

# Detailed Overview of Pharmacology of Active Ingredients in Tulla Botanicals Wellness Topical Products

# What is the pharmacology of Beta-Caryophyllene (BCP)?

Beta-caryophyllene is a natural bicyclic sesquiterpene that is found in many essential oils, including black pepper, cloves, rosemary, and other savory spices. One of its interesting properties is its interaction with the endocannabinoid system (ECS). BCP specifically targets the CB2 receptors in the body aiding in the reduction of inflammation and pain. Unlike other cannabinoids, BCP acts as a selective agonist of the CB2 receptors, which are primarily found in the immune system and peripheral tissues rather than the central nervous system. This unique interaction has led to investigations into its therapeutic potential. Here are some areas where beta-caryophyllene has shown therapeutic benefits:

<u>CB2 Receptor Activation</u>: Beta-caryophyllene is unique among terpenes because it acts as a selective agonist of the CB2 cannabinoid receptor. CB2 receptors are primarily found in immune cells, peripheral tissues, and the gastrointestinal tract. Activation of CB2 receptors has been associated with anti-inflammatory and immunomodulatory effects.

<u>Anti-Inflammatory Properties</u>: Beta-caryophyllene's activation of CB2 receptors is thought to contribute to its anti-inflammatory properties. By modulating immune responses and reducing inflammation, it may have potential therapeutic applications for conditions involving inflammation, such as inflammatory bowel disease.

<u>Pain Modulation</u>: The anti-inflammatory and analgesic properties of beta-caryophyllene may contribute to its ability to modulate pain perception. While research is ongoing, there is some evidence to suggest that it could be useful in managing pain, although more studies are needed to establish its efficacy and safety.

<u>Neuroprotective Effects</u>: Some studies suggest that beta-caryophyllene may have neuroprotective properties. By interacting with CB2 receptors in the central nervous system, it may help protect neurons and reduce neuroinflammation, potentially benefiting conditions like neurodegenerative diseases.

<u>Antioxidant Activity</u>: Beta-caryophyllene also exhibits antioxidant properties. Antioxidants help neutralize free radicals in the body, which can contribute to various health issues, including inflammation and oxidative stress.

#### What is the pharmacology of Emu Oil?

Emu oil is a natural oil obtained from the fat of the emu, a flightless bird native to Australia. It has been used traditionally by indigenous Australian populations for its purported therapeutic properties. While some people use emu oil for various skin conditions and inflammation, the scientific evidence supporting its pharmacological effects is limited, and more research is needed to fully understand its mechanisms of action and therapeutic potential. Here are some of the proposed pharmacological properties of emu oil:

<u>Anti-Inflammatory Properties</u>: Emu oil is believed by some to have anti-inflammatory effects when applied topically. It is often used for conditions such as arthritis, dermatitis, and other inflammatory skin



disorders. However, the specific mechanisms behind these potential anti-inflammatory effects are not well understood.

<u>Analgesic Effects</u>: Some people use emu oil topically for pain relief, especially for conditions like joint pain and muscle soreness. The purported analgesic effects may be related to the oil's anti-inflammatory properties, but the exact mechanisms are not well-established.

<u>Wound Healing</u>: Emu oil has been suggested to promote wound healing, possibly due to its moisturizing and anti-inflammatory properties. However, more research is needed to confirm its effectiveness in this regard.

<u>Antioxidant Properties</u>: Emu oil contains various antioxidants, such as vitamin E and carotenoids, which may contribute to its potential protective effects against oxidative stress. Antioxidants help neutralize free radicals in the body.

<u>Moisturizing and Skin Barrier Function</u>: Emu oil is known for its moisturizing properties. It contains fatty acids, including oleic acid, linoleic acid, and others, which are important for maintaining the integrity of the skin barrier. The oil is thought to penetrate the skin easily, providing hydration and potentially aiding in skin repair.

Before using emu oil or products containing emu oil, it's advisable to perform a patch test to check for any adverse reactions. If you have specific health concerns or conditions, consult with a healthcare professional before incorporating emu oil into your routine, especially if you are considering its use for medicinal purposes.

# What is the pharmacology of Squalane Oil?

Squalane oil is a saturated form of squalene, a natural compound derived from plant sources like olives or sugarcane. Squalane is widely used in skincare and cosmetic products due to its emollient and moisturizing properties. While it doesn't have the same well-defined pharmacological actions as pharmaceutical compounds, it does have several characteristics that make it beneficial for skin health. Here are some aspects of the pharmacology of squalane oil:

<u>Emollient and Moisturizing Properties</u>: Squalane is an excellent emollient, meaning it can soften and smooth the skin's surface. It helps to improve skin texture and prevents moisture loss, making it a popular ingredient in skincare products such as moisturizers, creams, and serums.

<u>Skin Barrier Function</u>: Squalane is similar to the skin's natural lipids and helps reinforce the skin barrier. By enhancing the skin barrier function, it contributes to the protection of the skin against external aggressors and helps maintain optimal hydration levels.

<u>Antioxidant Properties</u>: Squalane has antioxidant properties that can help protect the skin from oxidative stress caused by free radicals. This antioxidant activity may contribute to the oil's anti-aging effects by reducing damage caused by environmental factors.

<u>Non-comedogenic</u>: Squalane is non-comedogenic, meaning it is unlikely to clog pores. This makes it suitable for a wide range of skin types, including those prone to acne. It provides moisture without causing breakouts or exacerbating existing skin issues.

# Tulla Botanicals, Inc.Find Your Tranquil Balance616 Avondale Ln., MO 64083C: 816.518.2135 | drpat@tullabotanicals.comtullabotanicals.com



<u>Enhanced Penetration of Other Ingredients</u>: Squalane has the ability to enhance the absorption and effectiveness of other active ingredients in skincare products. It can act as a carrier oil, helping other beneficial compounds penetrate the skin more effectively.

While squalane oil is generally well-tolerated and considered safe for topical use, individual reactions may vary. It is often used in various skincare formulations, including moisturizers, serums, and anti-aging products. As with any skincare product, it's advisable to perform a patch test before widespread use, especially for individuals with sensitive skin or known allergies.

It's important to note that squalane is different from squalene. Squalene is a precursor to squalane and tends to be less stable, making squalane a more commonly used form in skincare products. Additionally, sustainable and plant-derived sources of squalane are preferred to avoid environmental concerns associated with traditional shark-derived squalene. Our formulations use olive-derived squalane, **not** shark-derived.

# What is the pharmacology of Palmitoylethanolamide (PEA)?

Palmitoylethanolamide (PEA) is a natural, protective, fatty molecule produced in our body, and in animals and plants. PEA can be found in food such as meat, eggs, soybeans, and peanuts. It is a naturally occurring fatty acid amide that belongs to the N-acylethanolamines family. PEA has been studied for its potential anti-inflammatory, analgesic (pain-relieving), and neuroprotective properties. While research on PEA is ongoing, some aspects of its pharmacology include:

<u>Anti-Inflammatory Effects</u>: PEA has been recognized for its anti-inflammatory properties. It is believed to exert its anti-inflammatory effects by interacting with various cellular targets involved in the inflammatory response. PEA may modulate immune cells and reduce the production of pro-inflammatory molecules.

<u>Pain Modulation</u>: PEA has analgesic properties and is thought to modulate pain signaling pathways. It interacts with receptors such as peroxisome proliferator-activated receptor alpha (PPAR- $\alpha$ ) and transient receptor potential vanilloid type-1 (TRPV1), which are involved in pain perception. By modulating these receptors, PEA may help in managing different types of pain.

<u>Neuroprotective Effects</u>: PEA has been investigated for its potential neuroprotective effects. It may have a role in protecting nerve cells and supporting overall neurological health. Some studies suggest that PEA may be beneficial in conditions involving neuroinflammation and neurodegeneration.

<u>Immune Modulation</u>: PEA is involved in modulating immune responses, particularly by influencing the activity of mast cells. Mast cells play a role in the immune system and are involved in inflammatory processes. PEA's modulation of mast cell activity contributes to its anti-inflammatory effects.

<u>Endocannabinoid System Modulation</u>: While PEA itself is not a cannabinoid, it may indirectly influence the endocannabinoid system. It can enhance the actions of anandamide, an endocannabinoid, by inhibiting its breakdown. Anandamide is known to have anti-inflammatory and analgesic effects.

<u>Antioxidant Activity</u>: PEA has antioxidant properties, contributing to its ability to neutralize free radicals. Antioxidants help protect cells from oxidative stress, which is implicated in various health conditions.



#### What is the pharmacology of Arnica Oil?

Arnica oil is derived from the flowers of the Arnica montana plant, which is a member of the Asteraceae family. Arnica has been traditionally used in folk medicine for various purposes, including the treatment of bruises, inflammation, and pain. However, it's important to note that the scientific evidence supporting the efficacy of arnica oil is limited, and its use should be approached with care.

The pharmacology of arnica oil is not fully understood, but some of its potential pharmacological actions may include:

<u>Anti-inflammatory effects</u>: Arnica is believed to contain compounds that have anti-inflammatory properties, which could help reduce swelling and inflammation when applied topically.

<u>Analgesic effects</u>: The oil may have analgesic (pain-relieving) properties, potentially providing relief from pain associated with bruises, sprains, or other injuries.

<u>Anti-bruising effects</u>: Arnica is often used topically to reduce bruising and promote healing. It is thought to improve blood circulation and prevent the accumulation of blood in the tissues.

<u>Antimicrobial effects</u>: Some studies suggest that arnica may have antimicrobial properties, which could help prevent infection in wounds or skin injuries.

Before using arnica oil or any arnica-containing products, it is advisable to consult with a healthcare professional, especially if you are pregnant, nursing, or have any underlying health conditions. Additionally, be cautious about potential interactions with other medications or skin sensitivities. Always perform a patch test on a small area of skin to check for any adverse reactions before widespread use.

#### What is the pharmacology of Castor Oil?

Castor oil is derived from the seeds of the Ricinus communis plant and has been used for various purposes, both topically and internally, for centuries. Its pharmacology involves a range of effects attributed to its chemical composition. Here are some key aspects of the pharmacology of castor oil:

<u>Anti-Inflammatory Properties</u>: Ricinoleic acid, the main component of castor oil, has demonstrated antiinflammatory effects in some studies. This property may contribute to the traditional use of castor oil in treating various inflammatory conditions.

<u>Antimicrobial Properties</u>: Castor oil has shown some antimicrobial activity in laboratory studies. This property may be attributed to compounds such as undecylenic acid, which is formed from ricinoleic acid during the processing of castor oil.

<u>Wound Healing</u>: The anti-inflammatory and antimicrobial properties of castor oil may contribute to its potential benefits in wound healing. It may help reduce inflammation and protect against infection when applied to minor wounds.

<u>Hydration and Moisturization</u>: When applied topically, castor oil is often used for its moisturizing properties. It can help hydrate the skin, making it a common ingredient in cosmetic and skincare products.



When using castor oil topically, it's advisable to perform a patch test to check for skin sensitivity. As with any natural remedy, individual responses can vary, and it's crucial to use caution and seek professional advice when needed.

#### **Disclaimer:**

This document is for informational purposes only and is not intended to be a substitute for professional medical advice, diagnosis, or treatment. Always seek the advice of your physician or other qualified health provider with any questions you may have regarding a medical condition. Never disregard professional medical advice or delay in seeking it because of something you have read in this document.

#### **References:**

#### **Beta-Caryophyllene**

1. <u>Protective Effects of (*E*)-β-Caryophyllene (BCP) in Chronic Inflammation.</u>

Scandiffio R, Geddo F, Cottone E, Querio G, Antoniotti S, Gallo MP, Maffei ME, Bovolin P.

Nutrients. 2020 Oct 26;12(11):3273. doi: 10.3390/nu12113273.

PMID: 33114564 Free PMC article. Review.

2. <u>β-caryophyllene and β-caryophyllene oxide-natural compounds of anticancer and analgesic</u> properties.

Fidyt K, Fiedorowicz A, Strządała L, Szumny A.

Cancer Med. 2016 Oct;5(10):3007-3017. doi: 10.1002/cam4.816. Epub 2016 Sep 30.

PMID: 27696789 Free PMC article. Review.

3. <u>Beta-caryophyllene enhances wound healing through multiple routes.</u>

Koyama S, Purk A, Kaur M, Soini HA, Novotny MV, Davis K, Kao CC, Matsunami H, Mescher A.

PLoS One. 2019 Dec 16;14(12):e0216104. doi: 10.1371/journal.pone.0216104. eCollection 2019.

PMID: 31841509 Free PMC article.

4. <u>β-Caryophyllene, a Natural Sesquiterpene, Attenuates Neuropathic Pain and Depressive-Like</u> <u>Behavior in Experimental Diabetic Mice.</u>

Aguilar-Ávila DS, Flores-Soto ME, Tapia-Vázquez C, Pastor-Zarandona OA, López-Roa RI, Viveros-Paredes JM.

J Med Food. 2019 May;22(5):460-468. doi: 10.1089/jmf.2018.0157. Epub 2019 Mar 13.

PMID: 30864870



5. <u>Hemp Seed Oil in Association with β-Caryophyllene, Myrcene and Ginger Extract as a Nutraceutical</u> Integration in Knee Osteoarthritis: A Double-Blind Prospective Case-Control Study.

Farì G, Megna M, Scacco S, Ranieri M, Raele MV, Chiaia Noya E, Macchiarola D, Bianchi FP, Carati D, Panico S, Di Campi E, Gnoni A, Scacco V, Inchingolo AD, Qorri E, Scarano A, Rapone B.

Medicina (Kaunas). 2023 Jan 18;59(2):191. doi: 10.3390/medicina59020191.

PMID: 36837393 Free PMC article. Clinical Trial.

6. <u>The CB2 Agonist β-Caryophyllene in Male and Female Rats Exposed to a Model of Persistent</u> <u>Inflammatory Pain.</u>

Ceccarelli I, Fiorenzani P, Pessina F, Pinassi J, Aglianò M, Miragliotta V, Aloisi AM.

Front Neurosci. 2020 Aug 18;14:850. doi: 10.3389/fnins.2020.00850. eCollection 2020.

PMID: 33013287 Free PMC article.

7. <u>Efficacy of a Combination of N-Palmitoylethanolamide, Beta-Caryophyllene, Carnosic Acid, and</u> Myrrh Extract on Chronic Neuropathic Pain: A Preclinical Study.

Fotio Y, Aboufares El Alaoui A, Borruto AM, Acciarini S, Giordano A, Ciccocioppo R.

Front Pharmacol. 2019 Jun 27;10:711. doi: 10.3389/fphar.2019.00711. eCollection 2019.

PMID: 31316381 Free PMC article.

8. Improvement of Oxidative Stress and Mitochondrial Dysfunction by β-Caryophyllene: A Focus on the Nervous System.

Ullah H, Di Minno A, Santarcangelo C, Khan H, Daglia M.

Antioxidants (Basel). 2021 Apr 1;10(4):546. doi: 10.3390/antiox10040546.

PMID: 33915950 Free PMC article. Review.

9. <u>Beta-caryophyllene is a dietary cannabinoid.</u>

Gertsch J, Leonti M, Raduner S, Racz I, Chen JZ, Xie XQ, Altmann KH, Karsak M, Zimmer A.

Proc Natl Acad Sci U S A. 2008 Jul 1;105(26):9099-104. doi: 10.1073/pnas.0803601105. Epub 2008 Jun 23.

PMID: 18574142 Free PMC article.

10. <u>Myrtenal and β-caryophyllene oxide screened from Liquidambaris Fructus suppress NLRP3</u> inflammasome components in rheumatoid arthritis.

Li WX, Qian P, Guo YT, Gu L, Jurat J, Bai Y, Zhang DF.

BMC Complement Med Ther. 2021 Sep 28;21(1):242. doi: 10.1186/s12906-021-03410-2.



### PMID: 34583676 Free PMC article.

11. (-)-β-Caryophyllene, a CB2 Receptor-Selective Phytocannabinoid, Suppresses Motor Paralysis and Neuroinflammation in a Murine Model of Multiple Sclerosis.

Alberti TB, Barbosa WL, Vieira JL, Raposo NR, Dutra RC.

Int J Mol Sci. 2017 Apr 1;18(4):691. doi: 10.3390/ijms18040691.

PMID: 28368293 Free PMC article.

12. <u>Plant Natural Sources of the Endocannabinoid (*E*)-β-Caryophyllene: A Systematic Quantitative Analysis of Published Literature.</u>

Maffei ME.

Int J Mol Sci. 2020 Sep 7;21(18):6540. doi: 10.3390/ijms21186540.

PMID: 32906779 Free PMC article.

13. The endocannabinoid system, cannabinoids, and pain.

Fine PG, Rosenfeld MJ.

Rambam Maimonides Med J. 2013 Oct 29;4(4):e0022. doi: 10.5041/RMMJ.10129. eCollection 2013.

PMID: 24228165 Free PMC article.

<u>Beta-caryophyllene as an antioxidant, anti-inflammatory and re-epithelialization activities in a rat skin</u> wound excision model.

Gushiken LFS, Beserra FP, Hussni MF, Gonzaga MT, Ribeiro VP, de Souza PF, Campos JCL, Massaro TNC, Hussni CA, Takahira RK, Marcato PD, Bastos JK, Pellizzon CH.

Oxid Med Cell Longev. 2022 Feb 3;2022:9004014. doi: 10.1155/2022/9004014. eCollection 2022.

#### PMID: 35154574 Free PMC article.

<u>Beta Caryophyllene-Loaded Nanostructured Lipid Carriers for Topical Management of Skin Disorders:</u> Statistical Optimization, In Vitro and Dermatokinetic Evaluation.

Ghazwani M, Hani U, Alqarni MH, Alam A.

Gels. 2023 Jul 6;9(7):550. doi: 10.3390/gels9070550.

PMID: 37504429 Free PMC article.

<u>B-Caryophyllene-Loaded Microemulsion-Based Topical Hydrogel: A Promising Carrier to Enhance the</u> <u>Analgesic and Anti-Inflammatory Outcomes.</u>



Alharthi S, Ziora ZM, Mustafa G, Chaubey P, El Kirdasy AF, Alotaibi G.

Gels. 2023 Aug 7;9(8):634. doi: 10.3390/gels9080634.

#### PMID: 37623089 Free PMC article.

1. <u>β-Caryophyllene, a CB2-Receptor-Selective Phytocannabinoid, Suppresses Mechanical Allodynia in a</u> Mouse Model of Antiretroviral-Induced Neuropathic Pain.

Aly E, Khajah MA, Masocha W.

Molecules. 2019 Dec 27;25(1):106. doi: 10.3390/molecules25010106.

# PMID: 31892132 Free PMC article.

2. <u>Protective Effects of (*E*)-β-Caryophyllene (BCP) in Chronic Inflammation.</u>

Scandiffio R, Geddo F, Cottone E, Querio G, Antoniotti S, Gallo MP, Maffei ME, Bovolin P.

Nutrients. 2020 Oct 26;12(11):3273. doi: 10.3390/nu12113273.

PMID: 33114564 Free PMC article. Review.

3. <u>β-Caryophyllene</u>, A Natural Dietary CB2 Receptor Selective Cannabinoid can be a Candidate to Target the Trinity of Infection, Immunity, and Inflammation in COVID-19.

Jha NK, Sharma C, Hashiesh HM, Arunachalam S, Meeran MN, Javed H, Patil CR, Goyal SN, Ojha S.

Front Pharmacol. 2021 May 14;12:590201. doi: 10.3389/fphar.2021.590201. eCollection 2021.

PMID: 34054510 Free PMC article.

4. (-)-β-Caryophyllene, a CB2 Receptor-Selective Phytocannabinoid, Suppresses Motor Paralysis and Neuroinflammation in a Murine Model of Multiple Sclerosis.

Alberti TB, Barbosa WL, Vieira JL, Raposo NR, Dutra RC.

Int J Mol Sci. 2017 Apr 1;18(4):691. doi: 10.3390/ijms18040691.

PMID: 28368293 Free PMC article.

5. <u>β-Caryophyllene, a CB2 receptor agonist produces multiple behavioral changes relevant to anxiety</u> <u>and depression in mice.</u>

Bahi A, Al Mansouri S, Al Memari E, Al Ameri M, Nurulain SM, Ojha S.

Physiol Behav. 2014 Aug;135:119-24. doi: 10.1016/j.physbeh.2014.06.003. Epub 2014 Jun 13.

PMID: 24930711

6. <u>A focused review on CB2 receptor-selective pharmacological properties and therapeutic potential of</u> <u>β-caryophyllene, a dietary cannabinoid.</u>



Hashiesh HM, Sharma C, Goyal SN, Sadek B, Jha NK, Kaabi JA, Ojha S.

Biomed Pharmacother. 2021 Aug;140:111639. doi: 10.1016/j.biopha.2021.111639. Epub 2021 Jun 3.

PMID: 34091179 Review.

7. <u>A mechanistic review on immunomodulatory effects of selective type two cannabinoid receptor β-</u> <u>caryophyllene.</u>

Baradaran Rahimi V, Askari VR.

Biofactors. 2022 Jul;48(4):857-882. doi: 10.1002/biof.1869. Epub 2022 Jun 1.

PMID: 35648433 Review.

8. <u>β-Caryophyllene Inhibits Cell Proliferation through a Direct Modulation of CB2 Receptors in</u> <u>Glioblastoma Cells.</u>

Irrera N, D'Ascola A, Pallio G, Bitto A, Mannino F, Arcoraci V, Rottura M, Ieni A, Minutoli L, Metro D, Vaccaro M, Altavilla D, Squadrito F.

Cancers (Basel). 2020 Apr 23;12(4):1038. doi: 10.3390/cancers12041038.

PMID: 32340197 Free PMC article.