ТЕХНОЛОГІЯ ЛІКАРСЬКИХ ПРЕПАРАТІВ

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PROSPECTS OF CREATING A NEW COMBINED MEDICINE WITH THE HEPATOPROTECTIVE ACTION

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Complex therapy of diseases of the hepatobiliary system of different genesis requires the use of safe, pharmacologically active, and multifunctional hepatoprotective medicines. Creation of a new original medicine containing several compounds of the natural origin in its composition is a perspective task of modern medicine.

Actuality problem of functional pathology of the hepatobiliary system is determined by considerable prevalence of these diseases not only in the structure of internal illnesses, but also in general population.

A modern lifestyle (stresses, surplus feed, low physical activity, smoking, alcohol, consumption of a plenty of medications), and also ecology, appeares as factors of risk of different diseases for internal organs, in particular a liver and biliary tract [1, 6, 22].

According to data of Worldwide Organization of Health Care, a more than 2 billion of people, suffering by the diseases of liver, is counted, that in 100 times exceeds prevalence of HIV-positive. For the last 20 years in a whole world there is a tendency to growth a number of liver diseases. Only in countries CIS is annually registered from 500 thousand till 1 million of people suffering that or other pathology of liver. In Ukraine for the last 10 years the prevalence of chronic hepatitis and cirrhosises of liver was multiplied at 2.2 times at least. So now only on a clinical account there are over 280 thousand of patients with chronic hepatitis of a different etiology and more than 40 thousand of patients with the cirrhosis of liver [2, 3].

Liver is an unique and difficult functional organ of the digestive system, which carrying out a big amount of various functions vitally necessary for the organism of man [3, 17] (Fig. 1).

Consequently, a therapy of diseases of the hepatobiliary system is one of the most main questions of modern medicine.

Illness of liver, gall-bladder and bilious ways are connected wiyh earch other, and the disease of one organ is accompanied by changes in other (biliary disorders function of liver are accompanied by the destructive changes of cellular membranes of hepatocytes). But an inflammatory process begins more frequently in a liver [14]. Hepatitis (acute and chronic), cirrhosis of liver, cholecystitis, discinesia at bilious ways, hepatic insufficiency, gall-bladder and bilious ways are concern to diseases of liver [5, 13, 21].

Diseases of gall-bladder appear at women, more frequently than at men, the. But such disease as cirrhosis, which is caused mainly by abuse by an alcohol, appears more frequently at men.

To hepatitis all are inclined, not depending on a sex and age. This illness usually appears in the school teams, kindergardens and even whiles the most severe quarantine; hepatitis B virus is spreading quickly [4, 6].

Complex medical treatment of liver diseases consists of two basic directions: causal and pathogenetic therapy. Causal therapy is used in viral hepatitis with parenteral mechanism of infection and is aimed to inhibition of viral replication, which caused to disease.

The basis of the pathogenetic therapy of liver disease includes drugs that increase the resistance of hepatocytes to pathological effects. It increases their antitoxic function and influence on the recovery of the disturbed functions of liver cells. These medicines of pathogenetic therapy are reflected by the term of gepatoprotector [4, 7, 15].

The mechanism of action hepatoprotectors:

- Amplification a disinfecting function of hepatocytes by increasing the reserves of glutathione, taurine, sulfates, or increasing the activity of enzymes, which takes part in the oxidation process;
- inhibition of the reactions of excessive lipid peroxidation and repair structures of cell membrane;
- anti-inflammatory action;
- blocking at fibrinogenezis by relief at necrosis of hepatocytes, the stimulation of activity in the liver and collagenosis block enzymes wich takes part in the synthesis of components at connective tissue [7, 17, 25].

Despite the large number hepatoprotectors presented in the pharmaceutical market in many countries remains a topical issue of creating a new domestic medicine,

Table 1

Classification and assortment of hepatoprotectors

The group of medicines	Examples of medicines	Country (producer)
Medicines that contains a natural or semi-synthetic flavonoids, silymarin is primarily	Karsil, dr.	Bulgaria
	Gepabene, caps.	Germany
	Gepatofalk planta, caps.	Germany
	Legalon, caps., dr.	Germany
	Silibor, tab.	Ukraine
	Darsil, tab.	Ukraine
	Sirotin, tab.	Slovenia
	Simepar, caps.	Switzerland
Medicines that contains a natural or semi-synthetic flavonoids other plants	Hophitol, tab.	France
	LIV – 52, tab.	India
	Gepatophit, coll.	Ukraine
	Flamin, tab.	Ukraine
	Sibectan, tab.	Russia
	Flacumin, tab.	Ukraine
	Tucveol, caps.	Russia
The organic medicines of animal origin	Sirepar, solut.	Hungary
	Gepatosan, caps.	Russia
	Liobil, tab.	Lithuania
	Holenzim, tab.	Russia
	Vigeratin, tab.	Belarus
	Allohol, tab., dr.	Ukraine
Drugs that contains essential phospholipids	Esenciale, caps.	Germany
	Phosphogliv, caps.	Russia
	Esliver, caps.	India
Medicines of different groups: aminoacids and their derivatives, vitamins, ursodeoxycholic acid	Geptral, tab.	Switzerland
	Ursofalk, tab.	Germany
	Ursosan, tab.	Czech Republic
	Metionin, tab.	Russia
	Lezitin, cap.	Russia
	Zitrarginin, sol.	France
	Lipin, pulv.	Ukraine
	Metadocsil, tab.	Italy
	Tiotriazolin, tab., cap.	Ukraine
	Espalipon, tab.	Germany
	Antral, cap., tab.	Ukraine
	Gepa-merz, pulv.	Germany
	Glutargin, tab.	Ukraine
Homoeopathic medecines	Galstena, tab.	Austria
	Gepar compozitum, sol.	Germany
	Rostoropsha compozitum , sol.	Germany

which will have significant advantages over existing ones.

Therefore, it was expedient to analyze the range of existing medicines hepatoprotectors at domestic and foreign production (Tabl. 1).

As the table shows, the range of medicines that are used for liver and biliary tract on the Ukrainian market is formed mainly due to foreign-made products (75%), which are taking part for about 70 producers (Russia, India, Germany, France etc.). Also known as the majority of foreign medicines do not always affordable to many patients in Ukraine, especially with prolonged use age of drugs [3].

Therapeutic efficacy while application of test substances depends on their medicinal form [19, 24]. Therefore, we analyzed the range at hepatoprotectors according to their medicinal form (Fig. 2).

The first group hepatoprotectors most widely represented by solid dosage form, namely, tablets (50%). Second seat in the assortment of pharmaceutical market is taken by capsules (25%). The far of medicines is represented in the form of solutions (10%) and drops (8%).

Plant collections, powders for preparation of solutions and other medications (syrups, suppositories), are represented in the least amount [22]. First of all in terms of biocompatibility for the body, anti-toxicity because of the the absence of cumulative properties, and finally, because of their accessibility to enzymatic processing to the final products that are excreted from the body physiologically. They also have wide variety therapeutic effects. A cost-effectiveness process allows applying these materials for domestic production of medicines [3, 11]. So it was necessary to analyze medicines hepatoprotectors according to the sources of origin (Fig. 3).

From the above results we can conclude that the pharmaceutical market is dominated by hepatoprotectors of plant origin, but it's primarily talking about their safety for the body, in connection with the minimum number of side effects. Medicines of animal origin constituted the smallest number (3%) of the total range of hepatoprotectors.

It is necessary to mark that now we have a situation, when products of beekeeping after the small interval of time is comparative become one of the most popular natural medicin compounds and found in a spotlight as a source of hepatoprotective medicines [16, 23].

Expedience of the use is scientifically led to in technology of medications of propolis, thanks to maintenance in their composition of valuable pharmacological active natural connections which show the wide spectrum of pharmacological action: anti-inflammatory, regenerative, reparative, antioxidant, antimicrobial, immunostimulating [18].

Very important is the fact that compounds which are part of propolis affect both the removal of the liver of bile, which takes part in digestion, and in decontaminating function of liver. The medical value also has ability of propolis to protect a liver from a different toxic influencing. Also, connections of propolis effective at some poisoning by medications, and at the promoted sensitiveness to action of medications. Furocoumarins, chromone and flavonoids, which are in propolis, are able to reduce the tone of the intestines, remove it spasms caused by various agents [8, 9, 12].

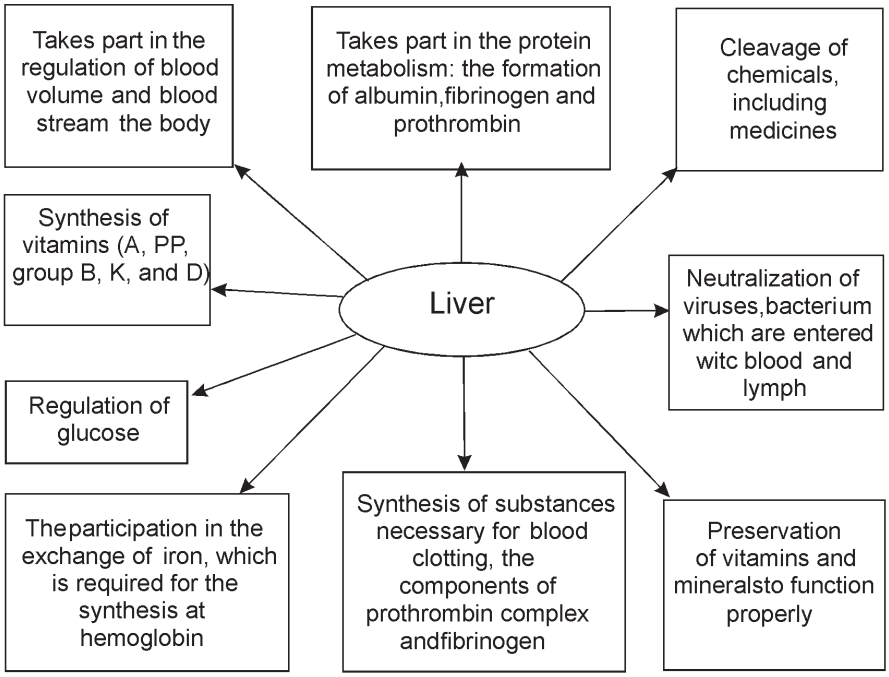

Fig. 1. Functions of liver and its part in the human body.

In such a way propolis is a valuable pharmacologically-active agent, which allows using it in the treatment of diseases hepatobilliari system.

One of enough study objects of biological animal is a bile, which has been used in folk medicine. Bile is the secret of polygonal cells, which is constantly, produces by liver of vertebrates' animals.

Organoterapeuthic medicines, which includes a medical bile are used widely in practical medicine for because at a wide range of biological effects diseases of the hepatobiliary system. The bile of cattle is used as an anti-inflammatory, analgesic and resolving agent, and is included in several national choleretic medicines. Recently, thanks to careful study of the chemical composition of bile became clear that it is complex the product of the liver in the biochemical, physical-chemical and physiological sense. It contains a number of compounds that determine its characteristic: bile lipids (cholesterol and its esters, bile acids, fatty acids, phospholipids), and bile pigments [3, 11].

On this basis, an analysis of domestic medicines with a bile as an active substance has been carried out. As a result, concluded that these medicines occupy too

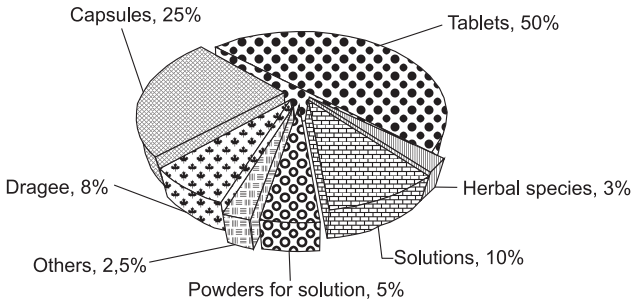

Fig. 2. Distribution of drugs according to pharmaceutical form.

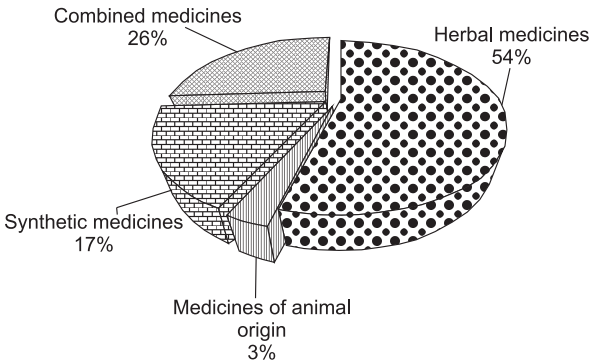

Fig. 3. Distribution of medicines according to the sources of origin.

Table 2

Assortment of medicines on the basis of bile cattle

The name product	Dosage form	Composition of the drug	Manufacturer of
Bile Medical canned	Solution: bottle, 250 ml, 100 ml	bile of cattle	«ChKP-Pharma» (Infuzia), Ukraine
Holenzim	Tablets	1 tab.: dried bile – 0.1 g; dried minced pancreas – 0.1g; dried mucous membranes of the intestines of beef cattle – 0.1 g;	«Lugapharm» Ukraine
Allohol	Tablets	1 tab.: dried bile – 80 mg, dried garlic powder – 40 mg, nettle leaves – 5 mg, activated charcoal – 25 mg;	«Borshchagovskiy» Ukraine

small number in the pharmaceutical market at Ukraine (Tabl. 2).

Today it is well known the age of combine therapy for patients with liver disease, gallbladder and biliary tract. From one side, there is a large clinical experience of efficiency of medicines combination. From the second, according to the modern notions in diseases of the hepatobiliary system takes part different mechanisms that interact with each other. A combination of two or more substances that interact with compensatory responses of each of them significantly increases the pharmacological effect at medicine as a whole. But the combination of substances of synthetic origin is applies generally [10, 20].

Thus, for the domestic production the creation of a new combined medicine, which can not to give foreign-made drugs, be available to many segments of the population, and suitable for prolonged usag in terms of pharmacotherapeutic safety is an actual task.

CONCLUSIONS

1. A modern range of medicines with hepatoprotective action consists a primarily of foreign medicines.

2. Medicines with active substances from plants and animals have an advantages over synthetic medicines by inex of bioavailability, and pharmacotherapeutic efficiency and level of safety.

3. Recently, great interest is the usage of combined medicines therapies, which includes some of the substances of natural origin.

4. Creation at original combine medicine on the basis of beekeeping products and a bile of cattle is a perspective scientific direction.

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ПЕРСПЕКТИВЫ СОЗДАНИЯ НОВОГО КОМБИНИРОВАННОГО ЛЕКАРСТВЕННОГО ПРЕПАРАТА ГЕПАТОПРОТЕКТОРНОГО ДЕЙСТВИЯ

Е.А.Дегтярева, А.И.Тихонов

Комплексная терапия заболеваний гепатобилиарной системы разного генеза требует применения безопасных, фармакологически активных, многофункциональных препаратов-гепатопротекторов. Создание нового оригинального препарата, в котором соединены несколько субстанций природного происхождения, является перспективным направлением современной медицины.

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ПЕРСПЕКТИВИ СТВОРЕННЯ НОВОГО КОМБІНОВАНОГО ЛІКАРСЬКОГО ЗАСОБУ ГЕПАТОПРОТЕКТОРНОЇ ДІЇ

К.О.Дегтярьова, О.І.Тихонов

Комплексна терапія захворювань гепатобіліарної системи різного генезу вимагає використання безпечних, фармакологічно активних, багатофункціональних препаратів- гепатопротекторів. Створення нового оригінального препарату, в якому поєднуються декілька сполук природного походження, є перспективним напрямком сучасної медицини.