The Impact of CBD on Health and Wellness: Assessing its Transformative Benefits in Skincare

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Introduction/Background

CBD has recently been making its way into the world of health and wellness. It is a naturally occurring compound derived from the cannabis plant and is known to potentially have therapeutic effects due to its anti-inflammatory and antioxidant properties. CBD interacts with the endocannabinoid system, which is a key player in regulating physiological processes in the body. Skin disorders, whether it be acne, psoriasis, eczema, etc. are common across all populations and can be mentally and physically damaging, which is why it is important to further explore new therapeutics and educate patients and healthcare providers about the current evidence of CBD in skin disorders. There are several physiological processes that are modulated through the endocannabinoid system that humans possess, making the incorporation of CBD into topical regimens an innovative road to look into. Topical cannabinoids can avoid first-pass metabolism with steady and sustained drug delivery and have minimal adverse effects. This is why it is also important to look further into transdermal delivery of CBD.

Pharmacokinetics

Topical application of CBD can decrease levels of pro-inflammatory cytokines, such as IL-6 and IL-17, and promote the release of anti-inflammatory cytokines (IL-10). Due to its high lipophilicity, CBD can reach to and accumulate in adipose tissues. Transdermal administration of cannabinoids also avoids first-pass metabolism and can lengthen drug plasma concentration. Transdermal drug delivery can increase medical efficacy and reduce adverse effects. Due to the several advantages of topical/transdermal cannabinoids, further studies on CBD's transcutaneous delivery with high lipophilicity and low bioavailability features should be implemented.

Pharmacodynamics

Current data suggest that high CBD/low Δ9-THC topical products appear to show little risk of inducing intoxication or impairment of cognitive/psychomotor functioning. On average, CBD/metabolite concentrations peaked after 7-10 days of product use and were highest for the lotion, which contained the most CBD and a permeation enhancer (vitamin E). Also, the detection limit in the blood for all products did not test "positive" for cannabis, when using current US federal workplace drug testing criteria.

Results

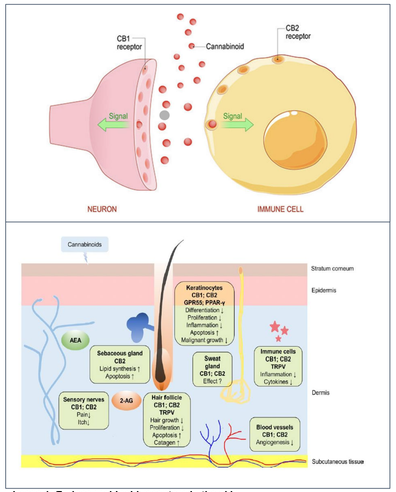

Image 1: Endocannabinoid receptors in the skin
Caterina MJ. TRP channel cannabinoid receptors in skin sensation, homeostasis, and inflammation. ACS Chem Neurosci. 2014;5(11):1107-1116. doi:10.1021/cn5000919

Figure 1: Human Studies

Article	Citation	# of participants	Dose	Duration	Frequency	Results
Hair Regrowth with Cannabidiol (CBD)-rich Hemp Extract - A Case Series	Smith GL, Satino J. Hair Regrowth with Cannabidiol (CBD)-rich Hemp Extract - A Case Series. *Cannabis*. 2021;4(1):53-59. Published 2021 Apr 22. doi:10.26828/cannabis/2021.01.003	35 subjects	3-4 mg per day	6 months		On average there was 93.5% increase in nonvellus hair after six months of once-daily use. All subjects had some regrowth.
An Observational Study of the Application of a Topical Cannabinoid Gel on Sensitive Dry Skin	Maghfour J, Rietcheck HR, Rundle CW, et al. An Observational Study of the Application of a Topical Cannabinoid Gel on Sensitive Dry Skin. *J Drugs Dermatol*. 2020;19(12):1204-1208. doi:10.36849/JDD.2020.5464	20		2 weeks		67% of participants reported a decrease in itch.
Efficacy of dietary hempseed oil in patients with atopic dermatitis	Callaway J, Schwab U, Harvima I, et al. Efficacy of dietary hempseed oil in patients with atopic dermatitis. J Dermatolog Treat. 2005;16(2):87-94. doi:10.1080/09546630510035832	16	30 mL (2tbsp) hempseed oil	20 weeks	Every 8 weeks with a 4 week washout period in between	Dietary hempseed oil improved clinical symptomsof atopic dermatitis.
The safety and efficacy of 3% cannabis seeds extract cream for reduction of human cheek skin sebum and erythema content	Ali A, Akhtar N. The safety and efficacy of 3% Cannabis seeds extract cream for reduction of human cheek skin sebum and erythema content. Pak J Pharm Sci. 2015;28(4):1389-1395.	11	3% cannabis seed extract cream	12 weeks	Measurements recorded every 2 weeks for 12 weeks	Skin sebum and erythmea content on treated side showed significant decrease compared with base treated side.
A therapeutic effect of cbd-enriched ointment in inflammatory skin diseases and cutaneous scars	Stella, A., Palmieri, B., Laurino, C., & Vadalà, M. (2019). A therapeutic effect of cbd-enriched ointment in inflammatory skin diseases and cutaneous scars. La Clinica Terapeutica, 170(2), e93–e99.	20		3 months	twice daily	The results showed that topical treatment with CBD-enriched ointment significantly improved the skin parameters, the symptoms. No irritant or allergic reactions were documented during the period treatment.

Figure 2: Animal Studies

Article	Citation	Number of Animals	Dose	Results
Cannabidiol-Loaded Lipid-Stabilized Nanoparticles Alleviate Psoriasis Severity in Mice: A New Approach for Improved Topical Drug Delivery	Zamansky M, Yariv D, Feinshtein V, Ben-Shabat S, Sintov AC. Cannabidiol-Loaded Lipid-Stabilized Nanoparticles Alleviate Psoriasis Severity in Mice: A New Approach for Improved Topical Drug Delivery. Molecules. 2023;28(19):6907. Published 2023 Oct 2. doi:10.3390/molecules28196907	For the study, male C57BL/6 8 to 11-weeks-old mice were used.	CBD—0.6% gel	CBD-loaded LSNs significantly reduced the PASI score and acanthosis and inhibited the IL-17A release compared to the control treatment groups. This demonstrated a substantial improvement in psoriasis symptoms. Moreover, the difference in response between CBD-loaded LSNs and CBD emulsion suggests deeper skin penetration and localization due to the LSN formulation. This study also emphasized the importance of lipid selection in topical drug delivery.
Analgesic and Anti-Inflammatory Effects of 1% Topical Cannabidiol Gel in Animal Models	Bunman S, Muengtaweepongsa S, Piyayotai D, et al. Analgesic and Anti-Inflammatory Effects of 1% Topical Cannabidiol Gel in Animal Models. Cannabis Cannabinoid Res. Published online September 5, 2023. doi:10.1089/can.2023.0070	Each group of studies included at least 10 mice and 8 rats.	1% CBD gel	It was shown that 1% CBD gel after 4 h of inflammatory induction reduced the severity of paw edema more than 1% diclofenac gel did, implying that 1% CBD had greater potential anti-inflammatory efficacy than 1% diclofenac. 1% CBD gel could help reduce inflammation and infiltration of inflammatory cells into the site of inflammation. Topical CBD could have analgesic and anti-inflammatory effects in animal models and can play a potential role in the clinical setting.
Transdermal cannabidiol reduces inflammation and pain-related behaviours in a rat model of arthritis	Hammell DC, Zhang LP, Ma F, et al. Transdermal cannabidiol reduces inflammation and pain-related behaviours in a rat model of arthritis. Eur J Pain. 2016;20(6):936-948. doi:10.1002/ejp.818	A total of 54 rats were used in the experiments described here of which 21 were used as naive controls and 23 were subjected to adjuvant-induced arthritis.	Animals were treated with CBD gel in 4 different doses: 0.62, 3.1, 6.2 and 62.3 mg/day for 4 consecutive days of treatment.	These data indicate that topical CBD application has therapeutic potential for relief of arthritis pain-related behaviours and inflammation without evident side-effects.

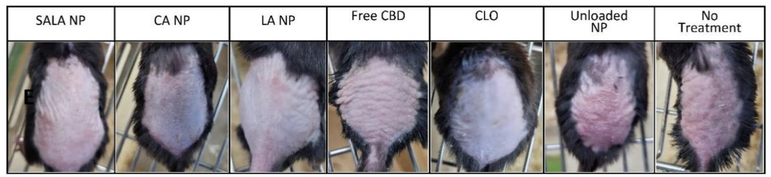

Image 2: Difference in progression of psoriasis in rat skin with different forms of topical treatment
Zamansky M, Yariv D, Feinshtein V, Ben-Shabat S, Sintov AC. Cannabidiol-Loaded Lipid-Stabilized Nanoparticles Alleviate Psoriasis Severity in Mice: A New Approach for Improved Topical Drug Delivery. Molecules. 2023;28(19):6907. Published 2023 Oct 2. doi:10.3390/molecules28196907

Methods

A literature review was performed utilizing PubMed. The following terms: (Cannabidiol, cannabis, topical, dermatological skin disorders, acne, psoriasis, transdermal) which produced a result of 57 articles. Some filters used while conducting this search were in vivo studies, human and animal studies, and topical route of administration. Of these 57 articles, 8 were used.

Conclusion

Many studies conducted in humans do not yield results that are measurable, do not indicate dosage forms, or the amount of CBD used. In the animal models there is an obvious positive outcome with the use of CBD on common disease states such as psoriasis and erythema; however, the measures of positive outcomes in humans are not as quantitative but more qualitative and self reported. Also, based on data found for the pharmacokinetics and pharmacodynamics for topical formulations of CBD, it has been shown to potentially increase medical efficacy and reduce adverse effects.We have shed light on the purported pharmacological action and current lack of human data to support the use.

Limitations

- Lack of studies in this area and its efficacy for medical use
- Many studies conducted have been done on animals rather than human subjects
- Limited findings of clinical studies with large sample sizes testing the efficacy of CBD in topicals
- Lack of a standardized dose across studies
- Lack of consistent biomarker for efficacy

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References

1. Caterina MJ. TRP channel cannabinoid receptors in skin sensation, homeostasis, and inflammation. ACS Chem Neurosci. 2014;5(11):1107-1116. doi:10.1021/cn5000919
2. Sivesind TE, Maghfour J, Rietcheck H, Kamel K, Malik AS, Dellavalle RP. Cannabinoids for the Treatment of Dermatologic Conditions. *JID Innov*. 2022;2(2):100095. Published 2022 Jan 13. doi:10.1016/j.xjidi.2022.100095
3. Baswan SM, Klosner AE, Glynn K, et al. Therapeutic Potential of Cannabidiol (CBD) for Skin Health and Disorders. Clin Cosmet Investig Dermatol. 2020;13:927-942. Published 2020 Dec 8. doi:10.2147/CCID.S286411
4. Peyravian N, Deo S, Daunert S, Jimenez JJ. The Anti-Inflammatory Effects of Cannabidiol (CBD) on Acne. *J Inflamm Res*. 2022;15:2795-2801. Published 2022 May 3. doi:10.2147/JIR.S355489
5. Gupta AK, Talukder M. Cannabinoids for skin diseases and hair regrowth. *J Cosmet Dermatol*. 2021;20(9):2703-2711. doi:10.1111/jocd.14352
6. Grinspoon P. The endocannabinoid system: Essential and mysterious. Harvard Health. Published August 11, 2021. https://www.health.harvard.edu/blog/the-endocannabinoid-system-essential-and-mysterious-202108112569
7. Osafo N, Yeboah OK, Antwi AO. Endocannabinoid system and its modulation of brain, gut, joint and skin inflammation. *Mol Biol Rep*. 2021;48(4):3665-3680. doi:10.1007/s11033-021-06366-1
8. Ramer R, Hinz B. Cannabinoid Compounds as a Pharmacotherapeutic Option for the Treatment of Martinez Naya N, Kelly J, Corna G, et al. An Overview of Cannabidiol as a Multifunctional Drug: Pharmacokinetics and Cellular Effects. *Molecules*. 2024;29(2):473. Published 2024 Jan 18. doi:10.3390/molecules29020473 *Control Release*. 2003;93(3):377-387. doi:10.1016/j.jconrel.2003.09.001
9. C Austin Zamarripa, Hayleigh E Tilton, Spencer Lin, Edward J Cone, Ruth E Winecker, Ronald R Flegel, David Kuntz, Melissa Beals, Martin Jacques, Michael Clark, Eric R Welsh, Lynn Wagner, Marcel O Bonn-Miller, Ryan Vandrey, Tory R Spindle, Pharmacokinetics and pharmacodynamics of five distinct commercially available hemp-derived topical cannabidiol products, *Journal of Analytical Toxicology*, Volume 48, Issue 2, March 2024, Pages 81–98, https://doi.org/10.1093/jat/bkae001
10. Mahmoudinoodezh H, Telukutla SR, Bhangu SK, Bachari A, Cavalieri F, Mantri N. The Transdermal Delivery of Therapeutic Cannabinoids. *Pharmaceutics*. 2022; 14(2):438. https://doi.org/10.3390/pharmaceutics14020438
11. Zamarripa CA, Tilton HE, Lin S, et al. Pharmacokinetics and pharmacodynamics of five distinct commercially available hemp-derived topical cannabidiol products. J Anal Toxicol. 2024;48(2):81-98. doi:10.1093/jat/bkae001