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REVIEW ARTICLE

Eczema treatments: A review of their effectiveness, limitations and future directions

Abstract

Eczema treatments are currently a very promising area of research, particularly due to recent advances in technology and their success. There are currently a myriad of available choices for eczema treatment, each possessing different efficacies, potencies and mechanisms of action. There are currently three main categories of eczema treatments: traditional, alternative and modern approaches. However, there are many debates over which treatments are the most effective and offer the greatest benefits. For instance, biologics are a promising avenue of research due to their potency and efficacy, though they are associated with more severe adverse effects than other treatments. Conversely, topical corticosteroids possess a wide range of potencies and are highly effective, but carry drawbacks related to application frequency or possible local side effects. Therefore, this literature review examines the most common eczema treatments across traditional, modern and alternative medicines, compares them, and evaluates possible future directions for the research and innovation of eczema treatments and their potential contribution towards the advancement in medical research.

Keywords: Translational Medical Sciences, Disease Treatments and Therapies, Dermatology, Eczema

1. Introduction

Since around 400 BC, when eczema was first described and labelled, it has persisted as a significant irritant and major health issue worldwide. Although considerable research and investment have been made to investigate treatments, the issue remains an unrelenting problem affecting approximately 1.5 million adults in the UK (*Change AD UK*, n.d.), underscoring its widespread impact throughout the country. Key treatments currently used most commonly include emollients, general improvements to hygiene and sanitary standards, topical corticosteroids, and some modern innovations, such as JAK inhibitors and biologics (Santer et al., 2024). Though the common treatments are effective on a wide scale, being more cost-effective and easily accessible, they do have some disadvantages, such as side effects like lichenification or erythema (Bhanot et al., 2019) with prolonged use of certain emollients and also skin thinning and stretching as side effects for topical corticosteroids. The newer innovations seem more promising, being long-lasting and highly effective at treating eczema, though a new issue arises: costs and malignancies

(Mansilla-Polo & Morgado-Carrasco, 2024). This is especially prevalent in JAK inhibitors, due to the effectiveness of their immunosuppressive nature, resulting in the weakening of the immune system, leading to greater vulnerabilities in the body, which eventually culminates in a greater risk for cancer. This vulnerability causes infections to develop within the body, particularly in the respiratory and urinary tracts (Klein et al., 2022). Biologics also have quite a few adverse side effects, including but not limited to conjunctivitis, injection site reactions and eosinophilia (*Long-Term Safety and Efficacy Study of Lebrikizumab* (*LY3650150*) *in Participants With Moderate-to-Severe Atopic Dermatitis* (*ADjoin*) (*ADjoin*), 2025). Therefore, while both traditional and newer innovations in eczema treatments have demonstrated various successes in terms of effectiveness in resolving eczema, they still have drawbacks in multiple ways, including side effects and costs. However, whilst these newer innovations do have drawbacks, further investment into them should be investigated to assess the assumptions that adverse side effects may be mitigated and eventually eliminated. This is evident in the possibility of investment into the mass production of biologics, slowly minimising costs and making them more affordable to the average person. This article ultimately aims to discuss various eczema treatments, some more well-known than others, evaluating their outlooks, various benefits and drawbacks. The key treatments discussed will include the most common traditional approaches and modern innovations, as well as some discussion on the prospect of alternative medicine. The key way in which this literature review differs from others is that it not only takes into account treatments which are very commercialised and recognised, but it also acknowledges the possibility of alternative medicine in its treatments and provides comprehensive comparisons to traditional and modern treatments for eczema.

2. Methodology

Search Strategy:

The primary strategy utilised for the identification of relevant literature reviews was through the thorough evaluation of key sources found on Google Scholar or ClinicalTrials.gov. The searching strategy was conducted using MeSH filtering and evidence-based analysis for clinical trials, which allowed me to achieve methodological rigour in mitigating bias, ensuring clinical relevance and statistical validity. Including terms such as “Biologics” and “Emollient efficacy” was vital in being able to filter relevant information when using keyword searching for Google Scholar.

Inclusion and exclusion Criteria:

Key criteria that were required for the consideration to use the source included:

- Sufficient data for analysis for clinical trials
- Peer-reviewed academic journals in terms of literature review evaluation

Exclusion criteria:

- Lack of empirical data
- Published as an editorial commentary

Study Selection and Data Extraction:

Screening was performed throughout the writing of this literature review, and each citation was independently reviewed and assessed. Ultimately, through the process of writing, a large proportion of literature reviews and clinical trials met all inclusion criteria to be included in the literature review.

Data extraction was conducted through comprehensive organisation through Zotero software to record the author, year of publication and area of eczema research, helping categorise research effectively through keyword searching within the software.

3. Analysis

Primary treatments: structure, functions, and limitations

The most common treatments prescribed are emollients. The main emollients prescribed by the NHS are creams and ointments, such as Aveeno creams and Cetraben cream. Aveeno creams and some Cetraben creams use colloidal oatmeal as a base, due to its natural healing acceleration benefits, which act as a barrier to retain moisture and gently cleanse the skin to optimise the reduction of eczema flaring and gradually help build up a natural barrier against eczema. The key chemical component contained within this colloidal oatmeal contains its anti-inflammatory and anti-itch properties, which are known as avenanthramides (Fig. 1) (Sur et al., 2008). Moreover, it also reduces hypersensitivity and thus is a very strong combatant against irritants. Avenanthramides act via inhibition of NF-κB, responsible for governing immune response and inflammation (Yang et al., 2014).

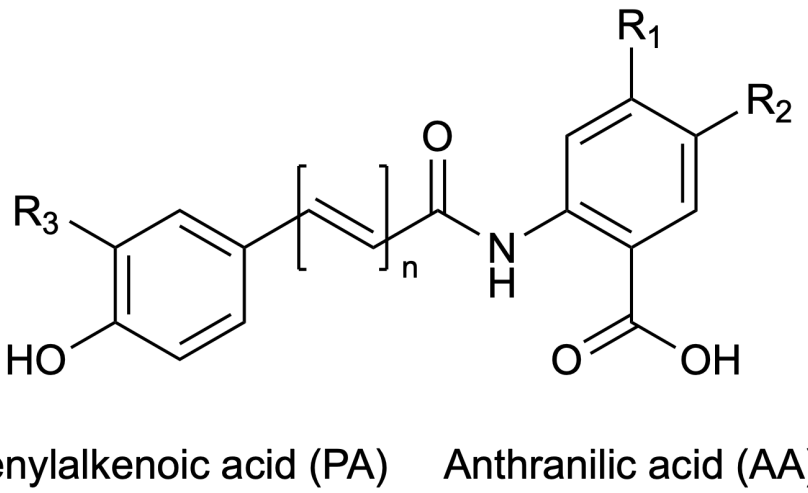


Figure 1. Chemical structure of avenanthramides (n = 1 or 2; R_1 = H, R_2 = OH, R_3 = H, OCH_3, or OH). Avenanthramides are formed by the N-acylation reaction between anthranilic acid (AA) and a phenylalkenoic acid (PA) to create an amide linkage.

Cetraben creams use soft paraffin and liquid paraffin as bases, which act as key chemical compounds for anti-inflammatory and anti-irritant properties. In a study, the SCORing Atopic Dermatitis index (SCORAD) score in patients using a paraffin-based cream was significantly lower than in those using a control cream, indicating a

notable reduction in eczema severity. It indicated a 28.6% decrease compared to the original SCORAD score. Therefore, it was concluded that the paraffin-based creams and ointments were effective in reducing the severity of eczema symptoms (Waked & Ibrahim, 2020). The key chemical compounds used in the creams are petrolatum, which is a mix of hydrocarbons. Studies have shown that it helps regulate antimicrobials and maintain the skin's epidermal barrier to help the retention of moisture and prevent irritants from coming into contact with the skin, which demonstrates its effectiveness in combating eczema in patients. One of the key chemical compounds in petrolatum is alkanes such as octadecane (Fig. 2) (Rogers & Skanupong, 1974). Petrolatum acts by forming a protective barrier on the skin, helping retain moisture and smooth the skin, making it both a comfortable and effective emollient.

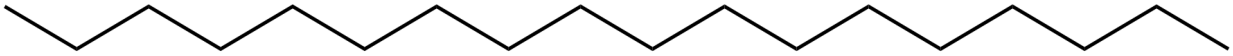


Figure 2. Chemical structure of octadecane, an alkane with 18 carbon atoms and 36 hydrogen atoms. It is a key component of petrolatum, and its skin-soothing and non-greasy properties make it a vital ingredient in petrolatum-based emollients.

Emollients have shown promising results, as evidenced by numerous clinical trials testing the effectiveness of colloidal oatmeal creams (*Study Results | NCT02691507 | Trial to Determine the Therapeutic Benefit of an OTC Cream on Dry, Itchy Skin of Adults and Children With Eczema | ClinicalTrials.Gov*, n.d.). Results indicated a significant increase in hydration and a substantial decrease in itchiness, with an average of 4.07 out of 10 on an arbitrary scale after application, demonstrating its short-term effectiveness. However, an issue arises after consolidating data for 7 days after cream application, with 4.22 out of 10. Though it has no significant impact on its overall success, it still shows diminished retention of its anti-itching properties compared to other commercial eczema treatments. Other studies also demonstrate this by recording hydration with a corneometer; the results showed that after 7 days, the unit of measure in arbitrary units was 208.52, compared to 14 days, when the unit of measure in arbitrary units was 158.65 (Johnson & Johnson Consumer Inc. (J& JCI), 2017). The greater the unit of measure in arbitrary units, the greater the hydration. This further emphasises the long-term decline in the effectiveness of emollients. Of course, it is crucial to consider that systematic reviews confirm they reduce flares in the long term when used proactively with anti-inflammatories.

A majority of emollients are effective with minimal side effects, providing a reliable short-term solution for mild to moderate eczema. However, situations in which adverse side effects occur must also be taken into account. In a study that examined the effects of a wide range of emollients, including variations in type (cream or lotion) and ingredients (botanicals, ceramides, and other components). From this study, it was found that many patients experienced the following side effects: erythema, irritation, papule formation, and further spreading of eczema, as well as other prominent side effects also being present (Emmett et al., 2023). It has been shown that overall botanical emollients may display more side effects due to the possibilities of irritants present in the natural ingredients compared to ceramides, as allergies may also arise from the use of botanical emollients (Corazza et al., 2009), whilst ceramide-based emollients remain effective and safe (Draelos, n.d.), due to the presence of ceramides in skin already.

Alongside emollients, topical corticosteroids remain a widely prescribed treatment worldwide. The key ways in which topical corticosteroids act are via binding to glucocorticoid response elements in DNA, which increases the production of anti-inflammatory proteins like lipocortin, and suppressing inflammatory genes (Mehta et al., 2016), as referenced previously, NF-κB, a protein complex that controls the body's inflammation. As a result, the body reduces the inflammatory response. Its fundamental chemical structure is often that of a steroid such as hydrocortisone (Fig. 3), which is $C_{21}H_{30}O_5$ (PubChem, n.d.). It has a four-ring structure known as a steroid nucleus, similar to other steroids. Due to its specific chemical structure, it can bind to the glucocorticoid receptor. At high concentrations, glucocorticoid receptor dimerisation can activate transcription of anti-inflammatory genes (Barnes, 2006). However, it should be noted that low doses of corticosteroids are what cause the anti-inflammatory effect (*Hydrocortisone*, n.d.).

Additionally, other commonly used topical corticosteroids contain betamethasone valerate (Fig. 3) at different concentrations based on the severity of the eczema (Brazzini & Pimpinelli, 2002). Betamethasone valerate has displayed significant decreases in common inflammatory-causing cytokines. Being one of the more potent corticosteroids, it has been a common prescription for patients with moderate or severe eczema. Clinical studies have shown its efficacy in reducing eczema severity (Gether et al., 2025). Moreover, in another study, betamethasone valerate showed potent effects in reducing symptoms of eczema relative to other common treatments, such as 0.5% and 2.5% desoximethasone, showing how it compares well against other frequent prescriptions against eczema (Ashton et al., 1987). Its chemical structure is $C_{27}H_{37}FO_6$. It has a valerate ester, a hydroxyl group and a ketone group as well (*Betamethasone Valerate Cream USP*, 0.1%, n.d.).

Evidently, Topical Corticosteroids have also shown significant success in reducing mild to moderate eczema. According to a study, transepidermal water loss was significantly lower when an irritant was applied to multiple patients than when the same irritant was applied to another patch of their skin, with a topical corticosteroid also applied. The study showed that significantly less erythema and lower values of the water loss were found, showing its potent effect on combating the inflammatory properties of eczema, as well as maintaining the water content of the skin (Ramsing & Agner, 1995). Another study also dictates its effectiveness relative to other alternatives of the treatment of eczema flare-ups, such as calcineurin inhibitors meant to suppress the inflammatory response of the immune system specifically. These studies show that the topical corticosteroids are more efficacious (Schmitt et al., 2011). Furthermore, potent corticosteroids can effectively eliminate potential bacteria, which could have helped amplify the effects of inflammation in eczema (Nilsson et al., 1992).

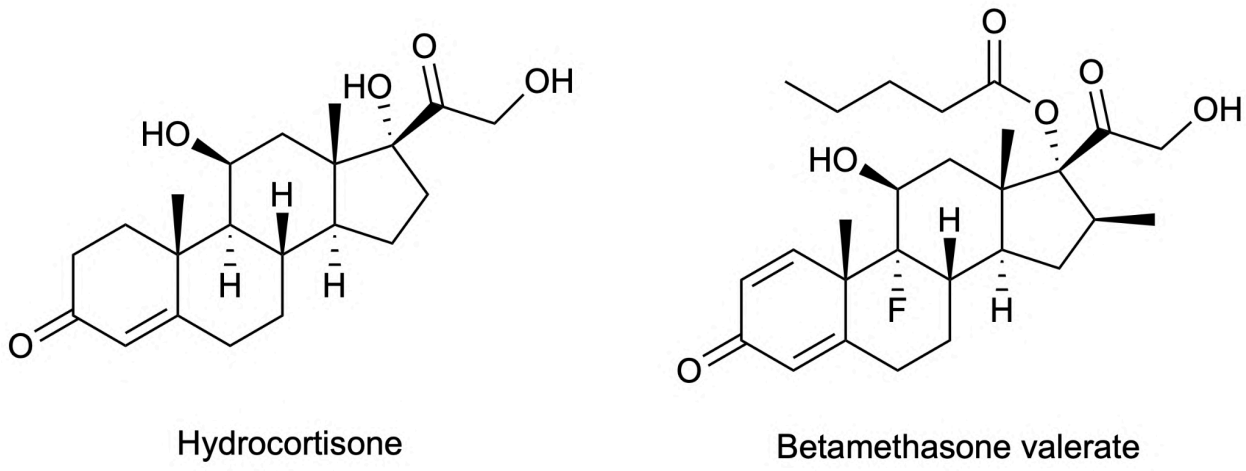


Figure 3. Chemical structures of hydrocortisone and betamethasone valerate. Both molecules are structurally similar and share a cyclopentanoperhydrophenanthrene steroid nucleus and multiple functional groups, including carbonyl and hydroxyl substituents.

Both hydrocortisone and betamethasone valerate have similar side effects, as they are topical corticosteroids in different forms. The most common side effects associated with the use of both medications are local side effects, such as skin atrophy, where the skin begins to thin, leading to easy bruising, and striae, which can result in stretch marks (Ference & Last, 2009). However, there are other side effects which, though rare, can occur, such as systemic side effects of Cushing's syndrome, where an increase in blood pressure and weight gain occurs or a decrease in the growth rate of children, though these systemic side effects have an amplified chance of occuring if the potency of the topical corticosteroid was too strong or there is prolonged use of the medication over a period of time (Dhar et al., 2014). Additionally, ocular symptoms may also be presented in glaucoma or cataracts (Daniel & Orchard, 2015). Despite these numerous side effects, the frequency of the occurrence is slim to none, thus being another reason why they prove to be such common prescriptions during treatment, with easily variable potencies based on the severity of the eczema.

Secondary treatments: structure, functions, and limitations

There are two key biologics currently used to treat eczema that are well known, namely Dupixent and Ebglyss. Dupixent (dupilumab) has been FDA-approved since March 2017 for the treatment of eczema. Its function is to inhibit the signalling of cytokines IL-4 and IL-13, resulting in reduced inflammation and, as a consequence, skin barrier dysfunction (Seegräber et al., 2018). Ebglyss (lebrikizumab) was FDA-approved in September 2024 for the treatment of eczema and works similarly to Dupixent by inhibiting cytokine signalling; however, it only inhibits IL13, preventing T cell Th2 signalling and consequently reducing both inflammation and eosinophilia (Khan et al., 2025). Lebrikizumab and dupilumab are both produced by inserting the genetic code into Chinese hamster ovary (CHO) cells to help mass-produce the antibodies; they must then be purified extensively to isolate the respective biologics in Dupixent and Ebglyss.

In a myriad of studies covering the efficacy of dupilumab, it has been extensively studied. Studies have shown its efficacy in treating eczema, as in one study on the effect of dupilumab on chronic hand eczema (CHE). Results showed that dupilumab was extremely effective in treating this particular eczema. According to the hand eczema severity index, patients had a significant decrease, and the dermatology life quality index (DLQI) increased overall. It showed an extremely high tolerance for patients and thus proved to be a very promising treatment for eczema, with high efficacy and a low rate of adverse side effects, making it relatively safe (Asamoah et al., 2025). Another study showed that 80.3% of patients in a clinical trial evaluating the effects of dupilumab on CHE achieved partial or complete resolution of their eczema, demonstrating both its potency and efficacy in treating chronic hand eczema (Riva et al., 2024). Its chemical structure is a monoclonal antibody of a subclass of immunoglobulin G4 that binds to the IL4 receptor. As a result of being able to bind to the IL-4 receptor, dupilumab can inhibit signalling along both the type 1 and type 2 receptors, thus resulting in a decrease in inflammation (*Dupilumab*, n.d.).

For lebrikizumab, there have been fewer studies due to its recent approval by the FDA for clinical trials; therefore, it has not been as thoroughly studied as lebrikizumab and has only recently become quite well known as a biologic. Studies, however, have also demonstrated its effectiveness in treating eczema. In a study that studied the long-term effects of lebrikizumab on patients with moderate to severe eczema, the results showed that a significant majority of patients experienced a substantial improvement in skin quality, having an investigator's global assessment (IGA) of 0 or 1, and there was no requirement to further take topical corticosteroids or other treatments to maintain these effects (release, n.d.). Additionally, a significant majority of patients had an extremely low EASI score, demonstrating lebrikizumab's potent effects on eczema. Its chemical structure is also that of an immunoglobulin G4 monoclonal antibody. It binds IL-13 with high affinity, thereby inhibiting its inflammatory effects.

The key potential adverse side effects that come about through the use of dupilumab for the treatment of eczema were head and neck eczema, conjunctivitis, eczema, peeling of skin and dryness in eyes, however overall dupilumab did show to have a high tolerance, as these adverse side effects only presented in less than 20% of patients, and are relatively minor and not severe or life threatening (Parmar et al., 2022). In another study, it was said that a small minority of patients had mild conjunctivitis, and a few patients had severe conjunctivitis, which may remain an issue; therefore, dupilumab must be researched slightly more to ensure the safety of patients who may decide to utilise it as a treatment for moderate to severe eczema. The key side effects of lebrikizumab are injection site reactions and conjunctivitis, and therefore it has similar side effects to dupilumab (Lin et al., 2024). However, studies show that relative to dupilumab, it seems that lebrikizumab seems to be more favourable due to its side effect profile and high tolerance. Moreover, it should be noted that dupilumab has a greater number of ocular effects (Loh et al., 2020).

Janus Kinase Inhibitors target the kinase domain of Janus Kinase proteins (JAK proteins). This prevents their activation, thus preventing JAK phosphorylation activity and, as a result, reducing the expression of inflammatory genes and the number of inflammatory and immune signalling pathways, thus significantly reducing inflammation and tissue damage. This is done as many of the signalling pathways are inhibited, such as IL-13 or IL-4, which are meant to produce an inflammatory response (*Basic Mechanisms of JAK Inhibition*, n.d.). In a literature review, it was stated that there are currently 11 FDA-approved JAK inhibitors which can be used. However, the key JAK inhibitors which are often used in the treatment of eczema are abrocitinib, ruxolitinib and upadacitinib (Fig. 4) (Key, n.d.) (Shawky et al., 2022).

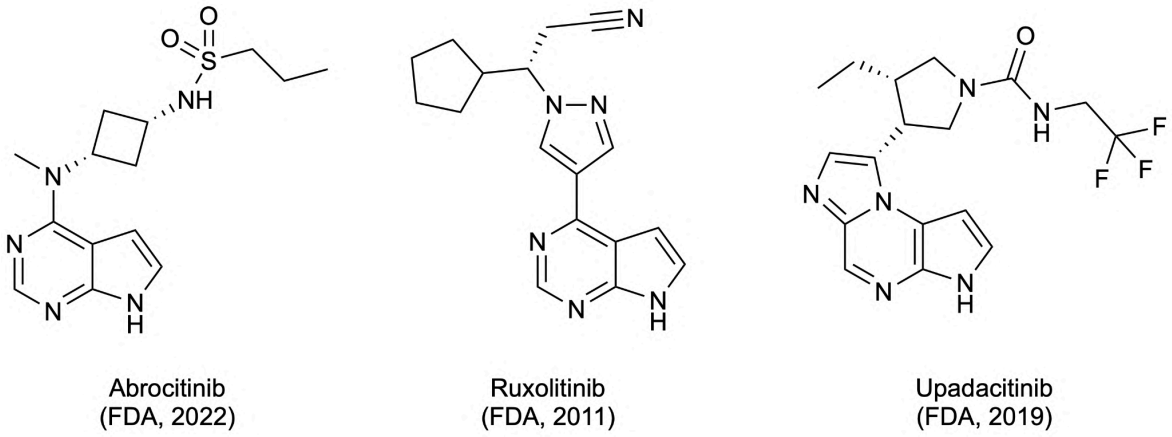


Figure 4. Chemical structures of the most commonly used JAK inhibitors to treat eczema. All 3 share a nitrile group that facilitates binding to the kinase, and they also have a pyrrolopyrimidine core. The nitrile group enables blocking of the JAK-STAT pathway.

Studies have shown that abrocitinib, ruxolitinib and upadacitinib are extremely effective in the treatment of eczema. This is evident in a study on the efficacy of abrocitinib and upadacitinib. For abrocitinib, results from the trial showed a significant reduction in pruritus for many patients, and 48.3% of patients demonstrated investigator's global assessment (IGA) scores of 0 or 1. Moreover, in week 1, there were also very substantial improvements in the eczema area severity index (EASI). This shows that abrocitinib has a high efficacy and can lead to skin clearance and relief. For upadacitinib, 50% of patients demonstrated an IGA score of 0 or 1 at 16 weeks, and there was a 90% improvement in EASI score as well at 16 weeks. There was also a general improvement in eczema symptoms, indicating relatively high efficacy, comparable to that of abrocitinib (Nezamololama et al., 2020). In another study, which evaluated the effects of ruxolitinib on eczema, it was found that there was a 51.6% decrease in EASI overall after 4 weeks, and there was a large percentage of patients who were able to achieve IGA scores of 0 or 1; therefore, the results also demonstrated ruxolitinib's efficacy (Mohney et al., 2023).

Generally, many of these JAK inhibitors do have the possibility of many side effects, such as non-specific side effects, such as nausea, vomiting or diarrhoea and also a 10% possibility of headaches, dizziness or fatigue. However, there are also very slim possibilities of many various specific side effects (Fig. 5) (Rajput Khokhar et al., 2025). In a recent clinical study, patients using ruxolitinib had a 38.3% risk of adverse side effects, which is quite high; therefore, whilst ruxolitinib has high efficacy and is extremely potent, it still has many side effects, but fewer systemic risks (Incyte Corporation, 2025). For upadacitinib, in a clinical trial, it was demonstrated that there was a 3.49% chance of a serious adverse event occurring, and there was a roughly 20% chance of a non-serious adverse event; however, the trial also indicated that many of the patients' eczema symptoms were substantially reduced through EASI and IGA scores (AbbVie, 2025). However, in a study with abrocitinib, there was a staggering 74% of patients who encountered treatment-emergent adverse events and 1.7% who encountered severe adverse events. Although this study demonstrated high rates of adverse events, real-world tolerability is often good, as shown in other clinical trials of JAK inhibitors. Therefore, similar to other JAK inhibitors, it has a frequency of adverse side effects (Pfizer, 2022). Though it is important to note that oral JAKs do carry these black box warnings for serious heart events, cancer,

clots and death and thus the serious risks mentioned are very consistent with these warnings for oral JAKs (Tokareva et al., 2023).

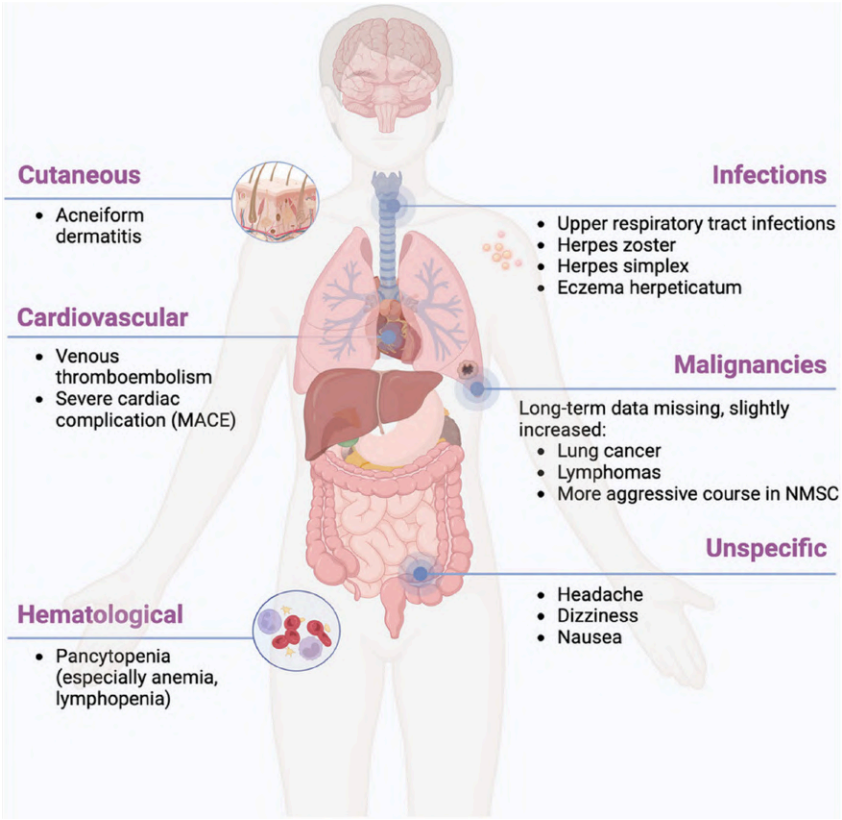


Figure 5. Summary of potential adverse effects of JAK inhibitor therapy. Overview of clinical complications categorised by organ system, highlighting increased risks of infection, cardiovascular events, cutaneous eruptions, and haematological abnormalities.

Alternative treatments: structure, functions, and limitations

Manuka honey remains a highly researched topic of discussion within the medical field, with the intention to evaluate its efficacy in reducing eczema. Its key function, for which it has been said to treat eczema, is due to its anti-inflammatory and moisturising properties (*Is Honey Good for Eczema?*, 2025a). It is also anti-bacterial, demonstrated in its effectiveness in preventing the development of the bacterium *S. aureus*, which often worsens eczema, due to further infection and flare-ups. It is anti-inflammatory, as it inhibits the signalling pathway of TLR1/2, toll-like receptors that often promote inflammation (Alangari et al., 2017). Moreover, it contains a high concentration of an anti-inflammatory chemical compound, known as methylglyoxal. Studies show that methylglyoxal inhibits the production of inflammatory cytokines; as a result, inflammation from eczema flare-ups is reduced significantly after application of this honey. This is achieved by activating NRF2, which suppresses

transcription of the IκBζ gene, thereby reducing the production of inflammatory cytokines substantially (Wei et al., 2023).

It contains a myriad of chemical compounds; however, the key anti-inflammatory compounds are methyl syringate and leptosin (Fig. 6). Methyl syringate acts by inhibiting neutrophil processes (Main et al., 2024), resulting in inflammation being significantly reduced; furthermore, it inhibits the expression of the enzyme cyclooxygenase-2 (J. Park et al., 2016), helping facilitate the reduction of inflammation and pruritus. The structure of methyl syringate comprises a benzene ring, along with a methyl ester group and a hydroxyl group. The structure of leptosin is comprised of a core of a benzene ring, which is bonded to a furan ring alongside a ketone group, as well as a phenyl group and 2 hydroxyl groups.

There are often minimal side effects that come about through the application of Manuka honey for the treatment of eczema; however, the key issues that often arise are related to contact irritation and allergic reactions. Some patients may be more susceptible to bee or pollen allergies, leading to honey irritating their skin. Its sticky properties also make it easy for dust and debris to stick onto it, leading to the possibility of the eczema worsening. Another key issue could be the quality or grading of the honey itself, as unpurified honey may contain bacteria that can worsen eczema; therefore, medical-grade honey should be used when applying (*Is Honey Good for Eczema?*, 2025b). However, other than these key potential side effects, honey, as a relatively safe chemical compound, will not often lead to other adverse side effects, resulting in its high tolerance level, mainly due to its low pH, moisturising efficacy and antibacterial properties (*Honey for Eczema*, 2022).

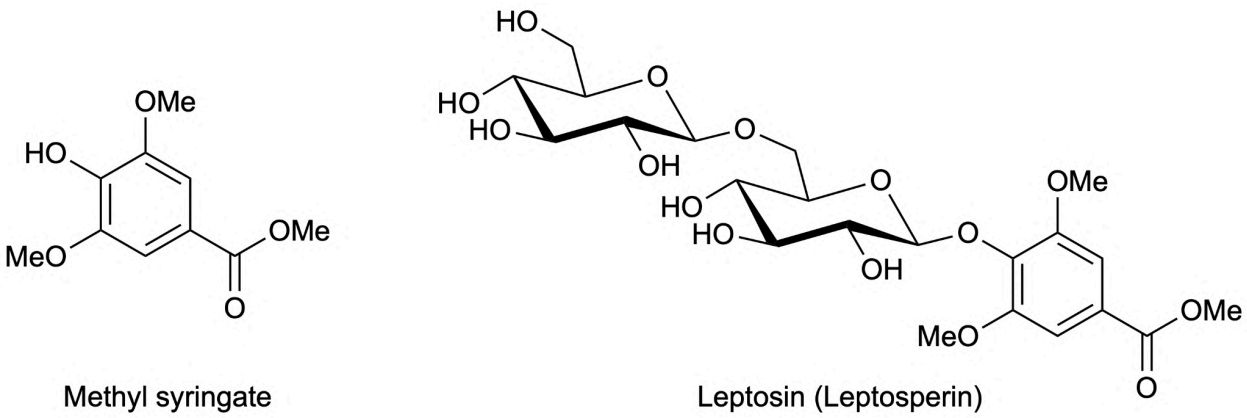


Figure 6. Chemical structures of methyl syringate and leptosin, also known as leptosperin, along with their respective functional groups, with both similarly having a hydroxyl group and benzene ring, but methyl syringate having a methyl ester group compared to leptosin with a furan ring, ketone group and phenyl group (J. Park et al., 2016).

Acupuncture works by stimulating the nervous system through the insertion of many tiny needles into various spots of the body. However, its key function in helping combat key symptoms of eczema is to activate the nervous system, stimulating nerves to release endorphins for pain relief, while inhibiting inflammatory cytokines (Li et al., 2021). Moreover, there are many classifications of specific areas for the needles to be inserted, for example, ST36 or PC6

(Fig. 7) (*Frontiers | Efficacy of Acupuncture on Upper Limb Dysfunction after Stroke: A Randomized Controlled Trial Protocol with Surface Electromyography Evaluation*, n.d.). These are key areas of insertion on the outer side of the shin and the inner wrist, respectively. Inserting needles into ST36 activates the sympathetic nervous system and, as a result, reduces inflammation (Oh & Kim, 2022). After inserting needles into PC6, this promotes the release of anti-inflammatory compounds and helps regulate the immune response to further reduce the severity of eczema symptoms (H.-J. Park et al., 2021).

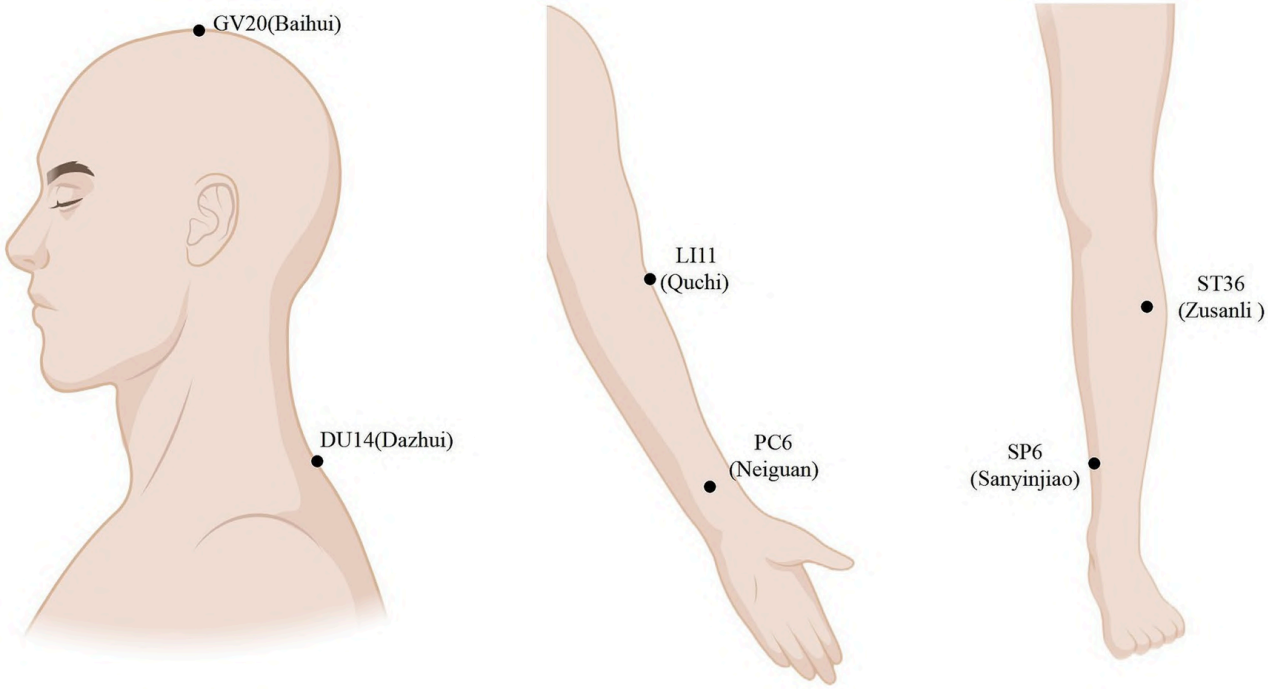


Figure 7. Schematic representation of acupuncture points of both ST36 and PC6, in which PC6 is in the inner wrist, and ST36 is in the outer shin.

There are a myriad of possible side effects which may come about through the use of acupuncture to treat eczema. This includes minor pain, bleeding and bruising at the sites of the needle insertion, dizziness, drowsiness, as well as the potential worsening of eczema, due to increasing the severity of eczema symptoms or causing a flare-up. There are also possibilities of infection and increased bleeding (Jones, 2019). The numerous severe side effects that come about through acupuncture outweigh its positive effects. Moreover, these side effects may or may not present, depending on the medical practitioner's experience and ability (Sreenivas, n.d.).

Evaluation of each treatment

Generally, there are numerous advantages to emollients becoming a standard for general prescription. Notable advantages include the effectiveness of moisture retention, helping improve the strength of the skin barrier. Studies

have shown that emollients have high efficacy in reducing the severity of flare-ups and eczema, as indicated by POEM scores, and have demonstrated considerable decreases in flare-ups and itching. However, this study also showed that adverse effects, whilst not fatal, are quite common as some patients did experience worsening of eczema, further itching, dryness and a burning sensation (Ridd et al., 2022). Moreover, relative to other medications, it is affordable for the average person and also easy to apply, though drawbacks also include frequency of application and potential clogging of pores, which may result in worsening of eczema (Table 1, Entry 1) (*How Parents and Children Evaluate Emollients for Childhood Eczema: A Qualitative Study | British Journal of General Practice*, n.d.).

Topical corticosteroids are highly effective in quickly resolving eczema flare-ups, relatively safe, and extremely versatile, with different potencies prescribed to patients depending on the severity of their eczema. An example of this would be hydrocortisone given to patients with very mild eczema, and betamethasone valerate at different concentrations for moderate and severe eczema. Moreover, they are often extremely affordable, as their over-the-counter availability has driven prices down. These advantages all make it a primary treatment for eczema. However, whilst topical corticosteroids are a very effective solution to eczema, it is crucial to be aware of the potential side effects as noted previously, as though they are of very low chance, local effects could still occur, such as striae or general irritation, with more severe side effects of Cushing's syndrome, which can come up as a side effect, though it is very unlikely to occur. It should also be noted that prices may increase significantly depending on the severity of the eczema, which should be a factor when considering other possible treatments. Therefore, overall, it is evident why topical corticosteroids are so commonly prescribed, having a very high efficacy, versatility, and being relatively affordable for the common person, whilst only having very slim chances of adverse side effects occurring (Table 1, Entry 2).

The key strengths of the use of dupilumab and lebrikizumab are that, overall, they help substantially reduce inflammation and pruritus, thus significantly improving skin health, holding this over many other traditional treatments for eczema due to being able to treat the underlying reasons for inflammation. They also reduce the number of systemic side effects because they are able to treat the underlying reasons for inflammation; moreover, they have been thoroughly researched, and as a result, there are minimal side effects, and they are relatively safe (Kumar et al., 2025). Studies mentioned previously have shown a consistent improvement in eczema symptoms, and the biologics themselves have an extremely high efficacy and potency, being able to combat eczema symptoms extremely effectively. However, the key weaknesses are cost and necessity for injection, as many patients will not be able to afford such a costly treatment on average, compared to the much cheaper alternative of an OTC medication for eczema treatment, whereas biologics cost a lot, leading to many patients having to pay out of their pockets for it. It is also important to note that many patients appear to be very sceptical of needles, therefore being a large barrier in biologics becoming widespread and used often. Due to biologics being able to suppress the immune system, there is a greater frequency of infection among patients who use these biologics compared to topical corticosteroid creams (Ameen et al., 2021). Therefore, overall, though biologics are an extremely optimistic avenue of research currently, some research should be invested towards clinical trials to further evaluate their safety profile and the reduction of cost via an investigation into the possibility of the industrialisation of biologics (Table 1, Entry 3).

The key strength of JAK inhibitors is their efficacy, which is evident in numerous clinical trials mentioned previously, where, using a variety of scales, such as EASI, IGA or DLQI, there have been significant improvements in all three scales using all three common JAK inhibitors in Abrocitinib, Ruxolitinib and Upadacitinib. Moreover, relative to other

common treatments, JAK inhibitors have much higher efficacy in skin clearance as well. Furthermore, compared to other treatments like biologics, where a needle is required for administration, most JAK inhibitors are orally administered, therefore being easier to administer and appealing to more patients (Harrington et al., 2020). However, though JAK inhibitors do possess high efficacy for treatment and are easy to administer, they still possess many downsides. As a result of its high efficacy, the likelihood of adverse events occurring increases. This is demonstrated by a greater frequency of serious side effects, such as cardiovascular events or blood clots. Another crucial weakness to note compared to other treatments is specificity, as JAK inhibitors affect multiple signalling pathways, which ultimately leads to many potential side effects. They are also extremely costly compared to OTC eczema treatments, costing tens of thousands of dollars (Table 1, Entry 4).

In general, the key advantages of utilising Manuka honey as an alternative medication relative to other common eczema treatments on the market are due to its inherent anti-inflammatory properties, along with its ability to retain moisture and reduce the severity of eczema flare-ups ("Is Manuka Honey Good for Eczema?," n.d.). Though the Manuka honey has been demonstrated to possess these important qualities in the effective treatment of eczema, it still contains many disadvantages, which would make it an unreliable choice for dermatologists to prescribe to patients with eczema. The key disadvantages involve its cost, feel, lack of research and risk factor for allergies. Regarding its cost, relative to other commercial products for treatment, the same potency of treatment is offered at a comparable efficacy, while being significantly cheaper compared to over-the-counter (OTC) emollients or topical corticosteroids. Due to a severe lack of research into alternative medications like Manuka honey compared to commonly researched treatments, such as topical corticosteroids, a greater number of clinical trials must be performed in order to further determine how it compares against traditional and modern treatments. Furthermore, it has been reported to feel very sticky and greasy, which a patient may find uncomfortable in daily life, especially with the frequency of application, compared to an emollient, which may be both soothing and won't feel as greasy. Many patients with allergies to pollen or bees, as stated previously, will not be able to use this medication; therefore, its versatility is substantially hindered by this factor compared to a topical corticosteroid (*Honey and Eczema*, n.d.). Lastly and overall, there is still only preliminary evidence for its potential antibacterial benefits and lesion improvement; therefore, no large randomised controlled trials (RCTs) confirm superiority over standards, and it is not recommended in major guidelines as a primary treatment (Table 1, Entry 5).

Table 1. Summary of primary, secondary and alternative eczema therapies: a comparison of treatment types, their delivery methods, efficacy, evidence level, main advantages and clinical limitations.

Entry	Type	Target	Delivery	Evidence	Advantages	Limitations
1	Emolients	Skin	Topical	High	OTC, cheap, hydro-retentive	Low potency, frequent application, potential pore clogging

2	Corticosteroids	Skin	Topical	High	OTC, safe, versatile potency, affordable	Potential adverse side effects, variable pricing
3	Biologics	Thigh or abdomen	Injection	Medium	High potencies and efficacy	Need for injection, costly, potential adverse side effects
4	JAK inhibitors	Skin and immune system	Oral or topical	High	High efficacy, easy to administer	Lack of specificity, high frequency of side effects, and costly
5	Alternative meds	Skin	Various	Low	Unproven	Adverse side effects, costly, unsafe, lack of thorough and evaluative trials

For acupuncture overall, the drawbacks outweigh the advantages due to the multiple severe side effects, which may be presented if in the care of an inexperienced medical professional, who may not be effective and accurate at inserting the needles into the patient, leading to multiple side effects occurring. Though it does have a few advantages, much research has been invested in the safety and efficacy of treating eczema with acupuncture, and studies have shown that when an experienced practitioner performs the treatment, eczema symptoms can be substantially reduced, and it is relatively safe. However, again, it still comes with very adverse side effects. It also needs to be considered that it is very costly compared to many OTC medications, such as topical corticosteroids, as an experienced practitioner of acupuncture is quite costly, yet necessary to ensure safety. Furthermore, though as stated previously, there has been quite a bit of research that has been invested into acupuncture, many other commercial treatments are even more rigorously evaluated and tested in clinical trials to be safer, more potent and cheaper. Lastly, the systematic reviews of acupuncture show mixed and low-quality evidence overall, with some mild itch and symptom reduction, which unfortunately come with heavy risks such as pain and infection, and the severe lack of thorough and evaluative trials makes it unreliable compared to conventional options (Zeng et al., 2021).

4. Conclusion

In conclusion, after extensive evaluation of a myriad of eczema treatments, modern and traditional approaches do remain the key treatments for both research and current usage. For traditional treatments, they remain reliable and affordable due to extensive research into the efficacy and safety of emollients and topical corticosteroids, as well as ways to reduce costs, which, as a result, leads to their prescription by more medical practitioners. For modern treatments, they remain an optimistic avenue for innovation and research, due to their potency and efficacy, though more research needs to be put towards reducing the frequency of adverse side effects, as well as making these treatments more accessible to the average person, due to the costly nature of JAK Inhibitors or Biologics, leading to substantial out-of-pocket costs for patients. Alternative medicines remain an area of scepticism, and rightly so, though research has been heavily invested in their safety and effectiveness. For the same effectiveness, both traditional and modern approaches to eczema treatment outperform alternative treatments, making them unreliable and rarely used in treatment. Therefore, overall, eczema treatments remain very promising for further research and innovation to optimise and refine both traditional and modern treatments in terms of cost, adverse side effects, and efficacy.

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Data & Code Availability Statement

No new raw data or software code were generated or analysed during this study. All data evaluated in this review were obtained from previously published literature and publicly available clinical trial registries at ClinicalTrials.gov. All primary sources and trial identifiers (NCT numbers) are cited within the article.

Acknowledgements

[Redacted]

Author Biography

[Redacted]

Mentor Contribution Statement

[Redacted]

Reviewer recommendation: Accept with major revisions, as detailed below

Comments

Abstract

- I would suggest cutting the first sentence as it is a little too general and does not contribute much to the overall message. I would also suggest adding one concluding sentence that sums up the research findings so the reader is left in no doubt about what your review uniquely adds to the field.

Introduction

- Since you mention eczema being described in 400 BC, it would be beneficial, to paint a much more vivid picture of the condition, if you can add 1-2 sentences of detail about how this disease was described in 400 BC.
- It would be beneficial to add a very short definition explaining what emollients, topical corticosteroids and JAK inhibitors/biologics are and how they work – even though this is discussed later in the paper, it is best to define things early.
- In general, lots of terminology is introduced without context or definition (e.g. lichenification, erythema). While you don't need a strict medical definition, this journal covers a broad range of fields (is not a specific medical or dermatology journal) and therefore it is important to have sufficient context such that the reader knows what this means without having to separately Google something while reading.

Methodology

- I am curious as to why Google Scholar and ClinicalTrials.gov were the only databases used given that other free ones also exist (PubMed for example). A minimum of three databases are usually required in order to ensure comprehensive overview of the literature. While it is not necessary to redo the analysis, I would suggest adding a sentence to explain why other databases were not used

Analysis

- "The key chemical component contained within this colloidal oatmeal contains its anti-inflammatory and anti-itch properties, which are known as avenanthramides" – this sentence is unclear grammatically, please rewrite
- "The key ways in which topical corticosteroids act are via binding to glucocorticoid response elements in DNA, which increases the production of anti-inflammatory proteins like lipocortin, and suppressing inflammatory genes" – is this correct? According to Eczema UK, steroids work by "attaching themselves to special receptors in cells, resulting in reduced production of

inflammatory mediators". In general, medication does not bind to DNA. I would suggest fact checking this particular statement, or rewording it since this makes it sound like the medication binds to DNA.

- Make sure all abbreviations (e.g. IL4, IL-13) are defined
- "In a myriad of studies covering the efficacy of dupilumab, it has been extensively studied. Studies have shown its efficacy in treating eczema, as in one study on the effect of dupilumab on chronic hand eczema (CHE). Results showed that dupilumab was extremely effective in treating this particular eczema." – awkward, please tighten and rephrase
- What is the citation (release, n.d.)? This likely needs to be reformatted.
- Figure 5 – this figure is taken directly from https://onlinelibrary.wiley.com/doi/10.1111/ddg.15796. This is not acceptable and needs to be cited.
- Table 1 should be modified so that it fits on one page, as opposed to straddling two pages

Peer review: Eczema treatments: A review of their effectiveness, limitations and future directions

Originality & significance

A strength of the paper is that it provides a broad overview of both established and emerging therapies. This is ranging from emollients and topical corticosteroids through to biologics, JAK inhibitors, and alternative therapies. The paper also describes the chemical structures of the treatments and provides context behind their mechanisms of action. In terms of providing a broad review, the paper does well!

Overall, the paper's unique contribution is not clear. Although the rightly states that it differs by incorporating alternative treatments alongside more established therapies, there are existing studies that provide overviews of conventional topical therapies, alternative therapies, and newer systemic biologics and JAK inhibitors. The student's paper is therefore not strongly differentiated from the existing literature. Relatedly, emollients and topical corticosteroids are well understood and thoroughly researched for mild-to-moderate eczema. Consequently, focussing on these established therapies for large parts of the paper makes it challenging to strengthen the paper's originality or significance (i.e., finding a research gap).

The paper can further strengthen its originality and significance by focussing on the newer therapies for moderate-to-severe eczema. For example, the paper's unique contribution could be to review the comparative evidence between biologics and JAK inhibitors in moderate-to-severe eczema, or to synthesise the available comparative evidence between individual biologics. This can answer important questions, such as, which biologic or JAK inhibitor may be preferred for patients with moderate-to-severe eczema. In other words, is there evidence to suggest that one therapeutic treatment for moderate-to-severe eczema is superior to others. Given these relatively new therapies, this could be a great contribution and original idea to explore. This would also shift the paper from a descriptive review to a more critically engaging review.

Ultimately, to strengthen originality and significance, the paper may consider focussing on patients with more severe eczema where newer therapeutics are present and more research is required. I highly encourage the student to prioritise originality and significance over breadth, as, covering all eczema treatments limits exploration of deeper questions.

Clarity

Overall, the clarity of the paper is good, and it is generally easy to follow. The student explains many of the key mechanisms behind eczema treatments, supported by figures illustrating chemical structures. The illustrations nicely complement the descriptions of the mechanisms. At times the mechanistic explanations are perhaps too detailed as the paper's objectives is on treatment effectiveness. For example:

Original: "Janus Kinase Inhibitors target the kinase domain of Janus Kinase proteins (JAK proteins). This prevents their activation, thus preventing JAK phosphorylation activity and, as a result, reducing the expression of inflammatory genes and the number of inflammatory and immune signalling pathways, thus significantly reducing inflammation and tissue damage. This is done as many of the signalling pathways are inhibited, such as IL-13 or IL-4, which are meant to produce an inflammatory response.

Modification: "Janus kinase (JAK) inhibitors reduce eczema severity by blocking intracellular signalling triggered by pro-inflammatory cytokines such as IL-4 and IL-13, thereby reducing immune-mediated inflammation."

This revision makes the explanation concise, linking the JAK inhibitors mechanisms to its ability to reduce eczema severity. Maintaining conciseness ensures the paper stays focussed on treatment efficacy, avoiding too much detail in mechanistic descriptions. I suggest similar modifications are implemented for such sections.

As a further minor comment, to improve clarity further, I encourage the student to ensure greater consistency in defining abbreviations at first use. For example, "JAK inhibitors" should be introduced as "Janus kinase (JAK) inhibitors," and "OTC" should be defined earlier as "over-the-counter."

Structure

The paper covers a wide range of eczema treatments, including emollients, topical corticosteroids, biologics, and oral JAK inhibitors. The paper currently categorises these under the headings "Primary treatments" and "Secondary treatments". While I understand the rationale for distinguishing established first-line topical therapies from newer systemic therapies, given the paper's focus on treatment effectiveness, this structure may unintentionally give the impression that the "primary treatments" are more effective than the "secondary treatments". To avoid this, I suggest structuring the review according to disease severity, which accurately reflects how treatments are selected in clinical practice. For example, emollients and topical corticosteroids are the mainstay of treatment for mild-to-moderate eczema, whereas biologics and oral JAK inhibitors are reserved for patients with moderate-to-severe disease whose eczema is inadequately controlled with topical therapies.

A structure based on disease-severity hierarchy may look like:

(1) Mild-to-moderate eczema

- Emollients
- Topical corticosteroids

(2) Moderate-to-severe eczema

- Biologics
- JAK inhibitors
- Comparative effectiveness between these biologics and JAK inhibitors (efficacy & safety)
    - This could form an additional section to strengthen the review's originality and significance (see my comments above).

(3) Alternative therapies

- Manuka honey
- Acupuncture

Organising the review in this way would better distinguish treatments according to the patient populations for whom they are intended, while also reflecting important differences in clinical management. For example, biologics and oral JAK inhibitors are prescription-only systemic therapies that are typically initiated and monitored by specialists. Furthermore, as correctly highlighted by the study, they have more severe adverse effects, but are, for this reason, given for more severe cases. Whereas emollients and topical corticosteroids form the foundation of treatment for milder disease and are often continued alongside systemic therapies in patients with more severe eczema. Overall, separating mild-to-moderate and moderate-to-severe eczema into distinct sections would provide a clearer structure for reviewing the treatments.

Use of Evidence & Research Methods

The paper is generally well-cited and demonstrates broad engagement with the literature across emollients, topical corticosteroids, biologics, JAK inhibitors, and alternative therapies. Overall, the student synthesises findings from a wide range of studies and appropriately uses evidence from clinical trials to support key statements on treatment efficacy.

The main area for improvement relates to the methodology section, particularly in terms of reproducibility and transparency. The following aspects can be clarified:

- **Search strategy:** While the use of Google Scholar and ClinicalTrials.gov is clearly stated, the search strategy is not fully specified. For example, it is noted that terms such as "Biologics" and "Emollient efficacy" were used, but it is unclear whether additional relevant terms were included (e.g., JAK inhibitors or specific drug names such as upadacitinib). Clarifying the full set of search terms would improve transparency, and if extensive, these could be presented in a table. In addition, specifying the date range of the literature search (or confirming if no restrictions were applied) would improve reproducibility.

- **Quality assessment of included studies:** It is positive that the paper attempts to address bias in the included papers. However, the current description ("MeSH filtering and/or evidence-based analysis for clinical trials") does not clearly explain how bias was assessed or reduced. In practice, formal tools such as the Cochrane risk-of-bias tool (RoB 2) are typically used for this purpose. If no formal quality assessment was conducted, which is acceptable for a student-level review, this should be acknowledged explicitly as a limitation (e.g., that included studies were not formally appraised for risk of bias and may therefore be subject to bias).

- **Data extraction:** It would also strengthen the methodology section to briefly specify what outcomes were extracted from the included studies. For instance, common eczema severity measures such as EASI, IGA, or other relevant clinical endpoints appear throughout the paper, and explicitly stating that these were systematically extracted would improve clarity and structure.

Overall, the methodology demonstrates a good initial approach to literature searching, but further detail and transparency would enhance reproducibility and strengthen the academic rigour of the review.

Engagement with Literature

The paper demonstrates a good broad engagement, covering a wide range of established and emerging eczema treatments, including emollients, topical corticosteroids, biologics, JAK inhibitors, and alternative therapies. Overall, the student successfully synthesises findings from multiple clinical trials and review articles and presents a clear descriptive overview of the mechanisms, efficacy, and adverse effects of each treatment class. This provides a useful foundation for understanding the therapeutic landscape. Overall, this is very well done!

Given the review's breadth, the paper is largely descriptive, with less scope for critical engagement. Specifically, the paper tends to summarise what is known about each therapy in isolation. As previously suggested, an opportunity for strengthening the paper would be to focus on the moderate-to-severe eczema treatment space. For example, the sections on biologics and JAK inhibitors both describe high efficacy in terms of outcomes such as EASI and IGA improvement, but there is little interpretation of how these drugs compare in terms of efficacy and safety. A more critical approach would attempt to contrast biologics (e.g., dupilumab vs lebrikizumab) and JAK inhibitors (e.g., upadacitinib vs abrocitinib) or evaluating how oral JAK inhibitors compare against biologics. This could then be followed by clearer interpretations and justified conclusions on whether certain therapies may be preferred in moderate-to-severe eczema. Overall, incorporating this evaluative layer would move the review from a descriptive review towards a more critically engaging paper.

Grammar and language

Overall good. Please see my comments under "clarity" where I recommend improvements to conciseness. There are also opportunities to improve medical language writing:

- **Title terminology:** The title *"Eczema treatments: A review of their **effectiveness**, limitations and future directions"* is likely more suitable if "**effectiveness**" is replaced with **"efficacy"**. In clinical research, *efficacy* refers to outcomes under controlled trial conditions (e.g., clinical trials), whereas *effectiveness* refers to performance in real-world practice. As the review predominantly draws on clinical trial data, "efficacy" is likely more appropriate.

- **Emotive language:** At times, emotive or intensifying language is used, particularly terms such as **"extremely"**. For example, *"Results showed that dupilumab was extremely effective in treating this particular eczema."* Such phrasing should be avoided in scientific writing. It is preferable to report outcomes directly and allow the quantitative results to demonstrate efficacy.

Final recommendation: Reject (with constructive feedback)

This is an ambitious and broad review that covers a wide range of eczema treatments. The paper demonstrates a solid understanding of multiple therapeutic options for eczema. The scope is commendable, particularly given the complexity of the treatment landscape, and the level of detail provided in describing drug mechanisms adds valuable context. Well done!

However, the originality and significance of the paper is limited. The paper is largely descriptive in its current form, which is linked to the paper's overall objective and structure. While the review is well-executed and broad in scope, strengthening its originality and significance would require a more focussed research question and methodology rather than revision of the existing manuscript. Thus, the paper is unlikely to reach publication standard with major revisions.

The recommendations outlined are intended to strengthen critical engagement, originality, and significance. One suggestion, within eczema, is comparing biologics and JAK inhibitors in terms of relative efficacy and safety. This would however require a reframed research question, revised title, and a different search strategy. This would effectively constitute a separate review rather than a revision. This would also require additional rigour, including clearer search reproducibility, formal quality assessment of included studies, and a more structured comparative synthesis of clinical trial evidence.

As a final point, I commend the student for their strong understanding of the literature and the evident effort behind this broad and ambitious review. For future work, I would encourage them to build on these strengths by focussing on a more defined area of the literature and avoid tackling too wide of a topic.

Convergence Journal Review

Eczema treatments: A review of their effectiveness, limitations and future directions

I had the pleasure of reading and reviewing the paper titled “Eczema treatments: A review of their effectiveness, limitations and future directions.” This is a genuinely useful topic to take on, and the student has clearly put in the work. Eczema affects an enormous number of people, the treatment landscape has shifted quickly with the arrival of biologics and JAK inhibitors, and a clear side-by-side account of what we have and where it falls short is worth writing. I liked the organizing structure of primary, secondary, and alternative treatments, and the summary comparison in Table 1 is a nice way to let the reader hold everything at once. The choice to include alternative approaches such as Manuka honey and acupuncture, and to compare them head-to-head with conventional options rather than treating them as an afterthought, is what makes the review feel original. That said, there are a few things to clean up. The manuscript has no abstract, only keywords, and a review of this scope really needs one to orient the reader. There is at least one clear error I would fix right away: in the biologics section the text says lebrikizumab “has not been as thoroughly studied as lebrikizumab,” which should read dupilumab. The section headings repeat the same “structure, functions, and limitations” phrasing three times, and Figure 7 for acupuncture is sourced from a stroke rehabilitation trial, which is an odd citation to lean on for a point about skin.

On evidence and engagement with the literature, the student did a lot right. They pulled real clinical trials with NCT identifiers from ClinicalTrials.gov, they explained mechanisms at a satisfying level of detail (NF-κB, the IL-4/IL-13 axis, JAK-STAT signalling), and the chemical structures are a nice touch that shows real effort. My main concern is the mix of source quality. A number of clinical claims lean on lay or secondary sources such as WebMD, HealthCentral, EverydayHealth, and a consumer blog, and for a research review those should be replaced with the primary literature or with formal guidelines like NICE or the American Academy of Dermatology. The other thing I would push on is comparison. The paper repeatedly ranks treatments against one another (“higher efficacy,” “more favourable”), but the numbers are drawn from different trials with different populations and endpoints, so those cross-trial comparisons need a caveat at minimum. The stronger move is to cite head-to-head data directly — for instance, the abrocitinib-versus-dupilumab trial the student already references (NCT04345367) is exactly the kind of comparison that would let them make these claims on solid ground. I would also resolve some internal contradictions: the Manuka honey section calls it “significantly cheaper” than OTC options in one place and lists cost as a disadvantage in another, and Table 1 similarly hedges. Finally, the acupuncture conclusion states that the severe side effects “outweigh” the benefits, which is a strong claim that the student's own cited evidence (described as mixed and low-quality) does not really support; I would soften it to match the evidence. The grammar and language are clean and professional, if a little wordy in places — tightening the run-on sentences and the recurring “a myriad of” would help.

Taking all of this together, this is a well-conceived and comprehensive review built on a sound premise, but it needs more than cosmetic changes before it is ready, so I would recommend accepting it with major revisions. The revisions should include: adding a structured abstract; replacing the lay and secondary web sources with primary literature or clinical guidelines; adding explicit caveats about cross-trial comparisons, or better, citing head-to-head trials such as the abrocitinib-versus-dupilumab study with more emphasis; resolving the Manuka honey cost contradiction and the dupilumab/lebrikizumab typo; tempering the acupuncture conclusion so it matches the strength of the evidence; and doing a light pass to tighten the prose. The premise and the methodology are solid, so I don't think this needs to go back out for a full second round of review — I would be happy to see it again once these revisions are made.

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REVIEW ARTICLE

Eczema treatments: A review of their effectiveness, limitations and future directions

Abstract

There are currently a myriad of available choices for eczema treatment, each possessing different efficacies, potencies and mechanisms of action. There are currently three main categories of eczema treatments: traditional, alternative and modern approaches. However, there are many debates over which treatments are the most effective and offer the greatest benefits. For instance, biologics are a promising avenue of research due to their potency and efficacy, though they are associated with more severe adverse effects than other treatments. Conversely, topical corticosteroids possess a wide range of potencies and are highly effective, but carry drawbacks related to application frequency or possible local side effects. Therefore, this literature review examines the most common eczema treatments across traditional, modern and alternative medicines, compares them, and evaluates possible future directions for the research and innovation of eczema treatments and their potential contribution towards the advancement in medical research. Overall findings dictate that modern and traditional eczema treatments remain the forefront for general usage due to reliability, accessibility and safety.

Keywords: Translational Medical Sciences, Disease Treatments and Therapies, Dermatology, Eczema.

1. Introduction

Since around 400 BC, when eczema was first described and labelled, it has persisted as a significant irritant and major health issue worldwide. During this time period, Hippocrates became the first to describe the condition now known as eczema, having described a patient with dry and scaly skin, as well as a chronic itch throughout the patient's body. Although considerable research and investment have been made to investigate treatments, the issue remains an unrelenting problem affecting approximately 1.5 million adults in the UK (*Change AD UK*), underscoring its widespread impact throughout the country. Key treatments currently used most commonly include emollients, general improvements to hygiene and sanitary standards, topical corticosteroids, and some modern innovations, such as Janus Kinase (JAK) inhibitors and biologics (Santer et al., 2024). Emollients are compounds which form a film on the outer surface of the skin, which aids in soothing irritation and hydrating the skin. JAK Inhibitors are a classification of medical compounds which reduce the transduction of cytokine signalling through the JAK-STAT

pathway and as a result reduce the transcription of genes related to the causation of inflammation and swelling. Biologics function as compounds which are composed of biological material, are grown in living cell structures, and are known for their potent efficacy in treating diseases. Though the common treatments are effective on a wide scale, being more cost-effective and easily accessible, they do have some disadvantages, such as side effects like lichenification (thickening of skin with leathery texture arising) or erythema (redness of skin due to increased blood flow to blood vessels near surface of skin) (Bhanot et al., 2019) with prolonged use of certain emollients and also skin thinning and stretching as side effects for topical corticosteroids. The newer innovations seem more promising, being long-lasting and highly effective at treating eczema, though a new issue arises: costs and malignancies (Mansilla-Polo & Morgado-Carrasco, 2024). This is especially prevalent in JAK inhibitors, due to the effectiveness of their immunosuppressive nature, resulting in the weakening of the immune system, leading to greater vulnerabilities in the body, which eventually culminates in a greater risk for cancer. This vulnerability causes infections to develop within the body, particularly in the respiratory and urinary tracts (Klein et al., 2022). Biologics also have a few adverse side effects, including but not limited to conjunctivitis (inflammation of the conjunctiva), injection site reactions and eosinophilia (*Long-Term Safety and Efficacy Study of Lebrikizumab (LY3650150) in Participants With Moderate-to-Severe Atopic Dermatitis (ADjoin) (ADjoin)*, 2025). Therefore, while both traditional and newer innovations in eczema treatments have demonstrated various successes in terms of effectiveness in resolving eczema, they still have drawbacks in multiple ways, including side effects and costs. However, whilst these newer innovations do have drawbacks, further investment into them should be investigated to assess the assumptions that adverse side effects may be mitigated and eventually eliminated. This is evident in the possibility of investment into the mass production of biologics, slowly minimising costs and making them more affordable to the average person. This article ultimately aims to discuss various eczema treatments, some more well-known than others, evaluating their outlooks, various benefits and drawbacks. The key treatments discussed will include the most common traditional approaches and modern innovations, as well as some discussion on the prospect of alternative medicine. The key way in which this literature review differs from others is that it not only takes into account treatments which are very commercialised and recognised, but it also acknowledges the possibility of alternative medicine in its treatments and provides comprehensive comparisons to traditional and modern treatments for eczema.

2. Methodology

Search strategy

The primary strategy utilised for the identification of relevant literature reviews was through the thorough evaluation of key sources found on Google Scholar or ClinicalTrials.gov. The searching strategy was conducted using MeSH filtering and evidence-based analysis for clinical trials, which allowed me to achieve methodological rigour in mitigating bias, ensuring clinical relevance and statistical validity. It is important to note that included studies were not formally appraised for risk of bias and may therefore be subject to bias. Including terms such as “Biologics” and “Emollient efficacy” was vital in being able to filter relevant information when using keyword searching for Google Scholar. The reason for which a third database was not used during the research into the manuscript was because Google scholar already yields many of the journals which are indexed in PubMed, thus its usage as a third database would yield nearly completely similar results, as a result usage of PubMed was used slightly in the initial research phase, though nearly similar papers would also appear on google scholar, as a result citations were primarily present on google scholar.

Additional relevant terms were used during the evaluation of different treatments, including: Abrocitinib, Ruxolitinib, Upadacitinib, Dupilumab, Lebikizumab, Hydrocortisone and Betamethasone Valerate. Additionally, the date range of the literature search had no restrictions applied. EASI, IGA and other clinical endpoints were systematically extracted.

Inclusion and exclusion criteria

Key criteria that were required for the consideration to use the source included:

- Sufficient data for analysis for clinical trials
- Peer-reviewed academic journals in terms of literature review evaluation

Exclusion criteria:

- Lack of empirical data
- Published as an editorial commentary

Study selection and data extraction

Screening was performed throughout the writing of this literature review, and each citation was independently reviewed and assessed. Ultimately, through the process of writing, a large proportion of literature reviews and clinical trials met all inclusion criteria to be included in the literature review.

Data extraction was conducted through comprehensive organisation through Zotero software to record the author, year of publication and area of eczema research, helping categorise research effectively through keyword searching within the software.

3. Analysis

Mild-to-moderate eczema

The most common treatments prescribed are emollients. The main emollients prescribed by the NHS are creams and ointments, such as Aveeno creams and Cetraben cream. Aveeno creams and some Cetraben creams use colloidal oatmeal as a base, due to its natural healing acceleration benefits, which act as a barrier to retain moisture and gently cleanse the skin to optimise the reduction of eczema flaring and gradually help build up a natural barrier against eczema. The key chemical components contained within this colloidal oatmeal are known as avenanthramides, which contain anti-inflammatory and anti-itch properties (Fig. 1) (Sur et al., 2008). Moreover, it also reduces hypersensitivity and thus is a very strong combatant against irritants. Avenanthramides act via inhibition of NF-κB, responsible for governing immune response and inflammation (Yang et al., 2014).

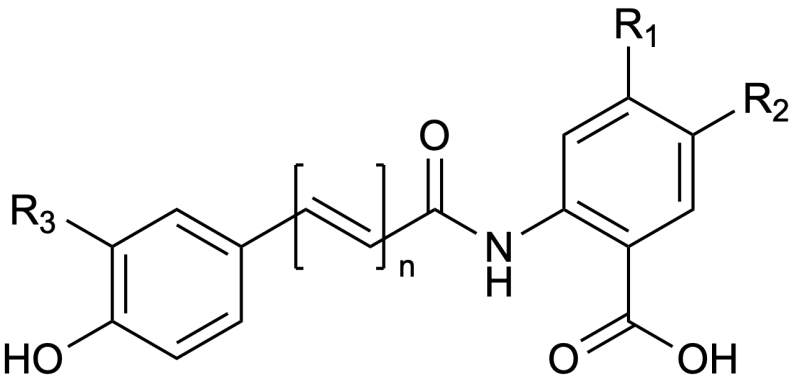


Figure 1. Chemical structure of avenanthramides (n = 1 or 2; R_1 = H, R_2 = OH, R_3 = H, OCH_3, or OH). Avenanthramides are formed by the N-acylation reaction between anthranilic acid (AA) and a phenylalkenoic acid (PA) to create an amide linkage.

Cetraben creams use soft paraffin and liquid paraffin as bases, which act as key chemical compounds for anti-inflammatory and anti-irritant properties. In a study, the SCORing Atopic Dermatitis index (SCORAD) score in patients using a paraffin-based cream was significantly lower than in those using a control cream, indicating a notable reduction in eczema severity. It indicated a 28.6% decrease compared to the original SCORAD score. Therefore, it was concluded that the paraffin-based creams and ointments were effective in reducing the severity of eczema symptoms (Waked & Ibrahim, 2020). The key chemical compounds used in the creams are petrolatum, which is a mix of hydrocarbons. Studies have shown that it helps regulate antimicrobials and maintain the skin's epidermal barrier to help the retention of moisture and prevent irritants from coming into contact with the skin, which demonstrates its effectiveness in combating eczema in patients. One of the key chemical compounds in petrolatum is alkanes such as octadecane (Fig. 2) (Rogers & Skanupong, 1974). Petrolatum acts by forming a protective barrier on the skin, helping retain moisture and smooth the skin, making it both a comfortable and effective emollient.

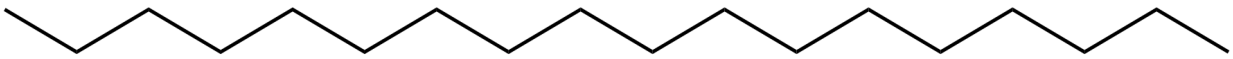


Figure 2. Chemical structure of octadecane, an alkane with 18 carbon atoms and 36 hydrogen atoms. It is a key component of petrolatum, and its skin-soothing and non-greasy properties make it a vital ingredient in petrolatum-based emollients.

Emollients have shown promising results, as evidenced by numerous clinical trials testing the effectiveness of colloidal oatmeal creams (*Study Results | NCT02691507 | Trial to Determine the Therapeutic Benefit of an OTC Cream on Dry, Itchy Skin of Adults and Children With Eczema | ClinicalTrials.Gov*, 2017). Results indicated a significant increase in hydration and a substantial decrease in itchiness, with an average of 4.07 out of 10 on an arbitrary scale

after application, demonstrating its short-term effectiveness. However, an issue arises after consolidating data for 7 days after cream application, with 4.22 out of 10. Though it has no significant impact on its overall success, it still shows diminished retention of its anti-itching properties compared to other commercial eczema treatments. Other studies also demonstrate this by recording hydration with a corneometer; the results showed that after 7 days, the unit of measure in arbitrary units was 208.52, compared to 14 days, when the unit of measure in arbitrary units was 158.65 (Johnson & Johnson Consumer Inc. (J& JCI), 2017). The greater the unit of measure in arbitrary units, the greater the hydration. This further emphasises the long-term decline in the effectiveness of emollients. Of course, it is crucial to consider that systematic reviews confirm they reduce flares in the long term when used proactively with anti-inflammatories.

A majority of emollients are effective with minimal side effects, providing a reliable short-term solution for mild to moderate eczema. However, situations in which adverse side effects occur must also be taken into account. In a study that examined the effects of a wide range of emollients, including variations in type (cream or lotion) and ingredients (botanicals, ceramides, and other components). From this study, it was found that many patients experienced the following side effects: erythema, irritation, papule formation, and further spreading of eczema, as well as other prominent side effects also being present (Emmett et al., 2023). It has been shown that overall botanical emollients may display more side effects due to the possibilities of irritants present in the natural ingredients compared to ceramides, as allergies may also arise from the use of botanical emollients (Corazza et al., 2009), whilst ceramide-based emollients remain effective and safe (Draelos, 2008), due to the presence of ceramides in skin already.

Alongside emollients, topical corticosteroids remain a widely prescribed treatment worldwide. The key ways in which topical corticosteroids act are via binding to glucocorticoid receptors within the cytoplasm. This causes a conformational change in the receptor, causing the dissociation of chaperone proteins from the chaperone complex. This corticosteroid-receptor complex then travels through the nuclear pores and inside the nucleus; two of these corticosteroid receptors bind together via homodimerisation, and this dimer then binds with DNA at sites known as glucocorticoid response elements. This process triggers transactivation and, as a result, the increased transcription and translation of anti-inflammatory proteins like lipocortin (Mehta et al., 2016). As referenced previously, NF-κB, a protein complex that controls the body's inflammation. As a result, the body reduces the inflammatory response. Its fundamental chemical structure is often that of a steroid such as hydrocortisone (Fig. 3), which is $C_{21}H_{30}O_5$ (PubChem, 2020). It has a four-ring structure known as a steroid nucleus, similar to other steroids. Due to its specific chemical structure, it can bind to the glucocorticoid receptor. At high concentrations, glucocorticoid receptor dimerisation can activate transcription of anti-inflammatory genes (Barnes, 2006). However, it should be noted that low doses of corticosteroids are what cause the anti-inflammatory effect.

Additionally, other commonly used topical corticosteroids contain betamethasone valerate (Fig. 3) at different concentrations based on the severity of the eczema (Brazzini & Pimpinelli, 2002). Betamethasone valerate has displayed significant decreases in common inflammatory-causing cytokines. Being one of the more potent corticosteroids, it has been a common prescription for patients with moderate or severe eczema. Clinical studies have shown its efficacy in reducing eczema severity (Gether et al., 2025). Moreover, in another study, betamethasone valerate showed potent effects in reducing symptoms of eczema relative to other common treatments, such as 0.5% and 2.5% desoximethasone, showing how it compares well against other frequent prescriptions against eczema

(Ashton et al., 1987). Its chemical structure is $C_{27}H_{37}FO_6$. It has a valerate ester, a hydroxyl group and a ketone group as well (*Betamethasone Valerate Cream USP*, 0.1%, 2010).

Evidently, Topical Corticosteroids have also shown significant success in reducing mild to moderate eczema. According to a study, transepidermal water loss was significantly lower when an irritant was applied to multiple patients than when the same irritant was applied to another patch of their skin, with a topical corticosteroid also applied. The study showed that significantly less erythema and lower values of the water loss were found, showing its potent effect on combating the inflammatory properties of eczema, as well as maintaining the water content of the skin (Ramsing & Agner, 1995). Another study also dictates its effectiveness relative to other alternatives of the treatment of eczema flare-ups, such as calcineurin inhibitors meant to suppress the inflammatory response of the immune system specifically. These studies show that the topical corticosteroids are more efficacious (Schmitt et al., 2011). Furthermore, potent corticosteroids can effectively eliminate potential bacteria, which could have helped amplify the effects of inflammation in eczema (Nilsson et al., 1992).

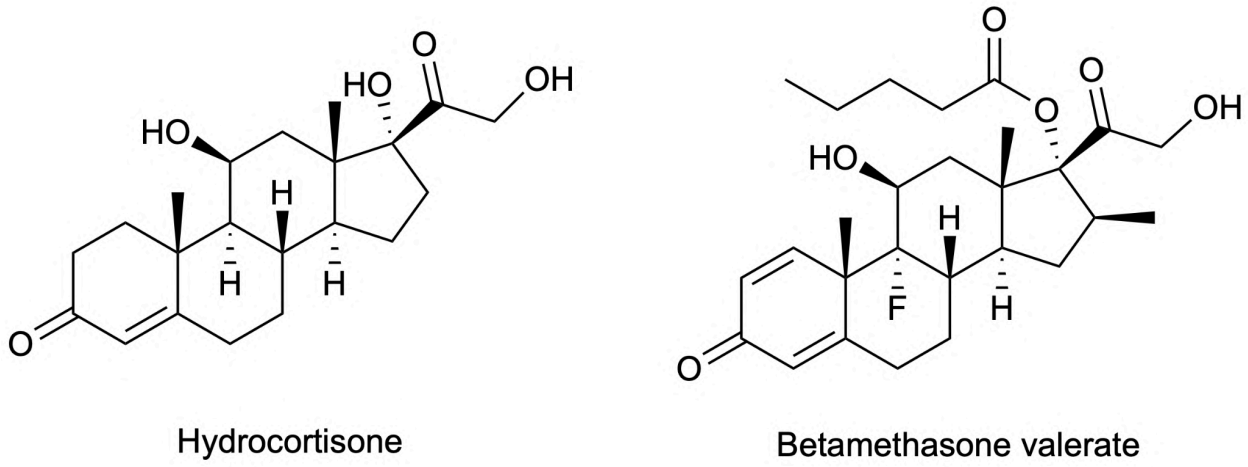


Figure 3. Chemical structures of hydrocortisone and betamethasone valerate. Both molecules are structurally similar and share a cyclopentanoperhydrophenanthrene steroid nucleus and multiple functional groups, including carbonyl and hydroxyl substituents.

Both hydrocortisone and betamethasone valerate have similar side effects, as they are topical corticosteroids in different forms. The most common side effects associated with the use of both medications are local side effects, such as skin atrophy, where the skin begins to thin, leading to easy bruising, and striae, which can result in stretch marks (Ference & Last, 2009). However, there are other side effects which, though rare, can occur, such as systemic side effects of Cushing's syndrome, where an increase in blood pressure and weight gain occurs or a decrease in the growth rate of children, though these systemic side effects have an amplified chance of occurring if the potency of the topical corticosteroid was too strong or there is prolonged use of the medication over a period of time (Dhar et al., 2014). Additionally, ocular symptoms may also be presented in glaucoma or cataracts (Daniel & Orchard, 2015). Despite these numerous side effects, the frequency of the occurrence is slim to none, thus being another reason why

they prove to be such common prescriptions during treatment, with easily variable potencies based on the severity of the eczema.

Moderate-to-severe eczema

There are two key biologics currently used to treat eczema that are well known, namely Dupixent and Ebglyss. Dupixent (dupilumab) has been FDA-approved since March 2017 for the treatment of eczema. Its function is to inhibit the signalling of cytokines IL-4 and IL-13, resulting in reduced inflammation and, as a consequence, skin barrier dysfunction (Seegräber et al., 2018). Ebglyss (lebrikizumab) was FDA-approved in September 2024 for the treatment of eczema and works similarly to Dupixent by inhibiting cytokine signalling; however, it only inhibits IL13, preventing T cell Th2 signalling and consequently reducing both inflammation and eosinophilia (Khan et al., 2025). IL-13 is a cytokine which regulates allergic responses, known as interleukin-13. Lebrikizumab and dupilumab are both produced by inserting the genetic code into Chinese hamster ovary (CHO) cells to help mass-produce the antibodies; they must then be purified extensively to isolate the respective biologics in Dupixent and Ebglyss.

Dupilumab has been extensively researched, and studies have shown its efficacy in treating eczema, as in one study on the effect of dupilumab on chronic hand eczema (CHE), results showed that dupilumab was effective in treating this particular eczema. According to the hand eczema severity index, patients had a significant decrease, and the dermatology life quality index (DLQI) increased overall. It showed a high tolerance for patients and thus proved to be a very promising treatment for eczema, with high efficacy and a low rate of adverse side effects, making it relatively safe (Asamoah et al., 2025). Another study showed that 80.3% of patients in a clinical trial evaluating the effects of dupilumab on CHE achieved partial or complete resolution of their eczema, demonstrating both its potency and efficacy in treating chronic hand eczema (Riva et al., 2024). Its chemical structure is a monoclonal antibody of a subclass of immunoglobulin G4 that binds to the IL4 receptor. IL-4 is a cytokine which regulates allergic responses, also known as interleukin-4. As a result of being able to bind to the IL-4 receptor, dupilumab can inhibit signalling along both the type 1 and type 2 receptors, thus resulting in a decrease in inflammation (Knox et al., 2024).

For lebrikizumab, there have been fewer studies due to its recent approval by the FDA for clinical trials; therefore, it has not been as thoroughly studied as Dupilumab and has only recently become well known as a biologic. Studies, however, have also demonstrated its effectiveness in treating eczema. In a study that studied the long-term effects of lebrikizumab on patients with moderate to severe eczema, the results showed that a significant majority of patients experienced a substantial improvement in skin quality, having an investigator's global assessment (IGA) of 0 or 1, and there was no requirement to further take topical corticosteroids or other treatments to maintain these effects (Stein-Gold et al., 2026). Additionally, a significant majority of patients had a low EASI score, demonstrating lebrikizumab's potent effects on eczema. Its chemical structure is also that of an immunoglobulin G4 monoclonal antibody. It binds IL-13 with high affinity, thereby inhibiting its inflammatory effects.

The key potential adverse side effects that come about through the use of dupilumab for the treatment of eczema were head and neck eczema, conjunctivitis, eczema, peeling of skin and dryness in eyes, however overall dupilumab did show to have a high tolerance, as these adverse side effects only presented in less than 20% of patients, and are relatively minor and not severe or life threatening (Parmar et al., 2022). In another study, it was said that a small minority of patients had mild conjunctivitis, and a few patients had severe conjunctivitis, which may remain an issue; therefore, dupilumab must be researched slightly more to ensure the safety of patients who may decide to utilise it as a treatment for moderate to severe eczema. The key side effects of lebrikizumab are injection site reactions and

conjunctivitis, and therefore it has similar side effects to dupilumab (Lin et al., 2024). However, studies show that relative to dupilumab, it seems that lebrikizumab seems to be more favourable due to its side effect profile and high tolerance. Moreover, it should be noted that dupilumab has a greater number of ocular effects (Loh et al., 2020).

Janus kinase (JAK) inhibitors reduce eczema severity by blocking intracellular signalling triggered by pro-inflammatory cytokines such as IL-4 and IL-13, thereby reducing immune-mediated inflammation.(*Basic Mechanisms of JAK Inhibition*, 2020). In a literature review, it was stated that there are currently 11 FDA-approved JAK inhibitors which can be used. However, the key JAK inhibitors which are often used in the treatment of eczema are abrocitinib, ruxolitinib and upadacitinib (Fig. 4) (Chovatiya & Paller, 2021, Shawky et al., 2022).

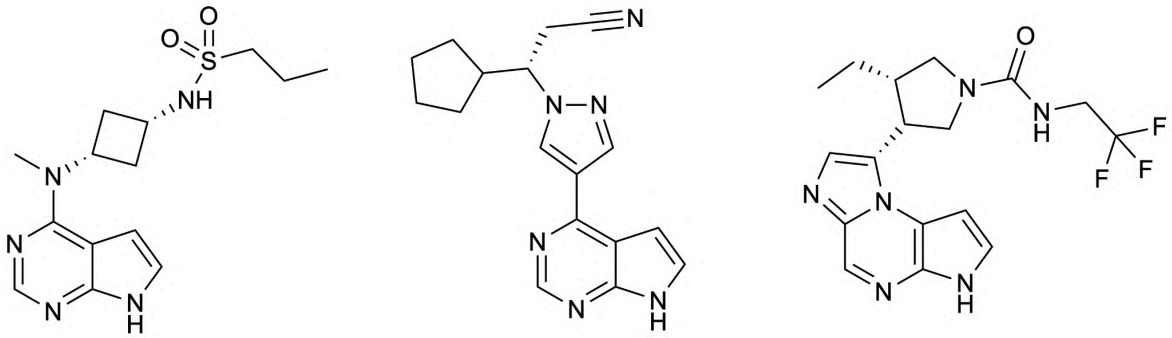


Figure 4. Chemical structures of the most commonly used JAK inhibitors to treat eczema. All 3 share a nitrile group that facilitates binding to the kinase, and they also have a pyrrolopyrimidine core. The nitrile group enables blocking of the JAK-STAT pathway.

Studies have shown that abrocitinib, ruxolitinib and upadacitinib are effective in the treatment of eczema. This is evident in a study on the efficacy of abrocitinib and upadacitinib. For abrocitinib, results from the trial showed a significant reduction in pruritus for many patients, and 48.3% of patients demonstrated investigator's global assessment (IGA) scores of 0 or 1. Moreover, in week 1, there were also very substantial improvements in the eczema area severity index (EASI). This shows that abrocitinib has a high efficacy and can lead to skin clearance and relief. For upadacitinib, 50% of patients demonstrated an IGA score of 0 or 1 at 16 weeks, and there was a 90% improvement in EASI score as well at 16 weeks. There was also a general improvement in eczema symptoms, indicating relatively high efficacy, comparable to that of abrocitinib (Nezamololama et al., 2020). In another study, which evaluated the effects of ruxolitinib on eczema, it was found that there was a 51.6% decrease in EASI overall after 4 weeks, and there was a large percentage of patients who were able to achieve IGA scores of 0 or 1; therefore, the results also demonstrated ruxolitinib's efficacy (Mohney et al., 2023).

Generally, many of these JAK inhibitors do have the possibility of many side effects, such as non-specific side effects, such as nausea, vomiting or diarrhoea and also a 10% possibility of headaches, dizziness or fatigue. However, there are also very slim possibilities of many various specific side effects (Fig. 5) (Rajput Khokhar et al., 2025). In a recent

clinical study, patients using ruxolitinib had a 38.3% risk of adverse side effects, which is high; therefore, whilst ruxolitinib has high efficacy and is potent, it still has many side effects, but fewer systemic risks (Incyte Corporation, 2025). For upadacitinib, in a clinical trial, it was demonstrated that there was a 3.49% chance of a serious adverse event occurring, and there was a roughly 20% chance of a non-serious adverse event; however, the trial also indicated that many of the patients' eczema symptoms were substantially reduced through EASI and IGA scores (AbbVie, 2025). However, in a study with abrocitinib, there was a staggering 74% of patients who encountered treatment-emergent adverse events and 1.7% who encountered severe adverse events. Although this study demonstrated high rates of adverse events, real-world tolerability is often good, as shown in other clinical trials of JAK inhibitors. Therefore, similar to other JAK inhibitors, it has a frequency of adverse side effects (Pfizer, 2022). Though it is important to note that oral JAKs do carry these black box warnings for serious heart events, cancer, clots and death and thus the serious risks mentioned are very consistent with these warnings for oral JAKs (Tokareva et al., 2023).

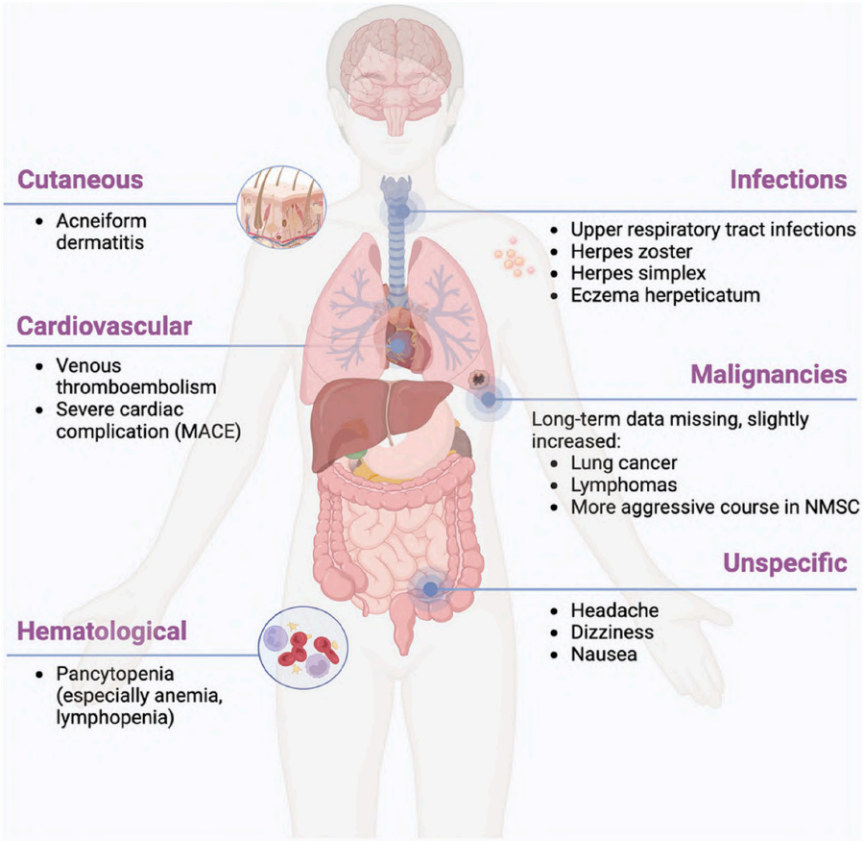


Figure 5. Summary of potential adverse effects of JAK inhibitor therapy. Overview of clinical complications categorised by organ system, highlighting increased risks of infection, cardiovascular events, cutaneous eruptions, and haematological abnormalities.

Alternative therapies

Manuka honey remains a highly researched topic of discussion within the medical field, with the intention to evaluate its efficacy in reducing eczema. Its key function, for which it has been said to treat eczema, is due to its anti-inflammatory and moisturising properties (Johnston et al., 2018a). It is also anti-bacterial, demonstrated in its effectiveness in preventing the development of the bacterium S. *aureus*, which often worsens eczema, due to further infection and flare-ups. It is anti-inflammatory, as it inhibits the signalling pathway of TLR1/2, toll-like receptors that often promote inflammation (Alangari et al., 2017). Moreover, it contains a high concentration of an anti-inflammatory chemical compound, known as methylglyoxal. Studies show that methylglyoxal inhibits the production of inflammatory cytokines; as a result, inflammation from eczema flare-ups is reduced significantly after application of this honey. This is achieved by activating NRF2, which suppresses transcription of the IκBζ gene, thereby reducing the production of inflammatory cytokines substantially (Wei et al., 2023).

It contains a myriad of chemical compounds; however, the key anti-inflammatory compounds are methyl syringate and leptosin (Fig. 6). Methyl syringate acts by inhibiting neutrophil processes (Main et al., 2024), resulting in inflammation being significantly reduced; furthermore, it inhibits the expression of the enzyme cyclooxygenase-2 (J. Park et al., 2016), helping facilitate the reduction of inflammation and pruritus. The structure of methyl syringate comprises a benzene ring, along with a methyl ester group and a hydroxyl group. The structure of leptosin consists of a core of a benzene ring, which is bonded to a furan ring alongside a ketone group, as well as a phenyl group and 2 hydroxyl groups.

There are often minimal side effects that come about through the application of Manuka honey for the treatment of eczema; however, the key issues that often arise are related to contact irritation and allergic reactions. Some patients may be more susceptible to bee or pollen allergies, leading to honey irritating their skin. Its sticky properties also make it easy for dust and debris to stick onto it, leading to the possibility of the eczema worsening. Another key issue could be the quality or grading of the honey itself, as unpurified honey may contain bacteria that can worsen eczema; therefore, medical-grade honey should be used when applying (Johnston et al., 2018b). However, other than these key potential side effects, honey, as a relatively safe chemical compound, will not often lead to other adverse side effects, resulting in its high tolerance level, mainly due to its low pH, moisturising efficacy and antibacterial properties (Mandal & Mandal, 2011).

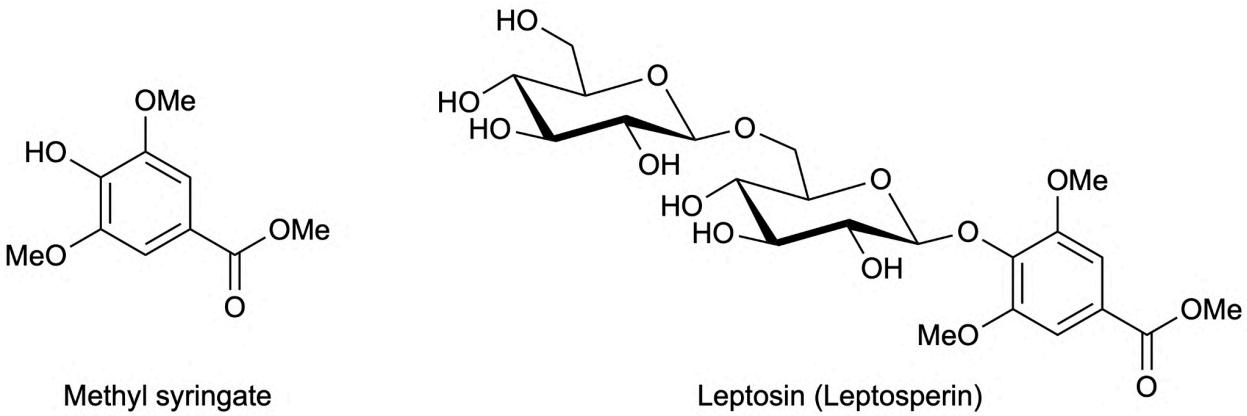
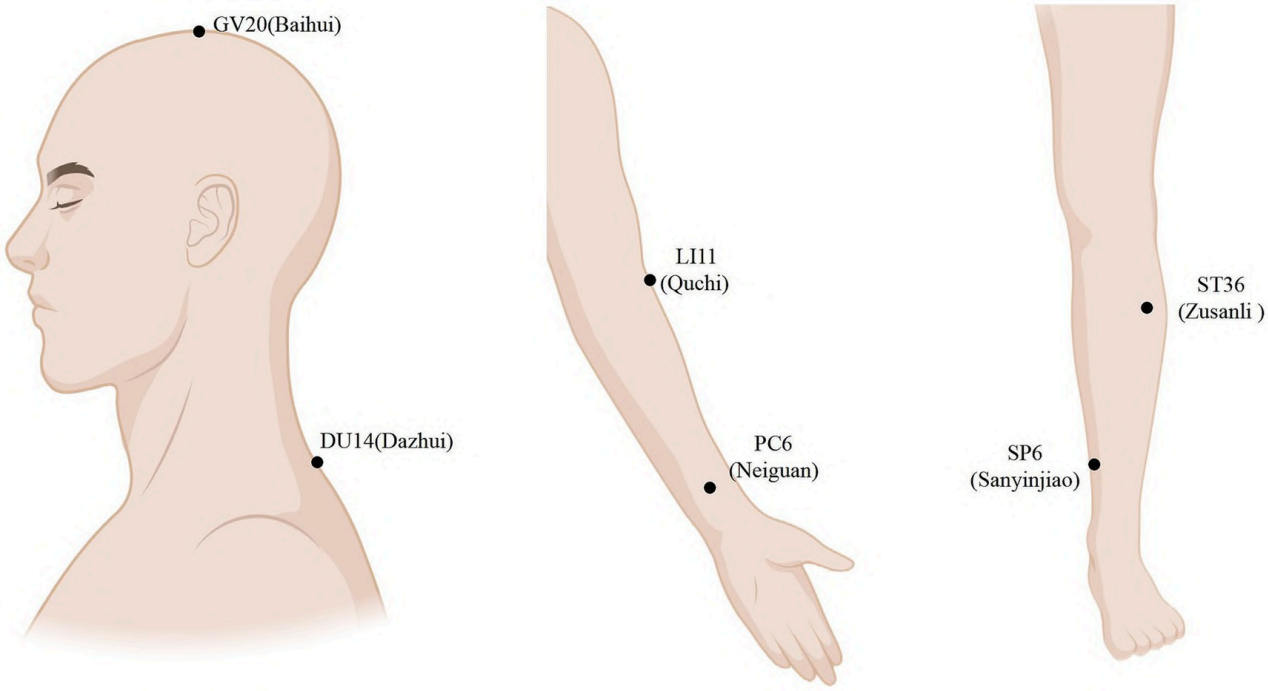


Figure 6. Chemical structures of methyl syringate and leptosin, also known as leptosperin, along with their respective functional groups, with both similarly having a hydroxyl group and benzene ring, but methyl syringate having a methyl ester group compared to leptosin with a furan ring, ketone group and phenyl group (J. Park et al., 2016).

Acupuncture works by stimulating the nervous system through the insertion of many tiny needles into various spots of the body. However, its key function in helping combat key symptoms of eczema is to activate the nervous system, stimulating nerves to release endorphins for pain relief, while inhibiting inflammatory cytokines (Li et al., 2021). Moreover, there are many classifications of specific areas for the needles to be inserted, for example, ST36 or PC6 (Fig. 7) (*Frontiers | Efficacy of Acupuncture on Upper Limb Dysfunction after Stroke: A Randomized Controlled Trial Protocol with Surface Electromyography Evaluation*, 2025). These are key areas of insertion on the outer side of the shin and the inner wrist, respectively. Inserting needles into ST36 activates the sympathetic nervous system and, as a result, reduces inflammation (Oh & Kim, 2022). After inserting needles into PC6, this promotes the release of anti-inflammatory compounds and helps regulate the immune response to further reduce the severity of eczema symptoms (H.-J. Park et al., 2021).



316

317 **Figure 7.** Schematic representation of acupuncture points of both ST36 and PC6, in which PC6 is in the inner wrist,
318 and ST36 is in the outer shin.

319 There are some possible side effects which may come about through the use of acupuncture to treat eczema. This
320 includes minor pain, bleeding and bruising at the sites of the needle insertion, dizziness, drowsiness, as well as the
321 potential worsening of eczema, due to increasing the severity of eczema symptoms or causing a flare-up. There are
322 also possibilities of infection and increased bleeding (Jones, 2019). The numerous severe side effects that come about
323 through acupuncture outweigh its positive effects. Moreover, these side effects may or may not present, depending
324 on the medical practitioner's experience and ability (Xu et al., 2013).

325 **Evaluation of each treatment**

326 Generally, there are numerous advantages to emollients becoming a standard for general prescription. Notable
327 advantages include the effectiveness of moisture retention, helping improve the strength of the skin barrier. Studies
328 have shown that emollients have high efficacy in reducing the severity of flare-ups and eczema, as indicated by
329 POEM scores, and have demonstrated considerable decreases in flare-ups and itching. However, this study also
330 showed that adverse effects, whilst not fatal, are common as some patients did experience worsening of eczema,
331 further itching, dryness and a burning sensation (Ridd et al., 2022). Moreover, relative to other medications, it is
332 affordable for the average person and also easy to apply, though drawbacks also include frequency of application and
333 potential clogging of pores, which may result in worsening of eczema (Table 1, Entry 1) (*How Parents and Children*
334 *Evaluate Emollients for Childhood Eczema: A Qualitative Study | British Journal of General Practice*, 2022).

Topical corticosteroids are highly effective in quickly resolving eczema flare-ups, relatively safe, and versatile, with different potencies prescribed to patients depending on the severity of their eczema. An example of this would be hydrocortisone given to patients with very mild eczema, and betamethasone valerate at different concentrations for moderate and severe eczema. Moreover, they are often affordable, as their over-the-counter availability has driven prices down. These advantages all make it a primary treatment for eczema. However, whilst topical corticosteroids are a very effective solution to eczema, it is crucial to be aware of the potential side effects as noted previously, as though they are of very low chance, local effects could still occur, such as striae or general irritation, with more severe side effects of Cushing's syndrome, which can come up as a side effect, though it is very unlikely to occur. It should also be noted that prices may increase significantly depending on the severity of the eczema, which should be a factor when considering other possible treatments. Therefore, overall, it is evident why topical corticosteroids are so commonly prescribed, having a very high efficacy, versatility, and being relatively affordable for the common person, whilst only having very slim chances of adverse side effects occurring (Table 1, Entry 2).

The key strengths of the use of dupilumab and lebrikizumab are that, overall, they help substantially reduce inflammation and pruritus, thus significantly improving skin health, holding this over many other traditional treatments for eczema due to being able to treat the underlying reasons for inflammation. They also reduce the number of systemic side effects because they are able to treat the underlying reasons for inflammation; moreover, they have been thoroughly researched, and as a result, there are minimal side effects, and they are relatively safe (Kumar et al., 2025). Studies mentioned previously have shown a consistent improvement in eczema symptoms, and the biologics themselves have a high efficacy and potency, being able to combat eczema symptoms effectively. However, the key weaknesses are cost and necessity for injection, as many patients will not be able to afford such a costly treatment on average, compared to the cheaper alternative of an over-the-counter (OTC) medication for eczema treatment, whereas biologics cost a lot, leading to many patients having to pay out of their pockets for it. It is also important to note that many patients appear to be very sceptical of needles, therefore being a large barrier in biologics becoming widespread and used often. Due to biologics being able to suppress the immune system, there is a greater frequency of infection among patients who use these biologics compared to topical corticosteroid creams (Ameen et al., 2021). Therefore, though biologics are an optimistic avenue of research currently, some research should be invested towards clinical trials to further evaluate their safety profile and the reduction of cost via an investigation into the possibility of the industrialisation of biologics (Table 1, Entry 3).

The key strength of JAK inhibitors is their efficacy, which is evident in numerous clinical trials mentioned previously, where, using a variety of scales, such as EASI, IGA or DLQI, there have been significant improvements in all three scales using all three common JAK inhibitors in Abrocitinib, Ruxolitinib and Upadacitinib. Moreover, relative to other common treatments, JAK inhibitors have much higher efficacy in skin clearance as well. Furthermore, compared to other treatments like biologics, where a needle is required for administration, most JAK inhibitors are orally administered, therefore being easier to administer and appealing to more patients (Harrington et al., 2020). However, though JAK inhibitors do possess high efficacy for treatment and are easy to administer, they still possess many downsides. As a result of its high efficacy, the likelihood of adverse events occurring increases. This is demonstrated by a greater frequency of serious side effects, such as cardiovascular events or blood clots. Another crucial weakness to note compared to other treatments is specificity, as JAK inhibitors affect multiple signalling pathways, which ultimately leads to many potential side effects. They are also costly compared to OTC eczema treatments, costing tens of thousands of dollars (Table 1, Entry 4).

In general, the key advantages of utilising Manuka honey as an alternative medication relative to other common eczema treatments on the market are due to its inherent anti-inflammatory properties, along with its ability to retain moisture and reduce the severity of eczema flare-ups (Patel & Cichello, 2013). Though the Manuka honey has been demonstrated to possess these important qualities in the effective treatment of eczema, it still contains many disadvantages, which would make it an unreliable choice for dermatologists to prescribe to patients with eczema. The key disadvantages involve its cost, feel, lack of research and risk factor for allergies. Regarding its cost, relative to other commercial products for treatment, the same potency of treatment is offered at a comparable efficacy, whilst being more costly compared to over-the-counter (OTC) emollients or topical corticosteroids. Due to a severe lack of research into alternative medications like Manuka honey compared to commonly researched treatments, such as topical corticosteroids, a greater number of clinical trials must be performed in order to further determine how it compares against traditional and modern treatments. Furthermore, it has been reported to feel very sticky and greasy, which a patient may find uncomfortable in daily life, especially with the frequency of application, compared to an emollient, which may be both soothing and won't feel as greasy. Many patients with allergies to pollen or bees, as stated previously, will not be able to use this medication; therefore, its versatility is substantially hindered by this factor compared to a topical corticosteroid (Alhabsi et al., 2026). Lastly and overall, there is still only preliminary evidence for its potential antibacterial benefits and lesion improvement; therefore, no large randomised controlled trials (RCTs) confirm superiority over standards, and it is not recommended in major guidelines as a primary treatment (Table 1, Entry 5). However, it is important to note that, compared with the other treatments discussed in the traditional and modern approaches, the figures for Manuka Honey are drawn from different trials with different patient populations, disease severity, and primary endpoints. As a result, it is vital to note that the interpretations of these trials may not be as strong, due to the lack of direct head-to-head clinical data to mitigate bias accordingly.

For acupuncture overall, the drawbacks outweigh the advantages due to the multiple side effects, which may be presented if in the care of an inexperienced medical professional, who may not be effective and accurate at inserting the needles into the patient, leading to multiple side effects occurring. Though it does have a few advantages, much research has been invested in the safety and efficacy of treating eczema with acupuncture, and studies have shown that when an experienced practitioner performs the treatment, eczema symptoms can be substantially reduced, and it is relatively safe. However, again, it still comes with very adverse side effects. It also needs to be considered that it is very costly compared to many OTC medications, such as topical corticosteroids, as an experienced practitioner of acupuncture is costly, yet necessary to ensure safety. Furthermore, though as stated previously, there has been a bit of research that has been invested into acupuncture, many other commercial treatments are even more rigorously evaluated and tested in clinical trials to be safer, more potent and cheaper. Lastly, the systematic reviews of acupuncture show mixed and low-quality evidence overall, with some mild itch and symptom reduction, which unfortunately come with heavy risks such as pain and infection, and the severe lack of thorough and evaluative trials makes it unreliable compared to conventional options (Zeng et al., 2021). Therefore, though through these findings the data does show the implication that overall acupuncture may not be a preferred option of treatment, it is still important to note that these interpretations should be approached with caution, being primarily preliminary insights.

Table 1. Summary of primary, secondary and alternative eczema therapies: a comparison of treatment types, their delivery methods, efficacy, evidence level, main advantages and clinical limitations.

Entry	Type	Target	Delivery	Evidence	Advantages	Limitations
1	Emollients	Skin	Topical	High	OTC, cheap, hydro-retentive	Low potency, frequent application, potential pore clogging
2	Corticosteroids	Skin	Topical	High	OTC, safe, versatile potency, affordable	Potential adverse side effects, variable pricing
3	Biologics	Thigh or abdomen	Injection	Medium	High potencies and efficacy	Need for injection, costly, potential adverse side effects
4	JAK inhibitors	Skin and immune system	Oral or topical	High	High efficacy, easy to administer	Lack of specificity, high frequency of side effects, and costly
5	Alternative meds	Skin	Various	Low	Unproven	Adverse side effects, costly, unsafe, lack of thorough and evaluative trials

Overall, the treatments summarised in Table 1 highlight the need for a personalised approach. Healthcare providers should evaluate severity using the EASI index and weigh the risk-benefit profile of each option. Selecting the optimal strategy requires balancing clinical efficacy with patient preferences to support long-term treatment adherence.

4. Conclusion

In conclusion, after extensive evaluation of many eczema treatments, modern and traditional approaches do remain the key treatments for both research and current usage. For traditional treatments, they remain reliable and affordable due to extensive research into the efficacy and safety of emollients and topical corticosteroids, as well as ways to reduce costs, which, as a result, leads to their prescription by more medical practitioners. For modern treatments, they remain an optimistic avenue for innovation and research, due to their potency and efficacy, though more research needs to be put towards reducing the frequency of adverse side effects, as well as making these treatments more accessible to the average person, due to the costly nature of JAK Inhibitors or Biologics, leading to substantial out-of-pocket costs for patients. Alternative medicines remain an area of scepticism, and rightly so, though research has been heavily invested in their safety and effectiveness. For the same effectiveness, both traditional and modern approaches to eczema treatment outperform alternative treatments, making them unreliable and rarely used in treatment. Therefore, overall, eczema treatments remain very promising for further research and innovation to optimise and refine both traditional and modern treatments in terms of cost, adverse side effects, and efficacy.

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Data & Code Availability Statement

No new raw data or software code were generated or analysed during this study. All data evaluated in this review were obtained from previously published literature and publicly available clinical trial registries at ClinicalTrials.gov. All primary sources and trial identifiers (NCT numbers) are cited within the article.

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Mentor Contribution Statement

Mentor, Dr Daria Sokolova, has helped in advisory and supporting roles throughout the process of this literature review.

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REVIEW ARTICLE

Eczema treatments: A review of their effectiveness, limitations and future directions

Abstract

There are currently a myriad of available choices for eczema treatment, each possessing different efficacies, potencies and mechanisms of action. There are currently three main categories of eczema treatments: traditional, alternative and modern approaches. However, there are many debates over which treatments are the most effective and offer the greatest benefits. For instance, biologics are a promising avenue of research due to their potency and efficacy, though they are associated with more severe adverse effects than other treatments. Conversely, topical corticosteroids possess a wide range of potencies and are highly effective, but carry drawbacks related to application frequency or possible local side effects. Therefore, this literature review examines the most common eczema treatments across traditional, modern and alternative medicines, compares them, and evaluates possible future directions for the research and innovation of eczema treatments and their potential contribution towards the advancement in medical research. Overall findings dictate that modern and traditional eczema treatments remain the forefront for general usage due to reliability, accessibility and safety.

Keywords: Translational Medical Sciences, Disease Treatments and Therapies, Dermatology, Eczema.

1. Introduction

Since around 400 BC, when eczema was first described and labelled, it has persisted as a significant irritant and major health issue worldwide. During this time period, Hippocrates became the first to describe the condition now known as eczema, having described a patient with dry and scaly skin, as well as a chronic itch throughout the patient's body. Although considerable research and investment have been made to investigate treatments, the issue remains an unrelenting problem affecting approximately 1.5 million adults in the UK (*Change AD UK*), underscoring its widespread impact throughout the country. Key treatments currently used most commonly include emollients, general improvements to hygiene and sanitary standards, topical corticosteroids, and some modern innovations, such as Janus Kinase (JAK) inhibitors and biologics (Santer et al., 2024). Emollients are compounds which form a film on the outer surface of the skin, which aids in soothing irritation and hydrating the skin. JAK Inhibitors are a classification of medical compounds which reduce the transduction of cytokine signalling through the JAK-STAT

pathway and as a result reduce the transcription of genes related to the causation of inflammation and swelling. Biologics function as compounds which are composed of biological material, are grown in living cell structures, and are known for their potent efficacy in treating diseases. Though the common treatments are effective on a wide scale, being more cost-effective and easily accessible, they do have some disadvantages, such as side effects like lichenification (thickening of skin with leathery texture arising) or erythema (redness of skin due to increased blood flow to blood vessels near surface of skin) (Bhanot et al., 2019) with prolonged use of certain emollients and also skin thinning and stretching as side effects for topical corticosteroids. The newer innovations seem more promising, being long-lasting and highly effective at treating eczema, though a new issue arises: costs and malignancies (Mansilla-Polo & Morgado-Carrasco, 2024). This is especially prevalent in JAK inhibitors, due to the effectiveness of their immunosuppressive nature, resulting in the weakening of the immune system, leading to greater vulnerabilities in the body, which eventually culminates in a greater risk for cancer. This vulnerability causes infections to develop within the body, particularly in the respiratory and urinary tracts (Klein et al., 2022). Biologics also have a few adverse side effects, including but not limited to conjunctivitis (inflammation of the conjunctiva), injection site reactions and eosinophilia (*Long-Term Safety and Efficacy Study of Lebrikizumab (LY3650150) in Participants With Moderate-to-Severe Atopic Dermatitis (ADjoin) (ADjoin)*, 2025). Therefore, while both traditional and newer innovations in eczema treatments have demonstrated various successes in terms of effectiveness in resolving eczema, they still have drawbacks in multiple ways, including side effects and costs. However, whilst these newer innovations do have drawbacks, further investment into them should be investigated to assess the assumptions that adverse side effects may be mitigated and eventually eliminated. This is evident in the possibility of investment into the mass production of biologics, slowly minimising costs and making them more affordable to the average person. This article ultimately aims to discuss various eczema treatments, some more well-known than others, evaluating their outlooks, various benefits and drawbacks. The key treatments discussed will include the most common traditional approaches and modern innovations, as well as some discussion on the prospect of alternative medicine. The key way in which this literature review differs from others is that it not only takes into account treatments which are very commercialised and recognised, but it also acknowledges the possibility of alternative medicine in its treatments and provides comprehensive comparisons to traditional and modern treatments for eczema.

2. Methodology

Search strategy

The primary strategy utilised for the identification of relevant literature reviews was through the thorough evaluation of key sources found on Google Scholar or ClinicalTrials.gov. The searching strategy was conducted using MeSH filtering and evidence-based analysis for clinical trials, which allowed me to achieve methodological rigour in mitigating bias, ensuring clinical relevance and statistical validity. It is important to note that included studies were not formally appraised for risk of bias and may therefore be subject to bias. Including terms such as “Biologics” and “Emollient efficacy” was vital in being able to filter relevant information when using keyword searching for Google Scholar. The reason for which a third database was not used during the research into the manuscript was because Google scholar already yields many of the journals which are indexed in PubMed, thus its usage as a third database would yield nearly completely similar results, as a result usage of PubMed was used slightly in the initial research phase, though nearly similar papers would also appear on google scholar, as a result citations were primarily present on google scholar.

Additional relevant terms were used during the evaluation of different treatments, including: Abrocitinib, Ruxolitinib, Upadacitinib, Dupilumab, Lebikizumab, Hydrocortisone and Betamethasone Valerate. Additionally, the date range of the literature search had no restrictions applied. EASI, IGA and other clinical endpoints were systematically extracted.

Inclusion and exclusion criteria

Key criteria that were required for the consideration to use the source included:

- Sufficient data for analysis for clinical trials
- Peer-reviewed academic journals in terms of literature review evaluation

Exclusion criteria:

- Lack of empirical data
- Published as an editorial commentary

Study selection and data extraction

Screening was performed throughout the writing of this literature review, and each citation was independently reviewed and assessed. Ultimately, through the process of writing, a large proportion of literature reviews and clinical trials met all inclusion criteria to be included in the literature review.

Data extraction was conducted through comprehensive organisation through Zotero software to record the author, year of publication and area of eczema research, helping categorise research effectively through keyword searching within the software.

3. Analysis

Mild-to-moderate eczema

The most common treatments prescribed are emollients. The main emollients prescribed by the NHS are creams and ointments, such as Aveeno creams and Cetraben cream. Aveeno creams and some Cetraben creams use colloidal oatmeal as a base, due to its natural healing acceleration benefits, which act as a barrier to retain moisture and gently cleanse the skin to optimise the reduction of eczema flaring and gradually help build up a natural barrier against eczema. The key chemical components contained within this colloidal oatmeal are known as avenanthramides, which contain anti-inflammatory and anti-itch properties (Fig. 1) (Sur et al., 2008). Moreover, it also reduces hypersensitivity and thus is a very strong combatant against irritants. Avenanthramides act via inhibition of NF-κB, responsible for governing immune response and inflammation (Yang et al., 2014).

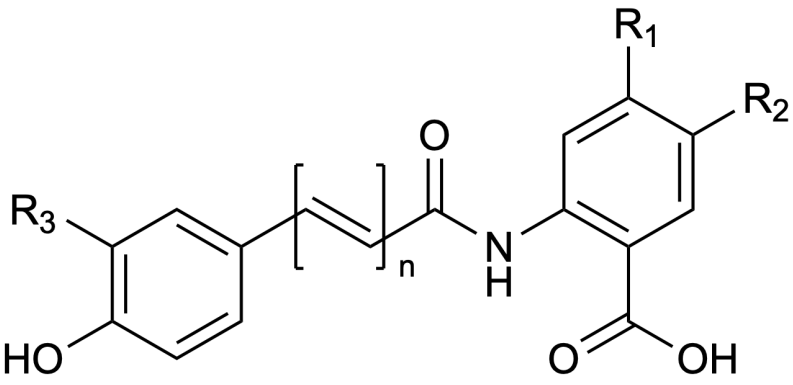


Figure 1. Chemical structure of avenanthramides (n = 1 or 2; R_1 = H, R_2 = OH, R_3 = H, OCH_3, or OH). Avenanthramides are formed by the N-acylation reaction between anthranilic acid (AA) and a phenylalkenoic acid (PA) to create an amide linkage.

Cetraben creams use soft paraffin and liquid paraffin as bases, which act as key chemical compounds for anti-inflammatory and anti-irritant properties. In a study, the SCORing Atopic Dermatitis index (SCORAD) score in patients using a paraffin-based cream was significantly lower than in those using a control cream, indicating a notable reduction in eczema severity. It indicated a 28.6% decrease compared to the original SCORAD score. Therefore, it was concluded that the paraffin-based creams and ointments were effective in reducing the severity of eczema symptoms (Waked & Ibrahim, 2020). The key chemical compounds used in the creams are petrolatum, which is a mix of hydrocarbons. Studies have shown that it helps regulate antimicrobials and maintain the skin's epidermal barrier to help the retention of moisture and prevent irritants from coming into contact with the skin, which demonstrates its effectiveness in combating eczema in patients. One of the key chemical compounds in petrolatum is alkanes such as octadecane (Fig. 2) (Rogers & Skanupong, 1974). Petrolatum acts by forming a protective barrier on the skin, helping retain moisture and smooth the skin, making it both a comfortable and effective emollient.

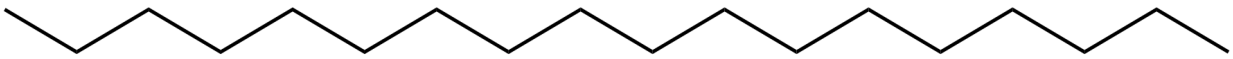


Figure 2. Chemical structure of octadecane, an alkane with 18 carbon atoms and 36 hydrogen atoms. It is a key component of petrolatum, and its skin-soothing and non-greasy properties make it a vital ingredient in petrolatum-based emollients.

Emollients have shown promising results, as evidenced by numerous clinical trials testing the effectiveness of colloidal oatmeal creams (*Study Results | NCT02691507 | Trial to Determine the Therapeutic Benefit of an OTC Cream on Dry, Itchy Skin of Adults and Children With Eczema | ClinicalTrials.Gov*, 2017). Results indicated a significant increase in hydration and a substantial decrease in itchiness, with an average of 4.07 out of 10 on an arbitrary scale

after application, demonstrating its short-term effectiveness. However, an issue arises after consolidating data for 7 days after cream application, with 4.22 out of 10. Though it has no significant impact on its overall success, it still shows diminished retention of its anti-itching properties compared to other commercial eczema treatments. Other studies also demonstrate this by recording hydration with a corneometer; the results showed that after 7 days, the unit of measure in arbitrary units was 208.52, compared to 14 days, when the unit of measure in arbitrary units was 158.65 (Johnson & Johnson Consumer Inc. (J& JCI), 2017). The greater the unit of measure in arbitrary units, the greater the hydration. This further emphasises the long-term decline in the effectiveness of emollients. Of course, it is crucial to consider that systematic reviews confirm they reduce flares in the long term when used proactively with anti-inflammatories.

A majority of emollients are effective with minimal side effects, providing a reliable short-term solution for mild to moderate eczema. However, situations in which adverse side effects occur must also be taken into account. In a study that examined the effects of a wide range of emollients, including variations in type (cream or lotion) and ingredients (botanicals, ceramides, and other components). From this study, it was found that many patients experienced the following side effects: erythema, irritation, papule formation, and further spreading of eczema, as well as other prominent side effects also being present (Emmett et al., 2023). It has been shown that overall botanical emollients may display more side effects due to the possibilities of irritants present in the natural ingredients compared to ceramides, as allergies may also arise from the use of botanical emollients (Corazza et al., 2009), whilst ceramide-based emollients remain effective and safe (Draelos, 2008), due to the presence of ceramides in skin already.

Alongside emollients, topical corticosteroids remain a widely prescribed treatment worldwide. The key ways in which topical corticosteroids act are via binding to glucocorticoid receptors within the cytoplasm. This causes a conformational change in the receptor, causing the dissociation of chaperone proteins from the chaperone complex. This corticosteroid-receptor complex then travels through the nuclear pores and inside the nucleus; two of these corticosteroid receptors bind together via homodimerisation, and this dimer then binds with DNA at sites known as glucocorticoid response elements. This process triggers transactivation and, as a result, the increased transcription and translation of anti-inflammatory proteins like lipocortin (Mehta et al., 2016). As referenced previously, NF-κB, a protein complex that controls the body's inflammation. As a result, the body reduces the inflammatory response. Its fundamental chemical structure is often that of a steroid such as hydrocortisone (Fig. 3), which is $C_{21}H_{30}O_5$ (PubChem, 2020). It has a four-ring structure known as a steroid nucleus, similar to other steroids. Due to its specific chemical structure, it can bind to the glucocorticoid receptor. At high concentrations, glucocorticoid receptor dimerisation can activate transcription of anti-inflammatory genes (Barnes, 2006). However, it should be noted that low doses of corticosteroids are what cause the anti-inflammatory effect.

Additionally, other commonly used topical corticosteroids contain betamethasone valerate (Fig. 3) at different concentrations based on the severity of the eczema (Brazzini & Pimpinelli, 2002). Betamethasone valerate has displayed significant decreases in common inflammatory-causing cytokines. Being one of the more potent corticosteroids, it has been a common prescription for patients with moderate or severe eczema. Clinical studies have shown its efficacy in reducing eczema severity (Gether et al., 2025). Moreover, in another study, betamethasone valerate showed potent effects in reducing symptoms of eczema relative to other common treatments, such as 0.5% and 2.5% desoximethasone, showing how it compares well against other frequent prescriptions against eczema

(Ashton et al., 1987). Its chemical structure is $C_{27}H_{37}FO_6$. It has a valerate ester, a hydroxyl group and a ketone group as well (*Betamethasone Valerate Cream USP*, 0.1%, 2010).

Evidently, Topical Corticosteroids have also shown significant success in reducing mild to moderate eczema. According to a study, transepidermal water loss was significantly lower when an irritant was applied to multiple patients than when the same irritant was applied to another patch of their skin, with a topical corticosteroid also applied. The study showed that significantly less erythema and lower values of the water loss were found, showing its potent effect on combating the inflammatory properties of eczema, as well as maintaining the water content of the skin (Ramsing & Agner, 1995). Another study also dictates its effectiveness relative to other alternatives of the treatment of eczema flare-ups, such as calcineurin inhibitors meant to suppress the inflammatory response of the immune system specifically. These studies show that the topical corticosteroids are more efficacious (Schmitt et al., 2011). Furthermore, potent corticosteroids can effectively eliminate potential bacteria, which could have helped amplify the effects of inflammation in eczema (Nilsson et al., 1992).

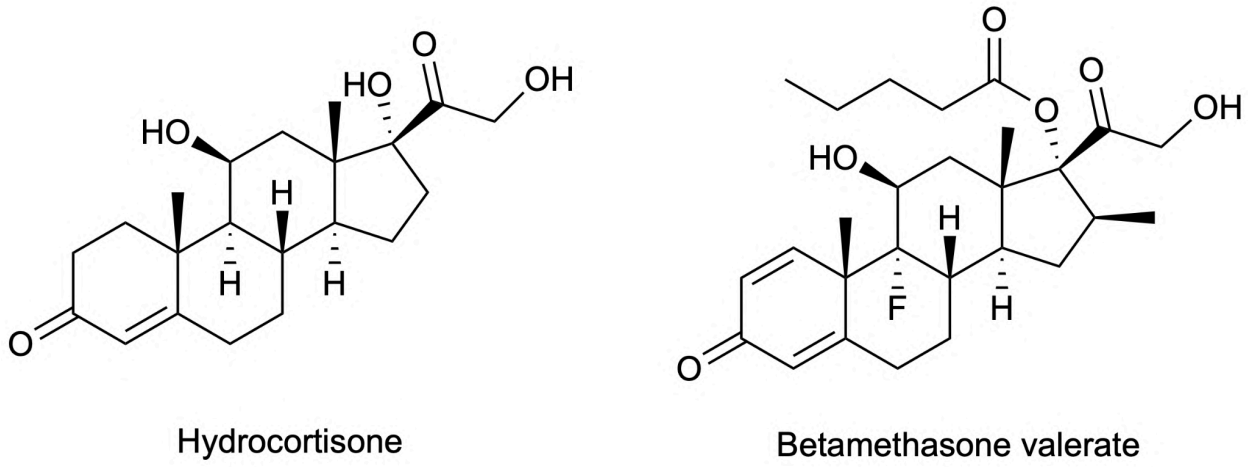


Figure 3. Chemical structures of hydrocortisone and betamethasone valerate. Both molecules are structurally similar and share a cyclopentanoperhydrophenanthrene steroid nucleus and multiple functional groups, including carbonyl and hydroxyl substituents.

Both hydrocortisone and betamethasone valerate have similar side effects, as they are topical corticosteroids in different forms. The most common side effects associated with the use of both medications are local side effects, such as skin atrophy, where the skin begins to thin, leading to easy bruising, and striae, which can result in stretch marks (Ference & Last, 2009). However, there are other side effects which, though rare, can occur, such as systemic side effects of Cushing's syndrome, where an increase in blood pressure and weight gain occurs or a decrease in the growth rate of children, though these systemic side effects have an amplified chance of occurring if the potency of the topical corticosteroid was too strong or there is prolonged use of the medication over a period of time (Dhar et al., 2014). Additionally, ocular symptoms may also be presented in glaucoma or cataracts (Daniel & Orchard, 2015). Despite these numerous side effects, the frequency of the occurrence is slim to none, thus being another reason why

they prove to be such common prescriptions during treatment, with easily variable potencies based on the severity of the eczema.

Moderate-to-severe eczema

There are two key biologics currently used to treat eczema that are well known, namely Dupixent and Ebglyss. Dupixent (dupilumab) has been FDA-approved since March 2017 for the treatment of eczema. Its function is to inhibit the signalling of cytokines IL-4 and IL-13, resulting in reduced inflammation and, as a consequence, skin barrier dysfunction (Seegräber et al., 2018). Ebglyss (lebrikizumab) was FDA-approved in September 2024 for the treatment of eczema and works similarly to Dupixent by inhibiting cytokine signalling; however, it only inhibits IL13, preventing T cell Th2 signalling and consequently reducing both inflammation and eosinophilia (Khan et al., 2025). IL-13 is a cytokine which regulates allergic responses, known as interleukin-13. Lebrikizumab and dupilumab are both produced by inserting the genetic code into Chinese hamster ovary (CHO) cells to help mass-produce the antibodies; they must then be purified extensively to isolate the respective biologics in Dupixent and Ebglyss.

Dupilumab has been extensively researched, and studies have shown its efficacy in treating eczema, as in one study on the effect of dupilumab on chronic hand eczema (CHE), results showed that dupilumab was effective in treating this particular eczema. According to the hand eczema severity index, patients had a significant decrease, and the dermatology life quality index (DLQI) increased overall. It showed a high tolerance for patients and thus proved to be a very promising treatment for eczema, with high efficacy and a low rate of adverse side effects, making it relatively safe (Asamoah et al., 2025). Another study showed that 80.3% of patients in a clinical trial evaluating the effects of dupilumab on CHE achieved partial or complete resolution of their eczema, demonstrating both its potency and efficacy in treating chronic hand eczema (Riva et al., 2024). Its chemical structure is a monoclonal antibody of a subclass of immunoglobulin G4 that binds to the IL4 receptor. IL-4 is a cytokine which regulates allergic responses, also known as interleukin-4. As a result of being able to bind to the IL-4 receptor, dupilumab can inhibit signalling along both the type 1 and type 2 receptors, thus resulting in a decrease in inflammation (Knox et al., 2024).

For lebrikizumab, there have been fewer studies due to its recent approval by the FDA for clinical trials; therefore, it has not been as thoroughly studied as Dupilumab and has only recently become well known as a biologic. Studies, however, have also demonstrated its effectiveness in treating eczema. In a study that studied the long-term effects of lebrikizumab on patients with moderate to severe eczema, the results showed that a significant majority of patients experienced a substantial improvement in skin quality, having an investigator's global assessment (IGA) of 0 or 1, and there was no requirement to further take topical corticosteroids or other treatments to maintain these effects (Stein-Gold et al., 2026). Additionally, a significant majority of patients had a low EASI score, demonstrating lebrikizumab's potent effects on eczema. Its chemical structure is also that of an immunoglobulin G4 monoclonal antibody. It binds IL-13 with high affinity, thereby inhibiting its inflammatory effects.

The key potential adverse side effects that come about through the use of dupilumab for the treatment of eczema were head and neck eczema, conjunctivitis, eczema, peeling of skin and dryness in eyes, however overall dupilumab did show to have a high tolerance, as these adverse side effects only presented in less than 20% of patients, and are relatively minor and not severe or life threatening (Parmar et al., 2022). In another study, it was said that a small minority of patients had mild conjunctivitis, and a few patients had severe conjunctivitis, which may remain an issue; therefore, dupilumab must be researched slightly more to ensure the safety of patients who may decide to utilise it as a treatment for moderate to severe eczema. The key side effects of lebrikizumab are injection site reactions and

conjunctivitis, and therefore it has similar side effects to dupilumab (Lin et al., 2024). However, studies show that relative to dupilumab, it seems that lebrikizumab seems to be more favourable due to its side effect profile and high tolerance. Moreover, it should be noted that dupilumab has a greater number of ocular effects (Loh et al., 2020).

Janus kinase (JAK) inhibitors reduce eczema severity by blocking intracellular signalling triggered by pro-inflammatory cytokines such as IL-4 and IL-13, thereby reducing immune-mediated inflammation.(*Basic Mechanisms of JAK Inhibition*, 2020). In a literature review, it was stated that there are currently 11 FDA-approved JAK inhibitors which can be used. However, the key JAK inhibitors which are often used in the treatment of eczema are abrocitinib, ruxolitinib and upadacitinib (Fig. 4) (Chovatiya & Paller, 2021, Shawky et al., 2022).

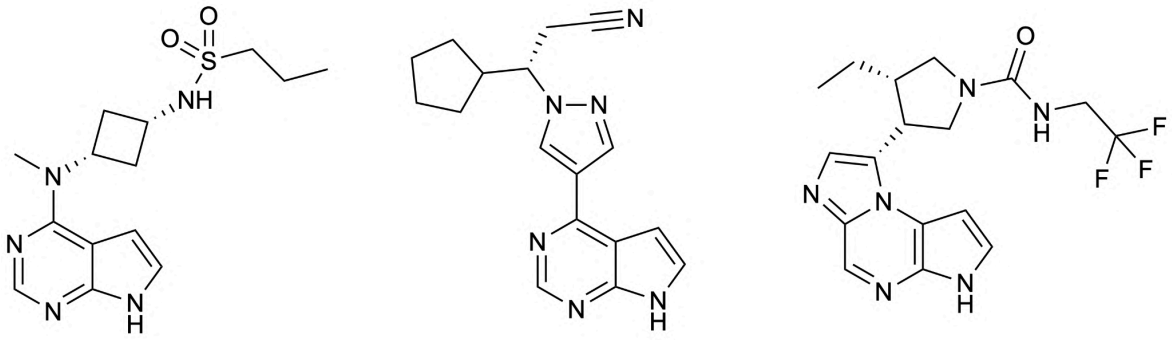


Figure 4. Chemical structures of the most commonly used JAK inhibitors to treat eczema. All 3 share a nitrile group that facilitates binding to the kinase, and they also have a pyrrolopyrimidine core. The nitrile group enables blocking of the JAK-STAT pathway.

Studies have shown that abrocitinib, ruxolitinib and upadacitinib are effective in the treatment of eczema. This is evident in a study on the efficacy of abrocitinib and upadacitinib. For abrocitinib, results from the trial showed a significant reduction in pruritus for many patients, and 48.3% of patients demonstrated investigator's global assessment (IGA) scores of 0 or 1. Moreover, in week 1, there were also very substantial improvements in the eczema area severity index (EASI). This shows that abrocitinib has a high efficacy and can lead to skin clearance and relief. For upadacitinib, 50% of patients demonstrated an IGA score of 0 or 1 at 16 weeks, and there was a 90% improvement in EASI score as well at 16 weeks. There was also a general improvement in eczema symptoms, indicating relatively high efficacy, comparable to that of abrocitinib (Nezamololama et al., 2020). In another study, which evaluated the effects of ruxolitinib on eczema, it was found that there was a 51.6% decrease in EASI overall after 4 weeks, and there was a large percentage of patients who were able to achieve IGA scores of 0 or 1; therefore, the results also demonstrated ruxolitinib's efficacy (Mohney et al., 2023).

Generally, many of these JAK inhibitors do have the possibility of many side effects, such as non-specific side effects, such as nausea, vomiting or diarrhoea and also a 10% possibility of headaches, dizziness or fatigue. However, there are also very slim possibilities of many various specific side effects (Fig. 5) (Rajput Khokhar et al., 2025). In a recent

clinical study, patients using ruxolitinib had a 38.3% risk of adverse side effects, which is high; therefore, whilst ruxolitinib has high efficacy and is potent, it still has many side effects, but fewer systemic risks (Incyte Corporation, 2025). For upadacitinib, in a clinical trial, it was demonstrated that there was a 3.49% chance of a serious adverse event occurring, and there was a roughly 20% chance of a non-serious adverse event; however, the trial also indicated that many of the patients' eczema symptoms were substantially reduced through EASI and IGA scores (AbbVie, 2025). However, in a study with abrocitinib, there was a staggering 74% of patients who encountered treatment-emergent adverse events and 1.7% who encountered severe adverse events. Although this study demonstrated high rates of adverse events, real-world tolerability is often good, as shown in other clinical trials of JAK inhibitors. Therefore, similar to other JAK inhibitors, it has a frequency of adverse side effects (Pfizer, 2022). Though it is important to note that oral JAKs do carry these black box warnings for serious heart events, cancer, clots and death and thus the serious risks mentioned are very consistent with these warnings for oral JAKs (Tokareva et al., 2023).

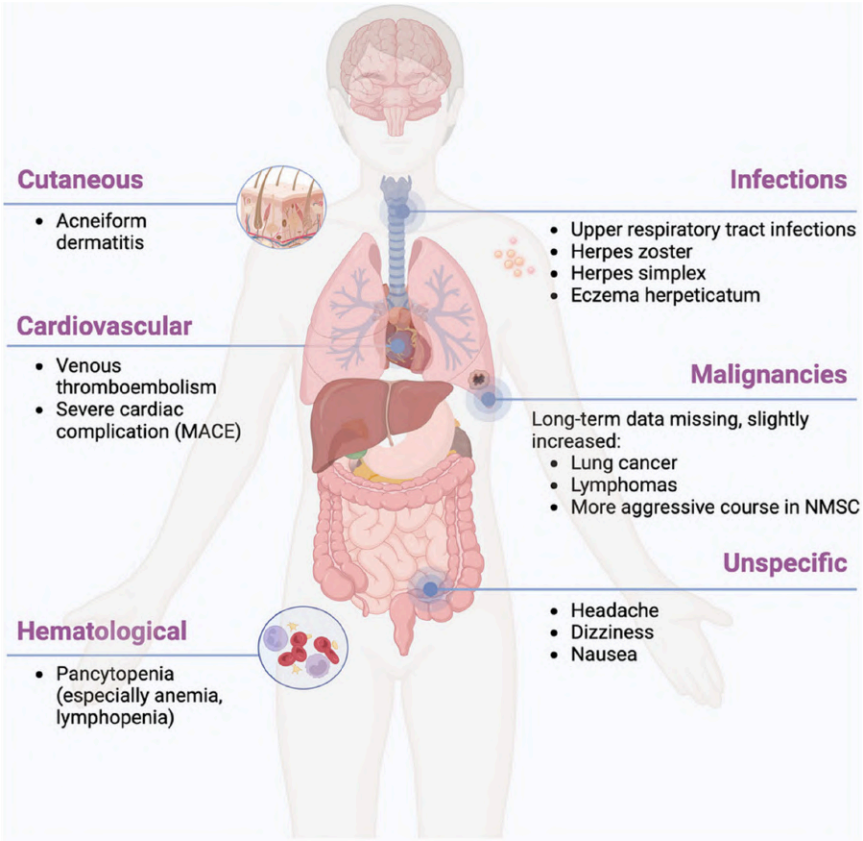


Figure 5. Summary of potential adverse effects of JAK inhibitor therapy. Overview of clinical complications categorised by organ system, highlighting increased risks of infection, cardiovascular events, cutaneous eruptions, and haematological abnormalities.

Alternative therapies

Manuka honey remains a highly researched topic of discussion within the medical field, with the intention to evaluate its efficacy in reducing eczema. Its key function, for which it has been said to treat eczema, is due to its anti-inflammatory and moisturising properties (Johnston et al., 2018a). It is also anti-bacterial, demonstrated in its effectiveness in preventing the development of the bacterium *S. aureus*, which often worsens eczema, due to further infection and flare-ups. It is anti-inflammatory, as it inhibits the signalling pathway of TLR1/2, toll-like receptors that often promote inflammation (Alangari et al., 2017). Moreover, it contains a high concentration of an anti-inflammatory chemical compound, known as methylglyoxal. Studies show that methylglyoxal inhibits the production of inflammatory cytokines; as a result, inflammation from eczema flare-ups is reduced significantly after application of this honey. This is achieved by activating NRF2, which suppresses transcription of the IκBζ gene, thereby reducing the production of inflammatory cytokines substantially (Wei et al., 2023).

It contains a myriad of chemical compounds; however, the key anti-inflammatory compounds are methyl syringate and leptosin (Fig. 6). Methyl syringate acts by inhibiting neutrophil processes (Main et al., 2024), resulting in inflammation being significantly reduced; furthermore, it inhibits the expression of the enzyme cyclooxygenase-2 (J. Park et al., 2016), helping facilitate the reduction of inflammation and pruritus. The structure of methyl syringate comprises a benzene ring, along with a methyl ester group and a hydroxyl group. The structure of leptosin consists of a core of a benzene ring, which is bonded to a furan ring alongside a ketone group, as well as a phenyl group and 2 hydroxyl groups.

There are often minimal side effects that come about through the application of Manuka honey for the treatment of eczema; however, the key issues that often arise are related to contact irritation and allergic reactions. Some patients may be more susceptible to bee or pollen allergies, leading to honey irritating their skin. Its sticky properties also make it easy for dust and debris to stick onto it, leading to the possibility of the eczema worsening. Another key issue could be the quality or grading of the honey itself, as unpurified honey may contain bacteria that can worsen eczema; therefore, medical-grade honey should be used when applying (Johnston et al., 2018b). However, other than these key potential side effects, honey, as a relatively safe chemical compound, will not often lead to other adverse side effects, resulting in its high tolerance level, mainly due to its low pH, moisturising efficacy and antibacterial properties (Mandal & Mandal, 2011).

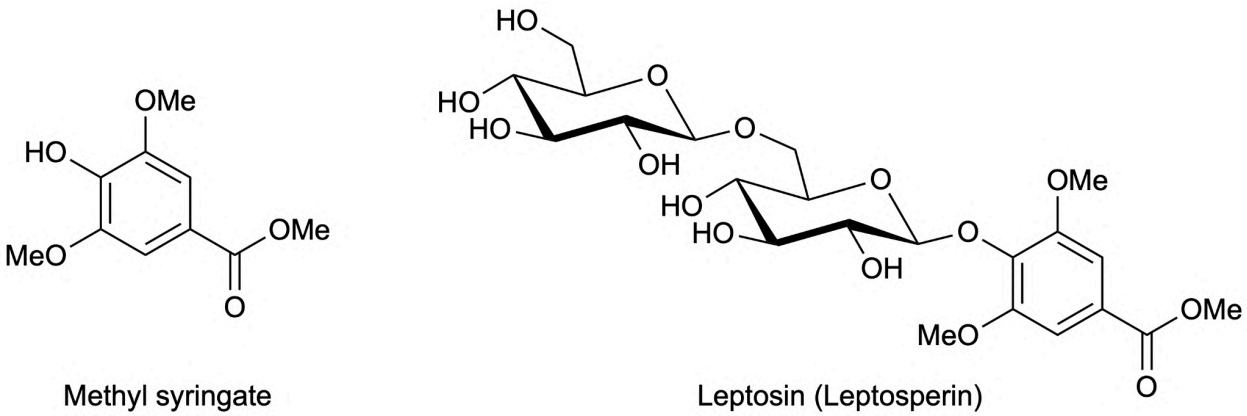


Figure 6. Chemical structures of methyl syringate and leptosin, also known as leptosperin, along with their respective functional groups, with both similarly having a hydroxyl group and benzene ring, but methyl syringate having a methyl ester group compared to leptosin with a furan ring, ketone group and phenyl group (J. Park et al., 2016).

Acupuncture works by stimulating the nervous system through the insertion of many tiny needles into various spots of the body. However, its key function in helping combat key symptoms of eczema is to activate the nervous system, stimulating nerves to release endorphins for pain relief, while inhibiting inflammatory cytokines (Li et al., 2021). Moreover, there are many classifications of specific areas for the needles to be inserted, for example, ST36 or PC6 (Fig. 7) (*Frontiers | Efficacy of Acupuncture on Upper Limb Dysfunction after Stroke: A Randomized Controlled Trial Protocol with Surface Electromyography Evaluation*, 2025). These are key areas of insertion on the outer side of the shin and the inner wrist, respectively. Inserting needles into ST36 activates the sympathetic nervous system and, as a result, reduces inflammation (Oh & Kim, 2022). After inserting needles into PC6, this promotes the release of anti-inflammatory compounds and helps regulate the immune response to further reduce the severity of eczema symptoms (H.-J. Park et al., 2021).

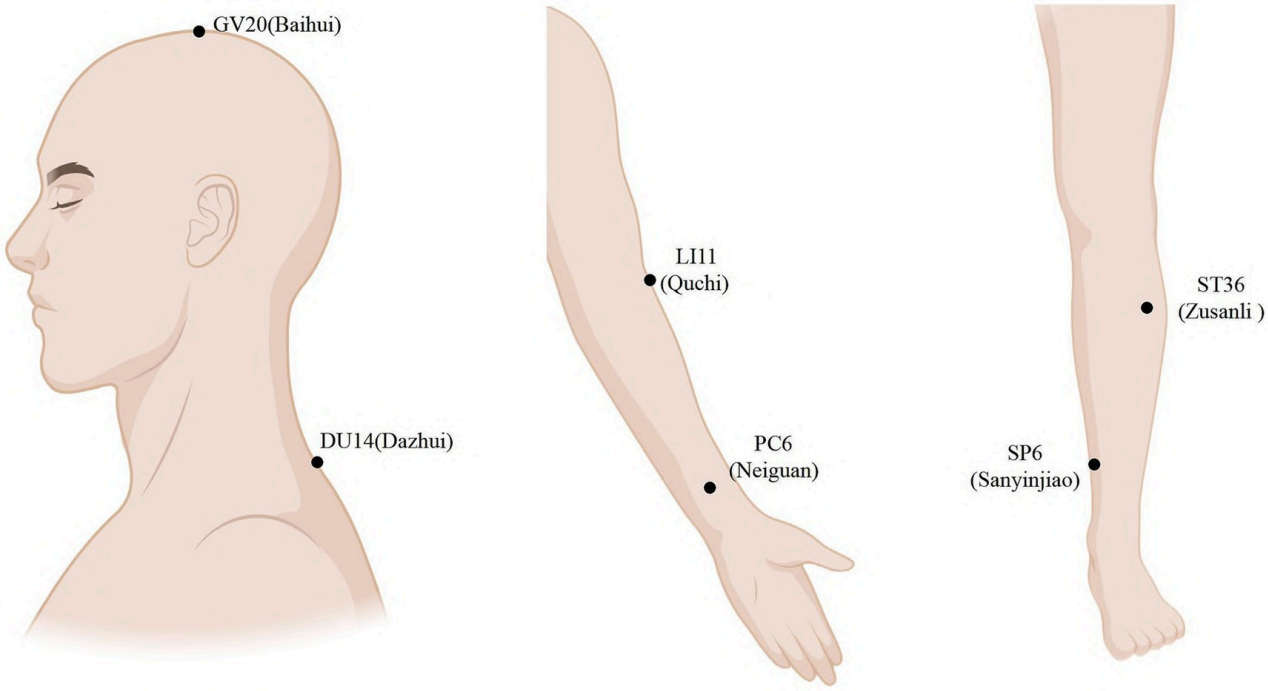


Figure 7. Schematic representation of acupuncture points of both ST36 and PC6, in which PC6 is in the inner wrist, and ST36 is in the outer shin.

There are some possible side effects which may come about through the use of acupuncture to treat eczema. This includes minor pain, bleeding and bruising at the sites of the needle insertion, dizziness, drowsiness, as well as the potential worsening of eczema, due to increasing the severity of eczema symptoms or causing a flare-up. There are also possibilities of infection and increased bleeding (Jones, 2019). The numerous severe side effects that come about through acupuncture outweigh its positive effects. Moreover, these side effects may or may not present, depending on the medical practitioner's experience and ability (Xu et al., 2013).

Evaluation of each treatment

Generally, there are numerous advantages to emollients becoming a standard for general prescription. Notable advantages include the effectiveness of moisture retention, helping improve the strength of the skin barrier. Studies have shown that emollients have high efficacy in reducing the severity of flare-ups and eczema, as indicated by POEM scores, and have demonstrated considerable decreases in flare-ups and itching. However, this study also showed that adverse effects, whilst not fatal, are common as some patients did experience worsening of eczema, further itching, dryness and a burning sensation (Ridd et al., 2022). Moreover, relative to other medications, it is affordable for the average person and also easy to apply, though drawbacks also include frequency of application and potential clogging of pores, which may result in worsening of eczema (Table 1, Entry 1) (*How Parents and Children Evaluate Emollients for Childhood Eczema: A Qualitative Study | British Journal of General Practice*, 2022).

Topical corticosteroids are highly effective in quickly resolving eczema flare-ups, relatively safe, and versatile, with different potencies prescribed to patients depending on the severity of their eczema. An example of this would be hydrocortisone given to patients with very mild eczema, and betamethasone valerate at different concentrations for moderate and severe eczema. Moreover, they are often affordable, as their over-the-counter availability has driven prices down. These advantages all make it a primary treatment for eczema. However, whilst topical corticosteroids are a very effective solution to eczema, it is crucial to be aware of the potential side effects as noted previously, as though they are of very low chance, local effects could still occur, such as striae or general irritation, with more severe side effects of Cushing's syndrome, which can come up as a side effect, though it is very unlikely to occur. It should also be noted that prices may increase significantly depending on the severity of the eczema, which should be a factor when considering other possible treatments. Therefore, overall, it is evident why topical corticosteroids are so commonly prescribed, having a very high efficacy, versatility, and being relatively affordable for the common person, whilst only having very slim chances of adverse side effects occurring (Table 1, Entry 2).

The key strengths of the use of dupilumab and lebrikizumab are that, overall, they help substantially reduce inflammation and pruritus, thus significantly improving skin health, holding this over many other traditional treatments for eczema due to being able to treat the underlying reasons for inflammation. They also reduce the number of systemic side effects because they are able to treat the underlying reasons for inflammation; moreover, they have been thoroughly researched, and as a result, there are minimal side effects, and they are relatively safe (Kumar et al., 2025). Studies mentioned previously have shown a consistent improvement in eczema symptoms, and the biologics themselves have a high efficacy and potency, being able to combat eczema symptoms effectively. However, the key weaknesses are cost and necessity for injection, as many patients will not be able to afford such a costly treatment on average, compared to the cheaper alternative of an over-the-counter (OTC) medication for eczema treatment, whereas biologics cost a lot, leading to many patients having to pay out of their pockets for it. It is also important to note that many patients appear to be very sceptical of needles, therefore being a large barrier in biologics becoming widespread and used often. Due to biologics being able to suppress the immune system, there is a greater frequency of infection among patients who use these biologics compared to topical corticosteroid creams (Ameen et al., 2021). Therefore, though biologics are an optimistic avenue of research currently, some research should be invested towards clinical trials to further evaluate their safety profile and the reduction of cost via an investigation into the possibility of the industrialisation of biologics (Table 1, Entry 3).

The key strength of JAK inhibitors is their efficacy, which is evident in numerous clinical trials mentioned previously, where, using a variety of scales, such as EASI, IGA or DLQI, there have been significant improvements in all three scales using all three common JAK inhibitors in Abrocitinib, Ruxolitinib and Upadacitinib. Moreover, relative to other common treatments, JAK inhibitors have much higher efficacy in skin clearance as well. Furthermore, compared to other treatments like biologics, where a needle is required for administration, most JAK inhibitors are orally administered, therefore being easier to administer and appealing to more patients (Harrington et al., 2020). However, though JAK inhibitors do possess high efficacy for treatment and are easy to administer, they still possess many downsides. As a result of its high efficacy, the likelihood of adverse events occurring increases. This is demonstrated by a greater frequency of serious side effects, such as cardiovascular events or blood clots. Another crucial weakness to note compared to other treatments is specificity, as JAK inhibitors affect multiple signalling pathways, which ultimately leads to many potential side effects. They are also costly compared to OTC eczema treatments, costing tens of thousands of dollars (Table 1, Entry 4).

In general, the key advantages of utilising Manuka honey as an alternative medication relative to other common eczema treatments on the market are due to its inherent anti-inflammatory properties, along with its ability to retain moisture and reduce the severity of eczema flare-ups (Patel & Cichello, 2013). Though the Manuka honey has been demonstrated to possess these important qualities in the effective treatment of eczema, it still contains many disadvantages, which would make it an unreliable choice for dermatologists to prescribe to patients with eczema. The key disadvantages involve its cost, feel, lack of research and risk factor for allergies. Regarding its cost, relative to other commercial products for treatment, the same potency of treatment is offered at a comparable efficacy, whilst being more costly compared to over-the-counter (OTC) emollients or topical corticosteroids. Due to a severe lack of research into alternative medications like Manuka honey compared to commonly researched treatments, such as topical corticosteroids, a greater number of clinical trials must be performed in order to further determine how it compares against traditional and modern treatments. Furthermore, it has been reported to feel very sticky and greasy, which a patient may find uncomfortable in daily life, especially with the frequency of application, compared to an emollient, which may be both soothing and won't feel as greasy. Many patients with allergies to pollen or bees, as stated previously, will not be able to use this medication; therefore, its versatility is substantially hindered by this factor compared to a topical corticosteroid (Alhabsi et al., 2026). Lastly and overall, there is still only preliminary evidence for its potential antibacterial benefits and lesion improvement; therefore, no large randomised controlled trials (RCTs) confirm superiority over standards, and it is not recommended in major guidelines as a primary treatment (Table 1, Entry 5). However, it is important to note that, compared with the other treatments discussed in the traditional and modern approaches, the figures for Manuka Honey are drawn from different trials with different patient populations, disease severity, and primary endpoints. As a result, it is vital to note that the interpretations of these trials may not be as strong, due to the lack of direct head-to-head clinical data to mitigate bias accordingly.

For acupuncture overall, the drawbacks outweigh the advantages due to the multiple side effects, which may be presented if in the care of an inexperienced medical professional, who may not be effective and accurate at inserting the needles into the patient, leading to multiple side effects occurring. Though it does have a few advantages, much research has been invested in the safety and efficacy of treating eczema with acupuncture, and studies have shown that when an experienced practitioner performs the treatment, eczema symptoms can be substantially reduced, and it is relatively safe. However, again, it still comes with very adverse side effects. It also needs to be considered that it is very costly compared to many OTC medications, such as topical corticosteroids, as an experienced practitioner of acupuncture is costly, yet necessary to ensure safety. Furthermore, though as stated previously, there has been a bit of research that has been invested into acupuncture, many other commercial treatments are even more rigorously evaluated and tested in clinical trials to be safer, more potent and cheaper. Lastly, the systematic reviews of acupuncture show mixed and low-quality evidence overall, with some mild itch and symptom reduction, which unfortunately come with heavy risks such as pain and infection, and the severe lack of thorough and evaluative trials makes it unreliable compared to conventional options (Zeng et al., 2021). Therefore, though through these findings the data does show the implication that overall acupuncture may not be a preferred option of treatment, it is still important to note that these interpretations should be approached with caution, being primarily preliminary insights.

Table 1. Summary of primary, secondary and alternative eczema therapies: a comparison of treatment types, their delivery methods, efficacy, evidence level, main advantages and clinical limitations.

Entry	Type	Target	Delivery	Evidence	Advantages	Limitations
1	Emollients	Skin	Topical	High	OTC, cheap, hydro-retentive	Low potency, frequent application, potential pore clogging
2	Corticosteroids	Skin	Topical	High	OTC, safe, versatile potency, affordable	Potential adverse side effects, variable pricing
3	Biologics	Thigh or abdomen	Injection	Medium	High potencies and efficacy	Need for injection, costly, potential adverse side effects
4	JAK inhibitors	Skin and immune system	Oral or topical	High	High efficacy, easy to administer	Lack of specificity, high frequency of side effects, and costly
5	Alternative meds	Skin	Various	Low	Unproven	Adverse side effects, costly, unsafe, lack of thorough and evaluative trials

Overall, the treatments summarised in Table 1 highlight the need for a personalised approach. Healthcare providers should evaluate severity using the EASI index and weigh the risk-benefit profile of each option. Selecting the optimal strategy requires balancing clinical efficacy with patient preferences to support long-term treatment adherence.

4. Conclusion

In conclusion, after extensive evaluation of many eczema treatments, modern and traditional approaches do remain the key treatments for both research and current usage. For traditional treatments, they remain reliable and affordable due to extensive research into the efficacy and safety of emollients and topical corticosteroids, as well as ways to reduce costs, which, as a result, leads to their prescription by more medical practitioners. For modern treatments, they remain an optimistic avenue for innovation and research, due to their potency and efficacy, though more research needs to be put towards reducing the frequency of adverse side effects, as well as making these treatments more accessible to the average person, due to the costly nature of JAK Inhibitors or Biologics, leading to substantial out-of-pocket costs for patients. Alternative medicines remain an area of scepticism, and rightly so, though research has been heavily invested in their safety and effectiveness. For the same effectiveness, both traditional and modern approaches to eczema treatment outperform alternative treatments, making them unreliable and rarely used in treatment. Therefore, overall, eczema treatments remain very promising for further research and innovation to optimise and refine both traditional and modern treatments in terms of cost, adverse side effects, and efficacy.

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Data & Code Availability Statement

No new raw data or software code were generated or analysed during this study. All data evaluated in this review were obtained from previously published literature and publicly available clinical trial registries at ClinicalTrials.gov. All primary sources and trial identifiers (NCT numbers) are cited within the article.

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Author Biography

Nathan Shiu is a 16-year-old student studying in the United Kingdom who attends Dulwich College. He has a strong interest in Medicine and Biochemistry due to a profound interest in the importance of healthcare in the wider community. His current academic efforts lie in understanding the efficacies of lab-made painkillers and how they

compare against over-the-counter painkillers. Outside of academic research, Nathan is the President of the Junior Doctors' Society, a founder of an Impact 500 project aiming to raise awareness and funds for the charity Doctors in Distress and a writer in the Pursuit of Knowledge article in their school.

Mentor Contribution Statement

Mentor, Dr Daria Sokolova, has helped in advisory and supporting roles throughout the process of this literature review.

Dear Reviewer,

Thank you for your thorough and constructive feedback on the manuscript, "Eczema treatments: A review of their effectiveness, limitations and future directions". We greatly appreciate the time you took to identify both the core conceptual issues and the more minor points, as your comments have helped to significantly improve the clarity, accuracy, and scientific rigour of the paper.

We have carefully addressed each of your concerns in the revised version. Below, we outline the specific changes made in response to your points:

Reviewer comment 1: *Abstract*
• I would suggest cutting the first sentence as it is a little too general and does not contribute much to the overall message. I would also suggest adding one concluding sentence that sums up the research findings so the reader is left in no doubt about what your review uniquely adds to the field.

We are grateful to the reviewer for highlighting this point and the abstract was adjusted accordingly, with the first sentence removed and a concluding sentence added:

There are currently a myriad of available choices for eczema treatment, each possessing different efficacies, potencies and mechanisms of action. There are currently three main categories of eczema treatments: traditional, alternative and modern approaches. However, there are many debates over which treatments are the most effective and offer the greatest benefits. For instance, biologics are a promising avenue of research due to their potency and efficacy, though they are associated with more severe adverse effects than other treatments. Conversely, topical corticosteroids possess a wide range of potencies and are highly effective, but carry drawbacks related to application frequency or possible local side effects. Therefore, this literature review examines the most common eczema treatments across traditional, modern and alternative medicines, compares them, and evaluates possible future directions for the research and innovation of eczema treatments and their potential contribution towards the advancement in medical research. **Overall findings dictate that modern and traditional eczema treatments remain the forefront for general usage due to reliability, accessibility and safety.**

Reviewer comment 2: *Introduction*
• Since you mention eczema being described in 400 BC, it would be beneficial, to paint a much more vivid picture of the condition, if you can add 1-2 sentences of detail about how this disease was described in 400 BC.
• It would be beneficial to add a very short definition explaining what emollients, topical corticosteroids and JAK inhibitors/biologics are and how they work – even though this is discussed later in the paper, it is best to define things early.
• In general, lots of terminology is introduced without context or definition (e.g. lichenification, erythema). While you don't need a strict medical definition, this journal covers a broad range of fields (is not a specific medical or dermatology

journal) and therefore it is important to have sufficient context such that the reader knows what this means without having to separately Google something while Reading.

We highly appreciate the reviewer's valuable insight on this matter, We have added extra context for the history of eczema in 400 BC, a few short definitions of terminology e.g. topical corticosteroids and JAK inhibitors/Biologics:

Since around 400 BC, when eczema was first described and labelled, it has persisted as a significant irritant and major health issue worldwide. **During this time period, Hippocrates became the first to describe the condition now known as eczema, having described a patient with dry and scaly skin, as well as an chronic itch throughout the patient's body.** Although considerable research and investment have been made to investigate treatments, the issue remains an unrelenting problem affecting approximately 1.5 million adults in the UK (*Change AD UK*, n.d.), underscoring its widespread impact throughout the country. Key treatments currently used most commonly include emollients, general improvements to hygiene and sanitary standards, topical corticosteroids, and some modern innovations, such as JAK inhibitors and biologics (Santer et al., 2024). **Emollients are compounds which form a film on the outer surface of the skin, which aids in the soothing of irritation and hydration of the skin. JAK Inhibitors are a classification of medical compounds which reduce the transduction of cytokine signalling, through the JAK-STAT pathway and as a result reduce the transcription of genes related to the causation of inflammation and swelling. Biologics function as compounds which are composed of biological material, and are grown in living cell structures, and are known for their potent efficacy in treating diseases.** Though the common treatments are effective on a wide scale, being more cost-effective and easily accessible, they do have some disadvantages, such as side effects like lichenification **(thickening of skin with leathery texture arising)** or erythema **(redness of skin due to increased blood flow to blood vessels near surface of skin)** (Bhanot et al., 2019) with prolonged use of certain emollients and also skin thinning and stretching as side effects for topical corticosteroids. The newer innovations seem more promising, being long-lasting and highly effective at treating eczema, though a new issue arises: costs and malignancies (Mansilla-Polo & Morgado-Carrasco, 2024). This is especially prevalent in JAK inhibitors, due to the effectiveness of their immunosuppressive nature, resulting in the weakening of the immune system, leading to greater vulnerabilities in the body, which eventually culminates in a greater risk for cancer. This vulnerability causes infections to develop within the body, particularly in the respiratory and urinary tracts (Klein et al., 2022). Biologics also have quite a few adverse side effects, including but not limited to conjunctivitis **(inflammation of the conjunctiva)**, injection site reactions and eosinophilia (*Long-Term Safety and Efficacy Study of Lebrikizumab (LY3650150) in Participants With Moderate-to-Severe Atopic Dermatitis (ADjoin) (ADjoin)*, 2025). Therefore, while both traditional and newer innovations in eczema treatments have demonstrated various successes in terms of effectiveness in resolving eczema, they still have drawbacks in multiple ways, including side effects and costs. However, whilst these newer innovations do have drawbacks, further investment into them should be investigated to assess the assumptions that adverse side effects may be mitigated and eventually eliminated. This is evident in the possibility of investment into the mass production of biologics, slowly minimising costs and making them more affordable to the average person. This article ultimately aims to discuss various eczema treatments, some more well-known than others, evaluating their outlooks, various benefits and drawbacks. The key treatments discussed will include the most common traditional approaches and modern innovations, as well as some discussion on the prospect of alternative medicine. The key way in which this literature review differs from others is that it not only takes into account treatments which are very commercialised and recognised, but it also acknowledges the possibility of alternative medicine in its treatments and provides comprehensive comparisons to traditional and modern treatments for eczema.

Reviewer comment 3: *Methodology*

• I am curious as to why Google Scholar and ClinicalTrials.gov were the only databases used given that other free ones also exist (PubMed for example). A minimum of three databases are usually required in order to ensure comprehensive overview of the literature. While it is not necessary to redo the analysis, I would suggest adding a sentence to explain why other databases were not used

The reviewer's comment is well taken, and we appreciate the opportunity to clarify this point *and have added a caveat sentence to explain the reasoning why other databases were not used during the process of writing this manuscript.*

The primary strategy utilised for the identification of relevant literature reviews was through the thorough evaluation of key sources found on Google Scholar or ClinicalTrials.gov. The searching strategy was conducted using MeSH filtering and evidence-based analysis for clinical trials, which allowed me to achieve methodological rigour in mitigating bias, ensuring clinical relevance and statistical validity. Including terms such as "Biologics" and "Emollient efficacy" was vital in being able to filter relevant information when using keyword searching for Google Scholar. **The reason for which a third database was not used during the research into the manuscript was because Google scholar already yields many of the journals which are indexed in PubMed, thus its usage as a third database would yield nearly completely similar results, as a result usage of PubMed was used slightly in the initial research phase, though nearly similar papers would also appear on google scholar, as a result citations were primarily present on google scholar.**

Reviewer comment 4: *Analysis*

• "The key chemical component contained within this colloidal oatmeal contains its anti-inflammatory and anti-itch properties, which are known as avenanthramides" – this sentence is unclear grammatically, please rewrite

We appreciate this insightful comment from the reviewer and have corrected this comment accoridngly.

The key chemical component contained within this colloidal oatmeal are known as avenanthramides, **which contain anti-inflammatory and anti-itch properties** (Fig. 1) (Sur et al., 2008).

• "The key ways in which topical corticosteroids act are via binding to glucocorticoid response elements in DNA, which increases the production of anti-inflammatory proteins like lipocortin, and suppressing inflammatory genes" – is this correct? According to Eczema UK, steroids work by "attaching themselves to special receptors in cells, resulting in reduced production of inflammatory mediators". In general, medication does not bind to DNA. I would suggest fact checking this particular statement, or rewording it since this makes it sound like the medication binds to DNA.

We thank the reviewer for this constructive suggestion, which has helped clarify the manuscript and have therefore rectified and corrected the incorrect statement in the manuscript.

Alongside emollients, topical corticosteroids remain a widely prescribed treatment worldwide. The key ways in which topical corticosteroids act are via binding to glucocorticoid receptors within the cytoplasm. **This causes a conformational change in the receptor, causing the dissociation of chaperone proteins from the chaperone complex. This corticosteroid-receptor complex then travels through the nuclear pores and inside the nucleus; two of these corticosteroid receptors bind together via homodimerisation, and this dimer then binds with DNA at sites known as glucocorticoid response elements. This process triggers transactivation and, as a result, the increased transcription and translation of anti-inflammatory proteins like lipocortin** (Mehta et al., 2016), as referenced previously, NF-κB, a protein complex that controls the body's inflammation.

• *Make sure all abbreviations (e.g. IL4, IL-13) are defined*

We thank the reviewer for this helpful comment and have subsequently defined the abbreviations stated accordingly

Ebglyss (lebrikizumab) was FDA-approved in September 2024 for the treatment of eczema and works similarly to Dupixent by inhibiting cytokine signalling; however, it only inhibits IL13, preventing T cell Th2 signalling and consequently reducing both inflammation and eosinophilia (Khan et al., 2025). **IL-13 is a cytokine which regulates allergic responses, known as interleukin-13**

Its chemical structure is a monoclonal antibody of a subclass of immunoglobulin G4 that binds to the IL4 receptor, **IL-4 is a cytokine which regulates allergic responses, known as interleukin-4.** As a result of being able to bind to the IL-4 receptor, dupilumab can inhibit signalling along both the type 1 and type 2 receptors, thus resulting in a decrease in inflammation

• *"In a myriad of studies covering the efficacy of dupilumab, it has been extensively studied. Studies have shown its efficacy in treating eczema, as in one study on the effect of dupilumab on chronic hand eczema (CHE). Results showed that dupilumab was extremely effective in treating this particular eczema." – awkward, please tighten and rephrase*

We thank the reviewer for drawing our attention to this important issue and have therefore tightened and rephrased this sentencing in order to provide more clarity in the manuscript.

Dupilumab has been extensively researched, and studies have shown its efficacy in treating eczema, as in one study on the effect of dupilumab on chronic hand eczema (CHE), results showed that dupilumab was extremely effective in treating this particular eczema. According to the hand eczema severity index, patients had a significant decrease, and the dermatology life quality index (DLQI) increased overall. It showed an extremely high tolerance for patients and thus proved to be a very promising treatment for eczema, with high efficacy and a low rate of adverse side effects, making it relatively safe (Asamoah et al., 2025). Another study showed that 80.3% of patients in a clinical trial evaluating the effects of dupilumab on CHE achieved partial or complete resolution of their eczema, demonstrating both its potency and efficacy in treating chronic hand eczema (Riva et al., 2024). Its chemical structure is a monoclonal antibody of a subclass of immunoglobulin G4 that binds to the IL4 receptor. As a result of being able to bind to the IL-4 receptor, dupilumab can inhibit signalling along both the type 1 and type 2 receptors, thus resulting in a decrease in inflammation (*Dupilumab*, n.d.).

• *What is the citation (release, n.d.)? This likely needs to be reformatted*

We thank the reviewer for this helpful comment and have reformatted the citation.

For lebrikizumab, there have been fewer studies due to its recent approval by the FDA for clinical trials; therefore, it has not been as thoroughly studied as lebrikizumab and has only recently become quite well known as a biologic. Studies, however, have also demonstrated its effectiveness in treating eczema. In a study that studied the long-term effects of lebrikizumab on patients with moderate to severe eczema, the results showed that a significant majority of patients experienced a substantial improvement in skin quality, having an investigator's global assessment (IGA) of 0 or 1, and there was no requirement to further take topical corticosteroids or other treatments to maintain these effects **(E_MCR-EADV-2024.Pdf, n.d.)**. Additionally, a significant majority of patients had an extremely low EASI score, demonstrating lebrikizumab's potent effects on eczema. Its chemical structure is also that of an immunoglobulin G4 monoclonal antibody. It binds IL-13 with high affinity, thereby inhibiting its inflammatory effects.

E_MCR-EADV-2024.Pdf.
https://conferences.medicom-publishers.com/wp-content/uploads/2024/11/E_MCR-EADV-2024.pdf (accessed 2026-07-14).

• *Figure 5 – this figure is taken directly from https://onlinelibrary.wiley.com/doi/10.1111/ddg.15796. This is not acceptable and needs to be cited.*

We are grateful to the reviewer for highlighting this point, however This citation was already present prior to the peer review in (Fig. 5) (Rajput Khokhar et al., 2025), which can be found in the manuscript in the paragraph prior to the diagram

• *Table 1 should be modified so that it fits on one page, as opposed to straddling two Pages*

We appreciate this insightful comment from the reviewer and have therefore shifted the table to fit on one page

Convergence
A Journal for Young Researchers

385 386 **Table 1.** Summary of primary, secondary and alternative eczema therapies: a comparison of treatment types, their delivery methods, efficacy, evidence level, main advantages and clinical limitations.

Entry	Type	Target	Delivery	Evidence	Advantages	Limitations
1	Emolients	Skin	Topical	High	OTC, cheap, hydro-retentive	Low potency, frequent application, potential pore clogging
2	Corticosteroids	Skin	Topical	High	OTC, safe, versatile potency, affordable	Potential adverse side effects, variable pricing
3	Biologics	Thigh or abdomen	Injection	Medium	High potencies and efficacy	Need for injection, costly, potential adverse side effects
4	JAK inhibitors	Skin and immune system	Oral or topical	High	High efficacy, easy to administer	Lack of specificity, high frequency of side effects, and costly
5	Alternative meds	Skin	Various	Low	Unproven	Adverse side effects, costly, unsafe, lack of thorough and evaluative trials

I believe these revisions resolve the core issues you raised and make the paper much stronger and more suitable for peer review.

Thank you again for your insightful critique, as it has been invaluable. We would be happy to make further adjustments if needed or provide additional clarifications.

Sincerely,

Nathan Shiu

Dear Reviewer,

Thank you for your thorough and constructive feedback on the manuscript, "Eczema treatments: A review of their effectiveness, limitations and future directions". We greatly appreciate the time you took to identify both the core conceptual issues and the more minor points, as your comments have helped to significantly improve the clarity, accuracy, and scientific rigour of the paper.

We have carefully addressed each of your concerns in the revised version. Below, we outline the specific changes made in response to your points:

Reviewer comment 1: Originality and Significance

•Overall, the paper's unique contribution is not clear. Although the rightly states that it differs by incorporating alternative treatments alongside more established therapies, there are existing studies that provide overviews of conventional topical therapies, alternative therapies, and newer systemic biologics and JAK inhibitors. The student's paper is therefore not strongly differentiated from the existing literature. Relatedly, emollients and topical corticosteroids are well understood and thoroughly researched for mild-to-moderate eczema. Consequently, focussing on these established therapies for large parts of the paper makes it challenging to strengthen the paper's originality or significance (i.e., finding a research gap). Ultimately, to strengthen originality and significance, the paper may consider focussing on patients with more severe eczema where newer therapeutics are present and more research is required. I highly encourage the student to prioritise originality and significance over breadth, as, covering all eczema treatments limits exploration of deeper questions.

We appreciate this insightful comment from the reviewer; however, we would like to respectfully disagree with this statement. This is due to the requirement of changing the premise of the paper, as the decision to cover a broad spectrum of eczema treatments was deliberate and therefore, by changing its approach, its impact would be reduced significantly.

Reviewer comment 2: Mechanism Clarity

Original: "Janus Kinase Inhibitors target the kinase domain of Janus Kinase proteins (JAK proteins). This prevents their activation, thus preventing JAK phosphorylation activity and, as a result, reducing the expression of inflammatory genes and the number of inflammatory and immune signalling pathways, thus significantly reducing inflammation and tissue damage. This is done as many of the signalling pathways are inhibited, such as IL-13 or IL-4, which are meant to produce an inflammatory response.

Modification: "Janus kinase (JAK) inhibitors reduce eczema severity by blocking intracellular signalling triggered by pro-inflammatory cytokines such as IL-4 and IL-13, thereby reducing immune-mediated inflammation." This revision makes the explanation concise, linking the JAK inhibitors mechanisms to its ability to reduce eczema severity. Maintaining conciseness ensures the paper stays focussed on treatment efficacy, avoiding too much detail in mechanistic descriptions. I suggest similar modifications are implemented for such sections.

We thank the reviewer for this perspective, which helped strengthen our discussion, and have accordingly revised the paragraph to reflect the modification the reviewer suggested, maintaining conciseness.

Janus kinase (JAK) inhibitors reduce eczema severity by blocking intracellular signalling triggered by pro-inflammatory cytokines such as IL-4 and IL-13, thereby reducing immune-mediated inflammation.

Reviewer comment 3: Acronym Clarity

As a further minor comment, to improve clarity further, I encourage the student to ensure greater consistency in defining abbreviations at first use. For example, "JAK inhibitors" should be introduced as "Janus kinase (JAK) inhibitors," and "OTC" should be defined earlier as "over-the-counter."

We thank the reviewer for drawing our attention to this important issue and have proceeded with the clarification of numerous acronyms to maintain clarity.

Key treatments currently used most commonly include emollients, general improvements to hygiene and sanitary standards, topical corticosteroids, and some modern innovations, such as **Janus Kinase (JAK)** inhibitors and biologics (Santer et al., 2024).

However, the key weaknesses are cost and necessity for injection, as many patients will not be able to afford such a costly treatment on average, compared to the much cheaper alternative of an **over-the-counter (OTC)** medication for eczema treatment, whereas biologics cost a lot, leading to many patients having to pay out of their pockets for it.

Reviewer comment 4: Structure

I suggest structuring the review according to disease severity, which accurately reflects how treatments are selected in clinical practice. For example, emollients and topical corticosteroids are the mainstay of treatment for mild-to-moderate eczema, whereas biologics and oral JAK inhibitors are reserved for patients with moderate- to-severe disease whose eczema is inadequately controlled with topical therapies.

We appreciate this insightful comment from the reviewer and have proceeded with structuring the review based on eczema severity.

(1) Mild-to-moderate eczema

• Emollients

• Topical corticosteroids

(2) Moderate-to-severe eczema

• Biologics

• JAK inhibitors

(3) Alternative therapies

• Manuka honey

• Acupuncture

Reviewer comment 5: Search Strategy

the search strategy specified. For example, it is noted that terms such as "Biologics" and "Emollient efficacy" were used, but it is unclear whether additional relevant terms were included (e.g., JAK inhibitors or specific drug names such as upadacitinib). Specifying the date range of the literature search (or confirming if no restrictions were applied) would improve reproducibility.

We thank the reviewer for this helpful comment, and additional relevant terms were used during the evaluation of different treatments, including: Abrocitinib, Ruxolitinib, Upadacitinib, Dupilumab, Lebikizumab, Hydrocortisone and Betamethasone Valerate. Additionally, the date range of the literature search had no restrictions applied.

Reviewer comment 6: Quality assessment of included studies

The current description ("MeSH filtering and/or evidence-based analysis for clinical trials") does not clearly explain how bias was assessed or reduced.

We thank the reviewer for this perspective, which helped strengthen our discussion and have decided to establish that included studies were not formally appraised for risk of bias and may therefore be subject to bias.

Reviewer comment 7: Data extraction

It would also strengthen the methodology section to briefly specify what outcomes were extracted from the included studies. For instance, common eczema severity measures such as EASI, IGA, or other relevant clinical endpoints appear throughout the paper,and explicitly stating that these were systematically extracted would improve clarity and structure.

The reviewer's comment is well taken, and we appreciate the opportunity to clarify this point and are therefore explicitly stating that EASI, IGA and other clinical endpoints were systematically extracted

Reviewer comment 8: Literature Engagement

Given the review's breadth, the paper is largely descriptive, with less scope for critical engagement. Specifically, the paper tends to summarise what is known about each therapy in isolation. As previously suggested, an opportunity for strengthening the paper would be to focus on the moderate-to-severe eczema treatment space. For example, the sections on biologics and JAK inhibitors both describe high efficacy in terms of outcomes such as EASI and IGA improvement, but there is little interpretation of how these drugs compare in terms of efficacy and safety. A more critical approach would attempt to contrast biologics (e.g., dupilumab vs lebrikizumab) and JAK inhibitors (e.g.,upadacitinib vs abrocitinib) or evaluating how oral JAK inhibitors compare against biologics. This could then be followed by clearer

interpretations and justified conclusions on whether certain therapies may be preferred in moderate-to-severe eczema. Overall, incorporating this evaluative layer would move the review from a descriptive review towards a more critically engaging paper.

We politely disagree with this comment, as the paper is described as "*largely descriptive*", though having a section for thorough evaluation (section "**Evaluation of each treatment**") and a table for summary and comparison (Table 1), as well as comparisons between treatments in each subsection of treatment. However, we will add a caveat to conclude the evaluation section and to further improve clarity.

Reviewer comment 9: Grammar and Language

Title terminology: The title "Eczema treatments: A review of their effectiveness, limitations and future directions" is likely more suitable if "effectiveness" is replaced with "efficacy". In clinical research, efficacy refers to outcomes under controlled trial conditions (e.g., clinical trials), whereas effectiveness refers to performance in real-world practice. As the review predominantly draws on clinical trial data, "efficacy" is likely more appropriate.

We are grateful to the reviewer for highlighting this point and therefore have decided to change the title to: "Eczema treatments: A review of their efficacy, limitations and future directions."

Reviewer comment 10: Emotive language

At times, emotive or intensifying language is used, particularly terms such as "extremely". For example, "Results showed that dupilumab was extremely effective in treating this particular eczema." Such phrasing should be avoided in scientific writing. It is preferable to report outcomes directly and allow the quantitative results to demonstrate efficacy.

The reviewer's comment is well taken, and we appreciate the opportunity to clarify this point; we have therefore removed all instances of "extremely" throughout the manuscript.

I believe these revisions resolve the core issues you raised and make the paper much stronger and more suitable for peer review.

Thank you again for your insightful critique, as it has been invaluable. We would be happy to make further adjustments if needed or provide additional clarifications.

Sincerely,

Nathan Shiu

Dear Reviewer,

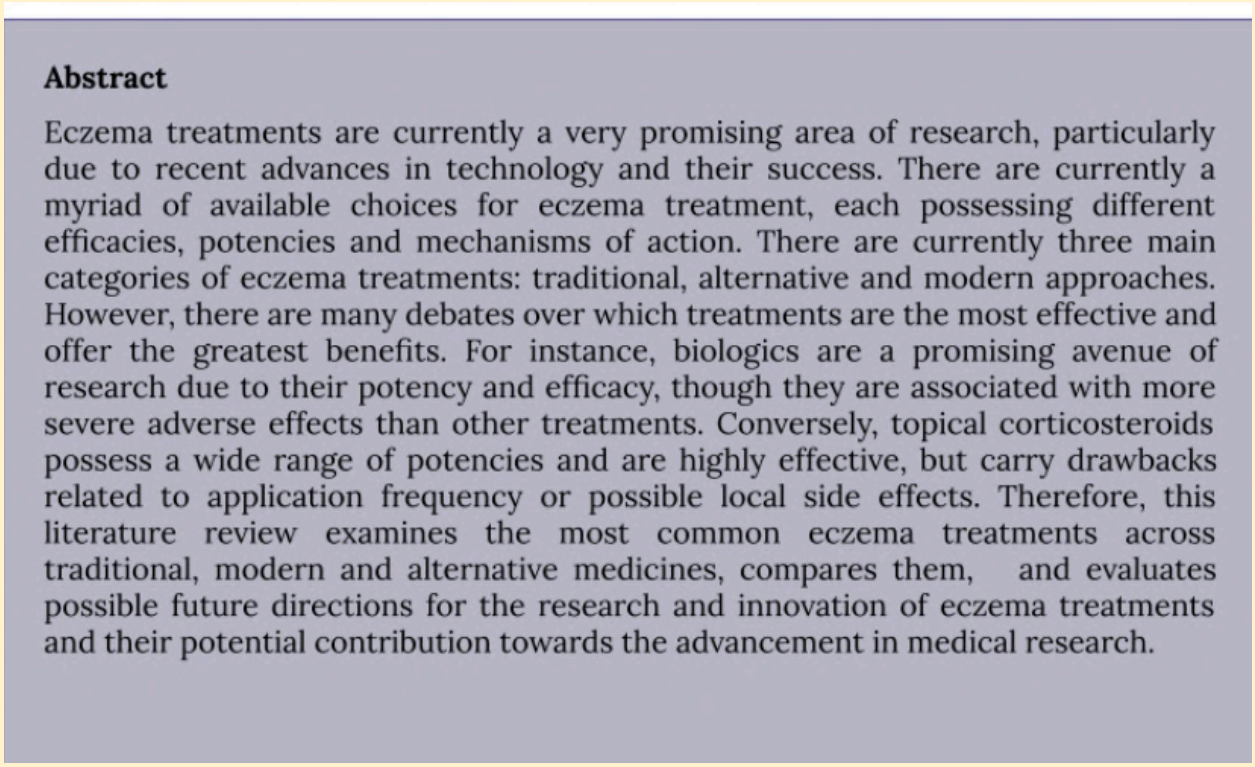
Thank you for your thorough and constructive feedback on the manuscript, "Eczema treatments: A review of their effectiveness, limitations and future directions". We greatly appreciate the time you took to identify both the core conceptual issues and the more minor points, as your comments have helped to significantly improve the clarity, accuracy, and scientific rigour of the paper.

We have carefully addressed each of your concerns in the revised version. Below, we outline the specific changes made in response to your points:

Reviewer comment 1: Abstract

• *The manuscript has no abstract, only keywords, and a review of this scope really needs one to orient the reader.*

We thank the reviewer for this helpful comment; however, an abstract is present on the finished Google document



Abstract

Eczema treatments are currently a very promising area of research, particularly due to recent advances in technology and their success. There are currently a myriad of available choices for eczema treatment, each possessing different efficacies, potencies and mechanisms of action. There are currently three main categories of eczema treatments: traditional, alternative and modern approaches. However, there are many debates over which treatments are the most effective and offer the greatest benefits. For instance, biologics are a promising avenue of research due to their potency and efficacy, though they are associated with more severe adverse effects than other treatments. Conversely, topical corticosteroids possess a wide range of potencies and are highly effective, but carry drawbacks related to application frequency or possible local side effects. Therefore, this literature review examines the most common eczema treatments across traditional, modern and alternative medicines, compares them, and evaluates possible future directions for the research and innovation of eczema treatments and their potential contribution towards the advancement in medical research.

Reviewer comment 2: Biologics section error

• *In the biologics section, the text says lebrikizumab "has not been as thoroughly studied as lebrikizumab," which should read dupilumab.*

We appreciate this insightful comment from the reviewer and have therefore changed Lebrikizumab into Dupilumab.

For lebrikizumab, there have been fewer studies due to its recent FDA approval for clinical trials; therefore, it has not been as thoroughly studied as **Dupilumab** and has only recently become widely known as a biologic.

Reviewer comment 3: Section Header conciseness

The section headings repeat the same "structure, functions, and limitations"

We thank the reviewer for this constructive suggestion, which has helped clarify the manuscript and we have decided to alter the section headers to make them less repetitive and improve conciseness and clarity, as recommended by one of the other reviewers, which is the way in which we envisioned the manuscript to be corrected

New Section headers:

Mild-to-moderate eczema
• Emollients
• Topical corticosteroids

Moderate-to-severe eczema
• Biologics
• JAK inhibitors

Alternative therapies
• Manuka honey
• Acupuncture

Reviewer comment 4: Figure choice

Figure 7 for acupuncture is sourced from a stroke rehabilitation trial, which is an odd citation to lean on for a point about skin.

We appreciate this insightful comment from the reviewer and would like to respectfully explain its reasoning.

The figure has been taken from a stroke-rehabilitation trial to use the diagram from this source to display the acupuncture areas, as though the citation pertains to a stroke rehabilitation trial, the method in which they present the acupuncture areas that I have made note of in the manuscript provides a useful, high quality optimal representation of those areas.

Reviewer comment 4: Citation Reliability

My main concern is the mix of source quality. A number of clinical claims lean on lay or secondary sources such as WebMD, HealthCentral, EverydayHealth, and a consumer blog, and for a research review those should be replaced with the primary literature or with formal guidelines like NICE or the American Academy of Dermatology.

We thank the reviewer for drawing our attention to this important issue and have therefore decided to change all the lay or secondary sources into primary sources, as shown here with the references in green being the new primary sources.

WebMD

Key, A. P. (n.d.). JAK Inhibitors for Atopic Dermatitis. WebMD. Retrieved November 23, 2025, from https://www.webmd.com/skin-problems-and-treatments/eczema/jak-inhibitors-atopic-dermatitis

Chovatiya, R., & Paller, A. S. (2021). JAK Inhibitors in the Treatment of Atopic Dermatitis. *The Journal of Allergy and Clinical Immunology*, *148*(4), 927–940. https://doi.org/10.1016/j.jaci.2021.08.009

Sreenivas, S. (n.d.). Acupuncture and Acupressure for Atopic Dermatitis. WebMD. Retrieved November 22, 2025, from https://www.webmd.com/skin-problems-and-treatments/eczema/acupuncture-acupressure-for-atopic-dermatitis

Xu, S., Wang, L., Cooper, E., Zhang, M., Manheimer, E., Berman, B., Shen, X., & Lao, L. (2013). Adverse Events of Acupuncture: A Systematic Review of Case Reports. *Evidence-Based Complementary and Alternative Medicine : eCAM*, *2013*, 581203. https://doi.org/10.1155/2013/581203

Health Central

Is Honey Good for Eczema? Benefits, Research, and How to Use It Safely. (2025a, January 28). HealthCentral. https://www.healthcentral.com/condition/eczema/honey-for-eczema

Is Honey Good for Eczema? Benefits, Research, and How to Use It Safely. (2025b, January 28). HealthCentral. https://www.healthcentral.com/condition/eczema/honey-for-eczema

Johnston, M., McBride, M., Dahiya, D., Owusu-Apenten, R., & Nigam, P. S. (2018). Antibacterial activity of Manuka honey and its components: An overview. *AIMS Microbiology*, *4*(4), 655–664. https://doi.org/10.3934/microbiol.2018.4.655

Everyday health

Honey and Eczema: Benefits, Types, Risks. (n.d.). EverydayHealth.Com. Retrieved November 21, 2025, from https://www.everydayhealth.com/eczema/honey-secret-clear-skin-you-have-eczema/

Alhabsi, A. N., Al Lawati, A., Al Hashmi, L., Al-Isaii, F., Alghammari, A., Das, S., & Al Hashmi, S. (2026). Clinical and Postoperative Applications of Manuka Honey in Wound Healing: An Evidence-Based Review. *International Wound Journal*, *23*, e70939. https://doi.org/10.1111/iwj.70939

Medicalnews today

Honey for eczema: Potential benefits and how to use it. (2022, August 31). https://www.medicalnewstoday.com/articles/honey-eczema

Mandal, M. D., & Mandal, S. (2011). Honey: Its medicinal property and antibacterial activity. *Asian Pacific Journal of Tropical Biomedicine*, *1*(2), 154–160. https://doi.org/10.1016/S2221-1691(11)60016-6

Business wire

release, 25 9 2024 12:45:00 CEST | Business Wire | Press. (n.d.). New Data Show Almirall´s EBGLYSS® (Lebrikizumab) Provided Sustained Disease Control for up to Three Years in More Than 80% of Adults and Adolescents With Moderate-to-severe Atopic Dermatitis | Business Wire. Retrieved November 23, 2025, from

Stein-Gold, L., DeBruin-Weller, M., Thaci, D., Kircik, L., Yang, C., Rueda, M. J., Gallo, G., & Paller, A. (2026). Lebrikizumab ADvocate1 and 2 Monotherapy and ADjoin (Long-Term) Trials: Use of Topicals Therapies. Dermatology and Therapy, 16(6), 2757–2772. https://doi.org/10.1007/s13555-026-01771-5

Scratchsleeves

Is Manuka honey good for eczema? Alternative remedies #3. (n.d.). *ScratchSleeves*. Retrieved November 21, 2025, from https://scratchsleeves.co.uk/scratchsleeves-blog/alternative-remedies-3-is-manuka-honey-good-for-eczema/

Patel, S., & Cichello, S. (2013). Manuka honey: An emerging natural food with medicinal use. *Natural Products and Bioprospecting*, *3*(4), 121–128. https://doi.org/10.1007/s13659-013-0018-7

Reviewer comment 5: Comparison reliability

The paper repeatedly ranks treatments against one another ("higher efficacy," "more favourable"), but the numbers are drawn from different trials with different populations and endpoints, so those cross-trial comparisons need a caveat at minimum. The stronger move is to cite head-to-head data directly — for instance, the abrocitinib-versus-dupilumab trial the student already references (NCT04345367) is exactly the kind of comparison that would let them make these claims on solid ground.

We thank the reviewer for this helpful comment and have added caveats when discussing the key advantages of manuka honey and the evaluation of acupuncture as an option for treatment in order to explain the reason why some cross-trial comparisons were used in the manuscript.

However, it is important to note that, compared with the other treatments discussed in the traditional and modern approaches, the figures for Manuka Honey are drawn from different trials with different patient populations, disease severity, and primary endpoints. As a result, it is vital to note that the interpretations of these trials may not be as strong, due to the lack of direct head-to-head clinical data to mitigate bias accordingly.

Therefore, though through these findings the data does show the implication that overall acupuncture may not be a preferred option of treatment, it is still important to note that these interpretations should be approached with caution, being primarily preliminary insights.

Reviewer comment 6: Internal contradictions

The Manuka honey section calls it "significantly cheaper" than OTC options in one place and lists cost as a disadvantage in another, and Table 1 similarly hedges. Finally, the acupuncture conclusion states that the severe side effects "outweigh" the benefits, which is a strong claim that the student's own cited evidence (described as mixed and low-quality) does not really support; I would soften it to match the evidence.

We thank the reviewer for this perspective, which helped strengthen our discussion and we have corrected these accordingly by softening statements to match the evidence.

Regarding its cost, relative to other commercial products for treatment, the same potency of treatment is offered at a comparable efficacy, **whilst being more costly** compared to over-the-counter (OTC) emollients or topical corticosteroids.

For acupuncture overall, the drawbacks outweigh the advantages due to the **multiple** side effects, which may be presented if in the care of an inexperienced medical professional, who may not be effective and accurate at inserting the needles into the patient, leading to multiple side effects occurring. Though it does have a few advantages, much research has been invested in the safety and efficacy of treating eczema with acupuncture, and studies have shown that when an experienced practitioner performs the treatment, eczema symptoms can be substantially reduced, and it is relatively safe. However, again, it still comes with **some** side effects.

Reviewer comment 7: Grammar rectification

Tightening the run-on sentences and the recurring "a myriad of" would help.

We appreciate this insightful comment from the reviewer and have tightened the run on sentences and changed some of the vocabulary with some of the "a myriad of" being changed to synonyms or removed.

I believe these revisions resolve the core issues you raised and make the paper much stronger and more suitable for peer review.

Thank you again for your insightful critique, as it has been invaluable. We would be happy to make further adjustments if needed or provide additional clarifications.

Sincerely,

Nathan Shiu

Eczema treatments: A review of their effectiveness, limitations and future directions

Reviewer 1

I have read through the student's responses to my comments as well as their responses to the insightful and constructive comments made by my fellow reviewers. The introduction reads much better now in my opinion, and does a better job of orienting the reader to the issue by going into more detail about existing treatments and the nature of the condition. The search criteria in the methodology is more detailed. A few minor points - is it possible to have a better diagram of octodecane as Convergence is an interdisciplinary journal, the chemical structure presented uses organic chemistry conventions which might not be immediately accessible to the reader? Otherwise, I think the scope and depth is good for a high-school student level and shows a high level of scientific understanding, furthermore the article is a useful overview of eczema treatments and therefore makes a valid contribution to the literature.

My opinion is to accept with minor revisions.

Post-review critical: Eczema treatments: A review of their effectiveness, limitations and future directions

The paper's coherence has improved by splitting sections into mild-to-moderate eczema, moderate-to-severe eczema and alternative therapies. This structure is logical as eczema treatments are indicated by the severity of disease and helps guide the review. Furthermore, additional details were provided in the search strategy and a date range which supports reproducibility and rigor. Overall, the paper has been improved, and the changes are welcoming!

Minor correction: The student did well to correct the methodology section by noting that studies were not formally appraised for risk of bias. However, the original text was not removed and still states that bias mitigation was achieved. Please remove: "*...which allowed me to achieve methodological rigour in mitigating bias, ensuring clinical relevance and statistical validity.*"

Response: originality (no revisions are required)

Thank you to the student's response, which notes that the paper's broad scope was a deliberate choice to avoid reducing impact. No revisions are required for addressing my previous comment on originality. I am happy with the paper's premise as is, **provided the literature engagement feedback below is addressed.** However, to highlight, originality is not about scope (i.e., number of treatments reviewed) but providing well-thought new perspectives or ideas, which aim to contribute to a knowledge gap. It is not expected for a student paper to be materially impactful, but new well-argued ideas or perspectives are. Referring to my original comments, the paper's premise of covering a broad spectrum of treatments likely guided the review to a largely descriptive synthesis of existing findings (too much scope makes it hard to apply evaluation throughout). As previously stated, I highly encourage originality over breadth as a recommendation for the student moving forward.

Response: Literature review engagement (actionable revisions required)

Thank you to the student's response, which highlights the "evaluation of each treatment" section and that treatments are compared in each subsection. A point was also added on healthcare providers requiring to assess risk-benefit profiles. However, my overall comment is not addressed, which is that paper needs more evaluation and critical engagement. Initially, I provided one example where the paper could introduce evaluation (e.g., one potential way is providing interpretations in terms of comparative drug efficacy & safety). Given that this was not actioned, I explicitly outline possible critical engagement for the paper to reach publication level. I have provided examples how critical engagement could strengthen the paper's sections on JAK's efficacy and biologic safety, shifting the papers descriptive synthesis to include critical engagement with the literature. These examples illustrate evaluative avenues to consider. Note, critical engagement does not necessarily need to be drug-to-drug comparisons to address my point that the paper is largely descriptive but is one example.

Page 8 on JAK inhibitors efficacy:

Statement on efficacy for abrocitinib: "For abrocitinib, results from the trial showed a significant reduction in pruritus for many patients, and 48.3% of patients demonstrated investigator's global assessment (IGA) scores of 0 or 1. Moreover, in week 1, there were also very substantial improvements in the eczema area severity index (EASI). This shows that abrocitinib has a high efficacy and can lead to skin clearance and relief....

Statement on efficacy for Upadacitinib: For upadacitinib, 50% of patients demonstrated an IGA score of 0 or 1 at 16 weeks, and there was a 90% improvement in EASI score as well at 16 weeks. There was also a general improvement in eczema symptoms, indicating relatively high efficacy, comparable to that of abrocitinib (Nezamololama et al., 2020)...

Statement on efficacy for ruxolitinib: In another study, which evaluated the effects of ruxolitinib on eczema, it was found that there was a 51.6% decrease in EASI overall after 4 weeks, and there was a large percentage of patients who were able to achieve IGA scores of 0 or 1; therefore, the results also demonstrated ruxolitinib's efficacy (Mohney et al., 2023).

Page 13 under "evaluation of each treatment" for JAK inhibitors efficacy:

Section on efficacy for JAK inhibitors: The key strength of JAK inhibitors is their efficacy, which is evident in numerous clinical trials mentioned previously, where, using a variety of scales, such as EASI, IGA or DLQI, there have been significant improvements in all three scales using all three common JAK inhibitors in Abrocitinib, Ruxolitinib and Upadacitinib. Moreover, relative to other common treatments, JAK inhibitors have much higher efficacy in skin clearance as well.

Examples of critical engagement to improve study

Currently, the JAK inhibitors efficacy is described in isolation of each other and not evaluated further in the paper. The evaluation of each treatment section repeats what had been stated, without expanding further. The sections on JAK inhibitor efficacy could be strengthened by critically considering the findings across the different inhibitors and whether the available evidence suggests that any particular inhibitor may have greater efficacy. For example, this could involve evaluating whether any inhibitor may appear most efficacious based on the trial findings (and/or other available evidence), while simultaneously considering whether it is appropriate to draw comparative efficacy conclusions from comparisons across trials (and/or other evidence), and highlighting any issues that may affect such interpretations. The discussion could then highlight any uncertainties regarding the comparative efficacy of these treatments and consider how these could inform recommendations for future research. This would add a very strong evaluative element.

Page 7 for adverse side effects for dupilumab and lebrikizumab:

Statement on safety for dupilumab: "The key potential adverse side effects that come about through the use of dupilumab for the treatment of eczema were head and neck eczema, conjunctivitis, eczema, peeling of skin and dryness in eyes, however overall dupilumab did show to have a high

tolerance, as these adverse side effects only presented in less than 20% of patients, and are relatively minor and not severe or life threatening (Parmar et al., 2022). In another study, it was said that a small minority of patients had mild conjunctivitis, and a few patients had severe conjunctivitis, which may remain an issue; therefore, dupilumab must be researched slightly more to ensure the safety of patients who may decide to utilise it as a treatment for moderate to severe eczema

…

Statement on safety for lebrikizumab: The key side effects of lebrikizumab are injection site reactions and conjunctivitis, and therefore it has similar side effects to dupilumab (Lin et al., 2024). However, studies show that relative to dupilumab, it seems that lebrikizumab seems to be more favourable due to its side effect profile and high tolerance. Moreover, it should be noted that dupilumab has a greater number of ocular effects (Loh et al., 2020)."

Examples of critical engagement to improve study

This is a good starting point describing some of the adverse effects of the biologics, but no evaluation expands on these further, leaving interesting avenues to critically explore (note that these points may be applied across the other eczema treatments covered in the review):

- Which adverse effects were most common with dupilumab? It is stated that less than 20% of patients were affected. If 19% of patients had side effects, this is quite a large proportion of patients having adverse effects. Related, do the adverse effects potentially affect the efficacy of the drug if patients must discontinue or adherence to dupilumab is negatively impacted? **This helps evaluate how safety could also impact efficacy.**

- Are there potential patient risk factors for an increased risk of side effects or does each patient generally have similar chance of adverse effects? Could the safety profile of dupilumab vary across different types of patients? Could this change potential recommendations on biologic preferences? **This critical engagement explores whether the safety profile of drugs may vary across patient characteristics.**

- It is stated that dupilumab must be researched more to ensure safety. However, it is not elaborated what exactly should be researched. Is more research needed on managing potential adverse events, or preventing them in the first place? Is research needed to identify patients who may have more severe side effects with dupilumab? **This critical engagement would link identified uncertainties in existing literature to well-argued and specific research recommendations.**

- It is a good that lebrikizumab is briefly compared to dupilumab, but this is not evaluated. What is the strength of evidence to suggest lebrikizumab has a more favourable safety profile? Are these

based on comparisons across trials? **The quality of evidence behind this favourable safety claim needs critical assessment to fully elucidate whether this is substantive.**

Page 12 under "evaluation of each treatment" for dupilumab and lebrikizumab:
"The key strengths of the use of dupilumab and lebrikizumab are that, overall, they help substantially reduce inflammation and pruritus, thus significantly improving skin health, holding this over many other traditional treatments for eczema due to being able to treat the underlying reasons for inflammation. They also reduce the number of systemic side effects because they are able to treat the underlying reasons for inflammation; moreover, they have been thoroughly researched, and as a result, there are minimal side effects, and they are relatively safe (Kumar et al., 2025)."

Example of critical engagement to improve study
The "evaluation of each treatment" section does not expand what had already been stated on biologic safety. It also appears contradictory, stating that dupilumab is thoroughly researched with minimal side effects, having previously noted that more research is required into dupilumab's safety profile. Deeper critical engagement would help bring these points together into a single, coherent argument, rather than allowing earlier statements to be dropped in a way that leads to inconsistences. As commented above, evaluating the literature would help identify well-argued recommendations for future research, avoiding potential inconsistencies through the paper.

Recommendation: Revise and Resubmit (major revisions needed, acceptance not guaranteed)

The paper is a good broad overview of eczema treatments, and has been improved following revision, including a clearer structure and clarification of the methodology. However, the paper's main area for improvement is its engagement with the literature, as the current content is largely a descriptive synthesis of the eczema drugs. The paper's critical engagement needs further strengthening to reach publication level. This area for improvement was highlighted in my first review, where I suggested incorporating an evaluative layer to, for example, compare individual drugs. The student's response acknowledged this by pointing me to the evaluation of each treatment section, and the treatment subsections. In response, I have provided examples of where critical engagement may be incorporated within the existing content. This clarifies what level of critical engagement would shift the paper from descriptive synthesis to one which also provides evaluative well-argued new ideas and perspectives. **It is not required for each evaluative avenue to be addressed above but are provided to prompt critical engagement. It would suffice to present a few well-argued evaluative contributions throughout the current review (not necessarily limited to JAK efficacy and biologic safety).** I

hope these comments are taken in the spirit they're intended to help and encourage the student to become a stronger researcher, and to improve the paper to the next level.

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REVIEW ARTICLE

Eczema treatments: A review of their effectiveness, limitations and future directions

Abstract

There are currently a myriad of available choices for eczema treatment, each possessing different efficacies, potencies and mechanisms of action. There are currently three main categories of eczema treatments: traditional, alternative and modern approaches. However, there are many debates over which treatments are the most effective and offer the greatest benefits. For instance, biologics are a promising avenue of research due to their potency and efficacy, though they are associated with more severe adverse effects than other treatments. Conversely, topical corticosteroids possess a wide range of potencies and are highly effective, but carry drawbacks related to application frequency or possible local side effects. Therefore, this literature review examines the most common eczema treatments across traditional, modern and alternative medicines, compares them, and evaluates possible future directions for the research and innovation of eczema treatments and their potential contribution towards the advancement in medical research. Overall findings dictate that modern and traditional eczema treatments remain the forefront for general usage due to reliability, accessibility and safety.

Keywords: Translational Medical Sciences, Disease Treatments and Therapies, Dermatology, Eczema.

1. Introduction

Since around 400 BC, when eczema was first described and labelled, it has persisted as a significant irritant and major health issue worldwide. During this time period, Hippocrates became the first to describe the condition now known as eczema, having described a patient with dry and scaly skin, as well as a chronic itch throughout the patient's body. Although considerable research and investment have been made to investigate treatments, the issue remains an unrelenting problem affecting approximately 1.5 million adults in the UK (*Change AD UK*), underscoring its widespread impact throughout the country. Key treatments currently used most commonly include emollients, general improvements to hygiene and sanitary standards, topical corticosteroids, and some modern innovations, such as Janus Kinase (JAK) inhibitors and biologics (Santer et al., 2024). Emollients are compounds which form a film on the outer surface of the skin, which aids in soothing irritation and hydrating the skin. JAK Inhibitors are a classification of medical compounds which reduce the transduction of cytokine signalling through the JAK-STAT

pathway and as a result reduce the transcription of genes related to the causation of inflammation and swelling. Biologics function as compounds which are composed of biological material, are grown in living cell structures, and are known for their potent efficacy in treating diseases. Though the common treatments are effective on a wide scale, being more cost-effective and easily accessible, they do have some disadvantages, such as side effects like lichenification (thickening of skin with leathery texture arising) or erythema (redness of skin due to increased blood flow to blood vessels near surface of skin) (Bhanot et al., 2019) with prolonged use of certain emollients and also skin thinning and stretching as side effects for topical corticosteroids. The newer innovations seem more promising, being long-lasting and highly effective at treating eczema, though a new issue arises: costs and malignancies (Mansilla-Polo & Morgado-Carrasco, 2024). This is especially prevalent in JAK inhibitors, due to the effectiveness of their immunosuppressive nature, resulting in the weakening of the immune system, leading to greater vulnerabilities in the body, which eventually culminates in a greater risk for cancer. This vulnerability causes infections to develop within the body, particularly in the respiratory and urinary tracts (Klein et al., 2022). Biologics also have a few adverse side effects, including but not limited to conjunctivitis (inflammation of the conjunctiva), injection site reactions and eosinophilia (*Long-Term Safety and Efficacy Study of Lebrikizumab (LY3650150) in Participants With Moderate-to-Severe Atopic Dermatitis (ADjoin)* (*ADjoin*), 2025). Therefore, while both traditional and newer innovations in eczema treatments have demonstrated various successes in terms of effectiveness in resolving eczema, they still have drawbacks in multiple ways, including side effects and costs. However, whilst these newer innovations do have drawbacks, further investment into them should be investigated to assess the assumptions that adverse side effects may be mitigated and eventually eliminated. This is evident in the possibility of investment into the mass production of biologics, slowly minimising costs and making them more affordable to the average person. This article ultimately aims to discuss various eczema treatments, some more well-known than others, evaluating their outlooks, various benefits and drawbacks. The key treatments discussed will include the most common traditional approaches and modern innovations, as well as some discussion on the prospect of alternative medicine. The key way in which this literature review differs from others is that it not only takes into account treatments which are very commercialised and recognised, but it also acknowledges the possibility of alternative medicine in its treatments and provides comprehensive comparisons to traditional and modern treatments for eczema.

2. Methodology

Search strategy

The primary strategy utilised for the identification of relevant literature reviews was through the thorough evaluation of key sources found on Google Scholar or ClinicalTrials.gov. The searching strategy was conducted using MeSH filtering and evidence-based analysis for clinical trials, which allowed me to achieve methodological rigour in mitigating bias, ensuring clinical relevance and statistical validity. It is important to note that included studies were not formally appraised for risk of bias and may therefore be subject to bias. Including terms such as “Biologics” and “Emollient efficacy” was vital in being able to filter relevant information when using keyword searching for Google Scholar. The reason for which a third database was not used during the research into the manuscript was because Google scholar already yields many of the journals which are indexed in PubMed, thus its usage as a third database would yield nearly completely similar results, as a result usage of PubMed was used slightly in the initial research phase, though nearly similar papers would also appear on google scholar, as a result citations were primarily present on google scholar.

Additional relevant terms were used during the evaluation of different treatments, including: Abrocitinib, Ruxolitinib, Upadacitinib, Dupilumab, Lebikizumab, Hydrocortisone and Betamethasone Valerate. Additionally, the date range of the literature search had no restrictions applied. EASI, IGA and other clinical endpoints were systematically extracted.

Inclusion and exclusion criteria

Key criteria that were required for the consideration to use the source included:

- Sufficient data for analysis for clinical trials
- Peer-reviewed academic journals in terms of literature review evaluation

Exclusion criteria:

- Lack of empirical data
- Published as an editorial commentary

Study selection and data extraction

Screening was performed throughout the writing of this literature review, and each citation was independently reviewed and assessed. Ultimately, through the process of writing, a large proportion of literature reviews and clinical trials met all inclusion criteria to be included in the literature review.

Data extraction was conducted through comprehensive organisation through Zotero software to record the author, year of publication and area of eczema research, helping categorise research effectively through keyword searching within the software.

3. Analysis

Mild-to-moderate eczema

The most common treatments prescribed are emollients. The main emollients prescribed by the NHS are creams and ointments, such as Aveeno creams and Cetraben cream. Aveeno creams and some Cetraben creams use colloidal oatmeal as a base, due to its natural healing acceleration benefits, which act as a barrier to retain moisture and gently cleanse the skin to optimise the reduction of eczema flaring and gradually help build up a natural barrier against eczema. The key chemical components contained within this colloidal oatmeal are known as avenanthramides, which contain anti-inflammatory and anti-itch properties (Fig. 1) (Sur et al., 2008). Moreover, it also reduces hypersensitivity and thus is a very strong combatant against irritants. Avenanthramides act via inhibition of NF-κB, responsible for governing immune response and inflammation (Yang et al., 2014).

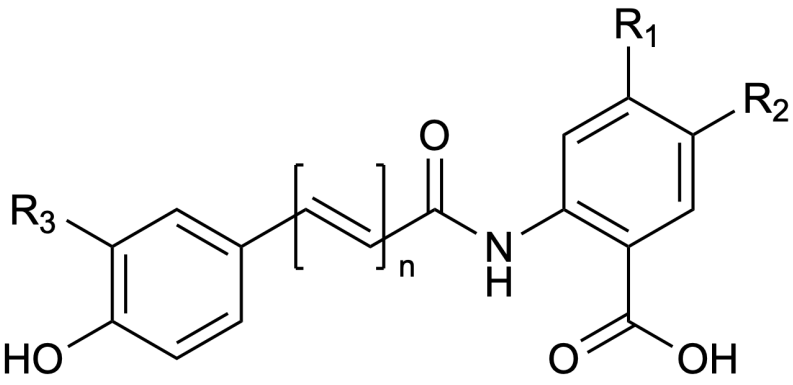


Figure 1. Chemical structure of avenanthramides (n = 1 or 2; R_1 = H, R_2 = OH, R_3 = H, OCH_3, or OH). Avenanthramides are formed by the N-acylation reaction between anthranilic acid (AA) and a phenylalkenoic acid (PA) to create an amide linkage.

Cetraben creams use soft paraffin and liquid paraffin as bases, which act as key chemical compounds for anti-inflammatory and anti-irritant properties. In a study, the SCORing Atopic Dermatitis index (SCORAD) score in patients using a paraffin-based cream was significantly lower than in those using a control cream, indicating a notable reduction in eczema severity. It indicated a 28.6% decrease compared to the original SCORAD score. Therefore, it was concluded that the paraffin-based creams and ointments were effective in reducing the severity of eczema symptoms (Waked & Ibrahim, 2020). The key chemical compounds used in the creams are petrolatum, which is a mix of hydrocarbons. Studies have shown that it helps regulate antimicrobials and maintain the skin's epidermal barrier to help the retention of moisture and prevent irritants from coming into contact with the skin, which demonstrates its effectiveness in combating eczema in patients. One of the key chemical compounds in petrolatum is alkanes such as octadecane (Rogers & Skanupong, 1974). Petrolatum acts by forming a protective barrier on the skin, helping retain moisture and smooth the skin, making it both a comfortable and effective emollient.

Emollients have shown promising results, as evidenced by numerous clinical trials testing the effectiveness of colloidal oatmeal creams (*Study Results | NCT02691507 | Trial to Determine the Therapeutic Benefit of an OTC Cream on Dry, Itchy Skin of Adults and Children With Eczema | ClinicalTrials.Gov*, 2017). Results indicated a significant increase in hydration and a substantial decrease in itchiness, with an average of 4.07 out of 10 on an arbitrary scale after application, demonstrating its short-term effectiveness. However, an issue arises after consolidating data for 7 days after cream application, with 4.22 out of 10. Though it has no significant impact on its overall success, it still shows diminished retention of its anti-itching properties compared to other commercial eczema treatments. Other studies also demonstrate this by recording hydration with a corneometer; the results showed that after 7 days, the unit of measure in arbitrary units was 208.52, compared to 14 days, when the unit of measure in arbitrary units was 158.65 (Johnson & Johnson; Johnson Consumer Inc., 2017). The greater the unit of measure in arbitrary units, the greater the hydration. This further emphasises the long-term decline in the effectiveness of emollients. Of course, it

is crucial to consider that systematic reviews confirm they reduce flares in the long term when used proactively with anti-inflammatories.

A majority of emollients are effective with minimal side effects, providing a reliable short-term solution for mild to moderate eczema. However, situations in which adverse side effects occur must also be taken into account. In a study that examined the effects of a wide range of emollients, including variations in type (cream or lotion) and ingredients (botanicals, ceramides, and other components). From this study, it was found that many patients experienced the following side effects: erythema, irritation, papule formation, and further spreading of eczema, as well as other prominent side effects also being present (Emmett et al., 2023). It has been shown that overall botanical emollients may display more side effects due to the possibilities of irritants present in the natural ingredients compared to ceramides, as allergies may also arise from the use of botanical emollients (Corazza et al., 2009), whilst ceramide-based emollients remain effective and safe (Draelos, 2008), due to the presence of ceramides in skin already.

Emollients sit in a completely different category of eczema care. Because they simply repair the physical skin barrier and do not target specific immune mechanisms, it does not make sense to test them head-to-head against systemic biologics. The more relevant research question is how daily, consistent moisturising can reduce the overall amount of steroid cream a patient needs over time.

Alongside emollients, topical corticosteroids remain a widely prescribed treatment worldwide. The key ways in which topical corticosteroids act are via binding to glucocorticoid receptors within the cytoplasm. This causes a conformational change in the receptor, causing the dissociation of chaperone proteins from the chaperone complex. This corticosteroid-receptor complex then travels through the nuclear pores and inside the nucleus; two of these corticosteroid receptors bind together via homodimerisation, and this dimer then binds with DNA at sites known as glucocorticoid response elements. This process triggers transactivation and, as a result, the increased transcription and translation of anti-inflammatory proteins like lipocortin (Mehta et al., 2016). As referenced previously, NF-κB, a protein complex that controls the body's inflammation. As a result, the body reduces the inflammatory response. Its fundamental chemical structure is often that of a steroid such as hydrocortisone (Fig. 2), which is $C_{21}H_{30}O_5$ (PubChem, 2020). It has a four-ring structure known as a steroid nucleus, similar to other steroids. Due to its specific chemical structure, it can bind to the glucocorticoid receptor. At high concentrations, glucocorticoid receptor dimerisation can activate transcription of anti-inflammatory genes (Barnes, 2006). However, it should be noted that low doses of corticosteroids are what cause the anti-inflammatory effect.

Additionally, other commonly used topical corticosteroids contain betamethasone valerate (Fig. 2) at different concentrations based on the severity of the eczema (Brazzini & Pimpinelli, 2002). Betamethasone valerate has displayed significant decreases in common inflammatory-causing cytokines. Being one of the more potent corticosteroids, it has been a common prescription for patients with moderate or severe eczema. Clinical studies have shown its efficacy in reducing eczema severity (Gether et al., 2025). Moreover, in another study, betamethasone valerate showed potent effects in reducing symptoms of eczema relative to other common treatments, such as 0.5% and 2.5% desoximethasone, showing how it compares well against other frequent prescriptions against eczema (Ashton et al., 1987). Its chemical structure is $C_{27}H_{37}FO_6$. It has a valerate ester, a hydroxyl group and a ketone group as well (*Betamethasone Valerate Cream USP*, 0.1%, 2010).

Evidently, Topical Corticosteroids have also shown significant success in reducing mild to moderate eczema. According to a study, transepidermal water loss was significantly lower when an irritant was applied to multiple patients than when the same irritant was applied to another patch of their skin, with a topical corticosteroid also applied. The study showed that significantly less erythema and lower values of the water loss were found, showing its potent effect on combating the inflammatory properties of eczema, as well as maintaining the water content of the skin (Ramsing & Agner, 1995). Another study also dictates its effectiveness relative to other alternatives of the treatment of eczema flare-ups, such as calcineurin inhibitors meant to suppress the inflammatory response of the immune system specifically. These studies show that the topical corticosteroids are more efficacious (Schmitt et al., 2011). Furthermore, potent corticosteroids can effectively eliminate potential bacteria, which could have helped amplify the effects of inflammation in eczema (Nilsson et al., 1992).

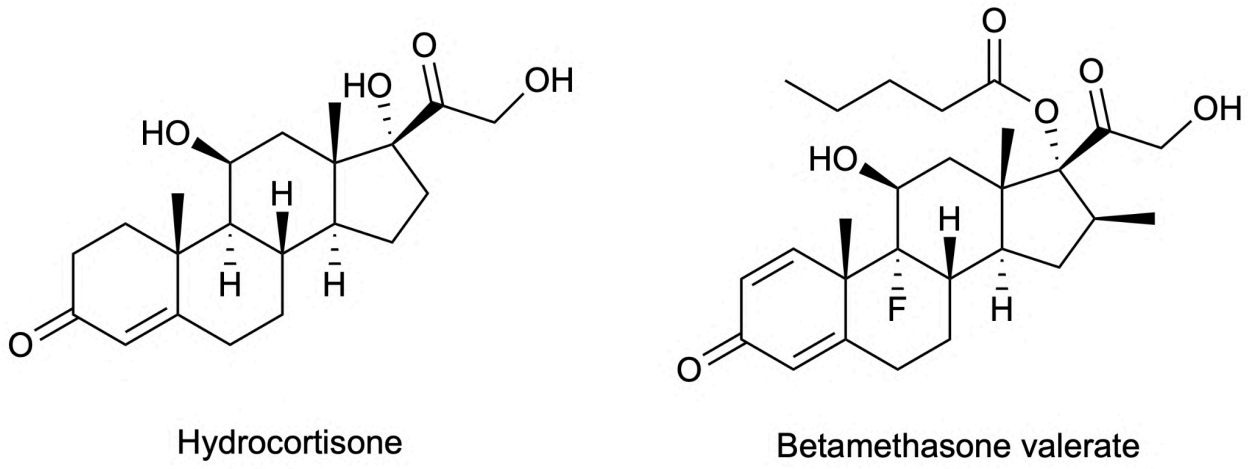


Figure 2. Chemical structures of hydrocortisone and betamethasone valerate. Both molecules are structurally similar and share a cyclopentanoperhydrophenanthrene steroid nucleus and multiple functional groups, including carbonyl and hydroxyl substituents.

Both hydrocortisone and betamethasone valerate have similar side effects, as they are topical corticosteroids in different forms. The most common side effects associated with the use of both medications are local side effects, such as skin atrophy, where the skin begins to thin, leading to easy bruising, and striae, which can result in stretch marks (Ference & Last, 2009). However, there are other side effects which, though rare, can occur, such as systemic side effects of Cushing's syndrome, where an increase in blood pressure and weight gain occurs or a decrease in the growth rate of children, though these systemic side effects have an amplified chance of occurring if the potency of the topical corticosteroid was too strong or there is prolonged use of the medication over a period of time (Dhar et al., 2014). Additionally, ocular symptoms may also be presented in glaucoma or cataracts (Daniel & Orchard, 2015). Despite these numerous side effects, the frequency of the occurrence is slim to none, thus being another reason why they prove to be such common prescriptions during treatment, with easily variable potencies based on the severity of the eczema.

Decades of medical use show that topical corticosteroids clear eczema lesions effectively, but doctors always have to balance this benefit against the risk of side effects. Using potent steroids over long periods can cause skin thinning, visible blood vessels, and even internal hormonal suppression. Because we already know these creams work, more standard efficacy trials would add little new knowledge. Instead, upcoming research needs to focus on application schedules. For example, studies could test proactive weekend therapy against reactive, on-demand use to determine which method keeps symptoms under control with the lowest overall amount of steroid exposure.

Moderate-to-severe eczema

There are two key biologics currently used to treat eczema that are well known, namely Dupixent and Ebglyss. Dupixent (dupilumab) has been FDA-approved since March 2017 for the treatment of eczema. Its function is to inhibit the signalling of cytokines IL-4 and IL-13, resulting in reduced inflammation and, as a consequence, skin barrier dysfunction (Seegräber et al., 2018). Ebglyss (lebrikizumab) was FDA-approved in September 2024 for the treatment of eczema and works similarly to Dupixent by inhibiting cytokine signalling; however, it only inhibits IL13, preventing T cell Th2 signalling and consequently reducing both inflammation and eosinophilia (Khan et al., 2025). IL-13 is a cytokine which regulates allergic responses, known as interleukin-13. Lebrikizumab and dupilumab are both produced by inserting the genetic code into Chinese hamster ovary (CHO) cells to help mass-produce the antibodies; they must then be purified extensively to isolate the respective biologics in Dupixent and Ebglyss.

Dupilumab has been extensively researched, and studies have shown its efficacy in treating eczema, as in one study on the effect of dupilumab on chronic hand eczema (CHE), results showed that dupilumab was effective in treating this particular eczema. According to the hand eczema severity index, patients had a significant decrease, and the dermatology life quality index (DLQI) increased overall. It showed a high tolerance for patients and thus proved to be a very promising treatment for eczema, with high efficacy and a low rate of adverse side effects, making it relatively safe (Asamoah et al., 2025). Another study showed that 80.3% of patients in a clinical trial evaluating the effects of dupilumab on CHE achieved partial or complete resolution of their eczema, demonstrating both its potency and efficacy in treating chronic hand eczema (Riva et al., 2024). Its chemical structure is a monoclonal antibody of a subclass of immunoglobulin G4 that binds to the IL4 receptor. IL-4 is a cytokine which regulates allergic responses, also known as interleukin-4. As a result of being able to bind to the IL-4 receptor, dupilumab can inhibit signalling along both the type 1 and type 2 receptors, thus resulting in a decrease in inflammation (Knox et al., 2024).

Individual patient traits also change how someone responds to a biologic. Having a past history of eye disease or certain allergic tendencies can increase the chance of getting conjunctivitis. At the same time, age and body weight affect how quickly a drug clears the body. An insufficient dose can easily make a drug look ineffective, when the real issue is simply underdosing. Grouping trial participants by baseline traits and physical profiles will be an important step toward personalised prescribing.

For lebrikizumab, there have been fewer studies due to its recent approval by the FDA for clinical trials; therefore, it has not been as thoroughly studied as Dupilumab and has only recently become well known as a biologic. Studies, however, have also demonstrated its effectiveness in treating eczema. In a study that studied the long-term effects of lebrikizumab on patients with moderate to severe eczema, the results showed that a significant majority of patients experienced a substantial improvement in skin quality, having an investigator's global assessment (IGA) of 0 or 1, and there was no requirement to further take topical corticosteroids or other treatments to maintain these effects (Stein-Gold et al., 2026). Additionally, a significant majority of patients had a low EASI score, demonstrating

lebrikizumab's potent effects on eczema. Its chemical structure is also that of an immunoglobulin G4 monoclonal antibody. It binds IL-13 with high affinity, thereby inhibiting its inflammatory effects.

Suggestions that lebrikizumab has a safer profile than dupilumab should be taken with caution. While both biologics met standard phase III licensing requirements, lebrikizumab has not been used in the real world for nearly as long. Variations in reported side-effect rates between trials may reflect differences in study protocols as well as patient groups rather than true biological differences. Direct, active-comparator trials are the only way to resolve this.

The key potential adverse side effects that come about through the use of dupilumab for the treatment of eczema were head and neck eczema, conjunctivitis, eczema, peeling of skin and dryness in eyes, however overall dupilumab did show to have a high tolerance, as these adverse side effects only presented in less than 20% of patients, and are relatively minor and not severe or life threatening (Parmar et al., 2022). In another study, it was said that a small minority of patients had mild conjunctivitis, and a few patients had severe conjunctivitis, which may remain an issue; therefore, dupilumab must be researched slightly more to ensure the safety of patients who may decide to utilise it as a treatment for moderate to severe eczema. The key side effects of lebrikizumab are injection site reactions and conjunctivitis, and therefore it has similar side effects to dupilumab (Lin et al., 2024). However, studies show that relative to dupilumab, it seems that lebrikizumab seems to be more favourable due to its side effect profile and high tolerance. Moreover, it should be noted that dupilumab has a greater number of ocular effects (Loh et al., 2020).

Though there is a positive correlation between clinical safety and efficacy, a majority of adverse events are minor, such as injection site reactions or mild conjunctivitis, and only a small percentage of these adverse events are serious; as the minor adverse events do not infer or correlate with worse efficacy, it should be concluded that there is no direct cause-and-effect relationship between safety and efficacy in the administration of dupilumab. It should also be noted that due to the method of administration being through injection with a needle, there would be a high prevalence of injection site reactions expected. This suggests a future investigation into the direct relationship between safety and efficacy as a clinical trial to mitigate bias in future research.

Janus kinase (JAK) inhibitors reduce eczema severity by blocking intracellular signalling triggered by pro-inflammatory cytokines such as IL-4 and IL-13, thereby reducing immune-mediated inflammation.(*Basic Mechanisms of JAK Inhibition*, 2020). In a literature review, it was stated that there are currently 11 FDA-approved JAK inhibitors which can be used. However, the key JAK inhibitors which are often used in the treatment of eczema are abrocitinib, ruxolitinib and upadacitinib (Fig. 3) (Chovatiya & Paller, 2021; Shawky et al., 2022).

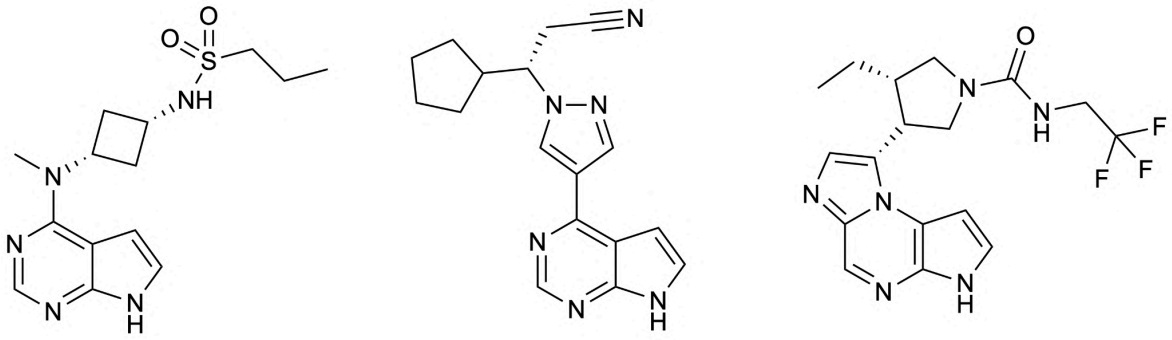


Figure 3. Chemical structures of the most commonly used JAK inhibitors to treat eczema. All 3 share a nitrile group that facilitates binding to the kinase, and they also have a pyrrolopyrimidine core. The nitrile group enables blocking of the JAK-STAT pathway.

Studies have shown that abrocitinib, ruxolitinib and upadacitinib are effective in the treatment of eczema. This is evident in a study on the efficacy of abrocitinib and upadacitinib. For abrocitinib, results from the trial showed a significant reduction in pruritus for many patients, and 48.3% of patients demonstrated investigator's global assessment (IGA) scores of 0 or 1. Moreover, in week 1, there were also very substantial improvements in the eczema area severity index (EASI). This shows that abrocitinib has a high efficacy and can lead to skin clearance and relief. For upadacitinib, 50% of patients demonstrated an IGA score of 0 or 1 at 16 weeks, and there was a 90% improvement in EASI score as well at 16 weeks. There was also a general improvement in eczema symptoms, indicating relatively high efficacy, comparable to that of abrocitinib (Nezamololama et al., 2020). In another study, which evaluated the effects of ruxolitinib on eczema, it was found that there was a 51.6% decrease in EASI overall after 4 weeks, and there was a large percentage of patients who were able to achieve IGA scores of 0 or 1; therefore, the results also demonstrated ruxolitinib's efficacy (Mohney et al., 2023).

Generally, many of these JAK inhibitors do have the possibility of many side effects, such as non-specific side effects, such as nausea, vomiting or diarrhoea and also a 10% possibility of headaches, dizziness or fatigue. However, there are also very slim possibilities of many various specific side effects (Fig. 4) (Rajput Khokhar et al., 2025). In a recent clinical study, patients using ruxolitinib had a 38.3% risk of adverse side effects, which is high; therefore, whilst ruxolitinib has high efficacy and is potent, it still has many side effects, but fewer systemic risks (Incyte Corporation, 2025). For upadacitinib, in a clinical trial, it was demonstrated that there was a 3.49% chance of a serious adverse event occurring, and there was a roughly 20% chance of a non-serious adverse event; however, the trial also indicated that many of the patients' eczema symptoms were substantially reduced through EASI and IGA scores (AbbVie, 2025). However, in a study with abrocitinib, there was a staggering 74% of patients who encountered treatment-emergent adverse events and 1.7% who encountered severe adverse events. Although this study demonstrated high rates of adverse events, real-world tolerability is often good, as shown in other clinical trials of JAK inhibitors. Therefore, similar to other JAK inhibitors, it has a frequency of adverse side effects (Pfizer, 2022). Though it is important to note that oral JAKs do carry these black box warnings for serious heart events, cancer,

clots and death and thus the serious risks mentioned are very consistent with these warnings for oral JAKs (Tokareva et al., 2023).

When reviewing the trial results for JAK inhibitors, ruxolitinib seems to achieve impressive skin clearance rates. However, comparing these numbers directly to oral treatments causes methodological issues. Ruxolitinib is a topical cream tested on localised eczema patches over just four weeks. In contrast, upadacitinib (50% achieving an IGA score of 0 or 1) and abrocitinib (48.3%) are daily oral tablets tested in patients with moderate-to-severe disease over twelve to sixteen weeks. The clinical trials had completely different time frames, baseline severity levels, and measuring points. Because the study setups vary so much, researchers cannot claim that one inhibitor works best without direct head-to-head trials or a network meta-analysis.

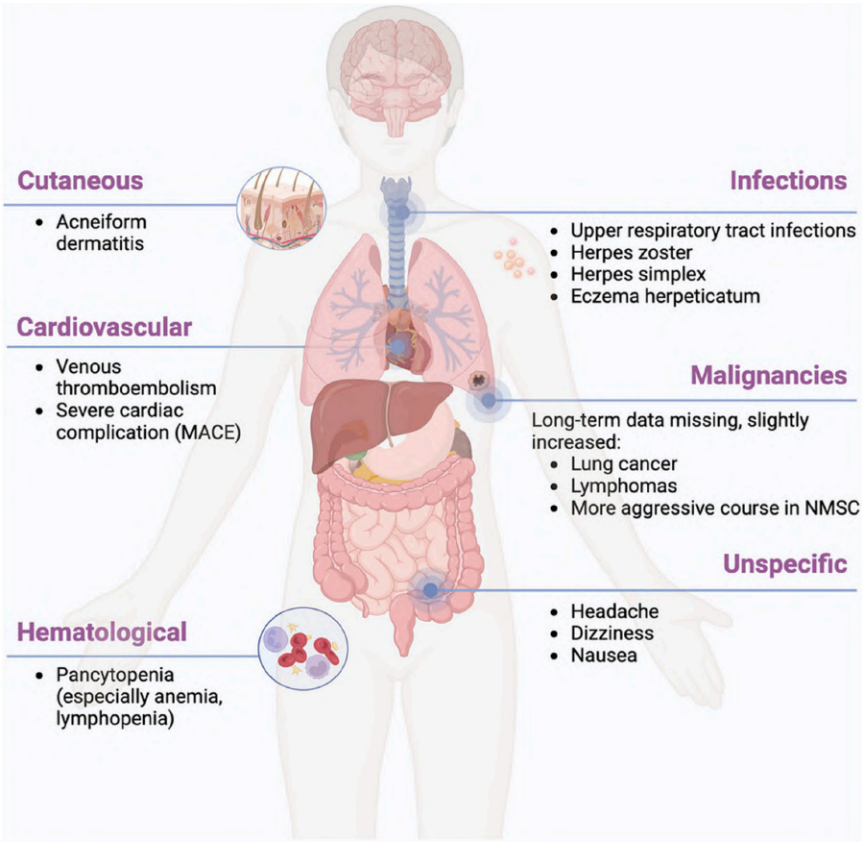


Figure 4. Summary of potential adverse effects of JAK inhibitor therapy. Overview of clinical complications categorised by organ system, highlighting increased risks of infection, cardiovascular events, cutaneous eruptions, and haematological abnormalities.

Alternative therapies

Manuka honey remains a highly researched topic of discussion within the medical field, with the intention to evaluate its efficacy in reducing eczema. Its key function, for which it has been said to treat eczema, is due to its anti-inflammatory and moisturising properties (Johnston et al., 2018a). It is also anti-bacterial, demonstrated in its effectiveness in preventing the development of the bacterium S. *aureus*, which often worsens eczema, due to further infection and flare-ups. It is anti-inflammatory, as it inhibits the signalling pathway of TLR1/2, toll-like receptors that often promote inflammation (Alangari et al., 2017). Moreover, it contains a high concentration of an anti-inflammatory chemical compound, known as methylglyoxal. Studies show that methylglyoxal inhibits the production of inflammatory cytokines; as a result, inflammation from eczema flare-ups is reduced significantly after application of this honey. This is achieved by activating NRF2, which suppresses transcription of the IκBζ gene, thereby reducing the production of inflammatory cytokines substantially (Wei et al., 2023).

It contains a myriad of chemical compounds; however, the key anti-inflammatory compounds are methyl syringate and leptosin (Fig. 5). Methyl syringate acts by inhibiting neutrophil processes (Main et al., 2024), resulting in inflammation being significantly reduced; furthermore, it inhibits the expression of the enzyme cyclooxygenase-2 (J. Park et al., 2016), helping facilitate the reduction of inflammation and pruritus. The structure of methyl syringate comprises a benzene ring, along with a methyl ester group and a hydroxyl group. The structure of leptosin consists of a core of a benzene ring, which is bonded to a furan ring alongside a ketone group, as well as a phenyl group and 2 hydroxyl groups.

There are often minimal side effects that come about through the application of Manuka honey for the treatment of eczema; however, the key issues that often arise are related to contact irritation and allergic reactions. Some patients may be more susceptible to bee or pollen allergies, leading to honey irritating their skin. Its sticky properties also make it easy for dust and debris to stick onto it, leading to the possibility of the eczema worsening. Another key issue could be the quality or grading of the honey itself, as unpurified honey may contain bacteria that can worsen eczema; therefore, medical-grade honey should be used when applying (Johnston et al., 2018b). However, other than these key potential side effects, honey, as a relatively safe chemical compound, will not often lead to other adverse side effects, resulting in its high tolerance level, mainly due to its low pH, moisturising efficacy and antibacterial properties (Mandal & Mandal, 2011).

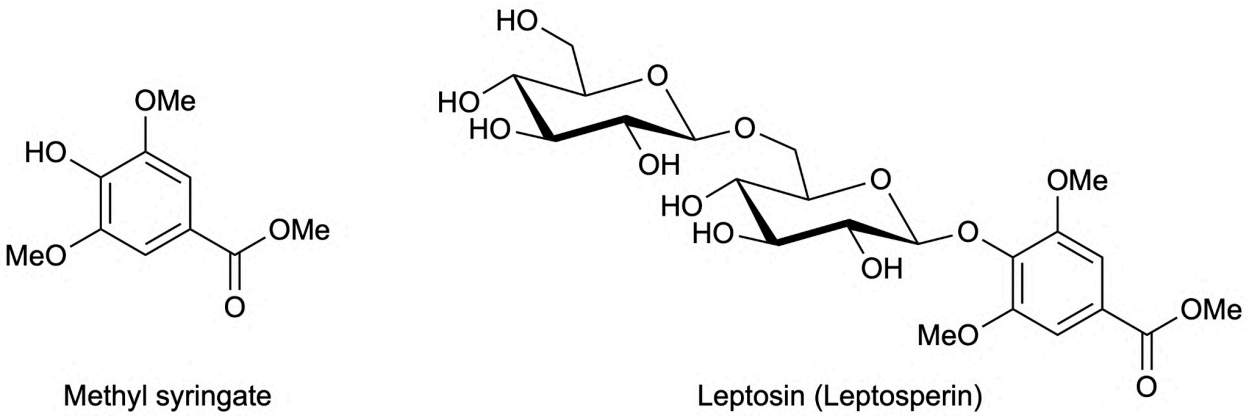


Figure 5. Chemical structures of methyl syringate and leptosin, also known as leptosperin, along with their respective functional groups, with both similarly having a hydroxyl group and benzene ring, but methyl syringate having a methyl ester group compared to leptosin with a furan ring, ketone group and phenyl group (J. Park et al., 2016).

Acupuncture works by stimulating the nervous system through the insertion of many tiny needles into various spots of the body. However, its key function in helping combat key symptoms of eczema is to activate the nervous system, stimulating nerves to release endorphins for pain relief, while inhibiting inflammatory cytokines (Li et al., 2021). Moreover, there are many classifications of specific areas for the needles to be inserted, for example, ST36 or PC6 (Fig. 6) (*Frontiers | Efficacy of Acupuncture on Upper Limb Dysfunction after Stroke: A Randomized Controlled Trial Protocol with Surface Electromyography Evaluation*, 2025). These are key areas of insertion on the outer side of the shin and the inner wrist, respectively. Inserting needles into ST36 activates the sympathetic nervous system and, as a result, reduces inflammation (Oh & Kim, 2022). After inserting needles into PC6, this promotes the release of anti-inflammatory compounds and helps regulate the immune response to further reduce the severity of eczema symptoms (H.-J. Park et al., 2021).

Finally, Manuka honey cannot yet be fairly compared with licensed medical treatments. The available evidence comes mostly from small, uncontrolled observational studies that lack placebo controls. Until researchers conduct proper randomised, placebo-controlled trials, claims about how well it works compared with conventional therapies remain unproven.

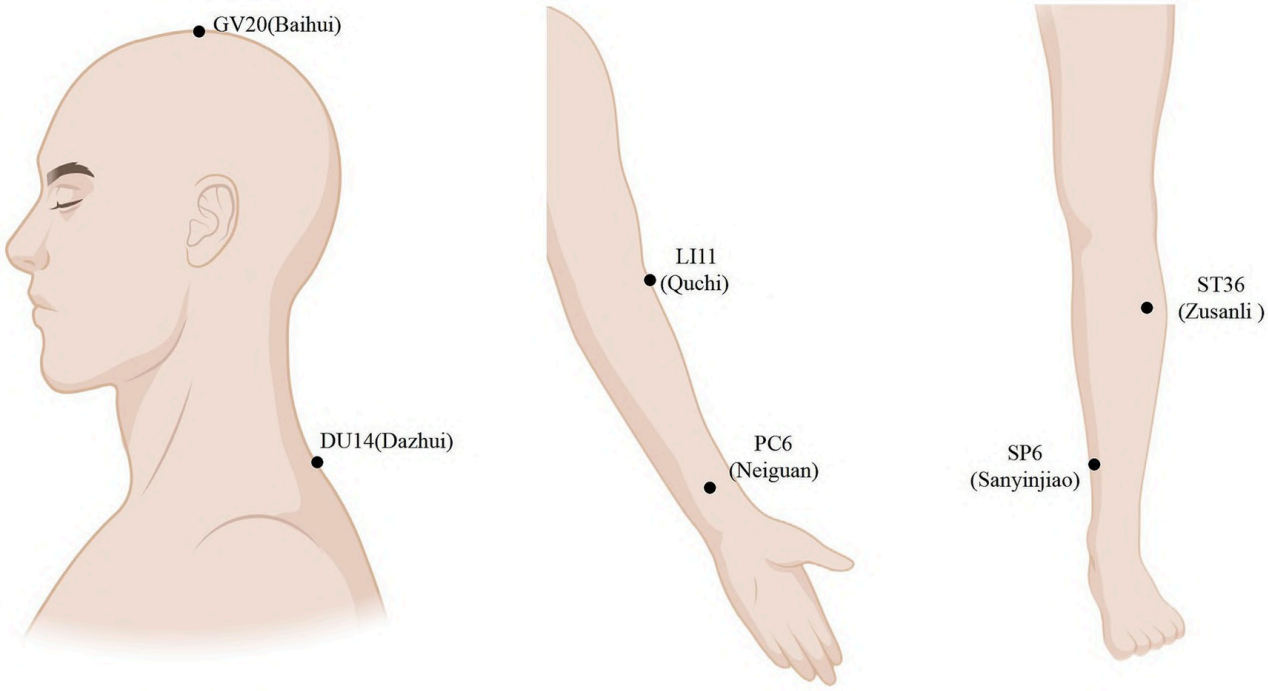


Figure 6. Schematic representation of acupuncture points of both ST36 and PC6, in which PC6 is in the inner wrist, and ST36 is in the outer shin.

There are some possible side effects which may come about through the use of acupuncture to treat eczema. This includes minor pain, bleeding and bruising at the sites of the needle insertion, dizziness, drowsiness, as well as the potential worsening of eczema, due to increasing the severity of eczema symptoms or causing a flare-up. There are also possibilities of infection and increased bleeding (Jones, 2019). The numerous severe side effects that come about through acupuncture outweigh its positive effects. Moreover, these side effects may or may not present, depending on the medical practitioner's experience and ability (Xu et al., 2013).

With acupuncture, adverse reactions usually happen because of specific existing risks, such as open skin lesions, bleeding disorders, or taking blood thinners. Future research into acupuncture should concentrate on creating clear patient screening checklists and running sham-controlled trials to see whether it provides real medical value as an add-on therapy.

Evaluation of each treatment

Generally, there are numerous advantages to emollients becoming a standard for general prescription. Notable advantages include the effectiveness of moisture retention, helping improve the strength of the skin barrier. Studies have shown that emollients have high efficacy in reducing the severity of flare-ups and eczema, as indicated by POEM scores, and have demonstrated considerable decreases in flare-ups and itching. However, this study also showed that adverse effects, whilst not fatal, are common as some patients did experience worsening of eczema,

further itching, dryness and a burning sensation (Ridd et al., 2022). Moreover, relative to other medications, it is affordable for the average person and also easy to apply, though drawbacks also include frequency of application and potential clogging of pores, which may result in worsening of eczema (Table 1, Entry 1) (*How Parents and Children Evaluate Emollients for Childhood Eczema: A Qualitative Study | British Journal of General Practice*, 2022).

Topical corticosteroids are highly effective in quickly resolving eczema flare-ups, relatively safe, and versatile, with different potencies prescribed to patients depending on the severity of their eczema. An example of this would be hydrocortisone given to patients with very mild eczema, and betamethasone valerate at different concentrations for moderate and severe eczema. Moreover, they are often affordable, as their over-the-counter availability has driven prices down. These advantages all make it a primary treatment for eczema. However, whilst topical corticosteroids are a very effective solution to eczema, it is crucial to be aware of the potential side effects as noted previously, as though they are of very low chance, local effects could still occur, such as striae or general irritation, with more severe side effects of Cushing's syndrome, which can come up as a side effect, though it is very unlikely to occur. It should also be noted that prices may increase significantly depending on the severity of the eczema, which should be a factor when considering other possible treatments. Therefore, overall, it is evident why topical corticosteroids are so commonly prescribed, having a very high efficacy, versatility, and being relatively affordable for the common person, whilst only having very slim chances of adverse side effects occurring (Table 1, Entry 2).

The key strengths of the use of dupilumab and lebrikizumab are that, overall, they help substantially reduce inflammation and pruritus, thus significantly improving skin health, holding this over many other traditional treatments for eczema due to being able to treat the underlying reasons for inflammation. They also reduce the number of systemic side effects because they are able to treat the underlying reasons for inflammation; moreover, they have been thoroughly researched, and as a result, there are minimal side effects, and they are relatively safe (Kumar et al., 2025). Studies mentioned previously have shown a consistent improvement in eczema symptoms, and the biologics themselves have a high efficacy and potency, being able to combat eczema symptoms effectively. However, the key weaknesses are cost and necessity for injection, as many patients will not be able to afford such a costly treatment on average, compared to the cheaper alternative of an over-the-counter (OTC) medication for eczema treatment, whereas biologics cost a lot, leading to many patients having to pay out of their pockets for it. It is also important to note that many patients appear to be very sceptical of needles, therefore being a large barrier in biologics becoming widespread and used often. Due to biologics being able to suppress the immune system, there is a greater frequency of infection among patients who use these biologics compared to topical corticosteroid creams (Ameen et al., 2021). Therefore, though biologics are an optimistic avenue of research currently, some research should be invested towards clinical trials to further evaluate their safety profile and the reduction of cost via an investigation into the possibility of the industrialisation of biologics (Table 1, Entry 3).

The key strength of JAK inhibitors is their efficacy, which is evident in numerous clinical trials mentioned previously, where, using a variety of scales, such as EASI, IGA or DLQI, there have been significant improvements in all three scales using all three common JAK inhibitors in Abrocitinib, Ruxolitinib and Upadacitinib. Moreover, relative to other common treatments, JAK inhibitors have much higher efficacy in skin clearance as well. Furthermore, compared to other treatments like biologics, where a needle is required for administration, most JAK inhibitors are orally administered, therefore being easier to administer and appealing to more patients (Harrington et al., 2020). However, though JAK inhibitors do possess high efficacy for treatment and are easy to administer, they still possess many

downsides. As a result of its high efficacy, the likelihood of adverse events occurring increases. This is demonstrated by a greater frequency of serious side effects, such as cardiovascular events or blood clots. Another crucial weakness to note compared to other treatments is specificity, as JAK inhibitors affect multiple signalling pathways, which ultimately leads to many potential side effects. They are also costly compared to OTC eczema treatments, costing tens of thousands of dollars (Table 1, Entry 4).

In general, the key advantages of utilising Manuka honey as an alternative medication relative to other common eczema treatments on the market are due to its inherent anti-inflammatory properties, along with its ability to retain moisture and reduce the severity of eczema flare-ups (Patel & Cichello, 2013). Though the Manuka honey has been demonstrated to possess these important qualities in the effective treatment of eczema, it still contains many disadvantages, which would make it an unreliable choice for dermatologists to prescribe to patients with eczema. The key disadvantages involve its cost, feel, lack of research and risk factor for allergies. Regarding its cost, relative to other commercial products for treatment, the same potency of treatment is offered at a comparable efficacy, whilst being more costly compared to over-the-counter (OTC) emollients or topical corticosteroids. Due to a severe lack of research into alternative medications like Manuka honey compared to commonly researched treatments, such as topical corticosteroids, a greater number of clinical trials must be performed in order to further determine how it compares against traditional and modern treatments. Furthermore, it has been reported to feel very sticky and greasy, which a patient may find uncomfortable in daily life, especially with the frequency of application, compared to an emollient, which may be both soothing and won't feel as greasy. Many patients with allergies to pollen or bees, as stated previously, will not be able to use this medication; therefore, its versatility is substantially hindered by this factor compared to a topical corticosteroid (Alhabsi et al., 2026). Lastly and overall, there is still only preliminary evidence for its potential antibacterial benefits and lesion improvement; therefore, no large randomised controlled trials (RCTs) confirm superiority over standards, and it is not recommended in major guidelines as a primary treatment (Table 1, Entry 5). However, it is important to note that, compared with the other treatments discussed in the traditional and modern approaches, the figures for Manuka Honey are drawn from different trials with different patient populations, disease severity, and primary endpoints. As a result, it is vital to note that the interpretations of these trials may not be as strong, due to the lack of direct head-to-head clinical data to mitigate bias accordingly.

For acupuncture overall, the drawbacks outweigh the advantages due to the multiple side effects, which may be presented if in the care of an inexperienced medical professional, who may not be effective and accurate at inserting the needles into the patient, leading to multiple side effects occurring. Though it does have a few advantages, much research has been invested in the safety and efficacy of treating eczema with acupuncture, and studies have shown that when an experienced practitioner performs the treatment, eczema symptoms can be substantially reduced, and it is relatively safe. However, again, it still comes with very adverse side effects. It also needs to be considered that it is very costly compared to many OTC medications, such as topical corticosteroids, as an experienced practitioner of acupuncture is costly, yet necessary to ensure safety. Furthermore, though as stated previously, there has been a bit of research that has been invested into acupuncture, many other commercial treatments are even more rigorously evaluated and tested in clinical trials to be safer, more potent and cheaper. Lastly, the systematic reviews of acupuncture show mixed and low-quality evidence overall, with some mild itch and symptom reduction, which unfortunately come with heavy risks such as pain and infection, and the severe lack of thorough and evaluative trials makes it unreliable compared to conventional options (Zeng et al., 2021). Therefore, though through these findings

the data does show the implication that overall acupuncture may not be a preferred option of treatment, it is still important to note that these interpretations should be approached with caution, being primarily preliminary insights.

Table 1. Summary of primary, secondary and alternative eczema therapies: a comparison of treatment types, their delivery methods, efficacy, evidence level, main advantages and clinical limitations.

Entry	Type	Target	Delivery	Evidence	Advantages	Limitations
1	Emollients	Skin	Topical	High	OTC, cheap, hydro-retentive	Low potency, frequent application, potential pore clogging
2	Corticosteroids	Skin	Topical	High	OTC, safe, versatile potency, affordable	Potential adverse side effects, variable pricing
3	Biologics	Thigh or abdomen	Injection	Medium	High potencies and efficacy	Need for injection, costly, potential adverse side effects
4	JAK inhibitors	Skin and immune system	Oral or topical	High	High efficacy, easy to administer	Lack of specificity, high frequency of side effects, and costly
5	Alternative meds	Skin	Various	Low	Unproven	Adverse side effects, costly, unsafe, lack of thorough and evaluative trials

Overall, the treatments summarised in Table 1 highlight the need for a personalised approach. Healthcare providers should evaluate severity using the EASI index and weigh the risk-benefit profile of each option. Selecting the optimal strategy requires balancing clinical efficacy with patient preferences to support long-term treatment adherence.

4. Conclusion

In conclusion, after extensive evaluation of many eczema treatments, modern and traditional approaches do remain the key treatments for both research and current usage. For traditional treatments, they remain reliable and affordable due to extensive research into the efficacy and safety of emollients and topical corticosteroids, as well as ways to reduce costs, which, as a result, leads to their prescription by more medical practitioners. For modern treatments, they remain an optimistic avenue for innovation and research, due to their potency and efficacy, though more research needs to be put towards reducing the frequency of adverse side effects, as well as making these treatments more accessible to the average person, due to the costly nature of JAK Inhibitors or Biologics, leading to substantial out-of-pocket costs for patients. Alternative medicines remain an area of scepticism, and rightly so, though research has been heavily invested in their safety and effectiveness. For the same effectiveness, both traditional and modern approaches to eczema treatment outperform alternative treatments, making them unreliable and rarely used in treatment. Therefore, overall, eczema treatments remain very promising for further research and innovation to optimise and refine both traditional and modern treatments in terms of cost, adverse side effects, and efficacy.

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Data & Code Availability Statement

No new raw data or software code were generated or analysed during this study. All data evaluated in this review were obtained from previously published literature and publicly available clinical trial registries at ClinicalTrials.gov. All primary sources and trial identifiers (NCT numbers) are cited within the article.

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Mentor Contribution Statement

Mentor, Dr Daria Sokolova, has helped in advisory and supporting roles throughout the process of this literature review.

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REVIEW ARTICLE

Eczema treatments: A review of their effectiveness, limitations and future directions

Abstract

There are currently a myriad of available choices for eczema treatment, each possessing different efficacies, potencies and mechanisms of action. There are currently three main categories of eczema treatments: traditional, alternative and modern approaches. However, there are many debates over which treatments are the most effective and offer the greatest benefits. For instance, biologics are a promising avenue of research due to their potency and efficacy, though they are associated with more severe adverse effects than other treatments. Conversely, topical corticosteroids possess a wide range of potencies and are highly effective, but carry drawbacks related to application frequency or possible local side effects. Therefore, this literature review examines the most common eczema treatments across traditional, modern and alternative medicines, compares them, and evaluates possible future directions for the research and innovation of eczema treatments and their potential contribution towards the advancement in medical research. Overall findings dictate that modern and traditional eczema treatments remain the forefront for general usage due to reliability, accessibility and safety.

Keywords: Translational Medical Sciences, Disease Treatments and Therapies, Dermatology, Eczema.

1. Introduction

Since around 400 BC, when eczema was first described and labelled, it has persisted as a significant irritant and major health issue worldwide. During this time period, Hippocrates became the first to describe the condition now known as eczema, having described a patient with dry and scaly skin, as well as a chronic itch throughout the patient's body. Although considerable research and investment have been made to investigate treatments, the issue remains an unrelenting problem affecting approximately 1.5 million adults in the UK (*Change AD UK*), underscoring its widespread impact throughout the country. Key treatments currently used most commonly include emollients, general improvements to hygiene and sanitary standards, topical corticosteroids, and some modern innovations, such as Janus Kinase (JAK) inhibitors and biologics (Santer et al., 2024). Emollients are compounds which form a film on the outer surface of the skin, which aids in soothing irritation and hydrating the skin. JAK Inhibitors are a classification of medical compounds which reduce the transduction of cytokine signalling through the JAK-STAT

pathway and as a result reduce the transcription of genes related to the causation of inflammation and swelling. Biologics function as compounds which are composed of biological material, are grown in living cell structures, and are known for their potent efficacy in treating diseases. Though the common treatments are effective on a wide scale, being more cost-effective and easily accessible, they do have some disadvantages, such as side effects like lichenification (thickening of skin with leathery texture arising) or erythema (redness of skin due to increased blood flow to blood vessels near surface of skin) (Bhanot et al., 2019) with prolonged use of certain emollients and also skin thinning and stretching as side effects for topical corticosteroids. The newer innovations seem more promising, being long-lasting and highly effective at treating eczema, though a new issue arises: costs and malignancies (Mansilla-Polo & Morgado-Carrasco, 2024). This is especially prevalent in JAK inhibitors, due to the effectiveness of their immunosuppressive nature, resulting in the weakening of the immune system, leading to greater vulnerabilities in the body, which eventually culminates in a greater risk for cancer. This vulnerability causes infections to develop within the body, particularly in the respiratory and urinary tracts (Klein et al., 2022). Biologics also have a few adverse side effects, including but not limited to conjunctivitis (inflammation of the conjunctiva), injection site reactions and eosinophilia (*Long-Term Safety and Efficacy Study of Lebrikizumab (LY3650150) in Participants With Moderate-to-Severe Atopic Dermatitis (ADjoin)* (*ADjoin*), 2025). Therefore, while both traditional and newer innovations in eczema treatments have demonstrated various successes in terms of effectiveness in resolving eczema, they still have drawbacks in multiple ways, including side effects and costs. However, whilst these newer innovations do have drawbacks, further investment into them should be investigated to assess the assumptions that adverse side effects may be mitigated and eventually eliminated. This is evident in the possibility of investment into the mass production of biologics, slowly minimising costs and making them more affordable to the average person. This article ultimately aims to discuss various eczema treatments, some more well-known than others, evaluating their outlooks, various benefits and drawbacks. The key treatments discussed will include the most common traditional approaches and modern innovations, as well as some discussion on the prospect of alternative medicine. The key way in which this literature review differs from others is that it not only takes into account treatments which are very commercialised and recognised, but it also acknowledges the possibility of alternative medicine in its treatments and provides comprehensive comparisons to traditional and modern treatments for eczema.

2. Methodology

Search strategy

The primary strategy utilised for the identification of relevant literature reviews was through the thorough evaluation of key sources found on Google Scholar or ClinicalTrials.gov. The searching strategy was conducted using MeSH filtering and evidence-based analysis for clinical trials, which allowed me to achieve methodological rigour in mitigating bias, ensuring clinical relevance and statistical validity. It is important to note that included studies were not formally appraised for risk of bias and may therefore be subject to bias. Including terms such as “Biologics” and “Emollient efficacy” was vital in being able to filter relevant information when using keyword searching for Google Scholar. The reason for which a third database was not used during the research into the manuscript was because Google scholar already yields many of the journals which are indexed in PubMed, thus its usage as a third database would yield nearly completely similar results, as a result usage of PubMed was used slightly in the initial research phase, though nearly similar papers would also appear on google scholar, as a result citations were primarily present on google scholar.

Additional relevant terms were used during the evaluation of different treatments, including: Abrocitinib, Ruxolitinib, Upadacitinib, Dupilumab, Lebikizumab, Hydrocortisone and Betamethasone Valerate. Additionally, the date range of the literature search had no restrictions applied. EASI, IGA and other clinical endpoints were systematically extracted.

Inclusion and exclusion criteria

Key criteria that were required for the consideration to use the source included:

- Sufficient data for analysis for clinical trials
- Peer-reviewed academic journals in terms of literature review evaluation

Exclusion criteria:

- Lack of empirical data
- Published as an editorial commentary

Study selection and data extraction

Screening was performed throughout the writing of this literature review, and each citation was independently reviewed and assessed. Ultimately, through the process of writing, a large proportion of literature reviews and clinical trials met all inclusion criteria to be included in the literature review.

Data extraction was conducted through comprehensive organisation through Zotero software to record the author, year of publication and area of eczema research, helping categorise research effectively through keyword searching within the software.

3. Analysis

Mild-to-moderate eczema

The most common treatments prescribed are emollients. The main emollients prescribed by the NHS are creams and ointments, such as Aveeno creams and Cetraben cream. Aveeno creams and some Cetraben creams use colloidal oatmeal as a base, due to its natural healing acceleration benefits, which act as a barrier to retain moisture and gently cleanse the skin to optimise the reduction of eczema flaring and gradually help build up a natural barrier against eczema. The key chemical components contained within this colloidal oatmeal are known as avenanthramides, which contain anti-inflammatory and anti-itch properties (Fig. 1) (Sur et al., 2008). Moreover, it also reduces hypersensitivity and thus is a very strong combatant against irritants. Avenanthramides act via inhibition of NF-κB, responsible for governing immune response and inflammation (Yang et al., 2014).

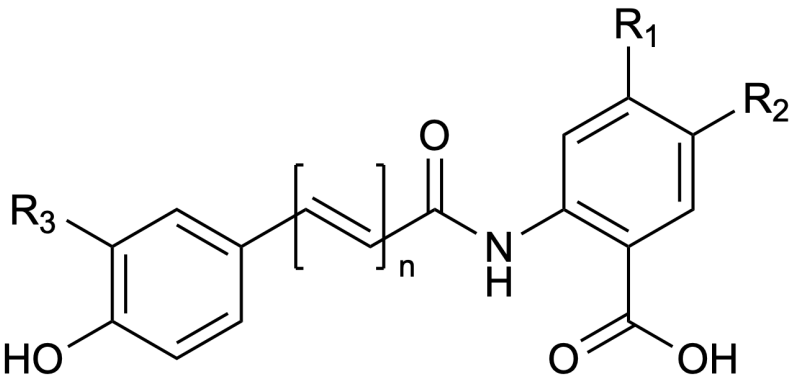


Figure 1. Chemical structure of avenanthramides (n = 1 or 2; R_1 = H, R_2 = OH, R_3 = H, OCH_3, or OH). Avenanthramides are formed by the N-acylation reaction between anthranilic acid (AA) and a phenylalkenoic acid (PA) to create an amide linkage.

Cetraben creams use soft paraffin and liquid paraffin as bases, which act as key chemical compounds for anti-inflammatory and anti-irritant properties. In a study, the SCORing Atopic Dermatitis index (SCORAD) score in patients using a paraffin-based cream was significantly lower than in those using a control cream, indicating a notable reduction in eczema severity. It indicated a 28.6% decrease compared to the original SCORAD score. Therefore, it was concluded that the paraffin-based creams and ointments were effective in reducing the severity of eczema symptoms (Waked & Ibrahim, 2020). The key chemical compounds used in the creams are petrolatum, which is a mix of hydrocarbons. Studies have shown that it helps regulate antimicrobials and maintain the skin's epidermal barrier to help the retention of moisture and prevent irritants from coming into contact with the skin, which demonstrates its effectiveness in combating eczema in patients. One of the key chemical compounds in petrolatum is alkanes such as octadecane (Rogers & Skanupong, 1974). Petrolatum acts by forming a protective barrier on the skin, helping retain moisture and smooth the skin, making it both a comfortable and effective emollient.

Emollients have shown promising results, as evidenced by numerous clinical trials testing the effectiveness of colloidal oatmeal creams (*Study Results | NCT02691507 | Trial to Determine the Therapeutic Benefit of an OTC Cream on Dry, Itchy Skin of Adults and Children With Eczema | ClinicalTrials.Gov*, 2017). Results indicated a significant increase in hydration and a substantial decrease in itchiness, with an average of 4.07 out of 10 on an arbitrary scale after application, demonstrating its short-term effectiveness. However, an issue arises after consolidating data for 7 days after cream application, with 4.22 out of 10. Though it has no significant impact on its overall success, it still shows diminished retention of its anti-itching properties compared to other commercial eczema treatments. Other studies also demonstrate this by recording hydration with a corneometer; the results showed that after 7 days, the unit of measure in arbitrary units was 208.52, compared to 14 days, when the unit of measure in arbitrary units was 158.65 (Johnson & Johnson; Johnson Consumer Inc., 2017). The greater the unit of measure in arbitrary units, the greater the hydration. This further emphasises the long-term decline in the effectiveness of emollients. Of course, it

is crucial to consider that systematic reviews confirm they reduce flares in the long term when used proactively with anti-inflammatories.

A majority of emollients are effective with minimal side effects, providing a reliable short-term solution for mild to moderate eczema. However, situations in which adverse side effects occur must also be taken into account. In a study that examined the effects of a wide range of emollients, including variations in type (cream or lotion) and ingredients (botanicals, ceramides, and other components). From this study, it was found that many patients experienced the following side effects: erythema, irritation, papule formation, and further spreading of eczema, as well as other prominent side effects also being present (Emmett et al., 2023). It has been shown that overall botanical emollients may display more side effects due to the possibilities of irritants present in the natural ingredients compared to ceramides, as allergies may also arise from the use of botanical emollients (Corazza et al., 2009), whilst ceramide-based emollients remain effective and safe (Draelos, 2008), due to the presence of ceramides in skin already.

Emollients sit in a completely different category of eczema care. Because they simply repair the physical skin barrier and do not target specific immune mechanisms, it does not make sense to test them head-to-head against systemic biologics. The more relevant research question is how daily, consistent moisturising can reduce the overall amount of steroid cream a patient needs over time.

Alongside emollients, topical corticosteroids remain a widely prescribed treatment worldwide. The key ways in which topical corticosteroids act are via binding to glucocorticoid receptors within the cytoplasm. This causes a conformational change in the receptor, causing the dissociation of chaperone proteins from the chaperone complex. This corticosteroid-receptor complex then travels through the nuclear pores and inside the nucleus; two of these corticosteroid receptors bind together via homodimerisation, and this dimer then binds with DNA at sites known as glucocorticoid response elements. This process triggers transactivation and, as a result, the increased transcription and translation of anti-inflammatory proteins like lipocortin (Mehta et al., 2016). As referenced previously, NF-κB, a protein complex that controls the body's inflammation. As a result, the body reduces the inflammatory response. Its fundamental chemical structure is often that of a steroid such as hydrocortisone (Fig. 2), which is $C_{21}H_{30}O_5$ (PubChem, 2020). It has a four-ring structure known as a steroid nucleus, similar to other steroids. Due to its specific chemical structure, it can bind to the glucocorticoid receptor. At high concentrations, glucocorticoid receptor dimerisation can activate transcription of anti-inflammatory genes (Barnes, 2006). However, it should be noted that low doses of corticosteroids are what cause the anti-inflammatory effect.

Additionally, other commonly used topical corticosteroids contain betamethasone valerate (Fig. 2) at different concentrations based on the severity of the eczema (Brazzini & Pimpinelli, 2002). Betamethasone valerate has displayed significant decreases in common inflammatory-causing cytokines. Being one of the more potent corticosteroids, it has been a common prescription for patients with moderate or severe eczema. Clinical studies have shown its efficacy in reducing eczema severity (Gether et al., 2025). Moreover, in another study, betamethasone valerate showed potent effects in reducing symptoms of eczema relative to other common treatments, such as 0.5% and 2.5% desoximethasone, showing how it compares well against other frequent prescriptions against eczema (Ashton et al., 1987). Its chemical structure is $C_{27}H_{37}FO_6$. It has a valerate ester, a hydroxyl group and a ketone group as well (*Betamethasone Valerate Cream USP*, 0.1%, 2010).

Evidently, Topical Corticosteroids have also shown significant success in reducing mild to moderate eczema. According to a study, transepidermal water loss was significantly lower when an irritant was applied to multiple patients than when the same irritant was applied to another patch of their skin, with a topical corticosteroid also applied. The study showed that significantly less erythema and lower values of the water loss were found, showing its potent effect on combating the inflammatory properties of eczema, as well as maintaining the water content of the skin (Ramsing & Agner, 1995). Another study also dictates its effectiveness relative to other alternatives of the treatment of eczema flare-ups, such as calcineurin inhibitors meant to suppress the inflammatory response of the immune system specifically. These studies show that the topical corticosteroids are more efficacious (Schmitt et al., 2011). Furthermore, potent corticosteroids can effectively eliminate potential bacteria, which could have helped amplify the effects of inflammation in eczema (Nilsson et al., 1992).

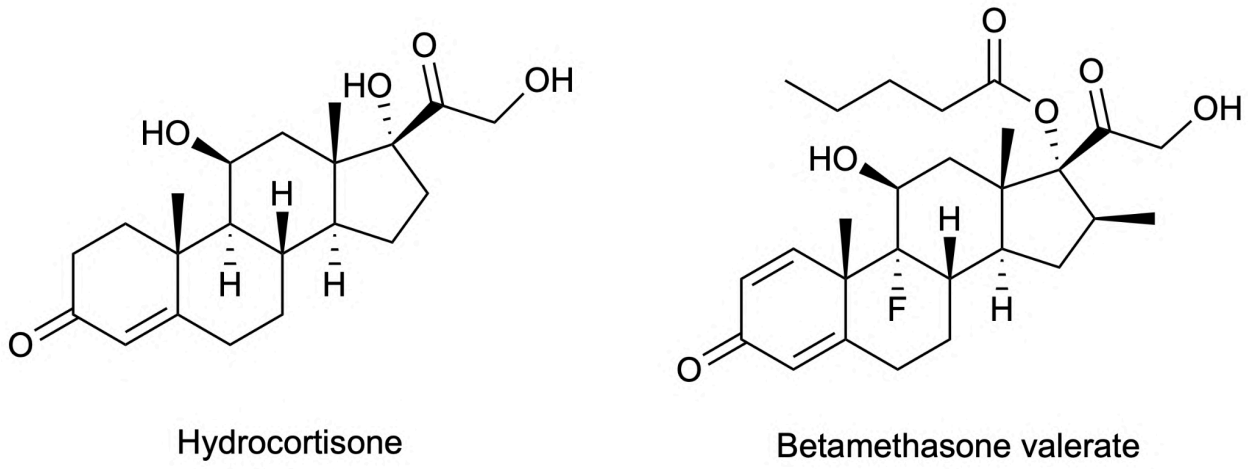


Figure 2. Chemical structures of hydrocortisone and betamethasone valerate. Both molecules are structurally similar and share a cyclopentanoperhydrophenanthrene steroid nucleus and multiple functional groups, including carbonyl and hydroxyl substituents.

Both hydrocortisone and betamethasone valerate have similar side effects, as they are topical corticosteroids in different forms. The most common side effects associated with the use of both medications are local side effects, such as skin atrophy, where the skin begins to thin, leading to easy bruising, and striae, which can result in stretch marks (Ference & Last, 2009). However, there are other side effects which, though rare, can occur, such as systemic side effects of Cushing's syndrome, where an increase in blood pressure and weight gain occurs or a decrease in the growth rate of children, though these systemic side effects have an amplified chance of occurring if the potency of the topical corticosteroid was too strong or there is prolonged use of the medication over a period of time (Dhar et al., 2014). Additionally, ocular symptoms may also be presented in glaucoma or cataracts (Daniel & Orchard, 2015). Despite these numerous side effects, the frequency of the occurrence is slim to none, thus being another reason why they prove to be such common prescriptions during treatment, with easily variable potencies based on the severity of the eczema.

Decades of medical use show that topical corticosteroids clear eczema lesions effectively, but doctors always have to balance this benefit against the risk of side effects. Using potent steroids over long periods can cause skin thinning, visible blood vessels, and even internal hormonal suppression. Because we already know these creams work, more standard efficacy trials would add little new knowledge. Instead, upcoming research needs to focus on application schedules. For example, studies could test proactive weekend therapy against reactive, on-demand use to determine which method keeps symptoms under control with the lowest overall amount of steroid exposure.

Moderate-to-severe eczema

There are two key biologics currently used to treat eczema that are well known, namely Dupixent and Ebglyss. Dupixent (dupilumab) has been FDA-approved since March 2017 for the treatment of eczema. Its function is to inhibit the signalling of cytokines IL-4 and IL-13, resulting in reduced inflammation and, as a consequence, skin barrier dysfunction (Seegräber et al., 2018). Ebglyss (lebrikizumab) was FDA-approved in September 2024 for the treatment of eczema and works similarly to Dupixent by inhibiting cytokine signalling; however, it only inhibits IL13, preventing T cell Th2 signalling and consequently reducing both inflammation and eosinophilia (Khan et al., 2025). IL-13 is a cytokine which regulates allergic responses, known as interleukin-13. Lebrikizumab and dupilumab are both produced by inserting the genetic code into Chinese hamster ovary (CHO) cells to help mass-produce the antibodies; they must then be purified extensively to isolate the respective biologics in Dupixent and Ebglyss.

Dupilumab has been extensively researched, and studies have shown its efficacy in treating eczema, as in one study on the effect of dupilumab on chronic hand eczema (CHE), results showed that dupilumab was effective in treating this particular eczema. According to the hand eczema severity index, patients had a significant decrease, and the dermatology life quality index (DLQI) increased overall. It showed a high tolerance for patients and thus proved to be a very promising treatment for eczema, with high efficacy and a low rate of adverse side effects, making it relatively safe (Asamoah et al., 2025). Another study showed that 80.3% of patients in a clinical trial evaluating the effects of dupilumab on CHE achieved partial or complete resolution of their eczema, demonstrating both its potency and efficacy in treating chronic hand eczema (Riva et al., 2024). Its chemical structure is a monoclonal antibody of a subclass of immunoglobulin G4 that binds to the IL4 receptor. IL-4 is a cytokine which regulates allergic responses, also known as interleukin-4. As a result of being able to bind to the IL-4 receptor, dupilumab can inhibit signalling along both the type 1 and type 2 receptors, thus resulting in a decrease in inflammation (Knox et al., 2024).

Individual patient traits also change how someone responds to a biologic. Having a past history of eye disease or certain allergic tendencies can increase the chance of getting conjunctivitis. At the same time, age and body weight affect how quickly a drug clears the body. An insufficient dose can easily make a drug look ineffective, when the real issue is simply underdosing. Grouping trial participants by baseline traits and physical profiles will be an important step toward personalised prescribing.

For lebrikizumab, there have been fewer studies due to its recent approval by the FDA for clinical trials; therefore, it has not been as thoroughly studied as Dupilumab and has only recently become well known as a biologic. Studies, however, have also demonstrated its effectiveness in treating eczema. In a study that studied the long-term effects of lebrikizumab on patients with moderate to severe eczema, the results showed that a significant majority of patients experienced a substantial improvement in skin quality, having an investigator's global assessment (IGA) of 0 or 1, and there was no requirement to further take topical corticosteroids or other treatments to maintain these effects (Stein-Gold et al., 2026). Additionally, a significant majority of patients had a low EASI score, demonstrating

lebrikizumab's potent effects on eczema. Its chemical structure is also that of an immunoglobulin G4 monoclonal antibody. It binds IL-13 with high affinity, thereby inhibiting its inflammatory effects.

Suggestions that lebrikizumab has a safer profile than dupilumab should be taken with caution. While both biologics met standard phase III licensing requirements, lebrikizumab has not been used in the real world for nearly as long. Variations in reported side-effect rates between trials may reflect differences in study protocols as well as patient groups rather than true biological differences. Direct, active-comparator trials are the only way to resolve this.

The key potential adverse side effects that come about through the use of dupilumab for the treatment of eczema were head and neck eczema, conjunctivitis, eczema, peeling of skin and dryness in eyes, however overall dupilumab did show to have a high tolerance, as these adverse side effects only presented in less than 20% of patients, and are relatively minor and not severe or life threatening (Parmar et al., 2022). In another study, it was said that a small minority of patients had mild conjunctivitis, and a few patients had severe conjunctivitis, which may remain an issue; therefore, dupilumab must be researched slightly more to ensure the safety of patients who may decide to utilise it as a treatment for moderate to severe eczema. The key side effects of lebrikizumab are injection site reactions and conjunctivitis, and therefore it has similar side effects to dupilumab (Lin et al., 2024). However, studies show that relative to dupilumab, it seems that lebrikizumab seems to be more favourable due to its side effect profile and high tolerance. Moreover, it should be noted that dupilumab has a greater number of ocular effects (Loh et al., 2020).

Though there is a positive correlation between clinical safety and efficacy, a majority of adverse events are minor, such as injection site reactions or mild conjunctivitis, and only a small percentage of these adverse events are serious; as the minor adverse events do not infer or correlate with worse efficacy, it should be concluded that there is no direct cause-and-effect relationship between safety and efficacy in the administration of dupilumab. It should also be noted that due to the method of administration being through injection with a needle, there would be a high prevalence of injection site reactions expected. This suggests a future investigation into the direct relationship between safety and efficacy as a clinical trial to mitigate bias in future research.

Janus kinase (JAK) inhibitors reduce eczema severity by blocking intracellular signalling triggered by pro-inflammatory cytokines such as IL-4 and IL-13, thereby reducing immune-mediated inflammation.(*Basic Mechanisms of JAK Inhibition*, 2020). In a literature review, it was stated that there are currently 11 FDA-approved JAK inhibitors which can be used. However, the key JAK inhibitors which are often used in the treatment of eczema are abrocitinib, ruxolitinib and upadacitinib (Fig. 3) (Chovatiya & Paller, 2021; Shawky et al., 2022).

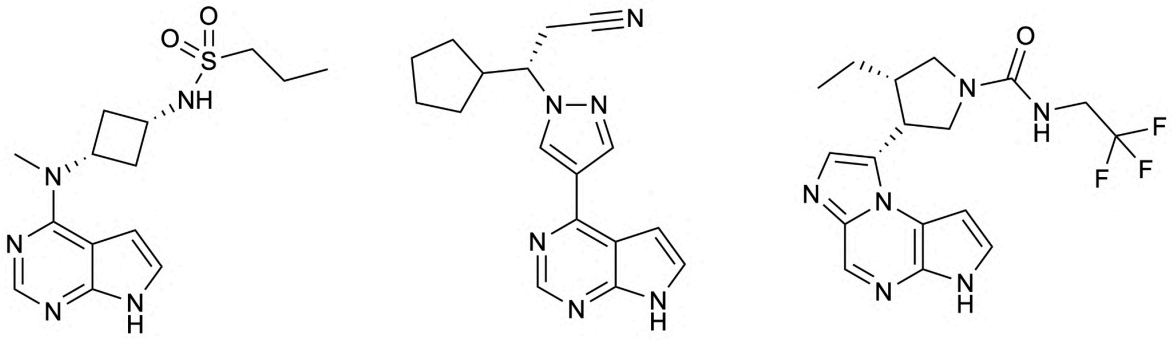


Figure 3. Chemical structures of the most commonly used JAK inhibitors to treat eczema. All 3 share a nitrile group that facilitates binding to the kinase, and they also have a pyrrolopyrimidine core. The nitrile group enables blocking of the JAK-STAT pathway.

Studies have shown that abrocitinib, ruxolitinib and upadacitinib are effective in the treatment of eczema. This is evident in a study on the efficacy of abrocitinib and upadacitinib. For abrocitinib, results from the trial showed a significant reduction in pruritus for many patients, and 48.3% of patients demonstrated investigator's global assessment (IGA) scores of 0 or 1. Moreover, in week 1, there were also very substantial improvements in the eczema area severity index (EASI). This shows that abrocitinib has a high efficacy and can lead to skin clearance and relief. For upadacitinib, 50% of patients demonstrated an IGA score of 0 or 1 at 16 weeks, and there was a 90% improvement in EASI score as well at 16 weeks. There was also a general improvement in eczema symptoms, indicating relatively high efficacy, comparable to that of abrocitinib (Nezamololama et al., 2020). In another study, which evaluated the effects of ruxolitinib on eczema, it was found that there was a 51.6% decrease in EASI overall after 4 weeks, and there was a large percentage of patients who were able to achieve IGA scores of 0 or 1; therefore, the results also demonstrated ruxolitinib's efficacy (Mohney et al., 2023).

Generally, many of these JAK inhibitors do have the possibility of many side effects, such as non-specific side effects, such as nausea, vomiting or diarrhoea and also a 10% possibility of headaches, dizziness or fatigue. However, there are also very slim possibilities of many various specific side effects (Fig. 4) (Rajput Khokhar et al., 2025). In a recent clinical study, patients using ruxolitinib had a 38.3% risk of adverse side effects, which is high; therefore, whilst ruxolitinib has high efficacy and is potent, it still has many side effects, but fewer systemic risks (Incyte Corporation, 2025). For upadacitinib, in a clinical trial, it was demonstrated that there was a 3.49% chance of a serious adverse event occurring, and there was a roughly 20% chance of a non-serious adverse event; however, the trial also indicated that many of the patients' eczema symptoms were substantially reduced through EASI and IGA scores (AbbVie, 2025). However, in a study with abrocitinib, there was a staggering 74% of patients who encountered treatment-emergent adverse events and 1.7% who encountered severe adverse events. Although this study demonstrated high rates of adverse events, real-world tolerability is often good, as shown in other clinical trials of JAK inhibitors. Therefore, similar to other JAK inhibitors, it has a frequency of adverse side effects (Pfizer, 2022). Though it is important to note that oral JAKs do carry these black box warnings for serious heart events, cancer,

clots and death and thus the serious risks mentioned are very consistent with these warnings for oral JAKs (Tokareva et al., 2023).

When reviewing the trial results for JAK inhibitors, ruxolitinib seems to achieve impressive skin clearance rates. However, comparing these numbers directly to oral treatments causes methodological issues. Ruxolitinib is a topical cream tested on localised eczema patches over just four weeks. In contrast, upadacitinib (50% achieving an IGA score of 0 or 1) and abrocitinib (48.3%) are daily oral tablets tested in patients with moderate-to-severe disease over twelve to sixteen weeks. The clinical trials had completely different time frames, baseline severity levels, and measuring points. Because the study setups vary so much, researchers cannot claim that one inhibitor works best without direct head-to-head trials or a network meta-analysis.

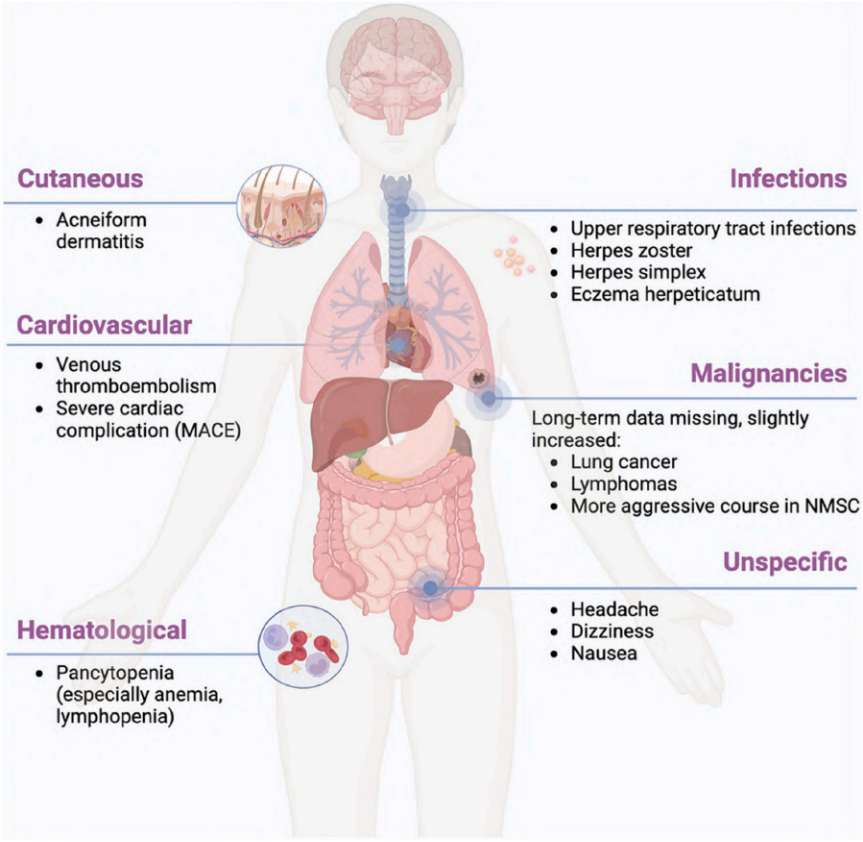


Figure 4. Summary of potential adverse effects of JAK inhibitor therapy. Overview of clinical complications categorised by organ system, highlighting increased risks of infection, cardiovascular events, cutaneous eruptions, and haematological abnormalities.

Alternative therapies

Manuka honey remains a highly researched topic of discussion within the medical field, with the intention to evaluate its efficacy in reducing eczema. Its key function, for which it has been said to treat eczema, is due to its anti-inflammatory and moisturising properties (Johnston et al., 2018a). It is also anti-bacterial, demonstrated in its effectiveness in preventing the development of the bacterium S. *aureus*, which often worsens eczema, due to further infection and flare-ups. It is anti-inflammatory, as it inhibits the signalling pathway of TLR1/2, toll-like receptors that often promote inflammation (Alangari et al., 2017). Moreover, it contains a high concentration of an anti-inflammatory chemical compound, known as methylglyoxal. Studies show that methylglyoxal inhibits the production of inflammatory cytokines; as a result, inflammation from eczema flare-ups is reduced significantly after application of this honey. This is achieved by activating NRF2, which suppresses transcription of the IκBζ gene, thereby reducing the production of inflammatory cytokines substantially (Wei et al., 2023).

It contains a myriad of chemical compounds; however, the key anti-inflammatory compounds are methyl syringate and leptosin (Fig. 5). Methyl syringate acts by inhibiting neutrophil processes (Main et al., 2024), resulting in inflammation being significantly reduced; furthermore, it inhibits the expression of the enzyme cyclooxygenase-2 (J. Park et al., 2016), helping facilitate the reduction of inflammation and pruritus. The structure of methyl syringate comprises a benzene ring, along with a methyl ester group and a hydroxyl group. The structure of leptosin consists of a core of a benzene ring, which is bonded to a furan ring alongside a ketone group, as well as a phenyl group and 2 hydroxyl groups.

There are often minimal side effects that come about through the application of Manuka honey for the treatment of eczema; however, the key issues that often arise are related to contact irritation and allergic reactions. Some patients may be more susceptible to bee or pollen allergies, leading to honey irritating their skin. Its sticky properties also make it easy for dust and debris to stick onto it, leading to the possibility of the eczema worsening. Another key issue could be the quality or grading of the honey itself, as unpurified honey may contain bacteria that can worsen eczema; therefore, medical-grade honey should be used when applying (Johnston et al., 2018b). However, other than these key potential side effects, honey, as a relatively safe chemical compound, will not often lead to other adverse side effects, resulting in its high tolerance level, mainly due to its low pH, moisturising efficacy and antibacterial properties (Mandal & Mandal, 2011).

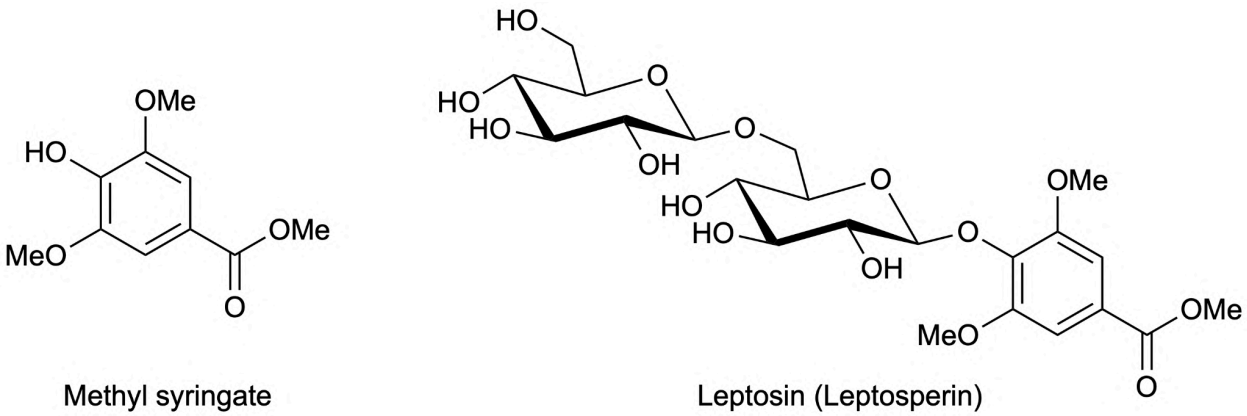


Figure 5. Chemical structures of methyl syringate and leptosin, also known as leptosperin, along with their respective functional groups, with both similarly having a hydroxyl group and benzene ring, but methyl syringate having a methyl ester group compared to leptosin with a furan ring, ketone group and phenyl group (J. Park et al., 2016).

Acupuncture works by stimulating the nervous system through the insertion of many tiny needles into various spots of the body. However, its key function in helping combat key symptoms of eczema is to activate the nervous system, stimulating nerves to release endorphins for pain relief, while inhibiting inflammatory cytokines (Li et al., 2021). Moreover, there are many classifications of specific areas for the needles to be inserted, for example, ST36 or PC6 (Fig. 6) (*Frontiers | Efficacy of Acupuncture on Upper Limb Dysfunction after Stroke: A Randomized Controlled Trial Protocol with Surface Electromyography Evaluation*, 2025). These are key areas of insertion on the outer side of the shin and the inner wrist, respectively. Inserting needles into ST36 activates the sympathetic nervous system and, as a result, reduces inflammation (Oh & Kim, 2022). After inserting needles into PC6, this promotes the release of anti-inflammatory compounds and helps regulate the immune response to further reduce the severity of eczema symptoms (H.-J. Park et al., 2021).

Finally, Manuka honey cannot yet be fairly compared with licensed medical treatments. The available evidence comes mostly from small, uncontrolled observational studies that lack placebo controls. Until researchers conduct proper randomised, placebo-controlled trials, claims about how well it works compared with conventional therapies remain unproven.

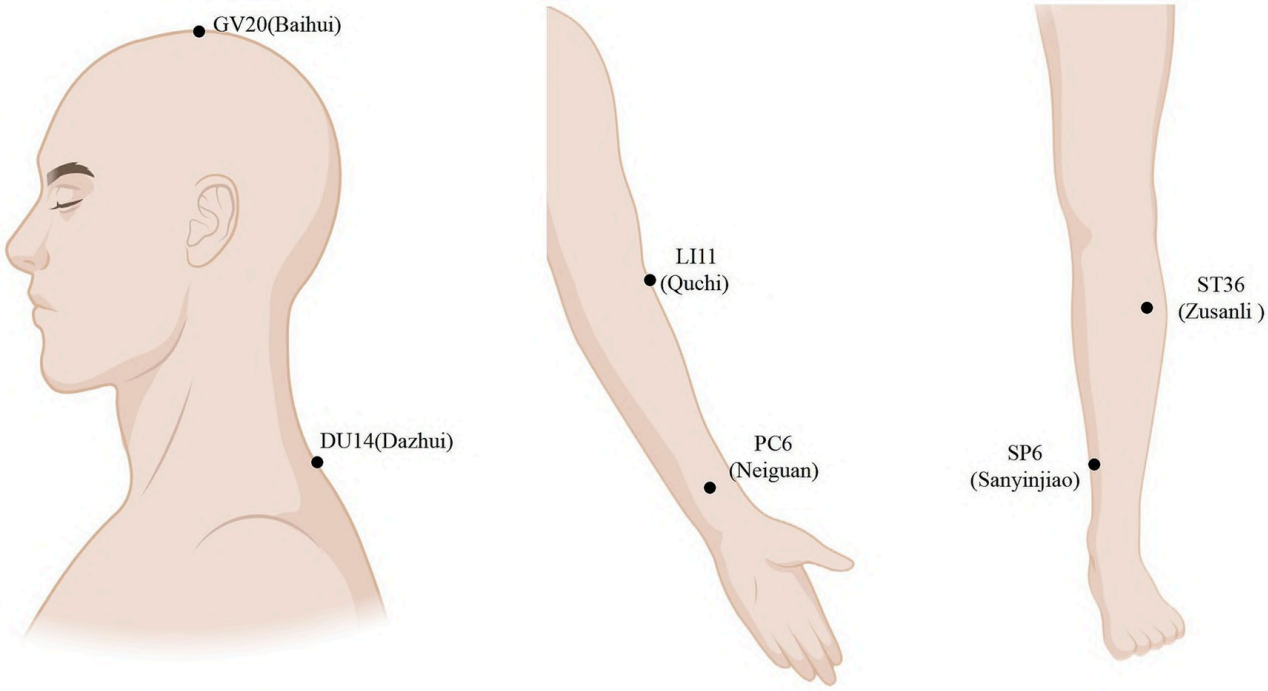


Figure 6. Schematic representation of acupuncture points of both ST36 and PC6, in which PC6 is in the inner wrist, and ST36 is in the outer shin.

There are some possible side effects which may come about through the use of acupuncture to treat eczema. This includes minor pain, bleeding and bruising at the sites of the needle insertion, dizziness, drowsiness, as well as the potential worsening of eczema, due to increasing the severity of eczema symptoms or causing a flare-up. There are also possibilities of infection and increased bleeding (Jones, 2019). The numerous severe side effects that come about through acupuncture outweigh its positive effects. Moreover, these side effects may or may not present, depending on the medical practitioner's experience and ability (Xu et al., 2013).

With acupuncture, adverse reactions usually happen because of specific existing risks, such as open skin lesions, bleeding disorders, or taking blood thinners. Future research into acupuncture should concentrate on creating clear patient screening checklists and running sham-controlled trials to see whether it provides real medical value as an add-on therapy.

Evaluation of each treatment

Generally, there are numerous advantages to emollients becoming a standard for general prescription. Notable advantages include the effectiveness of moisture retention, helping improve the strength of the skin barrier. Studies have shown that emollients have high efficacy in reducing the severity of flare-ups and eczema, as indicated by POEM scores, and have demonstrated considerable decreases in flare-ups and itching. However, this study also showed that adverse effects, whilst not fatal, are common as some patients did experience worsening of eczema,

further itching, dryness and a burning sensation (Ridd et al., 2022). Moreover, relative to other medications, it is affordable for the average person and also easy to apply, though drawbacks also include frequency of application and potential clogging of pores, which may result in worsening of eczema (Table 1, Entry 1) (*How Parents and Children Evaluate Emollients for Childhood Eczema: A Qualitative Study | British Journal of General Practice*, 2022).

Topical corticosteroids are highly effective in quickly resolving eczema flare-ups, relatively safe, and versatile, with different potencies prescribed to patients depending on the severity of their eczema. An example of this would be hydrocortisone given to patients with very mild eczema, and betamethasone valerate at different concentrations for moderate and severe eczema. Moreover, they are often affordable, as their over-the-counter availability has driven prices down. These advantages all make it a primary treatment for eczema. However, whilst topical corticosteroids are a very effective solution to eczema, it is crucial to be aware of the potential side effects as noted previously, as though they are of very low chance, local effects could still occur, such as striae or general irritation, with more severe side effects of Cushing's syndrome, which can come up as a side effect, though it is very unlikely to occur. It should also be noted that prices may increase significantly depending on the severity of the eczema, which should be a factor when considering other possible treatments. Therefore, overall, it is evident why topical corticosteroids are so commonly prescribed, having a very high efficacy, versatility, and being relatively affordable for the common person, whilst only having very slim chances of adverse side effects occurring (Table 1, Entry 2).

The key strengths of the use of dupilumab and lebrikizumab are that, overall, they help substantially reduce inflammation and pruritus, thus significantly improving skin health, holding this over many other traditional treatments for eczema due to being able to treat the underlying reasons for inflammation. They also reduce the number of systemic side effects because they are able to treat the underlying reasons for inflammation; moreover, they have been thoroughly researched, and as a result, there are minimal side effects, and they are relatively safe (Kumar et al., 2025). Studies mentioned previously have shown a consistent improvement in eczema symptoms, and the biologics themselves have a high efficacy and potency, being able to combat eczema symptoms effectively. However, the key weaknesses are cost and necessity for injection, as many patients will not be able to afford such a costly treatment on average, compared to the cheaper alternative of an over-the-counter (OTC) medication for eczema treatment, whereas biologics cost a lot, leading to many patients having to pay out of their pockets for it. It is also important to note that many patients appear to be very sceptical of needles, therefore being a large barrier in biologics becoming widespread and used often. Due to biologics being able to suppress the immune system, there is a greater frequency of infection among patients who use these biologics compared to topical corticosteroid creams (Ameen et al., 2021). Therefore, though biologics are an optimistic avenue of research currently, some research should be invested towards clinical trials to further evaluate their safety profile and the reduction of cost via an investigation into the possibility of the industrialisation of biologics (Table 1, Entry 3).

The key strength of JAK inhibitors is their efficacy, which is evident in numerous clinical trials mentioned previously, where, using a variety of scales, such as EASI, IGA or DLQI, there have been significant improvements in all three scales using all three common JAK inhibitors in Abrocitinib, Ruxolitinib and Upadacitinib. Moreover, relative to other common treatments, JAK inhibitors have much higher efficacy in skin clearance as well. Furthermore, compared to other treatments like biologics, where a needle is required for administration, most JAK inhibitors are orally administered, therefore being easier to administer and appealing to more patients (Harrington et al., 2020). However, though JAK inhibitors do possess high efficacy for treatment and are easy to administer, they still possess many

downsides. As a result of its high efficacy, the likelihood of adverse events occurring increases. This is demonstrated by a greater frequency of serious side effects, such as cardiovascular events or blood clots. Another crucial weakness to note compared to other treatments is specificity, as JAK inhibitors affect multiple signalling pathways, which ultimately leads to many potential side effects. They are also costly compared to OTC eczema treatments, costing tens of thousands of dollars (Table 1, Entry 4).

In general, the key advantages of utilising Manuka honey as an alternative medication relative to other common eczema treatments on the market are due to its inherent anti-inflammatory properties, along with its ability to retain moisture and reduce the severity of eczema flare-ups (Patel & Cichello, 2013). Though the Manuka honey has been demonstrated to possess these important qualities in the effective treatment of eczema, it still contains many disadvantages, which would make it an unreliable choice for dermatologists to prescribe to patients with eczema. The key disadvantages involve its cost, feel, lack of research and risk factor for allergies. Regarding its cost, relative to other commercial products for treatment, the same potency of treatment is offered at a comparable efficacy, whilst being more costly compared to over-the-counter (OTC) emollients or topical corticosteroids. Due to a severe lack of research into alternative medications like Manuka honey compared to commonly researched treatments, such as topical corticosteroids, a greater number of clinical trials must be performed in order to further determine how it compares against traditional and modern treatments. Furthermore, it has been reported to feel very sticky and greasy, which a patient may find uncomfortable in daily life, especially with the frequency of application, compared to an emollient, which may be both soothing and won't feel as greasy. Many patients with allergies to pollen or bees, as stated previously, will not be able to use this medication; therefore, its versatility is substantially hindered by this factor compared to a topical corticosteroid (Alhabsi et al., 2026). Lastly and overall, there is still only preliminary evidence for its potential antibacterial benefits and lesion improvement; therefore, no large randomised controlled trials (RCTs) confirm superiority over standards, and it is not recommended in major guidelines as a primary treatment (Table 1, Entry 5). However, it is important to note that, compared with the other treatments discussed in the traditional and modern approaches, the figures for Manuka Honey are drawn from different trials with different patient populations, disease severity, and primary endpoints. As a result, it is vital to note that the interpretations of these trials may not be as strong, due to the lack of direct head-to-head clinical data to mitigate bias accordingly.

For acupuncture overall, the drawbacks outweigh the advantages due to the multiple side effects, which may be presented if in the care of an inexperienced medical professional, who may not be effective and accurate at inserting the needles into the patient, leading to multiple side effects occurring. Though it does have a few advantages, much research has been invested in the safety and efficacy of treating eczema with acupuncture, and studies have shown that when an experienced practitioner performs the treatment, eczema symptoms can be substantially reduced, and it is relatively safe. However, again, it still comes with very adverse side effects. It also needs to be considered that it is very costly compared to many OTC medications, such as topical corticosteroids, as an experienced practitioner of acupuncture is costly, yet necessary to ensure safety. Furthermore, though as stated previously, there has been a bit of research that has been invested into acupuncture, many other commercial treatments are even more rigorously evaluated and tested in clinical trials to be safer, more potent and cheaper. Lastly, the systematic reviews of acupuncture show mixed and low-quality evidence overall, with some mild itch and symptom reduction, which unfortunately come with heavy risks such as pain and infection, and the severe lack of thorough and evaluative trials makes it unreliable compared to conventional options (Zeng et al., 2021). Therefore, though through these findings

the data does show the implication that overall acupuncture may not be a preferred option of treatment, it is still important to note that these interpretations should be approached with caution, being primarily preliminary insights.

Table 1. Summary of primary, secondary and alternative eczema therapies: a comparison of treatment types, their delivery methods, efficacy, evidence level, main advantages and clinical limitations.

Entry	Type	Target	Delivery	Evidence	Advantages	Limitations
1	Emollients	Skin	Topical	High	OTC, cheap, hydro-retentive	Low potency, frequent application, potential pore clogging
2	Corticosteroids	Skin	Topical	High	OTC, safe, versatile potency, affordable	Potential adverse side effects, variable pricing
3	Biologics	Thigh or abdomen	Injection	Medium	High potencies and efficacy	Need for injection, costly, potential adverse side effects
4	JAK inhibitors	Skin and immune system	Oral or topical	High	High efficacy, easy to administer	Lack of specificity, high frequency of side effects, and costly
5	Alternative meds	Skin	Various	Low	Unproven	Adverse side effects, costly, unsafe, lack of thorough and evaluative trials

Overall, the treatments summarised in Table 1 highlight the need for a personalised approach. Healthcare providers should evaluate severity using the EASI index and weigh the risk-benefit profile of each option. Selecting the optimal strategy requires balancing clinical efficacy with patient preferences to support long-term treatment adherence.

4. Conclusion

In conclusion, after extensive evaluation of many eczema treatments, modern and traditional approaches do remain the key treatments for both research and current usage. For traditional treatments, they remain reliable and affordable due to extensive research into the efficacy and safety of emollients and topical corticosteroids, as well as ways to reduce costs, which, as a result, leads to their prescription by more medical practitioners. For modern treatments, they remain an optimistic avenue for innovation and research, due to their potency and efficacy, though more research needs to be put towards reducing the frequency of adverse side effects, as well as making these treatments more accessible to the average person, due to the costly nature of JAK Inhibitors or Biologics, leading to substantial out-of-pocket costs for patients. Alternative medicines remain an area of scepticism, and rightly so, though research has been heavily invested in their safety and effectiveness. For the same effectiveness, both traditional and modern approaches to eczema treatment outperform alternative treatments, making them unreliable and rarely used in treatment. Therefore, overall, eczema treatments remain very promising for further research and innovation to optimise and refine both traditional and modern treatments in terms of cost, adverse side effects, and efficacy.

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Data & Code Availability Statement

No new raw data or software code were generated or analysed during this study. All data evaluated in this review were obtained from previously published literature and publicly available clinical trial registries at ClinicalTrials.gov. All primary sources and trial identifiers (NCT numbers) are cited within the article.

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The author is grateful to his mentor, Dr Daria Sokolova, for her guidance and support throughout the research and writing processes for this literature review. Figures in the literature review are credited and referenced.

Author Biography

Nathan Shiu is a 16-year-old student studying in the United Kingdom who attends Dulwich College. He has a strong interest in Medicine and Biochemistry due to a profound interest in the importance of healthcare in the wider community. His current academic efforts lie in understanding the efficacies of lab-made painkillers and how they compare against over-the-counter painkillers. Outside of academic research, Nathan is the President of the Junior Doctors' Society, a founder of an Impact 500 project aiming to raise awareness and funds for the charity Doctors in Distress and a writer in the Pursuit of Knowledge article in their school.

Mentor Contribution Statement

Mentor, Dr Daria Sokolova, has helped in advisory and supporting roles throughout the process of this literature review.

I am satisfied with the revisions the student has made in response to my comments. I have also reviewed the improvements made with respect to reviewer 1 and find that the student has made significant effort to improve their level of critical engagement with the scientific claims made by the articles reviewed; I am happy with these improvements. Overall the paper is well written and at a level far exceeding what is expected from high school students, therefore I am happy for it to be accepted now.

Dear Reviewer,

Thank you for your thorough and constructive feedback on the manuscript, "Eczema treatments: A review of their effectiveness, limitations and future directions". We greatly appreciate the time you took to identify both the core conceptual issues and the minor points, as your comments have significantly improved the clarity, accuracy, and scientific rigour of the paper.

We have carefully addressed each of your concerns in the revised version. Below, we outline the specific changes made in response to your points:

Reviewer Comment 1: Minor Correction

The student did well to correct the methodology section by noting that studies were not formally appraised for risk of bias. However, the original text was not removed and still states that bias mitigation was achieved. Please remove: "…which allowed me to achieve methodological rigour in mitigating bias, ensuring clinical relevance and statistical validity."

The primary strategy utilised for the identification of relevant literature reviews was through the thorough evaluation of key sources found on Google Scholar or ClinicalTrials.gov. The searching strategy was conducted using MeSH filtering and evidence-based analysis for clinical trials. It is important to note that included studies were not formally appraised for risk of bias and may therefore be subject to bias. Including terms such as "Biologics" and "Emollient efficacy" was vital in being able to filter relevant information when using keyword searching for Google Scholar. The reason for which a third database was not used during the research into the manuscript was that Google Scholar already yields many of the journals which are indexed in PubMed, thus, its usage as a third database would yield nearly completely similar results. As a result usage of PubMed was used slightly in the initial research phase, though nearly similar papers would also appear on Google Scholar, as a result, citations were primarily sourced from Google Scholar.

Reviewer Comment 2: Literature review engagement

Thank you to the student's response, which highlights the evaluation of each treatment section and that treatments are compared in each subsection. A point was also added on healthcare providers requiring to assess risk-benefit profiles. However, my overall comment is not addressed, which is that paper needs more evaluation and critical engagement. Initially, I provided one example where the paper could introduce evaluation (e.g., one potential way is providing interpretations in terms of comparative drug efficacy & safety). Given that this was not actioned, I explicitly outline possible critical engagement for the paper to reach publication level. I have provided examples how critical engagement could strengthen the paper's sections on JAK's efficacy and biologic safety, shifting the papers descriptive synthesis to include critical engagement with the literature. These examples illustrate evaluative avenues to consider. Note, critical engagement does not necessarily need to be drug-to-drug comparisons to address my point that the paper is largely descriptive but is one example.

We thank the reviewer for this perspective, which strengthened our discussion, and we have added evaluations accordingly to reflect the modification the reviewer suggested. The following information was added to the indicated line numbers in the revised manuscript.

Lines 293-299:

When reviewing the trial results for JAK inhibitors, ruxolitinib seems to achieve impressive skin clearance rates. However, comparing these numbers directly to oral treatments causes methodological issues. Ruxolitinib is a topical cream tested on localised eczema patches over just four weeks. In

contrast, upadacitinib (50% achieving an IGA score of 0 or 1) and abrocitinib (48.3%) are daily oral tablets tested in patients with moderate-to-severe disease over twelve to sixteen weeks. The clinical trials had completely different time frames, baseline severity levels, and measuring points. Because the study setups vary so much, researchers cannot claim that one inhibitor works best without direct head-to-head trials or a network meta-analysis.

Lines 250-256:

Though there is a positive correlation between clinical safety and efficacy, a majority of adverse events are minor, such as injection site reactions or mild conjunctivitis, and only a small percentage of these adverse events are serious; as the minor adverse events do not infer or correlate with worse efficacy, it should be concluded that there is no direct cause-and-effect relationship between safety and efficacy in the administration of dupilumab. This suggests a future investigation into the direct relationship between safety and efficacy as a clinical trial to mitigate bias in future research. It should also be noted that due to the method of administration being through injection with a needle, there would be a high prevalence of injection site reactions expected.

Lines 222-226:

Individual patient traits also change how someone responds to a biologic. Having a past history of eye disease or certain allergic tendencies can increase the chance of getting conjunctivitis. At the same time, age and body weight affect how quickly a drug clears the body. An insufficient dose can easily make a drug look ineffective, when the real issue is simply underdosing. Grouping trial participants by baseline traits and physical profiles will be an important step toward personalised prescribing.

Lines 236-239:

Suggestions that lebrikizumab has a safer profile than dupilumab should be taken with caution. While both biologics met standard phase III licensing requirements, lebrikizumab has not been used in the real world for nearly as long. Variations in reported side-effect rates between trials may reflect differences in study protocols as well as patient groups rather than true biological differences. Direct, active-comparator trials are the only way to resolve this.

Lines 194-199

Decades of medical use show that topical corticosteroids clear eczema lesions effectively, but doctors always have to balance this benefit against the risk of side effects. Using potent steroids over long periods can cause skin thinning, visible blood vessels, and even internal hormonal suppression. Because we already know these creams work, more standard efficacy trials would add little new knowledge. Instead, upcoming research needs to focus on application schedules. For example, studies could test proactive weekend therapy against reactive, on-demand use to determine which method keeps symptoms under control with the lowest overall amount of steroid exposure.

Lines 143-146:

Emollients sit in a completely different category of eczema care. Because they simply repair the physical skin barrier and do not target specific immune mechanisms, it does not make sense to test them head-to-head against systemic biologics. The more relevant research question is how daily, consistent moisturising can reduce the overall amount of steroid cream a patient needs over time.

Lines 361-364:

With acupuncture, adverse reactions usually happen because of specific existing risks, such as open skin lesions, bleeding disorders, or taking blood thinners. Future research into acupuncture should concentrate on creating clear patient screening checklists and running sham-controlled trials to see whether it provides real medical value as an add-on therapy.

Lines 347-350:

Finally, Manuka honey cannot yet be fairly compared with licensed medical treatments. The available evidence comes mostly from small, uncontrolled observational studies that lack placebo controls. Until researchers conduct proper randomised, placebo-controlled trials, claims about how well it works compared with conventional therapies remain unproven.

We believe these revisions resolve the core issues you raised and make the paper much stronger and more suitable for peer review.

Thank you again for your insightful critique, as it has been invaluable. We would be happy to make further adjustments if needed or provide additional clarifications.

Sincerely,

Nathan Shiu

Dear Reviewer,

Thank you for your thorough and constructive feedback on the manuscript, "Eczema treatments: A review of their effectiveness, limitations and future directions".

We have carefully addressed your concern regarding the figure in the revised version. Below, we outline the specific change made in response to your point:

Reviewer Comment 1: Minor Correction

A few minor points - is it possible to have a better diagram of octodecane as Convergence is an interdisciplinary journal, the chemical structure presented uses organic chemistry conventions which might not be immediately accessible to the reader?

The reviewer's comment is well taken, and we appreciate the opportunity to clarify this point. *Therefore, we have removed the diagram and citation of octadecane to reduce cognitive load for readers outside chemistry, given the paper's medical and biological focus and the journal's interdisciplinary scope.*

We believe this revision resolves the core issue you raised. Thank you again for your insightful critique, as it has been invaluable.

Sincerely,

Nathan Shiu

Final decision for: *"Eczema treatments: A review of their effectiveness, limitations and future directions"*

Decision: *Accept with minor revisions*

The student has put in great effort to improve the paper based on the received feedback. The paper has been substantially strengthened and some good evaluative sections having been added throughout. Interesting avenues of research have also been suggested with clear explanations. Very well done for the revisions! The paper meets standards for publication following remaining minor revisions.

Minor revision:

i) Please make sure that any new evaluative statements are appropriately supported by citations where relevant. For example: "a majority of adverse events are minor, such as injection site reactions or mild conjunctivitis, and only a small percentage of these adverse events are serious [**citation needed**] …" should be supported by a reference or even better quoting the exact numbers with the citation.

ii) Please double-check that the following is removed in the final version: *"…which allowed me to achieve methodological rigour in mitigating bias, ensuring clinical relevance and statistical validity"*. I appreciate that the student's response removed this text, but it still appeared in the tracked-changes document and the final version I received. Please double-check the text has been removed.