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IMPORTANCE OF PHYTOTHERAPY IN CHRONIC NON-INFECTIOUS DISEASES OF THE LIVER

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ABSTRACT

Currently, in the countries of Central Asia, as in most countries, 15-20% of the adult population suffers from acute and chronic liver pathology. Today, non-alcoholic fatty liver disease (NAFLD) is the most common non-communicable liver disease, accounting for approximately 70% of all chronic liver diseases. The complexity and versatility of the pathogenetic mechanisms of lipid metabolism disorders in the body requires effective pharmacological correction aimed at normalizing the composition, structure and ratio of various classes of lipoproteins. In this regard, the most harmless and therapeutically effective herbal remedies of natural origin, metabolic products of plant and animal cells, which have low toxicity and a wide spectrum of action, are of great importance. The advantage of phytotherapy is that it allows the use of plants for a long time without significant side effects, due to their compatibility with many drugs and with each other.

KEYWORDS: *phytotherapy, herbal remedies, lipid metabolism.*

Currently, in Russia and Central Asian countries, as in most countries, 15-20% of the adult population suffers from acute and chronic liver pathology. In recent years, due to the increase in the incidence of viral hepatitis and its various forms, as a result of the effects of toxins, drugs and allergic injuries of the hepatobiliary system, due to the increase in the incidence of environmental pollution, the tension in the supply of drugs, and the World Health organization (WHO) defines the problem of combating with these diseases as an exception of important medical and social importance. Today, non-alcoholic fatty liver disease (NAFLD) is the most common non-infectious liver disease, accounting for approximately 70% of all liver diseases [1,5,28,33,].

Non-alcoholic fatty liver disease (NAFLD) encompasses a wide range of liver damage, from steatosis to nonalcoholic steatohepatitis (NASG), fibrosis, and cirrhosis [1]. This pathology affects about 24% of the world's population. However, NAFLD is characterized by variable prevalence depending on geographic area, age, and the presence of other risk factors such as diabetes [3, 4]. For example, in the USA, its prevalence is 33.6% among adults and 10-20% among children, and 25% in Europe and Asia [5]. It should be noted that due to the prevalence of NAFLD and its association with obesity, insulin resistance, type II diabetes (D II), metabolic syndrome, and dyslipidemia, this disease is also a major risky factor for cardiovascular disease in the population [6]. In addition, NAFLD can also be found in non-obese individuals, and its prevalence in this group can vary from 3.5 to 27% [7, 8].

NAFLD also aggravates the severity and progression of other liver diseases such as hepatitis C and hemochromatosis. NAFLD incidence is thought to predominate among males, but females are also frequently affected [9]. Despite the different reasons that determine gender-specific responses to a high-fat diet (hormonal status, age, etc.), the gender factor in the development of NAFLD requires further study [10]. NAFLD is the most common chronic liver disease not only in adults, but also in children (from 8-17 to 38% among obese children) [6, 11]. If the simple steatosis (excess accumulation of fat in the form of triglycerides in the liver) observed in NAFLD is of good quality, the progression of the disease to NASG increases the risk of fibrosis, cirrhosis, liver failure, hepatocellular carcinoma and, accordingly, the development of death [2]. By 2030, NAFLD and its progressive form, NASG, are expected to be the main indication for liver transplantation [12]. NASG is known to be characterized by hepatocyte damage and inflammation in addition to steatosis, representing the most severe form of NAFLD [13].

There are a number of mechanisms that cause a violation of the metabolic function of the liver, which are primary (endogenous) factors, that is, secondary factors caused by the effect of gene mutations and exo- and endogenous xenobiotics. In their turn, they affect the function of hepatocytes and lead to disturbances in the metabolism of bilirubin, bile acids, protein and amino acids, carbohydrates and glycoproteins, lipoproteins and lipids, porphyrin, trace elements, mucopolysaccharides [1,2]. In particular, the liver regulates the distribution throughout the body of food components, in particular, fatty acids, brought from the small intestine through the portal vein. In the liver of a healthy person, lipids (mainly triglycerides, cholesterol, phospholipids) make up 0.8-1.5% of the liver mass. An increase in the amount of this type of lipids leads to the development of fatty liver disease [28,30].

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In addition, dyslipidemia, regardless of their etiopathogenesis, is accompanied by dysfunction in the main organ of lipid homeostasis - the liver. The primary role of the liver is related to the processes of lipid regulation, mobilization and biosynthesis, as well as the processes of inactivation of potentially toxic metabolites and compounds for the body [2]. In this case, the liver, as a target organ for lipid metabolism disorders, actively participates in the further development of dyslipidemia with the development of a systemic pathological reaction of the whole organism [25,27].

The complexity and versatility of the pathogenetic mechanisms of lipid metabolism disorders in the body requires effective pharmacological correction aimed at normalizing the composition, structure and proportions of different classes of lipoproteins [19].

There is no doubt that rational pharmacotherapy is one of the effective ways to correct not only the morphofunctional state of the liver, but also the multifaceted pathogenetic mechanisms of dyslipidemia. Despite the wide arsenal of hepatoprotective and lipid-lowering drugs, they do not always have the desired effect and in some cases can even cause serious adverse reactions [12]. In this regard, the search for new, active and less toxic drugs for early adequate prevention and treatment of hepatobiliary system pathologies and lipid metabolism disorders is an important problem.

At the end of the third millennium, humanity made one of the conclusions in the field of biology and medicine. These are the most harmless and therapeutically effective phytomedicines of natural origin, which have low toxicity and broad-spectrum effects as a product of the metabolism of plant and animal cells [26,27].

Plants, as the leading component of human nutrition, are naturally metabolized, have a positive effect on all organs and their functional activity, are maximally absorbed due to a wide range of biologically active substances, and have a complex effect on the body [13,20].

The advantage of phytotherapy is that it allows long-term use of plants without significant side effects, due to their compatibility with many drugs and with each other. Phytotherapy is intended for use at home and does not require special equipment [34,36].

Another advantage of this method of treatment is the polyvalent effect of plants. As a rule, one medicinal plant has several effects.

The gastrointestinal tract and liver respond better to phytotherapeutic treatment than other body systems. This is very natural, because many medicinal properties of plants (antimicrobial, wound healing, epithelizing, hemostatic) directly affect the mucous membrane of the gastrointestinal tract, providing local protection. It fully reveals itself when used. In addition, with the help of certain effects of medicinal herbs (choleretic, surgi, socogonal, etc.), by correcting the activity of the digestive system, heart, lung, joint and kidney pathologies and other diseases are treated. It is possible to improve the condition of sick patients [35,40].

Phytotherapy at different stages of the disease has its indications and properties, which include:

- In the initial stage of diseases, phytotherapy has a light effect on the body, and the therapeutic effect is used in limited quantities due to its development when used for a long time;
- In the acute phase of the disease, it can be used as a supportive treatment to increase the body's defenses, enhance the effect of important drugs and reduce their side effects;
- In the recovery phase, phytotherapy takes the leading place, especially in chronic diseases, because it can be used for a long time and gives good results in combination with synthetic drugs [18,22,23].

The potential of plants is huge, because plants have many medicinal properties: pain reliever, tonic and sedative, normalizes the work of the cardiovascular system, gastrointestinal tract, anti-inflammatory, diaphoretic, antimicrobial, etc. It should be noted that each medicinal herb has not one, but many properties that allow it to have a beneficial effect on the whole body. In addition, they normalize metabolic processes in the body, the hormonal background. Plants not only do not inhibit the body's defenses, but on the contrary, they are active against antibiotics that suppress many strains of microorganisms that are able to increase the human immunity, thus helping him to fight the disease. These properties - the effect on metabolism, hormonal and immune status - are used in the treatment of various chronic diseases [14,16,20].

However, it should be noted that all these would give an effective result only if they are used competently and correctly. The steps, sequence, continuity and duration of herbal medicinal use are very important [4,7]. Phytopreparations have their own characteristics - gradual development of the therapeutic effect, light, moderate effect.

Various infections, endogenous and exogenous intoxications (hepatotropic poisons, alcohol, food poisoning, etc.), blood circulation disorders, immune disorders, and side effects of drugs used in diseases of the hepatobiliary system lead to diseases.

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Existing scientific studies on the lipid-lowering activity of herbal preparations are based on its biologically active substances in various parts of plants, such as polysaccharides, pectins, saponins, phenolic compounds, tocopherol, unsaturated fatty acids, retinol, ascorbic acid, inositol, states that it is related to biotin, plant fiber, choline, sitosterols, trace elements, allicin, etc. [5]. These data show the effectiveness of medicinal plants, which can implement almost all directions of modern lipid-lowering drug therapy.

Early and adequate phytotherapy as a type of additional metabolic therapy helps to correct and restore disturbed lipid metabolism and prevents the development of organic changes in target organs [18]. According to the effect on lipid metabolism and the mechanism of action, herbal preparations with hypolipidemic properties are divided into several groups. Thus, they reduce the absorption of cholesterol in the intestine and limit its penetration into the endothelium of plant vessels containing sitosterols, which are plant sorbents [2]. The mechanism of their lipid-lowering action is explained by inhibition of absorption of exogenous cholesterol and inhibition of enterohepatic recirculation of bile acids [13]. These properties include the flowers of mountain arnica (arnica montana), the fruits of carrot-like vizanga (ammi visnaga), the bark of horned elm (ulmus laevis), the fruits and leaves of common viburnum (viburnum opulus), and the roots of medicinal burnet (sanguisorba officinalis) and rhizomes [7].

This group of medicinal plants includes the roots of Arctium lappa, Dioscorea Nipponica rhizomes, Tussilago farfara leaves, Hippophae rhamnoides fruits and leaves, Cydonia oblonga seeds, Aralia elata roots, sorghum (Avena sativa), sorghum (Avena sativa) roots, sesame (Sesamum) seeds, wheat (Triticum aestivum) seeds, brown rice (Oryza sativa) bran, black beech (Alnus glutinosa) includes seedlings, flowers of chamomile (Matricaria chamomilla), and bulbs of marsh sedum (Gnaphalium uliginosum) [4;5]. Sitosterols contain the bioactive chemical compound allicin, the high content of which is found in the rhizomes of garlic onion (Allium sativum) and blue cypress (Polemonium caeruleum). Large amounts of sitosterol [3-sitosterol] are found in the following plants: pistachios (Pistacia) (300 mg), pumpkin (Cucurbita) seeds (265 mg), pine nuts (Pinus sylvestris) and almonds (Prunus dulcis) (200 mg) per 100 g weight [6].

Other plants that contain sitosterols and are rich in monounsaturated fats have the ability to inhibit the synthesis of cholesterol and triglycerides, as well as increase their use in the body. It has been studied that monounsaturated fats have a positive effect on lipid metabolism, selectively reduce the atherogenic part of low-density lipoproteins [2]. This effect is found in the ripe fruits of walnut (Juglans regia), leaves of plantain (Plantago major), medicinal yellow tea (Agrimonia eupatoria), hairy astragal (astragalus dasyanthus) grass and roots, and tribulus terrestris grass and roots [14].

The same properties are found in red hawthorn (Crataegus sanguinea) leaves, cranberry (Vaccinium vitis-idaea) fruits and fresh leaves, and hypericum grass [14]. The richest in monounsaturated fats are olive and corn oils from seeds, as well as nuts, avocados, canola oil and peanut oil [11].

Plants with a large amount of pectin substances - polysaccharides present in all land plants and some algae belong to the group of phytochemicals that accelerate metabolism and accelerate the removal of lipids from the body [8]. Pectins are water-soluble fiber that cannot be digested or absorbed in the stomach and intestines [6]. They bind harmful and toxic substances that enter with food and remove them from the body, contribute to the normal secretion of bile fluid, prevent its condensation in the liver and gall bladder, and effectively reduce the level of cholesterol in the blood. The plants of this group include common hazelnut (Corylus avellana), sea buckthorn (Hippophae rhamnoides) oil, rosehip (Rosa cinnamomea) fruit, common fennel (Anethum graveolens) seeds, red hawthorn (Crataegus sanguinea) fruits, chetan (Sórbus aucupária) fruits, Japanese kelp (Saccharina japonica) thallus, common raspberry (Rúbus idáeus) fruits [3,8]. Due to the high content of pectins, all legumes and fruits, especially citrus fruits, as well as apples, watermelons, currants, plums, apricots, peaches, radishes, wild garlic, algae and lichens have a lipid-lowering effect. There are several publications on the effectiveness of beets and cauliflower, which are rich in essential organic acids, minerals, pectins, vitamins, saponins, and plant fiber [6].

The next group that significantly affects lipid metabolism is medicinal plants that contribute to the normalization of dyslipoproteinemia by increasing the fraction of anti-atherogenic high-density lipoproteins. This pharmacological activity is primarily associated with polyphenolic compounds present in black currant, strawberry, chokeberry, raspberry, pomegranate, cranberry, red grape and unfiltered olive oil [6,12]. The antioxidant properties of catechins, which are abundant in yellow and green teas, have been studied [6].

It is known that one of the principles of phytotherapy is a systematic and comprehensive approach. This condition is implemented in pharmacotherapy by using multicomponent herbal preparations, which have a number of advantages over monopreparations. In particular, due to their complex chemical composition and a rational combination of biologically active substances, they have a multifaceted effect on the body: on the one hand, they directly affect damage, on the other hand, they provides pharmacological correction of the functions of various systems, as well as increases the resistance of the body in general [16]. In addition, synergism is manifested in the use of collections consisting of plants, which allows to increase the beneficial properties of the ingredients that make up their composition [1,14].

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Taking into account the diversity of etiopathogenetic mechanisms in the disturbance of lipid homeostasis, it is clear that the selection and use of multi-component phytochemical preparations will be effective in the complex pharmacotherapy of diseases, where, in addition to the disturbance of lipid metabolism, other systems of the body are involved in the pathological process [19]. Thus, the hypolipidemic and angioprotective effect of wild mulberry (Fragaria vesca), horsetail (Equisetum arvense), Hypéricum perforátum grass, seeds of anéthum graveólens, birch (Betula pendula) leaves, peppermint (Méntha piperíta) herb, carrot seeds, eleutherococcus spiny root, senna (Senna alexandrina) leaf and elderberry (Arctium láppa) roots collection is carried out by phytocollection.

In the modern folk medicine of Central Asian countries, jam and jelly are made from Berberis vulgaris fruits. Fruits are used as a choleretic agent to increase appetite. A decoction of Zik bark is drunk in liver, bladder, and rheumatism diseases. In Ayurvedic medicine, zirk is used to treat fever, liver diseases and diabetes. In Russian folk medicine, tincture of zirk leaves is used for liver and gall bladder diseases [13]. The plant is very popular in modern scientific herbal medicine. Its antibacterial, antioxidant, anti-inflammatory, antiarrhythmic, sedative, choleretic, anti-leishmania and anti-malarial properties have been identified, which are attributed to the berberine alkaloid.

In studies, the use of zirk fruits significantly reduced the concentration of low-density lipoproteins and total cholesterol, and increased the concentration of high-density lipoproteins in patients with metabolic syndrome. 5% tincture of leaves is used for liver diseases, hepatitis, cirrhosis. Hepatoprotective properties of zirk have been experimentally determined [40]. Consumption of zirk extracts reduces the activity of ALT and AST in fatty liver and other liver diseases.

Saffron (Crocus sativus) extracts reduce appetite, induce rapid satiety, and are effective in the treatment of alimentary obesity. Its aqueous extracts inhibit histamine H1 receptors. Saffron consumption reduces blood triglycerides and inflammatory cytokines in metabolic syndrome [1].

Choleretic agents play an important role in the treatment of diseases of the hepatobiliary system. There are 3 groups of herbal choleretic agents: choleretic, cholekinetic, cholespasmolytic [2,17,19].

True choleretics stimulate the formation of bile and bile acids: zirk roots, mint, birch leaves, calendula, wormwood, coriander fruits, corn cobs (infusion and liquid extract) have this property [5,20].

Hydrocholeretics increase bile secretion due to the water component: medicinal valerian, valerian preparations, mineral waters.

Cholekinetics increase the tone of the gallbladder, relax the bile ducts, the sphincter of Oddi, eliminate the condensation of bile in the gallbladder and enhance the process of its release: This property is vegetable oils (corn, olive, sunflower); found in calamus rhizome, zirk roots, dandelion, immortelle flowers, cornflowers, calendula, coriander and nematode [19].

Cholespasmolytics relax the smooth muscles of the gallbladder, bile ducts, that is, eliminate spasm: these are the flowers of arnica (Arnica montana) and calendula (Calendula officinalis), medicinal valerian (Valeriana officinalis) roots and rhizome, field spices, mint leaves [22].

The high efficiency of herbal preparations depends on the complex of biologically active substances. Choleretic properties are associated with the presence of flavonoids, essential oils, resins and other substances. The mechanism of their action is complex and is related to the direct stimulation of the secretory function of hepatocytes; with an increase in the osmotic gradient between bile, blood and increased filtration of water and electrolytes into the bile ducts; by stimulating the receptors of the mucous membrane of the small intestine, it helps to activate the autocrine regulatory system and increase the production of bile [19]. Extracts from medicinal plants rich in magnesium ions can stimulate cholecystokinin secretion by duodenal epithelial cells. This effect may be due to the cholekinetic effect of preparations based on arnica and fennel. A reflex increase in the release of cholecystokinin causes bitterness. The combined use of plants with different mechanisms of cholekinetic action allows to achieve a very specific effect. In addition to the choleretic effect, most plants have antimicrobial, anti-inflammatory and antihypoxic properties, some of which are effective hepatoprotectors [23].

Medicinal plants with a choleretic effect, that is, to prevent the formation of stones in the liver and contribute to the elimination of stones: this is done through the roots of zirk, immortelle flowers, corn cobs and columns.

Thus, in the complex prevention and treatment of lipid metabolism disorders and hepatobiliary diseases, the use of a wide selection of available phytopreparations can be an important way to optimize the treatment and prevention process. Effective pharmacocorrection is possible if the basic principles of herbal treatment are followed, the main of which are the individual selection and dosage of herbal drugs, the adequate duration of use of herbal drugs, and a systematic and comprehensive approach based on science [13].

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