Review article

Specific features of cannabidiol metabolism and excretion during long-term consumption of cannabis

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ABSTRACT

The purpose of this study was to characterize the key patterns of cannabidiol metabolism and elimination. To fulfil this purpose, the study employed the latest scientific sources for the last 5-6 years from authoritative scientometric databases and archives, using bibliographic and bibliosemantic research methods. Cannabidiol has considerable therapeutic potential in the treatment of neurodegenerative diseases and neuropsychiatric disorders. Due to its properties, cannabidiol can be effective in treating conditions such as Alzheimer's disease, Parkinson's disease, multiple sclerosis (especially in young people), post-traumatic stress disorder, schizophrenia, etc. However, apart from therapeutic effects, it is necessary to consider the principles of drug metabolism and elimination. This substance is absorbed in the gastrointestinal tract after oral administration. The percentage of cannabidiol absorbed depends on the form of intake (capsules, oils, or food) and can range within 6-20%. The metabolism of cannabidiol is a multi-stage and complex process involving absorption in the digestive tract, intensive metabolism in the liver under the influence of digestive enzymes and cytochrome P450, and subsequent excretion of metabolites through the bile into the intestines. Understanding these processes is important for the optimised use of cannabidiol for medical purposes, considering its bioavailability and possible interactions with other drugs. The metabolism of cannabidiol is largely dependent on isoenzymes, specifically CYP2C19 and CYP3A4, which oxidise cannabidiol to active and inactive metabolites such as 7-hydroxycannabidiol (7-OH-CBD). Additional enzymes, such as CYP1A1, CYP1A2, CYP2C9, and CYP2D6, are also involved in this process, but their contribution is less significant.

***Keywords**:* Elimination, hepatobiliary system, law, narcotic substances, resistance,

INTRODUCTION

Cannabis, a plant with a rich history of use in folk medicine, is renowned for its therapeutic properties. Containing over one hundred chemical compounds, most notably cannabinoids like tetrahydrocannabinol (THC) and cannabidiol (CBD), cannabis has been employed to treat pain, inflammation, anxiety, and insomnia. Its leaves, flowers, and seeds have long been used in traditional remedies, while the hemp variety has been valued for its fiber in textiles and other industrial products. The growing recognition of cannabis as both a medicinal and industrial resource continues to shape modern health discussions. Recently, the popularization

of CBD has gained momentum worldwide, including in Ukraine, driven by increasing scientific research, demand for alternative therapies, and the widespread use of cannabinoids in countries like the USA, Italy, Switzerland, Germany, Canada, and Georgia.

For a long time, CBD was regarded as an exclusively narcotic substance in Ukraine. However, cannabis was legalized for medical use in 2024, as stated in the 2023 Draft Law No. 7457. Historically, cannabis has been used for various purposes, but its place in modern medicine remains controversial. Ukrainian law traditionally prohibits cannabis-related activities, with exceptions for scientific research. In contrast, researchers such as Babak and Kabrera-Lapitska (2022) highlight the growing legal discussions surrounding cannabis and its potential medical applications. Shevchuk and Hasiuk (2023) emphasize that CBD, unlike THC, does not produce typical narcotic effects like euphoria or altered consciousness. This makes it a promising candidate for medical use. Researchers like Hurtova and Kasianenko (2021) focus on CBD's therapeutic potential in treating neurological diseases such as epilepsy, Parkinson's, and Alzheimer's. They note that, since 2017, CBD derived from cannabis has been recognized as an effective treatment for these conditions.

Furthermore, the legal aspects of CBD are explored by scholars like Hurtova and Kasianenko (2021), who suggested that countries such as France and Switzerland, where medical cannabis is regulated through a doctor's prescription, could serve as models for Ukraine's legislative approach. Kalieniuk (2021) argues that cannabis use should be viewed not as a personal issue, but as a societal concern. Dispelling the myth that CBD is merely a recreational drug, researchers such as Stepaniuk and Lozova (2024) stress the need to provide evidence of its therapeutic properties. The metabolism of CBD is another critical area of study. Radish and Yevtushenko (2020) note that genetic factors, age, and health conditions can affect how individuals metabolize CBD, influencing its therapeutic effects. Despite the growing body of evidence, the exact mechanisms of CBD's action remain unclear.

Thus, most researchers have paid considerable attention to legal issues related to the use of cannabinoid substances for medicinal purposes, and only a few have raised the complexity of cannabidiol metabolism in the human body, the mechanisms of their effects on a healthy body and in pathology. The complexity and relevance of the problem lies in the fact that very few researchers have considered the elimination or excretion of cannabidiol by the human body. The purpose of this study was to analyse the key processes of CBD metabolism. The objectives of the study were to investigate the most common legislative documents on regulating the distribution of cannabis-based drugs; to find the benefits and dangers of CBD; and to investigate the specifics of CBD elimination.

MATERIALS AND METHODS

To fulfil the purpose set, the bibliographic and bibliosemantic research methods were used as the basis. The approach to the use of scientometric databases such as Scopus, Web of Science, PubMed, Google Scholar, as well as other scientific archives, including Research Gate, demonstrated a broad and comprehensive analysis of the current professional literature on the issues under study. The choice of searching by title rather than by topic helped to accurately identify relevant research topics, which contributed to the accuracy and relevance of the information obtained. The absence

of language restrictions helped to cover a wide range of scientific literature and consider different opinions and approaches to the problem under study. The literature search was conducted using keywords and phrases related to cannabidiol metabolism and elimination. The data obtained were thoroughly analysed, which helped to identify the key trends, problems, and areas for further investigation in this area. Bibliographic and bibliosemantic methods, as well as modern scientometric databases, helped to obtain comprehensive and up-to-date information on the metabolism and elimination of cannabidiol, which underlies further research and practical applications in this area. A series of terms, concepts, phrases, and keywords were used to search for scientific information: "cannabidiol", "cannabis", "marijuana", "analgesics", "narcotic substances", "law", "law and order", "permission", "draft law", "medicine", "palliative medicine", "headache", "neurology", "mental disorders", "panic", "fear", "anxiety", "stress", "metabolism", "elimination", "excretion", "absorption", "half-life", "liver", "gallbladder", "urination", "hepatobiliary tract", "pharmacokinetics", "pharmacodynamics", "diabetes mellitus", "oncology", "insulin resistance", "sphingolipids", "psoriasis", "skin accumulation", "toxicity", "coronavirus", "antioxidant properties", "metabolic regulators", "cytochrome P450".

Considering that the study of cannabidiol metabolism and elimination is a complex process and should be carried out under special conditions, a selection of the latest literature from the last 5-6 years on the pharmacodynamics and kinetics of cannabidiol, as well as legal issues related to this substance, has been compiled. In most sources, scientists performed preclinical studies on rats (*in vivo* animal models). To obtain the results, a dose of cannabidiol was experimentally administered by intravenous injection, orally or by inhalation. After that, blood samples were taken at different time intervals to determine the concentrations of cannabidiol and its metabolites. Bile collection by gallbladder cannulation. Furthermore, faecal samples were collected to determine the excretion of metabolites. The content and effect of cannabidiol on cellular structures were investigated using microscopy. Subsequently, standard cultivation of hepatocytes and other relevant cell lines was performed. Specific inhibitors were used to determine the role of individual enzymes (CYP450 enzyme inhibitors).

In the legal aspect, the following documents were analysed to investigate the legality and appropriateness of cannabidiol use in a more structural way: the Law of Ukraine No. 60/95-VR "On Narcotic Drugs, Psychotropic Substances and Precursors" (1995), the Law of Ukraine No. 123/96-VR "On Medicinal Products" (1996), the Draft Law of Ukraine No. 5596 "On Amendments to Certain Legislative Acts of Ukraine Regarding the Regulation of the Circulation of Cannabis for Medical, Scientific, and Scientific-Technical Purposes" (2021). These laws and draft laws are the principal regulations governing the circulation of drugs and the possible use of medical cannabis in Ukraine. They define the legal framework, restrictions, and requirements for the production, storage, use, and control of these substances.

RESULTS AND DISCUSSION

CBD products that have not been approved by regulatory authorities have gained considerable popularity as self-medication for various diseases due to widespread, but often unfounded, beliefs about their medicinal properties. Many people resort to CBT in the hope of

alleviating symptoms of anxiety, pain, insomnia, and other medical problems. However, due to the lack of scientifically proven data, the use of such products without proper consultation with medical professionals can be dangerous. These products may have an unknown composition, which creates additional risks for consumers. The lack of control by official authorities means that the quality and safety of such products are not absolutely guaranteed to the public, and they may contain impurities or have an inaccurate concentration of active substances. This complicates the assessment of their efficacy and safety, increasing the risk of adverse side effects.

Recently, the popularity of CBD has increased, which has led to the emergence of many CBD products on the market. Research includes both experimental and clinical trials aimed at investigating its effects on cognitive and anxiety disorders, movement disorders, and pain inflammation. However, existing research does not provide sufficient high-quality evidence on the effectiveness of CBT in the treatment of these conditions. In addition, not enough is known about its safety and the exact functions and dosage for each particular disorder or disease. Many people use these products to treat conditions such as chronic pain, anxiety, depression, and even epilepsy, despite the lack of reliable scientific evidence of the effectiveness of CBD in these cases (Britch *et al.*, 2021; Dashi *et al.,* 2015). Since these products are not properly regulated, there is an elevated risk that they may contain impurities or incorrect doses of the active ingredient, which can lead to unpredictable health consequences, and no one will be held responsible for this.

In 2024, Ukraine legalized the use of medical cannabis for various conditions, including cancer and post-traumatic stress disorder (PTSD) (Draft Law No. 7457, 2023). This step is aimed at alleviating pain, stress, and other symptoms in patients, including those affected by the war. The United Nations (UN) established the International Narcotics Control Board. This organization has emphasized the significance of the availability of medicines containing narcotic substances for patients who need them, following international standards and requirements (International Narcotics Control Board, 2024). The law also regulates the cultivation of hemp. It is allowed to grow technical hemp varieties with a THC content of less than 0.3% for industrial purposes, while for medical purposes the permissible THC level may be higher. This draft law was accompanied by a considerable number of discussions and amendments. Specifically, the law prescribes the creation of an electronic register of the Ministry of Agrarian Policy and the approval of medical protocols for the use of cannabis to treat certain diseases. However, there is some criticism about possible contradictions in the law that could affect doctors and patients.

The legalization of medical cannabis in Ukraine, effective from 2024, holds significant potential for the agricultural, pharmaceutical, and industrial sectors. The nation’s favourable climate and soil conditions make it ideally suited for cannabis cultivation, presenting an opportunity for agricultural diversification. Additionally, the growing demand for cannabis-based medicines could stimulate the pharmaceutical industry, positioning Ukraine as a key player in the European market. The industrial sector stands to benefit from the processing of hemp for textiles, biofuels, and other products, potentially leading to new manufacturing processes and products (Aliekperova *et al.,* 2023).

Beyond its medical applications, the legalization of CBD in Ukraine offers

considerable economic prospects, particularly in the agricultural sector, where large-scale hemp cultivation is permitted, with the expectation of increasing agricultural productivity and creating new markets for Ukrainian farmers. The pharmaceutical sector is also poised for growth, as cannabis-based medicines become more widely accepted (Vyshka *et al.,* 2014). Furthermore, industries such as textile production and biofuels, which utilize hemp fibres, are expected to experience an increase in production and innovation (Burlaka *et al.,* 2024). Collectively, these sectors present Ukraine with a unique opportunity to diversify its economy, attract foreign investment, and create new job opportunities.

Pharmacological studies have shown that lower doses of CBD (e.g., 10-20 mg) can effectively reduce anxiety in individuals with social anxiety disorder, whereas higher doses (e.g., 100-300 mg) may be needed to address generalized anxiety disorder (García-Gutiérrez *et al.,* 2020; Castillo-Arellano *et al.,* 2023). In one clinical trial, doses ranging from 5 mg to 400 mg per day were tested, demonstrating that while a moderate dose of 200 mg daily led to a marked reduction in anxiety symptoms in patients with generalized anxiety disorder, higher doses did not yield significantly better results, suggesting a dose-dependent effect (García-Gutiérrez *et al.,* 2020). For pain management, a dose of 10-20 mg CBD has been shown to significantly reduce pain and inflammation in chronic pain models (Britch *et al.,* 2021). In contrast, for neurodegenerative diseases like Parkinson's and Alzheimer's, higher dosages (50-100 mg) have been more effective in reducing symptoms and improving patient quality of life (Shevchuk and Volos, 2023; Lako *et al.,* 2023).

CBD affects various ion channels, including sodium and calcium channels. This can have a considerable impact on neural excitability and signal transmission in the nervous system. CBD's effect on ion channels contributes to its therapeutic properties, such as pain relief and seizure reduction. CBD also interacts with metabotropic receptors such as serotonin and adenosine receptors. The effect on these receptors may explain the anxiolytic and antidepressant properties of CBD, as serotonin receptors play a key role in the regulation of mood and anxiety (Fig. 1).

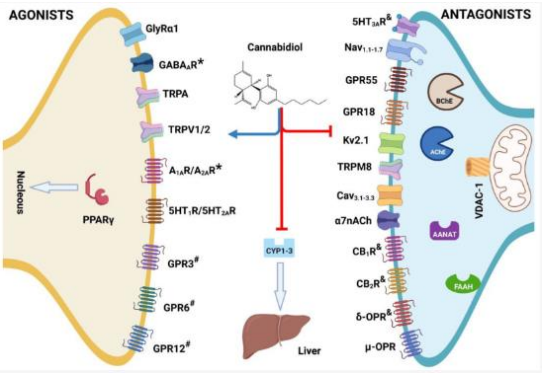

Fig. 1 : Molecular structure of cannabidiol and its relationship with receptors and synapses

Source: compiled by the authors based on Castillo-Arellano *et al.* (2023)

Increased doses of CBD can activate TRPV1 receptors, reducing anxiolytic effects. Blocking these receptors may enhance CBD's anxiolytic properties, reducing anxiety and stress (Fig. 2). CBD can also affect the levels of anandamide, an endocannabinoid that plays an important role in regulating mood and anxiety. The FAAH enzyme breaks down anandamide, reducing its levels in the brain. By inhibiting FAAH, CBD can increase the concentration of anandamide, which enhances its anxiolytic and antidepressant effects (Pivtoraiko *et al.,* 2022).

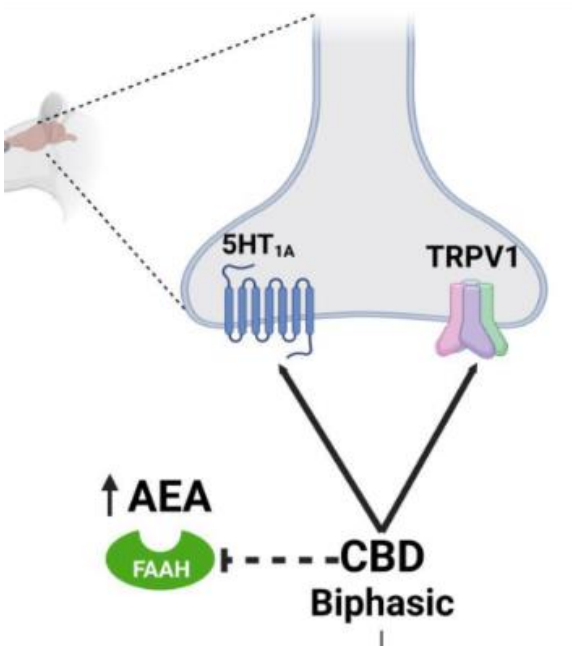

Fig. 2 : Schematic representation of the effect of cannabinoid on brain receptors in anxiety disorders

Source: compiled by the authors based on Castillo-Arellano *et al.* (2023)

These mechanisms underline the complexity of the action of CBD and the significance of understanding its dose-dependent effects. The choice of dose can have a considerable impact on its effectiveness in treating anxiety and other conditions. Blocking the TRPV1 receptor or inhibiting the FAAH enzyme may be potential strategies to enhance the anxiolytic effects of high doses of the compound.

Portillo *et al.* (2024) found that CBD disrupts tryptophan catabolism, potentially impairing fetal cognitive development through alterations in serotonin and kynurenine pathways. The cited study demonstrates that CBD considerably inhibits serotonin transport in the placenta, reducing its level by approximately 60% even at the lowest concentrations tested. This suggests that the compound may interfere with the natural mechanism of serotonin transport, which is important for foetal development.

CBD has been associated with metabolic disorders like diabetes and obesity, primarily through its interaction with cannabinoid receptors CB1 and CB2, which influence various physiological and immune processes (Charytoniuk *et al.,* 2021; Gochman *et al.,* 2023). Activation of the CB2 receptor is associated with anti-inflammatory effects and may have therapeutic value in the treatment of inflammatory and autoimmune diseases. Anandamide, also known as N-arachidonoylethanolamine, is one of the main endocannabinoids. It binds to both CB1 and CB2 receptors but has a higher affinity for CB1. Anandamide is involved in the regulation of mood, memory, appetite, and pain. It is metabolised by the enzyme FAAH, which breaks down anandamide into less active compounds. 2-arachidonoylglycerol (2-AG) is another important endocannabinoid that binds to both CB1 and CB2 receptors (Chayasirisobhon, 2021). It is involved in the regulation of many physiological processes, such as inflammation, immune response, and neuroprotection. 2-AG is metabolised via the enzymes monoacylglycerol lipase (MAGL) and α/β-hydrolase domain-6 (ABHD6).

CBD and cannabigerol (CBG) have anti-tumor effects, reducing glycolysis and lipid synthesis, and inducing oxidative stress in cancer cells (Mahmoud *et al.,* 2023). These cannabinoids can reduce the activity of the MAPK/ERK pathway, which plays a significant role in cancer cell proliferation, and inhibit angiogenesis, the formation of new blood vessels necessary for tumor growth.

CBD is primarily metabolized in the liver by cytochrome P450 enzymes, with CYP3A4 and CYP2C19 playing the most significant roles in its biotransformation. These enzymes oxidize CBD to primary metabolites, such as 7-hydroxycannabidiol

(7-OH-CBD) and 7-carboxycannabidiol (7-COOH-CBD), which may also be biologically active and contribute to its therapeutic effects. Additionally, CBD interacts with other drugs through inhibition of CYP450 enzymes, particularly CYP3A4 and CYP2C19, potentially altering the concentration and efficacy of other medications (Chan and Duncan, 2021; Nasrin *et al.,* 2021).

According to Martinez Naya *et al.* (2024), while CYP2C19 and CYP3A4 are the primary enzymes involved in CBD metabolism, other enzymes like CYP1A1, CYP1A2, CYP2C9, and CYP2D6 contribute to a lesser extent. 7-OH-CBD, one of the main active metabolites, is formed through hydroxylation by these enzymes and shows 38% lower plasma levels than CBD, indicating reduced bioavailability or faster excretion. After its formation, 7-OH-CBD can undergo additional transformations in the liver, producing further metabolites. In a similar manner, the hepatoprotective and choleretic properties of herbal compounds such as *Achillea* and *Tanacetum* are contingent on the liver for their metabolism and biliary excretion. The present study thus demonstrates the pivotal role of the liver in the metabolism and excretion of compounds, a finding that is further highlighted by the case of both CBD and the herbal compounds mentioned above (Kazakova *et al.,* 2024).

CBD and its metabolites are primarily excreted via feces, with key metabolic steps including hydroxylation, oxidation, and conjugation. These processes help prepare the metabolites for excretion, with glucuronidation and sulfation ensuring their water solubility. This facilitates their removal through bile or urine.

CBD metabolites are primarily excreted through the intestines, following secretion into the bile and passage through the gallbladder (Mamontov *et al.,* 2023). Most of the CBD metabolites are excreted from the body through the intestine, which emphasises the important role of the hepatobiliary pathway in the excretion of CBD. After the liver secretes the metabolites of the CBD into the bile, they pass through the gallbladder and enter the intestines. There, the metabolites continue their journey through the digestive system and are eventually eliminated from the body. This process is the main and key one for the effective circulation and elimination of CBD from the body. It emphasises the significance of the liver and gallbladder in the metabolism and excretion of cannabis-like substances. Knowledge of this mechanism is important for understanding the pharmacokinetics of CBD and for developing optimised regimens for its use, ensuring the effectiveness and safety of treatment.

A comprehensive understanding of the metabolism of CBD is essential for the accurate determination of its pharmacokinetic properties and the optimal utilisation of its therapeutic potential. Given the pivotal role of the hepatobiliary pathway in the excretion of CBD, it is equally important to explore the biological effects of CBD itself. CBD is renowned for its anti-inflammatory, antioxidant, and neuroprotective properties, and has consequently attracted considerable attention in the field of medical research with regard to its potential for the treatment of a wide range of conditions.

CBD is one of the key cannabinoids with considerable potential in medical research due to its biological properties, which include anti-inflammatory, antioxidant, and neuroprotective effects. However, to fully understand its pharmacokinetics and metabolic profile, it is necessary to investigate in detail the metabolic processes associated with this compound. CBD has anti-inflammatory,

antioxidant, and neuroprotective biological properties. CBD can reduce inflammation, which is useful in the treatment of various inflammatory diseases such as arthritis, Crohn's disease, etc. CBD exhibits antioxidant activity, helping to neutralise free radicals, which helps protect cells from oxidative stress and damage. Another undoubted fact is that it can help protect neurons and maintain the health of the nervous system, which is promising in the treatment of neurodegenerative diseases such as Alzheimer's and Parkinson's (Zotaj *et al.,* 2024).

The legal status of CBD remains unclear internationally, with some researchers questioning its marketed health benefits (Brunetti *et al.,* 2020; Aliekperova *et al.,* 2020). Considering the above facts, it is necessary to agree with Brunetti *et al.* (2020) and Aliekperova *et al.* (2020) as no regulatory framework for the regulation of cannabis-like substances has been identified. Despite the significant therapeutic potential of cannabidiol and other cannabinoids, their legal status stays ambiguous and often uncertain in many countries. Furthermore, the above researchers note that the practices of other countries such as the United States of America, the Netherlands, etc., cannot be used as an example in this case, as there is still a lack of information on the positive and negative effects of CBD, and some positive results of experimental data are overestimated. Furthermore, most of the studies have only undergone preclinical trials of the CBD and have not passed the clinical stage, which is scientifically incorrect.

CBD's anti-inflammatory and analgesic properties may aid recovery and improve performance in athletes (Schouten *et al.*, 2022; Sunda and Arowolo, 2020). Furthermore, CBD can help athletes cope with stress and improve sleep quality, which also has a positive impact on recovery and preparation for competition. The *in vivo* studies described by the scientist in his paper focus on the impact of CBD on living organisms, which allows for a more comprehensive understanding of its effects in real life. According to the data obtained, CBD has therapeutic and health-improving properties. However, the results of the study in the cited paper suggest more of a rehabilitative effect of CBD. It is impossible to agree with these researchers on the usefulness of CBD in sports, as these substances can clearly be considered doping for athletes, which is prohibited. In common with the present study, the in vitro studies conducted by Zhou *et al.* (2025) on cell cultures allow for a detailed analysis of the mechanisms of action of CBD at the molecular level. The results of these studies suggest the potential of CBD to improve skeletal muscle metabolism, reduce inflammation, accelerate tissue regeneration, and promote anabolism. Human trials show that CBD supplementation promotes muscle recovery, reducing pain and improving well-being. It was expected that CBD was effective in increasing the expression of metabolic regulators in the muscles of obese mice, such as Akt and glycogen synthase kinase-3 (GSK-3). Treatment with CBD in rodents also reduced muscle inflammation after eccentric exercise by affecting nuclear factor kappa B (NF-κB). In models of muscular dystrophy, CBD reduced the levels of inflammatory markers such as interleukin-6 (IL-6) and tumour necrosis factor alpha (TNF-α). Analogously, in obese rodents, CBD reduced inflammatory processes, specifically by affecting cyclooxygenase-2 (COX-2) and NF-κB.

In turn, Saraswat *et al.* (2023) highlighted data on the metabolism and mechanism of action of cannabidiol in coronavirus infection in their studies. Co-administration of CBD with intravenous

ramdivir may be a promising strategy to improve treatment efficacy in patients with COVID-19 by providing longer-lasting active levels of ramdivir or another drug in the body. This can be particularly useful for maintaining therapeutic drug concentrations and improving clinical efficacy.

Jarocka-Karpowicz *et al.* (2020) describe the relationship between psoriasis-affected skin and the use of cannabis-like substances such as CBD in this case. In contrast, the cited study investigates the anti-inflammatory and antioxidant effects of CBD and analogous substances. As a result of study, Jarocka-Karpowicz *et al.* cited findings differing from the present study, namely that CBD compounds can accumulate in the skin and are only partially eliminated. CBD has demonstrated the ability to modulate the redox state of cells and affect phospholipid metabolism, which may be important for psoriasis therapy and skin protection from UV radiation. These findings point to the potential therapeutic potential of CBD to reduce inflammation and oxidative stress in the skin, which may be useful for treating psoriasis and protecting the skin from the harmful effects of UV rays. Further research may help to determine the optimised regimens for the use of CBD to maintain skin health and treat dermatological diseases. In patients with psoriasis, CBD helps to reduce oxidative stress and lipid peroxidation, which can help to reduce inflammation and cell damage (Hartmane *et al.,* 2024; Rubins *et al.,* 1992). In healthy people, CBD affects these processes in a slightly different way, emphasising the difference in metabolic pathways between healthy and psoriasis-affected cells.

Berk *et al.* (2022) and Talwar *et al.* (2023) presented data analogous to the above. CBD affects metabolic processes and inflammation in various organs, and its role in regulating sphingolipid levels is one of the potential mechanisms for improving insulin sensitivity. Sphingolipids play a key role in cellular signalling pathways and may contribute to the development of insulin resistance (Belov *et al.,* 2005). However, the author refutes the long-term presence of cannabinoids in the skin. Considering the data obtained and the literature reviewed by these researchers, we can fully agree that CBD has a pronounced anti-inflammatory effect in the pathogenesis of psoriasis, but these theses require further in-depth investigation. The results suggest a direct influence on the metabolism and development of sphingolipid molecules and all fatty components of the skin.

The pharmacokinetics of CBD includes studies of its absorption, distribution, metabolism, and excretion. Absorption is next: CBD can be administered by various routes, including oral administration, inhalation, sublingual administration, and transdermal patches. The rate and efficiency of absorption depends on the method of administration. CBD is metabolised in the liver, mainly by cytochrome P450 enzymes (CYP3A4 and CYP2C19) (dos Santos *et al.*, 2023). Several metabolites are formed as a result of metabolism, including 7-OH-CBD and other compounds. The main routes of elimination of CBD and its metabolites from the body include excretion through the kidneys in the urine and through the intestines in the faeces. The elimination half-life of a CBD may vary depending on the route of administration, dose, and individual characteristics of the human body. Interaction with other drugs may also affect the metabolism and excretion of CBD, which is important to consider when using it for therapeutic purposes.

The metabolism of CBD is a multistructural and complex process involving several CYP450 isozymes (Le Bacquer *et al.*, 2024; Spelta *et al.*, 2024).

The main metabolites are 7-OH-CBD, which has a 38-45% lower amount of cannabis-like substance in plasma compared to the original CBD. Further metabolism in the liver leads to the formation of additional metabolites, which are excreted mainly in the faeces and to a lesser extent in the urine. An understanding of these metabolic pathways is crucial for the optimised and beneficial use of CBD for therapeutic purposes and for predicting possible interactions with other drugs.

The results of the study of the pharmacokinetics and metabolism of FDCs provide a foundation for the formulation of recommendations for specific population groups, including children and elderly patients. It is imperative to consider age-related differences in liver enzyme activity, body composition, and potential comorbidities when developing these recommendations. In pediatric patients, the metabolism of CBD may be slower due to the underdevelopment of liver enzymes in younger children, which matures with age (Tutchenko *et al.,* 2024; Rudyk *et al.,* 2024). This can necessitate lower starting doses and gradual dose escalation to monitor for adverse effects, especially in conditions like pediatric epilepsy. Since data on the safety and efficacy of CBD in children is still limited, careful monitoring is required. Additionally, variations in the absorption and bioavailability of CBD may be observed in this age group, depending on their body composition and the rate of enzyme maturation.

For elderly populations, CBD metabolism may be altered due to reduced liver function, which commonly occurs with aging, as well as changes in body fat composition that can affect the distribution and elimination of the compound (Komilova *et al.,* 2024). Therefore, a lower initial dose and gradual titration are recommended for older patients, with careful attention to the potential for drug interactions, particularly with medications metabolized by cytochrome P450 enzymes such as CYP3A4 and CYP2C19. Elderly individuals are also more susceptible to side effects like sedation and hypotension, making it crucial to adjust dosages accordingly (Niyazbekova *et al.,* 2023). Given the increased risk of polypharmacy in this demographic, monitoring for interactions and individualizing treatment plans will ensure both safety and efficacy. Further research is necessary to establish comprehensive age-specific dosing guidelines and evaluate the long-term safety of CBD in these vulnerable populations.

The analysis shows that most researchers point out that the lack of proper regulation and control by official bodies means that the quality and safety of such products can vary substantially. This creates a risk of not only ineffective treatment, but also potential side effects or interactions with other medications. Nevertheless, the CBD market continues to grow, attracting increasingly more consumers looking for alternative treatments. It is important to emphasise the need for further scientific research to determine the true capabilities and limitations of the CBD, as well as to develop clear recommendations for its safe use.

Thus, despite the potential benefits of CBD, the need for further research and controlled clinical trials stays urgent. This will help to ensure the proper level of safety and effectiveness of the CBD products, as well as to develop clear recommendations for their use. It is important to conduct further studies to confirm these results in clinical settings and to assess possible risks and interactions between the CBD and other pharmaceuticals. The prospects for additional investigation of the metabolism

of CBD involving cytochrome P450 are particularly valuable. This will enable the development of optimised treatment regimens and ensure patient safety when using these drugs simultaneously.

CONCLUSIONS

The potential of medical cannabis to significantly improve the treatment of various diseases in Ukraine is considerable; however, it is essential to overcome the legislative, social, and regulatory barriers that currently impede its use. In order to optimise its medical use, it is first necessary to gain a thorough understanding of its metabolism, particularly its interactions with other drugs that are metabolised by cytochrome P450 enzymes. Although the pharmacological parameters of cannabinoids, including metabolism and excretion, remain insufficiently understood, further research is required to investigate these aspects and the long-term safety and efficacy of cannabidiol. An investigation into the role of TRPV1 receptors and FAAH inhibition may facilitate an enhanced understanding of the anxiolytic effects of cannabidiol. It is imperative that further research be conducted on the endocannabinoid system in order to facilitate the advancement of therapeutic applications.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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