

**CASE REPORT**

# Self-initiated use of topical cannabidiol oil for epidermolysis bullosa

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**Abstract**

Epidermolysis bullosa is a rare blistering skin disorder that is challenging to manage because skin fragility and repeated wound healing cause itching, pain, limited mobility, and recurrent infections. Cannabidiol, an active cannabinoid found in cannabis, is postulated to have antiinflammatory and analgesic effects. We report 3 cases of self-initiated topical cannabidiol use in patients with epidermolysis bullosa in an observational study. One patient was weaned completely off oral opioid analgesics. All 3 reported faster wound healing, less blistering, and amelioration of pain with cannabidiol use. Although these results demonstrate promise, further randomized, double-blind clinical trials are necessary to provide scientific evidence of our observed benefits of cannabidiol for the treatment of epidermolysis bullosa.

**KEYWORDS**

blistering skin therapy, cannabidiol, cannabis, epidermolysis bullosa

## 1 | INTRODUCTION

Epidermolysis bullosa (EB) is a group of congenital blistering dermatoses affecting skin and mucosa that are caused by inherited defects in anchoring proteins between the epidermis and dermis, leading to mechanical fragility and predisposing patients to bullae, blisters, and scars with minor trauma. There are 4 major subtypes of EB based upon which proteins within the dermal-epidermal junction are altered: EB simplex, junctional EB, dystrophic EB, and Kindler syndrome. Injury prevention is paramount in the management of EB. Although new therapeutic options are being investigated, current treatment remains largely supportive and includes wound care, pain management, nutritional support, physical therapy, and social support.

Cannabidiol (CBD) oil has become increasingly popular for people with sleep disorders, anxiety, and chronic pain. Although studies have demonstrated its calming, relaxing, and antiinflammatory effects, clinical data are lacking. We present 3 cases of self-initiated CBD oil use in individuals with EB. Although family members noted fewer blisters, shorter healing time, and less analgesic need, these

results were not found in a randomized, double-blind, controlled study.

## 2 | REPORT OF CASES

### 2.1 | Case 1

A 6-month-old boy presented to a multispecialty EB clinic for routine evaluation. He had been born at 38 weeks gestation via cesarean section and was noted to have numerous intact blisters and aplasia cutis of the bilateral lower extremities. Biopsy followed by immunofluorescence and electron microscopic analysis showed absence of collagen VII and anchoring fibrils, confirming the diagnosis of recessive dystrophic EB.

Initial home wound care included over-the-counter petrolatum ointment, emu oil, and silicone-based dressing. Mupirocin was used intermittently to treat superficial infection and for secondary decolonization. Diphenhydramine and morphine were given before dressing changes. Because of persistent blistering and inadequate pain control with morphine, his parents self-initiated CBD spray, a

tincture of CBD oil that is misted over affected areas 2 to 3 times daily. They reported significant reduction of blistering since starting CBD spray (Figure 1), and he no longer required morphine before dressing changes. The parents also noted faster healing of chronic wounds.

## 2.2 | Case 2

A 3-year-old girl presented to the EB clinic for multispecialty care. She had been born at 40 weeks via spontaneous vaginal delivery and had erosions on the extremities and oral mucosa. Painful keratoderma on the soles limited her ambulation. Biopsy and electron microscopic analysis were consistent with EB simplex, generalized severe. Genetic testing confirmed a KRT5 mutation.

Home wound care included a mixture of petrolatum ointment with coconut oil followed by spot treatment with zinc oxide and allantoin 6% cream. For keratoderma, 10% urea was applied followed by gentle debridement. Dilute bleach baths and topical bacitracin were used to minimize skin infection. Based on recommendations from members of an EB social network, her mother began using a blend of emu oil and CBD oil applied topically to blisters on the face, trunk, and extremities at least twice daily, after which the patient was reported to have fewer blisters, and healing time for facial blisters was reduced by approximately half. Application of CBD to keratoderma also reduced pain associated with ambulation, allowing the patient to walk longer distances. Photo documentation over time supported the parents' subjective findings of less blistering (Figure 2).

## 2.3 | Case 3

A 10-year-old boy presented in whom easy blistering around the neckline had first been noticed at 1 month of age. Blisters on the palms and soles progressed at approximately 13 months of age, when he began walking. He was given a clinical diagnosis of localized EB simplex, because biopsy was declined. He continued to have frequent blistering of the neck, posterior upper arms, and soles as he aged. His regular wound care regime included emollients and over-the-counter topical antibiotics. He had debilitating, painful keratoderma that required wheelchair assistance and scheduled naproxen and gabapentin.

His parents self-initiated CBD oil and cream topically to his blisters and noted significant reduction in blistering with CBD use. They also noticed a lessening of his painful keratoderma, leading to more ambulation and less wheelchair use. He was able to discontinue naproxen and gabapentin after starting topical CBD.

## 3 | DISCUSSION

Cannabidiol is a naturally occurring compound of industrial hemp and marijuana, collectively referred to as cannabis. CBD is one of nearly 100 different cannabinoid compounds found in cannabis and is the

second most abundant phytocannabinoid after tetrahydrocannabinol (THC); but unlike THC, CBD does not have hallucinogenic effects.<sup>1</sup>

There are 2 known cannabinoid receptors in humans: cannabis (CB)1 and CB2.<sup>2</sup> CB1 receptors are expressed throughout the body, with a great proportion in the nociceptors of the brain and spinal cord.<sup>3</sup> The CB1 receptors are associated with the analgesic effects of cannabinoids. CB2 receptors are expressed in lymphoid tissue, and it is hypothesized that binding of CBD to CB2 receptors modulates cytokine release from immune cells and reduces inflammation.<sup>3</sup> CBD is also a direct agonist of vanilloid pain receptors (transient receptor potential cation channel subfamily V member 1 receptor), which are known to mediate pain perception, inflammation, and body temperature.<sup>4</sup> There are also many studies that have demonstrated the protective function of cannabinoids in acute and chronic inflammatory diseases,<sup>5,6</sup> although long-term safety and effects of its use have not been studied.<sup>7,8</sup>

Within the epidermis itself, CB agents have been shown to indirectly inhibit proliferation of cultured human epidermal keratinocytes and to stimulate apoptosis.<sup>9</sup> Other studies have shown that CB agents regulate epidermal differentiation through CB1 receptor-dependent inhibition of protein kinase C, activation protein-1, and transglutaminase.<sup>10,11</sup> Synthetic CB receptor agonists have also been linked to a reduction of histamine responses in human skin,<sup>12,13</sup> and there have been studies documenting its use in treating inflammatory acne vulgaris because of its ability to decrease proliferation of human sebocytes *in vitro*.<sup>14</sup>

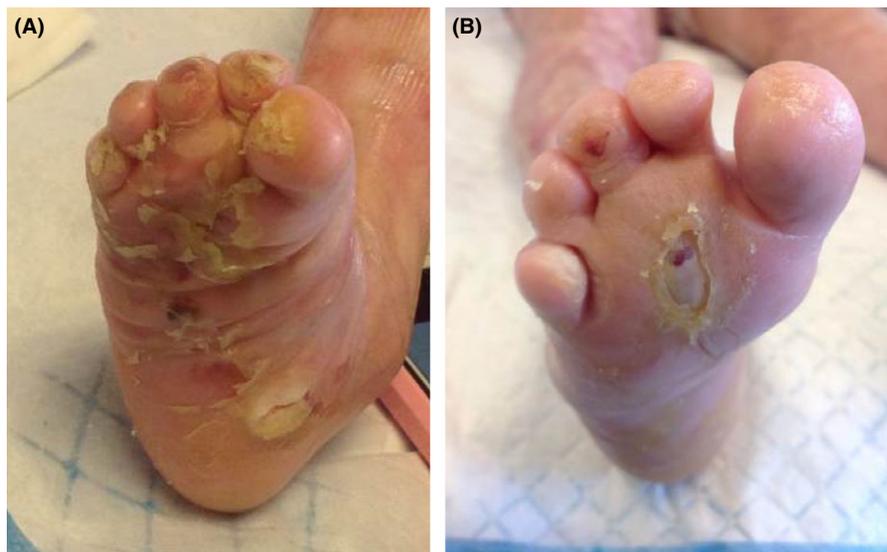
The use of CBD oil in individuals with EB is widely discussed in various online forums, but evidence supporting its use is anecdotal. Its topical formulations are available as oils, creams, and sprays. It is hypothesized that CBD decreases symptoms of EB by relieving chronic pain, modifying the itching sensation, and reducing inflammation.<sup>15</sup>

All 3 patients initiated treatment with CBD oil without physician recommendation. Two were able to stop oral analgesic medications (diphenhydramine and opiates in case 1; naproxen and gabapentin in case 3) after starting topical CBD. Cases 2 and 3 noted improvement in ambulation after application of CBD to hyperkeratosis on the soles. All patients noted fewer blisters and shorter healing time for active blisters. There were no self- or family-reported adverse effects from topical CBD.

To our knowledge, this is the first report in the medical literature on the use of topical CBD for EB. The mechanism of action for the observed benefits remains to be elucidated. We must exercise caution in interpretation of these findings, because randomized, double-blind, controlled studies are necessary to provide credible evidence of the benefits of CBD in EB. This is an observational study, which has inherent bias. For example, responders are more likely to divulge use of CBD than nonresponders, potentially magnifying the perceived clinical benefits. There is also potential for bias because results are self-reported. Furthermore, the study lacked a vehicle control group for comparison. Blistering in some subtypes of EB, such as EBS—generalized severe, is known to improve with age.



**FIGURE 1** Right leg before and after treatment with topical cannabidiol. A, At presentation, multiple intact blisters and aplasia cutis. B, After 6 mo of treatment, blisters are minimal and aplasia cutis is resolved



**FIGURE 2** Right foot before and after treatment with topical cannabidiol. A, At presentation, multiple intact blisters and skin erosions. B, After 8 mo of treatment, blisters and erosions are minimal

Although the perceived benefit of CBD could be spontaneous resolution because of older age and better skin care, the improvement reported occurred over a short period of time after initiating CBD. The perceived benefit of CBD could also be attributed to vehicle or placebo effects.

In conclusion, we have reported our observation of 3 individuals with EB who benefited from the use of topical CBD, specifically noting a reduction in pain and blistering and rapid wound healing. We chose to report the dramatic benefits patients described and the objective need for less analgesic to stimulate the scientific community to consider the study of CBD in EB. There have been no scientific randomized controlled studies of topical CBD use in children

with EB. Well-designed clinical trials are needed to further delineate the safety and efficacy of CBD use in EB.

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