

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Idrasil[™] safely and effectively. See full prescribing information for IDRASIL[™].

THESE STATEMENTS HAVE NOT BEEN EVALUATED BY THE FOOD AND DRUG ADMINISTRATION.

Idrasil[™] (cannabis) tablets

-----INDICATIONS AND USAGE------

Idrasil[™] consists of naturally extracted cannabinoid isolates that can be used to treat:

- Autoimmune Disease Syndrome (AIDS) (1.1)
- Attention Deficit Disorder (ADD) / Attentiondeficit hyperactivity disorder (ADHD) (1.2)
- Anorexia (ANA) (1.3)
- Addiction (1.4)
- Lou Gehrig's Disease (ALS) (1.5)
- Alzheimer's (ALZ) (1.6)
- Anxiety / Depression (1.7)
- Arthritis (RA) (1.8)
- Autism (AUT) (1.9)
- Autoimmune Disease (AID) (1.10)
- Cancers (CA) (1.11)
- Chronic Pain (CP) (1.12)
- Crohn's / Colitis / Irritable Bowel Syndrome (IBS) (1.13)
- Diabetes (DIA) (1.14)
- Endocrine Disorders (1.15)
- Epilepsy (EPI) (1.16)
- Fibromyalgia (FMA) (1.17)
- Gastrointestinal Disorders (GI) (1.18)
- Glaucoma (GLC) (1.19)
- Harm Reduction (1.20)
- Hepatitis C (HC) (1.21)
- Hypertension (HPT) / Cardio (1.22)
- Mental Disorder (MD) (1.23)
- Migraine Headache (MHA) (1.24)

- Muscular Dystrophy (MD) (1.25)
- Multiple Sclerosis (MS) (1.26)
- Nausea / Vomiting (N&V) (1.27)
- Neurodegenerative Disease (NDD) (1.28)
- Obsessive Compulsive Disorder (OCD) (1.29)
- Organ Failure (OF) / Transplant (TX) (1.30)
- Parkinson's Disease (PD) (1.31)
- Premenstrual Syndrome (PM)
- Posttraumatic stress disorder (PTSD) (1.33)
- Sleep Disorders (SD) (1.34)
- Tourette's Syndrome (TD) (1.35)

-----DOSAGE AND ADMINISTRATION-----Use the lowest effective dose consistent with treatment goals for the individual patient.

The typical dosage should consist of 6.25mg per 100 lbs (45.36 kg) every six hours; this may vary based on each patient's unique need and medical history.

----DOSAGE FORMS AND STRENGTHS----

Tablets: 12.5 mg, 25 mg, 100 mg.

-----CONTRAINDICATIONS------

- Patients with Cardiac Ischemia
- Possible adverse effects when consumed with alcohol

-----WARNINGS AND PRECAUTIONS------

- Before taking **Idrasil**[™], tell your doctor or pharmacist if you are allergic to it or have any other allergies.
- This product may contain inactive ingredients, which can cause allergic reactions or other problems. Talk to your doctor or pharmacist for more details.
- Before using this medication, tell your doctor or pharmacist your medical history. This drug may rarely make you dizzy or drowsy.
- Do not drive, use machinery, or do anything that needs alertness until you can do it safely. Limit alcoholic beverages.
- Before surgery, tell your doctor or dentist about all the products you use (including prescription drugs, nonprescription drugs, and herbal products).
- Older adults may be more sensitive to the side effects of the drug.

- This medication should only be used during pregnancy under a doctor's care. Discuss the risks and benefits with your doctor.
- This drug is unlikely to harm a nursing infant. Consult your doctor before breast-feeding.

-----ADVERSE REACTIONS------

If someone has overdosed and has severe symptoms such as passing out or trouble breathing, call 911. Otherwise, call a poison control center right away. US residents can call their local poison control center at 1-800-222-1222.

-----DRUG INTERACTIONS------

- Drug interactions may change how your medications work or increase your risk for serious side effects. This document does not contain all possible interactions. Keep a list of all your products (including prescription/nonprescription drugs and herbal products) and share it with your doctor and pharmacist.
- Do not start, stop, or change the dosage of any medicines without your doctor's approval.
- Some products that may interact with this drug are opioids, transdermal nicotine, antidepressants, Disulfiram, Fluoxetine, Sildenafil, Cisplatin, and Indomethacin.

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1. INDICATIONS AND USAGE

Carefully consider the potential benefits and risks of **Idrasil**[™] and other treatment options before deciding to use **Idrasil**[™]. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals.

1.1 Auto Immunodeficiency Syndrome (AIDS)/ Human Immunodeficiency Virus (HIV) Related Illness Idrasil™ may relieve the signs and symptoms (13.1)

1.2 Attention Deficit Disorder (ADD) / Attentiondeficit hyperactivity disorder (ADHD)
Idrasil[™] may relieve the signs and symptoms (13.2)

1.3 Addiction Recovery Idrasil[™] may relieve the signs and symptoms (13.3)

1.4 Lou Gehrig's Disease (ALS) Idrasil™ may relieve the signs and symptoms (13.4)

1.5 Alzheimer's (ALZ) Idrasil[™] may relieve the signs and symptoms (13.5)

1.6 Anorexia (ANA) Idrasil™l may relieve the signs and symptoms (13.6)

1.7 Anxiety / Depression Idrasil™ may relieve the signs and symptoms (13.7)

1.8 Arthritis (RA) Idrasil™ may relieve the signs and symptoms (13.8)

1.9 Autism (AUT) Idrasil[™] may relieve the signs and symptoms (13.9)

1.10 Autoimmune Disease Idrasil™ may relieve the signs and symptoms (13.10) **1.11 Cancer (CA) Idrasil**[™] may relieve the signs and symptoms (13.11)

1.12 Chronic Pain (CP) Idrasil[™] may relieve the signs and symptoms (13.12)

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1.18 Gastrointestinal Disorders (GI) Idrasil™ may relieve the signs and symptoms (13.18)

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1.25 Muscular Dystrophy (MD)

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1.26 Multiple Sclerosis (MS) Idrasil[™] may relieve the signs and symptoms (13.26)

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1:28 Neurodegenerative Disease (NDD) Idrasil™ may relieve the signs and symptoms (13.28)

1.29 OCD Idrasil[™] may relieve the signs and symptoms (13.29)

1.30 Organ Failure (OF) / Transplants (TX) Idrasil™ may relieve the signs and symptoms (13.30)

1.31 Parkinson's (PK) Idrasil™ may relieve the signs and symptoms (13.31)

1.32 Premenstrual Syndrome (PMS) Idrasil[™] may relieve the signs and symptoms (13.32)

1.33 Posttraumatic stress disorder (PTSD) Idrasil™ may relieve the signs and symptoms (13.33)

1.34 Sleep Disorders Idrasil™ may relieve the signs and symptoms (13.34)

1.35 Tourettes (TD) Idrasil[™] may relieve the signs and symptoms (13.35)

2. DOSAGE AND ADMINISTRATION

Use lowest effective dose for the shortest duration consistent with treatment goals for the individual patient. These doses can be given without regard to timing of meals.

3. DOSAGE FORMS AND STRENGTHS

Tablets: 12.5 mg, 25 mg, 100 mg.

4. CONTRAINDICATIONS

Idrasil[™] is contraindicated:

- In patients with Cardiac Ischemia
- When combined with Alcohol

5. WARNINGS AND PRECAUTIONS

- Cannabis is generally well-tolerated, and serious adverse effects, including increased risk of cardiovascular events, are rare.
- Adverse changes in cognitive function, especially executive function, may occur, especially with fetal or adolescent exposure.
- Cannabis should be avoided by adolescents, pregnant women, and nursing mothers.
- Cannabis should be avoided in those at risk of psychosis.
- Many studies show driving impairment, but on a much lower scale than alcohol.
- Drug interactions may be a concern.
- Cannabis enhances CNS depressant effects when combined with alcohol, barbiturates and benzodiazepines, but probably not opioids.
- THC induces CYP1A2 and can reduce levels of drugs metabolized by CYP1A2.
- CBD inhibits CYP3A4 and CYP2D6 and can increase levels of drugs metabolized by these isoenzymes.
- CPY3A4 metabolizes about a quarter of all drugs

6. ADVERSE REACTIONS

- Exacerbation of pre-existing cardiovascular disease, as cannabis use raises the heart rate.
- Decreased concentration levels, reduced short-term memory and difficulties with thinking and learning (resolved if cannabis use stops).
- Decreased sex drive in some people. Chronic use can lower sperm count in males and lead to irregular periods in females (resolved if cannabis use stops).
- Acute Intoxication may include acute anxiety, paranoia, and uncomfortably high heart rate or high blood pressure.

7. DRUG INTERACTIONS

7.1 Pharmacokinetics

Ingested cannabis does not appear to affect the pharmacokinetics of Docetaxel or Irinotecan.

7.2 Nicotine

Use of transdermal nicotine with cannabis enhances tachycardia and increases the stimulant effect of cannabis.

7.3 Antidepressants

Tachycardia has also been seen with combined use of tricyclic antidepressants and cannabis.

7.4 Morphine

Cannabis might increase the effects of opioids such as morphine.

7.5 Fluoxetine / Disulfiram

Isolated cases of hypomania have been seen when cannabis was used with disulfiram and with fluoxetine, and a man taking cannabis and sildenafil had a myocardial infarction.

7.6 Cisplatin

A case report describes a fatal stroke in a young man who received cisplatin and smoked cannabis.

7.7 Indomethacin

May antagonize some of the effects of smoking cannabis.

7.8 Alcohol

The detrimental effects of drinking alcohol and smoking cannabis may be additive on some aspects of driving performance. However, there is some evidence that regular cannabis use in itself does not potentiate the effects of alcohol. Smoking cannabis may alter the bioavailability of alcohol.

7.9 Chlorpromazine

Established interactions but of uncertain clinical importance. Be alert for the need to increase the dosages of chlorpromazine and related antipsychotics in patients who smoke, and reduce the dosages if smoking is stopped.

7.10 Docetaxel

Docetaxel is metabolized by the cytochrome P450 isoenzyme CYP3A4, and this does not appear to be affected by oral cannabis.

7.11 NSAIDs

It is suggested that prostaglandins have some part to play in some of the effects of cannabis and that these are antagonized by indomethacin, which is a prostaglandin inhibitor. Similarly, cannabis antagonizes the effects of NSAIDs.

7.12 Opioids

Cannabis use in methadone-maintained patients did not appear to affect treatment progress, although some psychological difficulties were slightly more prevalent.

7.13 Phenytoin

The in vitro data suggests that delta9tetrahydrocannabinol induces the cytochrome P450 isoenzyme CYP2C9. This appears to be the only evidence that cannabis might affect phenytoin levels and is only in vitro data. As such, it requires confirmation before any recommendations can be made. Note also that there are no reports in the literature of cannabis use affecting phenytoin levels.

7.14 Protease Inhibitors

There was no adverse effect on viral load or CD4 count in the patients receiving cannabis cigarettes or dronabinol.

7.15 Sildenafil

The vasodilatory effects of sildenafil necessitate caution in its use in patients with cardiovascular disease; myocardial infarction has rarely been associated with it, of an interaction to this case is unclear, but bear the use. The contribution possibility in mind in the event of adverse effects on concurrent use.

7.16 Theophylline

Little is known about the effects of smoking cannabis on theophylline levels but be alert for the need to increase the theophylline dosage in regular users. Note that irregular cannabis use might cause fluctuations in theophylline levels.

7.17 Tricyclic Antidepressants

Increased heart rates are well-documented adverse effects of both the tricyclic antidepressants and cannabis, and what occurred was probably due to the additive beta-adrenergic and antimuscarinic effects of the tricyclic, with the beta-adrenergic effect of the cannabis. Direct information is limited but it has been suggested that concurrent use should be avoided.

8. USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Cannabis may be unsafe when taken by mouth or smoked during pregnancy. Cannabis passes through the placenta and can slow the growth of the fetus. Marijuana use during pregnancy may also be associated with childhood leukemia and abnormalities in the fetus.

8.2 Nursing Mothers

Using cannabis, either by mouth or by inhalation is likely unsafe during breastfeeding. The THC in cannabis passes into breast milk and extensive cannabis use during breastfeeding may result in slowed development in the baby.

8.3 Pediatric Use

Unless your children are medically authorized to use cannabis, you should not be administering it to them, nor should you give them any unsupervised access whatsoever. Be conscious of how you use your cannabis and where you store it.

8.4 Geriatric Use

Some studies have shown elderly patients may be more sensitive to the effects of cannabis. It may be advisable to start with lower doses as a precaution.

8.5 Adult Males

Some studies show that heavy use of cannabis may decrease plasma testosterone and decreases sperm count, concentration, and motility.

9. OVERDOSE

Cannabis side effects from overdosing may include: acute anxiety, paranoia, increased heart rate and/or increase in blood pressure.

10. DESCRIPTION

Idrasil[™] is an aseptically processed and bacteria free, all-natural nutraceutical, it's processed and packaged in a sterile container using flash-heating to maintain sterility. The proprietary process isolates all the cannabinoids from the cloned cannabis plant, resulting in pure extraction in tablet form, which, is titrated and consistently dosed.

Eating Vs Smoking Cannabis



The difference between **inhaled** or **ingested** cannabis, in terms of the metabolic pathway, that THC takes through the body. When consumed, the liver breaks down the main psychoactive ingredient delta-9-THC into other molecules. First, enzymes turn delta-9-THC into 11-OH-THC, which is also psychoactive, and then to 11-COOH-THC, which is not psychoactive.

When cannabis is smoked or vaporized, delta-9-THC enters the bloodstream via absorption through the lungs. Once in the bloodstream, the delta-9-THC travels straight to the heart, and then the heart pumps it through the entire body, including the brain, allowing it to bind to cannabinoid receptors. The psychologically experienced high kicks in as the THC molecules pass through the blood barrier and bind to the receptors in the brain. When ingested, delta-9-THC enters the bloodstream through the walls of the stomach and intestines. When absorbed gastrointestinally, delta-9-THC travels first to the liver where most of it is eliminated or metabolized before it has ever had a chance to activate a receptor. After this first pass through the liver the remaining delta-9-THC and both, it's metabolites get to the heart and from there into circulation. Delta-9-THC and 11-OH-THC reach the brain simultaneously.

C/3

The recent identification of <u>cannabinoid receptors</u> and their endogenous lipid ligands has triggered an exponential growth of studies exploring the <u>endocannabinoid system</u> and its regulatory functions in health and disease. Such studies have been greatly facilitated by the introduction of selective cannabinoid receptor antagonists and inhibitors of endocannabinoid metabolism and transport, as well as mice deficient in cannabinoid receptors or the endocannabinoid-degrading enzyme fatty acid amidohydrolase.

In the past decade, the endocannabinoid system has been implicated in a growing number of physiological functions, both in the central and peripheral nervous systems and in peripheral organs. More importantly, modulating the activity of the endocannabinoid system turned out to hold therapeutic promise in a wide range of disparate diseases and pathological conditions, ranging from mood and anxiety disorders, movement disorders such as Parkinson's and Huntington's disease, neuropathic pain, multiple sclerosis and spinal cord injury, to cancer, atherosclerosis, myocardial infarction, stroke, hypertension, glaucoma, obesity/metabolic syndrome, and osteoporosis, to name just a few. An impediment to the development of cannabinoid medications has been the socially unacceptable psychoactive properties of plant-derived or synthetic agonists, mediated by $\underline{CB_1}$ receptors.

However, this problem does not arise when the therapeutic aim is achieved by treatment with a CB₁ receptor antagonist, such as in obesity, and may also be absent when the action of endocannabinoids is enhanced indirectly through blocking their metabolism or transport. The use of selective <u>CB₂</u> <u>receptor</u> agonists, which lack psychoactive properties, could represent another promising avenue for certain conditions.

The abuse potential of plant-derived cannabinoids may also be limited through the use of preparations with controlled composition and the careful selection of dose and route of administration. The growing number of preclinical studies and clinical trials with compounds that modulate the endocannabinoid system will probably result in novel therapeutic approaches in a number of diseases for which current treatments do not fully address the patients' need. Here, we provide a comprehensive overview on the current state of knowledge of the endocannabinoid system as a target of pharmacotherapy.

The American Society for Pharmacology and Experimental Therapeutics

Comparing THC and CBD



Cannabichromene (CBC)

Acid vs. Neutral Cannabinoid Decarboxylation



Non-psychoactive Phytocannabinoids



Health Effects of Cannabinoids



Why does pot do so many things to the human body and brain?

Non-THC Components of Cannabis

- \triangle 9-tetrahydrocannabinol (THC) is the primary • active ingredient in cannabis
- Secondary compounds may enhance the • beneficial effects of THC

- Other cannabinoids and non-cannabinoid compounds may reduce THC-induced anxiety, anticholinergic effects, and immunosuppression
- Terpenoids and flavonoids may increase cerebral • blood flow, enhance cortical activity, kill respiratory pathogens and provide antiinflammatory activity

Cannabidiol (CBD)

- Modulates the pharmacokinetics of THC •
- Very low affinity for CB1 And CB2 receptors
- Slight affinity for CB receptors as an antagonist •
- May modulate downstream signal transduction •
- Potent cytochrome P450 3A11 inhibitor thus • blocking the formation of 11-OH metabolite
- CBD possesses sedative properties, reduces anxiety and other unpleasant psychological side effects of pure THC

Idrasil[™] is CBD-Rich

- Second to THC as the most prevalent cannabinoid •
- Little binding affinity at CB1; mildly antagonizes • THC
- Reduces anxiety, paranoia, tachycardia, hunger, sedation
- Analgesic; neuroprotective antioxidant; • anticonvulsant, anti-nausea; antagonizes TNFalpha; anti-MRSA; agonistic at 5HT1a (antianxiety)
- Cytotoxic to many cancer cell line-• cytopreserative to normal cells
- Improves cognition in animal models of hepatic encephalopathy

12. NONCLINICAL TOXICOLOGY

- Adverse chemical reactions caused by the active compounds in IDRASIL such as THC, CBD, and/or THN.
- THC is a CYP1A2 inducer. •
- Theoretically, THC can decrease serum • concentrations of clozapine, duloxetine, naproxen, cyclobenzaprine, olanzapine, haloperidol, and chlorpromazine (Flockhart 2007, Watanabe et al 2007).
- CBD is a potent inhibitor of CYP3A4 and CYP2D6.
- As CYP3A4 metabolizes about a guarter of all drugs, CBD may increase serum concentrations of

macrolides, calcium channel blockers, benzodiazepines, cyclosporine, sildenafil (and other PDE5 inhibitors), antihistamines, haloperidol, antiretrovirals, and some statins (atorvastatin and simvastatin, but not pravastatin or rosuvastatin).

 CYP2D6 metabolizes many antidepressants, so CBD may increase serum concentrations of SSRIs, tricyclic antidepressants, antipsychotics, beta blockers and opioids (including codeine and oxycodone).

13. MEDICAL STUDIES

13.1 AIDS / HIV

Peer reviewed medical studies show the cannabis plant's efficacy in eliminating nausea, vomiting, and appetite loss. It also helps restoring weight and maintain essential nutrients. It targets neuropathic pain induced by HIV/AIDS therapy. It's also demonstrated some promise as an inhibitor of HIV/AIDS progression.

13.2 ADD / ADHD

Peer reviewed medical studies suggest that individuals suffering from ADHD, a dysfunction with a symptomatic change in activity levels, may - in some cases - benefit from cannabis treatment in that it appears to regulate activation to a level which may be considered optimum for performance. There was evidence, that the consumption of cannabis had a positive impact on performance, behaviour and mental state of the subject. The present observation corroborates previous data, suggesting that in patients suffering from Tourette syndrome, treatment with THC causes no cognitive defects.

13.3 ADDICTION

Peer reviewed medical studies have shown that the endocannabinoid system is involved in the common neurobiological mechanism underlying drug addiction. Accumulating evidence thus points to the ECBS as a critical target for the development of pharmacotherapies for the treatment of addiction to psychostimulants. Given the various neuropharmacological actions of exogenous cannabinoids, and their ability to modulate the acute reinforcing effects of drugs, data on Δ^9 -THC and CBD is particularly promising as to the potential use of cannabinoids in relapse prevention strategies for psychostimulant-dependent individuals. The effects of these compounds on stimulant use outcomes in humans remains to be clearly established and could be assessed with well-designed controlled trials. The neurobiological correlates of cannabinoids' impact on stimulant-seeking behaviors could also be examined with neuroimaging studies in stimulants dependent individuals.

13.4 ALS

Peer reviewed medical studies show given the highly favorable safety profile of whole-plant cannabis, and the severely debilitating symptoms caused by ALS, whole-plant cannabis medicine may be a safe and useful additional therapy for patients with ALS who are finding it difficult to control their symptoms with standard therapy.

13.5 ALZHEIMER'S

Peer reviewed medical studies show that THC could be a potential therapeutic treatment option for Alzheimer's disease through multiple functions and pathways. Compared to currently approved drugs prescribed for the treatment of Alzheimer's disease, THC is a considerably superior inhibitor of Abeta aggregation, and this study provides a previously unrecognized molecular mechanism through which cannabinoid molecules may directly impact the progression of this debilitating disease.

13.6 ANOREXIA

Peer reviewed medical studies show cannabis is a treatment option for anorexia, on average patients gain more weight, its well tolerated with no adverse effects.

13.7 ANXIETY / DEPRESSION

Peer reviewed medical studies have found that cannabis can be an effective treatment for depression. Cannabis doesn't cause the side effects that other pharmaceuticals would. Comprehensive reviews of research on medical cannabis use and mental health also found evidence that cannabis may help with symptoms of depression, PTSD and social anxiety.

13.8 ARTHRITIS

Peer reviewed medical studies finding that the endocannabinoid system has receptors present in the synovium of joints have suggested to researchers that cannabinoids may be beneficial for addressing the pain and inflammation associated with osteoarthritis and rheumatoid arthritis. Preclinical studies have also demonstrated cannabis' anti-inflammatory and pain-relieving effects, supporting the idea that the endocannabinoid system is involved in alleviating pain associated with arthritis.

Other studies have found evidence that synthetic cannabinoids offer strong anti-inflammatory and immunosuppressive properties and reduce joint damage in mice with osteoarthritis. Most recently, cannabinoid treatments were found effective for reducing osteoarthritis-related cartilage breakdown. These anti-inflammatory and anti-pain effects of cannabinoids are likely due to their interactions with the endocannabinoid system's CB₁ receptors, which have been specifically found to be associated with pain sensitivity in the osteoarthritic knee joints of rats.

13.9 AUTISM

A peer reviewed medical study showed 80% of the children's parents who participated in the study reported a decrease in problematic behavior, with 62% percent reporting that their child's behavior improved significantly.

The study also found that half of the children who participated in the study also reported an improvement in their level of communication, with 40% saying that their anxiety symptoms had significantly improved. A third of the participants did not show symptoms of anxiety before the study began.

13.10 AUTOIMMUNE DISEASE

Peer reviewed medical studies have discovered a novel pathway through which marijuana's main active constituent, THC, can suppress the body's immune functions. The recent findings show that THC can change critical molecules of epigenome called histones, leading to suppression of inflammation.

13.11 CANCER

Peer reviewed medical studies have shown that THC/CBD extract is efficacious for relief of pain in patients with advanced cancer pain not fully relieved by strong opioids. There is a consensus in the field of cancer research that targeting multiple pathways that control tumor progression is the best strategy for the eradication of aggressive cancers. Researchers have confirmed that the most potent effects against tumor growth occur when THC and CBD are combined. It has also shown to have an effect on the rate of metastasis, including for non-small cell lung cancer.

Harvard Medical School found that certain EGF lung cancer cells express CB1 and CB2 cannabinoid receptors. They found that the presence of THC effected metastasis of these cells by reducing the *"focal adhesion complex,"* which plays a vital role in cancer migration. Cannabinoids -- the active components of Cannabis sativa and their derivatives exert palliative effects in cancer patients by preventing nausea, vomiting and pain and by stimulating appetite. In addition, these compounds have been shown to inhibit the growth of tumor cells in culture and animal models by modulating key cellsignaling pathways. Cannabinoids are usually well tolerated, and do not produce the generalized toxic effects of conventional chemotherapies.

13.12 CHRONIC PAIN

Peer reviewed medical studies have found that cannabis is an extremely safe and effective medication for many patients with chronic pain. In stark contrast to opioids and other available pain medications, cannabis is relatively non-addicting and has the best safety record of any known pain medication (no deaths attributed to overdose or direct effects of medication). Average reported pain relief from medical cannabis was substantial. Average pretreatment pain on a zero to ten scale was 7.8, whereas average post-treatment pain was 2.8, giving a reported average improvement of 5 points. Both THC and CBD in cannabis are known to elicit analgesic effects, especially when used together due to their congruent chemical synergies. Studies are showing clinically and statistically significant evidence of an association between MCP enrollment and opioid prescription cessation and reductions and

improved quality of life warrants further investigations on cannabis as a potential alternative to prescription opioids for treating chronic pain.

13.13 CROHN'S / COLITIS / IBS

An eight-week study of THC-rich cannabis produced significant clinical, steroid-free benefits to 10 of 11 patients with active Crohn's disease, compared with placebo, without side effects.

13.14 DIABETES

Peer reviewed medical studies showed that when compared to a placebo, THCV significantly decreased fasting plasma glucose (estimated treatment difference [ETD] = -1.2 mmol/L; P < 0.05) and improved pancreatic β -cell function (HOMA2 β -cell function [ETD = -44.51 points; P < 0.01]), adiponectin (ETD = -5.9 × 10(6) pg/mL; P < 0.01), and apolipoprotein A (ETD = -6.02 µmol/L; P < 0.05), although plasma HDL was unaffected. Compared with baseline (but not placebo), CBD decreased resistin (-898 pg/ml; P < 0.05) and increased glucosedependent insulinotropic peptide (21.9 pg/ml; P < 0.05). THCV could represent a new therapeutic agent in glycemic control in subjects with type 2 diabetes

13.15 ENDOCRINE DISORDERS

The body's natural endocannabinoid system helps in the regulation of the body's activities, particularly in the maintenance of homeostasis (balance). These endocannabinoid type molecules also have been found to have anti-cancer effects on thyroid tumors in lab and studies involving animals. Endocannabinoid receptors have been located in regions of the brain that are responsible for sending out signals to the thyroid gland. In 2009 there was a research study that reported in the Journal of Endocrinology the abundance of CB1 receptors present on nerves in the brain that are involved in the hypothalamic-pituitary-thyroid axis and its regulation. This area controls the production of hormones by the thyroid gland. This distribution shows there is great potential for both excitatory and inhibitory inputs on this system.

13.16 EPILEPSY

Early evidence from laboratory studies, anecdotal reports, and small clinical studies over several years

suggest that cannabidiol (CBD) could potentially help control seizures. Several peer reviewed medical studies have shown the benefit of specific plantbased CBD products in treating specific groups of people with epilepsy who have not responded to traditional therapies.

13.17 FIBROMYALGIA

Peer reviewed medical studies show the use of cannabis was associated with beneficial effects on some FM symptoms.

13.18 GASTROINTESTINAL DISORDERS

The effectiveness of cannabis for treating symptoms related to gastrointestinal disorders is widely recognized. Its value as an antiemetic and analgesic has been proven in numerous studies and has been acknowledged by several comprehensive, government-sponsored reviews, including those conducted by the Institute of Medicine (IOM), the U.K. House of Lords Science and Technology Committee, the Australian National Task Force on Cannabis, and others. The IOM concluded, "For patients who suffer simultaneously from severe pain, nausea, and appetite loss, cannabinoid drugs might offer broadspectrum relief not found in any other single medication. "Research suggests that cannabis is effective in treating the symptoms of these GI disorders in part because it interacts with the endogenous cannabinoid receptors in the digestive tract, which can result in calming spasms, assuaging pain, and improving motility. Cannabis has also been shown to have anti-inflammatory properties and recent research has demonstrated that cannabinoids are immune system modulators, either enhancing or suppressing immune response.

13.19 GLAUCOMA

Cannabinoids have the potential of becoming a useful treatment for glaucoma, as they seem to have neuroprotective properties and effectively reduce intraocular pressure.

13.20 HARM-REDUCTION

Cannabis has been shown to be effective for treating nerve pain without the risk of fatal poisoning. This harm-reduction strategy may reduce the morbidity and mortality rates associated with prescription pain medications. Substituting cannabis for prescribed opioids may be considered a harm-reduction strategy.

13.21 HEPATITIS C

Peer reviewed medical studies suggest that modest cannabis use may offer symptomatic and virologic benefit to some patients undergoing HCV treatment by helping them maintain adherence to the challenging medication regimen.

13.22 HYPERTENSION / CARDIO

Peer reviewed medical study data shows that acute administration of CBD reduces resting BP and the BP increase to stress in humans, associated with increased HR. These hemodynamic changes should be considered for people taking CBD. Findings suggest that the positive chronotropic response to THC tends to maintain cardiac output which limits further decreases in blood pressure and the capillary filtration of aqueous humor decreases or the reabsorption of aqueous humor increases because of the systemic hypotensive effect attending THC inhalation

13.23 MENTAL DISORDERS

Researchers found evidence that cannabis can likely benefit people dealing with depression, social anxiety and PTSD. Studies also suggested that cannabis may have a place in dealing with addiction.

13.24 MIGRAINE HEADACHES

A peer reviewed medical study has found that the active compounds in cannabis are more effective at reducing the frequency of acute migraine pain. THC-CBD drug was very effective at reducing migraine pain, it was also effective at reducing the severity of pain in cluster headache sufferers with less side effects including fewer stomach aches and muscle pains.

13.25 MUSCULAR DYSTROPHY

Peer reviewed medical studies show reduction in MD symptoms with medical cannabis can lesson contractions, tightness, and pain in patients. Cannabis reduced spasticity measurements by onethird on the Ashworth Scale, which is commonly used to evaluate the overall mobility of the muscle. Pain scores improved by 50%.

13.26 MULTIPLE SCLEROSIS

Peer reviewed medical studies show reduction in MS symptoms with medical cannabis can lesson contractions, tightness, and pain in patients. Cannabis reduced spasticity measurements by onethird on the Ashworth Scale, which is commonly used to evaluate the overall mobility of the muscle. Pain scores improved by 50%.

13.27 NAUSEA / VOMITING

Peer reviewed medical studies show that Cannabis is an antiemetic, that is, cannabis stops you from vomiting. THC reduces vomiting by binding to cannabinoid CB1 receptors. CBD reduces nausea by interacting with serotonin receptors. When THC binds to the CB1 receptors in specific parts of the brain, it acts to reduce vomiting.

13.28 NEURODEGENERATIVE DISEASE

Extensive research on the impact of endocannabinoid system modulation and its effects on neurodegenerative disorders has occurred in the past several years. Signaling from the CB1 and CB2 [i.e. cannabinoid] receptors are known to be involved in the regulation of Ca2+ [calcium] homeostasis [i.e. the mechanism by which systems are kept balanced], mitochondrial function [i.e. function of components of cells that produce energy], trophic [i.e. growth] support and inflammatory status... while other receptors gated [i.e. modulated/controlled] by cannabinoids... are gaining interest in their antiinflammatory properties.

Through multiple lines of evidence, this evolutionarily conserved neural signaling system has shown neuroprotective capabilities and is therefore a potential target for neurodegenerative disorders. Given the highly favorable safety profile of wholeplant cannabis, and the severely debilitating symptoms caused by certain neurodegenerative diseases which could potentially be alleviated by its use, whole-plant cannabis medicine may be a safe and useful additional therapy for patients with certain neurodegenerative diseases who are finding it difficult to control their symptoms with standard therapy. Increased research on cannabinoid medicine and modulation of the endocannabinoid system in relation to neurodegeneration has the potential to lead to novel therapies which may help to prevent progression, and potentially initiation, of these diseases.

13.29 OCD

Medical cannabis may help control symptoms of OCD including impulsive behavior, repetitive behavior, repetitive thoughts, urges, anxiety, depression, stress, tension and social isolation. It may also curb the side effects of OCD medications such as nausea, headaches, restlessness, weight loss, insomnia, agitation, abdominal cramps and seizures.

13.30 ORGAN FAILURE / TRANSPLANTS

In peer reviewed medical studies, THC has helped to prevent rejection thru prevention of increases in the number of recipient T-cells in the recipient's lymph nodes (i.e. lower chance of rejection of donor tissue), decrease in inflammatory response signals. stimulation of <u>myeloid-derived suppressor cells</u> (which act to decrease the recipient T-cell response and prevent rejection), increased length of survival of donor skin cells. Cannabinoids are useful in modulating/reducing inflammatory processes, which are implicated not only in transplant rejection, but also in autoimmune disorders, cancer, and other debilitating diseases.

13.31 PARKINSON'S

Peer reviewed medical studies are showing improvements in Parkinson's related symptoms, both motor and non-motor, were relieved following the use of cannabis. The medical team registered important fluctuations in pain, sleep, and several motor symptoms, namely tremor, rigidity and bradykinesia. In addition to these results being the first study showing cannabis relieving motor and non-motor symptoms alike, no adverse effects were observed following the intake of cannabis. There was also significant improvement of sleep and pain scores. No significant adverse effects of the drug were observed.

13.32 PMS

Peer reviewed medical studies show that medical cannabis may make symptoms do to PMS easier to live with. Cannabis has been found to be very effective in treating hormonal and emotional disturbances, irritability, insomnia, depression, anxiety, and painful cramping.

13.33 PTSD

The results of a peer reviewed medical study indicated that patients in the sample reported an average of 75 percent reduction in all three areas of PTSD symptoms while using cannabis.

13.34 SLEEP DISORDERS

Parasomnia – abnormal or unusual behavior of the nervous system during sleep including sleepwalking, talking during sleep, grinding teeth, night terrors, head banging. Most patients reported that they fell asleep faster and easier and didn't wake up during the night. The time it took them to fall asleep was reduced, on average, by an hour.

13.35 TOURETTE'S SYNDROME

Peer reviewed medical studies results provide more evidence that THC is effective and safe in the treatment of tics. It, therefore, can be hypothesized that the central cannabinoid receptor system might play a role in TS pathology.



Distributed by:

C3® International, Inc. 13210 Harbor Boulevard, #187 Garden Grove, California 92843