Scientific name: *Cannabis sativa, Cannabis indica*

Also known as: banji, cannabis, ganja, hashish, marihuana, marijuana, pot, shisha, weed

Known active ingredients: tetrahydrocannabinol (THC), cannabidiol (CBD), cannabinol (CBN). Over 420 compounds, including 120 cannabinoids, have been isolated from *Cannabis* leaves and flowering tops.

INDICATIONS

People use this for: appetite stimulation, anxiety disorders, arthritis, depression, epilepsy, glaucoma, headache and migraine, Huntington's disease, insomnia, irritable bowel disease, management of chemotherapy-induced nausea, glaucoma, spasticity in multiple sclerosis, neuropathic pain, Parkinson's disease, sleep disorders, symptom control for psychiatric disorders such as anxiety or post-traumatic stress disorder (PTSD), Tourette syndrome

Effectiveness: possibly effective for chronic pain, fibromyalgia, management of chemotherapy-induced nausea, spasticity in multiple sclerosis, neuropathic pain. Few reliable studies are available regarding medical benefits of cannabis.

MECHANISM OF ACTION

Cannabinoids act on cannabinoid receptors, CB1 and CB2. CB1 receptors are found primarily in the CNS, but are also found in lower concentrations in the heart, liver, lung, GI system, reproductive organs, and other tissues throughout the body. CB2 receptors are found primarily in immune tissues, as well as retinal and microglia cells.

Cannabinoids such as THC and CBD act on cannabinoid receptors to suppress neuronal excitability and transmitter release, modulate cytokine release, and inhibit cyclooxygenase enzymes COX-1 and COX-2. THC is psychoactive and may produce euphoria, while CBD is not. Synergy and interactions may exist between different cannabinoids. For instance, CBD has been shown to modulate THC side effects through CB1 antagonism.

ADVERSE REACTIONS

Contraindicated for individuals with hypersensitivity to any cannabinoid, hypersensitivity to smoking (e.g. hyperactive airway disease, when using inhaled form), and psychotic disorders such as schizophrenia.

Use with caution in clients with cardiac disease (angina, peripheral vascular disease, cerebrovascular disease, arrhythmia) or respiratory disease, history of substance abuse or dependency, mania or depression, concomitant CNS medications; elderly individuals. Not recommended for pregnant or nursing women or individuals under the age of 25. Potential for dependence and abuse. Do not drive or operate machinery.

Common adverse reaction: dizziness or lightheadedness, cognitive impairment, dry mouth, fatigue, muscle weakness, myalgia, palpitations. Cough and throat irritation may occur with smoked cannabis. These side effects often diminish over time.

Less common adverse reactions: psychosis, respiratory events, cardiovascular events (including increases in blood pressure and heart rate, may increase risk of angina, myocardial

infarction (5x risk within one hour of smoking), stroke; may exacerbate arrhythmias), cannabis use disorder (addiction), cancer of the lung, head and neck, brain, cervix, prostate, and testes. May cause symptoms of chronic bronchitis and decrease ability to fight infection (e.g. pneumonia).

Cannabinoid hyperemesis syndrome/cyclic vomiting syndrome: Recurrent episodes of nausea, vomiting, and stomach pain, which disappears with discontinuation of cannabis. Frequent hot showers or baths usually relieve this. This reaction is often refractory to first-line antiemetics; acute nausea may be treated with lorazepam or haloperidol, IV normal saline, and discontinuation of cannabis.

Withdrawal: as per Diagnostic and Statistical Manual of Mental Disorders – 5th Edition (DSM-5), withdrawal symptoms may include irritability, nervousness or anxiety, restlessness, increased anger, sleep difficulty, strange or wild dreams, depressed mood, decreased appetite, sweating, shakiness or tremulousness, headaches, or stomach pains. Withdrawal is more common for individuals who report using cannabis regularly, typically defined as 20 or more days in the past month, as well as use of products with higher THC levels. Frequent use of cannabis is associated with a down-regulation of CB1 receptors; reversal of this state begins within two days of cessation of use, and returns to normal within four weeks. Withdrawal symptoms, when they occur, generally follow this pattern, and are generally believed to be similar in severity to symptoms of tobacco withdrawal or moderate alcohol withdrawal, although certain populations may experience more severe symptoms. Treatment is generally non-pharmacological, although short-term treatment of symptoms may be reasonable.

Elder Alert: increased risk of falling in older adults. Older adults may also be more susceptible to neurological, psychoactive, and blood pressure effects related to cannabis use.

PHARMACOKINETICS

Highly lipophilic with large volume of distribution. Terminal half-life of four days or longer. Hepatic metabolism with extensive first-pass metabolism. Excreted via biliary tract into feces, with urinary excretion of acid metabolites.

Smoked or vaporized: bioavailability is 95% or greater. Onset of action is 3-10 minutes; duration of action is 2-3 hours.

Orally ingested (oil, capsules, food): bioavailability is typically 10-35%, but may be as high as 50%. Onset of action is within 60-90 minutes; duration of action is typically 5-8 hours. Oral bioavailability and absorption are erratic.

INTERACTIONS

Interactions with drugs: THC is a substrate of CYP2C9 and 3A4; may weakly inhibit CYP3A4. Cannabidiol is a substrate of CYP2C19 and 3A4, and to a lesser extent 2C9; weakly inhibits CYP2C. Induction of CYP1A2 may occur; mechanism unknown.

Drug interactions include (but are not limited to) anticholinergic drugs, azelastine, CNS depressants, cocaine, droperidol, hydroxyzine, magnesium sulfate, methotrimeprazine, mirtazapine, paraldehyde, pramipexole, ropinirole, rotigotine, SSRIs, sympathomimetics, zolpidem.

Coadministration with ketoconazole may increase plasma levels of THC and its metabolites, as well as CBD. Coadministration with rifampin may decrease C_{max} and AUC of THC and its metabolites, as well as CBD. May increase clearance of theophylline.

Interactions with food and alcohol: additive effects with alcohol.

Interactions with diseases or conditions: may exacerbate arrhythmias; may trigger psychotic events for individuals who are predisposed (e.g. schizophrenia, bipolar).

DOSAGE AND ADMINISTRATION

***Dosage*:** there are very few guidelines available to establish dose ranges for dried cannabis or cannabis oil. It is recognized that the ratio of THC:CBD will have an impact on efficacy. As per Health Canada, dosing is highly individualized, and should be started at a very low dose and titrated to effect. Usual dosage range is 1-3 g daily. One "joint" is typically 0.5-0.75 g of dried cannabis. Oral doses are generally 2.5 times higher than smoked or vaporized doses.

Routes of administration: dried cannabis is typically smoked or vaporized for inhalation, or consumed orally in the form of an oil. Dried cannabis oil may also be incorporated into food products; note that manipulation of cannabis or cannabis oil into edible products is permitted only for the authorized user or responsible person, not for licensed producers/dealers of medical cannabis.