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Research Highlight

# Antiepileptic activity and potential mechanism of full-spectrum hemp extract

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ABSTRACT

Epilepsy is the fourth most common neuropsychiatric disorder. Although the approval of Epidiolex has ignited hope for patients, there is still a large gap in the field of anti-seizure research. The effect and underlying mechanism of full-spectrum hemp extract (HE) remains unclear. Here this study investigated the anti-seizure effect of HE on seizure models. The results showed that HE significantly reduced seizure susceptibility and prolonged seizure latency with better pharmacokinetic performance compared to CBD. This article then further explored the anti-seizure active components and their possible mechanism in HE. The results indicated that cannabichromene (CBC) and cannabinol (CBN) were involved in the anti-seizure process, especially CBC showed a strong allosteric enhancement effects on CBD binding site of the GABAA receptor, which implied that the GABAA receptor seemed to be the primary anti-epileptic target of HE. This article not only presents the great potential of HE as a candidate for new anti-epileptic drugs with less psychoactive, but also provides a valuable contribution to subsequent mechanism research and drug development on epilepsy.Abstract: Epilepsy is the fourth most coneuropsychiatric disorder. Although the approval of Epidiolex has ignited hope for patients, there is still a large gap in the field of anti-seizure research. The effect and underlying mechanism of full-spectrum hemp extract remains unclear. Here this study investigated the anti-seizure effect of HE on seizure models. The results showed that HE significantly reduced seizure susceptibility and prolonged seizure latency with better pharmacokinetic performance compared to CBD. This article then further explored the anti-seizure active components and their possible mechanism in HE. The results indicated that cannabichromene and cannabinol were involved in the anti-seizure process, especially CBC showed a strong allosteric enhancement effects on CBD binding site of the GABAA receptor, which implied that the GABAA receptor seemed to be the primary anti-epileptic target of HE. This article not only presents the great potential of HE as a candidate for new anti-epileptic drugs with less psychoactive, but also provides a valuable contribution to subsequent mechanism research and drug development on epilepsy.

Epilepsy is a chronic disorder characterized by sudden, abnormal discharges of neurons in the brain, leading to temporary brain dysfunction. According to the World Health Organization, epilepsy accounts for approximately 1% of the global burden of disease, making it the fourth most common neuropsychiatric disorder after depression, alcohol dependence, and cerebrovascular diseases, and one of the most prevalent neurological disorders [1].

Cannabis has been used to treat epilepsy for thousands of years. There are over 100 phyto-cannabinoids in cannabis, with the two primary components, Δ9-tetrahydrocannabinol (Δ9-THC) and cannabidiol (CBD) [2]. The use of Δ9-THC in medical treatment is limited due to its strong psychoactive and addictive properties. In contrast, CBD is non-addictive, presenting significant potential for therapeutic development. On June 25, 2018, the U.S. FDA approved an oral solution of CBD (trade name Epidiolex®) for the treatment of seizures associated with Dravet syndrome and Lennox-Gastaut syndrome in patients aged two years and older [3].

Industrial hemp, a unique variety of cannabis, contains less than 0.3% THC and has a higher concentration of CBD in its extracts. Due to these characteristics, hemp extract (HE) has gained widespread attention as a nutritional supplement among different populations. Previous studies suggest that HE has potential in alleviating chronic pain and im-

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proving cardiovascular health [4,5]. However, the neuroprotective effects of HE against epilepsy have not been widely studied. Based on this background, Huang et al. [6] employed various experimental methods to explore the anti-epileptic activity of HE and its possible mechanisms, providing data to support the discovery of anti-epileptic drugs and the investigation of HE.

Huang et al. reported that HE reduced seizure severity and prolonged seizure latency in mice with acute epilepsy, and showed improved absorption, enhanced distribution and prolonged elimination process in SD rats, exhibiting similar anti-seizure activity and better bioavailability compared to CBD. Then this article evaluated the anti-epileptic activity of five other phyto-cannabinoids in HE, whose results indicated that cannabichromene (CBC) and cannabinol (CBN) contribute to the anti-seizure process of HE.

The $GABA_A$ receptor is currently considered as one of the main anti-epileptic targets [7], and previous studies have reported that CBD enhances the allosteric modulation of the $GABA_A$ receptor [8]. Therefore, the researchers assessed the allosteric modulation effects of various phyto-cannabinoids in HE on the $GABA_A$ receptor. The findings showed that CBC exhibited strong allosteric enhancement effects on CBD binding site of the $GABA_A$ receptor, rather than other classic anti-epileptic targets such as KCNT1, Nav1.2, and Nav1.6 [9]. According to the results, the $GABA_A$ receptor seemed to be the primary anti-epileptic target of HE.

Huang's work comprehensively demonstrates the great potential of hemp extract as a candidate for new anti-epileptic drugs with less psychoactive than cannabis and discovers the mechanism of phyto-cannabinoids, such as CBC, which is non-addictive and exhibits positive allosteric modulating effects on GABAA receptor. This article not only presents a new opportunity for the development of anti-epileptic drugs with stronger safety and higher bioavailability, but also delves into its underlying mechanism, providing a valuable contribution to subsequent mechanism research and drug development on epilepsy.

## Declaration of competing interest

The authors declare that they have no conflicts of interest in this work.

## References

[1] A. Ali, Global Health: Epilepsy, Semin. Neurol. 38 (2) (2018) 191–199.
[2] Z. Breijyeh, B. Jubeh, S.A. Bufo, et al., Cannabis: A toxin-producing plant with potential therapeutic uses, Toxins (Basel) 13 (2) (2021) 117.
[3] D.A. Moss, M.K. Hawks, M.J. Snyder, et al., Integrative medicine: Cannabis and cannabis-related drugs, FP Essent 505 (2021) 28–34.
[4] A. Capano, R. Weaver, E. Burkman, Evaluation of the effects of CBD hemp extract on opioid use and quality of life indicators in chronic pain patients: A prospective cohort study, Postgrad. Med. 132 (1) (2020) 56–61.
[5] D. Rodriguez-Leyva, G.N. Pierce, The cardiac and haemostatic effects of dietary hempseed, Nutr. Metab. (Lond) 7 (2010) 32.
[6] Z.H. Wang, H.R. Zheng, H. Yang, et al., Cannabichromene from full-spectrum hemp extract exerts acute anti-seizure effects through allosteric activation of GABAA receptors, Fund. Res. 4 (5) (2024) 1357–1364.
[7] G.J. Sills, M.A Rogawski, Mechanisms of action of currently used antiseizure drugs, Neuropharmacology 168 (2020) 107966.
[8] T. Bakas, S. Van Nieuwenhuijzen P, S.O. Devenish, et al., The direct actions of cannabidiol and 2-arachidonoyl glycerol at GABAA receptors, Pharmacol. Res. 119 (2017) 358–370.
[9] J. Oyrer, S. Maljevic, I.E. Scheffer, et al., Ion channels in genetic epilepsy: From genes and mechanisms to disease-targeted therapies, Pharmacol. Rev. 70 (1) (2018) 142–173.

## Author profile

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