

# Medicinal preparations based on prickly artichoke (*Cynara scolymus L.*)

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**Annotation:** The basis of the article is the herbal medicinal raw material, the prickly artichoke *Cynara scolymus L.*, belonging to the family (*Asteraceae Dumort*).

**Keywords:** prickly artichoke *Cynara scolymus L.*, medicinal plants, raw materials, Cinaron Bio capsules, dietary supplement Hepatonorm, liquid extract.

**Relevance of the topic:** Currently, the world pays great attention to the development of hepatoprotective and choleric drugs based on medicinal plant materials and the identification of new biologically active additives (BAA) for quality control. In this regard, research is being carried out in priority areas of dynamic separation of biologically active substances in plant materials, assessment and standardization of the quality of developed drugs using gas-liquid and high-performance liquid chromatography, ultraviolet and mass spectroscopy.

In our country, especially in recent years, large-scale work is underway to produce medicines based on medicinal plants, including: drugs for the treatment of diseases of the liver and biliary tract, a lot of work is being done to develop their comprehensive improvement.

Of great interest is the study of plant objects that are used as food and at the same time may contain biologically active substances that exhibit hepatoprotective and choleric activity. Such objects include the prickly artichoke (*Cynara scolymus L.*) of the *Asteraceae* family. This species is used as a food product and medicinal plant, especially in Western Europe. Its nutritional value is explained by the presence of such biologically active substances as polyphenolic compounds, polysaccharides, organic acids and others. In Uzbekistan, large-scale work is also underway to grow prickly artichoke (*Cynara scolymus L.*) Figure 1.



**Figure 1.** The process of experimental observation of the growth of prickly artichoke (*Cynara scolymus L.*)

Decree of the President of the Republic of Uzbekistan of April 10, 2019 No. DP-5707 "On measures to accelerate the development of the pharmaceutical industry in 2019-2021"<sup>1</sup>, Decree of February 14, 2018 No. DP-3532 "On additional measures to accelerate the development of the pharmaceutical industry", Statement Cabinet of Ministers of the Republic of Uzbekistan No. 32 dated April 20, 2015 "On measures to develop the production of medicinal plants and biologically active additives (BAA) at local enterprises". This article to a certain extent contributes to the implementation of the tasks set in the regulations for this activity.

**The aim of the study** is to develop modern analytical methods for quality control and standardization of new preparations of hepatoprotectors and herbicides obtained on the basis of medicinal plant materials.

To achieve this goal, the following **tasks** were formulated in the work:

- development of methods for assessing, controlling and standardizing the quality of a liquid extract with a hepatoprotective and choleric effect, obtained on the basis of local raw materials of prickly artichoke;
- determination of the chemical composition of the choleric tea "Hepatonorm" and tincture of dietary supplements, developed on the basis of local raw materials of prickly artichoke;
- development of methods for assessing the quality, control and standardization of capsules "Cinaron Bio" 450 mg with hepatoprotective and choleric effects, obtained on the basis of local raw materials of prickly artichoke;
- study of the pharmaco-toxicological properties of the analyzed preparations;

**The object of the study** was a liquid extract based on prickly artichoke, capsules "Cinaron Bio", biologically active additives (BAA) "Hepatonorm", localized on the territory of Uzbekistan.

**The subject of the research** is the development of methods for the isolation and detection of biologically active substances (BAS) in drugs, the assessment and quality control, the introduction of analytical methods developed into the practice of control and analytical laboratories of pharmaceutical companies.

**Research methods.** The studies used chemical (thin-layer chromatography), physicochemical (spectrophotometry, mass spectrometry), modern instrumental (high-performance liquid chromatography) and pharmacological methods of analysis, as well as computer programs.

**The scientific novelty of the research** is as follows:

- for the first time, on the basis of local plant raw materials of prickly artichoke, in dry and liquid extracts, flavonoids, amino acids, ascorbic acid, vitamins, macro- and microelements, monosaccharides, additives were found in biologically active substances;
- a high-performance liquid chromatography method was developed for the authenticity and quantitative analysis of "Cinaron Bio" 450 mg capsules; standards were developed for standardizing the amount of oxidolinic acids to chlorogenic acid;
- the quality standards of the drug "Hepatonorm" BAA, developed on the basis of prickly artichoke, were established, its biological effectiveness and harmlessness were determined.

**The theoretical basis of the study** was the scientific research of scientists from all over the world such as O.S.Wolfbeis, X.F.Zhu, N.X.Zhang, Y.T.Tanaka, K.Tanaka, H.Kojima, A.Mutalib, E.Azzini, R.Bugianesi, F.Romano, G.Ben-Hod, S.Doğan, Y.Turan, H.Ertürk, R.Dosi, A.Daniele, V.Guida, L.Ferrara, A.S.El Senousy, M.A.Farag, D.A.Al-Mahdy, E.Fateh, B.Barrett, R.Bauer, H. Becker, M.A. Bukovsky, R. Cheminat, R.A.Zawatzky A.R.Burger, R.P.Torres, J.Warren, A. Rehman, H.D.Proksch, I.L. Luneva, V.A. Chelembitko, T.V. Orlovskaya, L.I. Dranik, T.A. Patsaev, N.T.Ilyasova, N.M.Mamedaliev, O.S.Leonovich, R.I.Stryuk, L.N.Pavlova, E.V.Sokolova, I.A.Utz, E.V.Avdeeva, N.N. Bogdashev, A.D. Gordienko, E.P. Fedorova, V.A. Kurkin, S.M. Nikolaev, A.D. Bakuridze, V.N. Samorodov on the development of drugs with hepatoprotective and choleric effects, study of their chemical composition, quality control and standardization<sup>2</sup>.

<sup>1</sup> Decree of the President of the Republic of Uzbekistan No. DP-5707 dated April 10, 2019 "On measures to accelerate the development of the pharmaceutical industry in 2019-2021".

<sup>2</sup> Information about foreign scientific research on the topic of the article is considered on the basis of sources [www.elsevier.com/locate/jethpharm](http://www.elsevier.com/locate/jethpharm), [www.springerlink.com/content](http://www.springerlink.com/content), [www.scopus.com](http://www.scopus.com)

On the basis of plant materials in the treatment of diseases of the liver and biliary tract, studies were carried out on the development of drugs used, the study of their pharmacological activity by such researchers as H.U. Aliyeva, A.N. Yunushodzhaeva, R.T. A.A.Abzalova, A.A.Yu.Ibragimova, Kh.M.Kamilova, N.K.Olimova, A.K.Saidvalieva.

#### **Practical basis of the research:**

- developed criteria for control without impurities of prickly artichoke extracts based on extracts and specific biologically active substances such as coffee, cinnamon and chlorogenic acids;
- "Hepatonorm" BAA was developed on the basis of prickly artichoke and its hepatoprotective pharmacological activity and non-toxicity were determined, and regulatory documents for this supplement were developed.

#### **Scientific and practical significance of the research results.**

The scientific significance of the results of the study is explained by the fact that the pharmacotherapeutic effect is not inferior to export drugs with the possibility of producing hepatoprotective and choleric drugs, and their quality can be controlled using gas-liquid and high-performance liquid chromatography and ultraviolet spectroscopy.

The practical significance of the results of the study is the inclusion of modern methods of phytocomposition "Cinaron Bio" capsules 450 mg and "Hepatonorm" in regulatory documents and their use in laboratory analysis for a quick assessment of the quality of these drugs and biologically active substances.

A method has been developed for obtaining a water-alcohol liquid extract based on prickly artichoke raw materials. The liquid extract was obtained as follows: 50 kg of crushed raw materials with a particle size of 2-6 mm were placed in an extractor, soaked in 40% ethyl alcohol for 1 hour, then extracted with 40% ethyl alcohol in a ratio of 1:5 for 7 hours. 85% (42.5 kg) of the extract relative to the total mass of the raw material was poured into a clean container and tightly closed with a lid (extract No. 1). After that, 40% ethyl alcohol was transferred to the extractor until a "glassy surface" was formed, and extraction was continued for 7 hours. Then all the liquid in the extractor was transferred to a clean, dry container (extract #2). The extraction was carried out in the same way 4 more times for 7 hours. After each extraction, the liquid was transferred to a container with extract No. 2. The extract in the second container was concentrated using a vacuum evaporator. The total volume of liquid was continued until 15% by weight (7.5 kg) of the raw material obtained for extraction was received, extracts No. 1 and No. 2 were combined and cooled at room temperature for 2-3 hours. The precipitated extract was filtered through a cotton filter into a clean, dry brown glass jar.

The following numerical indicators of the liquid extract were determined according to the requirements of the Global Fund: description, pH, heavy metals, dry residue, density, amount of alcohol. In appearance, the liquid extract was a brown liquid with a peculiar odor and a bitter taste, pH 5.14, dry residue 14.24%, density 1.076 g/cm<sup>3</sup>, the amount of alcohol was 23.86%, the quantitative content of heavy metals met the requirements of the Global Fund XI.

Quantitative analysis of biologically active substances of a liquid extract solution diluted (1:10 ratio) with purified water was carried out by HPLC, it was found that it contains relatively more chlorogenic (5119.32 µg/ml), caffeic (344.26 µg/ml) acids and cynaroside (2843.97 µg/ml).

The determination of the amount of hydroxycinnamic acids in the liquid extract in terms of chlorogenic acid was carried out using a spectrophotometer at a wavelength of 329 ± 2 nm. On average, the amount of hydroxycinnamic acids in terms of chlorogenic acid was 2.09%. The reference solution was 50% ethanol.

Vitamins B1 and B2 contained in the liquid extract were determined by the spectrophotometer method in accordance with the requirements of the Global Fund. According to the results of the study, vitamin B1 was 0.56 µg/ml, vitamin B2 - 0.25 µg/ml. The tannins contained in the liquid extract of prickly artichoke averaged 2.36%.

According to the results of mass spectrometric analysis of the elemental composition in the liquid extract, a relatively high content of such bioelements as sodium (1300.0 mg/kg), potassium (14000.0 mg/kg), magnesium (1000.0 mg/kg), phosphorus (730.0 mg/kg), calcium (540.0 mg/kg), sulfur (110.0 mg/kg), zinc (5.2 mg/kg) and copper (8.7 mg/kg).

Quantitative analysis of ascorbic acid in a liquid extract diluted with 0.1% orthophosphate acid (at a ratio of 1:10) was carried out by HPLC. The quantitative content of ascorbic acid was 14.2 µg/ml (retention time 2.455 min, peak area 53.17 mAU\*s).

As a result of studying the amino acid composition of a liquid extract based on prickly artichoke, 16 amino acids were identified, 9 of which are essential amino acids - valine, threonine, methionine, isoleucine, leucine, lysine, phenylalanine, histidine and arginine. The amount of protein was 15.0%, the content of proline, glutamine and asparagine in the protein is relatively higher than others.

### Conclusion.

As a result of the information and analytical study of scientific publications to determine the chemical properties, quality and quantity of preparations obtained on the basis of prickly artichoke, a methodological approach has been developed that determines the establishment of quality standards for the raw materials of this plant.

For an objective assessment of the chemical composition of a liquid extract based on prickly artichoke, modern methods for the analysis of high-performance liquid chromatography (HPLC) and spectrophotometric analysis (SPH) have been developed, and it is also recommended that these methods be included in the quality standards of extracts.

The chemical composition of Cinaron Bio 450 mg capsules has been studied, optimal quality standards have been established, and the preparation has been standardized. For the first time, quality standards for filter-packed tea and tincture of BAA "Hepatonorm" based on local prickly artichoke, proposed as methods of analysis in the production process, have been established.

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