Cannabis and Cannabinoids (PDQ®)

**Laboratory/Animal/Preclinical Studies**

**Antitumor Effects**
**Appetite Stimulation**
**Analgesia**

Cannabinoids are a group of 21 carbon terpenophenolic compounds produced uniquely by Cannabis sativa and Cannabis indica species.[1,2] These plant-derived compounds may be referred to as phytocannabinoids. Although delta-9-tetrahydrocannabinol (THC) is the primary psychoactive ingredient, other known compounds with biologic activity are cannabinol, cannabidiol, cannabichromene, cannabigerol, tetrahydrocannabivirin, and delta-8-THC. Cannabidiol, in particular, is thought to have significant analgesic and anti-inflammatory activity without the psychoactive effect (high) of delta-9-THC.

**Antitumor Effects**

One study in mice and rats suggested that cannabinoids may have a protective effect against the development of certain types of tumors.[3] During this 2-year study, groups of mice and rats were given various doses of THC by gavage. A dose-related decrease in the incidence of hepatic adenoma tumors and hepatocellular carcinoma was observed in the mice. Decreased incidences of benign tumors (polyps and adenomas) in other organs (mammary gland, uterus, pituitary, testis, and pancreas) were also noted in the rats. In another study, delta-9-THC, delta-8-THC, and cannabinol were found to inhibit the growth of Lewis lung adenocarcinoma cells in vitro and in vivo.[4] In addition, other tumors have been shown to be sensitive to cannabinoid-induced growth inhibition.[5-8]

Cannabinoids may cause antitumor effects by various mechanisms, including induction of cell death, inhibition of cell growth, and inhibition of tumor angiogenesis and metastasis.[9-11] Cannabinoids appear to kill tumor cells but do not affect their nontransformed counterparts and may even protect them from cell death. These compounds have been shown to induce apoptosis in glioma cells in culture and induce regression of glioma tumors in mice and rats. Cannabinoids protect normal glial cells of astroglial and oligodendroglial lineages from apoptosis mediated by the CB1 receptor.[10,11]

In an in vivo model using severe combined immunodeficient mice, subcutaneous tumors were generated by inoculating the animals with cells from human non-small cell lung carcinoma cell lines.[12] Tumor growth was inhibited by 60% in THC-treated mice compared with vehicle-treated control mice. Tumor specimens revealed that THC had antiangiogenic and antiproliferative effects.

In addition, both plant-derived and endogenous cannabinoids have been studied for anti-inflammatory effects. A mouse study demonstrated that endogenous cannabinoid system signaling is likely to provide intrinsic protection against colonic inflammation.[13] As a result, a hypothesis that phytocannabinoids and endocannabinoids may be useful in the prevention and treatment of colorectal cancer has been developed.[14]

Another study has shown delta-9-THC is a potent and selective antiviral agent against Kaposi...
sarcoma-associated herpesvirus (KSHV), also known as human herpesvirus 8.[15] The researchers concluded that additional studies on cannabinoids and herpesviruses are warranted, as they may lead to the development of drugs that inhibit the reactivation of these oncogenic viruses. Subsequently, another group of investigators reported increased efficiency of KSHV infection of human dermal microvascular epithelial cells in the presence of low doses of delta-9-THC.[16]

**Appetite Stimulation**

Many animal studies have previously demonstrated that delta-9-THC and other cannabinoids have a stimulatory effect on appetite and increase food intake. It is believed that the endogenous cannabinoid system may serve as a regulator of feeding behavior. The endogenous cannabinoid anandamide potently enhances appetite in mice.[17] Moreover, CB1 receptors in the hypothalamus may be involved in the motivational or reward aspects of eating.[18]

**Analgnesia**

Understanding the mechanism of cannabinoid-induced analgesia has been increased through the study of cannabinoid receptors, endocannabinoids, and synthetic agonists and antagonists. The CB1 receptor is found in both the central nervous system (CNS) and in peripheral nerve terminals. Similar to opioid receptors, increased levels of the CB1 receptor are found in sections of the brain that regulate nociceptive processing.[19] CB2 receptors, located predominantly in peripheral tissue, exist at very low levels in the CNS. With the development of receptor-specific antagonists, additional information about the roles of the receptors and endogenous cannabinoids in the modulation of pain has been obtained.[20,21]

Cannabinoids may also contribute to pain modulation through an anti-inflammatory mechanism; a CB2 effect with cannabinoids acting on mast cell receptors to attenuate the release of inflammatory agents, such as histamine and serotonin, and on keratinocytes to enhance the release of analgesic opioids has been described.[22-24]

**References**

3. National Toxicology Program.: NTP Toxicology and Carcinogenesis Studies of 1-Trans-Delta(9)-Tetrahydrocannabinol (CAS No. 1972-08-3) in F344 Rats and B6C3F1 Mice (Gavage Studies). Natl Toxicol Program Tech Rep Ser 446 (): 1-317, 1996. [PUBMED Abstract]