Medical Aspects of Cannabinoids

Gustavo Olaiz, Miguel Luján and Omar F Carrasco*

Politics, Population and Health Research Center, Mexico

Corresponding author: Omar F Carrasco, Politics, Population and Health Research Center, School of Medicine, Mexico

Introduction

Pain, seizures, anxiety and nausea, are some of the most common conditions treated in primary care settings worldwide. The current pharmacological options for these disorders include nowadays cannabinoids. Cannabis has an ancient history in ethnobotanical usage in Mesopotamia, India, China, Arabic and Islamic medicine for the treatment of distinct pathological entities [1-3]. Despite several types of cannabinoid medicines are available in some European countries as England or Germany and in American ones as Brazil, Canada, the United States and Uruguay, the medical use of cannabinoids needs scientific evidence, regulatory policies and social acknowledgement.

Scientific Evidence

Pharmacologic profile

The plant contains at least 750 chemicals and some 104 different cannabinoids. The principal cannabinoids in the cannabis plant include Tetrahydrocannabinol (THC), Cannabidiol (CBD), Cannabinol (CBN), Cannabigerol (CBG) and Cannabidivarin (CBDV). The action of the cannabinoids was determined with the discovery of the cannabinoid CB_1 and CB_2 receptors. The CB_1 receptors are found in high densities in the neuron terminals of the basal ganglia (affecting motor activity), cerebellum (motor coordination), hippocampus (short-term memory), neocortex (thinking), and hypothalamus and limbic cortex (appetite and sedation). To a lesser extent, the CB_1 receptors are found in periaqueductal gray dorsal horn (pain) and immune cells. CB_2 receptors are primarily found on immune cells and tissues and, when activated, can affect inflammatory and immunosuppressive activity [4,5].

The pharmacokinetic characteristics of cannabinoids (absorption, distribution, metabolism and elimination) have been primarily evaluated in clinical pharmacology studies. Cannabinoid's pharmacokinetic profile is unique for each cannabinoid, for example the elimination half-life of THC is highly variable with a mean of 30 hours and CBD has an elimination half-life of 9 hours [6,7]. Smoking cannabis turns approximately 50% of the THC content into smoke, with the remainder lost by heat or from smoke that is not inhaled. Up to 50% of inhaled smoke is exhaled again, and some of the remaining smoke undergoes localized metabolism in the lung [8]. Orally administered THC has a bioavailability ranging from 5-20% in the controlled environments of clinical studies but is often lower in users because of variations in gastric degradation (with the presence of acids) and extensive first-pass effects [9]. The bioavailability of oral CBD is also variable, reported to be 13-19% [10].

Clinical evidence pain

The analgesic effects of cannabis may be due to several different mechanisms including, modulation of rostral ventromedial medulla neuronal activity, antinociceptive effects in descending pain pathways, and anti-inflammatory properties by acting through prostaglandin synthesis inhibition. Different types of pain have been relieved with cannabinoids: neuropathic, chronic, postoperative, and that related to fibromyalgia, rheumatoid arthritis, multiple sclerosis, and cancer [11].

Clinical evidence muscle spasms

Spasticity is commonly associated with painful spasms and sleep disturbance and contributes to increased morbidity. A combination of two cannabinoids (THC: CBD) has been studied for the treatment of spasticity in patients with multiple sclerosis and has been shown to be effective as monotherapy and as add-on therapy for patients not fully relieved with other ant spasticity therapy [12].

Clinical evidence epilepsy

Tetrahydrocannabinol and cannabidiol have been shown to be effective and have similar potency in the maximal electroshock model of epilepsy [13], the action of THC was mediated via the CB_1 receptor. The mechanism of action of CBD was different than that of THC and is mediated via mechanism(s) different than the endocannabinoid system [14].

Clinical evidence anxiety

Anxiety is a pathology affecting in many aspects of life, including social life, productivity and health. CBD possesses an anxiolytic-like effect, because of the results of tests as the forced swimming test (FST), elevated plus maze (EPM) and Vogel conflict test (VCT) [15].

Clinical evidence nausea and vomiting

Cannabis-based medicines have been found to be effective anti-emetics and even exceed some modern treatments in their potential to alleviate nausea [16].

Regulatory Policies

Legislation around the World is inconsistent on the use, cultivation and possession of cannabis. The United Nations conventions on drugs authorize the use of psychotropic drugs only for medical or scientific purposes, but also considers "detention for personal use" as a crime. In Europe, Cannabis is illegal in France, Italy, Poland, Bulgaria, Cyprus, Denmark, Croatia, Finland, Great Britain, Luxembourg, Malta, Romania, Sweden, Austria, Latvia, Slovakia, Slovenia, Lithuania, Belgium, Hungary. It is legal in the Netherlands. It is decriminalized in: Germany, Portugal, United Kingdom, Czech Republic, Spain, Estonia [17]. In America is legal in Uruguay and it is decriminalized in: Canada, The United States, Mexico, Colombia and Brazil for medical purposes and research.

Social Acknowledgement

According to World Health Organization (WHO), Cannabis is the most commonly used illicit drug globally. The risk of developing dependence among those who have ever used cannabis was estimated at 9% in the USA in the early 1990s [18] compared to 32% for nicotine, 23% for heroin, 17% for cocaine, 15% for alcohol and 11% for stimulants [19]. A minority of first-time cannabis users become very anxious, have panic attacks, experience hallucinations and vomit. The daily use of cannabis over years and decades appears to produce persistent impairments in memory and cognition, especially when cannabis use begins in adolescence [20].

Future Directions

The use of Cannabinoids appears to improve the clinical course in patients with certain conditions such as pain and epilepsy. The World regulatory policies must recognize the health risks and benefits related to the therapeutics involving cannabinoids. The social recognition of cannabis-based treatments as complementary & alternative medicine must be reinforced by education and research.

References

1. Wilson JV, Reynolds EH (1990) Texts and documents. Translation and analysis of a cuneiform text forming part of a Babylonian treatise on epilepsy. Med Hist 34 (2): 185-198.

2. Jiang HE, Li X, Zhao YX, Ferguson DK, Hueber F, et al. (2006) A new insight into Cannabis sativa (Cannabaceae) utilization from 2500-year-old Yanghai Tombs, Xinjiang, China. J Ethnopharmacol 108(3): 414-422.

3. Lozano I (1998) Solaz del espíritu en el hachís y el vino y otros textos árabes sobre drogas. Universidad de Granada, Granada, Spain.

4. Pertwee RG (2006) Cannabinoid pharmacology: The first 66 years. Br J Pharmacol 147(suppl 1): S163-171.

5. Pertwee RG, Howlett AC, Abood ME, Alexander SP, Di Marzo V, et al. (2010) International union of basic and clinical pharmacology. LXXIX. Cannabinoid receptors and their ligands: beyond CB_1 and CB_2. Pharmacol Rev 62(4): 588-631.

6. Wall ME, Sadler BM, Brine D, Taylor H, Perez Reyes M (1983) Metabolism, disposition, and kinetics of delta-9-tetrahydrocannabinol in men and women. Clin Pharmacol Ther 34(3): 352-363.

7. Agurell S, Halldin M, Lindgren JE, Ohlsson A, Widman M, et al. (1986) Pharmacokinetics and metabolism of delta 1-tetrahydrocannabinol and other cannabinoids with emphasis on man. Pharmacol Rev 38(1): 21-43.

8. Marsot A, Audebert C, Attolini L, Lacarelle B, Micallef J, et al. (2017) Population pharmacokinetics model of THC used by pulmonary route in occasional cannabis smokers. J Pharmacol Toxicol Methods 85: 49-54.

9. Ohlsson A, Lindgren JE, Wahlen A, Agurell S, Hollister LE, et al. (1980) Plasma delta-9 tetrahydrocannabinol concentrations and clinical effects after oral and intravenous administration and smoking. Clin Pharmacol Ther 28(3): 409-416.

10. Mechoulam R, Parker LA, Gallily R (2002) Cannabidiol: An overview of some pharmacological aspects. J Clin Pharmacol 42(S1): 11S-19S.

11. Martin SE, Furukawa TA, Taylor J, Martin JL (2009) Systematic review and meta-analysis of cannabis treatment for chronic pain. Pain Med 10(8): 1353-1368.

12. Novotna A, Mares J, Ratcliffe S, Novakova I, Vachova M, et al. (2011) A randomized, double-blind, placebo-controlled, parallel-group, enriched-design study of nabiximols* (Sativex ®, as add-on therapy, in subjects with refractory spasticity caused by multiple sclerosis. Eur J Neurol 18(9): 1122-1131.

13. Karler R, Cely W, Turkanis SA (1974) Anticonvulsant properties of delta 9-tetrahydrocannabinol and other cannabinoids. Life Sci 15(5): 931-947.

14. Devinsky O, Cilio MR, Cross H, Fernandez RJ, French J, et al. (2014) Cannabidiol: Pharmacology and potential therapeutic role in epilepsy and other neuropsychiatric disorders. Epilepsia 55(6): 791-802.

15. de Mello SAR, de Oliveira RNP, Coutinho DS, Machado S, Arias CO, et al. (2014) Antidepressant like and anxiolytic-like effects of cannabidiol: Achemical compound of Cannabis sativa. CNS Neurol Disord Drug Targets 13(6): 953-960.

16. Cotter J (2009) Efficacy of crude marijuana and synthetic delta-9-Tetrahydrocannabinol as treatment for chemotherapy-induced nausea and vomiting: A systematic literature review. Oncol Nurs Forum 36(3): 345-352.

17. Zaami S, Di Luca A, Di Luca NM, Montanari VG (2018) Medical use of cannabis: Italian and European legislation. Eur Rev Med Pharmacol Sci 22(4): 1161-1167.

18. Anthony J, Warner L, Kessler R (1994) Comparative epidemiology of dependence on tobacco, alcohol, controlled substances and inhalants: Basic findings from the National Comorbidity Survey. Exp and Clin Psychopharm 2(3): 244-268.

19. Anthony JC (2006) The epidemiology of cannabis dependence. In: Roffman RA, Stephens RS (Eds.), Cannabis dependence: its nature, consequences and treatment. Cambridge University, Cambridge, UK, pp. 58-105.

20. Meier MH, Caspi A, Ambler A, Harrington H, Houts R, et al. (2012) Persistent cannabis users show neuropsychological decline from childhood to midlife. Proc Natl Acad Sci U S A, 109(40): E2657-E2664.

275

For possible submissions Click Here   Submit Article
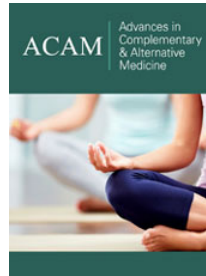
Advances in Complementary & Alternative Medicine

Benefits of Publishing with us

- High-level peer review and editorial services
- Freely accessible online immediately upon publication
- Authors retain the copyright to their work
- Licensing it under a Creative Commons license
- Visibility through different online platforms

276