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# A Preliminary Understanding of Cannabis Medicine and the Need for Further Characterization

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To date, the scientific study of the *Cannabis sativa* and *Cannabis indica* plants has been an arduous and complex process due to the limited availability of research funding and the extensive restrictions that have been in place for those trying to characterize the therapeutic properties of cannabis. Despite these hindrances, our understanding of this multifarious flora has grown significantly in the past 20 years. We have familiarized ourselves with the major constituents of interest in cannabis, the cannabinoids, which are responsible for acting upon the endocannabinoid system. Tetrahydrocannabinol (THC) has garnered the most attention primarily because of the psychoactive response that it elicits. However, THC is also a very robust molecule, acting as a powerful analgesic, muscle relaxant, anti-inflammatory, and anti-spasmodic [1]. There is also evidence that THC acts as a neurodegenerative antioxidant, in which it was effective in treating in a small clinical trial of agitated dementia patients with Alzheimer's disease [2]. Additionally, the propylated form of THC (THCV), induced weight loss, decreased body fat and serum leptin concentrations with increased energy expenditure in a murine study [3]. This particular study poses interest in creating molecules similar to THCV as potential dietary drugs. Homologous to THC is cannabidiol (CBD), which has been shown to modulate the psychoactive effects of THC, including anxiety, tachycardia, hunger, and sedation [4]. Recent cell studies indicate that CBD is effective *in vitro* against various lines of human tumor cells. Furthermore, CBD and the propylated analogue CBDV are effective anticonvulsants [5]. Cannabigerol (CBG) is the progenitor molecule of both THC and CBD and is effective in the treatment of inflammatory bowel disease (IBD) [6]. CBG is also a potent antiseptic and antibiotic, showing its powerful antibacterial activity against pathogens such as MRSA, a virulent form of *Staphylococcus aureus* [7]. During the oxidation of THC and CBD, cannabinol (CBN) is produced. CBN has demonstrated anticonvulsant [8] and anti-inflammatory [9] effects, in addition to reducing perceived thermal sensitivity, an attribute that could be utilized in the treatment of burns [10].

In addition to the cannabinoids, of which a small fraction of the hundreds of the putative cannabinoids are discussed here; cannabis also contains a myriad of terpene molecules. Terpenes are a diverse class of organic compounds that are primarily characterized as the flavoring agents of cannabis. In addition to taste and aroma, terpenes also provide a number of therapeutic benefits, ranging from anti-inflammatory to anti-microbial effects, even at parts-per-billion concentrations [11]. For example, D-limonene is responsible for the citrusy scent of some cannabis, such as the cultivar 'Tangerine Dream'. This fragrance is associated with stimulating and mood-elevating effects. Human clinical studies, in which hospitalized depressed patients were exposed with limonene aroma, demonstrated a significant anti-depressive effect [12]. Limonene has also been found to induce apoptosis of breast cancer cells [13] and successfully treat patients afflicted with gastro-oesophageal reflux [14]. α-pinene and β-pinene are also prominent cannabis terpenes that both exhibit act as anti-inflammatories [15], bronchodilators [16], and can act as acetylcholinesterase inhibitors aiding memory and mental sharpness [17]. Additionally, β-Myrcene and d-linalool are recognized as a sedative [18] and an anticonvulsant [19], respectively, whereas β-caryophyllene, caryophyllene oxide and nerolidol have antimalarial [20], antifungal [21], and anti-protozoal [22] properties, respectively.

Based on the available data it is easy to see the array of medical applications for this unique plant. However, the field of cannabis research is still in its embryonic stages due to the extensive restrictions and the societal stigmas that are associated with researching this Schedule 1 "drug". While we continue to reveal the therapeutic activity of the cannabinoids and terpenes molecules, there are other classes of compounds, such as the flavonoids and sterols, which have been relatively untouched scientifically. Furthermore, medical scientists need to collaborate more closely with analytical chemists to detect, quantify, and characterize novel cannabis constituents that are currently unresolved. Using high-resolution chromatography and mass spectrometry we can identify novel cannabis compounds and can elucidate their molecular structures through nuclear magnetic resonance (NMR) and/or X-ray crystallography. Furthermore, we can determine the effects that these molecules have *in vitro* and *in vivo*, through gene expression analysis and quantitative polymerase chain reaction (qPCR). As our understanding of the putative cannabis constituents continues to evolve, there is also a tremendous impetus for us to probe the unknown, given the medicinal potential of what has been uncovered by cannabis medicine to date. Just as a comprehensive effort was employed to account for and to characterize the genes within the human genome, so should a similar effort be commissioned to understand the full range of cannabis constituents. Such an effort, a Cannabinomics collective if you will, is the only way to unlock the therapeutic potential of this holistic medicine so that targeted cannabis-based therapies can be developed for specific illnesses. Cannabis is not a panacea; however, the growing body of scientific evidence indicates that the versatility of cannabis medicine is expanding.

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