Dereza fruits (Lycium chinense Miller, Lycium barbarum L.): a modern scientifically based view of a traditional remedy

T.L. Kiseleva, M.A. Kiseleva
(Federal Research Center for Nutrition, Biotechnology and Food Safety, Moscow)

Fruits of Goji (Lycium chinense Miller, Lycium barbarum L.): modern scientific evaluation of the traditional remedy

TL Kiseleva, MA Kiseleva
(Federal Research Center of Nutrition and Biotechnology, Moscow, Russia)

SUMMARY

Dereza fruits (Goji Berries) have a long tradition of medicinal and nutritional use in East Asian countries. In this work, an attempt is made to objectify the data of traditional oriental medicine on the medicinal properties of wolfberry fruits from the standpoint of modern scientific concepts (based on the results of phytochemical, toxicological, pharmacological and clinical studies published in the open press). An analysis of the results of phytochemical studies made it possible to establish that the main groups of biologically active substances responsible for the pharmacotherapeutic effect can be considered polysaccharides, carotenoids, flavonoids, vitamins.

In experimental studies in vitro and in vivo, the presence of antioxidant and immunomodulatory properties was revealed, especially in the context of age-related diseases, including atherosclerosis, neurodegeneration, and diabetes mellitus. The hypoglycemic, hypolipidemic, antihypertensive and neuroprotective effects of water-soluble extracts from fruits have also been established. The results of clinical studies confirm some of the actions established in experiments on animals, however, most experts agree that for reliable conclusions, additional modern studies are required on standardized extracts of wolfberry fruit.

The fruits are non-toxic raw materials, but there are reports of drug interactions with warfarin, as well as contraindications for use in accordance with the theoretical foundations of traditional Chinese medicine.

Key words: Goji, wolfberry, Berber wolfberry, Chinese wolfberry, traditional Chinese medicine.

RESUME

The fruit of Dereza (fruit of Goji) has an ancient tradition of medical and food use in East Asia. We analyzed the data of Traditional Oriental medicine on the therapeutic properties of the fruit of Dereza (Lycium spp.) From the perspective of modern scientific ideas (based on published in the open press the results of phytochemical, toxicological, pharmacological and clinical studies). Analysis of the results of phytochemical studies revealed that the main groups of biologically active substances responsible for pharmacotherapeutic action can be considered polysaccharides, carotenoids, flavonoids, vitamins.

In experimental studies in vitro and in vivo revealed the presence of antioxidant and immunomodulatory properties, especially in the context of agerelated diseases, including atherosclerosis, neurodegeneration and diabetes. Hypoglycemic, hypolipidemic, antihypertensive and neuroprotective effects of watersoluble fruit extracts have also been established. The results of clinical studies confirm some of the actions established in animal experiments, but most experts agree that additional modern studies on standardized extracts of Dereza fruit are required for reliable conclusions.

The fruits are not toxic, but there are reports of drug interactions with warfarin, as well as contraindications for use in accordance with the theoretical foundations of traditional Chinese.

Keywords: Goji, Wolfberry, Lycium barbarum, Lycium chinense, Traditional Chinese medicine.

INTRODUCTION

In recent years, Dereza berries, or Goji berries, have often been touted as a superfood with unique health benefits [111, 112]. Thanks to effective marketing strategies, since the beginning of the 21st century, goji fruits (berries and juices) have been actively sold in Western countries as healthy food products, as well as as a "miracle" remedy for well-being and an effective anti-aging agent. Moreover, the popularity of Goji-based products has grown especially rapidly in recent years. Now they are even included in everyday foods such as yoghurts, juices, biscuits, crispy bars, chocolate, muesli, as well as in sausages, beer, wine, and even soap [85, 87].

In the global functional food market, wolfberry is commonly referred to as the “Himalayan goji berry” or “Tibetan goji berry”. Goji products are heavily marketed online, but increasingly they can be found in pharmacies or organic stores. Dereza products are quite expensive; according to [85], on the Internet market, on average, you need to pay $ 30–50 for a 1 liter bottle of juice.

The commercial rise of wolfberry-based products in Western countries Dr. O. Potterat (2010) from the Department of Pharmaceutical Biology of the University of Basel (Switzerland) is largely explained by the publication of Dr. Earl Mindell's (2003) book "Goji, The Himalayan Secret of Health" [76]. The highly controversial Canadian-American pharmacist and nutritionist E. Mindell wrote a whole series of books on nutrition and nutritional supplements for the general public (publications caused deep skepticism in the scientific community) [85]. In the aforementioned goji publication, he recommends the use of Dereza fruit juice for the prevention of cancer, cardiovascular disease, diabetes and obesity, based on experience with traditional medicine and preliminary research conducted mainly in China.

In particular, E. Mindell declares the miraculous effect of goji berries, called the "Himalayan fruit of longevity," on life expectancy. His claims of Goji's "exceptional value" are consistently quoted in advertisements for Goji's products, including through MLM marketing. A detailed critical analysis is given in [41] (cited from [85]), where the authors conclude that, to date, there is no scientific or thoroughly verified evidence to support the claims for a reliable increase in life expectancy and some other statements.

Goji berries and goji berries are successfully and legally marketed as food or food supplements in Europe and the United States. However, there is a ban on advertising and promotion of these products as medicines (medicines supplied with therapeutic indications for use). In 2006, the FDA even had to send out warning letters to some distributors of goji juice about marketing claims that violate the Food Drug and Cosmetic Act [33], [32]. In Europe in 2007, the UK Food Standards Agency launched a special assessment procedure to determine if goji berries should receive Novel Food status, as was the case for Noni juice (Morinda citrifolia) in 2003 [86], [31]. After examining the scientific evidence and all the circumstances surrounding the use of wolfberry fruit in the UK and other countries, the agency concluded that before 1997 there were already sufficient records of food consumption of goji berries in the UK, and therefore, wolfberry fruit does not fall under the Novel Food legislation (Law on New Foods) [34]. In the United States, Goji is not on the FDA's GRAS List, which is generally regarded as safe (GRAS) [85].

With modern attempts to assess the scientifically based efficacy of wolfberry fruits, the following are usually studied:

1) the species diversity of the genus Lycium and the botanical species of Dereza, which were traditionally used in various medical schools and are applied in modern research and clinical practice;

2) differences in the use of wolfberry fruits in regions with different cultural and historical heritage;

3) the objectivity of the assessment of traditional and proven therapeutic and prophylactic types of action of dereza fruits on health and the function of individual body systems [112].

The purpose of this information and analytical study is to objectify the data of traditionaloriental medicine on the medicinal properties of wolfberry fruits from the standpoint of modern scientific concepts (based on the results of phytochemical, toxicological, pharmacological, clinical and historical studies published in the open press).

PLANT NAME AND SPECIES

Dereza (Goji berries, goji berries, Goji) - Lycium barbarum L., Lycium chinense Miller, Solanaceae family - Solanaceae Juss.

Goji (Goji) (from Chinese gouqi) [103, 118] is a relatively new name in Europe and America, which was given to two closely related botanical species of the genus Lycium (Dereza), which has an ancient tradition of use as medicinaland food plants in East Asia, in particular in China, Lycium barbarum and L. chinense [85]. Traditional Chinese language, the plant is known as Ningxia gouqi (Chinese trad. 寧夏枸杞, pinyin: Níngxià gǒuqǐ, literally: "Ningxiang Boxthorn").

Traditional names translated from English sound like a wolfberry (Wolfberry), Chinese wolfberry, matrimony wine (Barbary matrimony vine) [43]. In Japan, the plant is known askuko, in Korea as gugija, in Germany as Bocksdorn.

In domestic bibliographic sources on traditional Chinese medicine (TCM), historically, the name Chinese dereza is most often used - Lycium chinense Mill. According to some domestic TCM reference books, synonymsDereza Chinese are Dereza Berbers (barbarians) - Lycium barbarum L., goji berries [1, 2] and common wolfberry [7]. At the same time, the famous Russian botanist A.I. Schreter quite rightly did not consider these species as synonyms, in contrast to [1, 2, 7], and described various external features, phenology, range, habitat and cultivation features for the Chinese wolfberry and the Barbarian wolfberry (Berber) [8].

In various medical reference books, there are some discrepancies regarding the botanical species, which is advisable to use for medicinal purposes [85]. According to some foreign data, onlyL. barbarum can servedrug, although traditional medicine uses fruits (Fructus Lycii) and root bark (Cortex Radicis Lycii)of both types [85]. Other sources include both as raw materials for drugs or recommend eitherL. chinense or L. Barbarum. However, in essence, the indications for use coincide almost completely [85]. At the same time, only one type of fruit is included in the Pharmacopoeia of the PRC as a medicinal raw material -L. Barbarum (Pharmacopoeia of the People's Republic of China, 2000) [83].

According to O. Potterat (2010), Goji berry products sold outside Asia contain, according to suppliers, exclusively fruits L. barbarum. However, it is difficult for a layman to distinguish between fruits of different types and varieties, therefore, in commercial products are often counterfeit - the fruits of closely related species of wolfberry [85].

According to modern scientific concepts, out of 97 species of the genus Lycium known in the world, 31 species of wolfberry have been registered as food or medicinal plant raw materials (fruits are usually used) [112]. 85% species of the genusLycium are found in the Americas and Africa, of which 26% are used in traditional medical practice, with 9 of the 14 species being used in Eurasia. There are seven species and two varieties of the genus Lycium in China, of which 4 species were used by different ethnic groups. But onlyL. barbarum and L. chinense have received the status of "trade products (goods)" sold worldwide [112].

Lycium barbarum L. (synonym: L. Halimifolium Miller) (Chinese name - Gouqi, or Ningxiagouqi) and L. Chinense Miller (Gouqi) are two closely related species currently most commonly used as food and medicinal plants in East Asia. Some related species such asL. barbarum var. Aurantiocarpum(Huangguogouqi), L. Chinense var. Potaninii (Beifanggouqi), L. Ruthenicum (Heiguogouki) and L. Truncatum (Jieegouki) can be found on the market as an inexpensive supplement to two main types that are considered more valuable due to their traditional medical use [85, 118]. In China, the effectiveness of their use has been confirmed over the past two millennia. In particular, the use of Lycium fruits for rejuvenation, vision improvement and as a health food was documented as early as 500 BC (Mingi Bilu) [118].

USED PLANT PARTS

Fruits [1–6] and root bark [1, 2, 7], leaves [1, 2, 5, 6]. According to A.I. Schreter (2004), the fruits are usually used in the Berber (barbarians) Dereza, and the root bark of the Chinese Dereza. However, the bark of the roots of Chinese wolfberry in the Pharmacopoeia of the People's Republic of China (2000)

they are used along with the bark of Berber dereza roots [8, 83].

The fruits are harvested in summer and autumn when they turn orange-red. Dry in the shade. When the peel is covered with wrinkles, it is placed in the sun and dried until the peel is dry and firm and the pulp is soft [3, 4].

According to traditional medical sources, historically, for medicinal purposes, wolfberry leaves can also be used [1, 2, 5, 6, 102].

PLANT DESCRIPTION, ECOLOGY, CULTURE

Dereza is a creeping [5, 6] shrub 1–2 m [1, 2] or 1–3 m [8] high with soft half-curling stems [5, 6], small oval red or orange berries [3, 4]. Chinese experts describeL. barbarum as deciduousshrub with a height of 1 to 3 meters, and L. Chinense - slightly less. Leaves are lanceolate, can vary to ovoid.Oblong, orange or dark red fruits (berries) reach sizes up to 2 cm and have a bittersweet taste [103, 118].

Falsifications on the market are often related to the fact that the fruits of the Lycium species have very similar anatomy and histology (tissue structure). Differentiation based on morphological and histological analyzes is difficult. A significant difference requires molecular assays such as RAPD (random amplified polymorphic DNA) [103, 118].

The plant blooms in May-October [8] (September-October [5, 6]), bell-shaped purple flowers [5], juicy fruits [5, 6], ripen in June-November [8] (November [5]). It grows in river valleys, among thickets of bushes and on forest edges [8] in Japan, Korea, Eastern China [5, 6].

Dereza has been widely cultivated in China since ancient times (there are records in the book "Shih Jing", which contains the texts of the 11th-6th centuries BC) [1, 2]. Original habitatL. barbarum is still not definitively established, but,most likely, it can be found in the Mediterranean basin [39]. Currently, the plant is widespread in warm regions of the world, in particular in the Mediterranean, Southwest and Central Asia [89]. It is also cultivated in Europe and Central Asia [5, 6], in North America and Australia as a hedge [43].L. Chinense mainlydistributed in East Asia and grown, in particular, in South China, Korea and Japan [89].

Most of the commercially produced wolfberry fruit comes from plantations L. barbarum in the Ningxia Hui region(Ningxia Hui) in the north of central China and in the Xinjiang Uyghur region in the west of China. Moreover,L. barbarum is also grown in the river valleys of Mongolia [85].

As an ornamental plant, various types of wolfberry are grown in the North Caucasus, in the southern provinces of China, in European countries, Western Asia, North Africa and North America [8].

CHEMICAL COMPOSITION

Fruit. Ripe Dereza fruits contain on average3.39% beta-carotene, B vitamins$_{one}$ (0.23%), B_2 (0.33%), PP, C, free amino acids, macro- and microelements [8]. Modern scientific evidence makes it possible to explain the experience and effectiveness of their long-term traditional use and popularity at the present time. In particular, it is believed that polysaccharides, carotenoids - zeaxanthin dipalmitate, vitamins, betaine, and in general - complex (galenic) extracts and aqueous extracts are responsible for the rejuvenating effect, improving vision and efficacy against fatigue [111, 112].

Polysaccharides are considered the dominant and most important group of biologically active substances (BAS) in fruits. L. barbarum [85]. The results of their quantitative assessment, according to literature data, differ significantly, but a reliable indicator (after optimization of the extraction conditions) is currently considered to be a yield of 23% in terms of dried fruits [113].

Fraction of polysaccharides called polysaccharides Lycium barbarum (LBP - tab. 1), consists of a complex mixture of polysaccharides and proteoglycans with a high degree of branching, which have so far been only partially characterized. A review of the purified fractions in homogeneous form is published in [85] and is presented in table. one.

In most cases, the monosaccharide portion of the polysaccharides L. barbarum on 90–95% consists of arabinose, glucose, galactose, mannose, rhamnose, xylose and / or galacturonic acid [26, 30, 37, 47, 48, 79, 81, 82, 119, 120]. In 2009, L. barbarum polysaccharides were analyzed using preparative high performance size exclusion chromatography (HPSEC) [85].

Table 1

Homopolysaccharides isolated from fruits L. barbarum and L. chinense (by [85])

Glycoco-conjugates	Molecular weight	Content polysaccharides	Monosaccharides (molar ratio or%)	Bibliographic. a source
L. barbarum				
LbGp2	68200	90.7	Ara, Gal (4: 5)	[82]
LbGp3	92500	93.6	Ara, Gal (1: 1)	[47, 48]
LbGp4	214800	85.6	Ara, Gal, Rha, Glc (1.5: 2.5: 0.43: 0.23)	[47, 79]
LbGp5	23700	8.6	Rha, Ara, Xyl, Gal, Man, Glc (0.33: 0.52: 0.42: 0.94: 0.85: 1)	[47]
LbGp5B	23700		Rha, Ara, Glc, Gal, (0.1: 1: 1.2: 0.3), Galu (0.9%)	[81]
LBP3p	157000	92.4	Gal, Glc, Rha, Ara, Man, Xyl (1: 2.12: 1.25: 1.10: 1.95: 1.76)	[37]
LBPC2	12000	92.8	Xyl, Rha, Man (8.8: 2.3: 1)	[119, 120]
LBPC4	10000	95	Glc	[119, 120]
LBPA1	18000		Heteroglycan	[120]
LBPA3	66000		Heteroglycan	[120]
LBP1a-1	11500		Glc	[thirty]
LBP1a-2	9400		Glc	[thirty]
LBP3a-1	10300		GalA	[thirty]
LBP3a-2	8200		GalA	[thirty]
LBPF1	Ca 150,000	48.2 *		[26]
LBPF2	Ca 150,000	30.5 *		[26]
LBPF3	ca 150000	34.5 *		[26]
LBPF4	Ca 150,000	20.3 *		[26]
LBPF5	290000	23.5 *		[26]
L. chinense				
Cp-1-A	10000	87.8	Ara, Xyl (1: 1)	[91]
Cp-1-B	11000	89.4	Ara	[91]
Cp-1-C	42000	92.4	Ara, Gal (3: 1)	[91]
Cp-1-D	23000	90.7	Ara, Gal (1: 1)	[91]
Cp-2-A	89000	88.3	Ara (50.6%), Gal (22.8%), Man (8.4%), Rha (5.9%), Glc (5.6%)	[92]
Cp-2-B	71000	87.5	Ara (45.5%), Gal (47.4%)	[92]
Hp-2-A	8000	87.9	Ara (70.6%), Gal (13.5%)	[92]
Hp-2-B	11000	89.9	Ara (84.2%), Gal (10.7%)	[92]
Hp-2-C	120,000	90.7	Ara (49.5%), Gal (40.8%), Fuc (5.9%)	[92]
Hp-0-A	23000		Ara	[90]

* Carbohydrate content was determined using a phenol-sulfuric acid test. The content is significantly higher if it is estimated in relation to the protein content.

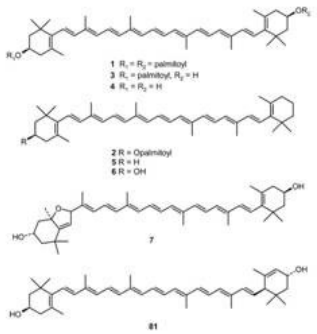
After protein hydrolysis, two main fractions with molecular weights of 79,250 and 24,470 amu (amu) were obtained, respectively [106]. The monosaccharide composition of the entire polysaccharide fraction was determined by gas chromatography after hydrolysis [85]. In the literature, there are some discrepancies in the results of the analysis of polysaccharidesL. barbarum, in particular inin relation to the presence of fucose and mannose, as well as the content of glucose [85]. In two similar studies conducted relatively recently, their composition was found to be Rha, Ara, Xyl, Man, Glc and Gal (molar ratio 0.3: 2.7: 0.3: 0.2: 2.7 : 0.9) [106] or Rha, Ara, Xyl, Fuc, Glc, Gal (1: 2.14: 1.07: 2.29: 3.59: 10.06) [69], respectively.

The second main group of biologically active substances L. barbarum are carotenoids, the content of which increases in the processripening of fruits [77, 84, 85]. In fig. 1 shows the fraction of carotenoids of fruits and leaves:

1 - zeaxanthin dipalmitate - the predominant component [108], the content of which is 56% of the total amount of carotenoids in fruits [80];

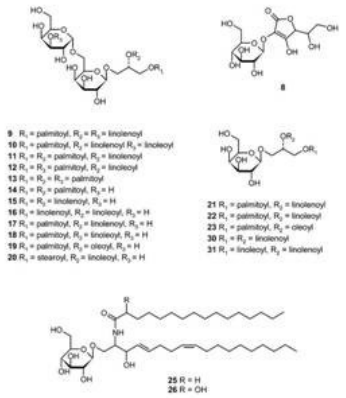
2 - βcryptoxanthin palmitate;3 -
zeaxanthin monopalmitate;

4 - free zeaxanthin (in minor amounts) and 5 - βcarotene (in
small amounts) [49].



Rice. 1. Carotenoids of fruits and leaves of wolfberry (according to [85]).

In addition, the fruits L. barbarum contains other vitamins, in particular riboflavin, thiamine and ascorbic acid, andalso its glucosylated precursor (Compound 8 - Fig. 2) [88, 105]. The content of vitamin C (42 mg / 100 g) is comparable to the content of ascorbic acid in fresh lemon fruits [85].



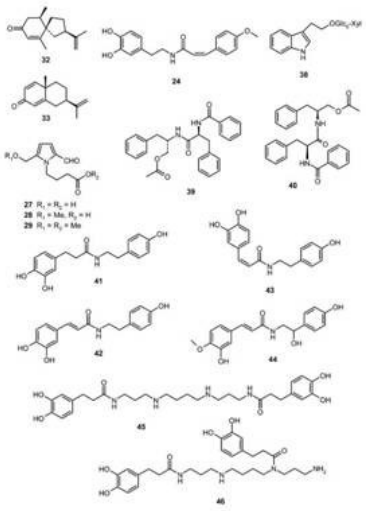
Rice. 2. Vitamin precursorC and glycolipids from dereza fruits (according to [85])

An important class of compounds L. barbarum are flavonoids: aglycones have been identified in fruits after hydrolysismyricetin, quercetin and kaempferol [60].

Essential oil and fatty acids L. barbarum was analyzed by gas chromatography with massspectrometry (GC-MS): hexadecanoic acid, linoleic acid, βelemen,myristic acid and ethylhexadecanoate [10].

Fruit L. barbarum also contains 1.0–2.7% free amino acids with proline as the main component. In addition, the non-proteinogenic amino acids taurine and γaminobutyric acid, as well as betaine (trimethylglycine) [19, 27].

A group of glycerogalactolipids was recently isolated from the fraction of nonpolar compounds [38] (Compounds 9–23 - Fig. 2.), as well as other compounds of various groups, including βsitosterol and its glucoside, daucosterol, scopoletin, pumaricacid [107], a dopamine derivative, licimide A (24 - Fig. 3.) [124], and L-monomenthyl succinate [45].



Rice. 3. Amides and other compounds from fruits and roots (according to [85])

Since many representatives of Solanaceae accumulate alkaloids, a certain interest was aroused by the publication [44], according to which in 1989 in a sample of fruits L. barbarum collected in India was reported to be quite highthe content of atropine is 0.95%.

According to [85], this study result seems to be very doubtful and is in clear contradiction with the long-term and widespread use of wolfberry fruits in the absence of any reports of their apparent toxicity. In this context, of interest are the results of an HPLC-MS study of goji berries from various regions [9], which revealed only traces of atropine in the analyzed samples - the maximum detected concentration was 19 ppb (w / w) - 19 parts per billion by weight (wt ./mas.) [9].

Fruit composition L. chinense is similar to the chemical composition of L. barbarum fruits: typical metabolites are polysaccharides, carotenoids and flavonoids. In the polysaccharide fraction, arabinoxylan (Cp-1-A), two arabinans (Cp-1-B and Hp-0-A) and a number of arabinogalactan proteoglycans were identified (Table 1) [90–92].

The main flavonoid is rutin, accompanying (in small amounts) - hyperoside, quercetin and morin [89]. Carotenoid fraction similar to that found in fruitsL. barbarum. Zeaxanthin dipalmitate (1 - fig. 1) is also the dominant compound, accounting for 49% of the total amount of carotenoids [80]. FruitL. chinense also containszeaxanthin (4 - Fig. 1) [55] and βcarotene (5 - fig. 1) [78]. In addition, two cerebroside (25, 26 - Fig. 2) [54] and three pyrrole derivatives (27-29 - Fig. 2) [28] with hepatoprotective properties (Fig. 3) have been isolated.

There are reports of identification in fruits L. barbarum tocopherols, phenolic acids, including gallic,coffee and protocatechus, chlorogenic and neochlorogenic [78].

In the study of volatile components, the main ketones were megastigmathenone, βionone and 3-hydroxy-βionone. Hydrocarbons include βelimen and δ-cadinene. Phenethyl alcohol and benzyl alcohol were accompanied by minorthe amounts of linalool and terpinen-4-ol [98]. Sesquiterpenes solavetivone (Compound 32 - Fig. 3) and 1,2-dehydro-αziperone (Compound 33 - fig. 3) [97]. Together with other esters of fatty acids C16 and C18, a large amount of methyl linoleate was found [98].

A study (by GC-MS and GC-ol-factometry) of aromatically active compounds made it possible to establish that 1-octen-3-ol, 3-hydroxy-2-butanone, acetic acid, hexanal and (E) -2-heptenal are the main components causing odor [61].

Seeds. Contains amino acids (L-aspartic acid, L-proline, L-alanine, leucine, L-phenylalanine, serine, glycine, L-glutamic acid, L-cysteine, L-lysine, L-arginine, L-isoleucine, L-threonine, L-histidine, L-tyrosine, L-tryptophan, Lmethionine), polysaccharides, taurine, many macro- and microelements (potassium, calcium, sodium, zinc, iron, copper, manganese, selenium, chromium, strontium, lead, cadmium, cobalt, magnesium, nickel) [eight].

Contains carotenoids - zeaxanthin (83% of the total carotenoids), βcryptoxanthin (6 - fig. 1) (7% of the total carotenoids), β carotene (0.9% of the total carotenoids), mutatoxanthin (7 - Fig. 1) (1.4%), as well as some minor carotenoids, some of which have not yet been even finally identified [77].

Seed sterols L. barbarum were analyzed in a series of studies for sterols contained in seedsvarious plants of the Solanaceae family. It was found that cycloartenol, cycloartanol and 24-methylenecycloartanol [50], gramisterol and citrostadienol [52] and 24-ethylcholesterol, 24-methylcholesta-5,24-dienol and 28-isofucosterol [51] are the main constituents of fractions 4,4- dimethyl, 4-methyl, 4-desmethylsterol, respectively [85]. A mixture of 6 ›-O-palmitoyl- and 6› -O-stearoyl-β sitosterol-3-O-glucoside was obtained together with two glycerogalactolipids (Compounds 30, 31 - Fig. 2) [53].

Root bark. Contains Betaine, Atropine, Hyoscyamine, Zeaxanthin, Physalien, Cryptoxanthin, Scopoletin [eight].

PHARMACOTHERAPEUTIC ACTION

For water extraction from fruits, the following types of action are described: immunotropic (immunostimulating [7]), antihypertensive [5, 6], hypoglycemic [7], anti-atherosclerotic [5], restorative and tonic [5, 6].

The antihypertensive effect is confirmed as in the experiment - it lowers blood pressure (BP) in a healthy rabbit [5] and in the clinic [7].

Fruits significantly reduce blood sugar levels [7]; in modern clinics they are considered beneficial for the liver and kidneys. [8]: "strengthens" the liver and promote its regeneration [7]. Reduce cholesterol levels [7]: inhibit the synthesis of total cholesterol and phospholipids, preferentially increasing the amount of neutral lipids [5]. Improves vision [8]. Relieve stubborn fever [8].

Experimental research in vitro and in vivo. Almost all major experimental (pharmacological)fruit research L. barbarum was carried out in China, as a rule, they were carried out for aqueous extracts or for more orless purified fractions of polysaccharides. There are no data on the pharmacokinetics of LBP, and the bioavailability of polysaccharides has not yet been studied [85]. Research has focused mainly on antioxidant and immunomodulatory properties in the context of age-related diseases, including atherosclerosis, neurodegeneration, and diabetes [22].

Antioxidant properties have been found in various studies like in vitro and in vivo. Antioxidantactivity is mainly attributed to polysaccharides (LBP) [65, 68] and flavonoids [60]. For both groups of biologically active substances, the mechanisms of action include a decrease in capacity, chelation of metal ions, and activity in absorbing radicals [60, 68]. It has been shown that betaine can also contribute to the antioxidant effect [95].

In [85], attention was focused on proteoglycans known as “polysaccharides Lycium barbarum ", whichhave shown antioxidant properties and some interesting pharmacological properties in the context of age-related diseases such as atherosclerosis and diabetes.

According to [85], the activity of polysaccharides is of particular interest, since this group of biologically active substances is characteristic of goji fruits. Polysaccharides extracted from fruits exhibited antioxidant activity in the β carotene / linoleic acid, as well as radical scavenging activity towards the superoxide anion and

reducing ability, which were similar to those of the synthetic antioxidant BHT [65]. They also strongly inhibited AAPH-induced [2,2'-azobis (2-amidinopropane) dihydrochloride] hemolysis of erythrocytes. LbGp5B Glyconoconjugate Inhibited LDL Oxidation in vitro [81].

LBP Demonstrated Protective Effect on Heat-Induced Damage in Rat Testes in vivo when administered per os and induced H_2O_2 oxidative damage in mouse testicular cells in vitro [73]. In rabbits fed 1.5% cholesterol for ten weeks, LBP gluten injection reduced triglyceride elevations, increased high density lipoprotein (HDL) cholesterol to total cholesterol ratio, and improved oxidation markers [74].

Oral administration of LBP reduced levels of low-density lipoprotein (LDL), triglycerides, and total cholesterol while increasing antioxidant enzyme activity in mice fed a high-fat diet [75]. Oral administration of LBP also had a protective effect on streptozotocin-induced oxidative stress and DNA damage in diabetic rats [63, 109]. In the same model, they markedly reduced plasma cholesterol, fasting insulin, and postprandial blood glucose. The improvement in insulin sensitivity has been associated with changes in the level of glucose transporter 4 (GLUT4) on the surface of skeletal muscle cells [121]. Hypoglycemic and hypolipidemic effects have also been observed in alloxan diabetic / hyperlipidemic rabbits [72] using an oral decoction of the fruit,

In the study of immunomodulatory properties (they attract a lot of attention, including in terms of cancer immunotherapy [85]), a number of experiments have shown that LBPs promote the proliferation of splenocytes [29, 37, 79, 81] in vitro. It was also reported about the proliferation of T-lymphocytes in vitro in mice that receivedLBP, LBPF4 or LBPF5 is injected or orally [26]. According to the results of the experiment, the LBP polysaccharide fraction caused the maturation of dendritic cells and increased their immunogenicity. LBP Activated Dentritic Cellsin vitro, amplified responses Th1 and Th2 as in vitro and in vivo [25].

Evidence has been published showing that LBPs act through increased expression of various cytokines and transcription factors. LbGp4 protein-polysaccharide complex stimulates the expression of nuclear factorkV (NF kV) andprotein activator 1 (AP-1) [79].

It was shown that LBP3 increases the expression of interleukin-2 (IL-2) and tumor necrosis factor-α (TNF-α) at the level of mRNA and protein in cultures of human peripheral blood mononuclear cells [35]. The antitumor properties that were found in experiments on mice are apparently explained by immunostimulatory activity [85]. Inhibition of the growth of S180 sarcoma tumors in mice treated orally with LBP3p, a purified fraction of LBP3, correlated with increased macrophage phagocytosis, spleen lymphocyte proliferation, CTL activity, and IL-2 mRNA expression [36]. In addition to immunostimulating effects, propapoptotic properties may also contribute to antitumor properties [85]. LBP inhibits cell proliferation with cell cycle arrest in S-phase and induces apoptosis of the human hepatoma cell linein vitro [117], and apoptosis is stimulated by an aqueous extract from the fruit of barbarian wolfberry in hepatocellular carcinoma cells [23]. Inhibition of PC3 prostate cancer cell proliferation has also been reportedin vitro. In the latest study, however, the activity was rather strangely attributed tomainly to scopoletin [71].

Recently, an aqueous extract has been shown to inhibit the growth of estrogen receptors in human breast cancer cell line MCF-7, and a change in the cellular metabolism of estradiol has been proposed as a mechanism [66]. Hematopoietic properties were also identified, which are mentioned in [85] in the context of potential use as an adjuvant in cancer therapy. In mice with radiation- or chemotherapy-induced myelosuppression, subcutaneous injections of LBP inhibited the reduction in erythrocyte and leukocyte counts. The effect may be due to the stimulation of PBMC (peripheral blood mononuclear cells) to produce the production of G-CSF (granulocyte colony stimulating factor) [40].

The neuroprotective properties of Berber Deresa fruit have been studied at the University of Hong Kong. Preventive treatment of rats with an aqueous extract from the fruitL. Barbarum protected animal cortical neurons against Aβ induced toxicityin vitro. According to the authors of the study, the main mechanism seems to include inhibition of the signaling pathway N-terminal kinase (JNK) with Aβ-triggered cJun [116]. Fruit extractL. barbarum also protected against stress caused by dithiothreitol, which indicates that neuroprotective activity is due not only to antioxidant properties [114]. The same authors observed a decrease in the activity of caspases 3 and 2, as well as inhibition of phosphorylation of double-stranded RNA-dependent protein kinase (PKR) [115].

In vivo neuroprotective effects were investigated in a glaucoma model with ocular hypertension. Rats that were watered water extract of the fruit L. barbarum showed significant reductions in retinal ganglion cell loss. During treatmentintraocular pressure did not change [20].

As you know, excessive consumption of fructose causes changes in the functioning of the central and peripheral nervous systems, which increases the vulnerability of peripheral nerves to traumatic injury. In a study [101], the electrophysiological parameters of responses of spinal cord motor neurons were experimentally evaluated during high-frequency stimulation of the distal part of the injured sciatic nerve in a model of diabetic stress under the influence of Lycium barbarum fetuses. Male albino rats were given 50% fructose water for 6 weeks to simulate diabetes. Then the left sciatic nerve was injured. One of the groups of animals after the injury continued to receive fructose for 3 weeks, the other - fructose and dry fruits of the wolfberry also for 3 weeks. As a result, in the fructose + trauma + deresis group, a relatively proportional separation of tetanic and post-tetanic potentiation and depression in the responses of ipsilateral and contralateral motoneurons was observed, which allowed the authors to suggest a modulating role for deresis fruits in the formation of short-term synaptic plasticity. Thus, dereza fruits are able to modulate the reorganization of the central nervous system, enhancing positive adaptive changes that improve functional recovery and promote selective targeted reinnervation in rats on a high fructose diet with sciatic nerve injury [101]. which allowed the authors to suggest a modulating role of wolfberry fruit in the formation of short-term synaptic plasticity. Thus, dereza fruits are able to modulate the reorganization of the central nervous system, enhancing positive adaptive changes that improve functional recovery and promote selective targeted reinnervation in rats on a high fructose diet with sciatic nerve injury [101]. which allowed the authors to suggest a modulating role of wolfberry fruit in the formation of short-term synaptic plasticity. Thus, dereza fruits are able to modulate the reorganization of the central nervous system, enhancing positive adaptive changes that improve functional recovery and promote selective targeted reinnervation in rats on a high fructose diet with sciatic nerve injury [101].

Significantly less research on fruits L. chinense. As with L. barbarum, the focus isresearchers found antioxidant properties, especially in the context of hepatoprotection (work was mainly carried out in

Seoul University, South Korea) [85]. It was shown that the properties of polar extracts absorbing free radicals against the DPPH radical correlated with the content of flavonoids [89]. CHCl extract3-MeOH showed protective activity against CCl_4-induced hepatotoxicity. The activity of the hexane-soluble fraction of this extract was attributed to zeaxanthin (Compound 4 - Fig. 1) and zeaxanthin dipalmitate (Compound 1 - Fig. 1) [55].

Zeaxanthin dipalmitate reduced liver fibrosis caused by ligation / dissection of the bile duct in rats at a dose of 25 mg / kg orally. Antifibrotic activity is, at least in part, mediated by antioxidant activity [56].

Two cerebroside (Compounds 25 and 26) were identified as active components in the EtOAc-soluble fraction after their isolation in order to study their biological activity [54]. Both compounds showed a protective effect on rat hepatocytes exposed to chloroform (CCl_4) [57] or galactosamine [58].

Hepatoprotective activity was also established for three pyrrole derivatives (Compounds 27-29), which demonstrated protective effects comparable to silybin in terms of toxicity induced by CCl_4, in rat hepatocytes [28].

Hepatoprotective action has also been demonstrated in vivo for aqueous extracts on the model CCl_4-induced liver toxicity. An anti-inflammatory effect was shown in a model of carrageenan-induced rat paw edema [70]. When analyzing the results of these studies in [85], a critical remark is made regarding the reliability of the data obtained, since a similar activity was obtained by the authors for various parts of the plant with different chemical composition. In addition, the authors of [70] failed to show clear dose-dependent effects (dose-response correlation has not been established).

The hepatoprotective effect of an aqueous extract of fruits, administered orally, was also shown in [42] in rats using a model of chloroform poisoning (CCl_4). The main mechanism, according to the authors of the study, includes antioxidant properties and a decrease in the expression of CYP2E1 [42].

According to V.S. Ibragimova (1994), in the experiment, 1% extract from the fruits together with betaine (1%) inhibited fatty degeneration of the liver of white mice, suppressed the growth of E. coli and candida white [5].

With respect to the root cortex, several compounds have shown hepatoprotective effects as well as inhibitory effects on the renin / angiotensin system, which may support traditional use in the treatment of hypertension [85].

Toxicology. Trace amounts of atropine found in fruits have no toxicological significance [85]. In this context, the assignment in some books [96, 99]Lycium barbarum cannot be considered a toxic plantreasonable [85]. The Chinese Materia Medica gives LD for water extract of goji berry$_{50}$ - 8.32 g / kg with subcutaneous administration in mice [21], which confirms the actual absence of fetal toxicity [85]. Thus, there is no risk when eating cultivated wolfberry fruits, although caution is advised when interacting with samples of unknown origin, since confusion with morphologically similar fruits of the nightshade cannot be ruled out [85]. Misidentification may also be the cause of some conflicting data regarding the alkaloids in goji berries [85].

The root bark also exhibits very low toxicity. Acute toxicity data have been reported, but at unrealistically high doses and without reference to original studies [85]: LD_{50} decoction for intraperitoneal injection is 12.8 g / kg in mice and 30 g / kg in dogs. LD_{50} when administered orally in dogs, it is 120 g / kg [46, 122]. Vomiting occurs in dogs receiving 120 g / kg orally or 30 g / kg intraperitoneally. In rabbits, drowsiness was observed at doses of 80 g / kg (oral) or 60 g / kg (injection) [122]. In addition to these data, for the root cortex (during the assessment of subacute toxicity in rats with high doses of 5 and 10 g / kg orally, for 14 days), an increase in the mass of the heart, liver and lungs was observed, an increase in the content of urea nitrogen in the blood was noted (BUN) and decreased creatinine levels, as well as increased white blood cell count. However, there were no signs of irreversible pathological damage or mortality in the rats. No changes in physical activity, food consumption and water consumption were also observed [110] (cited from [85]).

In the absence of acute toxicity, there is a danger of potential drug interactions between the fruits and bark of Dereza roots. Specifically, two reports document their possible interactions with warfarin. In a 61-year-old Chinese woman stabilized with warfarin, after drinking tea made from goji berries (for four days), an increase in the international normalized ratio (INR is a laboratory test reflecting the ratio of prothrombin time (PTT) values to the values of this indicator (PTT) of a healthy person). The values returned to normal after stopping the tea intake [59].Weak cytochrome inhibition was found in vitro CYP2C9. However, a very high dissociation constant (K_i = 3.4 mg / ml) suggests that drug interaction in vivo is influenced by other mechanisms [85].

In another described case, an 80-year-old Chinese woman receiving a stable dose of warfarin also experienced two episodes of increased INR after drinking an herbal tea containing L. Barbarum [62]. The report does not indicate the morphological group of raw materials (fruits or roots), which consisted of tea [85].

Clinical researches. Most of the research has come from China and has focused on anti-agingproblems. According to [85], most of the studies were small and insufficiently controlled. In most publications, it was unclear what kind of fruit was used in the study -L. Barbarum or L. Chinense [85].

In a representative study with 42 elderly participants, ingestion of 50 mg of dereza fruit extract twice daily for two months reduced dizziness, fatigue, chest congestion, sleep problems and anorexia [67] (cited in [17, 85]). The results have not been statistically evaluated [85].

In another study, as a result of taking 50 g of Goji berries per day in 25 elderly people for 10 days, hemoglobin and SOD (superoxide dismutase) increased, and the level of lipids in the blood significantly decreased [64] (cited from [17, 85]).

According to [85], a double-blind study conducted outside of China examined the overall effects of GoChi ™ (commercial goji juice) in young, healthy adults. Various parameters were assessed using a questionnaire. Blood pressure and body weight were monitored. Research has shown that consumption of GoChi ™ for 14 days increased subjective feelings of general wellness and improved neurological and gastrointestinal function [11]. However, [85] notes the small size of the study (N = 34) and the subjective assessment of

most of the parameters. In a subsequent double-blind study (N = 30), the authors demonstrated the effect of GoChi ™ on serum antioxidant markers in healthy Chinese adults aged 55–72 years. After 30 days, there was a significant increase in SOD and GSH-Px by 8.4 and 9.9%, respectively, with a concomitant decrease in MDA (malondialdehyde) by 8.7% [12]. These data are consistent with previous observations [17] and may indicate possible beneficial effects in oxidative stress, age-related conditions and age-associated diseases.

O. Potterat (2010) considers the most notable clinical study of goji berries to be the work in which the efficacy of wolfberry fruit as an adjuvant in cancer therapy was studied [85]. A study [18] was conducted in China on 75 patients with various common forms of cancer. Combination of IL-2 therapy with LAK (lymphokine-activated killer) and polysaccharidesL. barbarum had significantly higher response rates and a higher remission rate than oneonly IL-2 / LAK therapy [18] (cited from [85]). Commenting on the results of the study, O. Potterat (2010) notes the insufficient amount of information about the structure of the study and the products from wolfberry fruits included in the diet to fully assess the relevance of the data [85].

The clinical effects of goji berries are usually largely attributed to polysaccharides - LBP. Although to date, there is still no data on their bioavailability and pharmacokinetic behavior. In this context, O. Potterat (2010) notes that in addition to the direct effect of LBP on pharmacological targets, a number of researchers have proposed and described indirect mechanisms by which LBP can act in the intestine as bioactive fibers or prebiotics [12, 41] (cited from [85]).

The fraction of carotenoids from Dereza fruit has been investigated in the context of age-related eye diseases. There is no data showing the effect of taking goji berries themselves, but there is evidence to support a protective role for zeaxanthin. In particular, a decrease in the incidence of cataracts and macular degeneration has been reliably associated with the consumption of leafy green vegetables, which are a rich source of zeaxanthin and lutein [16, 17, 85, 100]. A study in twelve volunteers who received free or esterified carotenoids from goji berries (L. barbarum) suspended in yoghurt confirmed the bioavailability of zeaxanthin. The study also showedsignificantly higher absorption of zeaxanthin diplamitate (the dominant carotenoid in wolfberry fruit) compared to the non-esterified form [15].

APPLICATION

In medical practice, the fruits of both types of dereza are used for hypertension [5, 6, 8], diabetes mellitus [5, 8], cachexia [5], pulmonary tuberculosis [5, 6], pneumonia [5, 6], impotence [5, 6, 8], neurasthenia, general weakness, anemia, impaired vision [5, 6]. Root and root bark - as an antipyretic and thirst-quenching remedy for febrile diseases, edema of neurotic origin [5, 6].

Use in traditional medicine

Both are - L. Barbarum and L. Chinense - have been used in traditional Chinese medicine (TCM) for more than 2000 years - Early records date back to the Tang Dynasty (1000–1400 AD) [17]. The Chinese name Gouqizi refers to fruits [1, 2, 8], Digupi - to dried root bark [8], which are historically used in TCM [1, 2, 8, 85]. Several old traditional medicinal reference books also mention the medicinal use of leaves and seeds [1, 2, 102].

Traditionally in China, berries are eaten raw, made from them juice, wine or tea, processed into tinctures, recently - into powders, extracts and tablets [1, 2, 13, 123]. Besides China, goji berries are part of the medical tradition in other Asian countries, including Vietnam [14], Korea, and Japan [85].

Fruits in TCM. According to the classical Chinese pharmacological treatise "Shen-nong ben cao jing" (CanonOf the sacred farmer about roots and herbs) to products with exceptional healing properties, the regular intake of which gives lightness to the body, helps to resist aging, and prolongs the years of life [1, 2].

Goji berries are used in traditional Chinese medicine as a mild Yin tonic that enriches Yin in the liver, kidneys and moisturizes Yin in the lungs [13, 123, 24, 93]. In general, according to the TCM canons, fruits belong to the class of drugs that replenish Yin [3, 4] (mainly Yin of the Liver and Kidneys [1, 2]), which can be especially important for women, while the root bark is referred to as the category of drugs that help to cool the heat of the type of deficiency, that is, the heat arising from the lack of Yin [1, 2].

The taste of the fruit is sweet [1–4], spicy [7], neutral properties [1–4, 7] or slightly cool [1, 2]. Correlate with the channels of the Liver, Kidney [1–4, 7], Lungs [1, 2, 7].

The main function of dereza fruits is considered to be the replenishment of vital energy [8], the quintessence of Jing of the kidneys, nourishment of the liver to enlighten the eyes, moisturizing the lungs to stop coughing [3, 4], reducing the fever of the Blood and Lungs, and easing persistent fever [8]. In other words, the fruit medicine is used to “saturate the Yin of the Liver and Kidneys, saturate the Blood, clear the eyes” [7]. Typical signs of Liver Qi deficiency are impotence, back pain, stiffness and tinnitus, and possibly dullness [7].

In general, the indications for the use of Dereza fruits stem from the nutritional effect of Yin. They include blurred vision and decreased visual acuity, infertility, abdominal pain, dry cough, fatigue and headache [24, 93, 123]. The main indications in TCM are pain in the lower back [3, 4, 7] and knee joints [7], wet dreams [3, 4], dry cough [7], dizziness [3, 4, 7], spermatorrhea [7], decreased visual acuity [3, 4, 7, 8], blurred vision [3, 4], diabetes mellitus [1-4]. In particular, the fruits are considered particularly effective in diabetes arising from a lack of Liver and Kidney Qi [3,4], a lack of Kidney Yin (frequent and profuse urination with "thick" urine, dry mouth, dizziness, blurred vision, redness of the cheeks, night sweats, sensation of heat in the feet and palms, red tongue with a slight coating) [1, 2].

Goji berries are also highly regarded in Chinese folk medicine as a way to increase longevity.
[94] and against premature gray hair [24, 85]. Medicinal drinks and dietary soups based on goji berries are in some way at the interface between food and medicine and are still widely used in everyday practice in China [85].

In a modern BMT clinic, including in Western countries, fruits are prescribed for afternoon fever, nighttime

sweats in tuberculosis patients, coughing, hemoptysis, nosebleeds caused by heat of the lungs, as well as in diabetes mellitus caused by internal heat [8]. They are also prescribed for asthenia, lack of vital energy, accompanied by pain in the lower back and knees, dizziness, tinnitus, and impaired vision [8].

Root bark. Traditionally used as a coolant to "clear heat" and reduce fever fromfor yin deficiency [85]. In general, the bark of the dereza root belongs to the category of drugs that help to cool the heat of the deficiency type, that is, the heat arising from the lack of Yin [1, 2].

The taste is sweet, cold properties, correlates with the channels of the Lungs, Liver, Kidneys. Functions - cooling the heat of the negative type (Yin deficiency), cooling the heat of the Lungs, cooling the Blood [1, 2].

The drug, in particular, is prescribed for night sweats, "bone evaporation sensation" [24] and chronic low-grade fever. A decoction of the root bark is effective for the treatment of cough and is recommended against hemoptysis and hematuria [24], and is indicated for the treatment of hypertension and diabetes mellitus [46–48, 94, 122, 123]. In traditional sources, there is a clarification that the decoction is effective in diabetes with the properties of heat in the Lungs, heat in the Stomach or a lack of Yin of the Kidneys [1, 2].

It is popularly believed that if young leaves, flowers, root bark and fruits are consumed instead of tea all year round, then one can acquire excellent health and a blooming appearance (young leaves in China are also eaten) [1, 2, 5, 6, 85].

Mode of application. Leaves and crushed root are infused in water or boiled, fruits are boiled in water orinsist on wine [5, 6]. In the ancient tradition (Li Shi-chen) it was recommended to soak bright and shiny fresh berries in wine overnight, and in the morning to crush them to a pasty state [1, 2].

Currently, in addition to the classic version of natural dried fruits, standardized dry water-soluble fruit extracts are used. Both types of berries are very popular ingredients in Chinese cuisine. They are consumed in soups, as porridge (including medicinal one) with rice, and are added to numerous meat and vegetable dishes [85].

Wine is prepared as follows. 7.2 kg of fresh fruits are crushed, placed in a bag and immersed in 36 liters of alcohol, which is in a tightly sealed container in a cool place. Fruit soaking is carried out for 3 weeks [1, 2, 5, 6].

In ancient times, it was believed that "taking medicine [wolfberry] collected from thorny bushes will not bring any benefit" [2].

Dosage. In classical TCM, fruits are used in decoctions [3] at a dose (in terms of dry berries) 10-15 g [3, 4], according to other sources - 6-18 g [7], 2-4 g [5, 6], 6-12 g [8] or 5–12 g [13, 123]. A single dose of leaves (in a decoction or infusion) and root bark - 5–20 g [5, 6], according to other sources, root bark is used at a dose of 9–15 g [8] or 6–15 g [1, 2, 24 , 85].

QUOTES

"Dereza was very much appreciated by the followers of Taoism, who were keen on searching for the means of gaining immortality." “Those who take the pills of immortality value the root and fruit of dereza very much, calling them“ a cane in the hands of immortal saints ”[2].

"Long-term use helps to strengthen tendons and bones, gives lightness to the body, helps to resist aging." "It is used for the penetration of pathogenic Qi into the five tsang organs in diabetes due to fever in the Stomach, wandering pains throughout the body due to the perception of damp wind" (Shennong ben cao jing - The Sacred Farmer's Canon of Roots and Herbs). “Long-term use increases the body's resistance to cold and summer heat. In winter, the roots are harvested, in the spring and summer - the leaves, in the fall - the stems and fruits ”(Ming and Be Lu - added to the Shennong ben cao jing records of famous doctors, VI c) [Quot. by: 2].

CONTRAINDICATIONS

There are no signs of toxicity of wolfberry, but two reported cases of possible interactions with warfarin indicate a potential risk of drug interactions [85].

In TCM, the use of drugs from fruits is contraindicated in cases of Spleen Qi deficiency with loose stools [1–4], excessive fever and Spleen insufficiency in combination with excess moisture [7], and excess heat when external pathogenic Qi is perceived [1, 2]. Root bark in TCM is contraindicated in case of cold fever with wind-cold properties and in case of lack of Spleen qi with loose stools [1, 2].

ADVERSE REACTIONS

Despite a very long history of traditional use as a food or medicinal agent in herbal medicine, there are no reports of side effects caused by goji berries [85].

Only a few cases of allergic reactions have been reported, including urticaria or papular rash [13]. Chinese medicinal reference books recommend caution and avoidance of fruit for pregnant women, as well as for patients suffering from diarrhea, fever, arthritis and severe inflammatory conditions [24, 94, 104].

For root bark in high doses (50 g), side effects (dizziness, palpitations, nausea, vomiting and premature contractions) were reported, but only if the doses significantly exceeded the therapeutically recommended dose range of 5-15 g [13].

In modern BMT clinics, people with Yang deficiency and / or a weak Stomach or Spleen are advised to use cooling agents (cold Yin agents), in particular, Dereza preparations, very limited [93]. The root bark is also contraindicated in patients with "external wind-cold" or "wind-warm", and people with "true cold, but false heat" should be used with caution [24].

CONCLUSIONS

1. An attempt has been made to objectify the data of traditional oriental medicine on the medicinal properties of Dereza fruits with positions of modern scientific concepts (based on the results of phytochemical, toxicological, pharmacological and clinical studies published in the open press).

2. The carried out information and analytical research made it possible to establish that Goji berries have an ancient a tradition of medical and food use in East Asian countries.

3. Analysis of the results of phytochemical studies made it possible to establish that the main groups biologically active substances responsible for the pharmacotherapeutic action can be considered polysaccharides, carotenoids, flavonoids, vitamins.

4. In experimental research in vitro and in vivo revealed the presence of antioxidant and immunomodulatory properties (especially in the context of age-related diseases, including atherosclerosis, neurodegeneration and diabetes mellitus), as well as hypoglycemic, hypolipidemic, antihypertensive and neuroprotective effects.

5. The results of clinical studies confirm some of the actions established in experiments on animals, however, most experts agree that for reliable conclusions, additional modern studies are required on standardized extracts of wolfberry fruit.

6. The fruits are non-toxic raw materials, but there are reports of drug interactions with warfarin, and also contraindications for use in accordance with the theoretical foundations of traditional Chinese medicine.

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Author's address

D.Pharm.Sci. Kiseleva T.L., professor, leading researcher at the Federal Research Center for Nutrition, Biotechnology and Food Safety.

KiselevaTL@yandex.ru

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