

### INFLAMMATION & beta-caryophyllene

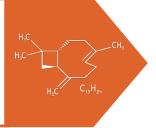
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An educational article highlighting current endocannabinoid system and functional medicine research

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# **OVERVIEW**



### Chronic inflammation is a fundamental, underlying feature of many neurological, metabolic and autoimmune disorders.

Researchers confirmed the link between obesity, diabetes, and chronic inflammation over 30 years ago. Recent studies also show the role that chronic inflammation plays in autoimmune and neurodegenerative disorders.

The body's own Endocannabinoid System (ECS) is providing exciting opportunities in the treatment of chronic inflammation, and thereby the serious disorders connected to chronic inflammation. The ECS is the twelfth and most recent body system composed of ligands, receptors, transporters, and enzymes that synthesize and degrade the signaling molecules. Since the ECS is present nearly everywhere in the human body and governs major body functions and systems, specifically regulating metabolism, inflammation, chronic pain, and neurological disorders. Scientists have identified multiple endocannabinoid substances that specifically regulates inflammatory changes.

This article explores the therapeutic potential of Beta-Caryophyllene (BCP) in addressing chronic inflammation.

Beta-Caryophyllene (BCP), a natural terpene and phytocannabinoid that is found in common food plants such as oregano, hops, and black pepper, works by targeting the body's endocannabinoid system to block the inflammatory process and to help with pain, stress disorders, diabetes, and high cholesterol. It binds to the Endocannabinoid System's CB2 receptor that regulates all immune cells proliferation, migration, and their release of inflammatory substances.

In addition to CB2 receptors BCP signals several other receptors to provide powerful therapeutic relief for chronic pain. In addition to analgesic effects BCP influences levels of glucose and cholesterol. It has shown potent therapeutic promise in neuropathic pain, neuro-degenerative and metabolic diseases, as well as having antibiotic, antifungal and anti-cancer effects.



# What is inflammation?

Inflammation is a process where your body activates your immune system as part of a protective response from outside threats, such as injury or invaders such as bacteria and viruses.

When your body activates your immune system, it sends out inflammatory cells. These cells in the M1 state attack invading agents such as bacteria or viruses, or degrade damaged tissue suffered from injuries. Once the acute M1 reaction is controlled the immune cells shift into M2 healing tissue and injuries. Inflammation can also affect body systems you can't see.

Inflammation can be either a short-term (acute) response, or long-lasting (chronic). In normal immune responses, acute inflammation usually goes away within hours or days after responding to the trigger, such as itching and redness from an insect bite.

Chronic inflammation can result when your body gets stuck in M1 state and continues to send out inflammatory cells even when there is no outside danger. Chronic inflammation can last days, months or even years after the trigger is gone.

Source: <u>https://www.webmd.com/a-to-z-guides/</u> <u>autoimmune-diseases</u>

Source: <u>https://www.hopkinsmedicine.org/health/</u> conditions-and-diseases/metabolic-syndrome

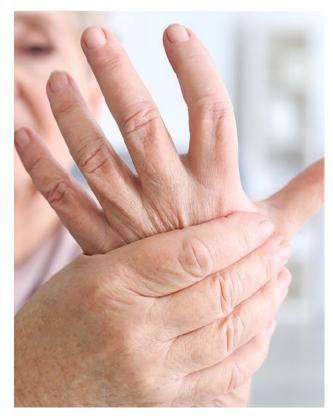
Inflammation can also affect body systems you can't see.

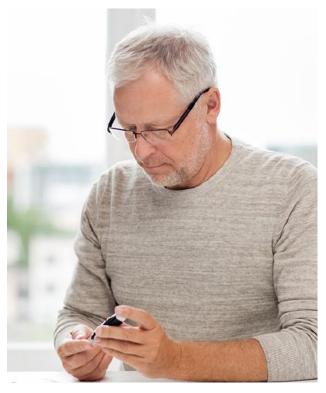
## Disorders linked to Chronic inflammation

There are numerous conditions linked to chronic inflammation, such as:

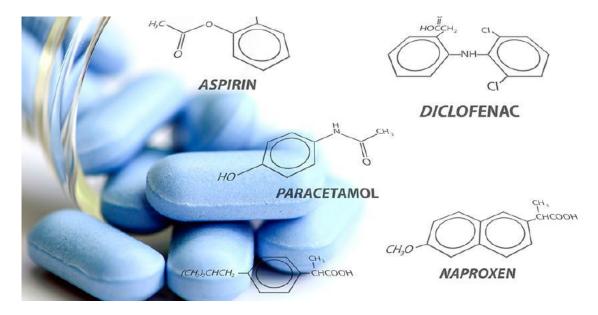
- Autoimmune disorders When the immune system targets and attacks healthy body tissues by mistake. Treatment for autoimmune disorders focuses on reducing immune system activity. Examples of autoimmune disorders include Rheumatoid arthritis, systemic lupus, inflammatory Bowel disease (IBD) and multiple sclerosis.
- Metabolic disorders Chronic inflammation (or vice versa) can create metabolic dysfunctions that can lead to a cluster of chronic disorders, such as diabetes type 2, obesity, and metabolic syndrome risk factors for cardiovascular disease (abdominal obesity, high blood pressure, impaired fasting glucose, high triglyceride levels and low HDL cholesterol levels). Metabolic syndrome greatly increases the risk of developing diabetes, heart disease, and/or strokes.
- Neuroinflammation An inflammatory response of immune cells occurs within the brain or spinal cord, especially after a traumatic brain or spinal cord injury. Chronic neuroinflammation involves the sustained activation of glial cells and recruitment of other immune cells into the brain with increased production of cytokines, reactive oxygen species (ROS) and other markers indicating damage and impairment to the central nervous system (CNS). Neuroinflammation can lead to serious neurodegenerative disorders, including anxiety, depression, and Alzheimer's.







# Autoimmune disorders: Conventional therapeutic approaches and risks



Focus is on bringing down inflammation and calming the overactive immune system. There are currently no cures for autoimmune disorders, and treatments focus on bringing down inflammation and calming the overactive immune system. Treatments range from overthe-counter medications to help relieve mild symptoms to immunosuppressant therapies that can have serious adverse consequences.

Common over-the-counter medications include non-steroidal anti-inflammatory drugs (NSAIDs) can help with inflammation, swelling, stiffness and pain, but they do pose health risks, especially long-term. Serious side effects of NSAIDs include increased bleeding risk, kidney damage, stomach upset/ulcers, and hypertension/strokes. Immunosuppressant medications generally target all parts of the immune system and suppress its overactivity. They are often used to control high levels of chronic inflammation and protect organ function. Corticosteroids are a familiar form of immunosuppressant.

Biologic therapies target specific parts of the immune system, such as blocking certain receptors on cells or the enzymes they activate.

Common side effects include increased risk of infections, nausea, diarrhea, stomach issues, dizziness, and fatigue. Use of JAK (Janus Kinase) inhibitors come with a risk of serious side effects, including heart-related events, cancer, blood clots, strokes, and death.

## Common therapeutic approaches for metabolic disorders



Some people can manage the impact of metabolic disorders through lifestyle changes, such as healthy eating, proper sleep, exercise, staying active, and managing their stress levels.

Healthcare practitioners often prescribe combinations of therapies that include lifestyle management and medications. Type 1 Diabetes therapy usually means insulin injections. Type 2 diabetes treatment is often carbohydrate restricting, weight loss and exercising, and medication that lowers blood glucose levels.

Obesity is a complex disorder that affects millions of children as well as adults. Many factors can contribute, including eating patterns, physical activity levels, genetics, sleep, and social routines.



Medications can also cause adverse side effects, including weight gain. Researchers are continuing studies on the role of other factors such as chronic stress, exposure to chemicals, and the gut microbiome. The Centers for Disease Control and Prevention advocate healthy lifestyle choices that include healthy eating and regular physical activity.

Healthcare professionals often advocate managing metabolic disorders with similar approaches to obesity – lifestyle changes and medication working together. The bad news for many patients is that common side effects of cholesterol-controlling medications include headaches, dizziness, nausea, weakness, diarrhea, and stomach issues. Statins can cause serious side effects including memory loss, confusion, and damage to kidneys and liver.



The Centers for Disease Control and Prevention advocate healthy lifestyle choices that include healthy eating and regular physical activity.

# Neuroinflammatory disorders: Conventional therapeutic approaches and risks

Research has shown that stress-induced neurologic responses serve as an important link between immune system dysfunction and the development of mood disorders.

When signals between the immune system and brain are blocked, behavior and mood can be affected. This is the basis of medical science behind many current moodrelated medications, including -adrenergic receptor blockers, benzodiazepines, and antidepressants.

The common side effects of antidepressants are drowsiness and fatigue. But people often report that they feel emotionally numb or not like themselves. Other reported side effects include weight gain, headaches, dizziness, sexual problems, gastrointestinal issues, and risk of suicide.<sup>1</sup>

Medications for neurodegenerative disorders such as Alzheimer's may slow the rate of decline, or help with symptoms such as changes in language, thinking abilities and movement. Several are cholinesterease inhibitors that can help prevent the breakdown of a brain chemical called acetylcholine, which is thought to be important for learning and memory. Medications such as memantine and ketamine, NMDA (N-Methyl-D-aspartate) receptor agonists, protect brain cells by blocking the effects of too much glutamate.<sup>2</sup>





People with Parkinson's disease often show low brain dopamine concentrations. Dopamine deficiency is usually addressed with medication that either converts to dopamine in the brain, or dopamine agonists that mimic the effect of dopamine in the brain. Potential side effects from these medications often include headaches, nausea, insomnia, and hallucinations. Over time, the benefits of such medications diminish or become less consistent.<sup>3</sup>

Alternative remedies for mental health disorders such as cannabis are popular. With the discovery of the endocannabinoid system, researchers are proving that Cannabis sativa's main psychotropic compound, Δ9-tetrahydrocannabinol (THC), modulates the release of the body's own endogenous (internally created) endocannabinoid neurotransmitters that regulate and affect many of the body's major biological processes, including inflammatory responses.

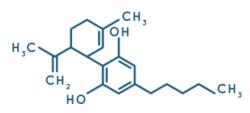
Common side effects of medical cannabis are dizziness, fatigue, light-headedness, drowsiness, and nausea. Some users also report slower reaction times, hallucinations, impaired concentration, and memory.

In contrast, the phytocannabinoid Cannabidiol (CBD) in addition to its calming effects on the Central Nervous System is showing promise in shifting immune cells away from proliferation, migration, and production of pro-inflammatory cytokines and toward antioxidation, anti-inflammatory cell types and cytokines. This results in the correction of the neuroinflammation and degeneration common to disorders such as Alzheimer's and Parkinson's.

Cannabidiol (CBD) is often well tolerated and comes without the "high" associated with Cannabis. However, it can also cause dry mouth, vivid dreams, and drowsiness.<sup>4</sup>

- Source: <u>https://my.clevelandclinic.org/health/treatments/9301-depression-medicines</u>
- 2. Source: Cannabinoid Modulation of Neuroinflammatory Disorders <u>https://</u> www.ncbi.nlm.nih.gov/pmc/articles/PMC3386505/
- 3. Source: <u>https://www.mayoclinic.org/diseases-conditions/parkinsons-disease/</u> <u>diagnosis-treatment/drc-20376062</u>
- 4. Source: <u>https://www.health.harvard.edu/blog/cannabidiol-cbd-what-we-know-and-what-we-dont-2018082414476</u>

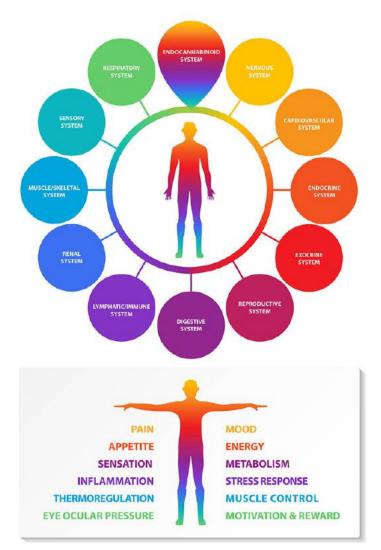
Cannabidiol (CBD) is derived directly from the hemp plant, related to marijuana. According to a report from the World Health Organization, "In humans, CBD exhibits no effects indicative of any abuse or dependence potential.... To date, there is no evidence of public health related problems associated with the use of pure CBD."



	Neurodegenerative Diseases Alzheimer's
7	Parkinson's
	Metabolic Disorders туре 2 Diabetes
	Fatty Liver Disease
Chronic	Musculoskeletal Disorders Osteoarthritis
Inflammation	Osteoporosis
	Sarcopenia
	Cardiovascular Diseases Cardiomyopathy
	Atherosclerosis
	Stroke
	Cancer Gastric
	Liver
	Lung
	Gall Bladder
	Colon
	Prostate
	Pancreatic
	Rectal

Chronic inflammation is a fundamental, underlying feature of many neurological, metabolic and autoimmune disorders. Researchers confirmed the link between obesity, diabetes and chronic inflammation over 30 years ago. Recent studies also show the role that chronic inflammation plays in autoimmune and neurodegenerative disorders.

# Inflammation and the Endocannabinoid System



#### The Endocannabinoid System (ECS) is an endogenous system that is the master regulator for many of the body's core systems.

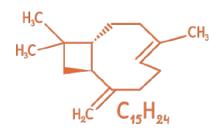
The endocannabinoid system (ECS) plays a critical role in our survival. This is due to its ability to maintain homeostasis (balance) of the human body, by integrating our neurologic, metabolic, endocrine, and immune system. It is present everywhere in the human body allowing it to function as a "master regulator" in the body. Humans are hard-wired with a system of cannabinoid receptors, ligands, enzymes and transporters throughout our brains and bodies. When these receptors are activated, they enable two-way communication between body systems; something previously thought to be impossible. The ECS supports vital communications between the control centers of the body and every other system. When this system is out of balance, we experience distress.

In particular, the ECS exerts regulatory control over metabolism, inflammation, chronic pain, and behavioral disorders such as depression and schizophrenia.<sup>1</sup>

Multiple endocannabinoids molecules affect the ECS. All of them seem to have a purpose in anti-proliferative, anti-inflammatory, and anti-metastatic effects (Madia & Daeninck, 2016). Additionally, it appears that they have a role in neurotransmission, immune system, and mitochondrial function.

 Source: Modulating the endocannabinoid system in human health and disease: successes and failures <u>https://www.ncbi.nlm.nih.gov/</u> pmc/articles/PMC3684164/

### What is Beta-Caryophyllene?



Beta-Caryophyllene (BCP) is a terpene (chemical compound) found in medicinal and food plants such as hemp, black pepper, clove oil, hops, oregano, allspice, chamomile, rosemary, and cinnamon. It is an oily liquid, usually pale yellow in color, with a scent that is woody and spicy, between cloves and turpentine.<sup>1</sup>

The U.S. Food and Drug Administration has classified it as a generally safe food additive2, with the ability to strongly activate the Endocannabinoid System's CB2 receptors. CB2 endocannabinoid activators have been proven to be neuroprotective and do not trigger psychotropic adverse effects normally seen with activation of CB1 receptors ("cannabis high").

When Beta-Caryophyllene binds to CB2 receptors, it provides a highly calming and soothing function, as well as protection. CB2 receptors located throughout the body including the brain increase



in numbers as a response to stress and inflammation as if preparing for a binding endocannabinoid. Research has shown that activation of the CB2 receptors has great therapeutic potential in the treatment of inflammation, pain, atherosclerosis, and osteoporosis.<sup>1</sup>

The U.S. Food and Drug Administration has classified Beta-Caryophyllene as a generally safe food additive<sup>2</sup>, with a strong ability to bind to and activate the Endocannabinoid System's CB2 receptors. <sup>2</sup>

1. Source: https://www.pnas.org/doi/10.1073/pnas.080360110

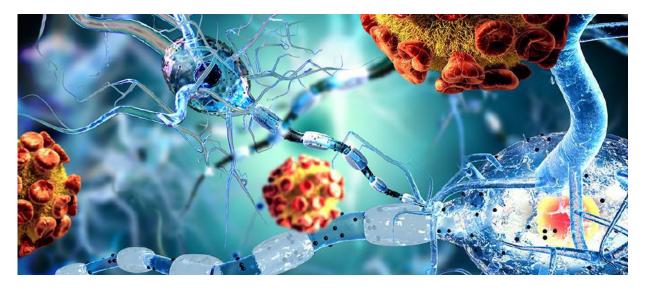
2. Source: https://www.accessdata.fda.gov/ scripts/cdrh/cfdocs/cfcfr/CFRSearch. cfm?fr=172.515&SearchTerm=caryophyllene



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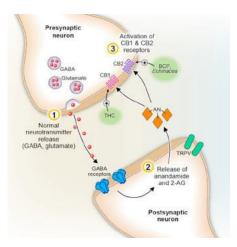
# CB2 Receptors, Inflammation & Beta-Caryophyllene



CB2 receptors are found throughout the body, but are primarily located in the immune system, such as white blood cells, the tonsils, and the spleen. But the brain maintains a separate immune system walled behind a blood brain barrier that filters out immune cells in the circulation. Instead, glial cells, astrocytes and microglia protect the brain.

Microglia are immune macrophages that are found in the brain and Central Nervous System (CNS). Their function is to provide a first line of defense against inflammation and injury, by destroying pathogens as well as removing damaged cells.<sup>1</sup>

In the case of chronic inflammatory conditions, the microglia maintain their function releasing inflammatory cytokines and chemokines that can



eventually result in serious damage if not mitigated.

"Microglial activation and neuroinflammation appear to be the upstream mechanism underlying the pathogenesis of neurodegenerative diseases including neuropathic pain, Alzheimer's disease, Parkinson's disease, multiple sclerosis, amyotrophic lateral sclerosis, AIDS, and Huntington's disease."<sup>2</sup>

Because beta-caryophyllene selectively activates the CB2 receptors, it is showing great potential in helping reduce and relieve chronic inflammation throughout the body. It can cross the blood brain barrier to reach the CNS and act on the CB2 receptors of overactive microglia.

This shifts the CNS immune system from reactive M1 state to resolution M2 decreasing microglia, cytokines, and increasing T-regulator cells to clean up debris. The overall effect is a protective role without the unwanted side-effects commonly associated with other conventional therapies previously mentioned in this article.

- Source: <u>https://faculty.sites.uci.edu/kimgreen/bio/microglia-in-the-healthy-</u> <u>brain/</u>
- 2. Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6035094/

Activation mechanism of CB1 and CB2 receptors Details from <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4120766/</u>

# RESEARCH SUMMARIES: Neuroinflammation, Neurodegenerative Disorders & Beta-Caryophyllene



Despite extensive research on Alzheimer's disease (AD), its diagnosis and treatment remain challenging, and no effective therapies are currently available. In this study, we explored whether the "JAK2-STAT3-BACE1" pathway is involved in neuroprotection conferred by the food flavoring agent beta-caryophyllene (BCP).

BCP exhibited the potential to dramatically increase PC-12 cell viability while protecting cell morphology. BCP inhibited APP, JAK2, STAT3, BACE1 mRNA and BACE1 protein over-expression, as well as JAK2 and STAT3 hyperphosphorylation. Molecular docking simulated the docking of BCP with JAK2, STAT3, BACE1, CB2. And JAK2 was found to be the most stable protein. In conclusion, inhibition of the "JAK2-STAT3-BACE1" signaling pathway may be one of the mechanisms through which BCP protects neurons and antagonizes Aβ's neurotoxicity.

Source: <u>https://www.frontiersin.org/articles/10.3389/</u> fnagi.2022.814432/full The cannabinoid receptor 2 agonist, betacaryophyllene, improves working memory and reduces circulating levels of specific proinflammatory cytokines in aged male mice

#### https://pubmed.ncbi.nlm.nih.gov/31173795/

Increased brain inflammation, or neuroinflammation, can sensitize the elderly brain to adverse effects, such as an increased vulnerability to the negative effects of stress [1]. The idea that aging is associated with a progressive decline in the ability to cope with stressors and a progressive increase in the whole body load of proinflammatory cytokines has been termed "inflammaging" It has been argued that inflamm-aging is driven by immunosenescence and may be a key component of the etiology and progression of many aging-related diseases, such as atherosclerosis, heart disease, and type II diabetes.

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A systematic review on the neuroprotective perspectives of beta-caryophyllene

#### https://pubmed.ncbi.nlm.nih.gov/30281175/

This study reviews published reports pertaining to the neuropharmacological activities of betacaryophyllene. A total of 545 research articles were recorded, and 41 experimental studies were included in this review, after application of exclusion criterion.

Search results suggest that beta-caryophyllene exhibits a protective role in a number of nervous system related disorders including pain, anxiety, spasm, convulsion, depression, alcoholism, and Alzheimer's disease.

Additionally, beta-caryophyllene has local anesthetic like activity, which could protect the nervous system from oxidative stress and inflammation and can act as an immunomodulatory agent. This review suggests a possible application of BCAR as a neuroprotective agent.

## RESEARCH SUMMARIES: Autoimmune Disorders & Beta-Caryophyllene



#### ADDITIONAL RESEARCH RESOURCES

Parkinson's disease. Beta-Caryophyllene exerts protective antioxidant effects through the activation of NQO1 in the MPTP model of Parkinson's disease. Flores-Soto et al. Neurosci Lett. 2021 Jan 742:135534;18

https://pubmed.ncbi.nlm.nih.gov/33271195/

Results reveal that betacaryophyllene improves the systemic inflammation and oxidative status of arthritic rats and, in addition, it was not associated with hepatotoxicity.

The current study investigated the action of betacaryophyllene, the major constituent of copaiba oil, on the systemic inflammation, oxidative status, and liver cell metabolism of rats with adjuvant-induced arthritis, a model for rheumatoid arthritis.

This study also compared the actions of betacaryophyllene with those previously reported for copaiba oil on arthritic rats.

These beneficial actions were of the same extension as those of copaiba oil (Copaifera reticulata) and, therefore, beta-caryophyllene is possibly responsible for the anti-inflammatory and antioxidant actions of the oil.

These results reveal that beta-caryophyllene improves the systemic inflammation and oxidative status of arthritic rats and, in addition, it was not associated with hepatotoxicity.

1. Source: <u>https://pubmed.ncbi.nlm.nih.gov/30132972/</u>



# RESEARCH SUMMARIES: Metabolic Disorders & Beta-Caryophyllene



#### Therapeutic Potential of Beta-Caryophyllene: A Dietary Cannabinoid in Diabetes and Associated Complications

Diabetes mellitus (DM), a metabolic disorder is one of the most prevalent chronic diseases worldwide across developed as well as developing nations.

Among the numerous therapeutic approaches, the health effects of dietary/nutraceutical approach due to the presence of bioactive constituents, popularly termed phytochemicals are receiving special interest for pharmacological effects and therapeutic benefits. Beta-caryophyllene (BCP) exhibits selective full agonism on cannabinoid receptor type 2 (CB2R), an important component of endocannabinoid system, and plays a role in glucose and lipid metabolism and represents the newest drug target for chronic inflammatory diseases.

BCP also showed agonist action on peroxisome proliferated activated receptor subtypes, PPAR-a and PPAR-y, the main target of currently used fibrates and imidazolidinones for dyslipidemia and IR, respectively.

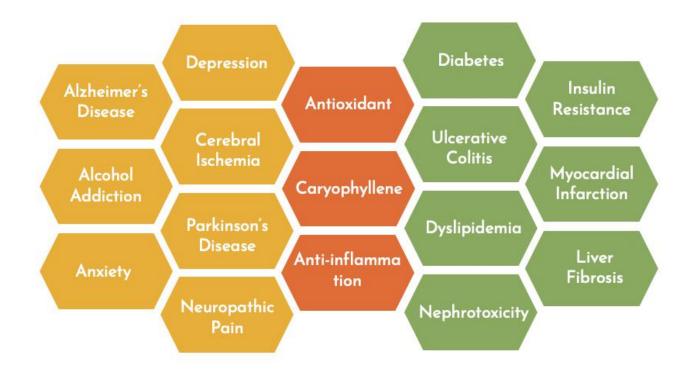
Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7599522/

Given the safe status, abundant natural occurrence, oral bioavailability, dietary use and pleiotropic properties modulating receptors and enzymes, BCP appears as a promising molecule for diabetes and its complications.

Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7599522/

OTHER APPLICATIONS OF BETA-CARYOPHYLLENE The Expanded Endocannabinoid System/Endocannabinoidome as a Potential Target for Treating Diabetes Mellitus https://pubmed.ncbi.nlm.nih.gov/31686231/

The endocannabinoid (eCB) system, i.e. the receptors that respond to the psychoactive component of cannabis, their endogenous ligands and the ligand metabolic enzymes, is part of a larger family of lipid signals termed the endocannabinoidome (eCBome). We summarize recent discoveries of the roles that the eCBome plays within peripheral tissues in diabetes, and how it is being targeted, in an effort to develop novel therapeutics for the treatment of this increasingly prevalent disease.



DISEASE	MAIN METABOLIC EFFECT	EXPERIMENTAL MODEL	<b>BCP ADMINISTRATION</b>	REFERENCES
Obesity and dyslipidemia	Decrease of visceral fat index. LDL and VLDL	Wistar rats fed with HFFD	30 mg/Kg b.w./day for 4 weeks by oral gavage	[10]
	Inhibition of adipogenesis	Bone marrow cells	0.1–100 µM for 3–4 days in differentiation medium	[85]
	Inhibition of lipid accumulation	Preadipocytes (3T3-L1 cells)	1 nM-10 μM for 9 days in differentiation medium	[133]
			5 or 10 µM for 6 days in differentiation medium	[134]
	Suppression of body weight gain	HFD-fed C57BL/6N mice	0.15% or 0.3% supplemented diets for 16 weeks	[134]
			0.02% or 0.2% supplemented diets for 4 and 8 weeks	[136]
	Reduction of total cholesterol, triglycerides, and LDL cholesterol levels	Hypercholesterolemic Wistar rats	1 mL/Kg b.w. for 3 days by oral gavage	[126]
			30 mg/Kg b.w./day for 4 weeks by oral gavage	[135]
	Decrease of hepatic HMG-CoA reductase activity	Hypercholesterolemic Wistar rats	1 mL/Kg b.w. for 3 days by oral gavage	[126]
			30 mg/Kg b.w./day for 4 weeks by oral gavage	[135]
Hepatic steatosis	Inhibition of palmitate-inducible lipid accumulation Downregulation of FAS and upregulation of ATGL Reduction of triglycerides. increase of FFA uptake and FFA oxidation	Human hepatocyte cell line (HepG2)	5 µM for 24h in serum free medium	[78]
			1, 10 or 100 μM for 24h	[23]
T2D	Increase of glucose uptake and GLUT4 translocation	Skeletal myotubes (C2C12 cells)	1, 10, 100 nM for 30 min in glucose and serum free medium	[133]
	Decrease of blood glucose levels and proinflammatory cytokines levels Increase of plasma insulin	Streptozotocin-Induced Diabetic rats	200 mg/Kg b.w. for 45 days by oral gavage	[138,139]
	Decrease of fasting blood glucose and fasting insulin	Wistar rats fed with a HFFD	30 mg/Kg b.w./day for 4 weeks by oral gavage	[10]
Cardiovascular disorders	Reduction of atherogenic and coronary risk index	Hypercholesterolemic Wistar rats	30 mg/Kg b.w./day for 4 weeks by oral gavage	[10]
	Protective role against isoproterenol-induced myocardial infarction	Male Sprague-Dawley rats	100 or 200 mg/Kg b.w/day for 21 days orally	[140]
	Protective effect against Doxorubicin-induced inflammation in the myocardium	Male Wistar Rats	25, 50, 100 mg/Kg b.w. for 5 days by intraperitoneal injection	[141]
			25 mg/Kg b.w. for 6 days a week for 5 weeks by intraperitoneal injection	[142]

HFFD: high fat/fructose diet; HFD: high fat diet; LDL: low density lipoprotein; HMG-CoA: Hydroxy methylglutaryl-Coenzyme A; FAS: fatty acid synthase; ATGL: adipose triglyceride lipase; GLUT4: glucose transporter 4; VLDL: very low density lipoprotein; FFA: free fatty acids.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7692661

# Introducing the BCPlus Product Family

Customized Beta-Caryophyllene (BCP) products that work with the body to enhance endocannabinoid health.

Our products are physician-formulated for maximum effectiveness and potency. They contain Beta-Caryophyllene from hops + carefully selected terpenes and essential oils to maximize effectiveness and potency.

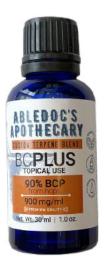
They can help support a wide range of health and wellness needs, from stress and anxiety relief, pain alleviation, inflammation reduction, healthy sleep cycles, skin conditions, digestive issues, and more.

All of our products are formulated and manufactured to strict quality standards, so you can be assured that you are getting reliable and consistent support for your body's needs.

- Physician-formulated blends for topical or oral uses
- Natural herbal food substances are FDAapproved
- Broad spectrum phytocannabinoid
- FDA accepted, low dosing, few adverse effects
- Synergistic with CBD
- Alternative to cannabis products
- Custom-blended formulations for topical or oral uses
- Contains NO THC will not show up in drug testing

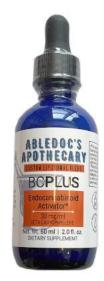
"57 year-old with diarrhea, NAFLD, gallbladder inflammation, obesity, depression, menopausal, brain fog, visual impairment, fatigue 5 years. Took Liposomal BCP 3ml had improved mental, vision, relieved GB pain, stopped diarrhea, almost immediate depression relief. Will do labs at 2 mo and report. Lost 13 lb. in two weeks." — A.O., Healthcare Professional

### BCPLUS Topical



Our topical blend is made from organically grown hops oil, distilled to a pure form of beta-caryophyllene. BCPlus Topical Tincture blocks overreacting immune conditions and pain receptors when applied locally to joints, muscles, neck, back or the back of hands. A few drops of the oil are all that are needed for reducing pain, inflammation or swelling, and providing a sense of calmness and relaxation.

### BCPLUS LIPOSOMAL ORAL



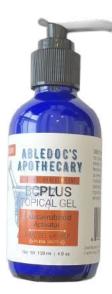
The first liquid liposomal betacaryophyllene product available. Liposomal formulations contain the active BCP inside very tiny, fat-like particles that are easier for the body to absorb, allowing the BCP to get to the targeted area of the body much faster. BCPlus Oral Liposomal helps block inflammatory processes and helps mitigate pain, stress disorders, diabetes, and high cholesterol.

### BCPLUS CRUNCHES

Our BCPlus Crunches contain all the beta-caryophyllene goodness of our oral formulation, made into tasty, crunchy little treats. Slightly sweetened with monkfruit, and enhanced with probiotics, BCPlus Crunches are low glycemic and Keto friendly. They come packaged in a small, round tin that is easy to store and transport in backpacks, bags or totes. Each crunch contains 9 mg of beta-caryophyllene. Safe for all ages.



### BCPLUS TOPICAL GEL



The BCPlus Topical Gel starts with our potent beta-caryophyllene topical formulation blended into a hydrating DMAE gel base that supports skin health and healing. We added Terpineol, an effective antioxidant, and Humulene (antiinflammatory substance found naturally in hops flowers) to enhance absorption into the skin. Essential oils are carefully chosen to enhance and support antiinflammatory, healing and calming properties. Our BCPlus Topical Gel is non-greasy and easy to apply.

### Endocannabinoid Health For EVERYONE!

Our beta-caryophyllene blends have no psychoactive effect, so that everyone could benefit from them. They work like CBD on the body, or maybe even better.

# OUR MISSION

At Blair Medical Group, we know that you want to be confident in the quality of the products that you use.

Our mission is to create and share natural, plantbased, non-prescription products that empower healing by balancing the Endocannabinoid System. We want people to feel better, create balance in their health, and be confident in the products they use.

### Empowering people's health & wellbeing through products that support the endocannabinoid system.

We supply and support individuals, professionals and practitioners by offering premium products that are free of preservatives, toxins, non-healthy product additives. Our physician-formulated product lines and educational resources will complement most healthcare protocols.



"I'm seeing the most improvements in cases that involve neuropathy and inflammation. Just got an email from a patient that has post-chemo neuropathy in her feet and legs, this was what she wrote: 'Wow! The BC plus is really working. I noticed changes within 3 days, especially in my feet. They are slowly waking up, and I have so much more mobility because of my feet now feeling the ground underneath. It is a slow progression but I will take it.' " — Naturopath, West Hartford, CT