IJBPAS, June, 2022, 11(6): 2609-2618

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

A BRIEF REVIEW ON CANNABIDIOL (CBD)

DAS M[1], BHATTACHARJEE M[1*], SARMA M[1], PAUL DC[1], SAIKIA D[1] AND SAIKIA AP[2]

1: Department of Biotechnology, Assam downtown University, Sankar Madhav Path, Gandhi Nagar Pin-781068, Guwahati Assam

2: Department of Computer Science, Assam downtown University, Sankar Madhav Path, Gandhi Nagar Pin-781068, Guwahati Assam

[*]**Corresponding Author: Dr. Minakshi Bhattacharjee:minakshibhattacharjee2007@gmail.com**

Received 18th June 2021; Revised 19th Aug. 2021; Accepted 18th Aug. 2021; Available online 1st June 2022

https://doi.org/10.31032/IJBPAS/2022/11.6.6046

ABSTRACT

The present review focuses on cannabidiol (CBD) which is a cannabinoid derived from cannabis. Cannabidiol is non-toxic in comparison to delta-9-tetrahydrocannabinol (THC). Cannabidiol is non-psychoactive in comparison to THC. It is found in both the species of the cannabis plant, *Cannabis sativa*, and *Cannabis indica* but cannabidiol percentage is higher in *Cannabis sativa.* The cannabidiol content in *Cannabis sp* can be determined by spectrophotometric assays and Liquid chromatography -Tandem Mass spectrometry (LC-MS). The general pharmacology is discussed, how the cannabidiol binds to the CB1 and CB2 receptors of the central nervous system. The antioxidant activity of cannabidiol and its implementation to prevent disease associated with redox imbalance and inflammation. Here, we have discussed how cannabidiol is related to lung cancer, breast cancer, arthritis. Nowadays CBD combined marketed authorized products are also discussed here like ARVISOL, Boheco Hemp seed oil.

Keywords: Cannabidiol, North East India, Medicinal Property

INTRODUCTION

Cannabidiol (CBD) is a chemical compound derived from the cannabis plant that belongs to the cannabinaceae family of plant species. Isolation of first natural cannabinoid as CBN to be obtained in pure form by Wood and colleagues in Cambridge in 1896 **[1]**. Cannabis is in use for the last thousands of years for fiber, nutritional seed oil, and medicinal use. In India, Uttara-khand state government has permitted cultivation of hemp crop, a rich source of high-quality fiber, and a host of medicinal use. Cannabidiol has had gained a major interest of study over the past few years ago. Abundant literature is available since 2008 over various search engines. Cannabidiol is the phytocannabinoids of the cannabis plant; it is one of the major cannabinoids of cannabis out of 113 identified cannabinoids. With the correct structure of Cannabidiol as CBD later was discovered early in the year 1940 **[1]**. CBD accounts for up to 40% of plant extracts. CBD devoid of psychoactive activity rather than tetrahydrocannabinol besides, CBD has analgesic, anti-inflammatory, antineoplastic and chemo-preventive activities. CBD can modulate endoplasmic reticulum stress, AKT/Motor signaling, thereby activating autophagy and promoting apoptosis. CBD inhibits cancer cell invasiveness and metastasis. CBD has broad therapeutic properties across a range of neuro-psychiatric disorders, stemming from diverse central nervous system actions **[2]**.

Studies have shown tetrahydrocannabinol (THC) is the main factor responsible for the effect of cannabis, but several reports have demonstrated that other cannabinoids including CBD have pharmacological activity **[3]**. The antagonism of the effect of THC when both CBD and THC are administered simultaneously to animals and humans. They concluded that although CBN increased the effect of THC in certain psychophysiology but these modulations were not significant enough. In neurological aspects, CBD is a cannabinoid 1 receptor (CB1) negative allosteric modulator, is a partial agonist of dopamine D2 high receptor sub-type and it increases anandamide (AEA) signaling, possibly through inhibition of the AEA catabolic enzyme, fatty acid amide hydrolase (FAAH) **[4]**.

Chemistry

As per "Cannabidiol (CBD) Critical Review Report (2018)", the **IUPAC Name of cannabidiol is** 2-[(6R)-3-methyl-6-prop-1-en-2-ylcyclohex-2-en-1- yl]-5-pentylbenzene-1,3-diol.

Chemical structure-

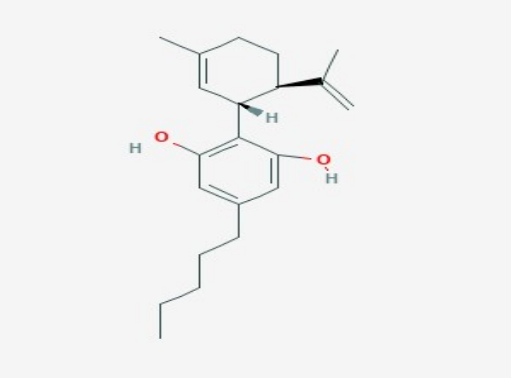

Figure 1: Chemical structure of cannabidiol (Adams *et al.* 1940)

Molecular formulae- C21H30O2

Molecular weight-314.469 g/mol

Melting point: 62-63 °C

Solubility: approx. 23.6 mg/mL in DSMO and ethanol

Identification and analysis

Cannabidiol is produced by both the species of *Cannabis sativa* and *Cannabis indica*, but literature reveals that, it can be found more in that *Cannabis sativa* than C*annabis indica* which has more psychoactive effect and a high percentage of tetrahydrocannabinol (THC).

Cannabis sativa: It is a herbaceous flowering plant found in eastern Asia. Flowers of the plant are unisexual (male/female) and arranged in racemes and produce hundreds of seeds. The major psychoactive ingredient is THC and known to produce 113 cannabinoids.

Cannabis indica: Found in Indian subcontinents. Tetrahydrocannabinol (THC) percentage is high both narrow-leaflet and wide-leaflet drugs are found under this taxonomy.

Analytical detection of CBD includes the following methods:

a) Spectrophotometric determination (plant sample)

Cannabidiol needs alkaline medium to react with 2, 4-dinitrophenol. The absorbance peak is at 500 nm. The detectable titer is 0.1 ug/10ml **[5]**.

b) Liquid Chromatography-

Tandem Mass Spectrometry (detection of cannabidiol in a whole blood sample)

c) The process of CBD extraction from blood sample. In the 1st phase, protein precipitation is done with acetonitrile followed by gradient elution for 16 min, and high-performance liquid chromatography. Electrospray ionization is utilized for CBD detection **[6]**.

General Pharmacology

Routes of administration: Currently, there is a lot of approved marketed cannabidiol (CBD) infused products namely:

• Health Horizon Ayurvedic Sativa Hemp Oil- Promotes cardiovascular health as it reduces the cholesterol rates can be used for an edible purpose, works on managing the hormonal balance of the body, facilitates hydration to the skin and provides

nourishment to hair and nails, helps to fortify the immune system.

• CBD is generally administered orally as a capsule, or dissolved in an oil solution (eg olive or sesame oil). A wide range of oral dosages has been reported in the literature, with most from 100-800 mg/day **[7]**.

Pharmacokinetics: Cannabidiol (CBD) induced a non-significant reduction of food intake, and it exerted beneficial effects on bone formation and fracture healing. Cannabidiol (CBD), when given to children ages 4-10 with a dose of 5, 10 and 20 mg/kg/d with Dravet syndrome produced dose-proportional increases in plasma concentrations of CBD. Aerosolised CBD accounts for greater bioavailability than oral route of administration **[8]**.

Cannabidiol (CBD) gets rapidly distributed in the tissue with a high rate of disruption. Cannabidiol is metabolized in the liver and its primary route is hydroxylation which is facilitated by the enzyme hydroxylases and further resulting in several metabolites that are excreted in feces and urine **[9]**.

Pharmacodynamics: The biological and psychological effects of cannabidiol on humans is further discussed as there are two main cannabinoid receptors CB1 located in the central nervous system, CB2 found in the periphery on cells along with immune function in the gastrointestinal tract and experimented on humans and animals, cannabidiol had shown very different effects from those of THC. In mice models, CBD did not suppress locomotor activity, hypothermia due to CB1 activation. THC produced all of the effects which occur when CB1 is activated. In comparison to THC, CBD has no effect on heart rate or blood pressure remains controlled, but in animal models of stress, it reduces heart rate and blood pressure **[10-11]**.

CBD may also interact with the endocannabinoid system through an indirect mechanism such as enhanced action of the endogenous cannabinoid ligand anandamide. This results from blockage of anandamide reuptake and the inhibition of its enzymatic degradation.CBD has been shown to modulate several non-endocannabinoid signaling systems **[12]**. Some of these mechanisms include:

• Inhibition of adenosine uptake, possibly resulting in indirect agonist activity at adenosine receptors.

• Enhanced activity at the 5-HT1a receptor.

• Enhanced activity at glycine receptor subtypes.

• Blockade of the orphan G-protein-coupled receptor GPR55.

Biological activity

i) Antioxidant property:

The antioxidant and anti-inflammatory properties of cannabidiol has been found. **[13]** have mentioned in their study that cannabidiol reduces oxidative conditions by preventing the formation of super-oxide radicals,which are mainly generated by xanthine oxidase and NADPH oxidase. Cannabidiol also reduces reactive oxygen species (ROS) production by chelating transition metal ions involved in the Fenton reaction to form extremely hydroxyl radicals **[23-24]**.

ii) Anticancer property:

CBD invade cancer cells by increasing tissue inhibitor of matrix metalloproteinase-1(TIMP-1). Cannabidiol is one of the non-psychoactive constituents of cannabis and it is considered as an antineoplastic agent based on its in vivo and in vitro activity against tumor cells **[14]**. Although by the use of CBD it is effective against the tumor, but the molecular mechanism of its action is not yet fully characterized **[15]**. Cannabidiol (CBD) is likely one of the phytocannabinoid present in cannabis which is lacking the psychoactive effect that makes it a therapeutic agent. It has been reported that CBD can exert an effect on metastasis and tumor angiogenesis **[16]**.

CBD of *Cannabis sativa* plant has a possible effect in breast cancer cell line and primarily effects on key neoplastic pathways. CBD binds to specific G-protein Coupled Receptor; downregulates ID1, a regulator of metastasis in breast cancer cell lines. Some review data regarding cannabidiol and its effects on breast cancer state that, alertness of breast tumor cells to anti-tumor agents depends on in part of estrogen receptor status. CBD induces both apoptosis and autophagy in breast cancer cells.CBD induces cell death via a mitochondria-mediated signaling pathway. Mitochondrion plays a central role in apoptotic cell death **[17]**.

iii) Antiarthritic property: Arthritis as one of the major problems causing inflammation of one or multiple joints in the human body. Over 100 different types of arthritis are known; these mostly common are Rheumatoid Arthritis (RA), and Oslo Arthritis **[18]**. Cannabis-based medicine (CBM) is a treatment of pain caused by rheumatoid arthritis. An experiment was conducted and using Sativex (CBM) over a group of 58 patients suffering from RA **[19]**. Sativex is a blend of whole plant-based extracts that delivers an approximately equal amount of THC and CBD. Minor cannabinoids including

cannabidiol, cannabichromene, and cannabigerol are also present and these three compounds have been found to have anti-inflammatory properties found in lab **[20]**.

iv) Antiepileptic property: In a study, the clinical use of CBD is most advanced in the treatment of epilepsy. In clinical trials, CBD has been demonstrated as an effective treatment for at least some forms of epilepsy, with one pure CBD product (Epidiolex) currently available.

15 patients with "secondarily generalized epilepsy with temporal focus" In response to CBD, 50% showed no seizures whereas others showed partial clinical improvement. In the placebo group, there was no change **[21]**.

A similar study recently on the safety and efficacy of CBD in patients with Lennox-Gastaut syndrome, a severe form of epileptic encephalopathy that produces various types of seizures (including drop seizures) that are often treatment-resistant. They found that treatment with CBD lowered drop seizures by median of 44% approximately **[22]**.

Cannabidiol combined products (marketing authorization)

Currently, there are a lot of authorized CBD products. However, there are some in development. Some authorized CBD products are as follows:

• Arvisol® tablets contain pure CBD and still under Phase I clinical trials. It has been developed by Echo Pharmaceuticals in the Netherlands and is intended to be registered for the treatment of various neurological disorders,
including schizophrenia and epilepsy.

• BOHECO hemp seed oil is a light non-greasy oil that's fortified with the goodness of the hemp plant and is derived from (*Cannabis sativa L.)* seed. Some benefit of this product is that it is rich in vitamins and minerals, contains omega3 and omega6 fatty acids, boosts metabolism, increase energy level, improves memory and brain function.

• Bionorica® (Germany) has produced a purified powdered CBD product from hemp plants.

• Nextgen Ayurveda Hemp seeds are seeds of Cannabis sativa L. that helps in improving metabolism and digestion, good for joint pains and muscles, super-rich in protein, safe to have orally.

CONCLUSION

In this present review on cannabidiol, certain data have come forward to how cannabidiol can be used for medicinal use and the general pharmacology of cannabidiol. However, the negative health effects are more. It is a

banned (synthetic drug) in India. Further, studies by many researchers are under progress.

CONFLICT OF INTEREST: NONE

FINANCIAL DISCLOSURE: NONE

ACKNOWLEDGEMENT: The authors acknowledge the infrastructure support received from the Assam down town University.

REFERENCES

[1] Giovanni Appendino. The early history of cannabinoid research, 2020 Rendiconti Lincei. Scienze Fisiche e Naturali.

[2] Angelo A. Izzo, Francesca Borrelli, Raffaele Capasso, Vincenzo Di Marzo and Raphael Mechoulam. Non-psychotropic plant cannabinoids: new therapeutic opportunities from an ancient herb, 2009 Trends in Pharmacological Sciences; Vol.30 No.10.

[3] E. A. Carlini, M. Santos, U. Claussen, D. Bieniek, and F. Korte. Structure Activity Relationship of Four Tetrahydrocannabinols and the Pharmacological Activity of Five Semi-Purified Extracts of Cannabis sativa, 1970 Psychopharmacologia (Berl.) 18, 82-93.

[4] Isac G. Karniol, Itiro Shirakawa, Reinaldo N. Takahashi, Elias Knobel and Richard E. Musty. Effect of Delta 9 – Tetrahydrocannabinol and Cannabinol in Man, 1975 Pharmacology13: 502-512.

[5] Tehseen Aman, Abdul Rashid & Irshad Khokhar. Spectrophotometric Determination of Cannabidiol 1993; Analytical Letters, 26(10), 21 13-2125.

[6] David M. Schwope, Karl B. Scheidweiler & Marilyn A. Huestis. Direct quantification of cannabinoids and cannabinoid glucuronides in whole blood by liquid chromatography–tandem mass spectrometry 2011; Anal Bioanal Chem 401:1273–1283.

[7] Pius S. Fasinu, Sarah Phillips, Mahmoud A. ElSohly and Larry A. Walker. **Current Status and Prospects for Cannabidiol Preparations as New Therapeutic Agents 2016;** *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*.

[8] Serena Deiana, Akihito Watanabe, Yuki Yamasaki, Naoki Amada, Marlene Arthur, Shona Fleming, Hilary Woodcock, Patricia Dorward,

Barbara Pigliacampo, Steve Close, Bettina Platt & Gernot Riedel. Plasma and brain pharmacokinetic profile of cannabidiol (CBD), annabidivarine (CBDV), Δ9-tetrahydrocannabivarin (THCV) and cannabigerol (CBG) in rats and mice following oral and ntraperitoneal administration and CBD action on obsessive–compulsive behavior 2012; Psychopharmacology 219:859–873.

[9] Sharon Rodner, Sznitman, Borje Olsson and Robin Room. A cannabis reader: global issues and local experiences 2008; EMCDDA series 8, Volume 1.

[10] Leonora E. Long, Rose Chesworth, Xu-Feng Huang, Iain S. McGregor, Jonathon C. Arnold and Tim Karl. A behavioural comparison of acute and chronic *D*9-tetra-hydro-cannabinol and cannabidiol in C57BL/6JArc mice 2010; International Journal of Neuro-psychopharmacology 13, 861–876.

[11] Salahaden R. Sultan, Sophie A. Millar, Timothy J. England and Saoirse E. O'Sullivan. A Systematic Review and Meta-Analysis of the Haemodynamic Effects of Cannabidi 2017; Frontiers in Pharmacology: Volume 8 | Article 81.

[12] Tiziana Bisogno, LumõÂr HanusÆ, Luciano De Petrocellis, Susanna Tchilibon, Datta E. Ponde, Ines Brandi, Aniello Schiano Moriello, John B. Davis, Raphael Mechoulam & Vincenzo Di Marzo. Molecular targets for cannabidiol and its synthetic analogues: efect on vanilloid VR1 receptors and on the cellular uptake and enzymatic hydrolysis of anandamide 2001; British Journal of Pharmacology: 134, 845 ± 852.

[13] Sinemyiz Atalay, Iwona Jarocka-Karpowicz and Elzbieta Skrzydlewska. Antioxidative and Anti-Inflammatory Properties of Cannabidiol2020; *Antioxidants: 9*, 21.

[14] SGB Neto, VI Moura and A Solange. Increasing the anti- cancer effect of CBD through PE supplementation to the cancer cell 2021; preprint.

[15] Vaccani A, Massi P, Colombo A and Rubino T, Parolaro D. Cannabid iol inhibits human glioma cell migration through a cannabinoid receptor-

independent mechanism 2005; Br J Pharmacol 144:1032–6.

[16] Robert Ramer, Jutta Merkord, Helga Rohde and Burkhard Hinz. Cannabidiol inhibits cancer cell invasion via upregulation of tissue inhibitor of matrix metalloproteinases 2010; Biochemical Pharmacology. 79: 955–966.

[17] Ashutosh Shrivastava, Paula M. Kuzontkoski, Jerome E. Groopman, and Anil Prasad. Cannabidiol Induces Programmed Cell Death in Breast Cancer Cells by Coordinating the Cross-talk between Apoptosis and Autophagy 2011; Therapeutic Discovery.

[18] Sumner Burstein. Cannabidiol (CBD) and its analogs: a review of their effects on inflammation 2015; *Bioorganic & Medicinal Chemistry:* S0968-0896(15)00083-8.

[19] D. R. Blake, P. Robson, M. Ho2, R. W. Jubb and C. S. McCabe. Preliminary assessment of the efficacy, tolerability and safety of a cannabis-based medicine (Sativex) in the treatment of pain caused by rheumatoid arthritis 2006; Rheumatology: 45: 50–52.

[20] Mark A. Lewis, Ethan B. Russo and Kevin M. Smith. Pharmacological Foundations of Cannabis Chemovars 2017; Thieme.

[21] Jomar M. Cunha, E. A. Carlini, Aparecido E. Pereira, Oswaldo L. Ramos, Camilo Pimentel, Rubens Gagliardi, W. L. Sanvito, N. Lander and R. Mechoulam.Chronic Administration of Cannabidiol to Healty Volunteers and Epileptic Patient 1980; Pharmacology 21:175-185.

[22] Elizabeth A Thiele, Eric D Marsh, Jacqueline A French, Maria Mazurkiewicz-Beldzinska, Selim R Benbadis, Charuta Joshi, Paul D Lyons, Adam Taylor, Claire Roberts, Kenneth Sommerville, on behalf of the GWPCARE4 Study Group. Cannabidiol in patients with seizures associated with Lennox-Gastaut syndrome (GWPCARE4): a randomised, double-blind, placebo-controlled phase 3 trial 2018; Thelancet.

[23] Sinemyiz Atalay, Iwona Jarocka-Karpowicz and Elzbieta Skrzydlewska. Antioxidative and Anti-Inflammatory Properties of

Cannabidiol 2020; *Antioxidants: 9*, 21.

[24] Hao Pan, Partha Mukhopadhyay, Mohanraj Rajesh, Vivek Patel, Bani Mukhopadhyay, Bin Gao, Gyo¨ rgy Hasko´ , and Pa´ l Pacher. Cannabidiol Attenuates Cisplatin-Induced Nephrotoxicity by Decreasing Oxidative/Nitrosative Stress, Inflammation, and Cell Death 2009; The Journal Of Pharmacology And Experimental Therapeutics: 328,708–714.