EFFECTS AND ACTIONS OF SILYBUM MARIANUM PHYTOPREPARATION

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Summary: *Providing the population of Uzbekistan with effective and safe medicines is one of the priority tasks of pharmacy. In accordance with the Decree of the President of the Republic of Uzbekistan dated May 20, 2022 N PP-251 "On measures to organize the cultural cultivation, processing and widespread use of medicinal plants in treatment", it becomes more significant. In this regard, herbal medicines (HRP) are of particular relevance, which have a wide range of therapeutic effects and a number of advantages compared to drugs of synthetic origin. PRP is distinguished by a relatively low risk of developing allergies, a milder therapeutic effect and safety.*

Keywords: *silybum marianum, hepatoprotectors, medicinal plants.*

Silybum marianum has been used as a medicinal plant since ancient times and is used in traditional medicine to treat liver diseases and normalize digestion, to stimulate lactation, and to treat inflammation of the upper respiratory tract and lungs. The main interest is the hepatoprotective activity of milk thistle. The dominant components are silybin, silydianin, silicristin, the sum of which is called silymarin [2].

Silybum marianum (popular names: black elecampane, lump, milk thistle, Maryino ostrichestro, Maryin thistle, Maryina thorns, white sow thistle, sharp pester) [10].

Silybum marianum grows in wastelands, in weedy places, along roads, in dry places, sometimes it is bred in gardens and kitchen gardens as an ornamental and medicinal plant. Silybum marianum is widely cultivated in Russia and Uzbekistan [8].

It is an annual (in cultivation conditions) or biennial (in nature) thorny plant 1.5-2 m high. The stem is erect, massive, furrowed, naked, or pubescent with villi, unbranched or slightly branched. The leaves are large with yellowish spines along the edge of the leaf and along the veins below, the leaf blade is green with white spots, shiny. Basal leaves are large, strongly wrinkled, pinnate, glabrous on petioles, stem leaves alternate, sessile [1]. The flowers are collected in large (up to 4 cm in diameter) inflorescences-baskets, located singly on the branches of the stem, the leaves of the wrapper of the baskets are arranged in several circles, with spikes along the edges, and with one larger spike at the top (up to 5 cm). The inflorescence bed is fleshy, covered with hairs. The flowers are all tubular, bisexual, purple-red. The fruit is a black achene with gray dots and a tuft of hairs at the end, 15-20 mm long, shiny [3].

It blooms from July to late autumn, the fruits ripen unevenly in August-September. Fruit picking is carried out in late August-September, during the drying period of the wrappers on most side baskets [5]. Harvesting is carried out by mowing the above-ground part in the first half of the day with the help of hay mowers, the

resulting mass is dried on a current and threshed. The fruits are separated from impurities and dried in dryers [9].

Quite mature and dried fruits of an annual cultivated herbaceous plant of milk thistle, collected in autumn, are used as raw materials. The fruits are ovoid achenes, slightly flattened laterally, 5 to 8 mm long, 2 to 4 mm wide, and 1 to 3 mm thick [15]. Apex obliquely truncated with protruding blunt thick remnant of style or without it. The base of the achene is blunt, the fruit scar is slit-like or rounded, slightly shifted to the side. The surface is smooth, sometimes longitudinally wrinkled, shiny or matte. Color - from black to light brown, sometimes with a lilac tint, often spotted fruits, the roller is lighter. There is no smell. The taste is slightly bitter.

When viewed under a microscope, the structure of the pericarp on a transverse section, consisting of several layers, is of diagnostic importance: the epidermal layer is palisade-like elongated cells, the outer and side walls are strongly thickened; pigment layer - one row of cells with brown content; a layer of fibrous cells of the mesocarp (6-7 rows of large cells with mesh and spiral thickening of the walls). The seed coat, tightly fused with the pericarp, is represented on the outside by a thick layer of elongated sclereoid with thickened walls. Seeds without endosperm [13].

Milk thistle powder contains fragments of the epicarp, consisting of colored cells, a group of parenchymal cells of the pigment layer, contains colored parts; a large group of sclereids with bright yellow thickened walls and a narrow plane; small-cell parenchyma fragments with perforated walls, thin-walled parenchymal cells containing oil, round and elongated calcium oxalate crystals [19].

Chemical composition: Milk thistle fruits contain flavolignans, flavonoids, fatty oils, essential oils, sterols, organic acids, bitterness, resins, mucus, sugars, amines, saponins and other substances. Milk thistle fruits contain a unique group of biologically active compounds - flavolignans. These are flavonoids containing a phenylpropanoid fragment (-C6-C3-) in their composition, constituting a small new group of natural compounds, which gives reason to attribute flavolignans to phenylpropanoids. Flavolignans were found in six families, and most of them (12 compounds) were isolated from the fruits of milk thistle (Silybum marianum (L. Gaertn). The flavonoid part of the compounds of this group is represented by flavonones (eriodic-tol), flavonols (taxifolin), flavones (luteolin, scutellarein, isoscutellarein, tricetin, tricine) and flavonols (herbacetin). The first representative of flavolignans, silybin, was isolated by a number of authors from the fruits of milk thistle, but due to the unusual chemical structure, it took more than 20 years to study its chemical structure [17].

Flavolignans, along with fatty oils, are the main group of biologically active compounds. Their content in the fruits of milk thistle, according to various sources, can range from 1.5 to 4%, depending on the variety and place of growth [8]. The flavolignans of silybum marianum are represented by the following compounds:

silybin, isosilybin, 2,3-dehydrosilybin, silandrin, silicristin, silydianin, silymonin, 2,3-dehydrosilicristin, isosilichristin, siligermine.

The dominant components are silybin, silydianin, silicristin, the sum of which is called silymarin [7].

An important class of biologically active compounds of milk thistle fruits is fatty oil, the content of which reaches 20-30%.

The composition of Silybum marianum fatty oil is characterized by the presence of: linoleic - 56.57%, oleic - 20.73%, palmitic - 8.01%, stearic - 4.79%, arachidic - 2.70%, behenic - 2.09 %, nonadecylic - 1.11%, lignoceric - 0.69%, myristic - 0.09% fatty acids [11].

Milk thistle fruits contain flavonoids of the classes flavonols (kaempferol), dihydroflavonols (taxifolin), and dehydrokaempferol [13]. Sugars that make up the fruits of Silybum marianum: arabinose, rhamnose, xylose, glucose.

The fruits of Silybum marianum contain ash, macronutrients (mg/g): K-9.20; Ca-16.60; Mg-4.20; Fe-0.08; trace elements: Mn-0.10; Cu-1.16; Zn-0.71; Cr-0.15; Al-0.02; V-0.01; Se-22.90; Ni-0.20; Sr-0.08; Pb-0.08; I-0.09; B-22.40.

The composition of the fruits of silybum marianum also includes up to 0.1% essential oil. Milk thistle leaves contain flavonoids (apigenin, luteolin, kaempferol and their glycosides), P-sitosterol and its glycosides. Silymarin was not found in milk thistle leaves [16].

Sterols are represented by cholesterol, campesterol and stigmasterol. Recently, six new hepatoprotective components of silybum marianum have been reported, with the 3-deoxyanalogues of silybin, silydianin, and silychristin showing more pronounced biological activity. With this in mind, it is of interest to study the possibility of creating medicines based on the raw materials of the white-flowered variety of this plant. Other lignoids with antihepatotoxic activity have also been found - these are neolignan Americanin A and Schisandra chinensis lignans. All this indicates the prospects for further studies of natural lignoids [9].

From the point of view of technology, the complex use of silybum marianum fruits is relevant, which makes it possible to obtain silybum marianum fatty oil, and from production waste (meal and fruit pulp) - flavolignan-containing galenical preparations.

To obtain dosage forms of silybum marianum, the optimal parameters of the technological process have been established; grinding of raw materials (recommended 0.5 mm); extractant (the most effective is 80% ethyl alcohol); the ratio of raw materials and extractant (liquid extract 1:1, tincture 1:5); absorption coefficient of raw materials - 1.5-1.7; extraction temperature regime (in laboratory conditions at a temperature of 70°C).

The total extract has a more pronounced biological activity than individual flavolignans [7].

There have been many scientific studies on the effects of silybum marianum. In the work of Yu. I. Brel, A. N. Lyzikov, the results of experimental studies confirm that milk thistle preparations have a pronounced antitumor effect against malignant neoplasms of various localizations (prostate, large intestine, lungs, bladder, ovaries, etc.). In vitro studies revealed the property of silymarin/silibinin to suppress the proliferation of cancer cells, and in vivo experiments - to inhibit the growth of tumor xenograft and reduce the incidence of neoplasms in chemically induced carcinogenesis. The antitumor properties of silymarin are due to a combination of its antioxidant and anti-inflammatory effects with mechanisms such as cell cycle regulation, apoptosis induction, angiogenesis inhibition, invasion and metastasis [2].

Due to the presence of antioxidant and anti-inflammatory properties, silymarin may be effective in the treatment and prevention of certain neurodegenerative and neurotoxic processes [14].

The results of experimental studies demonstrate the possibility of using silybum marianum preparations as a hypocholesterolemic agent. Krecman et al., studying the ability of silymarin and silybin to reduce diet-induced hypercholesterolemia in rats, found that the effect of these drugs on serum cholesterol concentration was comparable to that when using a hypocholesterolemic drug [5].

In addition to the hepatoprotective effect, silybum marianum preparations have antitumor, hypocholesterolemic, neuro- and cardioprotective properties, and can be effective in the treatment of diabetes mellitus, pancreatic and kidney diseases.

The current insufficient volume of clinical studies to determine the effectiveness of the use of milk thistle preparations in patients allows us to speak only about preliminary results.

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