

Cannabinoid Information

"Cannabinoids refers to a group of substances that are structurally related to Tetrahydrocannabinol (THC) or that bind to cannabinoid receptors. The term *cannabinoids* also refers to a unique group of secondary metabolites found in the cannabis plant, which are responsible for the plant's peculiar pharmacological effects."(1).

"Mechoulam and Gaoni (1967) defined "cannabinoids" as a group of C21 terpenophenolic compounds uniquely produced by cannabis. The subsequent development of synthetic cannabinoids (e.g., HU-210) has blurred this definition, as has the discovery of endogenous cannabinoids (e.g., anandamide), defined as "endocannabinoids" by DiMarzo and Fontana (1995). Thus, Pate (1999) proposed the term "phytocannabinoids" to designate the C21 compounds produced by cannabis."(2)

There are many different cannabinoids and terpenoids present in a sample of cannabis, however only the main cannabinoids have been linked to pharmacological activity so far. "The main cannabinoid types that are usually detected in each breeding strain or cultivar of cannabis are THC, CBD, CBN, CBG and CBC. However, there can be an enormous variation in their quantitative ratios."(3). THCV is now also considered to be a main cannabinoid.

"In fresh cannabis plant material, THC is predominantly present in the form of its acidic precursor THC-acid (THCA). Under the influence of heat or storage, THCA can be converted into free THC."(4). This statement about the acidic precursor is also true regarding CBD, CBG, CBC, and THCV as well. The test kit not only reveals the cannabinoids in their neutral/active form, it reveals the acidic cannabinoids in their natural form as well. "Cannabinoids are enzymatically biosynthesized in the plant as their corresponding carboxylic acid forms (Taura *et al.*, 2007). Neutral cannabinoids are formed via decarboxylation (loss of CO₂) of the acidic cannabinoids during exposure to light, heat (e.g. smoking), or as a result of prolonged storage (Thakur *et al.*, 2005). Cannabinol (CBN) is the most common oxidative degradation product of Δ⁹-THC found in aged cannabis (Fig. 1) (McPartland and Russo, 2001)."(5).

Studies have determined that the acidic precursor of the neutral cannabinoids have important pharmacological properties as well. "The therapeutic value of the acidic cannabinoid THCA as an immuno-modulating agent has only been discovered very recently [Verhoeckx, 2006], and its effect has been patented. Examples like these show that the study of medicinal cannabis should include the whole array of cannabinoids present, as far as possible [McPartland, 2001]. The therapeutic potential of cannabinoids can be further clarified by pointing out the central physiological

importance of the endocannabinoid system, and its homology to, and interaction with the endorphin system. In addition to the role as modulator of food intake, the cannabinoid system is involved in several physiological functions and might be related to a general stress-recovery system. This variety of effects was concisely summarized by Di Marzo *et al.* [1998], who stated that cannabinoids help you 'feel less pain, control your movement, relax, eat, forget (posttraumatic), sleep, and protect your neurons.'"(6)

"The most commonly used method for analysis of cannabinoids is gas chromatography [Raharjo, 2004]. But because this method is based on heating of sample components, it converts acidic cannabinoids present in the sample into their decarboxylated counterparts. Therefore, GC analysis is not suitable for the determination of the authentic composition of the cannabinoids in the plant.'"(7)

"The primary constituent of cannabis, THC, is approved by the Food and Drug Administration (FDA) for oral administration as appetite stimulant in the case of anorexia associated with weight loss in patients with HIV/AIDS.'"(8) The other main cannabinoids have also been found to hold medicinal value. For example, "CBD provides antipsychotic benefits (Zuardi *et al.* 1995). It increases dopamine activity, serves as a serotonin uptake inhibitor, and enhances norepinephrine activity (Banerjee *et al.* 1975; Poddar and Dewey 1980). CBD protects neurons from glutamate toxicity and serves as an antioxidant, more potently than ascorbate and α -tocopherol (Hampson *et al.* 1998)."(9)

"The human body possesses specific binding sites on the surface of many cell types for cannabinoids, and our body produces several endocannabinoids, fatty acid derivatives that bind to these cannabinoid receptors (CB) and activate them. CB receptors and endocannabinoids together constitute the endocannabinoid system...To date two cannabinoid receptors have been identified, the CB₁, and the CB₂ receptor. They differ in signaling mechanisms and tissue distribution.'"(10)

"CB₁ receptors regulate pain perception, cardiovascular functions, gastrointestinal functions, steroid and hypothalamic hormone regulation, and reproduction. CB₂ receptors seem to be involved in immuno-regulatory functions because of the relatively high level of expression in immune cells and tissues as well as the effects observed by compounds that interact with CB₂ receptors. The endocannabinoid system undergoes tissue specific changes in response to pathological conditions (Di Marzo and De Petrocellis, 2006). The number of physiological functions mediated by the cannabinoid receptor system makes it a highly attractive system to study for medicinal purposes both with the use of natural ligands and synthetically derived ligands.....CBD is also now under considerable investigation as a medicinal agent due to its numerous pharmacological activities and unlike THC, CBD does not exhibit psychoactive effects. Experimental evidence indicates that CBD may be useful as a neuro-protective agent,

an axiolytic, an anti-psychotic, and an anti-emetic agent. CBD may also be useful against autoimmune diseases such as type-1-diabetes and rheumatoid arthritis” (Mechoulam et al., 2007). ...Numerous researchers cite the importance of the plethora of chemical components found in Cannabis and preparations derived from Cannabis and the potential implications it may have on not only improving the therapeutic effect of the drug for a particular condition but also for alleviating the potential side effects caused by the main active ingredients in Cannabis such as THC (McPartland and Pruitt, 1999; McPartland and Russo, 2001b).” (11)

“The use of herbal marijuana as a medicine is here to stay. Both its safety and efficacy have been well established through much anecdotal and clinical experience.”(12)

Sources:

- 1) <http://en.wikipedia.org/wiki/Cannabinoid>
- 2) Cannabis and Cannabis Extracts: Greater Than the Sum of Their Parts? John M. McPartland, Ethan B. Russo
- 3) Cannabis; extracting the medicine, Arno Hazekamp, pg 15 Thesis, Leiden University
- 4) Cannabis; extracting the medicine, Arno Hazekamp, pg 32 Thesis, Leiden University
- 5) A Qualitative and Quantitative HPTLC Densitometry Method for the Analysis of Cannabinoids in Cannabis sativa L.-Justin Fishedick
- 6) Cannabis; extracting the medicine, Arno Hazekamp, pg 19 Thesis, Leiden University
- 7) Cannabis; extracting the medicine, Arno Hazekamp, pg 92 Thesis, Leiden University
- 8) Review on clinical studies... Hazekamp/Grotenhermen pg 16
- 9) Cannabis and Cannabis Extracts: Greater Than the Sum of Their Parts? John M. McPartland, Ethan B. Russo, •2001 by The Haworth Press, Inc. All rights reserved
- 10)Cannabinoids and the Endocannabinoid System Franjo Grotenhermen
Cannabinoids Vol 1, No 1, September 17, 2006
- 11)The Cannalogues: Thesis-Justin Fishedick Leiden University 2008
- 12)On the Future of cannabis as medicine. Thesis: Lester Grinspoon-Harvard Medical School pg 1