

External Epithelial Environment- change your external environment

- Baths – Be sure to not bathe in regular tap water- locate a water filter shower head to keep your aqueous solution free of as many extra chemicals and particulates as possible! You may even wish to use UVc light to destroy any exogenous DNA that the water may contain.
 - Baking Soda
 - Scaly skin and bath pH: Rediscovering baking soda
 - [https://www.jaad.org/article/S0190-9622\(09\)00493-9/fulltext](https://www.jaad.org/article/S0190-9622(09)00493-9/fulltext)
 - Old fashioned sodium bicarbonate baths for the treatment of psoriasis in the era of futuristic biologics: an old ally to be rescued
 - <https://pubmed.ncbi.nlm.nih.gov/15897164/>
 - Effects of sodium bicarbonate bath on the quality of sleep: An assessor-blinded, randomized, controlled, pilot clinical trial
 - <https://pubmed.ncbi.nlm.nih.gov/36528983/>
 - Antibacterial activity of baking soda
 - <https://pubmed.ncbi.nlm.nih.gov/12017929/>
 - The effects of bathing in neutral bicarbonate ion water
 - <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8576025/>
 - Taken together, our results show that percutaneously absorbed carbon dioxide changes to bicarbonate ions, which act directly on endothelial cells to increase NO production by phosphorylation of eNOS and thus improve blood flow.
 - Efficacy of a Topical Formulation of Sodium Bicarbonate in Mild to Moderate Stable Plaque Psoriasis: a Randomized, Blinded, Inpatient, Controlled Study
 - <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6704198/>
 - Antifungal activity of sodium bicarbonate against fungal agents causing superficial infections
 - <https://pubmed.ncbi.nlm.nih.gov/22991095/>
 - Epsom Salts
 - Permeation of topically applied Magnesium ions through human skin is facilitated by hair follicles
 - <https://pubmed.ncbi.nlm.nih.gov/27624531/>
 - Bathing in a magnesium-rich Dead Sea salt solution improves skin barrier function, enhances skin hydration, and reduces inflammation in atopic dry skin
 - <https://pubmed.ncbi.nlm.nih.gov/15689218/>
 - The effect of salt-water bath in the management of treatment-related peripheral neuropathy in cancer patients receiving taxane and platinum-based treatment
 - <https://pubmed.ncbi.nlm.nih.gov/34340926/>

- Coffee/Green tea (Caffeine and catechins)
 - Transdermal delivery of anticancer drug caffeine from water-in-oil nanoemulsions
 - <https://www.sciencedirect.com/science/article/abs/pii/S0927776509004202>
 - In vitro transdermal delivery of the major catechins and caffeine from extract of Camellia sinensis
 - <https://www.sciencedirect.com/science/article/abs/pii/S0378517304003436>
- Ion/Mineral sprays
 - Transdermal Mg sprays
 - Schweizer formula mineral spray
 - <https://www.schweitzerformula.com/the-formula/technical-details/>
 - Silver lotions
 - Transdermal uptake and organ distribution of silver from two different wound dressings in rats after a burn trauma
 - <https://pubmed.ncbi.nlm.nih.gov/25139317/>
 - Topical Silver for Infected Wounds
 - <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2742464/>
 - Electromagnetic Shielding Properties of Knitted Fabric Made from Polyamide Threads Coated with Silver
 - <https://www.mdpi.com/1996-1944/14/5/1281>
 - Room-temperature production of silver-nanofiber film for large-area, transparent and flexible surface electromagnetic interference shielding
 - <https://www.nature.com/articles/s41528-019-0050-8>
 - Oxygenated lotions
 - Topical Oxygen Emulsion: A Novel Wound Therapy
 - <https://jamanetwork.com/journals/jamadermatology/fullarticle/654413>
 - A Supersaturated Oxygen Emulsion for Wound Care and Skin Rejuvenation
 - <https://pubmed.ncbi.nlm.nih.gov/32550688/>
 - The antibacterial effect of topical ozone on the treatment of MRSA skin infection
 - <https://www.spandidos-publications.com/10.3892/mmr.2017.8148>
 - Ozonated Oils as Antimicrobial Systems in Topical Applications. Their Characterization, Current Applications, and Advances in Improved Delivery Techniques
 - <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7024311/>
- Silver tooth paste/mouth wash
 - Applications of Silver Nanoparticles in Dentistry: Advances and Technological Innovation
 - <https://www.mdpi.com/1422-0067/22/5/2485>
 - Dental Pulp Response to Silver-Containing Solutions: A Scoping Review
 - <https://www.mdpi.com/2304-6767/11/5/114>

- Bactericidal Activity of Silver Nanoparticles on Oral Biofilms Related to Patients with and without Periodontal Disease
 - <https://www.mdpi.com/2079-4983/14/6/311>
- Nebulization (clean lungs)
 - H₂O:H₂O₂ (1 part food grade hydrogen peroxide to 2 parts purified water + 3 drops of food grade iodine)
 - Use of a Hydrogen Peroxide Nebulizer for Viral Disinfection of Emergency Ambulance and Hospital Waiting Room
 - <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8934245/>
 - Inhalation Pneumonitis Caused by Nebulized Hydrogen Peroxide
 - <https://www.cureus.com/articles/147548-inhalation-pneumonitis-caused-by-nebulized-hydrogen-peroxide#!/>
 - Prospective Randomized Double-blind Placebo-controlled Study to Assess the Effects of Nano-ozonized Hydrogen Peroxide Nebulization on Results of RTPCR for Novel Coronavirus thus Infectivity and Clinical Course among Moderately Sick COVID-19 Patients
 - <https://www.jsafog.com/doi/JSAFOG/pdf/10.5005/jp-journals-10006-1986>
 - Efficacy assessment of different time cycles of nebulized hydrogen peroxide against bacterial and yeast biofilms
 - <https://www.sciencedirect.com/science/article/pii/S0195670122001529>
 - Colloidal silver
 - Colloidal silver for lung disease in cystic fibrosis
 - <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2443992/>
 - Treatment of infection and inflammation associated with COVID-19, multi-drug resistant pneumonia and fungal sinusitis by nebulizing a nanosilver solution
 - <https://www.sciencedirect.com/science/article/pii/S1549963423000059>
 - Silver colloidal nanoparticles: antifungal effect against adhered cells and biofilms of *Candida albicans* and *Candida glabrata*
 - <https://pubmed.ncbi.nlm.nih.gov/21756192/>
 - Silver Nanoantibiotics Display Strong Antifungal Activity Against the Emergent Multidrug-Resistant Yeast *Candida auris* Under Both Planktonic and Biofilm Growing Conditions
 - <https://www.frontiersin.org/articles/10.3389/fmicb.2020.01673/full>
 - Silver colloidal nanoparticle stability: influence on *Candida* biofilms formed on denture acrylic
 - <https://academic.oup.com/mmy/article/52/6/627/2804956?login=false>
 - Striking Back against Fungal Infections: The Utilization of Nanosystems for Antifungal Strategies
 - <https://www.mdpi.com/1422-0067/22/18/10104>
 - Antifungal activity of silver nanoparticles against *Candida* spp.
 - <https://www.sciencedirect.com/science/article/abs/pii/S0142961209008023>

- Sinus rinse with silver
 - The silver lining: towards the responsible and limited usage of silver
 - <https://ami-journals.onlinelibrary.wiley.com/doi/10.1111/jam.13525>
 - Topical Colloidal Silver for the Treatment of Recalcitrant Chronic Rhinosinuitis
 - <https://www.frontiersin.org/articles/10.3389/fmicb.2018.00720/full>
 - Evaluation of silver nanoparticles for the prevention of SARS-CoV-2 infection in health workers: In vitro and in vivo
 - <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0256401>

- Menthol

Biological properties [\[edit \]](#)



This section **needs additional citations to secondary or tertiary sources** such as review articles, monographs, or textbooks. Please add such references to provide context and establish the relevance of any **primary research articles** cited. Unsourced or poorly sourced material may be challenged and removed. *(September 2018)* (*Learn how and when to remove this template message*)

Menthol's ability to chemically trigger the cold-sensitive TRPM8 receptors in the skin is responsible for the well-known cooling sensation it provokes when inhaled, eaten, or applied to the skin.^[3] In this sense, it is similar to **capsaicin**, the chemical responsible for the spiciness of **hot chilis** (which stimulates **heat sensors**, also without causing an actual change in temperature).

Menthol's **analgesic** properties are mediated through a selective activation of **κ-opioid receptors**.^[4] Menthol blocks calcium channels^[5] and voltage-sensitive **sodium channels**, reducing neural activity that may stimulate muscles.^[6]

Some studies show that menthol acts as **GABA_A receptor positive allosteric modulator** and increases **Gabaergic** transmission in PAG neurons.^[7] Menthol also shares **anaesthetic** properties similar to **propofol**, by modulating the same sites of the **GABA_A receptor**.^[8]

Menthol is widely used in dental care as a topical antibacterial agent, effective against several types of **streptococci** and **lactobacilli**.^[9] Menthol also lowers blood pressure and antagonizes **vasoconstriction** through TRPM8 activation.^[10]

- Menthol cigarettes
 - Cellular and Molecular Targets of Menthol Actions
 - <https://www.frontiersin.org/articles/10.3389/fphar.2017.00472/full>
 - MAMMALIAN CILIATED RESPIRATORY EPITHELIUM: Studies with Particular Reference to Effects of Menthol, Nicotine, and Smoke of Mentholated and Nonmentholated Cigarettes
 - <https://jamanetwork.com/journals/jamaotolaryngology/article-abstract/597075>
 - Menthol Cigarette Smoke Induces More Severe Lung Inflammation Than Nonmenthol Cigarette Smoke Does in Mice With Subchronic Exposure – Role of TRPM8

- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6670025/>
- Cigarette smoke impairs airway epithelial barrier function and cell–cell contact recovery
 - <https://erj.ersjournals.com/content/39/2/419>
- Smoking, immunity, and DNA damage
 - <https://tlcr.amegroups.com/article/view/27925/html>
- Nicotine exposure and bronchial epithelial cell nicotinic acetylcholine receptor expression in the pathogenesis of lung cancer
 - <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC151841/>
- Control of Lung Epithelial Growth by a Nicotinic Acetylcholine Receptor
 - <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2770708/>
 - As ligand-gated ion channels, nAChRs undergo complex allosteric changes in response to binding either the endogenous ligand acetylcholine or exogenous ligands, including nicotine. Although nAChRs are classically linked to the plasma membrane depolarization required for neurotransmission, non-neuronal nAChRs in the lung act most frequently as calcium channels and have been linked to regulatory proteins such as src and phosphatidylinositol 3-kinase, which can control cell proliferation.
- Contribution of $\alpha 7$ nicotinic receptor to airway epithelium dysfunction under nicotine exposure
 - <https://www.pnas.org/doi/10.1073/pnas.1216939110>
- Electronic cigarette vapor with nicotine causes airway mucociliary dysfunction preferentially via TRPA1 receptors
 - <https://www.thoracic.org/about/newsroom/press-releases/ecigs-and-mucociliary-dysfunction.pdf>
- Nicotine induces cell proliferation, invasion and epithelial-mesenchymal transition in a variety of human cancer cell lines
 - <https://onlinelibrary.wiley.com/doi/full/10.1002/ijc.23894>
- Nicotine signals through muscle-type and neuronal nicotinic acetylcholine receptors in both human bronchial epithelial cells and airway fibroblasts
 - <https://respiratory-research.biomedcentral.com/articles/10.1186/1465-9921-5-27>
- Nicotinic alpha 7 receptor expression and modulation of the lung epithelial response to lipopolysaccharide
 - <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0175367>

- **Cannabinoids**

The **endocannabinoid system (ECS)** is a biological system composed of **endocannabinoids**, which are **endogenous lipid-based retrograde neurotransmitters** that bind to **cannabinoid receptors (CBRs)**, and cannabinoid receptor proteins that are expressed throughout the vertebrate **central nervous system** (including the **brain**) and **peripheral nervous system**.^{[1][2]} The endocannabinoid system remains under **preliminary research**, but may be involved in regulating physiological and **cognitive processes**, including **fertility**,^[3] **pregnancy**,^[4] **pre- and postnatal development**,^{[5][6][7]} various activity of immune system,^[8] **appetite**, **pain-sensation**, **mood**, and **memory**, and in mediating the **pharmacological effects of cannabis**.^{[9][10]} The ECS plays an important role in multiple aspects of **neural functions**, including the control of movement and motor coordination, learning and memory, emotion and motivation, addictive-like behavior and pain modulation, among others.^[11]

Two primary cannabinoid receptors have been identified: **CB1**, first cloned (or isolated) in 1990; and **CB2**, cloned in 1993. CB1 receptors are found predominantly in the brain and nervous system, as well as in peripheral organs and tissues, and are the main molecular target of the endogenous **partial agonist, anandamide (AEA)**, as well as exogenous **THC**, the most known active component of cannabis. Endocannabinoid **2-arachidonoylglycerol (2-AG)**, which was found to be two and three orders of magnitude more abundant in mammalian brain than AEA, acts as a full agonist at both CB receptors.^[12]

Binding and neuronal excitability [edit]



This section **provides insufficient context for those unfamiliar with the subject**. Please help improve the article by providing more context for the reader. (*January 2014*) (*Learn how and when to remove this template message*)

The molecular mechanisms of CB₁-mediated changes to the membrane voltage have also been studied in detail. Cannabinoids reduce calcium influx by blocking the activity of voltage-dependent **N-, P/Q- and L-type calcium channels**.^{[42][43]} In addition to acting on calcium channels, activation of **Gi/o** and **Gs**, the two most commonly coupled G-proteins to cannabinoid receptors, has been shown to modulate **potassium channel** activity. Recent studies have found that CB₁ activation specifically facilitates potassium ion flux through **GIRKs**, a family of **potassium channels**.^[43] Immunohistochemistry experiments demonstrated that CB₁ is co-localized with GIRK and **Kv1.4** potassium channels, suggesting that these two may interact in physiological contexts.^[44]

In the **central nervous system**, CB₁ receptors influence neuronal excitability, reducing the incoming synaptic input.^[45] This mechanism, known as **presynaptic inhibition**, occurs when a postsynaptic neuron releases endocannabinoids in retrograde transmission, which then bind to cannabinoid receptors on the presynaptic terminal. CB₁ receptors then reduce the amount of neurotransmitter released, so that subsequent excitation in the presynaptic neuron results in diminished effects on the postsynaptic neuron. It is likely that presynaptic inhibition uses many of the same ion channel mechanisms listed above, although recent evidence has shown that CB₁ receptors can also regulate neurotransmitter release by a non-ion channel mechanism, i.e. through Gi/o-mediated inhibition of **adenylyl cyclase** and **protein kinase A**.^[46] Direct effects of CB₁ receptors on membrane excitability have been reported, and strongly impact the firing of cortical neurons.^[47] A series of behavioral experiments demonstrated that **NMDAR**, an ionotropic **glutamate receptor**, and the **metabotropic glutamate receptors (mGluRs)** work in concert with CB₁ to induce **analgesia** in mice, although the mechanism underlying this effect is unclear.^[citation needed]

Immune system [edit]

In laboratory experiments, activation of cannabinoid receptors had an effect on the activation of **GTPases** in **macrophages**, **neutrophils**, and **bone marrow** cells. These receptors have also been implicated in the migration of **B cells** into the **marginal zone** and the regulation of **IgM** levels.^[62]

Autonomic nervous system [edit]

Peripheral expression of cannabinoid receptors led researchers to investigate the role of cannabinoids in the **autonomic nervous system**. Research found that the CB₁ receptor is expressed presynaptically by motor neurons that innervate visceral organs. Cannabinoid-mediated inhibition of electric potentials results in a reduction in noradrenaline release from **sympathetic nervous system** nerves. Other studies have found similar effects in endocannabinoid regulation of intestinal motility, including the innervation of smooth muscles associated with the digestive, urinary, and reproductive systems.^[25]

Analgesia [edit]

At the spinal cord, cannabinoids suppress noxious-stimulus-evoked responses of neurons in the dorsal horn, possibly by modulating descending **noradrenaline** input from the **brainstem**.^[25] As many of these fibers are primarily **GABAergic**, cannabinoid stimulation in the spinal column results in disinhibition that should increase noradrenaline release and attenuation of noxious-stimuli-processing in the periphery and **dorsal root ganglion**.

The endocannabinoid most researched in pain is **palmitoylethanolamide**. Palmitoylethanolamide is a fatty amine related to anandamide, but saturated and although initially it was thought that palmitoylethanolamide would bind to the CB1 and the CB2 receptor, later it was found that the most important receptors are the **PPAR-alpha** receptor, the **TRPV** receptor and the GPR55 receptor. Palmitoylethanolamide has been evaluated for its analgesic actions in a great variety of pain indications^[66] and found to be safe and effective.

Modulation of the endocannabinoid system by metabolism to N-arachidonyl-phenolamine (AM404), an endogenous cannabinoid neurotransmitter, has been discovered to be one **mechanism**^[67] for analgesia by acetaminophen (paracetamol).

Endocannabinoids are involved in **placebo** induced analgesia responses.^[68]

Thermoregulation [edit]

Anandamide and **N-arachidonyl dopamine** (NADA) have been shown to act on temperature-sensing **TRPV1** channels, which are involved in thermoregulation.^[69] TRPV1 is activated by the exogenous ligand **capsaicin**, the active component of chili peppers, which is structurally similar to endocannabinoids. NADA activates the TRPV1 channel with an **EC₅₀** of approximately of 50 nM.^[clarify] The high potency makes it the putative endogenous TRPV1 agonist.^[70] Anandamide has also been found to activate TRPV1 on sensory neuron terminals, and subsequently cause vasodilation.^[25] TRPV1 may also be activated by **methanandamide** and **arachidonyl-2'-chloroethylamide** (ACEA).^[13]

Types [edit]

CB₁ [edit]

Main article: Cannabinoid receptor type 1

Cannabinoid receptor type 1 (CB₁) receptors are thought to be one of the most widely **expressed** G_{ai} protein-coupled receptors in the brain. One mechanism through which they function is endocannabinoid-mediated **depolarization-induced suppression of inhibition**, a very common form of **retrograde signaling**, in which the depolarization of a single neuron induces a reduction in **GABA**-mediated neurotransmission. Endocannabinoids released from the depolarized post-synaptic neuron bind to CB₁ receptors in the pre-synaptic neuron and cause a reduction in GABA release due to limited presynaptic calcium ions entry.^[medical citation needed]

They are also found in other parts of the body. For instance, in the liver, activation of the CB₁ receptor is known to increase de novo **lipogenesis**.^[21]

CB₂ [edit]

Main article: Cannabinoid receptor type 2

CB₂ receptors are expressed on **T cells** of the **immune system**, on **macrophages** and **B cells**, in **hematopoietic cells**, and in the brain and CNS (2019).^[22] They also have a function in **keratinocytes**. They are also expressed on peripheral **nerve** terminals. These receptors play a role in **antinociception**, or the relief of **pain**. In the brain, they are mainly expressed by **microglial cells**, where their role remains unclear. While the most likely cellular targets and executors of the CB₂ receptor-mediated effects of endocannabinoids or synthetic agonists are the immune and immune-derived cells (e.g. leukocytes, various populations of T and B lymphocytes, monocytes/macrophages, dendritic cells, mast cells, microglia in the brain, Kupffer cells in the liver, astrocytes, etc.), the number of other potential cellular targets is expanding, now including endothelial and smooth muscle cells, fibroblasts of various origins, cardiomyocytes, and certain neuronal elements of the peripheral or central nervous systems (2011).^[8]

- Full spectrum hemp/Delta-8 THC/Medical Cannabis
 - Impact of Cannabis, Cannabinoids, and Endocannabinoids in the Lungs
 - <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5023687/>
 - Cannabinoids and Inflammations of the Gut-Lung-Skin Barrier
 - <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8227007/>
 - Inhaled marijuana smoke disrupts mitochondrial energetics in pulmonary epithelial cells in vivo
 - <https://journals.physiology.org/doi/full/10.1152/ajplung.00371.2005>

- The potential of cannabinoids and inhibitors of endocannabinoid degradation in respiratory diseases
 - <https://www.sciencedirect.com/science/article/pii/S0014299921007160>
- Cannabis compounds exhibit anti-inflammatory activity in vitro in COVID-19-related inflammation in lung epithelial cells and pro-inflammatory activity in macrophages
 - <https://www.nature.com/articles/s41598-021-81049-2>
- Differential inflammatory profile in the lungs of mice exposed to cannabis smoke with varying THC:CBD ratio
 - <https://link.springer.com/article/10.1007/s00204-023-03514-3>
- Not all vaping is the same: differential pulmonary effects of vaping cannabidiol versus nicotine
 - <https://thorax.bmj.com/content/early/2023/05/16/thorax-2022-218743>
- Effects of Marijuana Smoking on the Lung
 - <https://www.atsjournals.org/doi/full/10.1513/annalsats.201212-127fr>
- Cannabidiol inhibits SARS-CoV-2 replication through induction of the host ER stress and innate immune responses
 - <https://www.science.org/doi/10.1126/sciadv.abi6110>
- In search of preventive strategies: novel high-CBD Cannabis sativa extracts modulate ACE2 expression in COVID-19 gateway tissues
 - <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7746344/>
- Modulation of pulmonary immune function by inhaled cannabis products and consequences for lung disease
 - <https://respiratory-research.biomedcentral.com/articles/10.1186/s12931-023-02399-1>
- Involvement of the ACE2/Ang-(1–7)/MasR Axis in Pulmonary Fibrosis: Implications for COVID-19
 - <https://www.mdpi.com/1422-0067/22/23/12955>
- New AKT-dependent mechanisms of anti-COVID-19 action of high-CBD Cannabis sativa extracts
 - <https://www.nature.com/articles/s41420-022-00876-y>
- ACE2 Expression in Organotypic Human Airway Epithelial Cultures and Airway Biopsies
 - <https://www.frontiersin.org/articles/10.3389/fphar.2022.813087/full>
- Cannabinoids Block Cellular Entry of SARS-CoV-2 and the Emerging Variants
 - <https://pubs.acs.org/doi/10.1021/acs.inatprod.1c00946>