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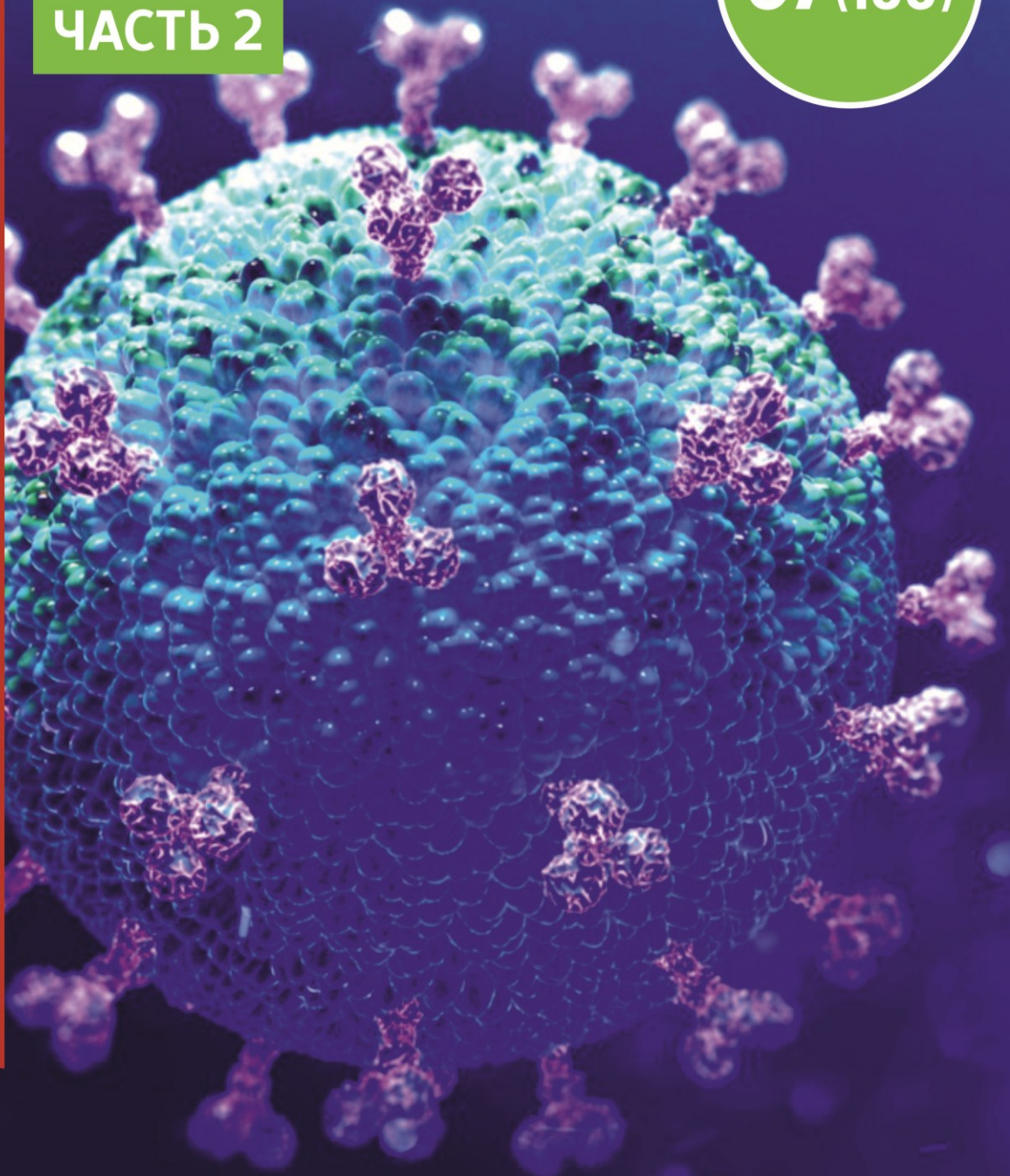
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<b>Содержание</b>	
<b>Papers in English</b>	<b>5</b>
<b>Information technology</b>	<b>5</b>
THE IMPORTANCE OF USING ELECTRONIC LESSON DEVELOPMENTS IN LESSONS OF COMPUTER SCIENCE AND INFORMATION TECHNOLOGIES Dilfuzaxon Kodirova	5
<b>Medicine and pharmacology</b>	<b>8</b>
HERBAL MEDICINE IN THE TREATMENT OF LIVER DISEASES Gulnora Rakhimova Muattar Yusupova Muslima Malikova Saodat Sharipova Oygul Rakhimova	8
<b>Pedagogy</b>	<b>13</b>
ROLES OF TEACHERS IN E-LEARNING HOW TO ENGAGE STUDENTS & EFFECTIVE WAYS OF E-LEARNING Yulchieva Mokhirakhon	13
<b>Engineering</b>	<b>15</b>
RESEARCH ON DETERMINATION OF THE FINAL SIZE OF THE LANDING OF THE BASES OF HYDROTECHNICAL STRUCTURES Rustam Khuzhakulov Altyngul Dzhumanazarova	15
DIGITAL ECONOMIC INFRASTRUCTURE. THE EFFECT OF THE DIGITAL ECONOMY ON EDUCATION Shahzod Kochkinov	19
THEORETICAL BACKGROUND FOR WEB APPLICATION Zainab Seger Anna Deytseva	21
<b>Philology</b>	<b>24</b>
NATIONAL CULTURAL FEATURES OF EUPHEMISM Nilufar Fayziyeva	24
OVERCOMING THE ISSUE OF LEARNING FOREIGN LANGUAGES AT HIGHER EDUCATION Malika Ulmasbaeva Shahnoza Omonova	26
TRANSLATION PROBLEMS Yorqinoy Madrimova	28
<b>Economics</b>	<b>30</b>
DIRECTIONS OF STATISTICAL ANALYSIS OF THE FINANCIAL SECTOR OF THE ECONOMY Dildorakhon Gafurova	30
<b>Law</b>	<b>34</b>
CRITERIA OF LEGAL LITERACY AND SPIRITUAL MATURITY Gulbahor Orzikulova	34
THE IMPORTANCE OF LEARNING ANCIENT ROMAN LAW Bahrom Orziqulov	36

## MEDICINE AND PHARMACOLOGY

## HERBAL MEDICINE IN THE TREATMENT OF LIVER DISEASES

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## ABSTRACT

The article provides a review of modern literature on the use of medicinal plants in the treatment of liver diseases. The hepatoprotective effect of medicinal plants develops on the basis of the antioxidant, anti-inflammatory, membrane-stabilizing effects of flavonoids, saponins, vitamins.

**Keywords:** herbal medicine; diseases of the hepatobiliary system; hepatoprotectors.

Liver disease remains a serious public health problem in Uzbekistan and abroad. Currently, liver diseases occupy one of the main places among the causes of disability of the population. Worldwide, there are approximately 200 million people with chronic liver disease, about 14 million of whom have cirrhosis of the liver (LC). Liver disease is one of the ten most common causes of death. The mortality rate in the development of liver failure remains high, despite the current advances in intensive care. WHO predicts that over the next 10–20 years, mortality from liver diseases will double. The liver is the central laboratory of the body and its functions are multifaceted. Among the factors that have a negative effect on liver function, the main ones are toxic substances, of which the main, of course, alcoholic effect, and our country is the leader in the purity and the amount of alcohol consumed per capita per year [1].

The liver is a complex and multifunctional organ with 300 billion cells. Taking part in digestion, blood formation and metabolic processes, it maintains the internal stability of the body. Therefore, in case of any violations in the liver, it is important to restore its normal functioning as soon as possible. The key to this is not only timely diagnosis, but also the complexity of treatment. And an effective additional component of the latter are products based on medicinal plants.

Liver function. The liver performs about 500 functions, responsible for important biochemical processes.

For this, the German physiologist Karl Ludwig was called “a large chemical laboratory”.

The main tasks of the liver in the body are:

- bile production;
- participation in the metabolism of proteins, fats, carbohydrates and other substances;
- neutralization of toxic compounds [2,3].

The secretion of bile is essential for the body. Its main components are phospholipids, cholesterol and bile pigments. They support the synthetic function of the liver and are involved in digestion. Also, some of the end products of metabolic metabolism are excreted along with bile. Failures in the liver and, as a result, a change in the composition of bile can cause the formation of calculi in the biliary tract.

All metabolic processes are somehow associated with the liver. Having a special location, this organ is an intermediate link between the portal and the general circulation. All compounds that are absorbed in the digestive tract pass through the liver. And then, having received a number of transformations, they are supplied to organs and tissues. The liver is involved in metabolic processes that maintain constant concentration and balance in the body:

- glucose;
- cholesterol;
- proteins;
- vitamins;

- water, etc.

Also, the liver is involved in the exchange of zinc, manganese, cobalt, copper and acts as a hormonal balance stabilizer.

The liver is involved in the detoxification of a number of toxic substances: both endogenous, that is, those produced inside the body, and exogenous, coming from outside. The liver detoxifies the products of cellular metabolism, for example, bilirubin, drugs, allergens, toxins, and the like. In addition, the liver removes excess vitamins, neurotransmitters and hormones from the body [4,5].

The liver has a unique ability - to remain resistant to negative factors that violate its integrity for a long time, and to regenerate itself. Studies have proven that even with the removal of up to 70% of this organ, it can reproduce the original mass. Despite this, in the structure of the general morbidity, there is a significant increase in the indicator of liver pathologies caused by:

- viral agents;
- intoxication;
- parasites;
- injuries;
- chronic diseases of other organs;
- heredity;
- hepatotoxic drugs.

The state of the liver is also influenced by unbalanced nutrition, stress, lack of rest and the like, without which the life of a modern person is impossible. The most common liver diseases are various types of hepatitis, fatty disease and cirrhosis.

*Due to the high biological activity, - important for the liver, hepatoprotective, anti-inflammatory and antitoxic properties, the absence of a large list of contraindications and the ability not to cause addiction, medicinal plants are used to prevent and treat liver diseases.*

Milk thistle. Numerous experiments have proven that milk thistle is one of the most effective natural remedies for treating liver disease.

*Milk thistle* included by WHO in the "Monograph of Medicinal Plants" and recommended as an element of adjuvant therapy for patients with:

- acute and chronic hepatitis;
- cirrhosis;
- toxic organ damage.

Milk thistle has a positive effect on the liver:

- protecting cells;
- stimulating the regeneration of new elements;
- blocking the influence of harmful substances (alcohol, toxins and heavy metals);
- preventing inflammation.

The mechanisms of action of milk thistle are primarily due to silymarin, the main active ingredient in the chemical composition of the plant. It is he who has a strong antioxidant effect, prevents destructive changes in liver cells and accelerates the recovery of damaged hepatocytes [6].

Bimmortelle. After milk thistle, sandy cumin, or immortelle, has a high therapeutic effect for the affected liver. *Immortelle inflorescence* contain a large amount of flavonoids. These compounds are characterized by

hepatoprotective activity. With antioxidant and anti-inflammatory effects, they protect liver cells from infection and poisoning. Thus, the immortelle helps the liver to cope with one of its main functions - detoxification. The immortelle is effective in treating diseases in which it is important to cleanse the body of toxins and increase the liver's resistance to viruses. Also, plant-based products provide choleric, cholekinetic, anti-inflammatory and antispasmodic effects. Decoctions and infusions are prepared from immortelle, which are used for cirrhosis, hepatitis, jaundice. The medicinal plant is useful for patients with chronic liver diseases: after taking it, pain decreases and bowel function improves. Also *immortelle* has a mild sedative effect and improves metabolic processes. Due to this, during the treatment, there is a normalization of well-being in general.

Silymarin. *Silybum marianum* (Milk thistle) has been used to treat liver diseases since the 16th century. Its major constituents are the flavonoids silibinin, silidianin, silichristin, and isosilibinin of which silibinin is the biologically most active compound and used for standardisation of pharmaceutical products [7]. The pharmacological profile of silymarin has been well defined and hepatoprotective properties of silymarin were investigated both *in vitro* and *in vivo*. Experimental studies demonstrated antioxidant and free radical scavenging properties, improvement of the antioxidative defence by prevention of glutathione depletion, and antifibrotic activity. To date, a major indication for silymarin treatment is *Amanita phalloides* (death cup fungus) intoxication in which silymarin acts as a hepatoprotectant through several mechanisms: 1. interruption of the enterohepatic recirculation of the hepatocyte toxin  $\alpha$ -amanitin; 2. inhibition of the binding of both phalloidin and  $\alpha$ -amanitin to hepatocyte membranes; and 3. competition with  $\alpha$ -amanitin for transmembrane transporters [8]. *Amanita* toxin given to dogs resulted in lethal hepatic failure in four animals treated with supportive care compared to no fatalities in animals treated with silymarin [9,10]. Although randomised trials were never performed in man for obvious reasons, one retrospective clinical report analysed 205 patients treated for amanita poisoning, of whom 46 died. Among the 16 individuals who received intravenous silibinin at 20–50 mg/kg/body weight daily, no fatalities occurred [11].

In addition to those described, for liver diseases, the following medicinal plants can also be prescribed:

- oregano (promotes better bile secretion);
- *chamomile*, knotweed, wormwood (have anti-inflammatory properties);
- nettle (reduces inflammation and normalizes metabolism);
- calendula (has choleric properties);
- corn stakes (neutralize toxins and have a good effect on metabolism);
- centaury (stimulates the secretion of bile).

The active search for new drugs with a hepatoprotective effect is determined by the global spread of viral hepatitis, a tendency towards a protracted and chronic course, an increase in the frequency of toxic drug-induced liver damage, non-alcoholic

steatohepatitis, an increased risk of progression of cirrhosis, liver failure and hepatocellular carcinoma in the absence of sufficiently effective treatments [ 11]. A significant achievement of recent years in hepatology is undoubtedly the development and introduction into clinical practice in the treatment of viral hepatitis of effective antiviral agents of the second generation, which have replaced interferon therapy [10]. The rapid increase in the number of effective antiviral drugs offered for the treatment of viral hepatitis, taking into account the genotype of the pathogen, typical toxic side effects, involved in the pathological process of organs, does not allow solving the problems associated with optimization and increasing the effectiveness of the treatment of liver diseases. The complexity of the correction of diseases is determined not only by the morphofunctional features of the organ, but also by the developing immunopathological reactions, cholestasis disorders, and often the fibrotic process of varying degrees of activity. Virus, toxic effects, metabolic disorders often play the role of a trigger, triggering a chain of pathological reactions of liver damage, which are difficult to correct in a number of patients in the future [7]. The complexity of the correction of diseases is determined not only by the morphological and functional characteristics of the organ, but also by the developing immunopathological reactions, disorders of cholestasis, and often the fibrotic process of varying degrees of activity. Virus, toxic effects, metabolic disorders often play the role of a trigger, triggering a

chain of pathological reactions of liver damage, which are difficult to correct in some patients in the future [8,9]. The complexity of the correction of diseases is determined not only by the morphofunctional features of the organ, but also by the developing immunopathological reactions, cholestasis disorders, and often the fibrotic process of varying degrees of activity. Virus, toxic effects, metabolic disorders often play the role of a trigger, triggering a chain of pathological reactions of liver damage, which are difficult to correct in a number of patients in the future [10].

#### Nomenclature of pharmaceuticals for liver protection

The nomenclature of pharmaceuticals with hepatoprotective action is small. In addition, despite the successes of chemistry, which has given medicine many effective drugs, the use of medicinal plants is gaining in scale. The increasing attention to medicinal plants is facilitated by a large number of cases of intolerance to a number of synthetic drugs, side effects during their use and, sometimes, the occurrence of the so-called "drug disease". Interest in herbal products is also associated with a change in the age structure of the population: there are more elderly and senile people who are characterized by chronic diseases. They require long-term medication, and in the case of the use of synthetic drugs that are alien to the human body, there is a great danger of side effects.

*Table 1.*

**Nomenclature of drugs with hepatoprotective action**

<b>P / p No.</b>	<b>Drug name</b>	<b>A country</b>	<b>Composition of the preparation</b>	<b>Indications for use</b>	<b>Release form</b>
<b>I. Preparations containing essential fatty acids.</b>					
1.	Essentiale	"Ronpulenc"	Essential phospholipids: phosphatidylcholine in combination with PUFA and vitamins	acute and chronic hepatitis, cirrhosis of the liver, fatty degeneration of the liver, liver damage by xenobiotics	capsules, ampoules
2.	Lipostabil	"Bosnaliek"	Essential phospholipids: phosphatidylcholine in combination with PUFA and vitamins	normalization of lipid metabolism	capsules
3.	Vitamin "F-99"	Switzerland "Divapharma"	Blend of linoleic and linolenic acid esters	metabolic disease	capsules, vials, ointments, cream
<b>P. Preparations from milk thistle.</b>					
4.	Silibinin		sum of flavonoids of milk thistle	acute (toxic) hepatitis	pills, capsules, suspension
five.	Legal	Germany "Medaus AG"	the sum of flavonoids of milk thistle	acute (toxic) hepatitis	pills, capsules, suspension
6.	Carsil	"Farmkhiholding"	the sum of flavonoids of milk thistle	acute (toxic) hepatitis	pills, capsules, suspension
7.	Silibor		the sum of flavonoids of milk thistle	hepatitis and cirrhosis of the liver	pills
8.	Milk thistle oil	Russia	the sum of flavonoids of milk thistle	hepatitis and cirrhosis of the liver	oil solution

<b>III. Preparations containing the amount of flavonoids</b>					
nine.	Flamin		the sum of flavonoids of flowers	hepatitis, cirrhosis of the liver, cholelithiasis	pills
ten.	Flacumin		sum of flavone aglycones from leaves of scumpia coggyria	as a choleric, cholelithiasis and anti-inflammatory agent in liver diseases	pills
eleven.	Konvaflavin		the sum of the flavonoids of the herb lily of the valley	viral, chronic hepatitis, liver damage by hepatotoxic agents	pills
12.	Katergen		flavonoids	viral hepatitis, toxic liver damage	pills
<b>IV. Preparations containing vitamin A</b>					
thirteen.	Retinol acetate	Russia "GSLM October" "Nizhpharm"	vitamin A	viral, chronic hepatitis, liver cirrhosis	ampoules, dragee, capsule tablets
fourteen	Retinol palmylate	Russia "KZM October" "Nizhpharm"	vitamin A	viral, chronic hepatitis, liver cirrhosis	Dragee bottles, capsule tablets
<b>V. Other drugs</b>					
fifteen.	Liv-52	India "Himalaya"	juices and decoctions of yarrow, cassia, chicory	infectious, toxic and chronic hepatitis	pills

Herbal remedies are also preferred in the treatment of children and adolescents: they are better perceived by the child's body, act more gently and most often do not give unwanted complications. The most famous hepatoprotectors, used for over fifty years and accepted by researchers as a reference in the development of new drugs, are the funds obtained from the milk thistle plant (*Silybum marianum* L.) silibor, silymarin. The active principle of preparations from the fruits of this plant are flavolignans silibinin (50%), as well as isosilybinin, silichristin and silidianin, which have a phenylchroman-ic structure. Legalon is a highly purified mixture of flavolignans isolated from the plant *Silybum marianum*. Preparations similar in composition and action are produced in different countries under various names Carsil, Silimarin, Silybin, Apihepar, Hepadestal, etc. [1, 7]. Numerous experimental data, obtained in in vitro and in vivo experiments on laboratory animals with modeling of acute and chronic liver damage in models of toxic liver damage with carbon tetrachloride, D-galactosamine, ethanol, praseodymium, drugs, in case of radiation injuries, indicated a high hepatoprotective activity of drugs obtained from milk thistle spotted [4, 5]. Flavonoid preparations, which have a beneficial effect on the functional state of the liver, have long been used as effective choleric agents. Flamin is a dry concentrate of sandy immortelle containing the amount of flavonoids. Convaflavin (Convaflavinum) is a total flavonoid preparation from the herb of lily of the valley (*Convallaria Keiskei* Mig.) Of this family. liliaceae (Liliaceae), the content of flavonoids in it is not less than 17% in the absence of cardiac glycosides. Flacumin (Flacuminum) is the sum of flavonoid aglycones obtained from the leaves of scumpia (*Cotinus coggyria* Scop.), Which previously served as a source of tannin. Flacoside, containing a flavonoid glycoside from the leaves of Amur velvet and Laval velvet, also has a

hepatoprotective effect. A comparative study of the hepatoprotective properties of flamin, convaflavin, flacumin, silibor and silymarin made it possible to reveal the hepatoprotective effect associated, according to the authors, with the suppression of lipid peroxidation and their stimulating effect on the synthesis of nucleic acids and protein. Datiscan, containing the sum of flavonoids from hemp datiska, had a distinct hepatoprotective, choleric effect in experimental hepatitis [2]. Flacumin (Flacuminum) is the sum of flavonoid aglycones obtained from the leaves of scumpia (*Cotinus coggyria* Scop.), Which previously served as a source of tannin. Flacoside, containing a flavonoid glycoside from the leaves of Amur velvet and Laval velvet, also has a hepatoprotective effect. A comparative study of the hepatoprotective properties of flamin, convaflavin, flacumin, silibor and silymarin made it possible to reveal the hepatoprotective effect associated, according to the authors, with the suppression of lipid peroxidation and their stimulating effect on the synthesis of nucleic acids and protein. Datiscan, containing the sum of flavonoids from hemp datiska, had a distinct hepatoprotective, choleric effect in experimental hepatitis [4]. Flacumin (Flacuminum) is the sum of flavonoid aglycones obtained from the leaves of scumpia (*Cotinus coggyria* Scop.), Which previously served as a source of tannin. Flacoside, containing a flavonoid glycoside from the leaves of Amur velvet and Laval velvet, also has a hepatoprotective effect. A comparative study of the hepatoprotective properties of flamin, convaflavin, flacumin, silibor and silymarin made it possible to reveal the hepatoprotective effect associated, according to the authors, with the suppression of lipid peroxidation and their stimulating effect on the synthesis of nucleic acids and protein. Datiscan, containing the sum of flavonoids from hemp datiska, had a distinct hepatoprotective, choleric effect in experimental hepatitis formerly



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effect associated, according to the authors, with the suppression of lipid peroxidation and their stimulating effect on the synthesis of nucleic acids and protein. Datiscan, containing the sum of flavonoids from hemp datiska, had a distinct hepatoprotective, choleric effect in experimental hepatitis [5,7]. Choleric and hepatoprotective action was caused by flavonoids from prostrate marigolds, hibiscus sabdarif, fruits of parsley, rose hips, herb of straight, abandoned and direct, from which the original preparations were obtained. The total preparation from caragana had a pronounced hepatoprotective effect. Extracts from Astragalus sainfoin, containing phenol carboxylic acids, flavonoids and saponins, had not only hepatoprotective and choleric, but also hypolipidemic effect. The well-known drug kaleflon, which is the sum of phenolic compounds from calendula officinalis L., mainly derivatives of flavonoids and phenol carboxylic acids, used in the treatment of gastric ulcer, demonstrated hepatoprotective properties, had a pronounced membrane stabilizing effect [10]. Bupleurum multinerve (L.), golden bupleur (B. aureum) and other plant species are distinguished by a rich content of flavonoids with P-vitamin activity, which made it possible to create the drug "Buplerin". Revealed the antihistamine effect of goat leaf bud; infusions of herbs and decoctions of roots had a hepatoprotective and choleric effect in cholecystitis, angiocholitis and hepatitis. Natural catechins inhibited the oxidation of low density lipoproteins and had a positive effect in experimental hepatitis in rats and in vitro [11].

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