

MARKETING RESEARCH OF THE MARKET OF DRUGS FOR THE TREATMENT OF HEPATOBILIARY SYSTEM DISEASES IN UKRAINE DURING THE COVID-19 PANDEMIC

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Introduction. Since the beginning of the COVID-19 pandemic, doctors around the world, including Ukraine, have seen an increase in liver disease, which, incidentally, leads to complications of coronavirus infection. This can be both acute liver damage by the virus itself and hepatotoxic effects of medicines used in COVID-19 [1-3].

In general, the total percentage of hepatobiliary system diseases in the structure of gastrointestinal diseases prevalence in Ukraine is about 30%. Every year, more than 1 million people die from chronic liver diseases and their complications. Among certain nosological forms in the class of gastrointestinal diseases, the highest share in the structure of mortality is occupied by liver fibrosis and cirrhosis (52.1%) and alcoholic liver disease (9.6%). The most common nosological cause of primary disability among patients with diseases of the gastrointestinal tract is cirrhosis of the liver (75.2%) [4].

Thus, it can be noted that diseases of the hepatobiliary system occupy a large percentage of all diseases of the digestive system and are the cause of a large percentage of complications and mortality.

The study of the Ukrainian market of hepatoprotectors was carried out by Matyashova N.O., Volkova A. V., Yakovlieva L.V. with coauthors [5-7].

Summarizing all the above, it can be concluded that the treatment of liver and biliary tract diseases remains an urgent task for Ukraine, given the epidemic situation that exists today in the country.

The purpose of our research was to study the range of drugs for the treatment of liver and biliary tract diseases registered in the pharmaceutical market of Ukraine since the beginning of the COVID-19 pandemic.

Materials and methods. The data of information resources, such as the State Register of Drugs, Compendium of Drugs, etc., which have been generalized by means of marketing methods, structural, statistical, and graphic analyzes, are used in the work.

Results and discussion.

A special place in the treatment of hepatobiliary pathology is occupied by medicines that belong to the group of hepatoprotectors. Hepatoprotectors are one of the most popular groups of medicinal products, whose action is aimed at restoring homeostasis in hepatocytes, which increases the body's resistance to pathogens, promotes normalization of functional activity, and stimulation of reparative and regenerative processes in the liver. Due to such effects, hepatoprotectors are used in liver diseases, pathologies of internal organs complicated by liver damage, and as a method of medical cover-up when using medicines that affect the liver [8, 9].

There are several classifications of hepatoprotectors. For example, SV Okovytyi proposes to divide hepatoprotectors by origin [9] (Table 1).

Table 1. Classifications of hepatoprotectors according to SV Okovytyi

Classification group	Brief description of the group	Examples of drugs
1. Preparations of plant origin		
1.1. Preparations containing natural or semi-synthetic flavonoids of milk thistle	Stimulate protein synthesis, protect liver cells from the penetration of toxins and free radicals	Carsil, Silibor, Silimar
1.2. Preparations containing licorice	Reduce inflammation, protect liver cells due to the antioxidant action	Phosphogliv
1.3. Preparations containing natural or semi-synthetic flavonoids of other plants	Have a choleric, diuretic and hepatoprotective effect	artichoke preparations (Hofitol, Holiver), catergen (Cyanidanol), Hepaliv, Tykveol
2. Preparations of animal origin		
		Sirepar, Hepatosan, Prohepar, Laenneka
3. Medicines containing essential phospholipids	They are part of the membranes of liver cells and help preserve their structure. Actively affect lipid metabolism.	Essentiale, Phosphogliv, Essliver, Eplir
4. Medicines with a predominant detoxifying effect	They are not classical hepatoprotectors, but have the ability to reduce toxemia associated with hepatocellular impairment by reducing the increased utilization of endogenous toxicants	
4.1. Medicines with direct detoxifying effect	These medicines are used to treat hepatic encephalopathy, regulate metabolism in liver cells, participate in the neutralization of ammonia	Ornithine-aspartate, Glutamine-arginine
4.2. Medicines with indirect detoxifying effect	reduce the formation of endogenous toxins; activate the formation of metabolites that provide a detoxifying effect;	Lactulose, Lactitol Ademethionine (which affects not only the liver but also the brain and

	accelerate the metabolism of toxicants	has an antidepressant effect, participates in the synthesis of aminoacids, participates in neutralization and excretion of bile acids into the biliary system) Metadoxin (breaks down alcohol, Phenobarbital)
5. Preparations of bile acids	stabilizes the membranes of hepatocytes	Ursodeoxycholic acid obethicholic acid
6. Medicines of different groups	Thioctic acid, affecting the peroxidation of lipids, inhibiting the synthesis of nitric oxide and thus protecting hepatocytes from toxins; thiazoic acid	Alpha lipon, Berlition Thiotriazolin

According to the classification proposed by ON Minushkin, LV Maslovskyi, AA Bukshuk hepatoprotectors are divided by mechanism of action [9] (Table 2).

Table 2. Classifications of hepatoprotectors according to ON Minushkin, LV Maslovskyi, AA Bukshuk

Classification group	Examples of drugs
1. Medicines that affect mainly the manifestations of cytolysis syndrome, reducing fatty infiltration of the liver	Essentiale forte
2. Medicines that affect mainly the manifestations of cholestasis syndrome:	
a) preparations of ursodeoxycholic acid	Ursosan, Ursofalk, etc.
b) preparations containing S-adenosylmethionine	Heptral
3. Medicines with predominantly detoxifying effect:	
a) used in acute and chronic alcohol intoxication	Metadoxyl, Roprene
b) used for medicinal and other toxic lesions	Ursosan
c) contain flavonoids of milk thistle	Hepabene, Legalon, Carsil
d) contain flavonoids of other plants	Hofitol
4. Medicines that prevent the development of fibrosis and are recommended for use at the stage of liver cirrhosis:	
a) preparations of ursodeoxycholic acid	Ursosan
b) preparations of the polyprenol group	Roprene
c) preparations containing flavonoids of milk thistle	Carsil
5. Medicines with possible antiviral activity (inhibiting hepatitis virus replication)	
a) preparations containing milk thistle flavonoids	Silibin, Silymarin
b) medicines that promote the transition of the virus into a latent state and stimulate the synthesis of interferon	Laenneka, Ursosan
6. Medicines that stimulate hepatocyte regeneration and modulate the immune system	Laenneka
7. Medicines with combined hepato- and neurotropic action, affecting the state of the central and peripheral nervous system	Metadoxyl, Roprene

As can be determined from the above data, hepatoprotectors can be of plant or animal origin, medicines that contain amino acids and essential phospholipids, medicines of synthetic origin.

Next, we have analyzed the Ukrainian market of hepatoprotective medicines.

The analysis was performed in group A05 "Bile and liver therapy" (according to the ATC classification) [8, 10]. Data are for September 2021.

The capacity of the hepatoprotector market in Ukraine is over 7.9 million packages worth over UAH 1.1 billion, and foreign brands such as Essentiale and Carsil are

among the top twenty in terms of sales of medicines in Ukraine [7].

Most hepatoprotectors for oral use (in the form of tablets, capsules, granules and powder for solution, drops, syrup, and herbal raw materials) are available over-the-counter.

Exceptions are:

- tablets: Bicyclol, Ursofalk, Ukrliv, Ursodiol. They include bicyclol and ursodeoxycholic acid;
- capsules: Ursofalk, Grinterol, Ursolizin, Ursoliv, Ursonost, Ursosan, Holudexan, Ursohol, Ursomax, Fumarta. The active substance of these medicines is ursodeoxycholic acid;

- oral suspension: Ursosalk, Ukrliv. They also contain ursodeoxycholic acid.

Thus, all preparations that contain ursodeoxycholic acid are prescription-only [11].

Hepatoprotectors for parenteral use (in the form of solution for injection, solution for infusion, concentrate for solution for infusion, powder for solution for infusion, lyophilisate for emulsions for injection), as well as suppositories, are available on prescription. Some over-the-counter drugs were re-registered as special food products in 2018 [8].

In 2001, the first National List of Essential Medicines included medicinal products used in liver diseases, namely: medicines based on essential phospholipids, silymarin, antral, thiotriazoline. The list applied to all finished dosage forms and dosage forms of drugs that were registered in Ukraine in accordance with these international non-proprietary names [12].

In 2006, the second National List of Essential Medicines included hepatoprotectors such as L-ornithine aspartate, antral, arginine, heparsuis, essential phospholipids, silymarin (monopreparation and its combinations), thiotriazoline, phosphatidylcholine. However, the group of these medicines was not included in the third National List of Essential Medicines, published in 2009 and based on the 19th edition of the Basic List of Essential Medicines recommended by the WHO [12].

However, they are included in the 13th issue of the State Form of Medicines (approved by Order No. 792 of the Ministry of Health of Ukraine dated 22.04.2021), which contains recommendations for the rational prescription and use of medicines. This group includes 25 trade names of hepatoprotective medicines. These are:

- Silymarin preparations: Darsil, Silibor 35, Hepar, Hepar forte, Carsil, Silymarol, Silybor Max, Silybor forte, Carsil forte, Legalon 140, Legalon 70;

- amino acid preparations: Hepatox, Heptor-Farmex, Larnamine Hepa-Merz, Orniliv (concentrate for solution for infusion), Ornitox (solution for injection), Larnamin, Hepa-Merz, Ornitox (granules for oral solution);

- combined medicines : Hepabene.

According to the standards of medical care in Ukraine, hepatoprotectors are used in 17 areas and medical specialties for different categories of patients: outpatients and inpatients; adults and children; pregnant and disabled.

In medical practice, hepatoprotectors are used as part of basic and symptomatic therapy to eliminate toxic hepatitis associated with side effects and complications of treatment of the patient's underlying disease with antibacterial, antifungal, antiretroviral drugs, cytostatics, delagil, ACE inhibitors, hypolipidemia; for the prevention of liver cirrhosis in cystic fibrosis; in case of impossibility of carrying out antiviral therapy of chronic viral hepatitis B without delta antigen; as a part of general strengthening therapy at pneumonia; as a part of medical and rehabilitation actions (radiation sickness, rehabilitation of invalids); in mild, moderate and severe poisoning to remove the poison that is absorbed into the bloodstream, to eliminate the syndrome of toxic hepatopathy [12].

Thus, despite the absence in the current National List of Essential Medicines and the WHO Base List, they are an important group of medicines that are present in the 13th issue of the State Form of Medicines and are widely used in medical practice in accordance with medical standards in Ukraine.

Both imported and domestic drugs are represented in the Ukrainian market (Fig. 1). A total of 73 trade names of hepatoprotectors have been registered so far.

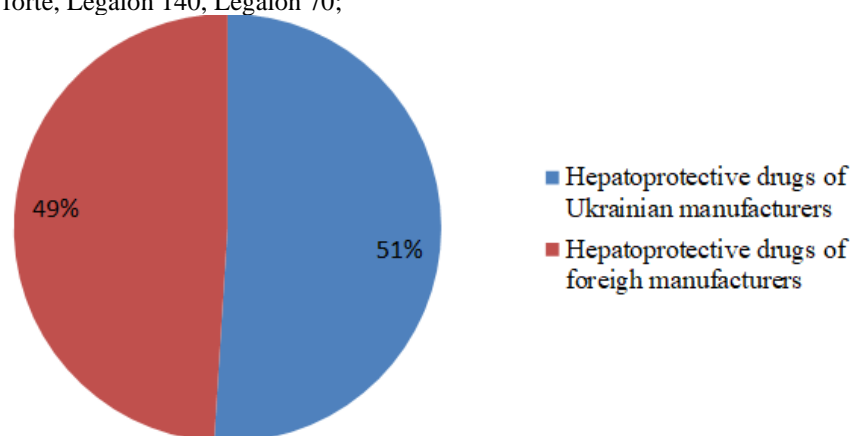


Fig.1. Percentage of domestic and imported hepatoprotective drugs.

As can be seen from Fig.1, domestic and imported drugs currently occupy almost the same market share. But we must remember that in monetary terms, the leading position is occupied by imported medicines because the difference in cost between the original drug and generics of domestic production can be one and a half to two times greater in favor of the original. Foreign manufacturers offer

mostly original medicines, the Ukrainian manufacturer's market is represented by generics and herbal medicines [8,10].

For a more detailed consideration of the segment of imported hepatoprotective medicines, it was distributed by country of origin, as shown in Fig. 2

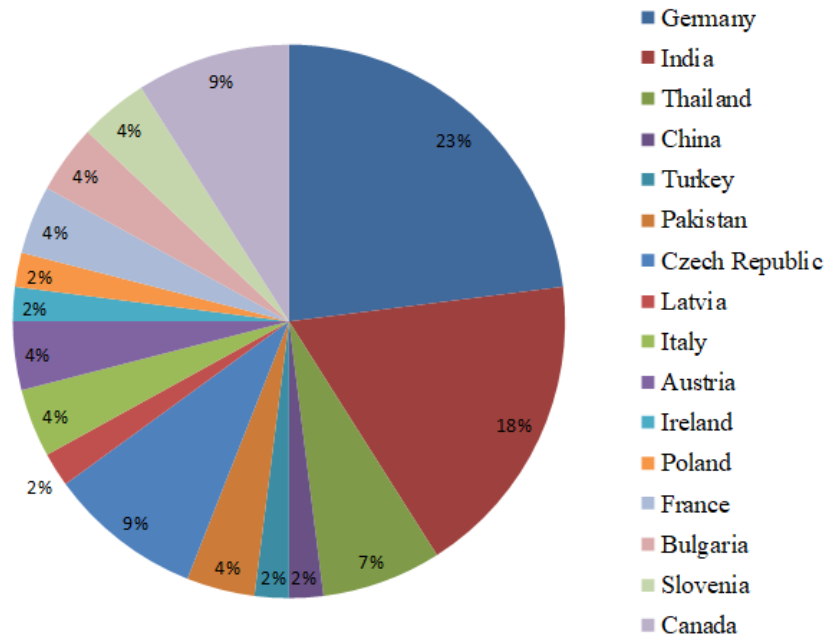


Fig. 2. Structuring of the Ukrainian market of imported hepatoprotective drugs by producer countries

As can be seen from the graph shown in Fig. 2, the first place in the number of names of medicines for the treatment of hepatobiliary system diseases, which are on the market of Ukraine, is occupied by Germany, the second - India, and the third - Czech Republic and Canada. In

general, hepatoprotective medicines from 16 countries are present on the Ukrainian market.

We have analyzed the distribution of hepatoprotective medicines by active substance, which is presented in Fig. 3.

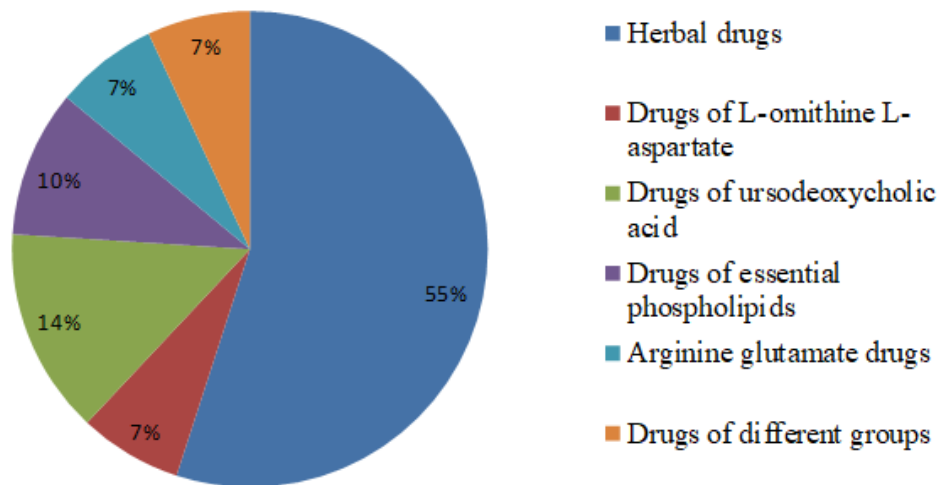


Fig. 3. Distribution of hepatoprotective medicines on the Ukrainian market by active substance

As can be seen in Fig. 3, the first place in prevalence is occupied by medicines of plant origin. Second place take ursodeoxycholic acid preparations, and in third place are preparations of essential phospholipids.

It can be concluded that the Ukrainian market of hepatoprotectors is filled with herbal preparations, but this only emphasizes their quality and effectiveness.

In the group of preparations of different groups are medicines that have the following active substances: bicyclol, thiotriazoline, antral, succinic acid.

The distribution of hepatoprotective drugs by dosage forms is presented in Fig.4.

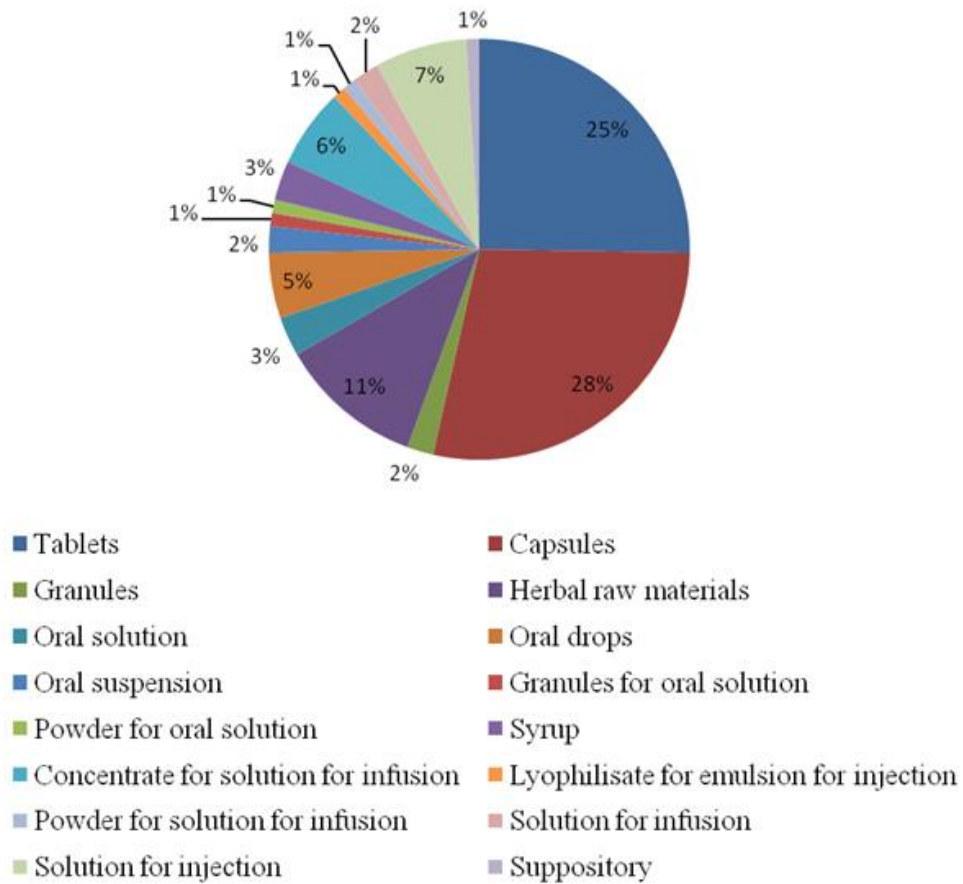


Fig. 4. Distribution of hepatoprotective medicines by dosage forms

Solid dosage forms for oral administration (tablets, capsules, granules) occupy more than half of the market of hepatoprotective medicinal products in Ukraine. They are followed by medicines for parenteral administration, which together occupy 17% of the market. Liquid oral dosage forms occupy 15%. It should also be

noted that medicinal plant raw materials (blends, parts of plants) occupy about 11% of the market.

Fig. 5 shows the distribution of medicines of group A05 by the presentation. As can be seen in Fig. 5 over-the-counter drugs make up 65% of the total number of hepatoprotectors registered in Ukraine.

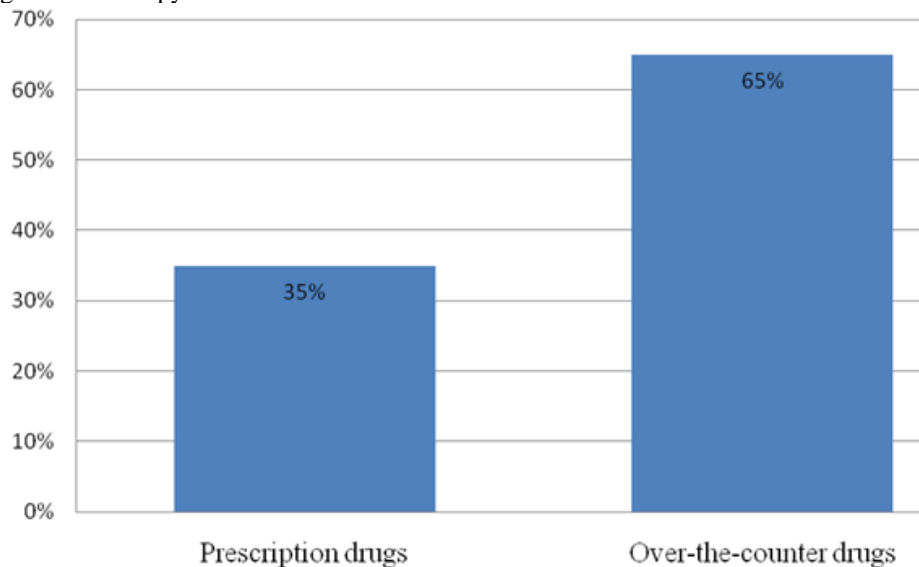


Fig. 5. Distribution of drugs by presentation

Thus, most hepatoprotective drugs are over-the-counter. These are mainly medicinal plant raw materials and oral preparations. Prescription medicines include all

injectable and infusion medicines, ursodeoxycholic acid medicines in all dosage forms.

Based on all the above data, it is possible to say that hepatoprotective medicines are widely represented in the pharmaceutical market of Ukraine. The market is

saturated with original and generic medicines, medicines of both imported and domestic production are presented; both prescription and over-the-counter medicines in various dosage forms are available.

Due to the fact that recently coronavirus infection has spread among children and adolescents, we consider promising research on the development of hepatoprotectors in the form of syrup.

Conclusions. A comparison of the National List of Medicines, the Basic List of Essential Medicines of the WHO and the State Form of Medicines on the content of medicines for the treatment of hepatobiliary system diseases has been carried out. It has been demonstrated that medicines of this group are currently excluded from the first two above-mentioned information sources.

Marketing research of the market of modern hepatoprotectors registered in Ukraine has been carried out. It is concluded that medicines of this group are widely represented in the pharmaceutical market of Ukraine. Both imported and domestic production medicines in various dosage forms are available. But given the epidemic situation in Ukraine and the spread of coronavirus infection among children and adolescents, we consider promising research on the development of hepatoprotectors in the form of syrup.

Marketing research of the market of drugs for the treatment of hepatobiliary system diseases in Ukraine during the COVID-19 pandemic

Kryklyva I., Karpenko L., Zaporozhska S., Saiko I., Sichkar A.

Introduction. Since the beginning of the COVID-19 pandemic, doctors around the world, including Ukraine, have seen an increase in liver disease, which, incidentally, leads to complications of coronavirus infection. This can be both acute liver damage by the virus itself and hepatotoxic effects of medicines used in COVID-19. The treatment of liver and biliary tract diseases remains an urgent task for Ukraine, given the epidemic situation that exists today in the country. The purpose of our research was to study the range of drugs for the treatment of liver and biliary tract diseases registered in the pharmaceutical market of Ukraine since the beginning of the COVID-19 pandemic. Materials and methods. The data of information resources, such as the State Register of Drugs, Compendium of Drugs, etc., which have been generalized by means of marketing methods, structural, statistical, and graphic analyzes, are used in the work.

Results and discussion. A special place in the treatment of hepatobiliary pathology is occupied by medicines that belong to the group of hepatoprotectors. There are several classifications of hepatoprotectors. For example, SV Okovytyi proposes to divide hepatoprotectors by origin. According to the classification proposed by ON Minushkin, LV Maslovskiy, AA Bukshuk hepatoprotectors are divided by mechanism of action. Thus hepatoprotectors can be of plant or animal origin, medicines that contain amino acids and essential phospholipids, medicines of synthetic origin. We have analyzed the Ukrainian market of hepatoprotective medicines. The analysis was performed in group A05

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"Bile and liver therapy" (according to the ATC classification). Data are for September 2021. Both imported and domestic drugs are represented in the Ukrainian market. A total of 73 trade names of hepatoprotectors have been registered so far. The first place in the number of names of medicines for the treatment of hepatobiliary system diseases, which are on the market of Ukraine, is occupied by Germany, the second - India, and the third - Czech Republic and Canada. In general, hepatoprotective medicines from 16 countries are present on the Ukrainian market. The first place in prevalence is occupied by medicines of plant origin. Second place take ursodeoxycholic acid preparations, and in third place are preparations of essential phospholipids. Solid dosage forms for oral administration (tablets, capsules, granules) occupy more than half of the market of hepatoprotective medicinal products in Ukraine. Most hepatoprotective drugs are over-the-counter. **Conclusions.** Given the state of treatment of hepatobiliary system diseases, which has not lost its relevance during the COVID-19 pandemic, the situation in the pharmaceutical market in terms of range of hepatoprotectors registered in Ukraine has been analyzed. It is demonstrated that hepatoprotective drugs are widely represented in the pharmaceutical market of Ukraine. The market is saturated with original and generic drugs, medicines of both imported and domestic production are presented; both prescription and over-the-counter drugs in various dosage forms are available.

Keywords: hepatobiliary system, liver disease, hepatoprotectors, market analysis

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