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APPLICATION OF MEDICAL CANNABIS IN PATIENTS WITH CENTRAL NERVE SYSTEM DISORDERS

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Abstract. *Cannabis sativa* is an annual plant in the Cannabaceae family, species of the genus *Cannabis*. Cannabis contains active elements, including Δ9-tetrahydrocanabinol (THC) and cannabidiol (CBD).
Neurological disorders are typically associated with neurodegeneration. It means that there is no causal treatment. Usually we can only modulate disease. It is very necessary to patients to reduce pain sensation or excessive muscle tension.
The paper contains a description of therapeutic possibilities treatment of cannabis in neurological disorders such as Alzheimer's disease, multiple sclerosis, Tourette syndrome and spasticity.

Key words: *Cannabis sativa*, cannabis, Alzheimer's disease, multiple sclerosis, Tourette's syndrome, dystonia

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Cannabis sativa L. is a herbaceous plant in the *Cannabis* genus, a species of the Cannabaceae family. Other names for cannabis are marijuana or weed. Each part of the plant is harvested differently, depending on the purpose of usage. Its seeds are used to make hempseed oil (for cooking, lamps or paints), bird feed. The flowers (and the leaves, stems, and seeds) contain psychoactive chemical compounds known as cannabinoids that can be use for medicinal, recreational, and spiritual purposes. Historically, *C. sativa* has been used as hallucinogenic, hypnotic, sedative, analgesic, and anti-inflammatory agent. Nowadays cannabis is used as a recreational or medicinal drug, and as part of religious rites. Modern cannabis has been subject to legal restrictions, currently illegal in most countries of the world. Medical marijuana can be use in Europe (Great Britain, the Netherlands, Spain and Belgium).

Cannabis contains more than 85 active elements, including Δ9-tetrahydrocanabinol (THC), cannabidiol (CBD), Cannabigerols (CBG), Cannabichromenes (CBC), Cannabinol (CBN) and Cannabinodiol (CBDL) (El-Alfy *et al.* 2010). THC is usually the main ingredient, but other substances – such as CBD – can also have an active effect. The composition determines both: the effects and the side effects of the cannabis. Three types of medicinal cannabis are available through pharmacies: Sativex, Bedrocan, Bedrobinol and Bediol. They have different composition and strength varies.

Types of cannabinoid receptors

The body's own cannabinoid system has been identified (El-Alfy *et al.* 2010). The discovery of this system, which comprises endocannabinoids: anandamid (AEA), 2-arachidonoiloglicerol (2-AG) and receptors, confirmed that cannabis has a positive effect on certain illnesses and conditions (Bisogno *et al.* 2005). Endocannabinoids (anandamid) and cannabinoids are also found at the intersection of the body's various systems, allowing communication and coordination between different cell types.

In human body two types of cannabinoid receptors have been identified: CB1 and CB2 receptors (Howlett *et al.* 2002). The first type

CB1 is mostly found in the central nervous system (CNS), connective tissues, gonads, glands, and organs. In CNS it takes a role in modulating pain. It also has an anti-emetic effect, and has influence on the memory and the motor system (Pacher *et al.* 2006). The second type of receptors CB2 is peripheral, and it is primarily found in immune system cells (in the spleen in particular) (Pacher & Mechoulam 2001). Probably it is responsible for the immunomodulatory effects of cannabinoids. Endocannabinoids and cannabinoids are also found at the intersection of the body's various systems, allowing communication and coordination between different cell types. They are synthesized on-demand from cell membrane arachidonic acid derivatives, have a local effect and short half-life before being degraded by the enzymes fatty acid amide hydrolase (FAAH) and monoacylglycerol lipase (MAGL).

Cannabinoids can be administered by smoking, vaporizing, transdermal patch, oral/sublingual or rectal ingestion, and injection. Data currently available shows that medicinal cannabis can help to relieve pain and muscle spasms/cramps associated with (MS) or spinal cord damage, long-term neurogenic pain caused by, nerve damage, phantom limb pain, facial neuralgia or chronic pain following an attack of shingles, tics associated with Tourette syndrome, nausea, reduced appetite, weight loss and debilitation associated with cancer or AIDS, nausea and vomiting caused by medication or radiotherapy for cancer and AIDS.

Patients generally tolerate medical cannabis well. Side effects of medicinal cannabis can be: mood-altering effects, insomnia or heart palpitations. Other effects are: relaxation, feeling hungry, heightened, sensitivity to the perception of colors and music. Also the time reaction may be slower, especially during the first hours after use.

Alzheimer's disease

Alzheimer's disease (AD) is a neurological disorder of unknown origin that is characterized by a progressive loss of memory and learned behavior (dementia). It begins slowly. It first involves the parts of the brain that control thought, memory and language. People with AD may have trouble remembering things that happened recently or names of people they know- mild cognitive impairment (MCI). Patients with Alzheimer's are also likely to experience depression, agitation and appetite loss, among other symptoms. There are no approved treatments or medications which can be available to stop the progression of AD. A review of the recent scientific literature indicates that cannabinoid therapy may provide symptomatic relief to patients afflicted with AD while also may moderate the progression of the disease (Pazos *et al.* 2004). Investigators from The Scripps Research Institute in California in 2006 reported that THC inhibits the enzyme responsible for the aggregation of amyloid plaque – the primary marker for Alzheimer's disease (Eubanks *et al.* 2006). Preclinical studies have demonstrated that cannabinoids can also prevent cell death by anti-oxidation (Hampson *et al.* 1998). Cannabinoids' neuroprotective properties could also play a role in moderating AD. Writing in the September 2007 issue of the British Journal of Pharmacology, investigators at Ireland's Trinity College Institute of Neuroscience concluded, that cannabinoids offer a multi-faceted approach for the treatment of Alzheimer's disease by providing neuroprotection and reducing neuro-inflammation. Manipulation of the cannabinoid pathway offers a pharmacological approach for the treatment of AD that may be efficacious than current treatment regimens (Campbell & Gowran 2007).

Dystonia

Dystonia is a neurological movement disorder characterized by abnormal high muscle tension and involuntary, painful muscle contractions. It is the third most common movement disorder after Parkinson's disease and tremor. CB1 receptors are highly expressed in the basal ganglia (a substantia nigra), in the cerebellum and in the brain regions involved in motor control (Hohmann & Herkenham

2000; Moldrich & Wenger 2000). In year 2002 case study has been published in the July issue of The Journal of Pain and Symptom Management (Chatterjee *et al.* 2002). It reported reduction symptoms of dystonia after smoking cannabis in a 42-year-old chronic pain patient. Investigators reported that subject's subjective pain score was extenuated from 9 to 0 (on a 0 to 10 visual analog scale) following cannabis inhalation (48 hours observation). In time of experiment patient did not require any conventional analgesics drags. A second case study reporting "significant clinical improvement" following cannabis inhalation in a single 25-year-old patient with generalized dystonia due to Wilson's disease. It was documented by an Argentinian research team in the August 2004 issue of the journal Movement Disorders (Uribe Roca *et al.* 2004). To contrast, in 2002 randomized, placebo-controlled study investigating the use of the synthetic oral cannabinoid naboline (Cesamet) in 15 patients afflicted with generalized and segmental primary dystonia did not show a significant reduction in dystonic symptoms. Investigators speculated that this result may have been dose-related, and that administration of a higher dosage may have yielded a different outcome (Fox *et al.* 2002).

Chronic pain

Neuropathic pain is nerve-related pain- a condition that is associated with numerous diseases, including diabetes, cancer, multiple sclerosis and AIDS. In most cases, the use of standard analgesic medications such as opiates and NSAIDS (non-steroidal anti-inflammatory drugs) is ineffective at relieving neuropathic pain. Long-term use of most conventional pain relievers, including acetaminophen, opioids, and NSAIDs, in future is associated with a host of potential adverse side effects, including hepatoxicity, stroke, heart-attack and accidental overdose death.

Use of cannabis is common in chronic pain populations and several recent FDA-designed clinical trials indicate that inhaled marijuana can significantly alleviate neuropathic pain. These include a pair of randomized, placebo-controlled clinical trials demonstrating that smoking cannabis reduces neuropathy in patients with HIV by more than 30 percent compared to placebo (Abrams *et al.* 2007). In 2008, double-blind, randomized clinical trial has been reported both high and low doses of inhaled cannabis reduced neuropathic pain of diverse causes in subjects unresponsive to standard pain therapies (Wilsey *et al.* 2008). In 2009, an international team of investigators from the United Kingdom, Belgium and Romania affirmed these preclinical findings in a clinical study of intractable cancer pain patients. They concluded: the THC/CBD extract showed a more promising efficacy profile than the THC extract alone (Johnson *et al.* 2009).

Finally, in 2010, at McGill University improved that, smoked cannabis significantly reduced pain, improves sleep quality and anxiety in participants with refractory pain when conventional therapies had failed (Ware *et al.* 2010). A review in 2011 in British Journal of Clinical Pharmacology concluded, that it is reasonable to consider that cannabinoids as a treatment option for the management of chronic neuropathic pain with evidence of efficacy in other types of chronic pain such as fibromyalgia and rheumatoid arthritis as well (Lynch & Campbell 2011).

Huntington's disease

Huntington's disease (HD) is an inherited degenerative brain disorder characterized by motor abnormalities and dementia produced by selective lesions in the cerebral cortex and, in particular, the striatum. It is caused by an unstable expansion of repeat a trinucleotide CAG in the N-terminal domain of a protein named huntingtin. The disease is characterized by motor disturbances, such as chorea (involuntary movements) and dystonia, psychiatric symptoms, and dementia. There are presently no known conventional therapies available to alleviate HD symptoms or delay HD-associated striatal degeneration (Melone *et al.* 2005).

Although the administration of cannabidiol in HD patients provided little symptomatic relief compared to placebo in a single clinical trial, more recent preclinical data indicates that cannabinoids may possess potential to moderate the advancement of the disease and similar neurodegenative disorders (Müller-Vahl *et al.* 1999a; Consroe *et al.* 1991; Luvone *et al.* 2009).

Tourette's syndrome

Tourette's syndrome (TS) is a complex neuropsychiatric disorder of unknown etiology that is characterized by involuntary vocal tics. Severity of this condition varies widely among patients. Though there is no cure for Tourette's syndrome, the condition often improves with age.

A review of the scientific literature reveals several clinical trials investigating the use of cannabinoids for the treatment of TS. Plant-derived cannabinoids have been found to be effective in the treatment of tics and behavioral problems in TS (Fox *et al.* 2002). Writing in the March 1999 issue of the American Journal of Psychiatry, investigators at Germany's Medical School of Hanover, Department of Clinical Psychiatry and Psychotherapy, reported successful treatment of Tourette's syndrome with a single dose of 10 mg of delta-9-THC in a 25-year-old male patient in an uncontrolled open clinical trial (Müller-Vahl *et al.* 1999b). Investigators again confirmed these preliminary results in a randomized, double-blind, placebo-controlled, crossover, and single dose trial of THC in 12 adult TS patients. Researchers reported a «significant improvement of tics and obsessive-compulsive behavior (OCB) after treatment with delta-9-THC compared to placebo (Müller-Vahl *et al.* 2003).

Multiple sclerosis

Multiple sclerosis (MS) is a chronic degenerative disease of the central nervous system that causes inflammation and a loss of motor coordination. Over time, MS patients typically become permanently disabled and in some cases the disease can be fatal. The administration of oral THC can boost immune function in patients with MS. It suggests pro-inflammatory disease-modifying potential of cannabinoids for MS (Killestein *et al.* 2003). THC treatment reduced CNS inflammation and improved neurological outcome (Wirguin *et al.* 1994).

Investigators at the University of California in San Diego reported in 2008 that inhaled cannabis significantly reduced objective measures of pain intensity and spasticity in patients with MS in a placebo-controlled, randomized clinical trial. Investigators concluded that «smoked cannabis was superior to placebo in reducing spasticity and pain in patients with multiple sclerosis and provided some benefit beyond currently prescribed treatment (Corey-Bloom 2010). Clinical and anecdotal reports of cannabinoids' ability to reduce MS-related symptoms such as pain, spasticity, depression, fatigue, and incontinence are plentiful in the scientific literature (Chong *et al.* 2006).

Clinical data reported in 2006 from an extended open-label study of 167 multiple sclerosis patients found that use of whole plant cannabinoid extracts relieved symptoms of pain, spasticity and bladder incontinence for an extended period of treatment (mean duration of study participants was 434 days) without requiring subjects to increase their dose (Wade *et al.* 2006).

Conclusions

1. There is internal human body system of receptors and related agonists-endocannabinoids.
2. The plant-derived cannabinoid preparation Sativex has already gained regulatory approval in Europe to MS patients.
3. Medical cannabis can be used under medical control to modify the perception of pain, spasticity and uncontrolled muscle movements.
4. Medical use in large-scale patients requires further study.

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