



AVICANNA™

MEDICAL CANNABIS INSIGHTS

WHAT'S NEW IN THE SCIENCE OF MEDICAL CANNABIS

CANNABINOID APPLICATIONS IN EPILEPSY MANAGEMENT

AVICANNA HIGHLIGHT

This newsletter explores cannabinoid applications in the treatment of epilepsy. Currently, there is significant evidence supporting medical cannabis as an adjunctive solution in epilepsy aside other treatments, however, there remains a paucity for research that proves cannabinoid-based therapies to be both independent and sustainable solutions to this disorder.

In this edition, we highlight a recent publication that reviews the potential for cannabinoid treatment in neurological disorders. We also delve into an expert perspective from Dr. Amza Ali on cannabinoid research and their applications in epilepsy specifically. Dr. Ali is the President of the Epilepsy Society of the Caribbean and a Fellow of the American Epilepsy Society and has received international recognition for his work in this field.

WHAT'S NEW?

PUBLICATION SPOTLIGHT

Safety, efficacy, and mechanisms of action of cannabinoids in neurological disorders

Daniel Friedman, Jacqueline A French, Mauro Maccarrone
Lancet Neurology, May 2019, Volume 18, Issue 5, pp 504-512

The recent success of the randomized controlled trials of plant-derived cannabidiol (CBD) have provided evidence of their anti-seizure and neuroprotective effects in cases of childhood-onset epilepsies (i.e. Lennox-Gastaut and Dravet Syndrome). These results have significantly increased the interest in the use of cannabinoids for the treatment of epilepsy and other neurological disorders. Efforts towards a better understanding of the pharmacokinetic challenges of oral cannabinoids and their mechanisms of action for exerting their therapeutic effects in neurological disorders are discussed as a "Personal View" in the article by Friedman et al. We chose to review this article as Avicanna is preparing formulations and designing controlled clinical trials for neurological disorders including epilepsy. Furthermore, this article provides a reputable review as it was written by distinguished scientists who only discussed well-controlled clinical studies that used standardized, regulated medical cannabis products.



Image of trichome taken under 20x magnification at Avicanna's analytical laboratory in Santa Marta, Colombia

Phytocannabinoids (plant-derived cannabinoids that are biologically active and include CBD and THC) have distinct differences in their chemical structure yet share 3-dimensional features that are common with endocannabinoids (endogenous cannabinoids produced within the human body) that allows them to bind to the same target receptors. THC for example, is known to bind and activate G-protein-coupled receptors CB1 and CB2, an interaction that can also be blocked by CBD via other cellular targets. Despite the growing knowledge, the precise molecular mechanism of phytocannabinoids is still unknown. This article highlights that the anti-seizure effects attributed to CBD have yet to be associated to its interactions with the endocannabinoid system or via interactions with non-selective cation channels, presynaptic G-protein receptors, or other targets that influence synaptic transmission. Although phytocannabinoids have potential for many therapeutic applications, without a complete understanding of these cellular and molecular mechanisms, they may lead to unpredictable and adverse effects.

The authors provided a summary of three large clinical studies that evaluated the safety and efficacy of CBD in Dravet Syndrome or Lennox-Gastaut syndrome, and briefly described several smaller open-label studies in Doose syndrome, Aicardi syndrome, tuberous sclerosis complex, drug resistant focal epilepsy and infantile spasms. Further discussions surrounding the challenges of assessing efficacy highlighted that CBD, as a potent hepatic enzyme inhibitor, can cause clinically significant drug interactions by influencing the metabolism of antiepileptic agents such as the benzodiazepine clobazam. Although the future of phytocannabinoid treatment in neurological disorders is promising, larger well controlled studies are still needed in order to recommend cannabinoids as second-line therapies for drug-resistant epilepsies.

EXPERT PERSPECTIVE

By: Dr. Amza Ali, *MBBS, DM, MSc, FRCP, FACP, FAAN, FAES, MBA*
Specialty Certification in Neurology (UK), Diplomate, American Board of Clinical Neurophysiology (ABCN)

Over the past few years we have seen a remarkable phenomenon: the resurgence of interest in derivatives of an ancient plant, cannabis, for the modern treatment of a number of diverse medical problems, including the medical disorder known as epilepsy. This term encompasses a markedly heterogeneous group of conditions all characterised by a tendency for recurrent unprovoked seizures, due to these abnormal and excessive electrical discharges from the brain. With presently 30% of patients refractory to all currently available medical treatments there is a great need for more research to find agents, preferably with novel mechanisms of action that can be used as adjuncts to existing treatments or even as monotherapy.



The recent publications of nearly pure non-psychoactive CBD in the treatment of the severe childhood epilepsy syndromes demonstrate its therapeutic efficacy even in these most difficult of epilepsies. A perplexing question however arises in there being such significant efficacy in Dravet Syndrome. This disorder is due to a single gene defect of a sodium channel subunit of inhibitory interneurons that results in neuronal hyperexcitability. There is however no evidence of endocannabinoid regulatory activity on these neurons. Thus, CBD's apparent efficacy in treating Dravet Syndrome cannot therefore be easily explained. Questions remain regarding the mechanism of CBD's true therapeutic efficacy in these childhood disorders, in view of its inhibitory effect on liver enzyme systems. This results in marked increases in serum levels of some standard anti-epileptic agents, particularly benzodiazepines, often used to treat these patients. Ultimately, only high quality basic science and clinical research will answer these questions and explain the true therapeutic potential of CBD in the treatment of epilepsy. Much work also remains to better characterise the anti-epileptic potential of many other cannabinoids including THC and CBG for example, as well as the interesting field of terpenes which themselves have many potential anti-epileptic and even anti-epileptogenic characteristics.

The stakes are high: epilepsy is not a benign disorder. Approximately 1 million people with epilepsy in North America are refractory to currently available medical treatments, as are tens of millions of other people worldwide. Many will die as a consequence of their seizures or are socially marginalised and made economically dependent because of pervasive stigma. In many countries the high social acceptability of cannabis and its derivatives has meant that many patients, or caregivers of under-aged patients, with epilepsy have been experimenting with highly variable and unstandardized preparations to treat their epilepsy symptoms or to lessen the side effects of their standard anti-epileptic drugs treatments. With rapid changes in the global regulatory landscape, developing standardized, safe, effective treatments derived from this widely accepted plant represents a unique clinical opportunity to change the lives of millions.

Provided by Avicanna Inc.

Avicanna is a Canadian biopharmaceutical corporation focused on the development, manufacturing and commercialization of plant-derived cannabinoid-based products through its two main business segments, cultivation and research and development. Avicanna's research and product development activities are primarily conducted out of Toronto, Canada including its headquarters in the Johnson & Johnson Innovation Centre, JLABS @ Toronto and the University of Toronto's Faculty of Pharmacy. Avicanna's scientists and researchers collaborate on the optimization and improvement of Avicanna's products. Avicanna's vertically integrated and international operations also include two majority owned cannabis cultivation subsidiaries - Sativa Nativa S.A.S. and Santa Marta Golden Hemp S.A.S., both located in Santa Marta, Colombia. Avicanna's scientists and researchers collaborate on the optimization and improvement of Avicanna's products ranging from cosmetics to phyto-therapeutics to pharmaceutical preparations.

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