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Perspective

PHARMACOLOGY OF MEDICINAL CANNABIS

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PERSPECTIVE

Medicinal cannabis, sometimes known as medicinal marijuana, is a treatment that has received a lot of press in recent years. Some of the challenges connected with this treatment include legal, ethical, and sociological implications of use; safe administration, packaging, and dispensing; adverse health consequences including deaths attributable to marijuana intoxication; and therapeutic indications based on inadequate clinical research. Marijuana is currently classified as a Schedule I controlled substance under the United States Drug Enforcement Administration's (DEA) Comprehensive Drug Abuse Prevention and Control Act (Controlled Substances Act) of 1970, which means it has a high potential for abuse, no currently accepted medicinal use in treatment in the United States, and a lack of accepted safety data for use of the treatment under medical supervision (Amin & Ali, 2019).

Pharmacology

The neurological system, internal organs, connective tissues, glands, and immunological cells all contain endocannabinoids (eCBs) and their receptors. The eCB system plays a homeostatic role, as it "eats, sleeps, relaxes, forgets, and protects." 26 eCBs are recognised to play a part in the pathophysiology of many ailments, as well as acting as a protective factor in several medical conditions (Brown et al., 2019). Migraine, fibromyalgia, irritable bowel syndrome, and other illnesses have been suggested to be clinical eCB deficient disorders (CEDS). Deficiencies in eCB signalling may also play a role in the development of depression. Defects in the eCB system have been linked to schizophrenia, MS, Huntington's disease, Parkinson's disease, anorexia, persistent motion sickness, and neonatal failure to thrive in human research (Ebbert et al., 2018).

The eCB system is a microcosm of psychoneuroimmunology, also known as "mind–body" medicine. Receptors, endogenous ligands, and ligand metabolic enzymes make up the eCB system. When cannabinoid receptors are triggered, a range of physiological activities occur. The most common G-protein–coupled receptor is cannabinoid receptor type 1 (CB1). The substantia

nigra, globus pallidus, hippocampus, cerebral cortex, putamen, caudate, cerebellum, and amygdala are all densely expressed in the central nervous system, with the substantia nigra, globus pallidus, hippocampus, cerebral cortex, putamen, caudate, cerebellum, and amygdala being the most densely expressed. Non-neuronal cells, such as adipocytes and hepatocytes, connective and musculoskeletal tissues, and the gonads, all express CB1. CB2 is mostly found in cells that regulate immunological activity, but it can also be found in the central nervous system.

N-arachidonyl-ethanolamide (anandamide or AEA) and sn-2-arachidonoyl-glycerol are the most well-known eCB ligands (2-AG). On demand, AEA and 2-AG are released from phospholipid precursors in the cell membrane. The discovery of secondary receptors, ligands, and ligand metabolic enzymes has enlarged the "traditional" eCB system. AEA, 2-AG, N-arachidonoyl glycine (NAGly), and the phytocannabinoids 9-THC and CBD, for example, may act as ligands for GPR55, GPR18, GPR119, and numerous transient receptor potential ion channels (e.g., TRPV1, TRPV2, TRPA1, TRPM8) with activities similar to capsaicin to varying degrees. 28 "Entourage chemicals" can improve the effects of AEA and 2-AG by inhibiting their hydrolysis via substrate competition and therefore prolonging their activity through synergy and augmentation. N-palmitylethanolamide (PEA), N-oleoylethanolamide (SEA), and cis-9-octadecenoamide (OEA or oleamide) are examples of entourage chemicals and may represent a novel route for molecular regulation of endogenous cannabinoid activity (Gertsch, 2018)

The majority of what we know about the negative effects of therapeutic cannabis comes from research on recreational marijuana users. Short-term cannabis usage has been linked to impairments in short-term memory, motor coordination, judgement, and paranoia or psychosis in large dosages. Addiction, altered brain development, cognitive impairment, poor educational outcomes (e.g., dropping out of school), and lower life satisfaction have all been linked to long-term or excessive cannabis use, particularly in teens. In people who are predisposed to such problems, long-term or excessive cannabis usage is linked to chronic bronchitis and an increased risk of chronic psychosis-related health conditions, such as schizophrenia and depressive variations. Myocardial infarction, stroke, and transient ischemic attack are among vascular disorders that have been studied. The use of cannabis for management of symptoms in neurodegenerative diseases, such as Parkinson's, Alzheimer's, and MS, has provided data related to impaired cognition in these individuals (Zinboonyahgoon et al., 2021).

Although cannabis and cannabinoid medicines are commonly used to relieve symptoms and cure disease, their usefulness for specific indications is unknown. The analgesic efficacy in chronic pain is unknown. Smoked cannabis, oromucosal extracts of cannabis-based medication, nabilone, dronabinol, and a new THC analogue were all studied in a systematic review of randomised controlled trials exploring cannabinoids in the treatment of chronic noncancer pain. Neuropathic pain, fibromyalgia, rheumatoid arthritis, and mixed chronic pain were among the pain syndromes studied. Cannabinoids were found to have a substantial analgesic effect in 15 of the 18 trials compared to placebo. The usage of cannabinoids was generally well tolerated, with the most

prevalent safe and modestly effective side effects being mild to moderate in severity. Overall, preliminary evidence suggests that cannabinoids are in the treatment of neuropathic pain.

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