

## About Beneficial Features of Medicinal Preparations of Licorice

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### Abstract

Rational phytotechnologies methods have been used to obtain a number of medicinal preparations from a natural national plant resource Glycyrrhiza Glabra, which approved regulatory documents in the form of patents and technological regulations. The firstly in the practice of world medical science, saponin-containing preparations of licorice naked were identified, allowing them to be widely used in medical practice for the treatment of oncological diseases, as well as diseases accompanied by a decrease in the Immune system. The scientific article presents the results of pharmaceutical and toxicopharmacological studies of medicinal preparations of the medicinal plant Glycyrrhiza glabra seu Licorice. For the first time in the practice of world medical science, the lymphotropic properties of saponin-containing licorice compounds, obtained in the form of dry and dense aqueous extracts, as well as in the form of therapeutic syrups, have been identified and substantiated. Toxicological experiments proved their low toxicity and safety. On the basis of the obtained dense and dry aqueous extracts of Glycyrrhiza glabra, a number of drugs and medicinal biologically active additives were developed for the first time and received certificates in the form of National and Eurasian Patents. It has been shown that the developed therapeutic agents have anti-inflammatory, immunostimulating, antitussive, antihemorrhoidal, cardiotonic, antiviral, sedative, diuretic, antitumor activities, which allows them to be recommended for widespread medical use. Developed licorice-based medicinal syrups: "Licorice syrup", "Licorice of Immunovit", "Licorice Hem", "Licorice Cardio", "Licorice Broncho", "Licorice Qripson", "Licorice Uro", "Licorice Sed" are produced by the national industry "Biyon Products LTD" and have been highly praised by buyers.

**Keywords:** Licorice, preparations, patent

### Introduction

The nature of Azerbaijan is rich and various. Along with surprising herbal flora and the fauna is diverse in addition with mineral rare objects. Therefore, usage of domestic natural resources as medicinal raw materials for elaboration and creation of pharmaceutical production is important and relevant purpose in pharmacy and medicine.

Among the representatives of appointed flora, using by the persons as remedies is difficult to find, perhaps, a plant with such ancient, documentary recorded history being possessed by Licorice.

Licorice or liquorice-"Glycyrrhiza" is a natural officinal and technical plant. It was known for Sumer's, Indians, Egyptians and being used as traditional medicine in ancient Chinese, Tibetan and Arabic medicine for a long time.

The medical book "Yadzur-Veda" being written in Sanskrit language (the science about life), being processed by doctor Sushrut, contains an information of Licorice root in the period of the 3rd century of our era.

The Indian aesculapian added to the list of recommendations of Chinese doctors the treatment method of external inflammations and eye diseases. Approaches of Indian doctors have been generally accepted by the Tibetan medicine. Licorice root under the name of "shingar" was being registered in many prescriptions for treatment of pulmonary diseases and other respiratory diseases.

The Licorice paid an attention the doctors of Greece, Rome, Burma where was delivered from China. By famous scientists such as Feofrast, Hippocrat, Pliny, Dioskorid the Licorice was included in one row with the most valuable curative plants.

Arabic intervention of the 6-8th century of our era also promoted for spreading of medical knowledge being accumulated since ancient times. The Licorice root began to be propagandized widely by the Arabic doctors as remedy.

Ar-Razi was living in the 9-th century, wrote: "The licorice softens a pulmonary tube and cleans it, satisfies thirst, helps at inflammation of a stomach, is useful at burning urine, inflammation of kidneys and a bladder". Just Arabic doctors have concentrated a maximum of knowledge of curative plants and experience of treatment with them, have transferred the art to Europe of an era of crusades. Huge contribution for development of medicine in Europe was created by Avicenna (Ibn-Sina) which widely applied the licorice root for treatment of various diseases. Avicenna was the first which has found salutary influence of a root of Licorice in cases of liver diseases.

The center of distribution of Arabic medicine experience was the medical school in Salerno. One of the first Europeans who have apprehended this knowledge was Konrad von Mankenber, the doctor of the 14th century. Thus, the Licorice has got in pharmacopeias of the majority of the countries in the world, and became a subject of attentive scientific research as remedy.

Related with natural reserves and preparations of licorice root the former Soviet Union occupied leading place in the world. The botanical sort of Licorice "Glycyrrhiza L", families of bean (Fabaceae) in world flora is generally presented by about 15 types (according to the latest data to 33 [2]. The kind of plants "licorice" attracts an attention as a source of natural raw materials for receiving valuable medicinal, food, perfumery and cosmetology, technical and other products [1]. Since 1901 for 2018 period of time valuable medicines related with licorice root over 7360 world security sources of information in the form of patents have been received. The analysis of these security documents allows creating a conclusion of great potential advantages for Licorice in medical field. The special interest for preparations of licorice was shown in medicine, medicinal means obtained from licorice find the application not less than by 12 pharmacotherapeutic groups, and therefore the application of licorice frequency has come out in medicine on top among floral herbs [3].

The licorice named by (*Glycyrrhiza glabra L. (F.)*) or a licorice smooth named by (*Liquiritia officinalis*) had been known as remedy in medical field more than 5000 years. Firstly, medical preparations were mentioned in the first book of herbs of China. The licorice root is a classical traditional medical means of Chinese and Tibetan doctors of medicine and being included in the "Gold Semerna" of the East. It is considered as a panacea of all diseases and also the means for saving of beauty and youth especially. By numerous scientific researches were being proved very useful medicinal properties of underground and elevated parts of a licorice.

So, firstly in the world medical scientific practice are being revealed: liotropic, immunotropic also being studied anti-inflammatory, anesthetics, laxative, diuretic, antiallergenic, hepatotropic, wound healing, antibecheic, antimicrobial, antiviral, adaptogenic, antioxidant, antidotal, against narcotic, anthelmintic anti-parasitic, anticoagulants pharmacotherapeutic properties [1].

At present, the licorice as a point of valuable source of natural crude attracts the general attention for obtaining of medicinal, perfumery cosmetology, food, technical and agricultural products.

Refer to modern physical and chemical chromatographic methods of analysis in part of the licorice had been discovered about 200 biologically active components and basically of them are triterpenic components these are: glycyrrhizic acid and its derivatives, aglykon-glyceric acid and its derivatives, phenolic components: flavonoids and its derivatives, polysaccharides; pectins, pitches, sugar, amino acids and so on [3].

Modern scientific research related with licorice is continued in several directions: expansion of a source of raw materials, allocation and division from made raw materials pharmacological of active agents and creation on the basis of

original medicines; chemical and pharmacological modifications of being known medicines; creation of new "pro-preparations" on the basis of the known biologically active components.

The Republic of Azerbaijan has huge stocks of Licorice roots. In the Republic of Azerbaijan 7 kinds of licorices grow, the most distribution was being gained by a licorice smooth or sweet.

The sweet licorice of the Republic of Azerbaijan gained the global recognition among all known species of licorices; refer to high content of the main valuable component of glycyrrhizic acid till 25% [4].

Since 19-th century, the sweet licorice of the Republic of Azerbaijan has been exporting for many countries of the world.

In fact the new licorice industry has been organized by other way in Independent, Democratic and Civil Republic of Azerbaijan.

So, since 2005 year on the basis of deep scientifically based researches had been organized the open joint stock company with production of preparations of licorice-"Biyann Products" MMC which is located in Agdash district of the country. "Biyann Products" MMC has 1000 hectares of a newly created licorice plantations and constructed plant with an area of 11 hectares. As a matter of fact that licorice industry takes the second place in the world after the American of the licorice industry "Licorice".

The year raw materials of a licorice are gain grown up 3-years are being processed in the plant with receiving a reasonable root, dense extract, also preparations and medically biologically active additives in the form of syrups. That plant has been working refer to exclusively newly developed standards and legal certificates. The special documents are the international patents and special certificates were being obtained from the Ministry of Health of the Republic of Azerbaijan: license for production, hygienic certifications, specifications, production schedules. The newly created licorice industry has a purpose for expansion of pharmaceutical, food, industry for color production, tobacco-growing, cosmetology production of construction materials, fertilizers of chemical household means and fodder products (schema-4).

Such big scale of planning is based on wide distribution of licorice in the territory of the country: the sweet licorice in the Republic of Azerbaijan is being widespreaded in Kura-Araks, Samur-Devechi, Primorsk, Mugan, Gobustan-Absheron, Alazan, Kurdamir, Ujar, Barda and Nakhchivan regions and also in the East Western direction of Great Caucasus and the central-southern parts of Lesser Caucasus. The sweet licorice growing in the territory of the Republic of Azerbaijan as appointed before the medicinal and technical plant is most qualitative and rich in content of pharmacologically active components.

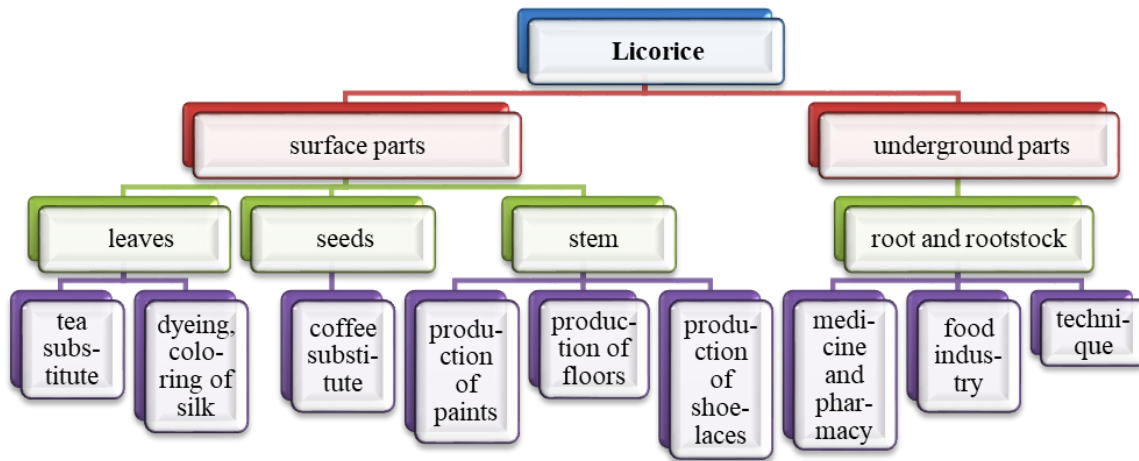


Fig 1: Schema 1.

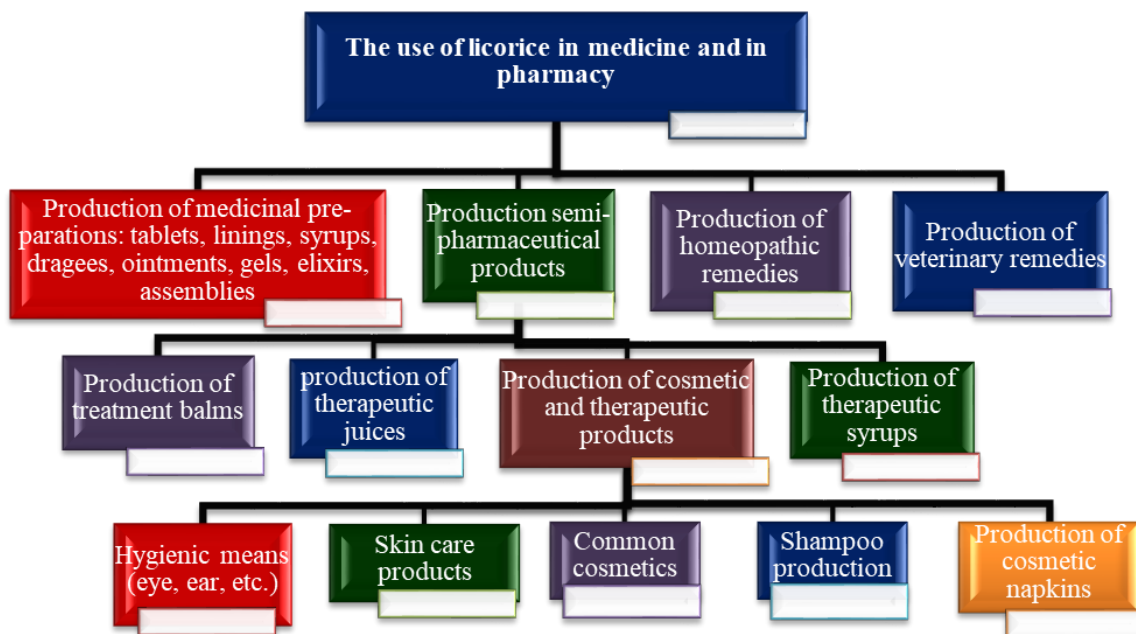


Fig 2: Schema 2.

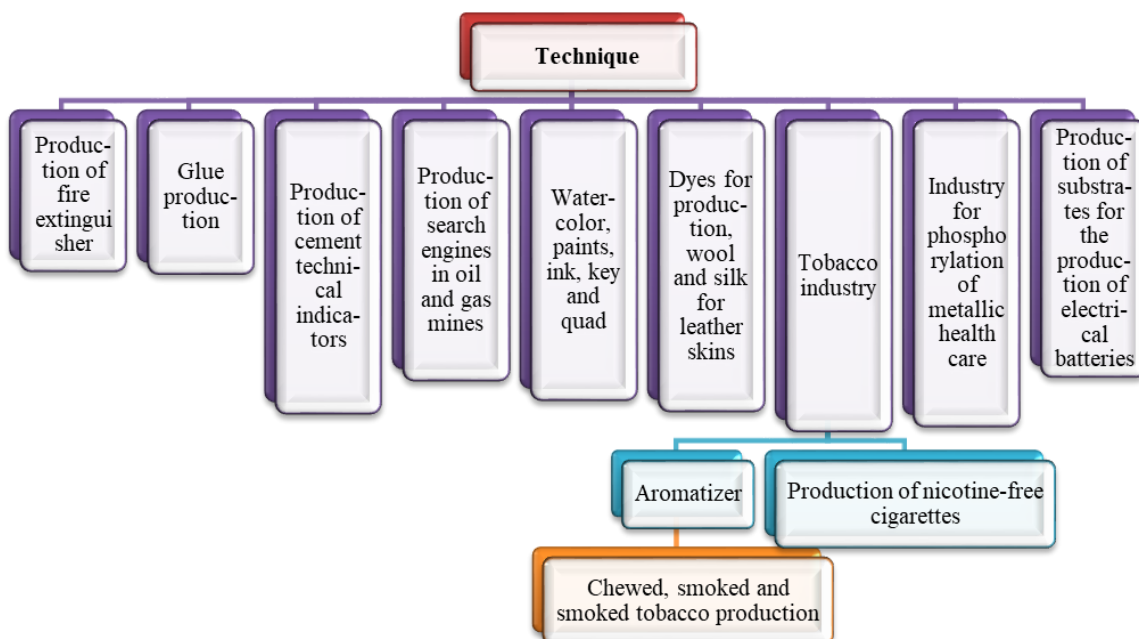


Fig 3: Schema 3.

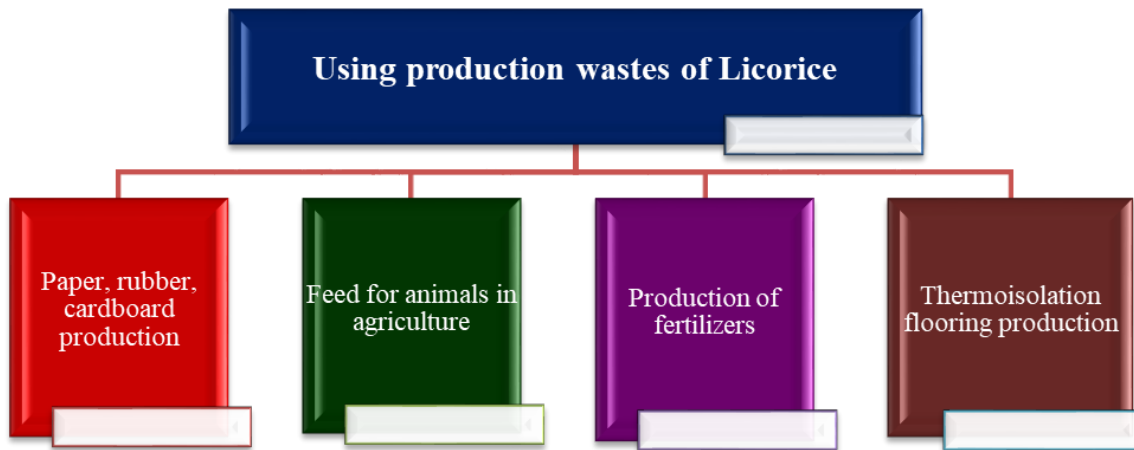


Fig 4: Schema 4.

Taking into account the scientific researches refer to chemical, technological, pharmacological-therapeutic studying of sweet licorice preparations and dietary biologically active supplements has been continuing from 1995 till 2018 years in the Azerbaijan Medical University.

Scientists of many countries of the world had proved anti-inflammatory properties of licorice preparations, including glycyrrhizic acid and its derivatives, it is revealed that glycyrrhizic acid and its aglicon enforcing influence of exogenous hormones of adrenal glands, inhibits oxidizing phosphorylation and biosynthesis of the sulfated mucopolysaccharides, creates lower an activity of a phosphoinositide 3-kinase, increases an activity of a glutamyltransferase [7]. It is shown, that glycyrrhizic acid inhibits activity of a farnesyltransferase in cellular membranes [8]. Glycyrrhizic acid and its derivatives, like nonsteroid resolvents influence a cascade of arachidonic acid, inhibiting biosynthesis of prostaglandins. Taking into account phased out before, we have paid an attention for development of a number of medicinal and parapharmaceutical means on the basis of licorice related with anti-inflammatory activities; which were being certified in a form of patents: "the obtaining method of means from the herbal raw materials which are possessed by anti-inflammatory activity". Eurasian Patent No. 028017 from 29.09.2017; «The means for prophylaxis and treatment of infectious and inflammatory diseases of a throat/throat and a mouth on the basis of medicinal herbs". Eurasian Patent No. 027691 from 31.08.2017; «The method of glucosamine obtaining". Az. Patent p960014 from 08.05.1996; "The method of licorice dense extract obtaining". Az. Patent a2007 0851 from 08.11.2007; «The method of obtaining of extractive substances from herbal raw materials" Az. Patent a2007 0246 from 05.03.2007; "Licorice syrup with immunotropic activity". Az. Patent a2007 0254 from 01.10.2007; "Anti-inflammatory and immunotropic" Az. Patent i2010 0112 from 12.05.2010; "Wound healing and antiburn means" Az. Patent i2013 0009 from 06.03.2013; "Remedy" of Az. Patent i2013 0008 from 06.03.2013.

Firstly, in practice of medical sciences had been discovered lymphotropic properties of being elaborated by us medical preparations.

It had been investigated the lymphatic properties in clinical practice during several pediatric diseases such as: anemia, pure meningitides, atopic dermatitis, several respiratory diseases and also in pathologic conditions as thymomegaly and thymico-lymphatic conditions. Also in adults in cases of oncologic diseases and different diseases continued by depressing of immune system.

The purpose of presented work is presentation of lymphotropic action of several preparation of licorice and practical usage them in several diseases.

#### Materials and Methods

The materials of investigation were newly elaborated pharmaceutical forms on the basis of Licorice: the dry water extract of Licorice, the dense water extract of Licorice, syrup of Licorice, syrup of "Licorice Broncho", syrup of Licorice "Qripson", syrup of Licorice "Sed", syrup of Licorice "Immunovit", syrup of Licorice "Hem", syrup of Licorice "Sed", syrup of Licorice "Cardio", syrup of Licorice "Broncho", syrup of Licorice, dry extract of Licorice, dense extract of Licorice.

The methods of studying of lymphotropic activity of being noted preparations had been held in 160 rabbits (kind of shinnilla) with weight of them 2, 5-3 kg. Firstly, had been determined influencing investigated preparations for lymphatic coagulation and them speed of lymph drainage. In experiments *in vitro* had been used fibrinogen, thrombin. In experiments *in vivo* had been used a hema coagulo graphic devise (ГК ГМ-4-02). About functional condition of coagulated activity of blood being proposed several results: the time of coagulation (Lee, White 1913), the time of recalcification (Berzerhorff, Roka, 1954), the time of thrombosis (Sirmai E., 1957), prothrombin index (Quick P.A., 1928), fibrinogen concentration (Rutberg 1961). The process of taking the blood portion was created in *v. auricularis* of rabbit and lymph portion was taking by method of A.A.Karnienko (1977) by modification of M. Kh.Aliyev and V.K.Mamedov (1989). The speed lymph drainage being determined refers to value of lymph. That was being drained from thoracic vessel.

#### Results and Discussion

The acute toxicity of all the listed pharmaceutical preparations of licorice on outbred white mice was studied. The acute toxicity of preparations had been held in white mice's (with weight 30,0-35,02) by total number of 80, that mice's beforehand being divided in 2 groups. We had 10 serial subgroups by 8 units. It had been noted lethal dosage ( $DL_{50}$ ) for being phased out preparations.

This way, had been discovered the water forms of dense and dry extracts and also syrups had less toxicity and practically harmless for per os usage.

The dry water extract of Licorice-1250 mg/kg, the dense water extract of Licorice-1260 mg/kg, syrup of Licorice-1350 mg/kg, syrup of "Licorice Broncho"-1320 mg/kg, syrup of

Licorice "Qripson"-1280 mg/kg, syrup of Licorice "Sed"-1310mg/kg, syrup of Licorice "Immunovit"-1420mg/kg, syrup of Licorice "Hem"-1380 mg/kg, syrup of Licorice "Sed"-1260 mg/kg, syrup of Licorice "Cardio"-1420 mg/kg, syrup of Licorice "Broncho"-1320 mg/kg, syrup of Licorice-1350 mg/kg, dry extract of Licorice-1250 mg/kg, dense extract of Licorice-1150 mg/kg.

It was found that the test substances Licorice bare harmless and low toxicity. Then the effect of individual medicinal

forms of licorice on blood clotting, antisloding and fibrinolysis of blood and lymph, as well as some parameters that allow to judge about the formation and outflow of lymph was studied.

Experimental studied have shown that drugs licorice: water extract, thick extract, dry extract in dose 0,1 ml/kq have a marked anticoagulant and pronounced lymphogenous effect (Table 1,2,3).

**Table 1:** The effect of dry licorice extract to lympho coagulation.

Determined indicators	Initial results	Obtained results (in hours)			
		0,5	1	3	24
Time of coagulation (sec.) M± % P	308 ± 10,2 100	520 ± 20,0 132 0,001	550 ± 16,2 138 0,001	520 ± 14,2 134 0,001	320 ± 5,2 103 0,001
Time of recalcification M± (sec.) % P	208 ± 5,2 100	260 ± 8,6 120 0,01	242 ± 12,2 120 0,01	228 ± 12,2 11,2 0,01	224 ± 20,6 101 0,01
Tolerance for heparin (sec.) M± % P	124 ± 4,6 100	340 ± 96 305 0,001	352 ± 2,0 329 0,001	342 ± 98 306 0,001	262 ± 5,2 240 0,001
Thrombin time (sec) M± % P	23 ± 0,8 100	45,1 ± 6,2 2015 0,01	47,2 ± 6,5 210 0,01	36,1 ± 1,7 170 0,01	25 ± 0,4 1104 0,001
Prothrombin index (%)M± % P	58 ± 1,7 1,0	44,2 ± 0,6 0,78 0,01	49,2 ± 0,5 0,75 0,001	38 ± 1,0 0,74 0,001	54 ± 0,4 0,96 0,001
Fibrinogen concentration (mq%) M± % P	72 ± 4,2 1,0	66 ± 4,2 0,92 0,05	50 ± 4,2 0,73 0,005	58 ± 6,4 0,78 0,005	64 ± 4,4 0,9 0,005
Lymphatic speed M±m (ml/min) % P	0,17 ± 0,01 108	0,3 ± 0,07 170 0,05	0,36 ± 0,04 260 0,05	0,38 ± 0,05 210 0,05	0,31 ± 0,08 175 0,05

**Table 2:** The effect of thick licorice extract to lympho coagulation.

Determined indicators	Initial results	Obtained results (in hours)			
		0,5	1	3	24
Time of coagulation (sec.) M± % P	408 ± 10,2 100	620 ± 2,0 132 0,001	650 ± 16,2 138 0,001	620 ± 14,2 134 0,001	420 ± 5,2 103 0,001
Time of recalcification M± (sec.) % P	206 ± 5,2 100	280 ± 8,6 120 0,01	240 ± 12,2 120 0,001	220 ± 12,2 11,2 0,01	204 ± 20,6 101 0,01
Tolerance for heparin (sec.) M± % P	104 ± 4,6 100	320 ± 96 305 0,001	332 ± 2,0 158 0,001	322 ± 98 306 0,001	242 ± 5,2 240 0,001
Thrombin time (sec) M± % P	22 ± 0,8 100	44,1 ± 6,2 201 0,01	46,2 ± 6,5 210 0,01	36,0 ± 1,7 170 0,001	24 ± 0,4 110 0,001
Prothrombin index (%) M± % P	66 ± 1,7 100	54,2 ± 0,6 0,78 0,001	50,2 ± 0,5 0,75 0,001	48 ± 1,0 0,74 0,001	64 ± 0,4 0,96 0,001
Fibrinogen concentration (mq%) M± % P	82 ± 4,2 1,0	76 ± 4,2 0,92 0,05	60 ± 4,2 0,73 0,005	68 ± 6,4 0,78 0,005	74 ± 4,4 0,9 0,005
Lymphatic speed M±m (ml/min) % P	0,18 ± 0,01 108	0,3 ± 0,07 170 0,05	0,45 ± 0,04 260 0,05	0,38 ± 0,05 210 0,05	0,32 ± 0,08 176 0,05

**Table 3:** The effect of water licorice extract to lympho coagulation.

Determined indicators	Initial results	Obtained results (in hours)		
		0,5	1	24
Time of coagulation (sec.) M± % P	480±20 100	540 ± 8,5 112	520 ± 8,8 109	520 ± 10 101
Time of recalcification M± (sec.) % P	130 ± 9 100	190± 11 145	214 ± 21 162	190 ± 16 142
Prothrombin index (%) M± % P	58 ± 4,7 1,0	34 ± 4,2 0,59 0,01	26 ± 2,1 0,45 0,05	54 ± 2,9 0,93 н.д.
Tolerance for heparin (sec.) M± % P	104 ± 8,5 100	230±21 224	215 ± 11 206	123 ± 11 118
Thrombin time (sec) M± % P	16 ± 1 100	27 ± 1,7 169	38 ± 2 244	25 ± 2,7 156
Fibrinogen concentration (mq%) M± % P	74 ± 7,5 1,0	37 ± 7,5 0,5 0,01	22 ± 6 0,3 0,01	52 ± 7,5 0,7 0,05
Lymphatic speed M±m (ml/min) % P	0,2 ± 0,03 100	0,3 ± 0,06 150 0,01	0,45 ± 0,03 265 0,01	0,45 ± 0,06 280 0,01

Comparative studied of lymph coagulation have shown that the drug causes a gradual increase in the clotting time of the lymph during the first hours of observation. The recalcification time increased but then quickly slowed down returning in a day to the initial level. The rate of lymphatic drainage increased 1,8 times in the first hours, and the next day it remained 1,5 times higher than the baseline.

Analysis of the results of studies conducted on a comparative pharmacological study of the lymphotropic activity of the listed medicinal plants provided a basis for judging about their high lymphogenous activity. In order to judge the bioavailability of the studied substances as well as to identify the products of their biotransformation in living organisms and biological fluids (blood and urine), a pharmacokinetic analysis was performed on rabbits. Optimal conditions for isolating the studied substances and their metabolites from bio objects, as well as methods for their qualitative identification were developed. Then a scheme and method of expression analysis of triterpen compounds of licorice and their metabolites from biological fluid of the body were developed for laboratory-diagnostic analysis.

This information allows making an opportunity to discuss, that the studied medicinal forms of licorice are safe and have a stimulating effect on both the lymph and the immune system. Identified lymphogenous or lympho-stimulating with a small anticoagulant effect, as well as immunotropic effects characterize the licorice naked as a source of valuable drugs with lymphotropic activity.

Experimental studied of the lymphotropic properties of bare licorice and its medicinal substances create the conditions for their possible use in practical medicine for the prevention and treatment of various diseases with reduced function of of the immune system.

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