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REVIEW ARTICLES

Corticosteroid and Antifungal Alternative Treatments for Seborrheic Dermatitis: A Review

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Corticosteroid and Antifungal Alternative Treatments for Seborrheic Dermatitis: A Review

SUMMARY

Alternative therapy is increasingly utilized as adjuncts to most commonly used conventional treatments (such as topical antifungal and corticosteroid) of seborrheic dermatitis (SD). Topical antifungal medications have been used with varying success, and long-term use of topical corticosteroid is widely known to cause various side effects. This article reviews trial studies of SD therapies other than corticosteroid and antifungal, aiming to offer information regarding existing alternative therapies and their side effects. Searches were performed on PubMed and Cochrane database focusing on clinical trials according to the PRISMA guidelines. A total 317 studies were identified from database searching. After duplicate removal and eligibility screening, 40 studies were included in the final analysis. Alternative modalities reviewed in this study include: herbal ingredients (herbal shampoo and handcream, Myrtus communis L., Quassia amara, tea tree oil, Vitreoscilla filiformis), calcineurin inhibitor, honey, isotretinoin, lipohydroxy acid, lithium, metronidazole, phototherapy, nicotinamide, oral homeopathic solution, solution of urea-lactic acid-propylene glycol (K301), and zinc pyrithione. For herbal ingredients, there is still no standardisation of active ingredients, purity, or concentrations. The most highly studied non-herbal alternative therapy was calcineurin inhibitors (pimecrolimus with twelve studies and tacrolimus with five studies) that yielded positive clinical improvements. The most common side effects observed were mild burning sensations, erythema, and pruritus. While most therapies appear to be beneficial and safe, further research is necessary before these therapies can be consistently recommended to patients, especially for long-term use.

Key Words: *Seborrheic dermatitis, alternative treatment, antifungal, corticosteroid, herbal, calcineurin inhibitor*

Seboreik Dermatit İçin Kortikosteroid ve Antifungal Alternatif Tedaviler: Bir Derleme

ÖZ

Seboreik dermatit (SD) için geleneksel tedavilerle (topikal antifungal ve kortikosteroid gibi) ilaveten alternatif tedavilerin kullanımı çoğaltmaya başlamıştır. Topikal antifungal ilaçlar değişen başarı oranlarıyla yaygın olarak kullanılmaktadır ve topikal kortikosteroidlerin uzun süreli kullanımının çeşitli yan etkileri olduğu iyi bilinmektedir. Bu makalede, mevcut alternatif tedaviler ve yan etkileri hakkında bilgi vermek amacıyla, kortikosteroid ve antifungal dışı SD tedavilerine ait klinik çalışmalar derlenmektedir. Çalışma PRISMA kılavuzlarına dayanarak Pubmed ve Cochrane veri tabanlarından araştırılan klinik calışmalara odaklanmaktadır. Veri tabanı araştırmalarından bulunan toplam 317 çalışma içerisinden duplikasyonların çıkarılması ve uygunluk taraması yapıldıktan sonra 40 çalışma nihai analize dahil edilmiştir. Bu çalışmada incelenen alternatif tedavi yaklaşımları: bitkisel içerikler (el kremleri ve bitkisel şampuanlar, Myrtus communis L., Quassia amara, çay ağacı yağı, Vitreoscilla filiformis), kalsinörin inhibitörleri, bal, izotretinoin, lipohidroksi asit, lityum, metronidazol, fototerapi, nikotinamid, oral homeopatik çözelti, üre-laktik asit-propilen glikol (K301) çözeltisi ve çinko piritiyon. Bitkisel içerikler için aktif maddelere ait herhangi bir standardizasyon, saflık tayini ya da konsatrasyona ait açık bilgiler bulunmamaktadır. Bitkisel olmayan tedaviler arasında pozitif klinik iyileşme ile sonuçlanan kalsinörin inhibitörleri en çok çalışılanlardır (pimekrolimus için 12 çalışma, takrolimus için 5 çalışma bulunmaktadır). Hafif yanma hissi, kızarıklık ve kaşıntılar en çok görülen yan etkilerdendir. Tedavilerin çoğunluğu olumlu ve güvenli sonuçlar gösterdiği halde, bu tedavilerin uzun süreli kullanım için hastalara tavsiye edilmeden önce daha fazla araştırma yapılması gerekmektedir.

Anahtar kelimeler: *Seboreik dermatit, alternatif tedavi, antifungal, kortikosteroid, bitkisel, kalsinörin inhibitörleri*

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INTRODUCTION

Seborrheic Dermatitis (SD) is a chronic papulosquamous disorder that affects infants and adults. It characteristically manifests in parts of the body with high concentrations of sebaceous follicles and active sebaceous glands, such as the face, scalp, ears, upper trunk, and flexures (inguinal, inframammary, and axillary) (Collins & Hivnor, 2012). SD often presents as well-demarcated erythematous plaques with greasy-looking, yellowish scales of varying extent (Borda, Perper, & Keri, 2019). Its pathogenesis is still not fully understood, some postulate that the disorder results from colonization of species from the genus *Malassezia* (formerly, *Pityrosporum*) on the skin (Berk & Scheinfeld, 2010). Although non-life threatening, SD can have a great impact on someone's quality of life, leading to low self-esteem and a negative social image especially among young female group and people who suffer from scalp lesions (Araya, Kulthanan, & Jiamton, 2015).

Seborrheic dermatitis is a common occurrence worldwide. Its incidence mostly occurs during three age periods – the first three months of life, puberty, and adulthood with the peak of 40-60 years of age (del Rosso, 2011). In adults, the SD incidence is around 1-3%, with men affected more frequently than women (3.0% vs. 2.6%) in all age groups. This suggests that sex hormones such as androgens may play a role in the development of SD. Various ethnic groups do not show any apparent difference in SD incidence (Sampaio et al., 2011).

Seborrheic dermatitis is a chronic condition which at some cases may require a long-term treatment, therefore it is imperative to choose a treatment modality with maximum benefits and most tolerable side effects. The treatment of SD involves eradicating fungus as well as reducing the inflammatory process and sebum production (Berk & Scheinfeld, 2010). With those mechanisms in mind, topical antifungal medications in conjunction with topical corticosteroids are often used. Topical antifungal medications have been used with varying success, and oral antifungals should only be reserved for severe, refractory cases due to potential drug interactions and side effects (Collins & Hivnor, 2012). Long term use of topical corticosteroid is also widely known to cause various dermatologic side effects (Coondoo, Phiske, Verma, & Lahiri, 2014). Therefore, this study reviews SD treatments other than antifungal medications and corticosteroid, to help physicians remain informed on evidence-based recommendations for various alternative SD therapies and hence better patient counseling could be performed. The articles used are trial studies published from January 1st, 2000 onwards, with the intention of offering fresh, up-to-date information.

METHODS/LITERATURE RESEARCH

A review of medical literatures was conducted according to the recommendations of PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. The keywords ("seborrheic dermatitis" OR "seborrhea") AND ("alternative" OR "treatment" OR "shampoo") were used to search trial studies from PubMed and Cochrane database. After removal of duplicates, eligible studies were screened by title and abstract. Studies were included if they described any clinical effects on SD following alternative therapies. Studies were excluded if they were irrelevant, there were no abstract available, the studies were published prior to January 1st, 2000, and they were conducted in in-vitro experiments. Irrelevant studies were the trials that did not include SD therapy other than antifungal medications and or corticosteroid. The remaining studies were then read in full text to confirm eligibility. Studies that do not have full-texts electronically available and studies that were not in English or do not have English translations were also excluded. Study selection and studies on alternative treatments for seborrheic dermatitis are shown in Figure 1 and Table 1 respectively.

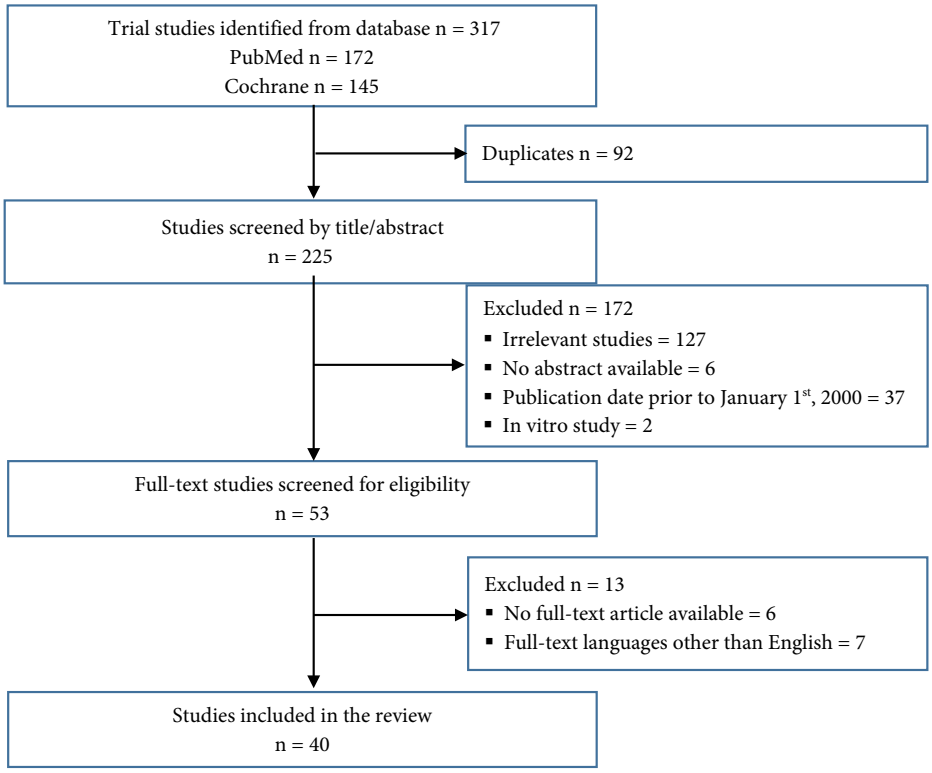

Figure 1. Seborrheic dermatitis: study selection for alternative treatment

RESULTS

Table 1. Studies on alternative treatments for seborrheic dermatitis

Alternative treatment; Reference	Number of patients	Treatment method /Duration (weeks)	Results	Adverse Effects
Herbal and Zinc Pyrithione Shampoo and Scalp Lotion. (Barak-Shinar & Green, 2018)	50	Shampoo at least twice weekly and the scalp lotion was used daily before bedtime for 42 days.	A reduction in erythema and flaking.	No adverse side effects were noted.
Honey. (Al-Waili, 2001)	30	Honey was applied every other day for 4 weeks. Improved patients were then divided into 2 groups, treatment was applied once weekly for 6 months. ▪ Prophylactic group: honey. ▪ Control group: vehicle.	A reduction in itching, scaling, and skin lesions. Subjective improvement in hair loss. Prophylactic group experienced no relapse compared to control group.	No adverse side effects were noted.
Isotretioin 10mg oral. (de Souza Leão Kamamoto, Sanudo, Hassun, & Bagatin, 2017)	45	Treatment for 6 months. ▪ Group ISO: 10mg isotretinoin every other day. ▪ Group X: topical treatment (antiseborrheic shampoo three times weekly, salicylic acid soap twice daily).	In group ISO, a reduction in rate of sebum production. Patient opinion, investigator, and quality of life assessments improved in both groups.	Group ISO: Cheilitis, abnormal serum lipids, body and facial skin fragility, headache, eczema, eye problems, nosebleeds. Less frequent: muscle ache, herpes simplex, tiredness, joint ache, pruritus, mood change, abnormal liver function.

Isotretinoin oral in very low dose. (Geißler, Michelsen, & Plewig, 2003)	11	Treatment for 6 months. ▪ Group I: 5mg daily. ▪ Group II: 2.5 mg daily. ▪ Group III: 2.5 mg three times weekly.	A reduction in sebum production and sebaceous gland size in all groups. A reduction of lipids in group I and II.	Facial redness, dryness of eyes and conjunctivitis, cheilitis, dry vestibulitis in group I and II.
Lipohydroxy acid containing shampoo. (Seite, Rougier, & Talarico, 2009)	100	Every other day for 4 weeks. ▪ Group I: 0.1% lipohydroxy acid (LHA) and 1.3% salicylic acid. ▪ Group II: 5% ciclopiroxolamine (CPO), 3% salicylic acid, and 0.5% menthol.	The tolerance, the global efficacy, and cosmetic acceptability of group I were significantly better.	No adverse side effects were noted.
Lithium gluconate. (Dreno & Moyse, 2002)	129	Twice daily for 8 weeks. ▪ Group I: 8% lithium gluconate. ▪ Group II: placebo	Clinical remission is better in group I.	Mild erythema and burning.
Lithium gluconate. (Dreno, Chosidow, Revuz, Moyse, & STUDY INVESTIGATOR GROUP, 2003)	557	Twice daily for 8 weeks. ▪ Intent to treat protocol (ITT): 288 patients. ▪ Patients protocol (PP): 269 patients.	In ITT and PP group, satisfaction rate was higher in those with lithium treatment.	Erythema, burning, dryness, and upper respiratory tract infections. Lithium gluconate was found to be sticky.
Metronidazole 0.75% gel. (Ozcan, Seyhan, & Yologlu, 2007)	67	Treatment gel or placebo for 4 weeks and were additionally followed up for another 4 weeks.	Metronidazole is only as effective as placebo. The disease severity quickly returns to the basal levels after treatment cessation.	No adverse side effects were noted.
Metronidazole 0.75% gel. (Koca, Altinyazar, & Eştürk, 2003)	84	Twice daily for 8 weeks. ▪ Group I: 0.75% metronidazole. ▪ Group II: placebo.	No statistically significant difference was found between the treatment groups.	No adverse side effects were noted.
Metronidazole 1% gel. (Mohamad Goldust, Rezaee, & Raghifar, 2013)	156	Twice daily for 4 weeks. ▪ Group I: 2% sertaconazole. ▪ Group II: 1% metronidazole.	Higher level of satisfaction was observed in group I.	No adverse side effects were noted.
Metronidazole 1% gel. (Siadat, Iraji, Shahmoradi, Enshaieh, & Taheri, 2006)	56	Twice daily for 8 weeks. ▪ Group I: 1% metronidazole. ▪ Group II: placebo.	In group I, a reduction in mean SD severity score.	Redness and pruritus.
Myrtus communis L. (Chaijan, Handjani, Zarshenas, Rahimabadi, & Tavakkoli, 2018)	90	Once every 3- 4 days for 30 days. ▪ Group I: anti-dandruff (*Myrtus communis L.*) shampoo. ▪ Group II: anti-dandruff (ketoconazole 2%) shampoo.	In both groups, significant improvement in all outcome measures (Excoriation Pruritus Grading, Adherent Scalp Flaking Score, Redness of Scalp Skin, Grading of Scalp Skin Involvement).	No adverse side effects were noted
Narrow-band ultraviolet B (TL-01) phototherapy. (Pirkhammer, Seeber, Hönigsmann, & Tanew, 2000)	18	Three times weekly until absence of symptoms or to a maximum of 8 weeks.	All patients responded well to treatment. Complete clearance in 6 patients, significant improvement in 12 patients.	Occasional moderate erythema.
Nicotinamide 4% cream. (Fabbrocini, Cantelli, & Monfrecola, 2014)	48	Once daily for 12 weeks. ▪ Group I: 4% nicotinamide. ▪ Group II: vehicle cream.	Reduction of 75% of the total score of erythema, scaling, and infiltration using four-point scale was observed in group I.	Minimal burning sensation and pruritus.

Novel Herbal-based Cream. (Barak-Shinar, Del Río, & Green, 2017)	32	Twice daily for 42 days.	A reduction in Investigator Static Global Assessment, desquamation (scaling), induration (inflammation), and erythema (redness) as well as self-assessed pruritus parameters.	No adverse side effects were noted.
Oral Homeopathic Solution. (Smith, Baker, & Williams, 2002)	41	Every morning for 10 weeks. ▪ Active group: homeopathic solution. ▪ Placebo group: vehicle drink.	The disease state of the active group was improved significantly compared to placebo group.	Mild stomach upset, stomach pain, and nausea.
Pimecrolimus 1% cream. (de Moraes et al., 2007)	21	Twice daily for 14 days.	Significant improvement from baseline in terms of erythema, scaling, and infiltration/population.	Mild burning.
Pimecrolimus 1% cream. (Firooz et al., 2006)	40	Twice daily for 2 weeks. Followed up every 2 weeks for 4 weeks. ▪ Group I: 1% pimecrolimus. ▪ Group II: 1% hydrocortisone acetate.	Group I and II have the same efficacy with no significant differences in patients' baseline data, response to treatment, and relapse rate.	Mild burning.
Pimecrolimus 1% cream. (M. Goldust, Rezaee, & Raghifar, 2013)	60	Twice daily for 4 weeks. ▪ Group I: 1% pimecrolimus. ▪ Group II: 2% sertaconazole.	Higher level of satisfaction was observed group II.	No adverse side effects were noted.
Pimecrolimus 1% cream. (High & Pandya, 2006)	5	Twice daily for 16 weeks.	All participants noted a marked decrease in the severity.	No adverse side effects were noted.
Pimecrolimus 1% cream. (B. S. Kim et al., 2007)	20	Twice daily for 4 weeks.	Improvements were noted in the global assessment of disease severity. Relapse was observed after discontinuation.	No adverse side effects were noted.
Pimecrolimus 1% cream. (Koc, Arca, Kose, & Akar, 2009)	48	Twice daily for 6 weeks. ▪ Group I: 1% pimecrolimus. ▪ Group II: 2% ketoconazole.	In both groups, effective results in clinical severity scores.	Mild burning, pruritus, irritation, and erythema.
Pimecrolimus 1% cream. (Ozden, Tekin, Lter, & Ankarali, 2010)	16	Twice daily for 2 weeks.	Statistically significant reductions in the scores of all parameters (clinically, 4-point score, Visual Analogue Scale).	Temporary pruritus.
Pimecrolimus 1% cream. (Rallis, Nasiopoulou, Kouskoukis, & Koumantaki, 2004)	19	Twice daily for 7 days. Additional period of 7 days, if needed, until complete clearance was achieved. In cases of recurrence a 5-day course was additionally applied.	Subjects' average assessment score was high (9.73).	Mild burning and irritation.
Pimecrolimus 1% cream. (Rigopoulos, Ioannides, Kalogeromitros, Gregoriou, & Katsambas, 2004)	22	Twice daily until absence of symptoms. ▪ Group I: 1% pimecrolimus. ▪ Group II: 0.1% betamethasone 17-valerate.	In group I, a reduction in erythema, scaling and pruritus, although slightly slower than betamethasone, but it is not statistically significant.	Mild burning sensation in group I.

Pimecrolimus 1% cream. (Tatlican, Eren, & Eskioglu, 2009)	52	Twice daily until lesions completely disappeared.	A reduction in pruritus, erythema, and scaling. The mean cure and mean remission times were 13.34 and 47.98 days, respectively.	Pruritus, burning, erythema.
Pimecrolimus 1% cream. (Warshaw et al., 2007)	96	Twice daily for 4 weeks. ▪ Group I: 1% pimecrolimus. ▪ Group II: placebo.	The superiority of pimecrolimus was observed	No adverse side effects were noted.
Pimecrolimus 1% cream. (Zhao et al., 2018)	30	▪ Group I: cream twice daily for 2 weeks, moisturizer twice daily for 2 weeks. ▪ Group II: cream twice daily for 2 weeks, then once daily for 2 weeks. ▪ Group III: cream twice daily for 4 weeks.	In all groups, a significant decrease in clinical severity scores. The improvement of total severity score in Group III was more remarkable than groups I and II.	Erythema, localized burning sensation, aggravated pruritus.
Quassia amara (Borda et al., 2019)	60	Twice daily for 4 weeks. ▪ Group I: 4% *Quassia amara* ▪ Group II: 2% ketoconazole ▪ Group III: 1% ciclopirox olamine	In all groups, a decrease in SD mean severity score. In group I, statistically significant difference in avoiding SD relapse.	No adverse side effects were noted.
Solution of urea, lactic acid, and propylene glycol. (Emtestam, Svensson, & Rensfeldt, 2012)	299	▪ Study I: once daily application for 4 weeks of K301 (K301a or K301b) or placebo, followed by maintenance treatment 3 times weekly for 4 weeks ▪ Study II: once daily application for 4 weeks of K301 (a) or placebo.	In both studies, 4-weeks desquamation scores were significantly improved for K301 compared to placebo.	Mild burning.
Tacrolimus 0.1% ointment. (Braza, Dicarlo, Soon, & Mccall, 2003)	16	Every night until absence of clinical symptoms, and then for 7 days thereafter.	Improvement in all the mean lesional erythema scores, mean scaling, mean investigator global assessment, and mean subject global assessment scores.	Mild-to-moderate application site pruritus/burning, mild sunburn.
Tacrolimus 0.03% cream. (Mohamad Goldust, Rezaee, Raghifar, & Hemayat, 2013)	60	Twice daily for 4 weeks. ▪ Group I: 2% sertaconazole. ▪ Group II: 0.03% tacrolimus.	In both groups, significant reductions in SI score, signs, and symptoms. In group I, a higher level of satisfaction was observed.	No adverse side effects were noted.
Tacrolimus 0.1% cream. (T. W. Kim et al., 2013)	75	Treatment for 10 weeks. ▪ Group I: cream, twice weekly. ▪ Group II: cream, once weekly. ▪ Group III: placebo twice weekly.	In group I and II, significant improvement in erythema, scaling and pruritus. The mean recurrence rate according to global assessment was significantly higher in group II compared to group I.	Burning and tingling sensation.
Tacrolimus 0.1% cream. (Meshkinpour, Sun, & Weinstein, 2003)	18	Treatment daily for 28 days or until complete absence of symptoms.	A complete clearance of SD with a grade of 0 for erythema, scaling, and global severity.	Mild local burning and irritation.

Tacrolimus 0.1% cream. (Papp, Papp, Dahmer, & Clark, 2012)	30	Twice daily for 12 weeks. ▪ Group I: 0.1% tacrolimus. ▪ Group II: 1% hydrocortisone.	Tacrolimus 0.1% cream was equally effective as hydrocortisone 1% cream but required significantly fewer treatment applications to achieve the same level of disease control.	Flushing and irritation in group I.
Tea tree oil 5% gel. (Roy et al., 2014)	54	Three times daily for 4 weeks. ▪ Group I: 5% tea tree oil gel. ▪ Group II: placebo gel.	In group I, a reduction in erythema, scaling, itching and greasy crusts	No adverse side effects were noted.
Tea tree oil 5% shampoo. (Satchell, Saurajen, Bell, & Barnetson, 2002)	126	Daily for 4 weeks. ▪ Group I: 5% tea tree oil shampoo. ▪ Group II: placebo.	In group I, an improvement in whole scalp lesion score, total area of involvement score, the total severity score, the itchiness, and greasiness.	No adverse side effects were noted.
Vitreoscilla filiformis biomass. (Guniche et al., 2008)	60	Once daily for 4 weeks. ▪ Group I: 5% LRP-biomass lotion ▪ Group II: vehicle lotion.	In group I, a high improvement of total clinical score (sum of erythema and scaling subscores) and level of pruritus.	No adverse side effects were noted.
Zinc pyrithione 1% shampoo. (Piérard-Franchimont, Goffin, Decroix, & Piérard, 2002)	343	Twice weekly for 4 weeks. ▪ Group I: 2% ketoconazole. ▪ Group II: 1% zinc pyrithione.	In both groups, flakiness improved significantly. In group I, the overall clearing was statistically greater and there was less clinical relapse.	Mild pruritus and erythema in both groups.
Zinc pyrithione (potentiated) shampoo. (Schwartz, Mizoguchi, & Bacon, 2013)	620	Three times weekly for 4 weeks. ▪ Group 1: potentiated zinc pyrithione shampoo ▪ Group II: zinc pyrithione/ climbazole combination	In group I, better adherent scalp flaking severity (ASFS) and overall scalp health.	No adverse side effects were noted.

Herbal and Zinc Pyrithione-based Therapy of Shampoo and Scalp Lotion

This therapy is a patented Kamedis Derma-Scalp Dandruff Therapy shampoo and scalp lotion (Kamedis Ltd., Tel-Aviv, Israel). The main ingredients are zinc pyrithione and botanical extracts of *Phellodendron amurense* bark, *Portulaca oleracea*, *Sapindus mukorossi* fruit, *Indigofera tinctoria*, and *Rheum palmatum* root. *Rheum palmatum* reduces sebum secretion. Zinc pyrithione and botanical ingredients especially in the scalp lotion offer potential anti-inflammatory, antimicrobial, and antifungal properties (Barak-Shinar et al., 2017).

Honey (Crude Honey)

In the study, honey was found to be beneficial due to its antibacterial, antifungal, and antioxidant properties (Al-Waili, 2001).

Isotretinoin oral

In these studies, oral isotretinoin was found effective due to its ability to suppress secretion of sebaceous glands by reducing their size, decreasing proliferation, and inducing basal sebocyte apoptosis. It has anti-inflammatory properties, including decreasing interleukin production by keratinocytes and sebocytes, polymorphonuclear cell migration, and Toll-like receptor 2 activity (de Souza Leão Kamamoto et al., 2017). In its higher dose (0.5-1.0mg/kg/day), oral isotretinoin has been controversially reported to trigger flaring, depression, suicidal ideation, and inflammatory bowel disease, and pseudotumor cerebri. It is still debated whether those adverse reactions are definitely caused by isotretinoin, and if they are, such reactions are rare (Geißler et al., 2003; Leyden, Del Rosso, & Baum, 2014).

Lipohydroxy acid containing shampoo

Lipohydroxy acid (LHA) was found useful in managing SD due to its ability to induce exfoliation and stimulate epidermal renewal. It also has antimicrobial and anti-inflammatory properties. In vitro experiments showed that LHA has similar antimicrobial properties to octopirox (piroctone olamine) against *Malassezia ovalis* (Seite et al., 2009).

Lithium

Lithium was more superior in controlling SD compared to ketoconazole 2% or placebo. The exact mechanism of action of lithium salts in SD remains unclear. It could act by inhibiting *Malasezzia furfur* which colonizes the cutaneous lesions. In also has an anti-inflammatory activity by inhibiting the production of arachidonic acid, which is the first step inducing the production of leukotriene and prostaglandin (Dreno et al., 2003; Dreno & Moyse, 2002)

Metronidazole

Metronidazole is an antibiotic with efficacy against anaerobic bacteria. It acts through DNA destruction and prevention of nucleic acid synthesis, in the anaerobic organisms and cells. It also has anti-inflammatory effect through inhibition of leukocyte chemotaxis and prevention of inflammatory mediators release from neutrophils, decreasing oxidative tissue damage. The exact mechanism of action of metronidazole in SD is not yet clear, it might be acting through these anti-inflammatory properties (Siadat et al., 2006).

***Myrtus communis L.* solution**

Myrtus communis L. is a shrub that grows from the Mediterranean region to the northwestern Himalayas. It has different components, such as polyphenols, myrtucommulone (MC), semi myrtucommulone (S-MC), 1 and 8-cineole, alpha-pinene, myrtenyl acetate, limonene, linalool and alpha-terpinolene. Those components contribute to myrtus solution having its anti-bacterial, anti-fungal and anti-inflammatory effect (Chaijan et al., 2018)

Narrow-band ultraviolet B (TL-01) phototherapy

This study showed favourable results, although the mode of action of narrow-band UVB in SD was still not fully understood. It may be related to its modulatory effect on inflammatory and immunological processes in the skin. There was also a report of a direct effect of UV irradiation on *P. ovale* leading to ultrastructural changes and growth inhibition (Pirkhammer et al., 2000).

Nicotinamide

Nicotinamide (NCT) shows effective result against SD because of its cellular inflammation regulation as well as its ability to regulate stratum corneum intercellular lipid synthesis. It blocks pro-inflammatory cytokines and poly(ADP-ribose) polymerase (PARP), which influences inflammatory processes through modulating different transcription factors. In stratum corneum, it increases ceramide and other intercellular lipids, maintaining the epidermal permeability barrier (Fabbrocini et al., 2014).

Novel herbal based handcream

This handcream is a patented Seborrheamedis Face Cream (Kamedis, Israel), which is a barrier-based, non-steroidal cream infused with herbal extracts to manage the clinical manifestations and symptoms of facial SD, such as erythema, scaling, and pruritus. The cream used in this study forms a dense layer over the affected areas and prevents oxygen supply, which resulted in anaerobic environment that inhibits pathogen growth. Its herbal ingredients namely dipotassium glycyrrhizate (also known as licorice), offers potential anti-inflammatory, antimicrobial, and antifungal, properties (Barak-Shinar et al., 2017).

Oral Homeopathic Solution Consisting of Potassium Bromide, Sodium Bromide, Nickel Sulfate, and Sodium Chloride

This study was based on information about how inorganic bromide was found to be effective to treat chronic skin conditions such as psoriasis, with has a similarity with SD in terms of its primary biochemical defect. Although the mechanism of action for nickel and bromide therapy is not fully understood, a theory is proposed whereby a genetic error of nickel-dependent metabolism exists. Bromide has also been found as an effective antipruritic agent (Smith et al., 2002).

Pimecrolimus 1% cream

Pimecrolimus cream 1% is a new topical macrolactam immunomodulator that inhibits T-cell activation and proinflammatory cytokine production (B. S. Kim et al., 2007), which is to prevent T-cell activation by down-regulating T-cell production of T-helper cells type 1 and type 2. Pimecrolimus also prevents the IgE/ antigen-mediated degranulation of mast cells (Warshaw et al., 2007)

Quassia amara

Quassia amara is a shrub from South America. It was effective for SD because of its high levels of active phytochemicals, including the triterpenoid quassi-

noids. It has anti-inflammatory properties, as well as antimicrobial and antifungal activities especially on *Malassezia spp.* Yeast (Borda et al., 2019).

Solution of urea, lactic acid, and propylene glycol (K301)

This study showed positive results. Propylene glycol, lactic acid, and urea have all been shown to inhibit growth of bacteria and or fungi. Therefore when combined, the ingredients of K301 provide a solution with keratolytic, exfoliating, anti-fungal and hydrating properties (Emtestam et al., 2012).

Tacrolimus 0.1% ointment

Tacrolimus 0.1% ointment showed great results against SD. It inhibits calcineurin, a calcium-dependent phosphatase essential for T-cell activation and proinflammatory cytokine production (Braza et al., 2003).

Tea tree oil

Tea tree oil (TTO) or *Melaleuca alternifolia* shows effective results in reducing SD symptoms. Although the exact mechanisms of TTO gel in treatment of SD is unknown. It may be associated with its antifungal properties, which may be due to its terpenoids content. It also has anti-inflammatory property (Roy et al., 2014; Satchell et al., 2002).

***Vitreoscilla filiformis* biomass**

Vitreoscilla filiformis is a Gram-negative bacteria found in thermal spa water classically used for dermatological treatment. In this test, the microorganism biomass was cultured in a medium prepared with La Roche Posay (LRP) spa water. LRP-biomass was shown effective in improving SD symptoms, probably due to its tolerogenic effect and its ability to modulate the defensins synthesis that may decrease scalp microflora dysregulation (Guniche et al., 2008).

Zinc pyrithione

As mentioned above, zinc pyrithione has anti-inflammatory, antimicrobial, and antifungal properties. Zinc pyrithione is known to have an efficacy against *M.furfur* (Barak-Shinar & Green, 2018). There is also a potentiated zinc pyrithione shampoo that shows better synergistic effect than normal zinc pyrthione shampoo during an in-vitro microbiology demonstration (Schwartz et al., 2013).

DISCUSSION

Nowadays, more people rely on non-conventional, alternative modalities to meet their healthcare needs. It is important that physicians remain informed on evidence-based recommendations for various alternative modalities. People often choose alternative modalities because of a perceived lower risk of side effects, and or dissatisfaction with traditional treatments (Farahnik, Sharma, Alban, & Sivamani, 2017).

Since the suggested underlying pathogenic mechanisms of SD are fungal proliferation and inflammation, the conventional treatments used are topical antifungal and anti-inflammatory agents such as corticosteroid (Borda et al., 2019). Topical antifungals have been used with varying success (Collins & Hivnor, 2012). In a study comparing antifungal agent ketoconazole and placebo, the results showed that the people treated with the topical antifungal agent achieved complete resolution of SD symptoms compared to those in the placebo group, but the results were statistically heterogeneous and could not be explained by subgroup analyses of dose, mode of delivery nor conflict of interest. Topical ketoconazole showed similar efficacy when compared to corticosteroids, but corticosteroids showed a two-fold greater risk of side effects (Okokon, Verbeek, Ruotsalainen, Ojo, & Bakhoya, 2015). Corticosteroids are effective in the short-term management of SD, but they have limited long-term use because of the potential for hypothalamic-pituitary-adrenal (HPA) axis suppression. In a case study of patients applying high-potency topical corticosteroids for up to one year, results showed low cortisol levels and clinical signs of Cushing syndrome as a result of HPA axis suppression (Gilbertson, Spellman, Piacquadio, & Mulford, 1998). In a clinical study where the majority of the patients applied topical corticosteroid for one week to one month with a regimen of twice or more per day, skin adverse effects emerged, such as: tinea incognito (49.46%), acne (30.27%), cutaneous atrophy (12.97%), rosacea (11.08%), topical steroid-dependent facies (9.73%), telangiectasia (8.38%), hypopigmentation (7.57%), irritant contact dermatitis (5.68%), striae (4.59%), pyoderma (4.32%), perioral dermatitis (2.70%), and hypertrichosis (1.35%) (Furue et al., 2003; Meena et al., 2017)546 children, and 515 adolescents and adults.

Herbal therapies for SD reviewed in this study include herbal shampoo and scalp lotion, honey, *Myrtus communis L.* solution, herbal handcream, *Quassia amara,* tea tree oil, and *Vitreoscilla filiformis.* For thousands of years, herbal therapies have been used with great results in treating dermatologic disorders in Europe and Asia. However, in the United States and many other countries herbal products are still considered as dietary supplements, which means there is still no standardisation of active ingredients, purity, or concentrations (Bedi & Shenefelt, 2002). Therefore,

even though the herbal studies showed favourable results in treating SD, learning about and using these non-conventional treatments remain challenging.

In this review, the most highly studied non-herbal alternative therapy for SD was calcineurin inhibitors (pimecrolimus with twelve studies and tacrolimus with five studies), where all showed positive clinical improvements. Even so, treatment periods varied largely between existing studies, ranging from 2 to 16 weeks. For pimecrolimus 1% cream, in a study comparing different courses to explore an optimal regimen, results showed that the regimen of 4-week twice-daily course may provide longer remission time and less frequent relapse (Zhao et al., 2018). As for tacrolimus 0.1% cream, there was a study where SD began to recur within 2 weeks after therapy was completed (Meshkinpour et al., 2003). A twice-weekly treatment with 0.1% tacrolimus ointment for facial SD seems to provide longer remission time (T. W. Kim et al., 2013).

The most common side effects observed in calcineurin inhibitor studies were mild burning sensations, erythema, and pruritus. However, the adverse effect profile of calcineurin inhibitors in terms of cellular activity and pharmacologic profile were still a lot safer than that of corticosteroids, making it more favourable for long term use. This is because the T-cell selectivity of pimecrolimus and tacrolimus contrasts with the multiple targets of corticosteroids, including inflammatory cells, fibroblasts, and keratinocytes. Due to the lack of effect of calcineurin inhibitors on fibroblasts and endothelial cells, there is no risk of skin atrophy and telangiectasia, as seen with corticosteroid use (Cook & Warshaw, 2009). In a study where sixteen healthy individuals applied topical pimecrolimus 1%, betamethasone valerate 0.1%, triamcinolone 0.1%, and a vehicle control; pimecrolimus did not induce epidermal atrophy when applied topically for 4 weeks, showing it has a low atrophogenic potential (Queille-Roussel et al., 2001)

There are limitations to this review and to the clinical trials included in the review. This review did not include unpublished studies in languages other than English. Another limitation of this review is the small amount of studies found for each treatment modality, often only one study was found, which can reduce the chance of cross referencing and finding meaningful correlation between studies if one exists. Given the lack of standardised outcome measure for SD, there were many trials that used a different subjective outcome measures, making it difficult to make comparisons across these studies. Some of the studies reviewed were sponsored by patented brands, which may increase the risk of outcome bias. Additionally, some of the studies included had small sample size or did not have a control group, making it difficult to draw specific conclusions about a particular therapy used.

CONCLUSION

Seborrheic dermatitis remains a challenging disease that may cause significant morbidity. With its still uncertain pathophysiology and etiology, there is a huge room for innovative therapies to emerge. While traditional therapies may offer immediate relief for many patients, risks of adverse effects may lead to explorations of complementary and alternative treatments. While clinical evidence and quality for these treatments are relatively less than that of more conventional therapy, well-designed trials do exist with occasional agreements between studies. Undeniably, more rigorous randomized controlled trials are needed to more accurately determine the safety and efficacy of these therapies. For now, it is imperative to know which alternative therapies exist and what potential side effects that may occur so better patient counseling could be performed.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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