The Benefits of Hemp-Derived Phytocannabinoids

WHITE PAPER ABSTRACT

By Cristiana Paul, MS & Nicole Spear, MS, CNS

WHAT ARE PHYTOCANNABINOIDS?

Phytocannabinoids are plant-derived compounds capable of directly interacting with cannabinoid receptors in the body. Cannabinoids, derived from the Cannabis plant, have been utilized the most for therapeutic purposes. Over 100 cannabinoids exist in various Cannabis species, but clinical research has focused primarily on the psychotropic cannabinoid, tetrahydrocannabinol (THC), and its non-psychotropic antagonist, cannabidiol (CBD). Hemp (*Cannabis sativa L.*) is a tall, narrow plant rich in CBD, which is harvested from its seeds and stalk fibers. This species is relatively low in THC, containing approximately 0.3%. (Contrast this with marijuana [*Cannabis indica*], which is short and densely populated with broad leaves that contain up to 30% THC and are virtually devoid of CBD.)

THE ENDOCANNABINOID SYSTEM

Both CBD and THC act upon the endocannabinoid system of the human body, which is a signaling system laced throughout the central nervous system and distributed among peripheral tissues including the immune and reproductive systems, gastrointestinal tract, sympathetic ganglia, endocrine glands, arteries, lungs and heart.[2]

The endocannabinoid system contains two subtypes of G-protein coupled cannabinoid receptors, CB1 and CB2, which are modulated by endocannabinoids. The primary endocannabinoids are arachidonoyl ethanolamide (anandamide) and 2-arachidonoyl glycerol (2-AG), derivatives of arachidonic acid.[3]

CB1 receptors are widely distributed throughout the brain, especially in the frontal cortex and the limbic system.[4] Their agonists, including THC, exert psychotropic affects as activation of CB1 receptors leads to retrograde inhibition of the neuronal release of acetylcholine, dopamine, GABA, histamine, serotonin, glutamate, cholecystokinin, D-aspartate, glycine, and noradrenaline.[5] CB1 agonists also have antispastic, analgesic, antiemetic, neuroprotective, and anti-inflammatory actions, and are effective against certain psychiatric diseases.[5]

CB2 receptors are distributed throughout the brain, immune system, spleen, and leukocytes.[4] Their agonists, such as CBD, modulate pain and inflammation, and are neuroprotective without producing negative side effects in the CNS.[6] There are some overlapping pathways between the cannabinoid receptors. Activation of either or both types of receptors by endocannabinoids can result in neuromodulation that offers a “protective role” in many medical conditions.[7] Research supports a role for modulation of the endocannabinoid system in managing a variety of issues, including emesis, pain, inflammation, multiple sclerosis, anorexia, epilepsy, glaucoma, schizophrenia, cardiovascular disorders, obesity, metabolic syndrome related diseases, Parkinson’s disease, Huntington’s disease, Alzheimer’s disease and Tourette’s syndrome.[7]

BENEFITS OF PHYTOCANNABINOIDS

Neuronal Health

- CB2 agonists offer neuroprotection by suppressing microglia activation via inhibiting the release of neurotoxic factors and by decreasing neuronal cell damage in cells or tissue.[4]
- Cannabinoids can also offer neuroprotection via their immunomodulatory properties which include 1) induction of apoptosis, 2) suppression of cell proliferation, 3) inhibition of pro-inflammatory cytokine/chemokine production and increase in anti-inflammatory cytokines, and 4) induction of regulatory T cells.[4]
- Neuroinflammatory conditions including MS, amyotrophic lateral sclerosis (ALS), Down syndrome, Alzheimer's disease, and stroke show upregulation of CB2 receptors in affected tissues, to enhance the opportunity for modulating inflammation and immunity.[4,15-17]
- CB2 agonists have been shown to reduce inducible nitric oxide synthase (iNOS) production and prevent neuronal injury during neuroinflammation.[4]
- In studies using primary human brain microvascular endothelial cells and human monocytes, CB2 agonists diminished adhesion of leukocytes to activated endothelium and down-regulated adhesion molecules. BBB injury and increased permeability were prevented.[4]
- Anti-psychotic effects of CBD have been noted as it attenuated the behavioral and glial changes observed in an animal model of schizophrenia based on NMDA receptor hypofunction.[8]

Pain Modulation

- Several CB2 agonists have reached clinical Phase II trials for pain management and numerous studies show their effectiveness against chronic nonmalignant neuropathic pain.[9,10]
- Joint pain is often rooted in central sensitization, characterized by significant spinal astrogliosis and increases in activity of metalloproteases MMP-2 and MMP-9 in the spinal cord. CB2 agonists exert analgesic effects in osteoarthritis models by attenuating the activity of these enzymes.[11]
- Analgesic actions of CB2 agonists may also be a result of their anti-inflammatory actions, reduction of basal NGF tone, induction of beta-endorphin release from keratinocytes, and direct action on nociceptors.[12]

Anti-inflammatory Properties

- Cannabinoids have shown therapeutic potential in a variety of chronic inflammatory conditions including inflammatory bowel disease, arthritis, autoimmune disorders, multiple sclerosis, HIV-1 infection, stroke, and Alzheimer's disease.[4]
- CB2 agonists have been shown to inhibit chemokine-induced chemotaxis of various cell types including neutrophils, lymphocytes, macrophages, monocytes and microglia. Migration of human monocytes is diminished in the presence of CB2 agonists.[4]
- In vitro studies showed CB2 agonists reduced TNF-α-induced activation of human coronary artery endothelial cells, but also reduced secretion of MCP-1 and attenuated monocyte transendothelial migration. Endothelium in the brain and other organs possess CB2 receptors allowing CB2 agonists to modulate inflammatory actions.[4]
- CB2 receptors are found in the enteric nervous system and colonic epithelium. The anti-inflammatory actions of CB2 agonists have shown both protective and healing effects on colitis and related inflammatory intestinal conditions.[13,14]
- CBD has been shown to reduce joint inflammation, including cartilage degradation and bone erosion in several animal models and suppressed release of TNF-α from synovial cells.[14]
- CBD treatment reduces mitochondrial superoxide, iNOS, nuclear factor kappa B (NF-κB) activation, and transendothelial migration of monocytes, attenuating inflammation induced by hyperglycemia in diabetic mice.[14]

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