Healing From the Outside In

The Therapeutic Powers of Cannabis Topicals

Introduction

As the body's largest organ and frontline defense, skin confronts constant assault from external pathogens, UV radiation, irritants, allergens, and injuries — mandating elaborate safeguarding of human biology. Our body's intricate protection system balances processes regulating epidermal cell proliferation and differentiation, pigmentation, vascular regulation, sweating, sensing, immunity, and inflammation through a complex molecular signaling network called the skin *Endocannabinoid System* (ECS) [1].

Human skin is composed of three main layers - the epidermis, dermis, and hypodermis. The outermost epidermis provides a protective barrier against the environment. It consists of several sublayers, with the stratum corneum at the very surface containing tough, dead skin cells.

Underneath lies the dermis, which contains connective tissue, hair follicles, sweat glands, and blood vessels giving skin its structure and elasticity. Deepest lies the hypodermis, composed mainly of fat and connective tissue which insulates the body and provides cushioning. Together, these layers dynamically interact to waterproof, shield, regulate temperature, sense stimuli, and synthesize key molecules upholding healthy barrier function.

The fabric of our skin is designed to "self-calibrate" via endocannabinoid lipids that engage cell receptors to maintain cutaneous equilibrium known as "homeostasis" [2].

However, exposure to modern stressors increasingly overloads the skin's adaptive capacity, thereby disturbing the ECS —which then manifests outwardly as inflammatory skin diseases including eczema, psoriasis, dermatitis, acne, infection, and chronic dryness/itch. Figure 1 below illustrates the skin's structure and diversity.

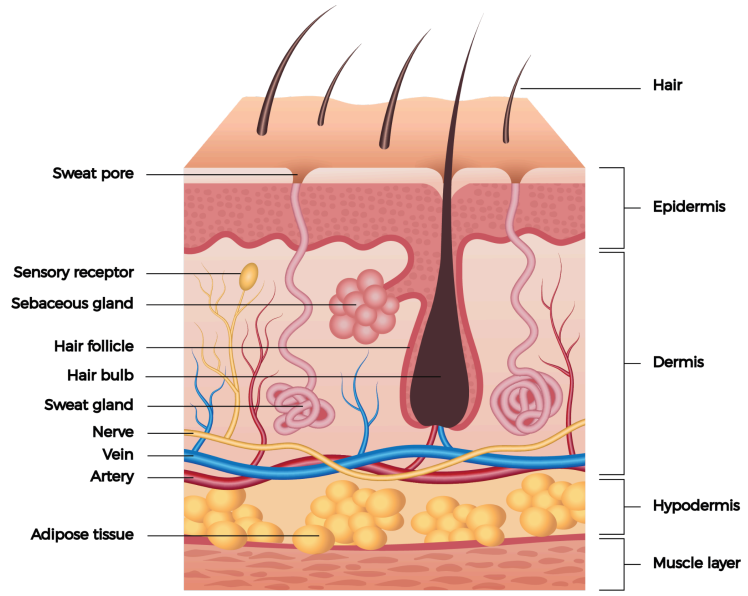

Figure 1: Human Skin Structure

Though topical steroids temporarily address symptoms, the unremitting nature and treatment risks calls for safer long-term solutions. Recent therapeutic newcomers taking the form of plant-derived cannabinoids have demonstrated anti-inflammatory, antimicrobial, antioxidant, anti-aging, and anti-itch benefits when topically applied.

Creams, lotions, and cosmetics infusing non-psychoactive cannabidiol (CBD) already line shelves bringing cannabis skin care into mainstream consciousness while further frontier compound and delivery advances loom imminent.

This white paper surveys mounting preclinical and other validation research supporting cannabinoids in helping maintain dermal health. It examines ECS architecture and endogenous signaling gone awry in common skin maladies, profiles major phytocannabinoids and their mechanisms and investigates new acidic cannabinoid variants. Lastly, we'll explore forthcoming opportunities and challenges marrying cannabis with dermatology.

Cannabinoids for Skin Health

Cannabis contains specialized compounds called cannabinoids that interact with skin cells to treat many inflammatory conditions. These cannabinoids work by binding receptors in the skin's endocannabinoid system (ECS). The ECS acts like a monitor, continually checking that skin cells work properly. When something disrupts the ECS, diseases can happen.

There are two main cannabinoid receptors in skin – CB1 and CB2. But cannabinoids also bind other receptors like *TRP channels* to exert healing effects. For example, the cannabinoid THC activates TRPV1 channels on pain sensing nerves. This stops pain signals, reducing discomfort in irritated skin. The cannabinoid CBG likewise battles skin bacteria by blocking inflammation. Different cannabinoids team up to ease symptoms by targeting various disease pathways simultaneously.

Cannabis also contains acidic cannabinoids like THCa and CBDa, possessing enhanced anti-inflammatory and antioxidant properties compared to traditional THC and CBD forms. For instance, CBDa tackles inflammation causing enzymes 500 times more powerfully than CBD. Additionally, inherent shelf stability advantages make cannabinoid acids superior choices managing inflammatory skin disorders.

Topical creams and lotions maximize cannabinoids' skin benefits while avoiding risks associated with internally taken options. Applied directly on affected areas, cannabinoid acids achieve high local concentrations which engage receptors underlying lesions that define conditions like eczema and psoriasis. This local action spares systemic distribution into the bloodstream, greatly reducing side effects. It also provides durable symptom relief as sufficient amounts stay active on the skin's surface.

Transient Receptor Potential (TRP) Channels

Transient Receptor Potential (TRP) channels are sensory channels that are activated by diverse physical and chemical signals. This enables them to evoke electrical signals or intracellular cascades to allow cells to sense their environments.

Transient Receptor Potential (TRP) channels are a large family of ion channels found in the membranes of many cell types. There are 27 different known TRP channel proteins in mammals, divided into 6 subfamilies based on their amino acid sequence homology – TRPA, TRPC, TRPM, TRPML, TRPP, and TRPV.

TRP channels play important roles in senses such as vision, taste, smell, touch, hearing, temperature sensation, and the encoding of molecular signals that generate a response.. They are also involved in other physiological processes like vascular tone regulation, insulin secretion, and Calcium and Magnesium ion reabsorption.

TRP channels are activated by diverse chemical, physical, mechanical, and thermal stimuli. For example, TRPA1 is activated by pungent compounds like mustard oil and cinnamaldehyde, TRPM8 is activated by cold temperatures and menthol, and TRPV1 is activated by capsaicin in hot chili peppers and noxious heat.

Some TRP channels contain sensory domains in their terminal regions that also react to temperature changes or chemical modifications.

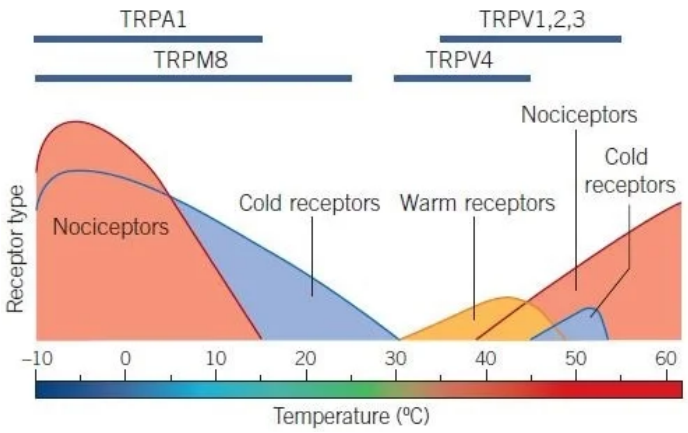

Figure 2: TRP Channels and External Stimuli

Conformational shifts[1] in these domains directly open the channel. Other TRP channels work downstream of receptors that use messenger molecules like diacylglycerol or IP3[2]. When these messenger levels rise, they trigger the TRP channel to open. Regardless of the initial trigger, the end result is that the channel opens to allow ion influx into the cell, converting environmental signals into electrical or biochemical responses.

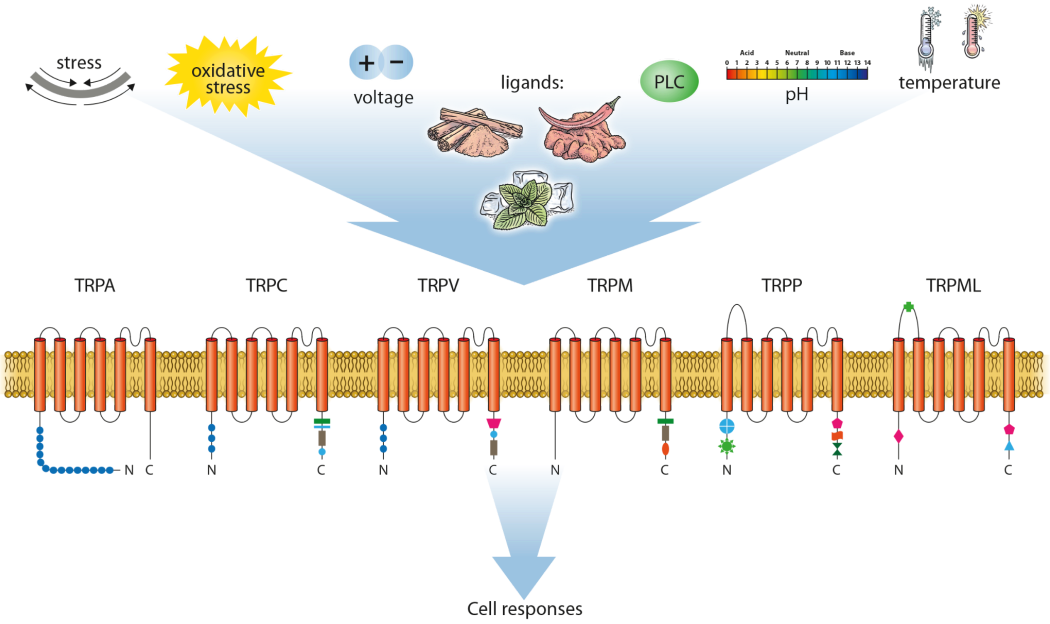

Figure 3: TRP Channels and Signal Sequencing

[1] A *Conformational Shift* refers to a change in the shape or structure of a protein. Such action occurs when external stimulus causes the protein to alter its shape by unfolding, bending, twisting or otherwise deviating from its original conformation.
[2] Inositol trisphosphate (IP3) and Diacylglycerol (DAG) are small molecules that act as a second messenger to regulate various cellular processes.

Once open, TRP channel pores are permeable to ionic versions of elements such as Calcium and Sodium, allowing these ions to flow into the cell. This ion influx then triggers action in some neurons or leads to other cell-type specific responses. Figure 3 illustrates the TRP channels and external stimuli.

Figure 4 shows the epidermal layer, key cell types, and the TRP channels that affect them. TRP's wide range of activating stimuli and involvement in many physiological processes make them important research targets for understanding sensation and for identifying potential therapeutic strategies.

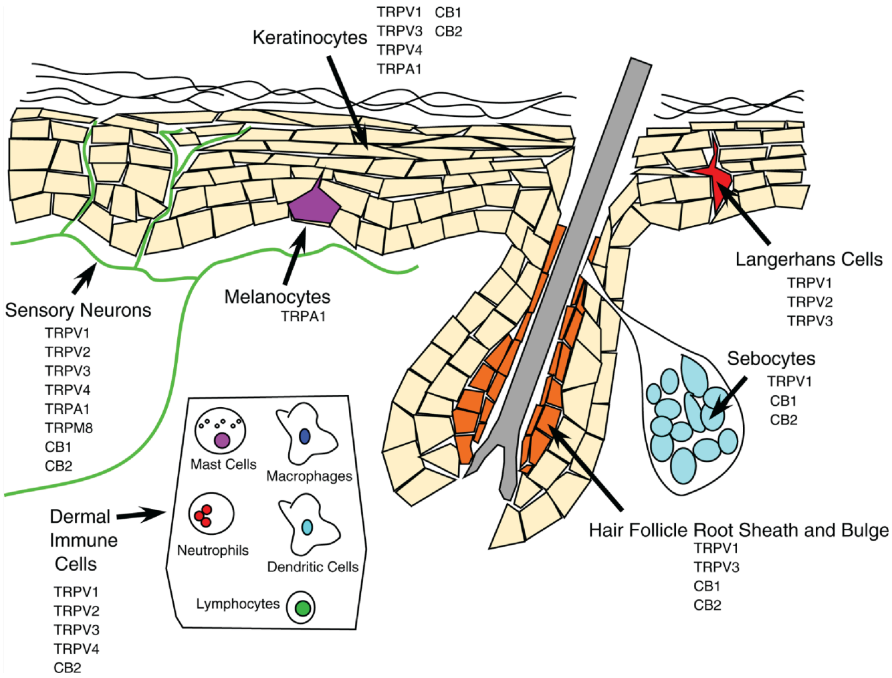

Figure 5: Epidermal Structure and TRP Channels

Cannabinoids Modulate Distinct Skin TRP Channels

As multiple signal integrators, some TRP channels serve as direct molecular targets for endo-, phyto-, and synthetic cannabinoids — termed "ionotropic cannabinoid receptors". The diverse TRP channels populate skin tissue — notably TRPV1-4, TRPA1 and TRPM8 — monitor inputs critical for maintaining tissue viability and immunological response. Clinical data indicates cannabinoids engage these entities and influence activation states with significant therapeutic implications.

For instance, endo- and phytocannabinoids activate the heat/pain sensor TRPV1. CBD likewise triggers inward movement, while higher cannabinoid concentrations desensitize channels and dampen inflammation. The skin TRP channel TRPA1 also responds to environmental irritants, resulting in inflammation and itch. Cannabinoids like THC, CBD and CBN activate TRPA1 directly but can likewise prompt desensitization at sufficient levels to reduce overactivity.

Research findings reveal cannabinoids wield intricate modulatory control over sensory and immunological skin TRP channels, thus expanding possibilities for therapeutic targeting of cutaneous tissues. Such an approach holds promise for managing afflictions involving inflammation, irritation, discomfort and barrier disruption. Continued exploration promises greater cannabinoid skin specificity while avoiding psychoactive effects accompanying systemic delivery.

The Skin Endocannabinoid System: Regulator of Cutaneous Balance

The skin's own endocannabinoid system is composed of bioactive lipids, metabolic enzymes, and various receptor families. Endocannabinoids like anandamide and 2-AG[3] activate ECS receptors to calibrate key functions involved in maintaining skin homeostasis. This delicate regulation goes awry in common disorders (like dermatitis) where endocannabinoid levels become abnormal [3].

Research confirms the skin generates endocannabinoids while also responding to plant cannabinoids applied externally from cannabinoids. These exogenous cannabinoids supplement the ECS through receptor pathways leading to anti-inflammatory, anti-itch, antioxidant, and anti-aging effects holding therapeutic promise [4].

Phytocannabinoids: Polymorphic Plants That Heal The Skin

Over 120 phytocannabinoids in Cannabis originate from biochemical immunity against pathogens now proving medicinal utility in people [5]. Best known tetrahydro-cannabinol (THC) and cannabidiol (CBD) constitute abundant neutral forms delivered directly from resin glands. Therapeutic attributes become augmented by lesser components like cannabichromene (CBC), cannabigerol (CBG), tetrahydro- cannabivarin (THCV) acting synergistically [6].

Though pure synthetic cannabinoid pharmaceuticals (e.g., Marinol, Cesamet, Sativex) exist, whole plant extracts combine far more remedial molecules that act to mitigate toxicity. This translates to increased potential application for inflammatory disease, including those of the skin [7].

Cannabinoids provide consistent anti-inflammatory relief by activating CB2 receptors. These receptors suppress the release of immune mediators that are involved in the pathways that generate inflammation and itch [8]. Additional TRP channel engagement on sensory neurons and mast cells further modulates pain and itch symptoms through separate desensitization pathways [9].

Cannabinoids also protect against damage from oxidation. They achieve this by both directly eliminating these damaging antioxidants and boosting natural antioxidant defenses (like superoxide dismutase[4]). This prevents collagen breakdown and skin aging caused by UV exposure to the Sun. Additionally, the combination of antioxidant, itch-reducing, cell growth-slowing and immune-calming effects allows cannabinoids to target multiple pathways to optimize skin healing [10].

[3] Anandamide and 2-AG are endogenous cannabinoid neurotransmitters that bind to cannabinoid receptors in the brain and body.
[4] Superoxide dismutase (SOD) is an antioxidant enzyme that plays a key protective role in cells exposed to oxygen.

Cannabinoid Acid Variants—Heightened Potency

While neutral cannabinoids like THC and CBD constitute most recognized forms, momentum shifts recognizing their biosynthetic acidic precursors retain enhanced therapeutic capacity concentrated in non-decarboxylated raw plants.

The acid forms of cannabinoids, CBDa and THCa, are more potent anti-inflammatory agents compared to their neutral counterparts. At smaller doses, CBDa and THCa can inhibit inflammation-promoting enzymes by up to 500 times more effectively than compounds like CBD and THC. Additionally, the acid forms do not cause psychotropic effects associated with activated cannabinoids [11].

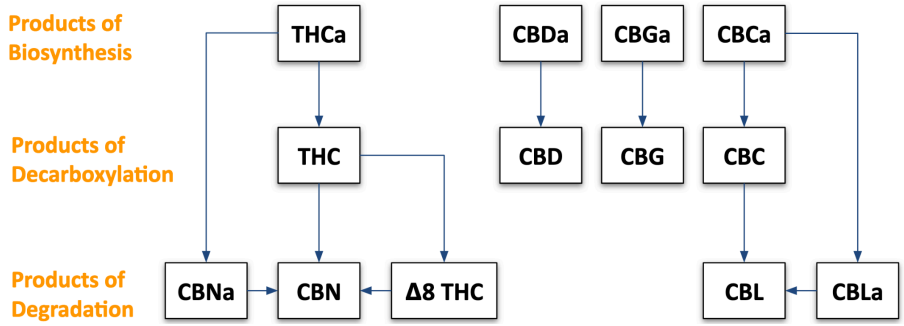

Figure 6: Cannabinoids and Their Precursors

Synthetic customization can further optimize actions for personalized therapy. Cannabinoid acids hold promise managing inflammation and skin conditions given superior bioactivity, stability, and tissue penetration[12]. Continued development extracting full cannabis benefits sees this molecular medicine applied balancing cutaneous needs.

Topical Cannabinoids – Direct Delivery

Beyond beneficial bioactivity, topical preparations maximize cannabinoid skin delivery while avoiding risks accompanying oral ingestion[13]. Transdermal creams, lotions, and patches allow sustained epidermal permeation reaching engaged receptors underlying plaques and lesions directly. This spares unnecessary systemic distribution reducing mood, fatigue and cognitive changes crossing the blood-brain barrier [14].

Acid in the GI tract partially compromises cannabinoid integrity, causing uneven absorption and effects [15]. In contrast, transdermal diffusion provides sustained symptom relief and bioavailability without gastric pitfalls. These inherent advantages make topical cannabinoids ideally suited concentrating activity where most required [16].

Treating Inflammation and Infection

Cannabinoids exhibit anti-inflammatory, antimicrobial, and anti-aging properties that are uniquely promising for treating inflammatory skin diseases. Conditions like eczema, psoriasis, acne, and chronic skin infections could potentially be managed by targeting multiple pathological pathways simultaneously [17]. Specifically, cannabinoids can:

- Suppress production of immune mediators and itch signals
- Combat infection-causing bacteria
- Reverse skin damage from UV exposure

Human studies already demonstrate CBD creams notably improving psoriatic plaques and lichenification associated with eczema just as well as standard topical steroids but without risks compelling treatment cessation [18]. Parallel emerging options harnessing non-psychotropic cannabinoid acids, spectrum botanical extracts, rationally devised combinations, and advanced modalities promises more comprehensive, personalized future skin therapy centered around homeostasis supporting skin health inside and out.

Halo Infusions Topicals - A Whole Plant Approach

Halo Infusions Intermediate Decarboxylation Process (IDP) judiciously extracts cannabinoid acids like THCa and CBDa alongside activated cannabinoids and terpenes retaining the full spectrum integrity matching the original flower's natural chemical ratios. This technique preserves anti-inflammatory acidic precursors alongside central analgesics THC and CBD among over 200 more compounds absent in isolates.

Controlled partial decarboxylation strikes an optimal balance maximizing diversity hitting the sweet spot between retained carboxyl groups combating irritation and freed hydrogens easing discomfort.

Insights gained in recent studies specifically show excellent anti-inflammatory, antioxidant and regenerative properties of cannabinoid precursors including THCa and THCV for inflammatory skin conditions. Topical THCa creams have been shown to significantly resolve dermatitis, psoriasis and acne symptoms given superior bioactivity and dermis penetration.

Figure 7 illustrates the decarboxylation process. In the figure, the red vertical dashed line indicates where Intermediate Decarboxylation occurs. It's at this specific sweet spot that decarboxylation is halted in order to maximize cannabinoid and precursor expression.

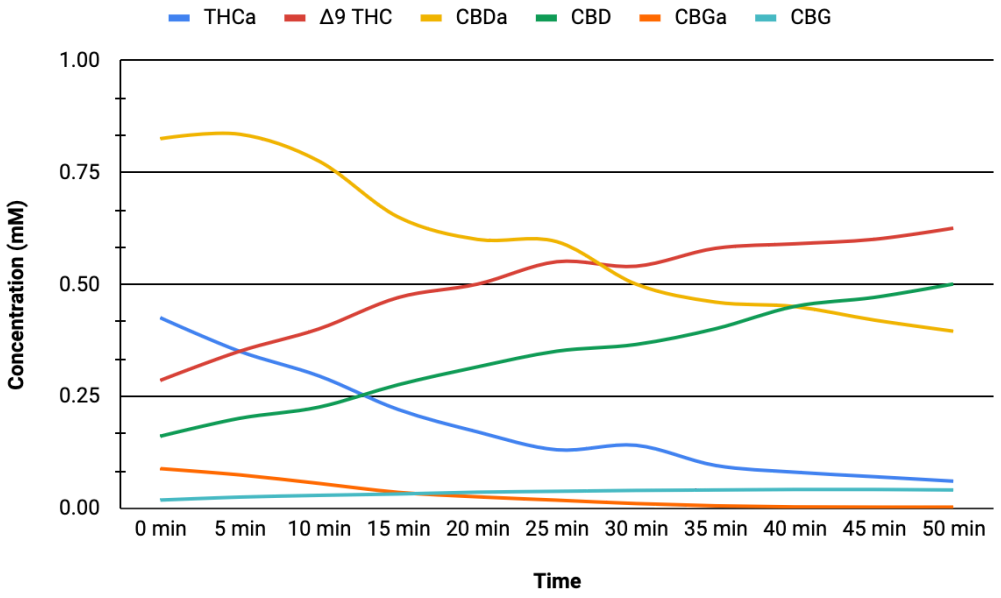

Figure 7. Decarboxylation Over Time

Conclusion

Plant cannabinoids can interact directly with the human endocannabinoid system to restore balance in the skin. Consistent clinical results demonstrate that customized cannabinoid treatments can effectively treat stubborn skin conditions without impairing the central nervous system.

But what is only beginning to be understood is the synergetic interaction that cannabinoids and other cannabis compounds have in interacting with tissues in the skin, including and especially the TRP channels present. The resulting interaction creates a cascade effect that has profound and immediate benefits in terms of pain relief.

Studies referenced in this paper demonstrate the potential of cannabinoids to improve dermatological therapies for many patients through complementary care focused on the skin. As the outermost organ, skin is uniquely situated at the intersection of internal physiology and external environment.

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