International Journal of Medicine and Medical Research

Journal homepage: https://ijmr.com.ua/
Volume 9, No. 1. 2023

UDC 615.3
DOI: 10.61751/ijmmr.2413-6077.2023.1.47

Article's History:
Received: 17.02.2023; Revised: 26.04.2023; Accepted: 30.05.2023

Pharmacological and morphological features and socioeconomic aspects of cannabidiol: A literature review

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Abstract. The relevance of detailed analysis of the available scientific research on the effects of cannabidiol on the human body is determined by the growing popularity of the non-psychoactive substance in cannabis products as a medicine. The research aimed to collect and systematise information about the positive and negative effects of cannabidiol, as well as the possibilities of its use in medicine. An analysis of 3375 scientific articles, publications and reports was conducted, of which 68 were selected that best met the terms of the request. The collected data was summarised and presented in a structured format. The results of the review indicate the remarkable pharmacological potential of cannabidiol, which can be used as a promising therapeutic agent in various medical fields. In the studies reviewed, cannabidiol showed anticonvulsant and antiepileptic effects, as well as a positive impact on drug substitution programmes. However, the possibility of negative reactions and potentially harmful effects of cannabidiol was also noted: it can lead to the development of psychological and physical dependence; increases the risk of physiological disorders, including the impact on spermatogenesis and disruption of the female microflora; affects behaviour and leads to developmental abnormalities. The effects of cannabidiol on the human body are still not well understood, and its distribution in the absence of sufficient legal regulation may pose a risk to the health and safety of consumers. Understanding all aspects of cannabidiol use will ensure proper management of its use and development of the relevant legislative framework, as well as facilitate further research and development of new drugs based on this plant extract

Keywords: cannabis; toxicology; law; epilepsy; chronic pain; generalised anxiety disorder

Introduction

Cannabidiol, as one of the active cannabinoids in cannabis plants, is finding more and more applications in medicine, but its potential benefits and impact on various aspects of human functioning remain a subject of debate in scientific circles. Data on cannabinol is contradictory, and its legality and safety are being questioned globally. Understanding the potential risks, side effects and interactions with other medicines is critical to ensuring the safety and efficacy of cannabidiol in clinical practice.

Many studies have already been conducted on the effects of cannabidiol on the human body. Since 2018, Ukrainian scientists have been actively working on this issue and have reached certain conclusions. For example, G.V. Zaychenko & P.V. Simonov [1] investigated the positive properties of cannabinoids associated with the activation of CB2 receptors. Activation of CB2 receptors had a cardioprotective effect, reduced cerebral ischaemia, suppressed inflammation, oxidative-nitrosative stress and cell death, slowed the progression of atherosclerosis and had a nephroprotective effect. By contrast, activation of CB1 receptors in vascular and cardiac tissues contributed to the development of cardiovascular disease through oxidative and nitrosative stress and protein kinase activation. B. Hinz & R. Ramer [2] also demonstrated the probable carcinogenic properties of cannabinoids, which showed carcinogenic effects both when used alone and in combination with

Suggest Citation:
Hasiuk OP. Pharmacological and morphological features and socioeconomic aspects of cannabidiol: A literature review. Int J Med Med Res. 2023;9(1):47–59. DOI: 10.61751/ijmmr.2413-6077.2023.1.47
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other anticancer drugs. The authors noted that this area required further study. O. Sulaieva *et al.* [3] also found that CB2 receptors may be involved in the malignant transformation and progression of non-small cell lung cancer (NSCLC). However, some issues remained unexplored. For example, data on the effects of cannabidiol on the nervous system and its potential role in the treatment of mental and neurological diseases are limited.

Regarding the market of cannabinoids, and cannabidiol in particular, in Ukraine, scientists N. Aliekperova *et al.* have written [4]. Their study noted serious prospects for the development of the cannabidiol market in Ukraine. The authors pointed out that interest in cannabidiol products was growing, and this could create new opportunities for the development of the medical and pharmaceutical industries. According to the researchers, the Ukrainian market had significant potential for the production and consumption of cannabidiol-based products, including oils, creams, and other medicines. The authors also stressed that the development of the cannabidiol market could have a positive impact on the country's economy, providing new jobs, attracting investment, and stimulating the development of industries related to the production of cannabidiol products.

N. Aliekperova *et al.* [5] also studied the attitudes of Ukrainian pharmacists towards the legalisation of medical cannabis and cannabidiol-based products. The study showed that only half of the professionals supported the legalisation of these products. Other participants in the experiment expressed some doubts and reservations related to the safety, dosage, and quality of cannabidiol products. The safety of this plant extract has already been the subject of debate, and in some cases, its effectiveness has been questioned [6]. This indicated the need for further research to determine the efficacy and safety of cannabidiol in medicine. The purpose of this study was to review the pharmacological profile of cannabidiol and its effects on various body systems, as well as to consider possible mechanisms of action of this compound, especially in the context of the treatment of mental and neurological diseases.

In this study, a literature review of relevant scientific sources and publications was conducted through a systematic analysis of scientific sources to identify trends, develop key findings, and formulate scientific recommendations. Scientific databases such as PubMed, Google Scholar, Scopus, and Cochrane Database of Systematic Reviews were used to collect relevant scientific publications. The search for scientific sources was conducted using keywords related to the research topic, such as "cannabidiol", "cannabidiol toxicity", "cannabidiol treatment", "cannabidiol side effects", "cannabidiol pharmacy", "cannabidiol prevalence", "cannabidiol harm", "cannabidiol therapeutic properties", "cannabidiol marketing", "cannabidiol legal status".

The selected scientific sources were read in detail, critically comprehended, and analysed to collect information related to the research topic, and the quality of the sources was assessed, including verification of the authors' credibility, research methodology and availability of substantiated evidence. Key aspects, conclusions and recommendations related to the topic were identified. Data from scientific sources were organised and summarised for further analysis. Information from the sources obtained was systematised, summarised, and presented in the literature review.

Analysis of Chemical, Pharmacodynamic and Pharmacokinetic Features and Properties of Cannabidiol

Active research on cannabidiol began in 2016. The main topics investigated included cannabidiol's properties, its interaction with various drugs, pharmacological profile, health effects, etc (Fig. 1).

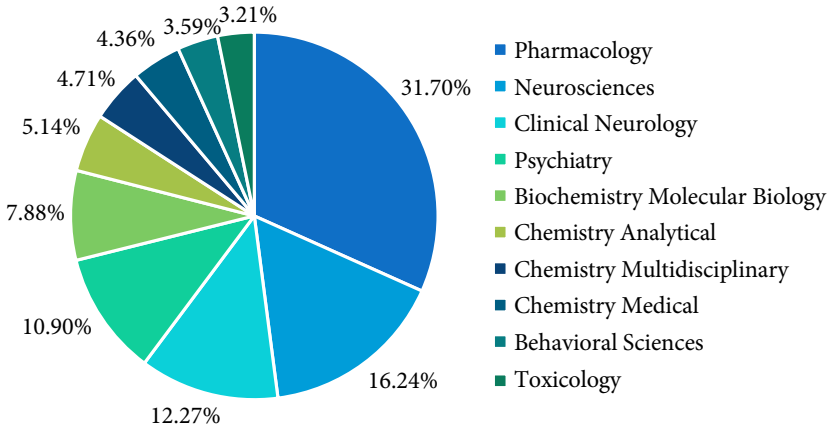
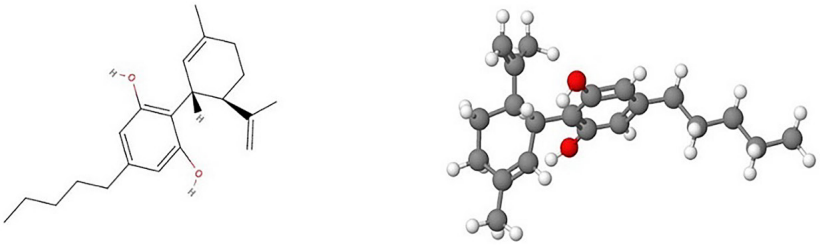


Figure 1. Visualisation of research areas on the effects of cannabidiol
Source: compiled by the author based on [7]

The results showed that cannabidiol was a complex research object that was studied concerning various aspects of health and disease. However, it was evident that the harmful effects and toxicity of cannabidiol were not sufficiently studied (only 3.21%), and therefore further research was needed [7].

The cannabis plant, "marijuana", or "cannabis" has been used for many years as a medicine to relieve pain and

seizures. Cannabis contains approximately 540 naturally occurring compounds, including more than 100 that have been identified as phytocannabinoids due to their common chemical structure [3]. The predominant psychotropic component is Δ9-tetrahydrocannabinol (Δ9-THC), while the main non-psychoactive ingredient is cannabidiol (CBD). These compounds are partial agonists or antagonists of the prototypical cannabinoid receptors, CB1 and CB2. Δ9-THC and CBD can act as analgesics, antiemetics, anti-inflammatory agents, anticonvulsants, and as protective agents against neurodegeneration. However, there has been a lack of well-controlled, randomised clinical trials to provide evidence of the effectiveness of Δ9-THC or CBD as therapeutic agents, as well as to fully understand their effects on the human body. The legalisation of cannabis for medicinal and recreational use in some regions would allow for the necessary research on its pharmacokinetics and pharmacology [8]. Particular attention has been paid to the non-psychoactive substance in cannabis products – CBD. CBD was first isolated from cannabis extracts by R. Adams *et al.* in 1940 [9]. Cannabidiol is a cyclohexene substituted with a methyl group at position 1, a 2.6-dihydroxy-4-pentylphenyl group at position 3, and a prop-1-en-2-yl group at position 4 (Fig. 2).



a b

Figure 2. Molecular structure of cannabidiol
Notes: a – structural model; b – 3D model of a structure
Source: [10]

At room temperature, cannabidiol is a colourless crystalline solid [11]. In the industry, cannabidiol can be produced in dry form, oil, capsules, and supplements. M. Premoli *et al.* [12] report that cannabidiol has a low ability to bind to the CB1 and CB2 cannabinoid receptors, although it acts as an agonist/antagonist of these receptors. The main effect of CB1 and CB2 receptor antagonism is to reduce the binding capacity of tetrahydrocannabinol (THC) and its related isomers [13]. T. Bosquez-Berger *et al.* [14] also studied its ability to exhibit partially antagonistic properties to serotonin receptors. Cannabidiol is also an allosteric opioid receptor modulator. The pharmacological effects of CBD may include peroxisome proliferator-activated receptor (PPARγ) agonism, inhibition of voltage-dependent cation channels, and intracellular calcium release [15].

L.J. Martin *et al.* found [16] that cannabidiol has a multifaceted pharmacology due to its ability to bind to cholesterol on the cell membrane. The oral bioavailability of cannabidiol in humans is approximately 6%, while its inhalation bioavailability ranges from 11 to 45% (average 31%) [17]. The half-life of CBD is 18-32 hours [18]. Studies conducted by G. della Rocca *et al.* [19] showed that when CBD was taken in capsule form, the peak concentration (Cmax) was reached 4-5 hours after ingestion. But if CBD was consumed in the form of oil, the Cmax was reached much faster – in 1-2 hours. At the same time, the use of oil provided a higher bioavailability of CBD compared to capsules. Cannabidiol was absorbed more rapidly by inhalation than by ingestion (maximum concentration – Tmax – was 5 minutes, respectively) [20]. Plasma CBD concentrations showed a nonlinear increase with dose and 6.5% bioavailability at a dose of 3000 mg. The absorption of CBD increased threefold with a high-fat meal, indicating the accumulation of CBD in body fat tissue. CBD is not able to be absorbed in the oral epithelium or absorption is limited, instead, the main absorption of the substance occurs in the gastrointestinal tract [19]. Cannabidiol is metabolised in the liver and intestine by cytochrome P450 enzymes CYP2B6, CYP2C19, CYP2D6, CYP2J2 and CYP3A4, as well as by isoenzymes UGT1A7, UGT1A9 and UGT2B7, forming various metabolites [21]. CBD metabolism is very complex, especially in hepatocytes (Fig. 3).

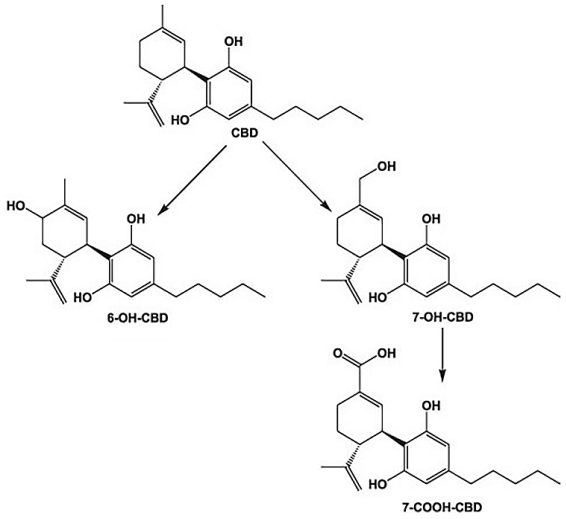


Figure 3. CBD metabolism in a liver
Notes: CBD – cannabidiol

The main human metabolite is 7-carboxycanabidiol (7-COOH-CBD; ~90% of all measured in plasma) [22], as well as 6α- and 6β-hydroxyisomers and derivatives hydroxylated on the alkyl side chain with subsequent glucuronidation. In general, Q. Rao *et al.* [23] identified 24 CBD metabolites in the liver. The main concern with 7-COOH-CBD was its reactive acyl glucuronide. CBD is excreted from the body in faeces (84%) and also in urine (8%) [24]. This indicates that the main route of elimination of CBD is through the intestine, which may affect the efficiency of its pharmacokinetics and the possibility of accumulation in the body with prolonged use.

Cannabidiol interacts with a variety of neurotransmitter systems, including serotonin and opioid receptors, which can affect a variety of aspects of neural activity and body physiology. Regarding serotonin receptors, some studies indicate that CBD can interact with 5-HT1A receptors, which are responsible for controlling mood, sleep, and other mental functions [6, 12, 24]. This may partially explain the anxiolytic (anti-anxiety) and antineuropathic properties of CBD. Experiments [13, 15, 17] have demonstrated the effect of CBD on other serotonin receptors, which can affect various aspects of mood and mental state. Regarding opioid receptors, there is some evidence to suggest that CBD may interact with the body's opioid systems. Studies have shown that CBD can affect the activity of opioid receptors, causing a reduction and presentation of pain [17, 18]. However, the mechanisms of this interaction are not yet fully understood and require further study. In general, the interaction of cannabidiol with these neurotransmitter systems shows that CBD can have a complex effect on nervous activity, mood, pain, and other physiological processes in the body [6].

Allosteric modulation of opioid receptors opens up interesting opportunities for the development of new approaches to the management of pain and other conditions associated with the opioid system. This could lead to an increase in the effectiveness of opioid therapy, providing more intense analgesia with lower doses of opioids. As noted by R.A. Vlad *et al.* [24], it is possible to reduce side effects associated with opioid therapy, such as constipation and respiratory depression. Allosteric modulators can slow down the development of opioid tolerance, make opioid therapy more individualised, and reduce the risk of psychological and physiological dependence. Allosteric modulation of opioid receptors can affect biological systems in various ways. According to studies [23, 24], this process can lead to an increase in the analgesic effect of opioid drugs and provide more effective pain control. At the same time, it is possible to reduce the dose of opioids, which can reduce the risk of side effects and the development of drug tolerance. Another important aspect is the ability of allosteric modulation to minimise the adverse effects associated with opioid therapy, such as respiratory depression and constipation. Additionally, the use of allosteric modulators may reduce the risk of opioid dependence due to the ability to achieve the desired effect at lower doses. Cannabidiol is one of the main non-psychoactive components of cannabis. It interacts with various receptors and neurotransmitter sys tems, exhibiting potential therapeutic properties. Cannabidiol is metabolised in the liver to form various metabolites and is primarily excreted in the faeces. Studies of the pharmacokinetics and pharmacodynamics of cannabidiol are important for understanding its effects and developing optimal patterns of use.

Legal Status, Prevalence and Potential Impacts of Cannabis

The legal status of CBD varies by country and jurisdiction. In some countries, such as Canada and some US states, legislation has allowed the use of marijuana and its constituents, including CBD, as a medicinal product [25]. In the European Union, CBD was classified as a "novel food substance", which meant that it had to be registered and approved before being used in food [26]. In many other countries, such as Australia, Japan, and Singapore, CBD has not yet been legal, regardless of its use as a medicinal product or in food [27]. Some countries only allow the use of CBD if it contains less than 0.2-0.3% of the psychoactive substance found in marijuana (THC) [25]. Internationally, CBD is not under the control of the United Nations (UN) on Narcotic Drugs and Psychotropic Substances because it has no psychoactive properties and does not cause a narcotic effect [27]. On 7 April 2021, the Ukrainian government legalised the use of isolated cannabidiol [28]. Thus, the legal status of CBD has been constantly changing, and different countries have taken different approaches to regulating its use.

CBD-based products were distributed across European countries with different legal statuses. The expected effect of CBD use depended on social status. For example, people with lower incomes reported improved well-being and reduced anxiety and stress [27]. At the same time, the use of cannabidiol by people with a higher level of education was associated with a desire for increased concentration and headache relief [27]. Thus, it could be argued that CBD products were widespread among different segments of the population. This was facilitated by the availability and variety of products. The main way of distributing CBD was through the Internet (64%), where it was easy to order and deliver goods without proper age verification, and the number of stationary sales shops and pharmacies was also increasing, with a 17% share of sales, with the rest of the turnover carried out by shadow and unregistered outlets [29]. In most countries, the laws governing the use of CBD were not clear, thus turning it into an unregulated sector [30]. Despite a ruling by the Court of Justice of the European Union stating that CBD was not a drug, its status remained unclear [31]. Part of the reason for the tightness of the legal framework was due to insufficient research on the effects of CBD-based products on the human body, which created room for further research and a phased study of the effects of CBD in different population groups. The main regions of distribution of cannabidiol were North America and Europe, and to a lesser extent Latin America, Asia, the Middle East, and Africa (Fig. 4).

Figure 4. Global cannabis market outlook for 2024

Source: [32]

The first innovative companies for the industrial production and distribution of cannabis products received a total of $128.5 million in investment [32]. The investment market in this sector continued to grow. A recent report by the Centre for Medical Cannabis estimated that 8-11% of European adults have tried CBD for various purposes [33]. The size of the global cannabidiol market in 2023 was estimated at USD 9.4 billion (Fig. 5).

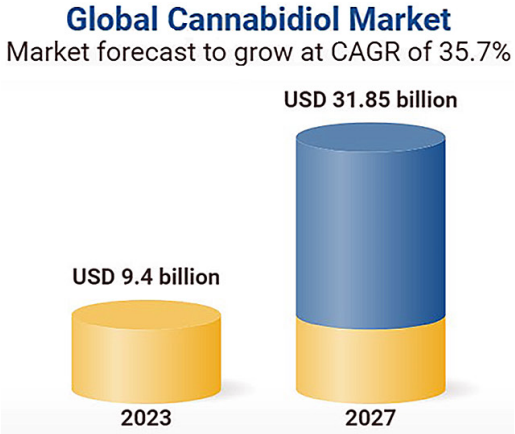


Figure 5. Global market value and revenue forecast for 2027

Source: [34]

The scientific community has shown interest in the chemical compound cannabidiol due to its positive effects and neuroprotective properties in several neurodegenerative diseases, including amyotrophic lateral sclerosis, Parkinson's disease, Huntington's disease, and Alzheimer's disease [10]. According to the findings of R. Kaufmann *et al.* [35], improved well-being was highlighted as the main reason for CBD use among a relatively healthy population. Reduced anxiety, improved sleep, and reduced stress were also described as the most expected effects of CBD. This study included a sample of 469 in patients who were treated as inpatients. Overall, 33.3% of patients reported using CBD, with the most common uses being to reduce anxiety (52.4%), improve insomnia symptoms (33.3%), and reduce pain (23.8%). The majority of patients (61.9%) said that CBD use did not affect their substance dependence, but some (16.7%) reported that CBD use helped them reduce their use of other substances [36].

CBD has also been used in treatment programmes for other drugs and alcohol addiction [37]. As CBD has demonstrated many therapeutic effects in neural circuits involved in the development of drug addiction and drug-seeking behaviour, it has become a promising candidate for the treatment of substance abuse disorders. Studies have shown that CBD reduced the drive to obtain amphetamine and prevented its recurrence in rats

that had previously been trained to find amphetamine independently [38]. In addition, it was found that CBD modulated D1- and D2-receptor levels in the mesocorticolimbic areas of the rat brain. This indicated that CBD could be a potential treatment for drug addiction, in particular, to prevent the recurrence of drug seeking [39]. As a result of the experiment by K. Nouri *et al.* [40] proved that cannabidiol reduced intrusive drug-seeking thoughts using dopaminergic receptors in the nucleus accumbens. The results also indicated the potential benefit of CBD to reduce inflammation in people with cocaine use disorder. The interaction between cannabidiol and the CB1 receptor could be an important factor in the treatment of cocaine dependence. A CB1 receptor antagonist could reverse the effectiveness of CBD in reducing cocaine seeking [41]. Y. Qian *et al.* [42] found that cannabidiol reduced cocaine withdrawal symptoms and craving, and improved cognitive function and mood in mice. The possibility of using cannabidiol and its analogues as an alternative treatment for pain and prevention of opioid abuse in rats [43], gambling and behavioural addiction [44] has also been identified. A recent double-blind, randomised study by R.M. Vitale *et al.* [38] reported the effect of reducing cravings and drug-induced anxiety in people with heroin use disorder. The legal status of cannabidiol varies in different countries and jurisdictions. CBD-based products are common among different segments of the population. Cannabidiol is being researched as a potential remedy for a variety of conditions, including anxiety, insomnia, pain, and the treatment of drug and alcohol addiction.

Cannabidiol Toxicity and Side Effects: A Review of Studies on the Effects on the Body

A significant claim is that cannabidiol can alter the liver metabolism of other drugs, making them ineffective or toxic [42]. Cannabidiol both metabolises and inhibits the cytochrome P450 enzyme pathway, in particular CYP2C19 and CYP3A4. Cannabidiol has been reported to cause significant increases in the serum levels of other drugs metabolised through this pathway, such as macrolide antibiotics [39]. Given that other common medications are also metabolised through this pathway, the greatest danger of cannabidiol may not have been its direct side effects, but rather the inhibition of metabolic pathways in the liver, which could have caused significant drug interactions. The concomitant use of cannabidiol and methadone led to a marked increase in serum methadone levels, most likely due to cannabidiol-induced inhibition of the CYP isoenzyme [45]. Studies have shown that the simultaneous use of cannabidiol and antibiotics in rats increased the area under the concentration-time curve (AUC) of the antibiotic, indicating an increase in its bioavailability [46]. In addition, cannabidiol reduces the excretion of the antibiotic from the blood plasma, which could lead to an increase in the toxicity of this drug.

In clinical trials of the only certified cannabidiol-based drug (EPIDIOLEX), using the maximum recommended maintenance doses, significant increases in liver to body weight (LBW), plasma alanine aminotransferase (ALT), aspartate aminotransferase (AST) and total bilirubin were observed. CBD increased the ratio of LBW, ALT, AST, and total bilirubin [45]. Hepatotoxicity gene expression arrays showed that CBD differentially regulated more than 50 genes, many of which were associated with oxidative stress responses, lipid metabolism pathways, and drug-metabolising enzymes [46]. CBD has also shown clear signs of hepatotoxicity, possibly of a cholestatic nature. The involvement of numerous pathways related to lipid and xenobiotic metabolism has raised serious concerns about potential drug interactions as well as the safety of CBD itself [47]. Another study demonstrated an interaction between cannabidiol and plasma biological parameters [48], where the average daily dose of CBD was 50.3 mg, and the prevalence of elevated ALT was 9.1%, AST 4.0%, alkaline phosphatase 1.9%, and total bilirubin 1.7%.

Women might have a higher risk of side effects and other responses to CBD therapy compared to men [49]. Subsequent studies have also noted an effect on spermatogenesis. Thus, treatment with 0.5 μM CBD significantly reduced sperm concentration [50]. Mice exposed to CBD showed a decrease in the size of the seminiferous tubules, a narrowing of the diameter of the tubular lumen in these tubules, and a reduction in the height of the seminiferous epithelium. In an experiment conducted by R.K. Carvalho *et al.* [51], sperm DNA damage worsened, the activity of the antioxidant enzyme SOD in sperm decreased, the percentage of motile elements decreased significantly, and more abnormal shapes were found. Another study reported that oral administration of 30-300 mg/kg body weight/day of CBD for 90 days caused a decrease in testicular size and inhibition of spermatogenesis [47]. 30 mg/kg body weight/day of CBD administered orally for 34 consecutive days, followed by a 35-day recovery period, caused a decrease in Sertoli cells, abnormal sperm morphology, and decreased plasma testosterone levels. Z. Pandelides *et al.* [50] found the effect of CBD on the development of Dario fish. It was noted that cannabidiol had a significant effect on larval behaviour and developmental abnormalities. During development, CBD caused significant adverse effects at both the cellular and tissue levels of the organism. Based on the molecular changes observed in this study, the authors identified the main pathways of CBD toxicity, such as binding of Cnr1, Cnr2 and/or PPAR receptors and alteration of metabolic pathways (e.g., retinol) (Fig. 6). The oral route of administration of CBD products is one of the most common. CBD can transform in the acidic environment of the stomach to THC. This conversion was found in studies with gastric fluid modelling (Fig. 7). CBD is a compound rich in pharmacological interactions. The most commonly reported results are neurological, carcinogenic and drug interactions (Fig. 8).

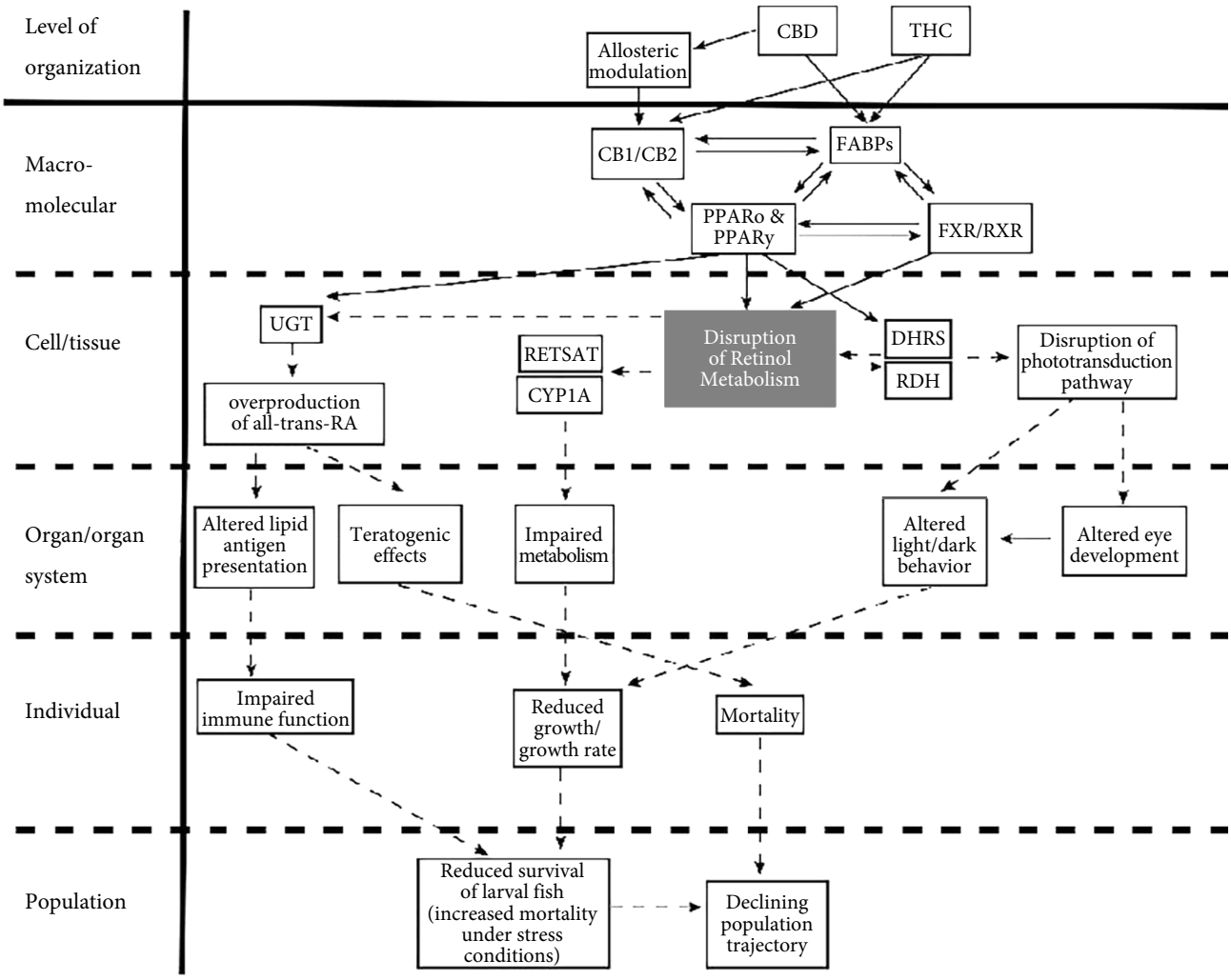


Figure 6. Potential adverse effects of cannabinoid toxicity

Notes: continuous lines with arrows indicate known linkages, while dashed lines with arrows represent likely pathways of adverse effects; CBD – cannabidiol; THC – tetrahydrocannabinol; CB1/CB2 – cannabinoid receptors; FABP – fatty-acid-binding proteins; PPAR – peroxisome proliferator-activated receptors; FXR/RXR – farnesoid X receptor/retinoid X receptor; UGT – UDP-glucuronosyltransferase; RETSAT – retinol saturate; CYP1A – cytochrome P450 1A; DHRS – dehydrogenase; RDH – retinol dehydrogenase

Source: [52]

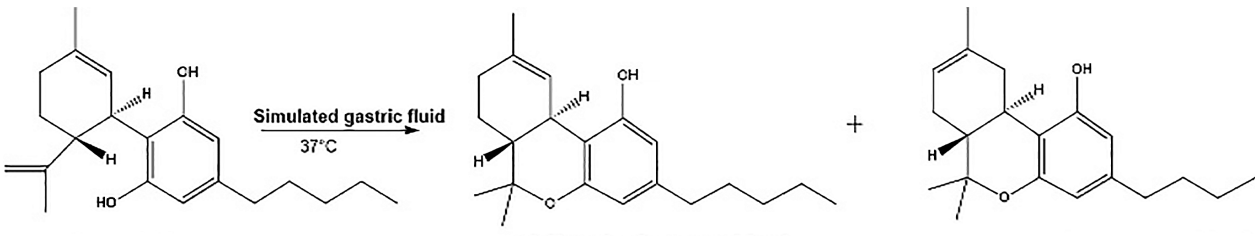


Figure 7. Psychoactive products of acid-catalysed cyclisation of cannabidiol in the presence of simulated gastric fluid at 37°C

Source: [53]

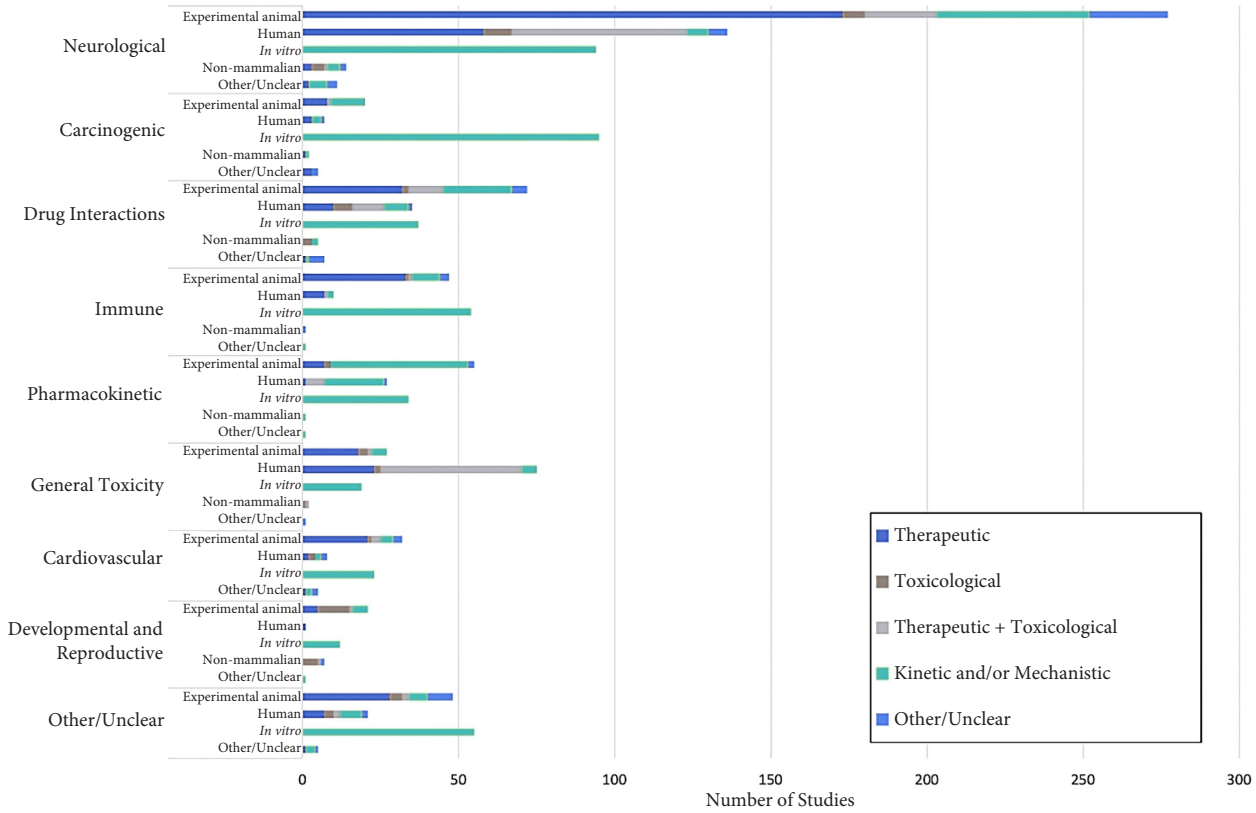


Figure 8. Studies on the safety of cannabidiol

Source: [54]

Cannabinoids have been linked to multiple types of cancer. The use of cannabidiol plant material and liquid extracts has been associated with an increased risk of prostate cancer [55]. Testicular cancer was found to be most strongly associated with cannabis exposure. The area under the cumulative exponential E-Value curve for tobacco, alcohol use disorders (AUD), cannabis, THC, cannabidiol, cannabichromene, cannabinol, and cannabigerol was 34, 32, 13, 0, 103, 58, 25, 31, indicating that cannabidiol was most involved in carcinogenesis [56]. Another effect of CBD was observed in the excretory system. Participants without chronic kidney disease (CKD) who consumed cannabidiol had a faster decline in glomerular filtration rate [57]. Despite its anti-inflammatory properties, B. Carmona-Hidalgo *et al.* [58] found that CBD worsened diabetic nephropathy and led to an earlier end-stage renal disease in a mouse model.

To exploit the full potential of cannabidiol's therapeutic value, pharmaceutical companies have been working to create new forms of cannabinoids with reduced side effects and toxicity. One of them was a method of producing a new cannabinoid, 8.9-dihydrocannabidiol (8.9-DHCBD). The antibacterial and antioxidant properties of the substance were studied. The results of the study showed that 8.9-DHCBD had strong antibacterial activity against some strains of bacteria that are pathogenic to humans, as well as significant antioxidant activity. The authors of the article argued that 8.9-DHCBD could have potential applications as a new natural antibiotic and antioxidant [59].

On the other hand, it is worth noting that most of the statements about the positive and beneficial effects of using CBD-based products have avoided the issue of the effects on the body and the consequences of use. J.A. Crippa *et al.* [60] have proposed CBD as a promising therapeutic tool to overcome several clinical problems. Since 2001, more than two hundred clinical trials have focused on the use of CBD for the treatment of seizures, cancer, post-traumatic stress disorder, and other health problems [61]. The evidence of a positive effect on anxiety, depression, sleep disorders or other psychological conditions is limited and contradictory and was mostly based on subjective testimonies of the subjects [62]. It is also worth noting that according to the European Food Safety Authority (EFSA) statement on the safety of cannabidiol as a novel product, based on an assessment of the available data, there are uncertainties in the data on the safety of cannabidiol as a novel product [63].

CBD and CBD-containing products have been growing quantitatively in markets around the world, yet despite their high popularity among consumers, knowledge about the negative effects of CBD-containing products remained limited. Accumulating evidence indicated that CBD when administered in clinically relevant doses or over a long period, had a significant potential for hepatotoxicity, as well as for interactions with various conventional medications [64]. The US Food and Drug Administration (FDA), while acknowledging the potential benefits of CBD, also argued that questions remained about its safety, including the

potential for liver damage [65]. Another significant claim was that cannabidiol could alter the liver metabolism of other drugs, making them ineffective or toxic [66].

Among natural extracts from cannabis plants, synthetic analogues of CBD have also gained popularity on the market and have been actively used in e-cigarettes. Numerous cases in 2012 linked synthetic cannabinoids to acute kidney injury [67, 68]. In particular, nephrotoxicity could be associated with an effect on proximal tubular mitochondrial function. Renal biopsies in such cases most often demonstrated acute tubular necrosis, with some cases of acute interstitial nephritis [67]. In the context of e-cigarettes used to heat CBD oil, an important aspect is the prevalence of E-cigarette or Vaping Use-Associated Lung Injury (EVALI). This syndrome has a significant association with the use of vaping products with cannabidiol, in particular CBD. The study selected seventeen international cases from 13 countries for analysis [68]. Countries outside the US had more men in the cohorts (76% compared to 58-83%), and the average age of patients from these countries was slightly higher (31 years compared to 27, 19, and 27 years). The use of nicotine/flavoured e-liquids was more common among patients outside the US (100% vs. 58-67%), and the use of cannabinoid-based products was less common (24% vs. 78-92%) [68]. Cannabidiol has potential side effects and toxicity. It can interact with other drugs, inhibiting their metabolism in the liver. Hepatotoxicity, nephrotoxicity, and reproductive toxicity of cannabidiol have been observed. Its conversion to psychoactive substances in the stomach and its association with certain types of cancer is a concern. However, evidence for positive effects is often contradictory and limited.

Conclusions

Cannabidiol, as one of the active cannabinoids contained in cannabis plants, is gaining increasing recognition in medical practice. However, its potential benefits and effects on various aspects of human body functioning continue to be the subject of debate in scientific circles. In this study, the main focus was on a thorough analysis of the therapeutic properties of cannabidiol, as well as the study of possible negative effects and toxicity associated with its use. Additionally, the relevance of CBD as a chemical compound in the modern global market was studied and the main areas of its application were identified. The data obtained in the course of the study revealed a significant interest of the scientific community in this complex compound.

The features and properties of cannabidiol as one of the main components of cannabis, which affects the body through interaction with receptors and neurotransmitter systems, have been studied. It has a complex metabolism in the liver and is mainly excreted in the faeces. Cannabidiol affects serotonin and opioid receptors, which opens up prospects for the treatment of pain and other conditions. Even though CBD-based products have been legalised by regulators in the United States and Europe, there have been legitimate concerns about possible negative effects on the body. There was considerable ambiguity in the views and opinions on cannabidiol. At the same time, it is important to note that its use as a therapeutic agent is widespread in neurology, psychiatry, addiction medicine and palliative care. After analysing the results, some major concerns were identified about the possible negative effects of cannabidiol on the body. The main ones included the issues of hepatotoxicity, possible carcinogenicity, impact on reproductive health, possible adverse reactions, and possible interaction with other medicines. It is important to note that at the time of the study, information on the impact of cannabidiol on certain body systems, such as the excretory, immune, and cardiovascular systems, remained insufficiently studied.

Further scientific research is needed to fully unlock the potential of cannabidiol and objectively assess its benefits and risks. Topics for further research may include an analysis of the comprehensive effects of cannabidiol on the body and a general overview of its mechanism of action. Particular attention should be devoted to the interaction of cannabidiol with other drugs and its effect on various body systems. It is important to note that the effective and safe use of cannabidiol can play an important role in improving the quality of life of patients, but this requires in-depth study and proper regulation of its use in medical practice.

Acknowledgements

None.

Conflict of Interest

The author declares no conflict of interest.

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Фармако-морфологічні особливості та соціально-економічні аспекти канабідіолу: огляд літератури

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Анотація. Через зростаючу популярність непсихоактивної речовини продуктів коноплі як лікувального засобу, необхідно було провести детальний аналіз наявних наукових досліджень з теми впливу канабідіолу на людський організм. Метою цього огляду був збір та систематизація інформації про позитивні та негативні впливи канабідіолу, а також про можливості його використання в медицині. Проведений аналіз 3375 наукових статей, публікацій і звітів, з яких відібрано 68 тих, що найбільше відповідали умовам запиту. Зібрані дані були узагальнені і представлені в структурованому форматі. Отримані результати огляду вказують на значний фармакологічний потенціал канабідіолу, який може використовуватися, як перспективний терапевтичний засіб у різних медичних сферах. В розглянутих дослідженнях канабідіол виявляв протисудомний, протиепілептичний ефект, а також позитивний вплив в програмах заміни наркотичних речовин. Проте також було відзначено можливість негативних реакцій та потенційно шкідливого впливу канабідіолу: може призводити до розвитку психологічної та фізичної залежності; підвищує ризик розвитку фізіологічних порушень, зокрема вплив на сперматогенез та порушення жіночої мікрофлори; впливає на поведінку та призводить до відхилень у розвитку. Дія канабідіолу на організм людини досі залишається недостатньо вивченою, а його розповсюдження в умовах недостатнього законодавчого регулювання може чинити ризик для здоров'я та безпеки споживачів. Розуміння всіх аспектів використання канабідіолу забезпечить належне управління його використанням і розвитком відповідної законодавчої бази, а також сприятиме подальшому вивченню та розробці нових препаратів на основі даного рослинного екстракту

Ключові слова: канабіс; токсикологія; право; епілепсія; хронічний біль; генералізований тривожний розлад