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The Importance of Dry Extract from Plants of Central Asia for Eliminating Alterations of Functional State of Liver in Its Alcoholic Lesion

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Abstract The influence of dry extract from the collection of Central Asian medicinal herbs - *Hipericum scabrum L., Ziziphora pedicellata Pazij Vved., Mediazia macrophylla and Glycirhiza glabra L.* on bile excretory function of liver in alcoholic hepatitis was studied. The model of alcoholic hepatitis was developed with the introduction of 40% ethanol in a dose 0,7 ml for 100 gr weight once in a day during 21 days. The introduction of dry extract in a dose of 25 mg/kg to rats with the alcoholic hepatitis promoted restoration of bile excretory function of liver. The bile excretion statistically significant increased to 67,9% in comparison with untreated group. Besides dry extract raised significantly excretion of bilious acids, cholesterin and bilirubin to 60,7%, 103,5% and 104,6% respectively. The dry extract from medicinal plants of Central Asia can be recommended as pathogenetic preparation for the treatment of diseases of hepatobiliary system.

Keywords Dry extract, Bile, Bilious acids, Bilirubin, Cholesterin

1. Introduction

The excessive consumption of alcohol leads to a wide spectrum of somatic complications. Especially, the parenchymatous organs are vulnerable to the toxic influence of alcohol [1]. Thus, the lesion of liver is the most frequent manifestation of alcoholic disease [2, 3]. The results of studies of some researchers showed that continued alcohol consumption increased the risk of progression to cirrhosis to 30%, and fibrosis or cirrhosis to 37%. Fatty liver develops in about 90% of individuals who drink more than 60 g/day of alcohol but may also occur in individuals who drink less [1, 4, 5, 9]. Alcoholic liver disease represents a spectrum of clinical illness and morphological changes that range from fatty liver to hepatic inflammation and necrosis (alcoholic hepatitis) to progressive fibrosis (alcoholic cirrhosis) [6, 7]. Simple, uncomplicated fatty liver is usually asymptomatic and self-limited, and may be completely reversible with abstinence after about 4-6 weeks [8]. Moreover, sustained excessive alcohol intake favours the progression of other liver diseases, such as virus-related chronic hepatitis, also increasing the risk of hepatocellular carcinoma [6, 10, 11]. The methods of treatment including many pathogenetic agents do not have convincing favourable effect on a course and an outcome of this pathology that it causes to the further study and development the effective remedies for treatment [12]. The development of multicomponent phyto-preparations owing a number of advantages over the monopreparations is considered perspective in this direction of study. In particular, thanks to the difficult and balanced chemical compound, phyto-collection has multilateral effect to the body: on the one hand favorably influence directly to the focus of lesion and on the other hand provide pharmacological regulation of functional systems as well as raise the resistance of whole organism [13]. The medicinal herbs can serve as the potential resources of the new useful compounds for creating and developing remedies that are effective for the therapy of liver diseases with various aetiologies. Many plants have hepatoprotective effect; however, there are not enough scientific data about the plants possessing hepatoprotective properties, which confirm their pharmacological efficiency. Therefore, the purposeful regular researches of pharmacological effects of medicines developed from the herbal raw materials are required [14].

The herbal plants growing in territory of Central Asia such as *Hipericum scabrum L., Ziziphora pedicellata Pazij Vved., Mediazia macrophylla and Glycirhiza glabra L.* have been used in traditional medicine for many centuries. *Hipericum scabrum L.* contains biological active substances such as flavonoids, which increase bile outflow as well as interfere stasis of bile in the gallbladder and by that prevent possibility of formation of gallstones, facilitate bile secretion [15]. This

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herbal plant along with flavonoids (hyperoside, rutins, quercetrin, izoquercetrin and quercitin) contains vitamins P and PP, choline, anthocyans and ascorbic acid [16]. *Ziziphora pedicellata Pazij Vved.* contains organic acids, essential oil, vitamin C, saponins and flavonoids [17]. There are high fatty acids (palmitic, olein, linoleic and others), glycosides, essential oils and flavonoids in the content of *Mediazia macrophylla* growing in Uzbekistan [18]. The roots of *Glycirhiza glabra L.* contains glycyrrhizic acid (6-30%), flavonoids and others pharmacological active substances. The glycyrrhizic acid that is considered triterpenoids glycoside possesses anti-inflammatory properties. The pharmacologic activity of *Glycirhiza glabra L.* also expresses by the presence of flavonol glycoside such as liqueritin, liqueritigenin and liqueritoside [19, 20].

The purpose of present work was to study the influence of dry extract from collection of medicinal herbs: *Hipericum scabrum L., Ziziphora pedicellata Pazij Vved., Mediazia macrophylla and Glycirhiza glabra L.* on bile excretory function of liver in alcoholic hepatitis. It is known that the most important, sensitive and specific function of liver is the bile producing function. Bile excretory activity of liver and chemical compound of bile is the objective and significant indicators reflecting the functional condition of liver [21].

2. Material and Methods

2.1. Plant Material and Preparation of Dried Extract

Aerial parts of *Hypericum perforatum L., Ziziphora pedicellata Pazij et Vved.* and *Mediazia macrophylla* as well as root and rhizome parts of *Glycirhiza glabra L.* were obtained in summer of 2013 from foothills to medium zones of mountains of Tashkent region, Fergana, Samarkand and Surkhandaryo regions of Uzbekistan. Plant material was dried under dark conditions at room temperature for 10 days. The dry material was milled, obtaining 4-6 mm particles and mixed in proportion 1,25:1,0:1,25:1,5 (productivity of dried extract was higher than other proportions) then extracted by water at 93-95ºC temperature for 3 hours. The extract was then separated from the sample residue by filtration through filter paper. The resulting extracts were concentrated in vacuum until remaining a crude solid extract, which then was dried in dryer apparatus.

2.2. Experiment

The experiments were carried out on white adult rats weighting 160-210 gr. The animals kept in condition of vivarium on the standard ration. Animals kept in vivarium condition on standard food allowance. The animals were divided into 4 groups and each group consisted 6-8 animals. The healthy animals were in the first group (1-group) and they were treated with drinking water in a volume 0,7 ml/100 gr into the stomach through metallic cannula. The animals with alcoholic hepatitis without treatment were in second group (2-group). The model of alcoholic hepatitis was developed with the introduction of 40% ethanol in a dose 0,7 ml for 100 gr weight once in a day during 21 days [22]. After the last introduction of ethanol, the solution of dry extract in a dose 25 mg/kg was introduced into the stomach to the animals of third group (3-group) during 6 days. LIV-52 in a dose 100 mg/kg was introduced to the animals of fourth group (4-group) per os during 6 days after inducing alcoholic hepatitis. Later 24 hours after a final introduction of preparations, the bile excretory function of liver was investigated through the inserting polyethylene catheter into the common bile duct of animals under the parenteral anesthesia (sodium pentobarbital 50 mg/kg, intraperitonial).

We judged about the choleretic action of dry extract by the analysing the quantity of the excreted bile for 4 hours as well as analysing the concentration and quantity of chemical compounds of bile that are bilirubin, cholesterin and common bile acids. The concentration (mg%) and common quantity (mg on 100 g weight of body) of bile acids (mg), cholesterin (mg) [23] and bilirubin (mkg) [24] were determined in two hour portions.

The experiments were carried out by the following the rules, which were accepted in European convention on protection of vertebrate animals, used for experiments or in other scientific purposes (ETS N 123) Strasbourg, 18.03.1986г.

The received results were subjected to the statistic processing with the using of standard software package Biostat 2009 on well-known method of variation statistics with an estimation of the statistic significance of indicators (M±m) and differences between groups were analyzed using the Student's t-test. $P<0.05$ was considered significant.

3. Results and Discussion

The results of study showed that the noticeable disturbances are observed in the excretory function of liver at acute hepatitis, which was induced by the administration of ethanol. In particular, speed of secretion of bile statically significantly reduced on average to 41,7% in control group's animals in comparisons with healthy animals for 4 hours of experiment. At the same time, there were reducing of the quantity of bilious acids to 39,8%, cholesterin to 63,4% and bilirubin to 57,2% in the excreted bile in comparison with healthy animals. Consequently, the functional state of liver depresses at the recurring influence of alcohol that it is expressed not only in reduction of excretion of bile, but also decreasing of main chemical components of it. The received results conform with the results of other authors [22].

The main cause of damage of functional activity of hepatocytes under the influence of alcohol is an intensifying of free radical oxidation mechanism of cellular damage, as a result of oxidation of alcohol. The toxic metabolite acetylaldehyde is produced in a high concentration, which induces enzyme aldehydeoxidase leading to the formation of the active forms of oxygen and activation of peroxidation of

membrane lipids [25]. Indeed, the content of malonic dealdehyde in liver increases twice under the influence of alcohol and the concentration of phospholipids decrease [22]. It is considered that a accumulation of products of lipid's peroxidation influence as a labializing agents on lysosomes that lead to releasing of phospholipase A2 and other hydrolytic enzymes [26]. Probably, it explains the development of disbalance in content of separate phospholipid fractions which characterising by the sharp increasing of extremely toxic products-lysophopholipids resulting to the destruction of hepatocyte membranes and infringements of their functional condition [22]. It is logical to consider that the formation of bilious acids from cholesterin and conjugation of them with taurine, glycine and glicurinidation of bilirubin reduce in such conditions. In a result, the content of them in the excreted bile decrease. Thus, the reduction of excretion of cholesterin leads to accumulation it in the liver and to the development fatty infiltration of liver.

Table 1. The influence of dry extract (25 mg/kg per os) to the intensity of bile secretion and its chemical content in rats with alcoholic hepatitis (for 4-hour experiment 100-gr body weight)

Group	Bile, ml	Bilious acids, mg	Choleste-rin, mg	Biliru-bin, mkg
1-group	1,44±0,07	8,59±0,53	0,31±0,02	112,4±7,5
2-group	0,84±0,04*	5,17±0,36*	0,11±0,01*	48,1±2,9*
3-group	1,41±0,09[a]	8,31±0,49[a]	0,23±0,03*[a]	98,4±7,9[a]
4-group	1,13±0,11*[a]	6,30±0,85*[b]	0,20±0,02*[a]	66,5±9,9*[b]

Statistically significant difference: *- in comparison with 1-group; a - in comparison with 2-group; b- in comparison with 3-group.

The introduction of dry extract in a dose of 25 mg/kg to rats with the alcoholic hepatitis promoted restoration of bile excretory function of liver. After 6 day treatments, the bile excretion statistically significant increased to 67,9% in comparison with untreated group. Besides dry extract raised significantly excretion of bilious acids, cholesterin and bilirubin to 60,7%, 103,5% and 104,6% respectively. Thus, apparently from table 1, significance treated and healthy animals considerably do not differ between themselves. The quantity of excreted bile at animals of 4th group was 34,5% more than 2nd group's animals but at the same time, it was 19,9% less then animal 3rd group which were treated with the solution of dry extract. The quantity of bilious acids, cholesterin and bilirubin in the content of excreted bile were significant 21,9%, 81,8% and 38,3% more than animals of 2nd group respectively. The numbers of bilious acids, cholesterin and bilirubin were 31,9%, 15,0% and 48,0% less respectively in comparison with results of 3rd group. Probably, the disturbances of biochemical processes, which express by the reduction of bile excretory function of liver and main chemical contents of bile are eliminated under the influence of dry extract in alcoholic hepatitis.

Thus, it is necessary to remember that some herbal preparations, such as dry extract, possess anti-oxidant action and interrupt the influence of active forms of oxygen to the membrane phospholipids of cells and their burning. Based on this, it can be supposed that the herbal preparation dry extract also possesses anti-oxidant property which lies on the basis of restoring action on the functional condition of liver at its damage by ethanol. Such assumption was supported with the results of our previous researches, in which it has been established a positive pharmaco-therapeutic actions of dry extract in toxic hepatitis which was induced by tetrachlormethane [12].

4. Conclusions

1. Alcoholic damage of liver is accompanied by the reduction of excretory function of liver and chemical components in bile - bilious acids, cholesterin and bilirubin.
2. Experimental therapy with dry extract eliminates disturbances of bile excretory function of liver and content of the main components of bile.
3. Application dry extract as pathogenetic agent in alcoholic damage of liver allows raising efficiency of treatment of complications of alcoholism.
4. The dry extract from collection of Central Asian medicinal herbs *Hipericum scabrum L., Ziziphora pedicellata Pazij Vved., Mediazia macrophylla and Glycirhiza glabra L.* is more effective comparing to LIV-52.

Generalizing results of the present work, it is possible to conclude that dry extract from Central Asian medicinal herbs makes distinct restoring impact on the functional condition of liver at its damage by alcohol and can be recommended as pathogenetic preparation for the treatment of diseases of hepatobiliary system.

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