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Perspective

Cannabidiol: The "Trojan Horse" of our times

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Abstract

The spread in humans is considered one of the most studied issues among other illicit products. Nevertheless, cannabis/cannabinoids' safety remains unsolved and controversial. Cannabidiol, a component of recreational cannabis, is now found in a multitude of legal or illegal medicinal cannabis preparations, dietary supplements, foods, cosmetics, etc., in uncontrollable combinations with the psychoactive tetrahydrocannabinol (THC). Despite the conflicting findings of many research groups regarding the safe administration of cannabinoids in general, in all age/race groups, these limitations have not been particularly emphasized. Fortunately, the significant increase in its consumption in the elderly has led reliable international organizations to strongly question the long-term cannabidiol toxicological "immunity", highlighting these risks by classifying it as a particularly *CMR substance* (ANSES). Serious elderly problems have also been recently recorded, especially at dosages greater than 2mg/day of Cannabidiol (EFSA). In this short article, some of the Cannabidiol receptors, their potential therapeutic applications, side effects, and their interactions with prescription drugs/comorbidities are listed.

In conclusion, Cannabidiol must immediately be addressed by law, as a multi-potent and not harmless drug, with the aim of an effective measure against the public and individual health "invisible siege", on a global scale, otherwise its negative cost outweighs any healing benefit.

Introduction

It is well known that the intense pharmacological interest in phytocannabinoids, such as cannabidiol (CBD), is due lately to the discovery of the endocannabinoid system (ECS) in the human body, which supports many physiological processes and has regulatory effects on a variety of seemingly distinct disorders and is mainly associated with G protein-coupled cannabinoid receptors named CB1 and CB2 [1,2].

It has also been experimentally proven that CBD has physicochemical affinity with more than 65 molecular targets, e.g., the serotonin 1A (5-HT1A) receptor, the G protein-coupled receptor GPR55, the transiently active vanilloid receptor 1 (TRPV1), the ETN1-type nucleoside transport protein, the nuclear factor erythroid 2-related factor 2, the T-type calcium channels, and the 1 anion channel VDAC1. CBD is the main ingredient in many free-market products, mostly sold without any quality control [2,3].

Based on studies to date, CBD, which is not "harmless," is a powerful bioactive molecule. CBD, acting on a multitude of bodily receptors, beyond competition in the ECS, exhibits several controversial actions (antioxidant, anti-inflammatory, analgesic, etc.), alleviating thus certain symptoms of

chemotherapy (nausea, pain) and certain neurodegenerative diseases [4].

Unfortunately, the ever-increasing legal/illegal circulation and overdose use of products/preparations containing CBD has created considerable confusion not only among health scientists but also among consumers. In the July 2025 issue of *JAMA*, cannabis use has reached a new record high of 4.8% since 2021 among people aged 65 and older [5].

In the US, recreational cannabis is now legal in 24 states, while medical use is legal in an additional 15. In this group of older adults, who often take multiple prescription medications, several interactions with cannabinoids (CBD/THC) can cause unpredictable effects, including the risk of dangerous falls. On the other hand, serious interactions of CBD have already been observed with comorbidities, as well as interactions with widely prescribed drugs, such as anticonvulsants [6], antihypertensives, antiemetics, simple sedatives, antibiotics, steroids, anticancer drugs, etc. [7].

These adverse effects are due to the competitive interference of CBD with isoforms of hepatic drug-metabolizing enzymes CYP [3,8], the cellular drug transporter p-glycoprotein, as well as the accumulating effect of cannabinoids on the addiction protein ΔFosB, which is also associated with biological

phenomena as diverse as memory formation, drug addiction, stress resilience, and immune cell activity. Δ FosB is a highly stable transcription factor that turns specific genes on or off that accumulates in the brain's reward circuitry in response to chronic drug use, including cannabinoids [9].

Lately, the French agency ANSES has proposed a new classification of CBD as a CMR substance (Carcinogenic, Mutagenic or Toxic to Reproduction) according to the CLP Regulation (EC 1272/2008). The proposal is currently in public consultation until 16 May 2025, which could mark a turning point in CBD regulation. Thus, the indiscriminate use of CBD forced the EFSA to recently release the urgent warning document: *"The European Food Safety Authority (EFSA) has launched a public consultation process on its updated opinion on the safety of cannabidiol (CBD) as a 'novel food' [10]. The preliminary document, published on September 9, provisionally establishes a daily dose considered safe at just 2 milligrams per day for a 70-kg adult, a value on which there is no consensus.* The available literature from human and animal studies indicated primarily potential effects of CBD on the liver, gastrointestinal tract, endocrine system, nervous system, and psychological functions. In addition, several animal studies triggered concerns of reproductive toxicity, and the extent to which this could occur in humans needed further clarification" [11]. Since then, EFSA has consistently monitored and assessed newly available data and has endeavoured to update its statement on the safety of CBD as a NF pursuant to Regulation (EU) 2015/2283 by the end of 2025.

Based on the above remarks, Cannabidiol should be treated by the competent regulatory authorities as a multi-potential drug, which involves strict quality control, titration, synergy studies, and clinical intervention studies, to identify promptly any adverse effects from chronic cumulative action and interactions per patient and co-administered drug or morbidity [12]. The implementation of the above measures is a one-way street, because otherwise unauthorized Cannabidiol preparations could, if it has not already done so, lead to a modern health and social "Trojan horse".

Conclusion

Cannabidiol has quickly shifted from a niche chemical to a common ingredient in both health and everyday products. While purified and regulated formulations have shown benefits in certain clinical settings, the growing availability of over-the-counter options raises serious safety concerns. There are significant risks, especially for older adults who take multiple medications, due to variations in product composition, unclear dosing, and the potential for serious drug interactions with anticancer drugs, particularly from cytochrome P450 inhibition.

Recent assessments by regulatory agencies reveal ongoing concerns about liver, hormonal, and reproductive effects, highlighting that CBD is not harmless. In today's mixed regulatory environment, it is more difficult to monitor safety and ensure quality.

A careful, evidence-based plan that focuses on standardizing manufacturing, clear labeling, and ongoing clinical research is needed. CBD should be regarded as a biologically active substance that requires close monitoring to ensure that its health benefits do not bring additional risks to public health.

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