

Cannabinoid Addiction: Pharmacotherapy, Forensic and Pharmaceutical Practice, Availability of Drugs

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Abstract. Data from the scientific literature on the current state of the spread of dependence on psychoactive substances of plant origin – cannabinoids was processed. The problem of cannabinoid addiction has been studied. Forensic and pharmaceutical practice was analyzed. The development of organizational measures in order to provide drug patients with cannabinoid addiction (F12) with a comprehensive approach was substantiated.

The peculiarities of pharmacotherapy and the availability of drugs for drug addicts have been clarified. The methods of assessing the availability and effectiveness of hepatoprotectors based on pharmacoeconomic, forensic and pharmaceutical indicators have been improved.

Keywords: addiction, cannabinoids, drug addicts, forensic pharmacy, drugs, pharmacotherapy, hepatoprotectors.

Introduction. Forensic and pharmaceutical practice shows intensive abuse of cannabis by minors and young people with other psychoactive substances (medicines, alcohol) [1-9]. Abuse of cannabinoids leads to cannabinoid addiction and comorbid disorders (cardiovascular, gastrointestinal, oncological, psychiatric, HIV/AIDS) against the background of a pandemic of infections (COVID-19, monkeypox virus, influenza) in accordance with ICD-11 [10-21].

The legalization of cannabis in the world led to [22-25]:

- increase in the level of use of cannabis and marijuana among young people;
- increase in the number of comorbid mental illnesses, suicides, and hospitalizations;
- increase in tax revenues;
- decrease in the number of arrests for actions related to the illegal circulation (storage) of cannabis;
- increase in drug patients in Africa, South and Central America with cannabinoid addiction.

In the USA, the DEA is actively trying to stop the spread of cannabis cultivation [26]. The Domestic Cannabis Eradication Program (DCE/SP) has been adopted and is aimed exclusively at:

- control over the activities of organizations involved in the cultivation of cannabis;
- financing of the cannabis eradication program in Hawaii and California (1979);
- providing resources to support 126 state and local law enforcement agencies that are actively involved in the implementation of the program.

According to the DEA service, in 2020 during the implementation of the DCE/SP program:

- court decisions and 4,992 arrests of citizens who committed crimes;
- disposal of 830,922 indoor plants with a total number of 4,541,962 marijuana plants;
- disposal of 3,711,040 cultivated hemp plants outdoors;
- court decisions on the arrest of 4,992 citizens who committed crimes;
- confiscation of assets in the amount of more than 41.0 million dollars.

At the same time, we note that in Ukraine, as in the USA, law enforcement agencies conduct measures aimed at countering of illegal circulation of psychoactive substances. Thus, during the joint meeting (2021) of the heads of law enforcement and other state bodies on combating the illegal circulation of weapons, ammunition and explosives, narcotics, psychotropic substances, precursors, as well as human trafficking, it was emphasized that [27]:

- the rate of growth of drug addiction in Ukraine is one of the highest in the world;
- in 2020, 24,500 criminal offenses were recorded in the sphere of circulation of narcotic drugs and other psychoactive substances;

- the largest number of such crimes were recorded in the Dnipropetrovsk, Donetsk, Odesa and Kharkiv regions, as well as in the city of Kyiv;
- the number of narcotic drugs and other psychoactive substances seized by the National Police of Ukraine from illegal circulation has decreased by almost five times;
- every year, narcotics cause the death of about a thousand citizens of different age groups;
- about 120,000 people die from the consequences of drug addiction and associated diseases;
- about 20% of the volume of illegal traffic of psychoactive substances in Ukraine is distributed due to the use of the Internet.

Forensic and pharmaceutical practice shows that the main illegal traffic of marijuana in Ukraine is carried out "through hands", special Telegram channels and other social networks. These are closed groups of 200-300 people. Administrators accept applications. The client deposits money into the dealer's account. After some time, they send the coordinates where the bag with marijuana is located [28-31].

Forensic pharmaceutical studies of the illegal circulation of psychoactive substances and cannabinoid drug addiction were conducted in Ukraine [32-37].

The purpose of the study was to conduct a review of the literature on the features of pharmacotherapy of cannabinoid addiction, to generalize forensic and pharmaceutical practice on the illegal circulation of cannabinoids, to study the availability of drugs for drug addicts.

Materials and methods. The study was conducted from January 2022 to December 2022. More than 200 scientific sources on the topic of the work were used. The forensic and pharmaceutical practice of cannabinoid addiction was analyzed.

To solve the problems, the following was used:

- mathematical and graphic methods; statistical evaluation and mathematical processing of data was carried out using modern computer technologies;
- documentary, comparative, regulatory and historical analysis, forensic and pharmaceutical monitoring;
- analytical and descriptive analysis (for questionnaires of pharmacy, medicine, jurisprudence specialists and patients);
- pharmacoeconomic analysis (index and ABC analysis – to study the effectiveness and availability of drugs with the aim of including them in the pharmacotherapy of cannabinoid addiction);
- statistical analysis (to determine the reliability of the obtained results).

The study is a fragment of the research works of the Kharkiv Medical Academy of Postgraduate Education on the topics "Improvement of the organizational and legal procedure of providing drugs to patients from the position of forensic pharmacy, organization and management of pharmacy" (state registration number 0116U003137, implementation period 2016-2020), "Pharmaceutical and medical law: integrated approaches to the drug circulation system from the standpoint of forensic pharmacy and the organization of the pharmaceutical case" (state registration number 0121U000031, implementation period 2021-2026), Lviv Medical Institute LLC on the topic "Improvement of the drug circulation system during pharmacotherapy on the basis of evidentiary and forensic pharmacy, organization, technology, biopharmacy and pharmaceutical law" (state registration number 0120U105348, implementation period 2021-2026), Petro Mohyla Black Sea National University on the topic "Conceptual interdisciplinary approaches to the drug circulation system, taking into account organizational and legal, technological, biopharmaceutical, analytical, pharmacognostic, forensic and pharmaceutical, clinical and pharmacological, pharmacoeconomic, pharmacotherapeutic aspects" (state registration number 0123U100468, implementation period 2023-2028) and State Enterprise "Luhansk State Medical University" on the topic "Conceptual interdisciplinary approaches to pharmaceutical provision and availability of drugs, taking into account organizational and legal, technological, analytical, pharmacognostic, forensic and pharmaceutical, clinical and pharmacological, pharmacoeconomic, marketing, social and economic competence" (state registration number 0123U101632, implementation period 2023-2027).

Results and discussion. Pharmacotherapy of cannabinoid addiction requires a comprehensive approach, taking into account medical care and pharmaceutical support. The peculiarities of the formation of cannabinoid addiction were studied by summarizing forensic pharmaceutical practice. Among the reasons for the growth of illegal cannabinoid circulation, drug crime and the spread of cannabinoid addiction are the lack of funding for pharmaceutical support for patients with cannabinoid addiction, the shortcomings of the regulatory framework, the lack of proper interaction between state authorities, self-government, law enforcement agencies and advocacy [38-41].

To counteract the illegal circulation of narcotic drugs, psychotropic substances, and precursors, it is necessary to [42]:

- ✓ continue reforming the law enforcement system and bringing it into line with international legal standards;
- ✓ provide material, technical and personnel support for special units that fight against drug trafficking;
- ✓ deepen cooperation between Ukraine and the EU in this area;
- ✓ ensure adaptation of national legislation to EU legislation;
- ✓ organize a large-scale sociological study of the latency of drug addiction and drug crime in Ukraine;
- ✓ create social and psychological rehabilitation services for drug addiction patients and change approaches to the drug accounting system;
- ✓ increase, on the basis of interdepartmental interaction, the effectiveness of preventive measures aimed at promoting a healthy lifestyle among minors and youth;
- ✓ strengthen explanatory work in pedagogical teams;
- ✓ encourage the participation of non-governmental public organizations, charitable foundations, and religious centers in the promotion of combating the illegal circulation of South Africa;
- ✓ develop and ensure an effective system of combating the leakage into illegal circulation of psychoactive substances from objects of entrepreneurial activity, which have been issued a license for such activity.

Revenue from the trade in narcotic drugs ranks second after the arms trade, amounting to USD 400 billion, ahead of the oil trade. The use of the Internet for the illegal circulation of psychoactive substances is growing [43]. The improvement of technical devices for using Internet resources stimulates the improvement of methods of illegal distribution of cannabinoids [43].

The analysis of some characteristics of drug crimes in Ukraine makes it possible to conclude that the existence of official statistical information and indicators that indicate a decrease in the level of drug crime in Ukraine does not reflect the actual state of crimes committed by this group, namely [44]:

- the most widespread crimes in the sphere of illegal circulation of narcotic drugs, psychotropic substances, and other psychoactive substances: illegal production, manufacture, acquisition, storage, transportation, forwarding or sale of narcotic drugs, psychotropic substances with the purpose of sale (Article 307 of the Criminal Code) and without the purpose of sale (Article 309 of the Criminal Code);
- in regions with the highest concentration of drug crimes per 100,000 population, there are no effective regional crime prevention programs;
- it is necessary to conduct a further study of the state of combating drug crime in Ukraine in order to develop a mechanism to combat this "background" phenomenon.

In his work Melnyk O.M. notes that: – in our society, a persistent search, improvement, and implementation of a large-scale system of combating drug addiction is underway, in particular, it is placed on a solid legislative and regulatory basis; as a member of the United Convention on Narcotic Substances of 1961, Ukraine takes an active part in international actions to stop the spread of narcotic drugs. Everything that the Ukrainian state has done in this field is a small part of what needs to be done. Unfortunately, the highest legislative body of the country deals with social policy mostly on paper, and the issue of drug addiction is bypassed altogether, although the problem is becoming increasingly acute and especially relevant, because the age of drug addicts is rapidly getting younger.

Undoubtedly, the mentioned problems require deep study and comprehensive analysis by specialists and scientists, taking into account both positive changes and the probability of harmful consequences. The criminal law policy of Ukraine in this area should be balanced and consistent, should be based on international experience and should provide for a continuous search for new approaches to, if not complete taming, then at least to reducing the destructive impact of drug addiction on society. Therefore, the problem of combating drug addiction among minors is a problem of a national scale and requires immediate, adequate measures [45-48].

For the purpose of practical consideration of the facts of the illegal circulation of psychoactive substances, five examples from forensic and pharmaceutical practice were given, which clearly show the level of the problem in Ukraine.

Forensic and pharmaceutical example No. 1. Criminal proceedings were opened by the investigator of the Zolochiv district of the National police in Lviv region under the procedural guidance of the prosecutor's office of the Lviv region under Part 2 of Art. 310 and Part 3 of Art. 309 of the Criminal Code of Ukraine [48]. It was established that on September 23, 2022, police officers detained a 33-year-old man from Zolochiv district. A. who illegally traded (growing, storing) cannabis for his own needs in particularly large quantities. During the search of the suspect's house, A. the police discovered and seized from illegal circulation 3.5 kg of plant material, which, according to the forensic examination, is cannabis. The suspect in the case was declared a suspect, and a pre-trial investigation is currently underway.

Forensic and pharmaceutical example No. 2. The investigator of the Ivano-Frankivsk District of the National police in Ivano-Frankivsk region opened a criminal proceeding under Part 2 of Art. 307 of the Criminal Code of Ukraine [49]. It was established that on October 15, 2022, police officers detained a 21-year-old girl after receiving a parcel at the Ivano-Frankivsk post office. B. During the examination of the parcel in the presence of the witnesses, there were 2 bags with a vegetable substance weighing 1 kg. After conducting an express test, it was established that the plant substance is cannabis (marijuana), a narcotic drug, worth about 280,000 hryvnias.

Forensic and pharmaceutical example No. 3. The investigator of the Mukachiv district of the National police in Transcarpathian region opened a proceeding under Part 1 of Art. 309 and Part 1 of Art. 310 of the Criminal Code of Ukraine [50]. It was established that on August 19, 2022, police officers in Mukachiv region and Berehiv region in the household of B. removed: 66 bushes of hemp plants; 0.5 kg of a substance that is a narcotic drug – marijuana.

Forensic and pharmaceutical example No. 4. Investigators of the Supreme Administration of the National police in Poltava region, under the procedural guidance of the Poltava regional prosecutor's office, opened proceedings under Part 1 of Art. 309 and Part 1 of Art. 310 of the Criminal Code of Ukraine [51]. It was established that a 51-year-old resident of Poltava ordered seeds of various varieties of hemp through the Internet. Illegally grew narcotic plants. From the collected "harvest" K. produced cannabis. During the authorized search on the land plot and the household, K. police investigators discovered and seized from illegal circulation: 20 cannabis plants; containers and packages with cannabis with a total weight of 0.700 kg; special devices for crushing cannabis and using marijuana. Seized material evidence was sent for forensic examination.

Forensic and pharmaceutical example No. 5. The Voznesenskii Court of Ukraine on December 17, 2019 completely acquitted gr. R., disabled person of the 1st group, for growing hemp for the treatment of his pain syndrome. Gr. R. used marijuana by smoking to relieve joint pain [52]. The court found the evidence inadmissible, and the fact of growing hemp bushes unproven. The court agreed with the argument of human rights defenders and the lawyer of the Center for Strategic Legal Defense of the Ukrainian Helsinki Union for Human Rights about the violation of the right to protection.

The right of drug patients with cannabinoid addiction to medical care and pharmaceutical support is guaranteed by Articles 3, 27, 46 and 49 of the Constitution of Ukraine [53]; Resolution of the Cabinet of Ministers of Ukraine dated August 17, 1998 No. 1303 [54].

Interdisciplinary studies of the circulation of psychoactive substances, pharmacotherapy of addictive addiction, forensic pharmaceutical practice was conducted by Ukrainian scientists

Trachtenberg I.M., Linsky I.V., Minko O.I., Galatsan O.V., Shapovalov V.V. (Jr.), Chuiev Yu.F., Gudzenko A.O., Zbrozhek S.I., Khalin M.M., Galavan Z.S., Petrenko S.L., Vasina Y.V., Malinina N.G., Shapovalov V.V., Negretskyi S.M., Kurizheva O.O. It is also necessary to note the great role of the following Ukrainian scientists: [Sosin I.K.], [Danilenko V.S.], [Kutko I.I.], [Viktorov O.V.], [Stefanov O.V.], [Gubskiy Yu.I.], [Volokh D.S.], [Georgievskiy V.P.], [Voloshyn P.V.], [Vyshar H.M.], [Abrosimov O.S.]

The conducted forensic and pharmaceutical studies showed [33] that:

- ❖ criminality related to the illegal circulation of cannabis in the structure of general crime related to the illegal circulation of psychoactive substances of various classification and legal groups is 58.75%; in the structure of drug crime related to the illegal circulation of narcotics of plant origin – 62.66%;
- ❖ in the Kharkiv region, on average, 22.58% to 23.33% of cannabis narcotics are seized from illegal circulation per month;
- ❖ 86.0% of men aged 21 to 51 participate in the drug business;
- ❖ there are cause-and-effect relationships between the increase in the illegal circulation of cannabinoids, the spread of cannabinoid addiction, polydrug addiction, polytoxicomania and the increase in the level of crime, drug crime and drug addiction in society.

Above became the basis for defining of the four directions for the development of regulatory measures to combat the illegal circulation of cannabinoids and cannabinoid addiction [34]:

- 1) organizational and legal (forensic pharmacy);
- 2) medical and pharmaceutical (health care organization, pharmaceutical business organization);
- 3) social and economic;
- 4) moral and ethical, informational and explanatory work (IEW), cultural and educational.

Scientific studies have developed a two-level system of regulatory measures (Fig. 1).

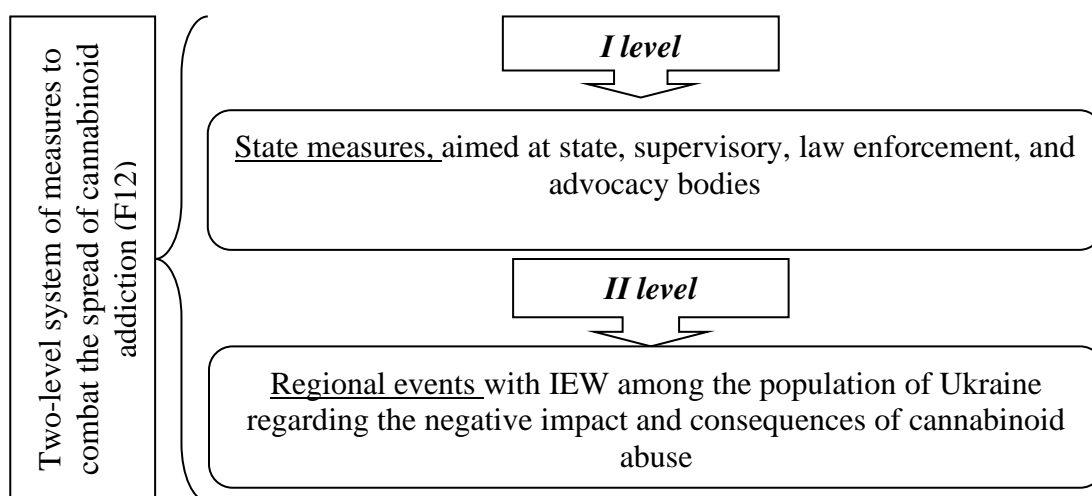


Fig. 1. A two-level system of regulatory measures to counter the spread of cannabinoid addiction and illegal cannabinoid circulation [28].

The method of assessing the availability and effectiveness of drugs for drug addicts according to pharmacoeconomic and forensic pharmaceutical criteria was improved on the basis of evidence-based medicine and evidence-based pharmacy. The inclusion of hepatoprotectors according to a set of indicators (effectiveness, availability, control regime) in the pharmacotherapy schemes of drug patients with cannabinoid addiction is substantiated. The informational and physical components of the availability of hepatoprotective drugs according to the forensic pharmaceutical indicator "control mode" were determined. It has been proven that, according to the clinical and pharmacological group, hepatoprotectors have the ATS code – A05BA; according to the classification and legal feature – classified as a general group; according to the nomenclature and legal group – l'esfal, essentielle and glutargin assigned to the prescription group; antral, karsil and hepabene – to the OTC group.

The economic components of the availability of hepatoprotectors were calculated according to pharmacoeconomic indicators (price volatility coefficient, availability coefficient, ABC analysis). L'esfal and antral prove to have the least price fluctuations (volatility coefficients of 13.78 and 16.89, respectively); the highest value of availability coefficients (at the level of 97.8 and 98.1, respectively) for drug addicts with cannabinoid (hashish) addiction (F12).

According to the results of ABC analysis, group A included 4 drugs according to INN (glutargin, essentielle, hepabene, l'esfal), group B included 2 drugs according to INN (antral, karsil). Group C did not include any drugs. Established that group A included the most expensive (77.8%) drugs (glutargin, essentielle, hepabene, l'esfal).

The study of the effectiveness of hepatoprotectors was carried out using a questionnaire of medical specialists (60 respondents) using statistical analysis of questionnaire data. Based on the results of the data, a rank matrix was constructed (Table 1).

Table 1. Matrix of ranks of hepatoprotectors of injectable and tablet dosage form.

The number of respondents and statistical indicators of their evaluations	Injectable dosage forms			Tableted dosage forms		
	L'Esfal (X1)	Essentiale (X2)	Glutargin (X3)	Antral (X1)	Carsil (X2)	Hepabene (X3)
$m = 60$						
$\sum_{i=1}^n a_{ij}$	6	6	6	6	6	6
$\sum_{i=1}^n \sum_{j=1}^m a_{ij}$	176	119	65	172	122	66
\bar{Z}_{ij}	2,93	1,98	1,08	2,86	2,03	1,10
Rank Z_j	3	2	1	3	2	1

Based on the obtained results, a histogram of the distribution by ranks (weighted average) of the respondents' conclusions was constructed (Fig. 2).

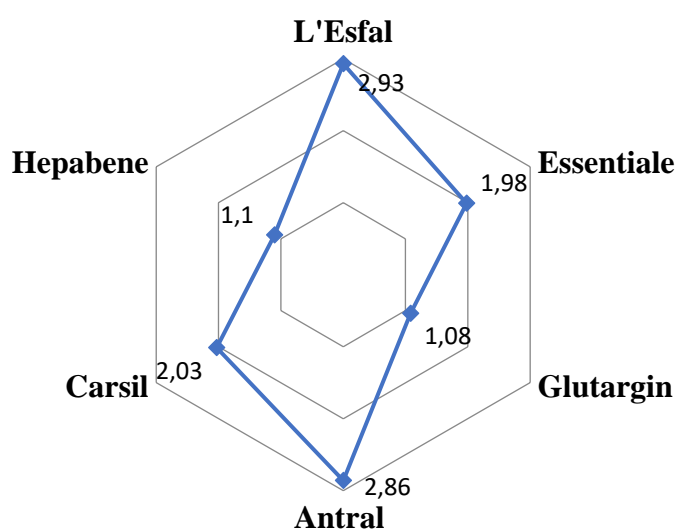


Fig. 2. Histogram of the distribution of the effectiveness of hepatoprotectors according to the ranks of respondents' conclusions.

Based on the study of the effectiveness of hepatoprotectors, established that the highest ranks were given to the drugs L'Esfal (2.93) and Antral (2.86).

According to pharmacoeconomic studies, the most available drugs are L'Esfal ($K_{nc} = 13.78$; $K_d = 97.8$) and Antral ($K_{nc} = 16.89$; $K_d = 98.1$).

The obtained results showed that the injectable form of the drug L'Esfal and the tablet form of the drug Antral can be recommended for inclusion in pharmacotherapy schemes of cannabinoid (hashish) addiction.

The simultaneous use of L'Esfal and Antral drugs in the pharmacotherapy schemes of cannabinoid (hashish) addiction (F12) was tested on the basis of the Healthcare Facility "Kharkiv Regional Narcological Dispensary" under the leadership of Prof. Sosin I.K. [55-59].

The study of the problem in recent years showed that specialists of the Ministry of Health of Ukraine propose to legalize the circulation of medical cannabis by adopting the draft law "On regulation of the circulation of plants of the genus hemp (*Cannabis*) for medical, industrial purposes, scientific and scientific and technical activities" [60]. Cannabis preparations will help to save the traumatized psyche of patients due to hostilities, create new jobs, prevent the illegal circulation of cannabis preparations, reduce criminogenic tension in the regions (thefts, road accidents, suicides, etc.), increase financial revenues to the budget of Ukraine [61].

Conclusions. Data from the scientific literature on the current state of the spread of addiction on psychoactive substances of plant origin – cannabinoids was processed. The problem of cannabinoid addiction has been studied. Forensic and pharmaceutical practice was analyzed. The specific weight of offenses related to the illegal circulation of cannabinoids is more than 58%. According to the statistical data, 86.0% of men aged 21 to 51 participate in the drug business. For the first time, the development of organizational measures for the provision of drugs to drug patients with cannabinoid addiction (F12), which involve a comprehensive approach, has been scientifically substantiated. A two-level system of control and permitting measures has been developed, which includes state (I level) and regional (II level). The peculiarities of pharmacotherapy and the availability of drugs for drug addicts have been clarified. The informational and physical components of the availability of hepatoprotectors of the new generation according to the forensic pharmaceutical indicator "control mode" were determined. The economic components of the availability of hepatoprotectors were calculated based on the pharmacoeconomic indicators of the coefficients of price volatility and availability, as well as ABC analysis.

Conflict of interest. The author declares that he is the sole author of this work and has approved it for publication. The author certifies that the research was conducted in the absence of any commercial or financial relationships that could be interpreted as a potential conflict of interest.

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