HERBAL MEDICINAL COMPOUNDS IN THE EFFECTIVE TREATMENT OF LIVER DISEASES

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Abstract. *As a result of liver damage, changes in cellular metabolism occur in the immune system against various toxic substances and microbes. It is characterized by a decrease in the functional activity of the liver, a violation of its chemical and immunological mechanisms.*

Keywords: *toxic substances, metabolism, hepatocyte, plasma membrane, homeostasis.*

ЛЕКАРСТВЕННЫЕ ПРЕПАРАТЫ РАСТИТЕЛЬНОГО ПРОИСХОЖДЕНИЯ В ЭФФЕКТИВНОМ ЛЕЧЕНИИ ЗАБОЛЕВАНИЙ ПЕЧЕНИ

Аннотация. *В результате поражения печени в иммунной системе происходят изменения клеточного метаболизма в отношении различных токсических веществ и микробов. Характеризуется снижением функциональной активности печени, нарушением ее химических и иммунологических механизмов.*

Ключевые слова: *токсические вещества, метаболизм, гепатоцит, плазматическая мембрана, гомеостаз.*

INTRODUCTION

Currently, the number of people affected by acute and chronic hepatitis is increasing in the countries of the world. In connection with this situation, several scientific laboratories and centers are conducting research in search of medicinal compounds showing hepatoprotective properties.

Modern methods of treatment of diseases caused by liver damage cover two main directions. The first direction, in clinical practices, the etiotropic treatment method was adopted in the case of viral hepatitis. The second direction is the method of pharmacological treatment in accordance with the pathogenetic treatment in accordance with the different time links of the pathogenesis. Pharmacological correction is aimed at different levels of liver damage and all changes in the pathogenesis of liver cells with the help of medicinal compounds. [1, 12, 13].

MATERIALS AND METHODS

Hepatoprotectors are the pharmacological basis of treatment of liver diseases. The main hepatoprotective compounds used in clinical practice are plant compounds, i.e. phytohepatoprotectors [2, 3, 11]. Phytohepatoprotectors are of particular importance with the following properties.

- First, phytohepatoprotectors have exotic effects in the treatment of liver diseases [4]. The participation of synthetic drugs in liver metabolism often occurs with the participation of cytochrome R 450. Changes in metabolism can occur not only in the presence of synthetic hepatoprotectors, but also in the presence of drugs prescribed in parallel. In general, in simpler terms, treatment of the diseased liver with synthetic compounds leads to a violation of the action of hepatoprotectors and other medicinal compounds in the liver metabolism, further increasing the damage to the liver in pathological conditions. Phytohepatoprotectors protect the liver and its function to a high degree from foreign influences [1, 2, 4].

- Secondly, phytohepatoprotectors have several other pharmacological properties (antimicrobial, anti-inflammatory, antioxidant, immunomodulatory, choleretic, etc.). Phytohepatoprotectors effectively affect several pathogenetic links of liver diseases, as well as other pathologies in the body [3].
- Thirdly, the therapeutic effect of phytohepatoprotectors depends on the amount of the compound used and its easy access to the liver [2, 3].
- Fourthly, phytohepatoprotectors have the characteristics of safe, harmless, mild effect for patients in ambulatory conditions.
- Fifth, the biologically active substances extracted from plants are in the optimal amount and ratio, easily reach organs, and are agents for pathogenetic and symptomatic treatment [5].
- Sixth, the effect of phytohepatoprotectors during the treatment of the disease is stable compared to the effect of synthetic drugs, even if it is carried out for a longer period of time [2].
- Seventh, phytohepatoprotectors are economical as well as active pharmacological agents [3].

RESULTS

At the same time, a large number of plant compounds (up to 54%) are used as hepatoprotectors in the treatment of liver diseases, while phospholipid preparations are used by 16%, and other compounds, including synthetic, organopreparations and amino acid preparations by 30% [7, 9, 10].

Among plant hepatoprotectors, flavonoids and polyphenols occupy the main place [7, 9, 10].

Polyphenols are a large group of natural biologically active compounds. This class of compounds includes substances containing 2 or more molecules of phenolic groups. Polyphenolic compounds have high antioxidant activity due to the displacement of hydrogen atoms in the molecule. Polyphenolic compounds are widely used as hepatoprotectors in the treatment of liver pathologies of various etiologies [5].

The most studied polyphenol is gossypol, which is isolated from the plant species Gossypium L. and the related Malvaceae family. Gossypol and its derivatives are compounds that have an active effect on membranes and are capable of increasing the permeability of biological and artificial membranes, as well as changing the activity of a number of enzymes. It is assumed that the high binding property of gossypol with the lipid layer causes it to accumulate in the lipid bilayer region of the membrane, affecting protein structures, enzyme systems and ion channels located in the membrane. The study of the effect of gossypol on the passive permeability of the inner membranes of energized mitochondria shows an increase in permeability for monovalent and divalent cations.

In particular, the permeability of the membrane to the H+ ion increases several times. As a result of the activity of proton-oxidative phosphorylation of gossypol, the process of oxidative phosphorylation is separated in mitochondria. Due to the toxic effect of gossypol on the body, pharmacological use is somewhat limited.

Another group of compounds with hepatoprotective properties are flavonoids. Researchers studied the effects of polyphenolic compounds isolated from different natural compounds on mitochondrial functional parameters in vitro and in situ.

Ginkgo biloba L. plant leaves extract contains bilobalide 24%, flavonoid glycosides, terpenoid lactones 6%, as well as proanthocyanid and organic acids [11]. Ginkgo biloba extract

has been shown to inhibit apoptosis in in vitro experiments. These data confirm that Ginkgo extract has a protective effect on mitochondria. The protective effect of Ginkgo extract may be attributed to its antioxidant properties, mainly the anti-ischemic activity of flavonoids and bilobalide on mitochondria.

Also, studies have investigated the hepatoprotective properties of natural and artificial flavonoids [10]. Among them, the silymarin (Silybum marianum) component stands out with a more pronounced effect. Silymarin includes three isomeric compounds (silycristin, silydianin, silibinin). Silymarin has high biological activity [10]. Because silibinin has a phenolic structure, it is able to bind with radicals and participate in the process of peroxidation of lipids. Silibinin significantly increases the amount of glutathione returned in the liver, thereby protecting the liver from oxidative stress, participating in the restoration of its normal detoxification function [7]. The positive effects of silymarin in liver diseases are due to its antioxidant potential and "membrane stabilizing" properties. The antioxidant effect of silymarin is related to the interaction with free radicals generated in mitochondria, their transformation into less aggressive compounds [10]. Silymarin protects the cell internal structure, as well as hepatocyte cells and mitochondrial membranes from several pathogenic effects [7].

Also, the hepatoprotective effect of cathergen (cyanidanol-3) from plant substances has been studied [7, 10].

Catergen affects the biochemical reactions related to the increase of synthesis of ATF in liver cells, as well as energy expenditure. Catheteric cells have the effect of reducing the permeability of cell membranes to water-soluble small molecule compounds and ensuring membrane stability [7].

The effects of bemethyl are also well studied in studies, it sufficiently increases the activity of antioxidant enzymes in mitochondria and exhibits antioxidant properties [12].

Licorice plant (Glycyrrhiza Glabra L.) is distinguished by its medicinal properties, it has been used in folk medicine for centuries.

When extracting the root of licorice root, it was found that glycyrrhizic acid (GzK) is up to 25% of the total weight. Its aglycon - glycyrrhetinic acid (GrK) is notable for its structural similarity to hormones of the cortex of the adrenal glands.

Currently, GzK and GrK are widely used in medicine as a remedy against colds, allergies, viral diseases, and tumor diseases. In addition, in recent years, licorice preparations are used in the treatment of viral hepatitis.

Shirinmia drugs are widely used in the treatment of various pathologies, as well as in various scientific and practical studies. The main biologically active compounds of this drug are GzK belonging to the class of triterpenoids and its derivative - GrK.

At the same time, alkaloids can have a special place among some biologically active substances that have a positive effect on liver function. Among medicinal substances used in medicine, the specific activity of various alkaloids depends on their structure.

Alkaloids contain analgesic and narcotic compounds (morphine, codeine): active nervous system regulators (strychnine, brucine), mydriatic (pupil dilator) agents (atropine, hyoscyamine) and miotic (pupil constrictor) agents (physostigmine, pilocarpine) have been identified. Some alkaloids retain adrenergic activity, stimulate the sympathetic nervous system, raise blood pressure and increase heart activity (ephedrine). However, little information is given in the literature about plant alkaloids exhibiting hepatoprotective properties.

Based on the above-mentioned information, in this thesis work, changes in the functional parameters of animal liver mitochondria in the case of toxic hepatitis were analyzed.

In addition, the effects of protopine, cryptopine, α-allocryptopine and zeravshanizin alkaloids isolated from plants on the functional parameters of animal liver mitochondria in the state of healthy and toxic hepatitis were studied and their hepatoprotective properties were evaluated.

Studies were conducted in vitro and in vivo. 4 alkaloids provided by the UzR FA O'MKI in carrying out this work: Protopine ($C_{20}H_{19}NO_5$), cryptopine ($C_{21}H_{23}NO_5$), α-allocryptopine ($C_{21}H_{23}O_5N$) and diterpenoid alkaloids ($C_{29}H_{33}NO_6$) from Aconitum zeravschanicum were used.

In preliminary experiments on the effect of alkaloids on the functional parameters of rat liver mitochondria, the antioxidant property of protopine alkaloid was more evident than other alkaloids. Therefore, in the next stages of our research, in vivo experiments, protopine alkaloid was selected in order to fully study the hepatoprotective properties.

Studies were carried out in purebred white rats with a body weight of 120-140 g. Feeding of laboratory animals was carried out under normal vivarium conditions. Researches were carried out in three stages, interdependently, in vitro and in vivo conditions.

DISCUSSION

The study of the physicochemical properties of mitochondrial membranes shows that its inner membrane selectively passes certain compounds, for example, medicinal substances. The effect of pharmacological agents on the functional parameters of mitochondria should be considered not only from the toxicological, but also from the therapeutic point of view. A potential "target" for several pharmacological agents has been identified at the mitochondrial level. For example, an antiviral analogue of a nucleoside has a toxic effect on mitochondria due to the inhibition of ɣDNA polymerase. Several other substances affect different components of mitochondrial channels, leading to disruption of MRT or ion homeostasis. Also, several inhibitors of the electron transport system in mitochondria affect one or several complexes of the respiratory chain. For example, nonsteroidal anti-inflammatory compounds are mediators of oxidation-phosphorylation. Mitochondrial toxicity of compounds may also be due to free radical products. Most of them (papaverine, oligomycin, cyclosporine A, bilobalide, various polyphenols and flavonoids) are natural compounds.

Nowadays, many alkaloids are used as medicinal compounds in various fields of medicine. The effective effect of alkaloids depends on their physicochemical structure and physiological activity. Currently, in modern scientific laboratories, many alkaloids are isolated, their derivatives are synthesized, and their effects on the body are studied.

CONCLUSIONS

Based on the above considerations, in the first stage of our work, we studied the effect of plant alkaloids protopine, cryptopine, α-allocryptopine and zeravshanizin on mitochondrial functional parameters in in vitro and in vivo experiments.

It is known that identifying the mechanisms of the origin of diseases and their effective treatment is one of the urgent issues of medicine. Currently, in the treatment of diseases, the use of plant biological medicinal compounds is widely established. In the treatment of diseases, plant biological medicinal compounds are more important than synthetic drugs due to the fact that they have a quick and effective effect.

One of the important tasks of hepatology is to study changes in physiological and biochemical processes in the body in liver diseases. Liver damage caused by various toxic substances depends on the dose, chemical structure and duration of exposure.

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