TOPICALS

Clinical Summary

by HARVEST MEDICINE | 2021

Topicals & Skin Disorders

Skin disorders rank among the leading causes of non-fatal disease burden worldwide. Atopic dermatitis (AD), acne, and pruritus are among the most common skin disorders and can have a profound impact on an individual's well-being, mental health, and social participation.[1, 2] Numerous studies implicate dysregulation of the cutaneous endocannabinoid system (ECC) in the pathogenesis of these disorders and cite topical medical cannabis (MC) as a potential remedy.[3] Naturally, demand for topical MC has increased and a wide assortment of topical MC products are available on the Canadian market.[4] Therefore, this review will focus on the clinical literature that pertains to the use of topical MC in the treatment of AD, acne, and pruritus.

Atopic dermatitis (Eczema) is a chronic, relapsing, inflammatory condition that presents as dry, itchy, red, and inflamed patches of skin (Illustration 1).

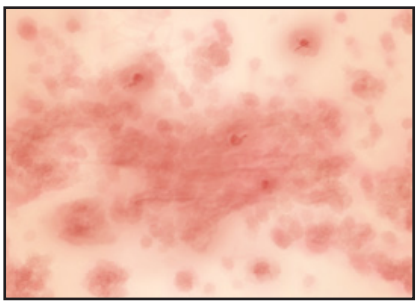


Illustration 1: Typical appearances and common location of atopic dermatitis; Eczema on back of knees. Adapted from JAMA Dermatogy[14]

Illustration 2: Eczema: Steroids and other topical medications. Adapted from InformedHealth.org[15]

Treatment for AD typically involves application of a topical corticosteroid (Illustration 2). Although corticosteroids are effective, these agents can cause serious adverse drug reactions (ADR) including the development of striae, skin atrophy, perioral dermatitis, acne rosacea, and adrenal suppression.[5]

A 2-week, prospective, observational, study evaluating application of a topical CBD (Cannabidiol) gel in 20 participants with AD demonstrated a statistically significant reduction in AD symptom severity after treatment compared to baseline. There were no ADRs reported.[6] These findings were corroborated by a 12-week, prospective, observational study evaluating a topical cannabis sativa seed oil applied twice daily to inflamed lesions in 50 participants with AD, psoriasis, or irritative contact dermatitis.

Following treatment, 60% and 40% of participants demonstrated complete or partial healing respectively (photo 1 & 2).[7]

Photo 1: Bilateral, erythematous & squamous lesions of the palms.

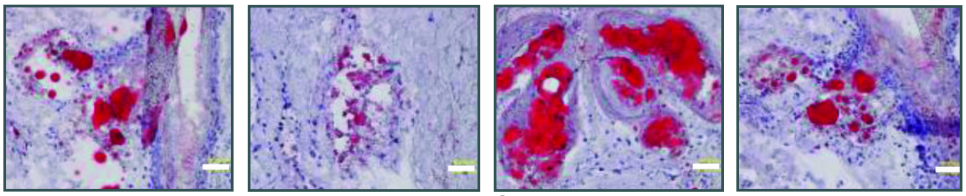
After 12 weeks, we observed a complete healing with restitutio ad integrum in 30 patients. In the other 20 patients, we revealed a partial healing.[7]

Photo 2: Cutaneous aspect after 12-week topical therapy.

Lastly, a 4-6 week prospective, observational, cohort study evaluating a cream containing the endocannabinoid, palmitoylethanolamine (PEA), in 2456 participants with AD reported a mean reduction in AD symptom severity of 58.6% compared to baseline. The PEA cream also demonstrated a steroid-sparing effect as earlier use of topical corticosteroids was discontinued by 56% participants. With respect to safety, mild irritation, erythema, and pruritus were reported in 3.4% of participants. Otherwise, the PEA cream was well tolerated.[8]

Topicals & Skin Disorders

Acne is a highly prevalent condition that presents as comedones, papules, pustules, nodules, and varying degrees of scarring. Consequently, acne often contributes to serious psychological disorders including depression, anxiety, and poor self-image. Treatments for acne include topical benzoyl peroxide and topical and oral retinoids and antibiotics. These treatments are effective but problematic with respect to side effects.[9] Topical MC has been proposed as a treatment for acne by exerting antibacterial activity and reducing sebum production and inflammation (Figures 1-4 & A-D).[10] A 12-week prospective, placebo-controlled, split body trial evaluating a 3% cannabis sativa seed extract applied twice daily in 11 male participants reported a statistically significant reduction in skin sebum and erythema compared to placebo.



Figures A–D: hSOC of (A) control, (B) 10 μM CBD, (C) 30 μM AEA, and (D) 30 μM AEA plus CBD 10 μM (14 days; sebum: Oil Red O staining, red; nuclei: hematoxylin, blue).[10]

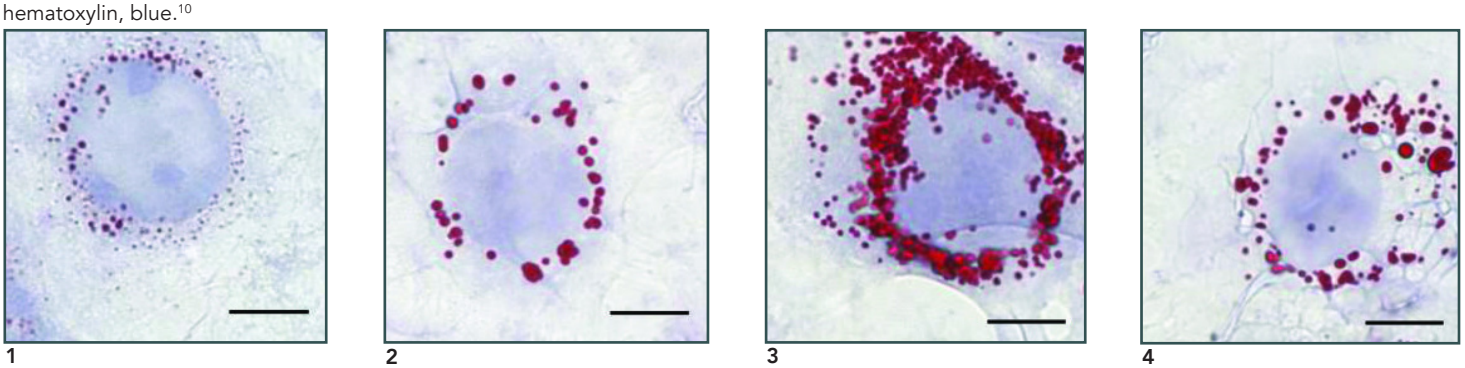
Abbreviations: CBD = Cannabidiol; AEA = Anandamide

With respect to safety, the topical was well tolerated and there were no ADRs reported.[11] Pruritus is defined as an unpleasant sensation that causes a desire to scratch. Chronic pruritus often causes significant physical and psychological effects such as skin injury, loss of sleep, anxiety, and depression. While many patients can achieve relief easily with current therapies, for others, managing pruritus is extremely challenging.[12] A prospective, observational, study evaluating a cream containing PEA in 22 participants suffering from chronic pruritus demonstrated a mean reduction in pruritus symptoms of 86.4% in 14/22 of participants. The topical was well tolerated and there were no ADRs reported.[13]

AD, acne, and pruritus are serious conditions with treatments that are often either inadequate in terms of efficacy or poorly tolerated. The safety and efficacy of topical MC in treating these conditions has been demonstrated in numerous clinical studies. For patients where conventional therapies are not appropriate, topical MC could certainly be a reasonable alternative. Patients seeking to treat symptoms of skin disorders with MC are encouraged to follow the guidance of an experienced MC clinician and routinely follow-up to monitor ongoing treatment.

-Harvest Medicine 2021
& Wade, I., University of Toronto Pharmacy Intern 2021

Figures 1, 2, 3, and 4: Semiquantitative determination of lipid synthesis for (1) control, (2) 10 μM CBD, (3) 30 μM AEA, and (4) 30 μM AEA plus 10 μM CBD.
Sebum droplets: Oil Red O staining, red; nuclei: hematoxylin, blue.[10]



References

1. Seth, D., Cheldize, K., Brown, D., & Freeman, E. E. (2017). Global Burden of Skin Disease: Inequities and Innovations. Current Dermatology Reports, 6(3), 204–210. https://doi.org/10.1007/s13671-017-0192-7
2. Hay, R. J., Johns, N. E., Williams, H. C., Bolliger, I. W., Dellavalle, R. P., Margolis, D. J., Marks, R., Naldi, L., Weinstock, M. A., Wulf, S. K., Michaud, C., J L Murray, C., & Naghavi, M. (2014). The global burden of skin disease in 2010: an analysis of the prevalence and impact of skin conditions. The Journal of investigative dermatology, 134(6), 1527–1534. https://doi.org/10.1038/jid.2013.446
3. Sheriff, T., Lin, M. J., Dubin, D., & Khorasani, H. (2019). The potential role of cannabinoids in dermatology. Journal of Dermatological Treatment, 31(8), 839–845. https://doi.org/10.1080/09546634.2019.1675854
4. Ligaya, A. (2019, June 3). Canadian edibles, topicals market worth $2.7B; ramp up over 3-5 years: Deloitte. The Toronto Star. https://www.thestar.com/business/2019/06/03/canadian-edibles-topicals-market-worth-27b-ramp-up-over-3-5-years-deloitte.html.
5. Lee, J. H., Son, S. W., & Cho, S. H. (2016). A Comprehensive Review of the Treatment of Atopic Eczema. Allergy, asthma & immunology research, 8(3), 181–190. https://doi.org/10.4168/aair.2016.8.3.181
6. Maghfour, J., Rietcheck, H. R., Rundle, C. W., Runion, T. M., Jafri, Z. A., Dercon, S., Lio, P., Fernandez, J., Fujita, M., Dellavalle, R. P., & Yardley, H. (2020). An Observational Study of the Application of a Topical Cannabinoid Gel on Sensitive Dry Skin. Journal of drugs in dermatology, 19(12), 1204–1208. https://doi.org/10.36849/JDD.2020.5464
7. Tammaro, A., Magri, F., Chello, C., Giordano, D., Parisella, F. R., De Marco, G., & Persechino, S. (2019). A successful topical treatment for cutaneous inflammatory diseases:an additional or alternative therapy to topical steroids. European annals of allergy and clinical immunology, 51(3), 129–130. https://doi.org/10.23822/EurAnnACI.1764-1489.79
8. Eberlein, B., Eicke, C., Reinhardt, H. W., & Ring, J. (2008). Adjuvant treatment of atopic eczema: assessment of an emollient containing N-palmitoylethanolamine. Journal of the European Academy of Dermatology and Venereology, 22(1), 73–82. https://doi.org/10.1111/j.1468-3083.2007.02351.x
9. Tan, A. U., Schlosser, B. J., & Paller, A. S. (2017). A review of diagnosis and treatment of acne in adult female patients. International journal of women's dermatology, 4(2), 56–71. https://doi.org/10.1016/j.ijwd.2017.10.006
10. Oláh, A., Tóth, B. I., Borbíró, I., Sugawara, K., Szöllõsi, A. G., Czifra, G., Pál, B., Ambrus, L., Kloepper, J., Camera, E., Ludovici, M., Picardo, M., Voets, T., Zouboulis, C. C., Paus, R., & Bíró, T. (2014). Cannabidiol exerts sebostatic and antiinflammatory effects on human sebocytes. The Journal of clinical investigation, 124(9), 3713–3724. https://doi.org/10.1172/JCI64628
11. Ali, A., & Akhtar, N. (2015). The safety and efficacy of 3% Cannabis seeds extract cream for reduction of human cheek skin sebum and erythema content. Pakistan journal of pharmaceutical sciences, 28(4), 1389–1395.
12. Tivoli, Y. A., & Rubenstein, R. M. (2009). Pruritus: an updated look at an old problem. The Journal of clinical and aesthetic dermatology, 2(7), 30–36
13. Ständer, S., Reinhardt, H. W., & Luger, T. A. (2006). Topische Cannabinoidagonisten. Eine effektive, neue Möglichkeit zur Behandlung von chronischem Pruritus [Topical cannabinoid agonists. An effective new possibility for treating chronic pruritus]. Der Hautarzt; Zeitschrift fur Dermatologie, Venerologie, und verwandte Gebiete, 57(9), 801–807. https://doi.org/10.1007/s00105-006-1180-1
14. Silverberg JI. Atopic Dermatitis. JAMA Dermatol. 2014;150(12):1380. https://dor.org/10.1001/jamadermatol.2014.2757
15. InformedHealth.org [Internet]. Cologne, Germany: Institute for Quality and Efficiency in Health Care (IQWiG); 2006-. Eczema: Steroids and other topical medications. 2017 Feb 23. Available from: https://www.ncbi.nlm.nih.gov/books/NBK424899/