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Development of Cannabidiol as a Drug

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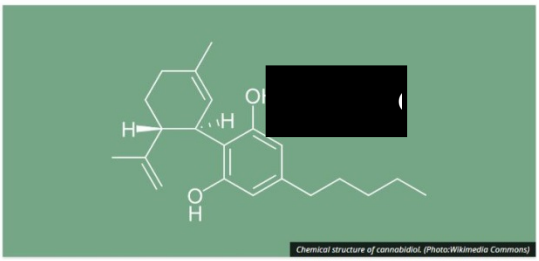
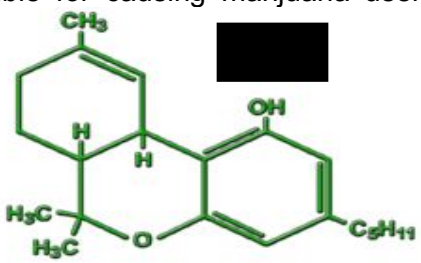
Introduction :

Cannabis also known as marijuana is a preparation of cannabis plant for its use as a drug or medicine. Cannabis contains many compounds. THC , CBD constitute majority of them. CBD (Cannabidiol) is extracted and separated from varieties of cannabis. CBD is one of 85 chemical substances known as cannabinoids, which are all found in the cannabis plant. CBD is the second most abundant compound, typically representing up to 40% of its extracts.The most abundant constituent of cannabis is the cannabinoid known as THC, an intoxicating and illegal substance that is responsible for causing marijuana users to get



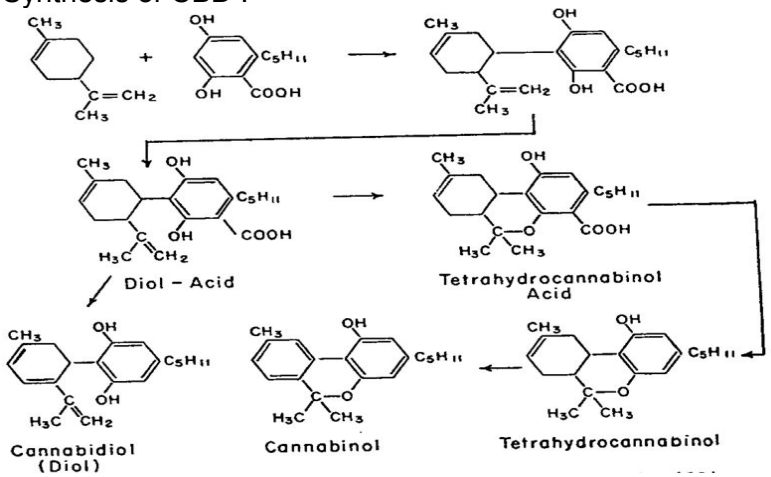


"high."

Unlike the main psychoactive cannabinoid in marijuana, CBD does not produce euphoria or intoxication. Cannabinoids have their effect mainly by interacting with specific receptors on cells in the brain and body: the CB1 receptor, found on neurons and glial cells in various parts of the brain, and the CB2 receptor, found mainly in the body's immune system. The euphoric effects of THC are caused by its activation of CB1 receptors. CBD has a very low affinity for these receptors (100 fold less than THC) and when it binds it produces little to no effect. There is also growing evidence that CBD acts on other brain signaling systems, and that these actions may be important contributors to its therapeutic effects[10].

Chemistry of CBD : Insoluble in water. Soluble in organic solvents. Colorless crystalline liquid at room temperature. In acidic condition it cyclizes to THC and under basic condition in presence of air it gets oxidized to Quinone.

Synthesis of CBD :



1) CBD has a wide range of medicinal benefits

Medicinal properties of CBD	Effects
Anti-cancer	Combats tumor cells
Anti-inflammatory	Combats inflammatory disorder
Anti-oxidant	Combats neurodegenerative disorders
Anti-depressant	Combats anxiety
Antiemetic	Reduces nausea and vomiting
Anticonvulsant	Suppresses seizure activity
Antipsychotic	Combats psychosis disorders

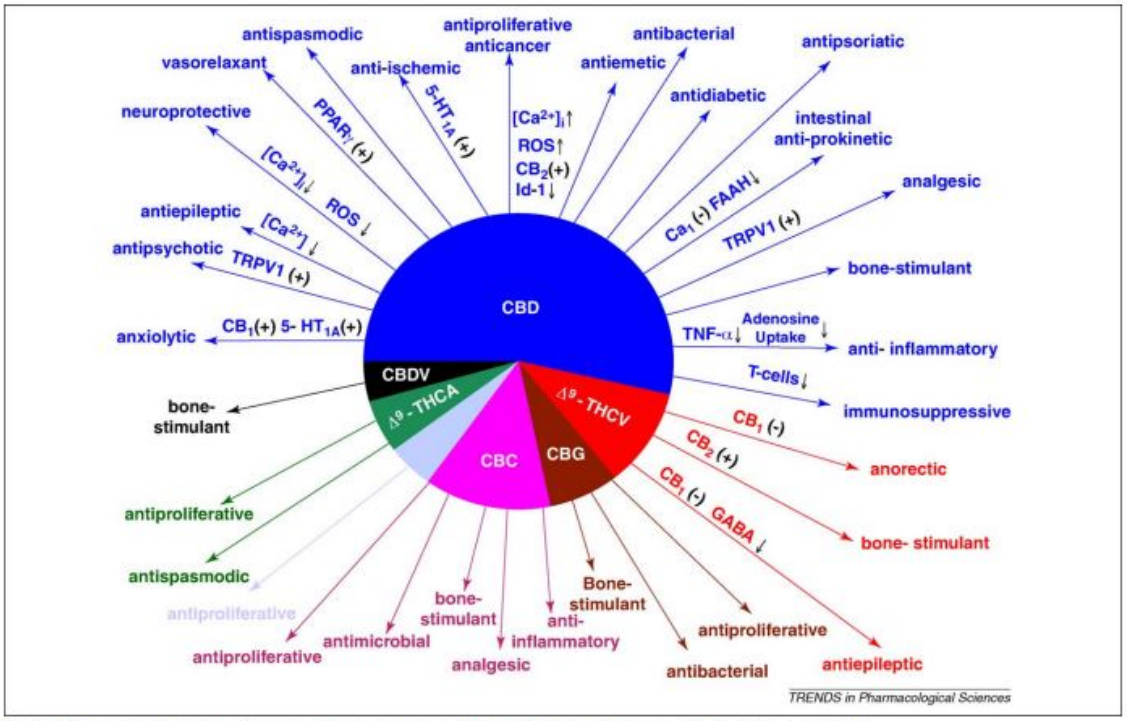


Figure 1. Pharmacological actions of non-psychotropic cannabinoids (with the indication of the proposed mechanisms of action).
Abbreviations: Δ^9-THC, Δ^9-tetrahydrocannabinol; Δ^8-THC, Δ^8-tetrahydrocannabinol; CBN, cannabinol; CBD, cannabidiol; Δ^9-THCV, Δ^9-tetrahydrocannabivarin; CBC, cannabichromene; CBG, cannabigerol; Δ^9-THCA, Δ^9-tetrahydrocannabinolic acid; CBDA, cannabidiolic acid; TRPV1, transient receptor potential vanilloid type 1; PPARγ, peroxisome proliferator-activated receptor γ; ROS, reactive oxygen species; 5-HT$_{1A}$, 5-hydroxytryptamine receptor subtype 1A; FAAH, fatty acid amide hydrolase. (+), direct or indirect activation; ↑, increase; ↓, decrease.

Pharmacology of CBD :

There are two types of cannabinoid receptors CB1 and CB2. CB1 receptors are expressed in the central nervous system whereas CB2 receptors are expressed mainly in the immune system.

CBD has low binding affinity to these receptors. THC binds well with these receptors. But when CBD binds to these receptors we can say that it inhibits the action of THC which is psychotic and thereby reduces the effects of THC.

CBD is non-psychoactive because it does not act on the same pathways as THC. These pathways, called CB1 receptors, are highly concentrated in the brain and are responsible for the mind-altering effects of THC. So we can say CBD has two receptors. When CBD binds to CB1 receptor and CB1 is a neuron terminal located receptor. CB1 is inhibitory to transmitter release at neuron terminal from this we can explain the analgesic effects, high food intake response,etc. When CBD binds to CB2 receptor it activates downstream regulation that helps in cytokine release and we know that *cytokines* are cell signalling molecules that aid cell to cell communication in immune responses and stimulate the movement of cells towards sites of inflammation, infection and trauma. So from this we can explain that CBD regulates inflammatory response. But both these receptors are GPCR's and so they have cross-talks with non-CB receptors and so we cannot find the sole action of CBD.

CBD has antitumor properties in lung cells. CBD binds and overexpresses intercellular adhesion molecule-1 (ICAM-1) a sticky protein which increases the adhesive nature of lung cancer cells thereby decreasing its invasiveness and their ability to spread. But we don't know the exact mechanism of how CBD promote cancer cell death. So they took a standard of lung cancer cell lines and cells from lung cancer patient and looked at how CBD induced ICAM-1 affects the adhesion of cancer cells to lymphokine activated killer (LAK) cells. From this we can say that CBD enhanced the susceptibility of these tumor cells to stick to LAK cells, thereby promoting their lysis[17,2].

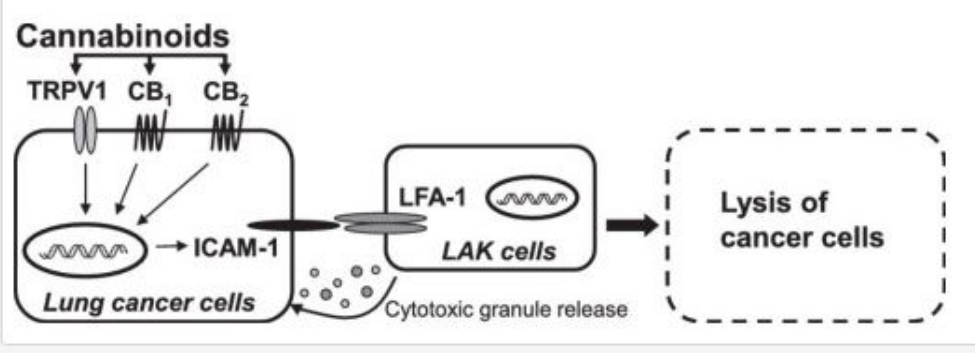


fig [2]

CBD

Pros	Cons
Can counter psychoactivity of THC	Not all pathways are known
Has neuroprotective & neurogenic effects	Illegal status hampers research
No human fatality because of overdose reported	GW pharma said CBD has better effect with THC but THC is psychoactive element

Available drugs in market : Sativex- mixture of THC and CBD (for muscle spasms and stiffness). Marinol and cesamet – approved for treatment of nausea in patients undergoing chemotherapy.

Future of CBD as a drug : CBD can have many more health benefits than any single drug that is prescribed today. It can be brought to use in many critical medical conditions like cancer, diabetes,etc. From this we can say that a lot of research will be required and clinical trials to bring this drug into effect.

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