Chapter VII: Dermatological Health and Dermatological Disease

Learning Objectives
1. Discuss assessment protocols to determine level of endocannabinoid deficiencies of the dermatological system.
2. Discuss therapeutic strategies to address endocannabinoid deficiencies of the dermatological system.
3. Discuss patient care guidelines to implement cannabinoid therapy with standard of care pharmaceutical regimens pertaining to the dermatological system.
4. Discuss educational guidelines for patients to monitor clinical outcomes when implementing cannabinoid protocols for dermatological disorders.

The Endocannabinoid System and Cannabidiol (CBD) - Introduction

The endocannabinoid system (ECS) is a lipid-derived signaling system discovered within the past decade. Cannabinoids, which are homeostatic regulators, circulate throughout human and animal systems continuously, affecting all physiological processes. The endocannabinoid system is comprised of CB1 and CB2 receptors, which bind directly or indirectly to cannabinoids and phytocannabinoids. CB1 receptors are excitatory and are located in the central nervous system, lungs, liver, and kidney. CB2 receptors regulate immunological responses and are located in the immune and circulatory systems. Endogenous compounds, such as anandamide and arachidonylglycerol (2-AG), are made by mammals from lipids and bind directly to the CB1 and CB2 receptors, serving as neurotransmitters for cannabinoids. Cannabidiol (CBD oil), a non-psychotropic cannabinoid naturally occurring in human and animal species, is also a phytocannabinoid, derived from the industrial hemp plant. While CBD does not bind directly with receptors, it does affect stress genes, such as Soat2 and Cyp27a1, which control sterol (i.e., cholesterol) metabolism. CBD increases the amount of anandamide and other vital lipids, thereby indirectly increasing the availability of circulating cannabinoids to bind with CB1 and CB2 receptors.

Research has shown that cannabidiol, in the form of CBD oil, has therapeutic benefits individually and adjunctively with other interventions. Cannabidiol (CBD) made from legal, industrial hemp contains less than .3% THC, rendering it non-psychoactive. CBD oil has antiemetic, anxiolytic, antitumoral, and immunologically inhibitory properties. Three categories differentiate the types of clinical endocannabinoid deficiency (CECD), which are associated with different disease processes and disorders: genetic, acquired, and idiopathic autoimmune. Many disorders have a combination of CECD origins, and supplementation with cannabidiol (CBD) requires ongoing assessment to facilitate optimal benefit for the individual.

The Human Endocannabinoid System
The human endocannabinoid system is responsible for memory networks in the brain, both excitatory and inhibitory, including the neurogenesis of hippocampal granule cells, which regulate the timing of the endocannabinoids in accordance with the brain’s needs, pain perception, mood, synaptic plasticity, motor learning, appetite and taste regulation, and metabolic function, which regulates the storage of energy and transport of cellular nutrition. Cannabinoid receptor binding sites are located in the forebrain areas associated with higher cognitive function, forebrain, midbrain, and hindbrain areas associated with movement control, and hindbrain areas associated with motor and sensory functions attributed to the autonomic nervous system. The endocannabinoid system affects the lipocytes and fat cells, collectively
known as adipocytes, hepatocytes, in the gastrointestinal tract, musculoskeletal system, and endocrine system. The endogenous arachidonate-based lipids, anandamide and 2-arachidonoylglycerol (2-AG) are physiological ligands for the cannabinoid receptors. Cannabinoid receptors CB1 and CB2, two G-protein-coupled receptors, facilitate the responses of the endocannabinoid system in the body, which are critical to maintaining homeostasis. CB1 receptors are located in the central and peripheral nervous systems as well as the lungs, kidneys, and liver. CB2 receptors are predominantly expressed in the immune system and hematopoietic cells.

The direct effect of the endocannabinoid deficiency (CECD) correlates with multisystemic clinical outcomes in such conditions as hyperinsulinemia, osteoporosis, diabetes, dementia, cardiovascular disease, multiple sclerosis, and obesity. Three primary categories are herein defined to discuss endocannabinoid deficiency (CECD): genetic, acquired, and idiopathic autoimmune. Genetic endocannabinoid deficiency relates to hereditary acquisition of a disorder; acquired refers to an infectious of traumatic origination, and idiopathic autoimmune refers to etiologies for endocannabinoid deficiencies (CECD) which do not have direct associations. Diseases and disorders are assigned to one or more of these categories because often secondary disorders arise with physiological changes associated with the primary diagnosis. For example, dermatitis has been associated with endocannabinoid deficiency (CECD) and the disease is often categorized as acquired, originating from an extrinsic source. The presentation of scleroderma, which is multisystemic, supports adding the category of idiopathic autoimmune as well to the assessment. Because the endocannabinoid system facilitates communication and coordination between various cell types, deficiencies directly affect physiological homeostasis.

Cannabidiol (CBD), a non-psychotropic cannabinoid naturally occurring in human and animal species, occurs as a phytocannabinoid, CBD oil, which is derived from the industrial hemp plant. The restorative effects of cannabidiol (CBD oil), which increases anandamide and other lipid neurotransmitters, thereby restoring the endocannabinoid system, are of interest in the medical management of multiple disorders, including disorders of the dermatological system, which is directly affected by the immunological and neurological systems. Indeed, research supports that plant-derived cannabidiol (CBD) has analgesic, anti-tumoral, and anti-inflammatory benefits.

Cannabidiol (CBD)
Cannabidiol (CBD) is a non-psychotropic and non-toxic compound, which has been demonstrated to positively affect the human endocannabinoid system. Cannabidiol (CBD), derived from the hemp plant, demonstrates anti-inflammatory and immune-modulating properties. Cannabidiol (CBD) has a low affinity for CB1 and CB2 receptors in the human body, but acts as an indirect antagonist of their agonists. (Antagonists are defined as substances that stop or inhibit the effects of another substance on the cellular surface, producing the same effect as a substance which would normally bind to the receptor. Agonists are chemicals that bind to receptors and elicit a biological response.) Therefore, cannabidiol (CBD) may enhance the therapeutic effects of THC, possibly by increasing the density of the CB1 receptors. Cannabidiol (CBD) has been demonstrated to cross the blood-brain barrier and exert antioxidant, antimicrobial, and antitumoral properties, rendering it valuable in the prevention and treatment of oxidative dermatologic disorders and diseases.
Human Dermatological System
The largest organ of the human body is the skin, which protects and armors the underlying adipose tissue, muscle, ligaments, viscera, and skeletal system. Multiple layers of ectodermal tissue facilitate insulation, temperature regulation, sensation and synthesis of vitamin D and B for the human body. As the initial line of defense, the skin protects the body from pathogens and minimizes dehydration, managing water loss. Pigmentation of the skin varies in the world and originated from geographical location and climate category.

The endocannabinoid system facilitates immunological and nervous system responses throughout the dermatological system via CB1, autonomically through CB1 receptors, and immunologically through CB2 receptors. Various manifestations of endocannabinoid deficiency affect the dermatological structures, increasing the incidence of diseases that affect the skin and underlying tissues.

Cannabidiol (CBD) and Dermatological Disorders and Diseases: Dermatitis
Chronic dermatological conditions, such as psoriasis, and acute conditions, such as contact dermatitis, cause rash, pruritus, increased risk of infection, and psychological stress. The immunological response often increases symptoms associated with dermatitis. CB1 and CB2 receptors in genetic and acquired clinical endocannabinoid deficiency (CECD) in dermatitis respond to the administration of cannabidiol (CBD). Research indicates that cannabidiol (CBD) possesses anti-inflammatory and analgesic properties, which reduce symptoms. Further, the increased uptake of administered cannabidiol (CBD) has been found to regulate the immunological responses to dermatitis, thereby improving symptoms and reducing anxiety and depression associated with dermatitis. Cannabidiol (CBD) is suggested as adjunctive therapy in the management of both chronic and acute dermatitis.

Diabetic Ulcer
Diabetic ulceration occurs when decreased circulatory perfusion accompanies diabetes. Reduced blood flow to the periphery, including legs and feet, causes chronic ulceration, cellulitis and recurring infection. Clinical endocannabinoid deficiency (CECD) in diabetes mellitus responds to adjunctive administration of CBD oil with oral hypoglycemic agents and insulin. CB1 and CB2 receptors are restored with cannabidiol (CBD) administration, reducing sensory and dysfunctional immunological responses, respectively. Cannabidiol (CBD) possesses anti-inflammatory and anti-bacterial properties, which potentiate therapeutic healing options, such as hyperbaric oxygen therapy, in the management of diabetic ulcerations.

Scleroderma
Scleroderma, a systemic autoimmune disorder manifesting initially and most frequently as a dermatologic exacerbation, causes hardening of the skin and tissues. Alterations in oxygen perfusion and aberrant immunological responses contribute to symptoms of pain and fatigue. Clinical endocannabinoid deficiency (CECD) in scleroderma is considered idiopathic autoimmune, affecting CB1 and CB2 receptors throughout the human body. Administration of cannabidiol (CBD) has been shown to improve skin elasticity, reduce dermatological exacerbations, and relieve discomfort associated with this chronic disorder.
Skin Cancer
Malignancy of the skin includes such malignancies as squamous cell carcinoma and malignant melanoma. Tumoral growth and visceral dissemination of malignancy characterizes carcinoma of the skin, categorized as acquired and idiopathic autoimmune clinical endocannabinoid deficiency (CECD). Administration of cannabidiol (CBD) triggers malignant cell death, inhibiting tumor growth, and metastasis to viscera. Further, autophagy, which removes cellular waste, is enhanced by cannabidiol (CBD), expediting malignant cell death. Administration of cannabidiol (CBD) is warranted given conclusive research which supports anti-tumoral, anti-bacterial, and analgesic effects of CBD oil.

Endocannabinoid Deficiency (CECD) Classification: Dermatological Disorders

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Origin of CECD</th>
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<tbody>
<tr>
<td>Dermatitis</td>
<td>Genetic, Acquired</td>
</tr>
<tr>
<td>Diabetic Ulcer</td>
<td>Acquired</td>
</tr>
<tr>
<td>Scleroderma</td>
<td>Idiopathic Autoimmune</td>
</tr>
<tr>
<td>Skin Cancer</td>
<td>Idiopathic Autoimmune</td>
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</tbody>
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CEN Medical Cannabis Pharmacological Prescription and Coding System: Dermatological Disorder Application
The CEN Medical Cannabis Pharmacological Prescription and Coding System (CEN/MCPPCS) provides language that enables the health care practitioner to communicate with the dispenser of medical cannabis. The first two letters of the system refer to the cannabis type: cannabis sativa, cannabis indica, or cannabis hybrida. The numerical value in percentage to the right of the colon refers to the recommended THC content in percentage, and the numerical value in sequence to the right of the THC percentage refers to the recommended CBD content.

**Example:** Cannabidiol (CBD oil) is recommended for the patient. The concentration of the CBD oil is 19.5% and the patient is to ingest 50 mg. of CBD oil four times each day every six hours, as adjunctive therapy in the treatment of dermatitis, (ICD-9:690.1). The prescription would therefore read:

Triana Bartholomew
Date of Birth: 09-01-1939.
Diagnosis: Seborrheic dermatitis, ICD-9 code: 690.1
CBD: 0.00%/ 19.5%. Take 50 mg. of CBD oil by mouth four times daily, every 6 hours. Use dropper as indicated.
David Posner, M.D.

The patient would then be able to purchase the CBD oil online or at a dispensary, offering the prescription to the pharmacist or technician.
Composition Assignments:
1. Please suggest a plan of care based upon the following patient information. Discuss if CBD oil would be indicated with rationale and the type of endocannabinoid deficiency (s)(CECD) for the dermatological disease process.
   a. A 65-year-old male complains of localized itching of the left leg. Upon examination, skin appears reddened and cellulites is evident. The patient states he was recently prescribed an oral hypoglycemic agent by his physician.
2. Please choose an article from the CEN library on an aspect of cannabidiol (CBD) and the dermatological system. Write a two-hundred-word critical analysis paper on this research article and determine the following in your paper:
   a. Author and affiliation
   b. Study population
   c. Purpose
   d. Outcome of the study
   e. Importance of the research

Bibliography


