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Opinion Article

Cannabinoids and their Medicinal use in Man and Animals (Plenary Session)

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Introduction

The use of Cannabis spp. and Cannabis-derived products is increasing. The legal human "medicinal marujana" industry was estimated in the Economist Magazine in 2022 to be worth US$ 4.9 billion and is predicted to increase to US$ 47 billion within 6 years. In some countries it is the most rapidly growing agribusiness sector and of recent years. Many countries have legislation permitting medicinal use of cannabis derived products in humans, and some have legalised recreational use. Conclusive controlled double-blinded randomised efficacy studies of adequate power are lacking in all species.

As cannabis-derived products have become more widely available therapeutic applications in humans have expanded vastly and veterinarians have also seen more animal use and concomitant increases of toxicosis. There are thousands of chemovars (strains) containing varying combinations of cannabinoids, terpenes, flavonoids ad other substances which are pharmacologically active. The three main species of Cannabaceae are: C. indica, C. sativa (includes hemp) and Ruderalis spp. Cannabis was used medicinally by the Ancient Greeks for dressing wounds, for nosebleed and tapeworms in humans and horses. Cannabis was used until more recent centuries in medications designed to treat colic and stimulate weight gain in horses.

Hemp (Cannabis sativa) is legally defined in the United States (US) and European Union (EU) as any part of the cannabis plant that contains less than or equal to 0.3% THC (delta-9-trans tetrahydrocannabinol or tetrahydrocannabinol) on a dry weight basis. Hemp has traditionally been farmed for industrial uses (e.g., textiles, paper, biodiesel, constructions materials), as well as for food (hemp seeds and hemp seed oil). Typically, hemp contains high amounts of non-psychoactive cannabinoids. In the US, "hemp" is not legally recognized as a dietary supplement for humans or animals.

The term "Marijuana" is typically used for the psychoactive dried resinous flower buds and leaves of the cannabis plant (C. sativa or C. indica) but can refer to any part of the cannabis plant that contains greater than 0.3% of THC. Marijuana is commonly smoked, vaped, or ingested orally. Sublingual oral preparations are convenient for concentrating, titrating and individualizing doses.

Over 480 cannabinoids and other substances have been isolated. The amount of each substance depends on the subspecies, the age of the plant, the time of year the leaves were harvested, the way they have been dried, and other factors including lighting regimen and watering cycles. Cannabidiol (CBD) is a non-psychoactive lipid cannabinoid and has been used in human medicine to mitigate anxiety, improve appetite, relieve nausea, control seizures, and assist in the management of sleep disorders. THC appears to have an allosteric effect modulating and often increasing the efficacy of endocannabinoid receptors which has been termed the "entourage effect" even at levels of THC that are not overtly psychoactive.

Human use with combined THC: CBD has expanded into chronic pain management, opioid addiction withdrawal, insomnia, post-traumatic stress and other forms of chronic anxiety, muscle spasm and other uses. The art of prescribing generally involves attention to the relative proportions of THC: CBD, timing and the overall dose for the right constellation of indications as well as awareness of mental health history and the potential impact on mental health. Starting low and building up to the point where receptor occupation may allow dose reduction after a period of weeks is typical prescribing practice.

The US Agricultural Improvement Act of 2018 (2018 Farm Bill) authorized the production of hemp and removed hemp and hemp seeds from the Drug Enforcement Administration's (DEA) schedule of Controlled Substances (defined as Cannabis sativa with ≤0.3% THC on a dry weight basis). As a result, hemp is no longer subject to the restrictions of the US Controlled Substances Act. Many manufacturers have interpreted this to mean that hemp products can now be marketed for human or animal use with no further federal regulation, which is not the case. As for the European industry, many cannabis products in the US are marketed with claims of therapeutic efficacy without having gone through approval process to substantiate those claims and are therefore being marketed illegally.

The safety of THC in foodstuffs was reviewed in 2015 by the European Food Safety Authority (EFSA) which concluded that consuming food containing THC at greater than 1 µg/kg body weight in one sitting, or in a day, may have adverse effects. Following a request from the European Commission, the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP of EFSA) delivered a scientific opinion on the safety of hemp (Cannabis genus) for use as animal feed. Different types of feed materials may be derived from the hemp plant: hemp seed meal/cake, hemp seed oil and whole hemp plant), flour (ground dried hemp leaves) and hemp protein isolated from seeds. Hemp seed and hemp seed cake may be used as feed materials for all animal species and EFSA defined maximum incorporation rates in the complete feed per species e.g., 3–7% in poultry, 2–5% in pigs for hemp seed and hemp seed cake, 5% in ruminants for hemp seed cake and 5% in fish for hemp seed. Feeding efficacy trials demonstrate that hemp and its derivates are a good source of crude protein and essential fats. There are many companies in the EU marketplace today selling "nutritional supplement" cannabis-derived products for dogs, cats, and horses, some of which make therapeutic claims. These products have been promoted as aids for itching, anxiety, nausea, poor appetite, seizures, cancer, digestive problems, inflammation, immune disease, and reduced mobility due to joint pain in animals. Whilst early data may support some of these claims, it is against the law to make therapeutic feed claims for nutritional products. Under the EU Regulations, products for which therapeutic claims are made must firstly be approved by a National Medicinal Health Product Agency (i.e., national competent authority) or European Medicines Agency (EMA), to become a medicine and be legally manufactured and marketed with supporting scientific data on the quality, efficacy and safety of products. Veterinarians should not offer scientific advice on the effectiveness of these feed products to treat disease, as they are not approved medicines and such claims are (a) illegal (b) unproven and (c) potentially unsafe.

Unlike in the EU, US regulations pertaining to "dietary supplements" for humans do not apply to products intended for use in animals. Products marketed as animal supplements are accordingly regulated as either foods or drugs (not as dietary supplements) depending on their intended use. If their intended use is therapeutic, as indicated by a therapeutic claim or the circumstances of their use, such products are regulated as drugs and must meet US Food and Drug Administration (FDA) approval to be legally marketed; otherwise, they are regulated as foods. However, under US federal law, foods cannot contain substances that are the active ingredients in approved pharmaceuticals. US federal authorities have concluded that, because THC and CBD are active ingredients in approved drugs, they cannot be incorporated into food. Human dietary supplements also cannot contain substances that are the active ingredients in approved pharmaceuticals, including THC and/or CBD.

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