

Comment on “Cannabinoids in dermatologic surgery”



To the Editor: In view of the rapid growth in our understanding of the ubiquitous endocannabinoid signaling system together with the global trends toward cannabis legalization, we commend Kong et al¹ for their manuscript entitled “Cannabinoids in Dermatologic Surgery.” Their detailed review discusses the potential impact of cannabinoids in integumentary conditions. They recount evidence to suggest the benefit of cannabinoids on parameters of skin health, including wound healing and analgesia, and they highlight the current and potential therapeutic applications of cannabinoids. However, their discussion is centered upon a single cannabinoid, cannabidiol (CBD), while overlooking the more than 70 other cannabinoids and hundreds of other chemical compounds, including terpenes and flavonoids, which are derived from cannabis. It is important to emphasize that multiple chemical compounds play roles in the medicinal benefits of cannabis through their complex interactions with the endocannabinoid signaling system.²

The authors misrepresented some of the available literature by identifying cannabidiol (CBD) as the principal mediator of beneficial impact. They reference the 2017 systematic review by the National Academies of Sciences, Engineering, and Medicine on the therapeutic applications of cannabinoids.³ They erred by stating that this report recommends CBD as effective for chronic pain, chemotherapy-induced nausea and vomiting, and muscle spasticity. This report details that other cannabinoids contribute to these benefits. Oral cannabinoids, including synthetic analogs of Δ -9-tetrahydrocannabinol, dronabinol (Marinol) and nabilone (Cesamet), are effective for chemotherapy-induced nausea and vomiting. Oral cannabinoids and cannabis are effective for chronic pain. Lastly, nabiximols (Sativex) are effective for refractory cancer pain and spasticity associated with multiple sclerosis. These non-CBD cannabinoids deserve attention for their proven medicinal benefits. Within the field of dermatology, the combined use of cannabinoids, terpenes, and flavonoids from cannabis, instead of CBD alone, is garnering attention due to their potentiated effects in chronic pain and wound healing as a result of the entourage effect.^{1,4,5}

The use of topical CBD in epidermolysis bullosa highlighted by the authors is one published example of the benefit of cannabinoids in dermatologic conditions. However, there are more recently published data on successful outcomes in similarly challenging integumentary wounds caused by

calciphylaxis and sickle cell disease using topical cannabis-based medicines (TCBM). These TCBM comprise multiple active components of the cannabis plant from different chemical classes, including cannabinoids, terpenes, and flavonoids.

In a cohort of recalcitrant leg ulcers in complex patients with nonuremic calciphylaxis, TCBM led to complete wound closure within a mean of 2.5 months, while altogether negating the need for analgesics after 2.1 months.⁴ A case report involving 3 recalcitrant leg wounds in a complex patient with sickle cell disease showed complete wound closure within a mean of 1.4 months after TCBM application.⁵ These reports highlight the greater potential within the cannabis plant as a tool for the healing of integumentary conditions.

In summary, interactions with the endocannabinoid signaling system are complex and involve multiple compounds derived from botanical medical-grade cannabis. Indeed, their combined effects may be greater than the sum of their individual contributions. Therefore, cannabis-based therapies hold significant promise for the broad domain of dermatology.

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Conflicts of interest

Dr Maida is the President and CEO of VinSan Therapeutics Inc, which holds intellectual property and patents pertaining to cannabis-based medicines for integumentary and wound management. Author Fazzari has no conflict of interest to declare.

REFERENCES

1. Kong HE, Pollack BP, Blalock TW. Cannabinoids in dermatologic surgery. *J Am Acad Dermatol*. 2021;85:1565-1570. <https://doi.org/10.1016/j.jaad.2021.01.016>
2. Weigelt MA, Sivamani R, Lev-Tov H. The therapeutic potential of cannabinoids for integumentary wound management. *Exp Dermatol*. 2021;30(2):201-211. <https://doi.org/10.1111/exd.14241>

3. National Academies of Sciences, Engineering, and Medicine. *The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research*. The National Academies Press; 2017. <https://doi.org/10.17226/24625>
4. Maida V, Shi RB, Fazzari FGT, Zomparelli L. Topical cannabis-based medicines – a novel paradigm and treatment for non-uremic calciphylaxis leg ulcers: an open label trial. *Int*

Wound J. 2020;17(5):1508-1516. <https://doi.org/10.1111/iwj.13484>

5. Maida V, Shi RB, Fazzari FGT, Zomparelli L. A new treatment paradigm for sickle cell disease leg ulcers: topical cannabis-based medicines. *Exp Dermatol.* 2021;30(2):291-293.

<https://doi.org/10.1016/j.jaad.2021.05.074>