three sections from each joint. The sections were stained with hematoxylin and eosin. All stages of micropreparation were performed in accordance with OARSI (Osteoarthritis Research Society International) recommendations. Microscopic examination was performed under a microscope Granum Trino R 6003 (DSM-310). Statistical processing of the obtained digital data was performed using the non-parametric criterion (Statistics 6, Mann-Whitney U Test, Fisher test).

Results and discussion. The introduction of Freund's adjuvant to rats leads to the development of morphological signs of arthritis of the ankle joints: proliferative synovitis; formation of pannus; destructive-dystrophic changes of cartilage tissue; inflammatory infiltration in periarticular tissues. The nonsteroidal anti-inflammatory drug diclofenac sodium has a pronounced normalizing effect on morphological changes in rat joints in adjuvant arthritis. Cartilage destruction is absent, hyperplasia of the covering tissues occurs six times less often than in untreated animals. Residual effects in periarticular tissues are noted. The use of thick extract of the tanacetum reduced the number of animals with destruction of articular cartilage by 2.6 times compared with control pathology and the number of animals with severe inflammation in the synovial membrane and periarticular tissues by 3 times.

Conclusions. The ability of tanacetum **(*Tanacetum parthenium* L.)** thick extract to reduce the severity of articular cartilage destruction, inflammation in the synovial membrane and periarticular tissues in rats with a model of adjuvant arthritis justifies the feasibility of creating a new anti-inflammatory phytomedicine.

THERAPEUTIC ACTIVITY OF *CANNABIS SATIVA*

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Introduction. Cannabis, first traced back to Central Asia, is one of the most traditional psychotropic medications to humans. Agreeing to archaeological revelations, it has been known in China at least since the Neolithic time frame, around 4,000 BC [1]. The most famous form of the cannabis plant is marijuana and hashish. Marijuana is a Mexican term at first ascribed to cheap tobacco but today referred to the dried leaves and flowers of the cannabis plant. Hashish, the Arabic name for Indian hemp, is the resin gum of the plant [2]. For hundreds of years, cannabis has been utilized as a source of fiber, food, oil and for religious, recreational, and therapeutic purposes [3]. It contains various mixtures of structurally active agents, for example, cannabinoids, terpenoids, flavonoids, and alkaloids [4]. The major psychoactive chemical of cannabis is delta-9-tetrahydrocannabinol (THC), commonly known as THC. Various other cannabinoids include delta-8-THC, cannabinol, cannabidiol (CBD), cannabicyclol, cannabichromene, and cannabigerol; however, they are

available in little amounts and have no significant psychotropic activity as compared with THC [1, 5]. Presently, cannabinoids are used for symptomatic treatment, but there is evidence that states that they can be used to slow down the progression of neurodegenerative diseases [6]. Further, Cannabinoids, especially CBD, retard breast cancer cell proliferation [7], while THC retarded glioblastoma multiforme growth in animal. Models and a pilot clinical study showed that it depresses tumor cell proliferation *in vitro* [8] and have evidence for other cancers like prostate, lung, and blood cancers. Other clinical conditions such as nausea, glaucoma, chronic pain, inflammation, multiple sclerosis, and epilepsy have shown relief or improvement from medical cannabis. Despite some contentious discussion on its medical use, unprescribed marijuana may lead to addiction. Its use during adolescence can affect mental development, and regular use could also lead to a high risk of anxiety and depression, especially in people with a genetic vulnerability [9].

Cannabis extracts contain several active compounds called cannabinoids. Among this, the most abundant ones are THC, its precursor CBD, and cannabinol. CBD lack psychoactive abilities but has other medical indications such as anticonvulsant effect and anticancer effects [10]. Cannabinoids are highly lipophilic compounds and were originally thought to simply diffuse through the cell membrane [11]. But in 1988, using saturable high-affinity binding of titrated cannabinoid in the homogenized brain of rat led to the discovery of cannabinoid receptors. They are now termed as CB receptors which were further classified into CB1 and CB2 [10]. CB1 was mainly identified in the central nervous system, while CB2 was subsequently identified in the peripheral tissue [12]. Since the abundance of CB1 was found to be in CNS, it is known to have effects on motor coordination and short-term memory processing, while CB2 is primarily expressed in leukocytes and used as hematopoietic development [13]. Discovery of cannabinoid receptors led to a search of endogenous transmitters. In 1992, with radiolabeled extracts of pig brain was identified the first endogenous mediator, N-arachidonoylethanolamide [14]. A few years later, the second endocannabinoid, 2-arachidonoyl glycerol, was identified, and recently, 3 endocannabinoids with selectivity to CB1 and CB2 were discovered. The well-established endocannabinoids are anandamide and 2-arachidonoyl glycerol, which have numerous roles, including working as "retrograde" mediator passing data from postsynaptic to presynaptic neurons [10]. THC and CBD are the most abundant cannabinoids that are scientifically studied as of now [15]. A synthetic version of THC, Marinol (dronabinol), is available on prescription. A newer synthetic THC developed was Cesamet (nabilone) for nausea and vomiting [16].

The aim of the study. This work expects to fill in as an educational tool with appropriate evidences about the benefits that therapeutic cannabis can offer. This information is primarily relevant as very recently, in July 2018, a cannabis-based product for epilepsy has been approved by the United States Food and Drug Administration (US FDA). Here, we give an outline of the history of cannabis in traditional system of medicine, fundamental science behind cannabis and the endocannabinoids framework, its

evidence as a therapeutic agent in Alzheimer's, epilepsy, chronic pain, and cancer studies and along with its molecular mechanism and legal aspects.

Materials and methods. We performed a literature search on databases such as PubMed and Google Scholar. Pre-printed articles, clinical studies, preclinical studies, meta-analysis, systematic reviews, and narrative reviews are included, and those papers that are not having adequate information were excluded.

Results. According to WHO, Alzheimer's disease (AD) is portrayed by a dynamic decrease in psychological function. Promotion of AD is generously expanded among individuals matured 65 years or more, with a dynamic decrease in memory, thinking, language, and learning capacity. According to Alzheimer's association, 1 in 10 people of age above 65 years have Alzheimer's dementia, as of 2019, and risk of it increases with age. One of the main factors in Alzheimer's progression is the accumulation of β-amyloid proteins in the patient. A randomized, double-blind clinical study at the University of Toronto suggested that nabilone, a synthetic cannabinoid, was effective in treating agitation and other behavioural symptoms of Alzheimer's. Medical cannabis oil containing THC as an add-on leads to a significant decrease in neurobehavioral symptoms such as delusions, agitation/aggression, irritability, apathy, sleep, and caregiver distress. Medical cannabis can help prevent or delay the onset of Alzheimer's and slow the disease's progression. Furthermore, THC competitively represses the compound acetylcholinesterase and additionally prevents acetylcholinesterase-actuated amyloid β-peptide aggregation, the key neurotic marker of Alzheimer's disease. Compared to present medications recommended for the treatment of Alzheimer's disease, THC is an impressively predominant inhibitor of amyloid β-peptide aggregation. Night-time agitation has been one of the major symptoms of severe dementia and has become the main problem for caregivers. In an open-label pilot study, 6 patients with severe dementia were treated with dronabinol, a pure isomer of THC, for 2 weeks. This investigation recommends that dronabinol could lessen night-time agitation and motor activity in extremely demented patients. Hence, it creates the impression that dronabinol might be a safe new treatment alternative for behavioural and circadian disturbances in dementia. Dronabinol treatment diminished the seriousness of disturbed behavior. These results demonstrated that dronabinol is a promising novel therapeutic agent that may be significant for the treatment of anorexia just as to improve disturbed behaviour in patients with AD. Cannabinoid receptor agonist anandamide and noladin ether inhibit amyloid-peptide, which is responsible for neurodegenerative changes during Alzheimer's. At very low concentration, nanomolar, anandamide, and noladin ether showed concentration-dependent inhibition of A peptide toxicity. Behavioural disturbances in patients with dementia associated with Alzheimer's have a significant therapeutic effect using dronabinol and perhaps other cannabinoids.

Parkinson's disease (PD) is the second most common neurodegenerative disease, the number of which is significantly increasing. Since 1990 (over 26 years), the number of individuals with PD doubled to over 6 million globally, and it is found that it affects men more than women. PD is identified by the presence of TNF-α, ILs, and other inflammatory

mediators in the cerebrospinal fluids as well as in substantia nigra pars compacta of PD patients. Presence of the inflammatory mediators may chronically increase reactive oxygen species, playing a role in the progression of disease. A study showed the neuroprotective effect of CBD in animal model, where administration of CBD for 2 weeks protected medical forebrain bundle from 6-hydroxydopamine toxicity. Further, CBD protective effect against striatal atrophy caused by 3-nitropropionic acid, in vivo, confirmed its therapeutic effect. An open-labelled pilot study on 6 outpatients of PD also received a flexible dose of CBD (150 mg/day) regimen for 4 weeks with usual therapy. There was a significant decrease in total score of scale used to follow-up PD patients and a decrease in psychotic symptoms, suggesting therapeutic benefits of CBD in PD patients.

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease where motor neuron of brain and spinal cord are selectively degenerated, leading to muscle wasting and atrophy and further paralysis and death. Presence of cytokines and immune cell, including T cells, activated microglia, and astrocytes in degenerated motor neurons of ALS patients and mouse models became a biomarker for the progression of the disease. ALS is found to develop with a uniform frequency in major western countries. Various epidemiological studies report that it is prevalent in 4.1–8.4 individuals in 100,000 people. A study showed the involvement of CB receptors in transgenic animal model for ASL, and efficacy of CB2 agonist AM-1241 demonstrated an increase of 56% of survival interval, concluding that it may slow motor neurodegeneration, opening a new therapeutic domain for ASL. Multiple sclerosis is an autoimmune chronic condition where immune system attacks axonal myelin sheaths of the neuron. MS affects 2.2 million people worldwide, as for 2016. Axonal damage is followed by inflammation and neurodegeneration. At present, drugs targeting immune system are used to treat MS, but they have moderate and not satisfactory effects. THC, Δ8-THC (a stable, less psychoactive analogy of THC), and dexanabinol showed beneficial effects by reducing severity and incidence of neurological deficits in rats with experimental autoimmune encephalomyelitis. A multicentred clinical trial with 660 MS patients checked the efficacy of cannabis extracts and its synthetic products for its therapeutic effects.

Conclusions. This study has analysed and reviewed the historical, botanical, chemical, ethnopharmacological, and legal aspects of C. Sativa from the first human use to the present medical applications with an analysis of its multiple therapeutic applications for various diseased conditions in the contemporary scientific context. There is an abundance of support for its several medicative uses as well as a possible benefit in various diseased conditions. Extensive pharmacological examination is still needed to better understand the clinical significance and uses of active cannabinoids in the treatment and prevention of chronic diseases. With the majority of the United States currently legalizing medicinal cannabis and/or restricted CBD-only use, physicians need to be educated on the history and correct clinical use of cannabis, as a result of which patients can know more and more about possible treatment utilizing cannabis. Medical cannabis has shown to have clinical efficacy in our past, and in present, data show its therapeutic effects.

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