Review Article

Topical Integrative Treatments for Pruritus: A Comprehensive Review

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Background

Pruritus is one of the most common symptoms experienced by patients and can be a significant burden in daily life. A wide variety of topical treatment options are available for itch.

Objective

This review aims to provide a comprehensive summary of integrative/alternative topical treatment options for pruritus.

Methods

A comprehensive review of the literature regarding integrative topical treatments for itch was conducted using PubMed and PubMed Central.

Results

Some of the most commonly utilized integrative topical treatments for pruritus include oatmeal baths, urea cream, various herbal and botanical dressings/oils, cannabinoids, topical vitamin B12 and vitamin E, and honey.

Conclusion

Pruritus remains a challenging symptom to manage, despite the availability of a wide range of both conventional and unconventional treatment options. Utilizing an integrative approach may help decrease symptom severity and improve quality of life for patients with pruritus.

INTRODUCTION

Itch, also known as pruritus, is a common and non-specific symptom characterized by an uncomfortable sensation that prompts a desire to scratch.[1] Chronic pruritus is a frequently reported complaint, with the estimated 12-month cumulative incidence of chronic pruritus being approximately 7%.[2] While itch may be common, its impact on quality of life should not be underestimated: chronic itch has been proven to have significant impacts on sleep, personal relationships, mood, and overall well-being.[3]

Pruritus can be a challenging symptom to manage clinically due to its variable presentation, complex pathophysiology, and wide range of etiologies.[4] There are many available treatment options for patients with pruritus. Some of the most commonly used treatments come in the form of topical creams, lotions, and oils. Topical treatments for pruritus include commonplace conventional therapies including topical corticosteroids, emollients, and calcineurin inhibitors, as well as alternative and complementary therapies including oatmeal, various herbal/botanical formulations, cannabinoids, and honey. Despite the plethora of options, unmet needs remain in treating itch. In a survey of dermatologists, chronic pruritus was rated as having the highest level of unmet need among 9 dermatologic conditions.[5] Perhaps because of these therapeutic gaps, concerns about safety, and sometimes simply to find care more congruent with their own values, many patients seek treatments outside of the evidence-based pharmacologic canon of therapy (See Table 1).[6]

PATHOPHYSIOLOGY OF ITCH

The physiologic pathways involved in the sensation of itch in humans are complex and have yet to be fully characterized. However, ongoing research on the pathogenesis of pruritus has identified promising therapeutic targets that have revolutionized the treatment of this distressing symptom. It is well understood that the sensation of itch is transmitted in the skin via type C and type Aδ nerve fibers when exogenous and/or endogenous pruritogens bind to their sensory receptors.[4] Research has identified numerous pruritogens involved in itch. The most well-studied pruritogens are Th2 cytokines (interleukin-4, interleukin-13,

interleukin-31, interleukin-33, thymic stromal lymphopoietin), which utilize Janus kinase (JAK) pathways to produce the sensation of itch.[4]

Itch can be caused by a wide variety of etiologies, including dermatologic, renal, hepatobiliary, paraneoplastic, psychogenic, and neuropathic causes.[1] Some of the most common dermatologic diagnoses associated with pruritus include atopic dermatitis, psoriasis, lichen planus, prurigo nodularis, cutaneous malignancies, and bacterial, fungal, viral, or parasitic skin infections.[1] Of the many non-dermatologic diagnoses that also often present with pruritus, some of the most common include chronic kiney disease, cholestatic liver disease, diabetes, hyperthyroidism, systemic sclerosis, systemic lupus erythematosus, polycythemia vera, Hodgkin lymphoma, and iron-deficiency anemia.[1] In all of these etiologies, the type of itch produced can be broadly categorized into itch that follows either histaminergic or non-histaminergic pathways.[4] The histaminergic itch pathway is typically responsible for the acute sensation of itch and is mediated by mast cell, basophil, and/or keratinocyte release of histamine.[4] A wide range of receptors and pruritogens other than histamine released from mast cells, granulocytes, macrophages, lymphocytes, keratinocytes, neurons, and basophils can be involved in non-histaminergic itch pathways, and these tend to be more chronic forms of itch, often the ones seen presenting to dermatology.[4]

METHODS

In March 2024, an extensive literature review was conducted by two independent reviewers on integrative approaches to pruritus. This review utilized a comprehensive search of both PubMed and PubMed Central, spanning publications from 1987 through early March, 2024. The search included clinical trials, systematic reviews, and literature reviews, all available in English to maintain linguistic consistency. Search terms employed included "topical pruritus treatment," "topical itch treatment," "integrative pruritus treatment," "integrative itch treatment," "alternative pruritus treatment," and "alternative itch treatment."

INTEGRATIVE TOPICAL TREATMENTS FOR ITCH

BOTANICAL OILS

COCONUT OIL

The use of topical coconut oil application for itch relief has been studied in the contexts of atopic dermatitis and uremic itch.[7,8] Coconut oil is rich in medium-chain fatty acids, making it an excellent emollient and occlusive agent. In vitro studies have also found coconut oil to have anti-inflammatory and antioxidant properties that can help improve skin barrier function.[9] Coconut oil also contains monolaurin, a short-chain fatty acid compound with antimicrobial properties.[10]

In a study by Muliani et al, topical application of virgin coconut oil was found to be effective in reducing symptoms of pruritus in patients on hemodialysis for chronic kidney disease.[7] A randomized clinical trial studying the effects of topical virgin coconut oil in pediatric patients with atopic dermatitis also found that treatment with virgin coconut oil decreased pruritus scores in patients and also improved skin barrier function.[11] Another study found that 3 months of treatment with topical coconut oil with vitamins A and E decreased pruritus severity scores in pediatric patients with cholestatic liver disease.[12]

SWEET ALMOND OIL

Sweet almond oil contains essential fatty acids including oleic, linoleic, palmitic, and stearic acids.[13] These essential fatty acids reduce itching and inflammation and protect the skin, and deficiencies in essential fatty acids are thought to play a role in the pathogenesis of pruritus.[13] In a randomized control trial involving 42 patients with uremic pruritus on hemodialysis, topical application of sweet almond oil for two weeks was found to significantly reduce uremic pruritus symptoms.[13]

In another study of 20 patients with pruritus related to end-stage renal disease, massage with a mixture of mint, lavender, and tea tree oils diluted to 5% in sweet almond oil was found to relieve symptoms of pruritus.[14] Furthermore, a study of 80 patients with uremic pruritus found that aromatherapy massage with lavender, tea tree, almond, and jojoba oils significantly reduced pruritus severity.[15] However, since these studies did not investigate the effects of sweet almond oil in isolation, the effects of the treatment can not be credited with certainty to the sweet almond oil in the mixture.

CLOVE OIL

Clove, a fragrant plant prevalent in tropical climates, is high in antioxidants and has gained widespread attention for its many applications including utility in perfume, food, and health industries.[16] In dermatology, clove oil has been of interest due to its anti-inflammatory and wound-healing effects. Eugenol, one of its active ingredients, is thought to reduce itch by inhibition of COX-2 expression and subsequent reduction in synthesis of inflammatory mediators.[16]

A clinical trial was conducted by Ibrahim et al to investigate clove oil's potential utility in relieving pruritus. Fifty patients who had been diagnosed with chronic pruritus resulting from a range of diseases, such as renal, hepatic, and diabetic were divided into two groups of 25 participants each. Group II applied petrolatum topically, and Group I was instructed to moisturize their skin before applying topical clove oil.[17] The 5-D itch scale was used to evaluate treatment efficacy. Results indicated a significant improvement in all of the individual parameters on the 5-D itch scale for clove oil users. No significant treatment effect was seen in the petrolatum group. A comparison of total scores on the 5-D itch scale between the two groups indicated a significantly greater improvement with clove oil than with the placebo/petrolatum ($P>.05$).[17]

PEPPERMINT OIL

Peppermint, a flowering herb native to North America and Europe, has a long history of medical use.[18] The oil, obtained from fresh leaves via steam distillation, has several benefits including antibacterial and anti-inflammatory properties as well as the ability to modulate psychosocial stress. Peppermint oil has also been shown to affect the physiology of the esophagus, stomach, small intestine, and gallbladder.[18] In the context of itch, peppermint oil is thought to reduce the sensation of itch by cooling the skin and activating A-delta and k-opioid receptors, creating a mild analgesic effect.[19] Despite the popularity of topical peppermint oil treatments in dermatology, published research on the subject remains scarce.[20]

Elsaie et al conducted a study to evaluate the efficacy of topical peppermint oil in treating chronic pruritus stemming from hepatic, renal, or diabetic causes.[20] The 5-D itch scale (5D-IS) was used to assess outcomes. Results indicated that topical peppermint oil treatment resulted in a significant reduction in pruritus compared to the control group across all domains measured—duration, degree, direction, disability, and distribution (P-value <0.05).[20] In another study by Akhavan Amjadi et al, twice daily topical application of peppermint oil was shown to decrease severity of itching associated with pregnancy (pruritus gravidarum).[19] The efficacy of this treatment has also been studied in the context of treating pruritus associated with burn-induced hypertrophic scars.[21] In a study by Wu et al, daily application of a formula containing peppermint oil, menthol, and methyl salicylate was found to significantly reduce pruritus severity in 74 patients with severe intractable pruritus due to burn-induced hypertrophic scars.[21]

OTHER BOTANICAL FORMULATIONS/EXTRACTS

OATMEAL

Oatmeal is a natural substance with a high safety profile and a long history of treating dermatological diseases due to its antioxidant and anti-inflammatory properties.[22] The anti-itch properties of oat-derived treatments are thought to be mediated by phytochemicals known as avenanthramides.[10,23] Avenanthramides inhibit activation of NF-kB, thereby reducing local inflammation and associated itch.[10,23] In a study by Sur et al using a murine itch model, topical application of isolated avenanthramides effectively reduced oxazolone-induced contact hypersensitivity, resiniferatoxin-induced neurogenic inflammation, and histamine-mediated itch.[23]

Oats can be used as a topical treatment for pruritus in various ways, including oatmeal baths, oat oil, and oat oil-based creams.[10] The oatmeal bath treatment contains 100% natural colloidal oatmeal, which is produced by grinding and boiling oats to extract a mixture mainly consisting of starch (65-85%), protein (15-20%), lipids (3-11%), fiber (5%), and beta-glucans (5%).[22] 15-20 minutes of soaking in a bath containing this colloidal oatmeal substance cleans and soothes sensitive skin.[22] Oatmeal baths have been shown in numerous trials to be effective in reducing pruritus. Matheson et al conducted a comparative study to determine the efficacy of two bath and shower oils in relieving pruritus in burn patients. One product had liquid paraffin and 5% colloidal oatmeal, whereas the other only contained liquid paraffin. The formulation including colloidal oatmeal considerably reduced itching and resulted in a significant decrease in antihistamine use among patients.[24] Oat oil-based lotion has also been shown to improve symptoms of itch, as demonstrated in a study by Southall et al. in which 29 patients with severe xerosis and itch underwent a 2-week treatment course with daily topical oat oil-based lotion application.[25]

CANNABINOIDS

Throughout history, cannabis has been utilized for industrial, medical, and recreational purposes. The medicinal applications of cannabinoids have been gaining public attention in recent years, resulting in a subsequent increase in clinical trials and research. The biologically active compounds in cannabis, known as cannabinoids, are divided into three main groups: endocannabinoids, phytocannabinoids, and synthetic form.[26] Endocannabinoids are naturally produced in the human body and play a crucial role in maintaining skin homeostasis. Phytocannabinoids are naturally derived from Cannabis plants, and synthetic cannabinoids are produced chemically in laboratories.[26]

Cannabinoids are ligands for cannabinoid receptors CB1R and CB2R. Previous studies have shown that both receptors are present in various skin components, such as keratinocytes, mast cells, hair follicles, and sensory nerve fibers. Generally, increased activity at these receptors has been associated with a reduction in pruritus.[26,27]

In a study by Yuan et al, 60 patients with asteatotic eczema were enrolled in a double-blind randomized controlled trial. After 4 weeks of treatment with an emollient cream containing 0.3% N-palmitoylethanolamine (PEA) and 0.21% N-acetylethanolamine (AEA), the majority of patients experienced significant improvements specifically in the part of the Eczema Area and Severity Index assessing itch severity.[28]

An observational cohort study of 2456 pediatric and adult patients with atopic eczema also demonstrated that treatment with a cream containing PEA led to “very much improved” or “improved” intensity of itch in 82.5% of patients.[29] In another study of 21 patients with uremic pruritus on hemodialysis, 3 weeks of treatment with a cream containing PEA and AEA was shown to significantly decrease pruritus, with 8 patients experiencing total resolution of pruritus.[30]

CHAMOMILE

Chamomile is one of the oldest medicinal herbs known to mankind. Chamomile tea and herbal extracts are prepared from the dried flowers of *Matricaria* species, containing numerous terpenoids and flavonoids that contribute to its medicinal properties.[31] Chamomile is thought to have anti-pruritic effects via inhibition of pro-inflammatory cy-

tokines, improvement of skin hydration and barrier function, effects on the metabolism of arachidonic acid, and interaction with sensory nerve endings that modulate itch signal transmission.[32,33] Chamomile has also been shown to have anti-allergic properties via inhibition of mast cell degranulation and decrease in histamine release.[34]

In a randomized study with 72 patients observing the effects of a proprietary chamomile extract-containing cream on the symptoms of atopic eczema, a 2-week treatment course with the cream was shown to be more effective than both placebo and hydrocortisone 0.5% cream in relieving pruritus.[32] Studies have also shown that topical application of 8% chamomile gel was effective in reducing itch in patients with dermatitis secondary to radiation treatment for head and neck cancer, and the use of twice daily chamomile compresses was more effective than 1% hydrocortisone ointment in relieving itch associated with peristomal skin lesions in colostomy patients.[35,36]

CALENDULA

Calendula officinalis, otherwise known as marigold, is an herbaceous flowering plant with a long history of medicinal use in a variety of contexts including digestive problems, headaches, wounds, menstrual irregularities, and more.[33] In the treatment of skin conditions, *Calendula* has been recognized for its anti-inflammatory, immunomodulatory, healing, antibacterial, and antifungal properties.[33] The flowers, roots, and leaves of *Calendula* contain many bioactive compounds including terpenes, phenols, and alkaloids.[33] While the mechanism by which *Calendula* relieves pruritus has not yet been elucidated, *Calendula* is thought to improve skin barrier function due to its high fatty acid content and attenuate inflammation.[33]

Studies have investigated the use of topical *Calendula* in various formulations including creams, oils, and gels. While studies on the impacts of *Calendula* on itch in particular remain limited, *Calendula* has been reported to decrease itch severity in patients with vaginal dystrophy associated with menopause, bacterial vaginosis, xerosis with pruritus, and diabetes-related foot injuries/infections.[37-40]

ALOE VERA

Aloe vera is a green cactus-like plant from the *Liliaceae* family that produces a colorless, mucilaginous gel, which is widely used for both medicinal and cosmetic purposes.[41] Because aloe vera possesses anti-inflammatory, antibacterial, and wound-healing qualities, it has long been used to treat digestive problems and skin injuries like burns, wounds, insect bites, and eczema.[42]

Mahboub et al conducted a study to compare the effects of silver sulfadiazine cream and aloe vera gel on first- and second-degree burns.[43] While both groups' wounds healed fully in two weeks, the wounds of patients in the group being treated with aloe vera gel healed more quickly. Interestingly, both groups' wound itching peaked on day seven, but drastically decreased 30 minutes after using aloe vera gel, revealing the plant's powerful calming properties.[43] Aloe vera was also shown in a double blind, placebo-controlled clinical trial to significantly reduce pruritus and scaling in 58% of patients with seborrheic dermatitis.[44] Studies have also reported that topical aloe vera decreases itching in psoriasis, atopic dermatitis, and xerosis.[33]

TEA DRESSINGS/BATHS

Black tea is made by soaking the oxidized leaves of *Camellia sinensis* in hot/boiling water and has been suggested to have anti-inflammatory properties.[45] Since facial skin is thinner and more susceptible to topical corticosteroid-related skin atrophy, black tea dressings are commonly used in Germany as a non-steroidal topical intervention for facial dermatitis.[45] While the mechanisms by which black tea dressings reduce itch are still unclear, astringent compounds found in black tea like tannins and flavonoids are thought to play a role.[45] The therapeutic effects of black tea dressings can also be further enhanced by the subsequent application of emollient cream to help repair epidermal barrier damage and reduce inflammation.[45] A small study on the effects of treatment with black tea dressings and subsequent cold cream (mixture of peanut oil, water, cetyl palmitate, and yellow wax) application in 22 patients with facial dermatitis found that this treatment regimen significantly decreased pruritus by day 3 of treatment.[45] One adverse event (eczema herpeticum) was reported, however, this was determined not to be related to the black tea dressing treatment.[45]

Similarly, green tea baths have been studied and suggested to be an effective treatment for itch in atopic dermatitis, specifically AD associated with *Malassezia sympodialis* infection.[46] Green tea is rich in catechins, which have been found to have antioxidant, antimutagenic, antibacterial, and antitumor properties.[46] In a small clinical study of four pediatric patients with *Malassezia*-related atopic dermatitis, bathing in green tea (700 mL of 5% extract in 150 L of filtered water at 37° C) for 30 minutes 3 times a week for 4 weeks led to a marked decrease in pruritus and no serious adverse effects were reported during the study.[46]

ST. JOHN'S WORT

St. John's wort (*Hypericum perforatum*), a flowering plant native to Europe and Asia, has been primarily used as an over-the-counter antidepressant for many years. Additionally, it exhibits anti-inflammatory and anti-neoplastic properties due to its anthraquinone content.[47] The use of St. John's wort in dermatological applications has been explored in several clinical trials and pilot studies.[48,49]

In one such study, Mansouri et al conducted a double-blind, placebo-controlled pilot study involving twenty patients with mild to moderate plaque-type psoriasis. Participants were treated with St. John's wort ointment and a placebo, each applied to opposite sides of the body twice daily for four weeks. Clinical evaluations and two punch biopsies from symmetrically preferred lesions on both sides were performed to assess and compare treatment outcomes. The results showed a significant reduction in overall disease severity after one month of treatment with the St.

John's wort ointment, with pronounced decreases in thickness, scaling, and pruritus scores.[48]

In another study, Schempp et al conducted a placebo-controlled, double-blind clinical trial involving twenty-one patients to assess the efficacy of a cream containing St. John's wort extract, standardized to 1.5% hyperforin (verum), in comparison to a placebo for treating subacute atopic dermatitis. Treatment with either verum or placebo was randomly assigned to either the right or left side of the body, and patients were treated twice daily for four weeks. The group receiving the St. John's wort extract/verum treatment reported significant improvements in eczematous lesions, and the treatment was well-tolerated.[49]

LICORICE ROOT

Originating from the root of the *Glycyrrhiza glabra* plant, licorice has been valued for its extensive range of therapeutic benefits since ancient times, particularly as a traditional herbal medicine in China.[50,51] It is traditionally used to treat gastrointestinal and liver diseases, as well as oral and skin diseases. Human intestinal microflora converts the active component, glycyrrhizin, into glycyrrhetinic acid, which inhibits 11β-hydroxysteroid dehydrogenase (11β-HSD) and mimics the effects of corticosteroids.[51]

Due to licorice's renowned anti-inflammatory properties, its effectiveness has been explored in treating various skin conditions. Saeedi et al conducted a double-blind clinical trial with 60 patients to investigate the impact of licorice extract (1% and 2%) vs. a base gel applied topically on atopic dermatitis.[52] Reduction in erythema scores was 35.02% for the 1% licorice extract and 60.76% for the 2% licorice gel. Additionally, oedema scores decreased by 56.64% with the 1% licorice group and 83.76% with the group receiving the 2% formulation. Itching scores also saw significant reductions, dropping 44.1% for the 1% gel and 72.53% for the 2% gel by the conclusion of the study.[52] In another study, treatment with shampoo containing glycyrrhetinic acid was shown to significantly decrease pruritus in patients with seborrheic dermatitis.[44]

TURMERIC

Turmeric is a yellow-colored spice used in cooking, cosmetics, and as a natural medicine.[53] The active phytochemical in turmeric, curcumin, has been shown to have anti-inflammatory, antimicrobial, antioxidant, and anti-neoplastic properties.[53] Turmeric can be used both orally and topically in the treatment of a variety of diseases including dermatologic conditions like skin eruptions and infections.[53] Studies have also demonstrated topical turmeric formulations' efficacy in treating symptoms of itch/pruritus in atopic dermatitis, uremic pruritus, and itch related to external cancerous lesions.[53,54] The biochemical mechanism used by turmeric to alleviate itch remains unknown, however it has been hypothesized that turmeric reduces itch by acting on TNF-a, IL-4, IgE-antigen complexes, and compound 48/80.[33]

SANGRE DE DRAGO (AMAZONIAN DRAGON TREE RESIN)

Sangre de drago (Dragon's blood) is a natural resin from the Amazonian dragon tree (*Croton lechleri*) that reduces neurogenic cutaneous inflammation via the inhibition of substance P release.[55] *Sangre de drago* is used both topically and orally as a natural medicine by indigenous cultures of the Amazon River basin for a number of afflictions including hives, sore throat, insect bites, wound healing, hemostasis, and diarrhea, but few scientifically rigorous studies have investigated the mechanisms and efficacy of this natural medicine.[56,57] While rodent studies have shown that the use of *Sangre de Drago* may decrease itch, clinical studies in human participants are severely lacking.[55] A small clinical study on the effects of a commercially available *Sangre de Drago* balm formulation on symptoms of insect bites/stings and other skin conditions in 10 pest control workers did find that all 10 participants reported itch relief with the use of the active balm, while the placebo balm offered itch relief in none of the cases.[56] Interestingly, symptom relief was reported to occur rapidly in less than two minutes on average, suggesting that the active compounds likely act on sensory afferent nerves.[56]

TOPICAL VITAMINS

VITAMIN B12 TOPICAL

Vitamin B12 has been shown to be an effective nitric oxide (NO) scavenger.[58] Excess nitric oxide (indicated by high levels of nitric oxide synthase in the skin) has been shown to be implicated in the pathogenesis of psoriasis and atopic dermatitis, which suggests that vitamin B12 may be useful in the treatment of these conditions.[58]

In a randomized placebo-controlled trial with 49 patients with atopic dermatitis, twice daily topical application of vitamin B12 cream (0.07% cyanocobalamin DAB) was found to reduce symptoms of atopic dermatitis with significant superiority over placebo.[58] The treatment was well tolerated with low safety risk, with only 6 cases of skin irritation being reported during the study (two "possible" and four "probable" cases related to the B12 cream treatment).[58]

TOCOTRIENOL (VITAMIN E)

Vitamin E is a natural phenolic antioxidant often found as an ingredient in skincare products thought to provide dermatologic benefits via stabilization of lipid bilayers of the stratum corneum and inhibition of lipid peroxidation.[59] Vitamin E is also thought to upregulate the expression of genes that drive keratinocyte differentiation, suggesting that vitamin E may provide therapeutic benefit in the treatment of atopic dermatitis.[59]

In a clinical study of 30 pediatric patients with atopic dermatitis, 12 weeks of treatment with a topical cream containing vitamin E in the form of α-, β-, γ-, and δ- tocopherols and tocotrienols and 3-O-ethyl ascorbic acid was found to significantly decrease pruritus intensity/severity, with a relative reduction of 46.3% over the 12-week treat-

ment course.[59] The treatment was very well tolerated, with no reported adverse reactions.[59]

OTHER/MISCELLANEOUS

COAL TAR

Coal tar is rich in phenols, polycyclic aromatic hydrocarbons and heterocyclic compounds and has been proven to have antimicrobial, anti-inflammatory, and antipruritic effects.[60,61] Coal tar is thought to exert these effects via restoration of filaggrin expression and activation of the aryl hydrocarbon receptor (AHR), thus counteracting Th2-mediated downregulation of skin barrier function.[62] Coal tar for topical use is often compounded with glucocorticoids, but steroid-free formulations using petrolatum or unguentum leniens are also available.[60] Coal tar is a second-line treatment for atopic dermatitis, and studies have also demonstrated efficacy in the treatment of psoriasis.[60,61]

Coal tar does have a variety of side effects that may limit its use including burning, local irritation, contact dermatitis, folliculitis, and phototoxicity.[60] Furthermore, its strong odor, tendency to stain skin and clothing, and poor cosmetic acceptance may deter patients from this treatment option and/or negatively impact patient compliance.[61,62] Overall, topical coal tar application is a long-standing treatment with moderate efficacy, but declining use in clinical practice.[62]

HONEY

Honey has long been used as a natural medicine in the treatment of various ailments. Honey has been shown to reduce inflammation, possess anti-microbial properties, promote wound healing, stimulate tissue regeneration, and more.[63,64]

In a study of 21 patients with moderate-to-severe atopic dermatitis or psoriasis vulgaris, topical application of a honey, beeswax, and olive oil mixture was shown to be effective in reducing symptoms of pruritus.[64] The treatment was also very well tolerated, with no side effects being reported during the course of the study.[64] In another study on 29 patients with recurrent cold sores, treatment with a medical grade honey-based formula was found to be more effective than conventional treatments in reducing itching.[63] Furthermore, the honey-based formula was preferred over conventional treatment by 100% of patients.[63] Lastly, in a study of 28 patients who had received split-thickness skin grafts on the scalp or face, treatment with an ointment containing 70% honey, 20% aloe vera, and 10% peppermint was shown to effectively reduce pruritus and was also associated with significantly better treatment satisfaction in comparison to standard treatment (petroleum jelly).[65]

VINEGAR

Vinegar, aside from its culinary utility, is also renowned for its antimicrobial properties and is produced through a two-step fermentation process involving yeast and Acetobacter, which converts sugars to ethanol and then acetic acid, resulting in a solution of acetic acid and water.[66,67] Historically, its dermatological applications date back to 420 BC when Hippocrates used it to treat wounds. Over the years, numerous clinical trials have explored its benefits in dermatology.[66]

In one such trial, Nakhaee et al studied 23 hemodialysis patients suffering from uremic pruritus, dividing them into three groups. The first group applied *Avena sativa* lotion twice daily for two weeks; the second group used diluted vinegar (30 mL synthetic white vinegar 5% in 500 ml of water); and the third group was treated with hydroxyzine tablets over the same period. Following a three-day washout period, the treatments were crossed over.[68] The effectiveness of each treatment was measured using a pruritus scale and a visual analogue scale before and after the interventions. The results showed that both vinegar and hydroxyzine significantly reduced all pruritus scale scores, providing strong evidence of vinegar's potential to treat pruritus.[68]

SERICIN CREAM

Sericin is a high molecular weight biopolymer derived from the silkworm (*Bombyx mori*) that functions as a moisturizer with anti-inflammatory properties.[69] Serine, the predominant amino acid in natural moisture factor (NMF), comprises 32% of sericin and contributes to its moisturizing properties.[69] Sericin is also thought to reduce inflammation by decreasing levels of TNF-α and IL-1β.[69]

In a study of 47 patients with uremic pruritus on hemodialysis, 6 weeks of treatment with a topical sericin cream significantly decreased symptoms of itching (from moderate to severe pre-treatment to mild post-treatment) and led to increased quality of life.[69]

SODIUM BICARBONATE BATH

Alkaline baths, particularly ones containing sodium bicarbonate, have long been utilized in the Mediterranean region to treat psoriasis. While the exact mechanism by which sodium bicarbonate baths reduce pruritus remain unknown, it is hypothesized that an alteration of pH may inactivate molecules or pathways involved in the pathogenesis of diseases associated with pruritus.[70] Sodium bicarbonate baths are also thought to have some keratolytic activity, as demonstrate by their efficacy in reducing hyperkeratosis in patients with psoriasis.[70]

In a study by Verdolini et al involving thirty-one patients with mild to moderate psoriasis, sodium bicarbonate baths (350-500 g of sodium bicarbonate dissolved in average 85 L of bath water) every other day for 3 weeks were found to result in considerable improvement at the end of the trial.[70] Participants noted improvements in itching and irritation and expressed intentions to use the treatment even after the study.[70]

While sodium bicarbonate baths have been reported to be effective in the prevention of aquagenic pruritus in some studies, other studies have documented treatment failure or loss of treatment efficacy over time.[71,72] While evidence for the efficacy of sodium bicarbonate for aquagenic pruri-

tus is mixed, it is a safe and low-cost intervention that may provide symptomatic relief.[71]

ICE/COOLING

Cooling the skin via the application of ice, cold air, or other cooling agents such as menthol has been shown to be effective in decreasing the sensation of itch.[73,74] Cooling the skin has been hypothesized to provide symptomatic relief of pruritus via vasoconstriction of blood vessels and subsequently decreased local release of pruritogens.[74] Cooling the skin is also thought to attenuate nerve membrane excitability and facilitate interactions between itch-mediating C fibers and cold-mediating Aδ fibers that may decrease the sensation of itch.[74]

In a study of 15 healthy volunteers, cold exposure (achieved by exposing the skin to CO2 snow-cooled air at ~8.2° C or topical 1% menthol solution application) was found to rapidly attenuate itch sensation in the setting of experimental histamine-induced itch.[74] Furthermore, in a study of 60 patients with pruritus secondary to chronic kidney disease on hemodialysis, treatment with a self-operated ice roller was found to significantly decrease pruritus severity as well as distribution of pruritus-associated body parts.[75] Given that cooling the skin via the application of ice is a simple, accessible, and low-risk treatment with proven efficacy, this alternative/integrative treatment may improve symptomatic relief in patients with pruritus, especially when utilized in combination with other conventional and/or integrative therapies.

CONCLUSION

Pruritus is a common, yet often difficult to manage symptom with a complex and not yet fully understood pathophysiology. Itch is associated with a diverse range of dermatologic, renal, hepatobiliary, paraneoplastic, psychogenic, and neuropathic conditions. There are many topical treatment options, both conventional and unconventional, that can be offered to patients suffering from this unpleasant and sometimes debilitating symptom. In order to optimize symptomatic relief and maximize quality of life improvement, it is important that providers engage patients in a thorough and collaborative conversation that includes discussion of integrative treatments when discussing treatment options for pruritus.

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No funding was secured for this study.

DISCLOSURE

PL reports being on the speaker's bureau for AbbVie, Arcutis, Eli Lilly, Galderma, Hyphens Pharma, Incyte, La Roche-Posay/L'Oréal, Pfizer, Pierre-Fabre Dermatologie, Regeneron/Sanofi Genzyme, Verrica; reports consulting/advisory boards for Alphyn Biologics (stock options), AbbVie, Almirall, Amyris, Arcutis, ASLAN, Bristol-Myers Squibb, Burt's Bees, Castle Biosciences, Codex Labs (stock options), Concerto Biosci (stock options), Dermavant, Eli Lilly, Galderma, Janssen, LEO Pharma, Lipidor, L'Oréal, Merck, Micreos, MyOR Diagnostics, Regeneron/Sanofi Genzyme, Sibel Health, Skinfix, Suneco Technologies (stock options), Theraplex, UCB, Unilever, Verdant Scientific (stock options), Verrica, Yobee Care (stock options). In addition, Dr. Lio has a patent pending for a Theraplex product with royalties paid and is a Board member and Scientific Advisory Committee Member emeritus of the National Eczema Association.

AP and LW have no financial relationships or conflicts of interest relevant to this article to disclose.

AUTHOR CONTRIBUTIONS

Study conception and design was by Dr. Lio. Literature search, article screening/review, and data extraction were performed by Aileen Park and Leo Wan. Data analysis was performed by Aileen Park and Leo Wan. The final draft of the manuscript was written by Aileen Park and Leo Wan. All authors contributed to the revision of previous drafts. The final manuscript was reviewed and approved by all authors.

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Table 1. Summary of integrative topical treatments for various etiologies of itch/pruritus

Integrative Topical Treatments for Itch			
Treatment Class	**Treatment**	**Mechanism of Action**	**Indications**
Botanical Oils	Coconut Oil	emollient, occlusive agent, anti-inflammatory and anti-oxidant	atopic dermatitis, uremic pruritus
	Sweet Almond Oil	anti-inflammatory, improvement in barrier function	uremic pruritus
	Clove Oil	anti-oxidant, anti-inflammatory (inhibits COX-2)	chronic pruritus due to hepatic, renal, or diabetic causes
	Peppermint Oil	antibacterial, anti-inflammatory	chronic pruritus due to hepatic, renal, or diabetic causes
Other Botanical Formulations/ Extracts	Oatmeal	anti-oxidant, anti-inflammatory	burn-related itch, histamine-mediated itch, contact hypersensitivity itch, neurogenic inflammation
	Cannabinoids	maintenance of skin homeostasis, reduction of itch by binding to cutaneous CB1R and CB2R receptors	eczema
	Chamomile extract	anti-inflammatory (effects on arachidonic acid metabolism)	atopic eczema, radiation dermatitis, itch associated with peristomal skin lesions
	Calendula officinalis	anti-inflammatory, immunomodulatory, healing, antibacterial, and antifungal	vaginal dystrophy, bacterial vaginosis, xerosis with pruritus, diabetes-related foot injuries/infections
	Aloe vera	anti-inflammatory, antibacterial	burn-related itch
	Tea dressings/ baths	anti-inflammatory, astringent properties	facial dermatitis, atopic dermatitis
	St. John's wort	anti-inflammatory, anti-neoplastic	plaque psoriasis, atopic dermatitis
	Licorice root	anti-inflammatory (glycyrrhetic acid inhibits 11β-hydroxysteroid dehydrogenase (11β-HSD) and mimics the effects of corticosteroid)	atopic dermatitis
	Turmeric	anti-inflammatory, antimicrobial, antioxidant, anti-neoplastic	atopic dermatitis, uremic pruritus, itch related to external cancerous lesions
	Sangre de drago	reduction of neurogenic inflammation (inhibition of substance P release)	itch due to insect bites/stings
Topical Vitamin Oils	Vitamin B12	nitric oxide (NO) scavenger	atopic dermatitis
	Vitamin E	antioxidant, lipid bilayer stabilization, upregulation of genes driving keratinocyte differentiation	atopic dermatitis
Other/ Miscellaneous	Coal tar	restoration of filaggrin expression, activation of the aryl hydrocarbon receptor (AHR)	atopic dermatitis, psoriasis
	Honey	anti-inflammatory, antimicrobial, wound healing, tissue regeneration	atopic dermatitis, psoriasis, cold sores
	Vinegar	antimicrobial	uremic pruritus
	Sericin cream	moisturizer, anti-inflammatory	uremic pruritus
	Sodium bicarbonate baths	unknown, potentially local alterations in pH inactivating itch-mediating molecules/pathways, keratolytic activity	psoriasis
	Ice/cooling	local vasoconstriction, mediation of interactions between itch-mediating C fibers and cold-mediating Aδ fibers	histamine-induced itch, uremic pruritus

REFERENCES

1. Roh YS, Choi J, Sutaria N, Kwatra SG. Itch: Epidemiology, clinical presentation, and diagnostic workup. *J Am Acad Dermatol*. 2022;86(1):1-14. doi:10.1016/j.jaad.2021.07.076

2. Matterne U, Apfelbacher CJ, Vogelgsang L, Loerbroks A, Weisshaar E. Incidence and determinants of chronic pruritus: a population-based cohort study. *Acta Derm Venereol*. 2013;93(5):532-537. doi:10.2340/00015555-1572

3. Yosipovitch G, Rosen JD, Hashimoto T. Itch: From mechanism to (novel) therapeutic approaches. *J Allergy Clin Immunol*. 2018;142(5):1375-1390. doi:10.1016/j.jaci.2018.09.005

4. Sutaria N, Adawi W, Goldberg R, Roh YS, Choi J, Kwatra SG. Itch: Pathogenesis and treatment. *J Am Acad Dermatol*. 2022;86(1):17-34. doi:10.1016/j.jaad.2021.07.078

5. High unmet need in severe chronic pruritus in the United... *Itch*. doi:10.1097/itx.0000000000000018

6. Astin JA. Why Patients Use Alternative Medicine. Accessed June 28, 2024. https://jamanetwork.com/journals/jama/fullarticle/187543

7. Muliani R, Vitniawati V, Rakhman DA. Effectiveness of Olive Oil with Virgin Coconut Oil on Pruritus Grade Scores Among Hemodialysis Patients. *Int J Adv Life Sci Res*. Published online October 1, 2021:25-33. doi:10.31632/ijalsr.2021.v04i04.004

8. Hussain Z, Thu HE, Shuid AN, Kesharwani P, Khan S, Hussain F. Phytotherapeutic potential of natural herbal medicines for the treatment of mild-to-severe atopic dermatitis: A review of human clinical studies. *Biomed Pharmacother Biomedecine Pharmacother*. 2017;93:596-608. doi:10.1016/j.biopha.2017.06.087

9. Varma SR, Sivaprakasam TO, Arumugam I, et al. In vitro anti-inflammatory and skin protective properties of Virgin coconut oil. *J Tradit Complement Med*. 2019;9(1):5-14. doi:10.1016/j.jtcme.2017.06.012

10. Natural Oils for Skin-Barrier Repair: Ancient Compounds Now Backed by Modern Science - PubMed. Accessed July 23, 2024. https://pubmed-ncbi-nlm-nih-gov.proxy.hsl.ucdenver.edu/28707186/

11. Evangelista MTP, Abad-Casintahan F, Lopez-Villafuerte L. The effect of topical virgin coconut oil on SCORAD index, transepidermal water loss, and skin capacitance in mild to moderate pediatric atopic dermatitis: a randomized, double-blind, clinical trial. *Int J Dermatol*. 2014;53(1):100-108. doi:10.1111/ijd.12339

12. El-Koofy NM, Salah El-Din A, Mostafa S, Abdelkader HA, Elmonem MA, El-Naggar WM. Coconut Oil with Vitamins A and E as a New Topical Emollient Mixture for Pruritus in Children with Cholestatic Liver Disease. *Indian J Pediatr*. 2021;88(5):512-513. doi:10.1007/s12098-020-03593-5

13. Afrasiabifar A, Mehri Z, Hosseini N. Efficacy of Topical Application of Sweet Almond Oil on Reducing Uremic Pruritus in Hemodialysis Patients: A Randomized Clinical Trial Study. *Iran Red Crescent Med J*. Published online 2016. doi:10.5812/ircmj.34695

14. Shahgholian N, Dehghan M, Mortazavi M, Gholami F, Valiani M. Effect of aromatherapy on pruritus relief in hemodialysis patients. *Iran J Nurs Midwifery Res*. 2010;15(4):240-244.

15. Cürcani M, Tan M. The effect of aromatherapy on haemodialysis patients' pruritus. *J Clin Nurs*. 2014;23(23-24):3356-3365. doi:10.1111/jocn.12579

16. Haro-González JN, Castillo-Herrera GA, Martínez-Velázquez M, Espinosa-Andrews H. Clove Essential Oil (Syzygium aromaticum L. Myrtaceae): Extraction, Chemical Composition, Food Applications, and Essential Bioactivity for Human Health. *Mol Basel Switz*. 2021;26(21). doi:10.3390/molecules26216387

17. Ibrahim IM, Elsaie ML, Almohsen AM, Mohey-Eddin MH. Effectiveness of topical clove oil on symptomatic treatment of chronic pruritus. *J Cosmet Dermatol*. 2017;16(4):508-511. doi:10.1111/jocd.12342

18. Chumpitazi BP, Kearns GL, Shulman RJ. Review article: the physiological effects and safety of peppermint oil and its efficacy in irritable bowel syndrome and other functional disorders. *Aliment Pharmacol Ther*. 2018;47(6):738-752. doi:10.1111/apt.14519

19. Akhavan Amjadi M, Mojab F, Kamranpour SB. The Effect of Peppermint Oil on Symptomatic Treatment of Pruritus in Pregnant Women. *Iran J Pharm Res IJPR*. 2012;11(4):1073-1077.

20. Elsaie LT, El Mohsen AM, Ibrahim IM, Mohey-Eddin MH, Elsaie ML. Effectiveness of topical peppermint oil on symptomatic treatment of chronic pruritus. *Clin Cosmet Investig Dermatol*. 2016;9:333-338. doi:10.2147/CCID.S116995

21. Wu J, Xu R, Zhan R, et al. Effective symptomatic treatment for severe and intractable pruritus associated with severe burn-induced hypertrophic scars: A prospective, multicenter, controlled trial. *Burns J Int Soc Burn Inj*. 2016;42(5):1059-1066. doi:10.1016/j.burns.2015.09.021

22. Pazyar N, Yaghoobi R, Kazerouni A, Feily A. Oatmeal in dermatology: a brief review. *Indian J Dermatol Venereol Leprol*. 2012;78(2):142-145. doi:10.4103/0378-6323.93629

23. Sur R, Nigam A, Grote D, Liebel F, Southall MD. Avenanthramides, polyphenols from oats, exhibit anti-inflammatory and anti-itch activity. *Arch Dermatol Res*. 2008;300(10):569-574. doi:10.1007/s00403-008-0858-x

24. Matheson JD, Clayton J, Muller MJ. The Reduction of Itch During Burn Wound Healing. *J Burn Care Rehabil*. 2001;22(1):76-81. doi:10.1097/00004630-200101000-00017

25. Southall M, Pappas A, Nystrand G, Nebus J. Oat Oil Improves the Skin Barrier.

26. Yoo EH, Lee JH. Cannabinoids and Their Receptors in Skin Diseases. *Int J Mol Sci*. 2023;24(22). doi:10.3390/ijms242216523

27. Avila C, Massick S, Kaffenberger BH, Kwatra SG, Bechtel M. Cannabinoids for the treatment of chronic pruritus: A review. *J Am Acad Dermatol*. 2020;82(5):1205-1212. doi:10.1016/j.jaad.2020.01.036

28. Yuan C, Wang XM, Guichard A, et al. N-palmitoylethanolamine and N-acetylethanolamine are effective in asteatotic eczema: results of a randomized, double-blind, controlled study in 60 patients. *Clin Interv Aging*. 2014;9:1163-1169. doi:10.2147/CIA.S65448

29. Eberlein B, Eicke C, Reinhardt HW, Ring J. Adjuvant treatment of atopic eczema: assessment of an emollient containing N-palmitoylethanolamine (ATOPA study). *J Eur Acad Dermatol Venereol*. 2008;22(1):73-82. doi:10.1111/j.1468-3083.2007.02351.x

30. Szepietowski JC, Szepietowski T, Reich A. Efficacy and tolerance of the cream containing structured physiological lipids with endocannabinoids in the treatment of uremic pruritus: a preliminary study. *Acta Dermatovenerol Croat ADC*. 2005;13(2):97-103.

31. Srivastava JK, Shankar E, Gupta S. Chamomile: A herbal medicine of the past with bright future. *Mol Med Rep*. 2010;3(6):895-901. doi:10.3892/mmr.2010.377

32. Patzelt-Wenczler R, Ponce-Pöschl E. Proof of efficacy of Kamillosan(R) cream in atopic eczema. *Eur J Med Res*. 2000;5(4):171-175.

33. Gonçalves S, Fernandes L, Caramelo A, Martins M, Rodrigues T, Matos RS. Soothing the Itch: The Role of Medicinal Plants in Alleviating Pruritus in Palliative Care. *Plants*. 2024;13(24):3515. doi:10.3390/plants13243515

34. Chandrashekhar VM, Halagali KS, Nidavani RB, et al. Anti-allergic activity of German chamomile (Matricaria recutita L.) in mast cell mediated allergy model. *J Ethnopharmacol*. 2011;137(1):336-340. doi:10.1016/j.jep.2011.05.029

35. Charousaei F, Dabirian A, Mojab F. Using chamomile solution or a 1% topical hydrocortisone ointment in the management of peristomal skin lesions in colostomy patients: results of a controlled clinical study. *Ostomy Wound Manage*. 2011;57(5):28-36.

36. Maleki M, Mardani A, Manouchehri M, Ashghali Farahani M, Vaismoradi M, Glarcher M. Effect of Chamomile on the Complications of Cancer: A Systematic Review. *Integr Cancer Ther*. 2023;22:15347354231164600. doi:10.1177/15347354231164600

37. Pazhohideh Z, Mohammadi S, Bahrami N, Mojab F, Abedi P, Maraghi E. The effect of Calendula officinalis versus metronidazole on bacterial vaginosis in women: A double-blind randomized controlled trial. *J Adv Pharm Technol Res*. 2018;9(1):15-19. doi:10.4103/japtr.JAPTR_305_17

38. Cioinac SE. Use of calendula cream balm to medicate the feet of diabetic patients: Case series. *Int J Nurs Sci*. 2016;3(1):102-112. doi:10.1016/j.ijnss.2015.12.001

39. Tedeschi C, Benvenuti C, Research Group EG. Comparison of vaginal gel isoflavones versus no topical treatment in vaginal dystrophy: results of a preliminary prospective study. *Gynecol Endocrinol Off J Int Soc Gynecol Endocrinol*. 2012;28(8):652-654. doi:10.3109/09513590.2011.650764

40. Yahya YF, Vani O, Putra DEW, et al. The Efficacy and Safety of Plant Oil Mixtures in the Treatment of Xerosis with Pruritus in Elderly People: Randomized double blind Controlled Trial. *Biosci Med J Biomed Transl Res*. 2021;5(3):255-262. doi:10.32539/bsm.v5i3.206

41. Farahnik B, Sharma D, Alban J, Sivamani RK. Topical Botanical Agents for the Treatment of Psoriasis: A Systematic Review. *Am J Clin Dermatol*. 2017;18(4):451-468. doi:10.1007/s40257-017-0266-0

42. Sánchez M, González-Burgos E, Iglesias I, Gómez-Serranillos MP. Pharmacological Update Properties of Aloe Vera and its Major Active Constituents. *Mol Basel Switz*. 2020;25(6). doi:10.3390/molecules25061324

43. Mahboub M, Aghazadeh Attari AM, Sheikhalipour Z, et al. A Comparative Study of the Impacts of Aloe vera Gel and Silver Sulfadiazine Cream 1% on Healing, Itching and Pain of Burn Wounds: A Randomized Clinical Trial. *J Caring Sci*. 2022;11(3):132-138. doi:10.34172/jcs.2021.036

44. Borda LJ, Perper M, Keri JE. Treatment of seborrheic dermatitis: a comprehensive review. *J Dermatol Treat*. 2019;30(2):158-169. doi:10.1080/09546634.2018.1473554

45. Witte M, Krause L, Zillikens D, Shimanovich I. Black tea dressings - a rapidly effective treatment for facial dermatitis. *J Dermatol Treat*. 2019;30(8):785-789. doi:10.1080/09546634.2019.1573306

46. Kim HK, Chang HK, Baek SY, et al. Treatment of Atopic Dermatitis Associated with Malassezia sympodialis by Green Tea Extracts Bath Therapy: A Pilot Study. *Mycobiology*. 2012;40(2):124-128. doi:10.5941/MYCO.2012.40.2.124

47. Peterson B, Nguyen H. St. John's Wort. In: *StatPearls*. StatPearls Publishing; 2024.

48. Mansouri P, Mirafzal S, Najafizadeh P, Safaei-Naraghi Z, Salehi-Surmaghi MH, Hashemian F. The impact of topical Saint John's Wort (Hypericum perforatum) treatment on tissue tumor necrosis factor-alpha levels in plaque-type psoriasis: A pilot study. *J Postgrad Med*. 2017;63(4):215-220. doi:10.4103/0022-3859.201423

49. Schempp CM, Windeck T, Hezel S, Simon JC. Topical treatment of atopic dermatitis with St. John's wort cream--a randomized, placebo controlled, double blind half-side comparison. *Phytomedicine Int J Phytother Phytopharm*. 2003;10(Suppl 4):31-37. doi:10.1078/1433-187x-00306

50. Yang R, Yuan BC, Ma YS, Zhou S, Liu Y. The anti-inflammatory activity of licorice, a widely used Chinese herb. *Pharm Biol*. 2017;55(1):5-18. doi:10.1080/13880209.2016.1225775

51. Kwon YJ, Son DH, Chung TH, Lee YJ. A Review of the Pharmacological Efficacy and Safety of Licorice Root from Corroborative Clinical Trial Findings. *J Med Food*. 2020;23(1):12-20. doi:10.1089/jmf.2019.4459

52. Saeedi M, Morteza-Semnani K, Ghoreishi MR. The treatment of atopic dermatitis with licorice gel. *J Dermatol Treat*. 2003;14(3):153-157. doi:10.1080/09546630310014369

53. Vaughn AR, Branum A, Sivamani RK. Effects of Turmeric (Curcuma longa) on Skin Health: A Systematic Review of the Clinical Evidence. *Phytother Res PTR*. 2016;30(8):1243-1264. doi:10.1002/ptr.5640

54. Kuttan R, Sudheeran PC, Josph CD. Turmeric and curcumin as topical agents in cancer therapy. *Tumori*. 1987;73(1):29-31. doi:10.1177/030089168707300105

55. Pfab F, Schalock PC, Napadow V, Athanasiadis GI, Yosipovitch G, Ring J. Complementary integrative approach for treating pruritus. *Dermatol Ther*. 2013;26(2):149-156. doi:10.1111/dth.12031

56. Miller MJ, Vergnolle N, McKnight W, et al. Inhibition of neurogenic inflammation by the Amazonian herbal medicine sangre de grado. *J Invest Dermatol*. 2001;117(3):725-730. doi:10.1046/j.0022-202x.2001.01446.x

57. Pona A, Cline A, Kolli SS, Taylor SL, Feldman SR. Review of future insights of Dragon's Blood in dermatology. *Dermatol Ther*. 2019;32(2):e12786. doi:10.1111/dth.12786

58. Stücker M, Pieck C, Stoerb C, Niedner R, Hartung J, Altmeyer P. Topical vitamin B12--a new therapeutic approach in atopic dermatitis-evaluation of efficacy and tolerability in a randomized placebo-controlled multicentre clinical trial. *Br J Dermatol*. 2004;150(5):977-983. doi:10.1111/j.1365-2133.2004.05866.x

59. Open-label, single-arm, single-center clinical study on the effectiveness and safety of a moisturizer containing tocotrienol-rich composition in children with mild to moderate atopic dermatitis - How - 2023 - Journal of Cosmetic Dermatology - Wiley Online Library. Accessed June 12, 2024. https://onlinelibrary.wiley.com/doi/10.1111/jocd.15793

60. Farmer WS, Marathe KS. Atopic Dermatitis: Managing the Itch. *Adv Exp Med Biol*. 2017;1027:161-177. doi:10.1007/978-3-319-64804-0_13

61. Leung AK, Barankin B, Lam JM, Leong KF. Childhood guttate psoriasis: an updated review. *Drugs Context*. 2023;12. doi:10.7573/dic.2023-8-2

62. Wollenberg A, Christen-Zäch S, Taieb A, et al. ETFAD/EADV Eczema task force 2020 position paper on diagnosis and treatment of atopic dermatitis in adults and children. *J Eur Acad Dermatol Venereol JEADV*. 2020;34(12):2717-2744. doi:10.1111/jdv.16892

63. Naik PP, Mossialos D, van Wijk B, Novakova P, Wagener FADTG, Cremers NAJ. Medical-Grade Honey Outperforms Conventional Treatments for Healing Cold Sores—A Clinical Study. *Pharmaceuticals*. 2021;14(12):1264. doi:10.3390/ph14121264

64. Al-Waili NS. Topical application of natural honey, beeswax and olive oil mixture for atopic dermatitis or psoriasis: partially controlled, single-blinded study. *Complement Ther Med*. 2003;11(4):226-234. doi:10.1016/s0965-2299(03)00120-1

65. Abbasi MS, Rahmati J, Ehsani AH, Takzare A, Partoazar A, Takzaree N. Efficacy of a Natural Topical Skin Ointment for Managing Split-Thickness Skin Graft Donor Sites: A Pilot Double-blind Randomized Controlled Trial. *Adv Skin Wound Care*. 2020;33(7):1-5. doi:10.1097/01.ASW.0000666916.00983.64

66. Elhage KG, St Claire K, Daveluy S. Acetic acid and the skin: a review of vinegar in dermatology. *Int J Dermatol*. 2022;61(7):804-811. doi:10.1111/ijd.15804

67. Gaurav V, Bhoi AK, Mehta N. Home Remedies in Dermatology. *Indian Dermatol Online J*. 2023;14(6):864-870. doi:10.4103/idoj.idoj_166_23

68. Nakhaee S, Nasiri A, Waghei Y, Morshedi J. Comparison of Avena sativa, vinegar, and hydroxyzine for uremic pruritus of hemodialysis patients: a crossover randomized clinical trial. *Iran J Kidney Dis*. 2015;9(4):316-322.

69. Aramwit P, Keongamaroon O, Siritientong T, Bang N, Supasyndh O. Sericin cream reduces pruritus in hemodialysis patients: a randomized, double-blind, placebo-controlled experimental study. *BMC Nephrol*. 2012;13:119. doi:10.1186/1471-2369-13-119

70. Verdolini R, Bugatti L, Filosa G, Mannello B, Lawlor F, Cerio RR. Old fashioned sodium bicarbonate baths for the treatment of psoriasis in the era of futuristic biologics: an old ally to be rescued. *J Dermatol Treat*. 2005;16(1):26-30. doi:10.1080/09546630410024862

71. Bircher AJ. Water-induced itching. *Dermatologica*. 1990;181(2):83-87. doi:10.1159/000247891

72. Dannaker CJ, Greenway H. Failure of sodium bicarbonate baths in the treatment of aquagenic pruritus. *J Am Acad Dermatol*. 1989;20(6):1136. doi:10.1016/s0190-9622(89)80205-1

73. Interventions for chronic pruritus of unknown origin - Andrade, A - 2020 | Cochrane Library. Accessed June 12, 2024. https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013128.pub2/full

74. Bromma B, Scharein E, Darsow U, Ring J. Effects of menthol and cold on histamine-induced itch and skin reactions in man. *Neurosci Lett*. 1995;187(3):157-160. doi:10.1016/0304-3940(95)11362-Z

75. Effects of an ice roller on chronic kidney disease-associated pruritus in patients receiving haemodialysis - Lin - Journal of Renal Care - Wiley Online Library. Accessed June 12, 2024. https://onlinelibrary.wiley.com/doi/10.1111/jorc.12491