MORUS SPECIES THROUGH CENTURIES IN PHARMACY AND AS FOOD

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The use of various *Morus* species in pharmacy, as well as in traditional medicine is well known worldwide. In Serbia there is a proverb "Health comes in through the mouth", i.e. through food. So, the aim of the present review paper is the construction of a mosaic from many known uses of *Morus* species which have been in use through centuries and in different cultures as a remedy, but also as an important nutrient.

Keywords: mulberry, pharmacy, food

Introduction

Coloured fruits are good sources of phenolic compounds including anthocyanins, flavonoids and carotenoids [1-4]. Mulberry fruits are rich in phenols and have a unique sour and refreshing taste [5]. They are used as a traditional medicine in curing dental diseases, diabetes, hypertension, arthritis and anemia [6]. With the aim of finding new sources of natural antioxidants, fruits, vegetables and other plants with the antioxidant activity were investigated [7-12].

Genus *Morus* belongs to Moraceae family, and the names of over 150 species have been published. Different sources usually cite different selections of accepted names. Only 10-16 are generally cited as being accepted by the vast majority of botanical authorities [13]. The best known mulberry species are white mulberry (*Morus alba* L.), red mulberry (*Morus rubra* L.) and black mulberry (*Morus nigra* L.) (Figure 1).

(b)

(c)

(a)

Figure 1. a) White mulberry (*Morus alba* L.) b) Red mulberry (*Morus rubra* L.) c) Black mulberry (*Morus nigra* L.)

Table 1 gives the scientific mulberry classification.

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Table 1. The scientific mulberry classification

Kingdom	<i>Plantae</i>
Subkingdom	<i>Tracheobionta</i>
Division	<i>Magnoliophyta</i>
Class	<i>Magnoliopsida</i>
Subclass	<i>Hamamelididae</i>
Order	<i>Urticales</i>
Family	<i>Moraceae</i>
Genus	<i>Morus</i> L.
Species	<i>Morus alba</i> L., <i>Morus rubra</i> L., <i>Morus nigra</i> L., etc.

Morus alba L. is a native to India, China and Japan. It became naturalized in Europe a few centuries ago. The tree was introduced to America for silkworm cultivation in early colonial times and it was naturalized and hybridized with the local red mulberry. White mulberry has a long history of medicinal use in Chinese medicine [14]. Red mulberry or American mulberry originates from the eastern part of the USA and black mulberry came from Asia. Red mulberry fruits arrived in Europe before Roman times. Black mulberry is distributed in Asia, Europe, North and South America and Africa [1, 6].

White mulberry, and to a lesser extent red mulberry, is resistant to drought, pollution and poor land. Black mulberry is more sensitive, particularly in cold climate areas and wet summers. White mulberry is the most resistant among the mentioned three mulberry species, although resistance depends on the clone. Some of them can be harmed at -3.8 °C, while some of them are durable even to -31.6 °C. Red mulberry is durable below 0 °C, while black mulberry is very sensitive to low temperatures and the sensitivity varies depending on the clone [3, 4].

All three mulberry trees are deciduous trees of different sizes [15, 16]. White mulberry tree can be 24 meters tall and of different shapes (relaxed or pyramidal). On rich land, red mulberry can be 21 meters tall, while black mulberry is the shortest and can be 9 meters tall. The durability of mulberry depends on the species. Red mulberry very rarely reaches the age of 75 years, while black mulberry can give fruits for centuries.

White mulberry was named after the colour of its buds, not the colour of its fruits [16].

There are excellent review papers on the history and active pharmacokinetic principles of mulberry [17-21]. The aim of this paper is to give a brief summary of its use in pharmacy and as food in different countries and times.

Antimicrobial activity of mulberry

Antimicrobial activities of compounds isolated from different parts of white and black mulberry are presented in Table 2.

Table 2. Antimicrobial activity of compounds isolated from different parts of mulberry

Sample	Compound	Part of the plant	Activity	MIC (µg/ml)	Literature
<i>Morus alba</i> L.	Kuwanon G	Root	<i>Streptococcus mutans</i>	8	[22]
			<i>Streptococcus sanguis</i>	8	
			<i>Streptococcus sobrinus</i>	8	
			<i>Porphyromonas gingivalis</i>	8	
			<i>Staphylococcus aureus</i>	125	
			<i>Actinobacillus</i>	1000	
			<i>actinomycetemcomitans</i>	1000	
			<i>Candida albicans</i>	>1000	
			<i>Lactobacillus acidophilus</i>	>1000	
<i>Morus alba</i> L.	Mulberrofuran G	Root	<i>Lactobacillus casei</i>	>1000	[23]
			<i>Candida albicans</i>	>60	
			<i>Saccharomyces cerevisiae</i>	>60	
			<i>Escherichia coli</i>	30	
			<i>Salmonella typhimurium</i>	7.5	
			<i>Staphylococcus epidermis</i>	6.25	
			<i>Staphylococcus aureus</i>	5	
			<i>Candida albicans</i>	>60	
			<i>Saccharomyces cerevisiae</i>	>60	
<i>Morus alba</i> L.	Albanol B	Root	<i>Escherichia coli</i>	20	[23]
			<i>Salmonella typhimurium</i>	5	
			<i>Staphylococcus epidermis</i>	5	
			<i>Staphylococcus aureus</i>	5	
			<i>Micrococcus luteus</i>	1.56	
	Chalcomoracin	Leaves	<i>Bacillus subtilis</i>	3.13	[23]
			<i>Escherichia coli</i>	>100	
			<i>Klebsiella pneumoniae</i>	>100	
			<i>Pseudomonas aeruginosa</i>	>100	
			<i>Staphylococcus aureus</i>	125	
			<i>Bacillus subtilis</i>	125	
<i>Morus nigra</i> L.	Extract	Stem	<i>Micrococcus flavus</i>	500	[24]
			<i>Streptococcus faecalis</i>	500	
			<i>Salmonella abony</i>	250	
			<i>Pseudomonas aeruginosa</i>	500	

Morus alba L., a good source of ascorbic acid, over 90%) is present in the reduced form. It also contains carotene, vitamin B1, folic acid, folinic acid, isoquercetin, quercetin, tannins, flavonoids and saponins [26].

Oxyresveratrol, arylbenzofuran moracin M2, cyclo-morusin, morusin, kuwanon C5, kuwanon C6, betulinic acid, α -amyryn acetate and β sitosterol-3-O- β -D-glucoside were isolated from stems of black mulberry from Botswana [24]. Oxyresveratrol and arylbenzofuran moracin M2 showed antibactericidal activity against *Staphylococcus aureus* (MBC=125 and 62.5 µg/mL, respectively); arylbenzofuran moracin M2 also showed bactericidal activity against *Streptococcus faecalis* (MBC=500 and 250 µg/ml, respectively) [24]. The antibacterial test was conducted on different microorganisms such as *Staphylococcus mutants* ATCC 25175, known as oral pathogen, *Streptococcus sanguis* ATCC 35105, *Streptococcus sobrinus* ATCC 27351, *Staphylococcus aureus* ATCC 10231, *Candida albicans* ATCC 10231, *Actinobacillus actinomycetemcomitans* ATCC 33384, *Lactobacillus acidophilus* ATCC 4356, *Lactoba-*

cillus casei ATCC 4646 and *Porphyromonas gingivalis* W50.

The antibacterial activity of kuwanon G was investigated by the comparison of MIC with some commercially available appliance in use against caries. MIC of kuwanon G against *Streptococcus* was 8 µg/ml, which is less comparing to 32 µg/ml of sanguinarine, 125 µg/ml of carvacrol and 500 µg/ml of thymol and eucalyptol which are commercial agents with antibacterial activity. This shows that kuwanon G has a stronger antibacterial activity comparing to commercial agents. Antibacterial activity of kuwanon can be compared with antibiotics such as vancomycin and chlorhexidine which possess harmful effects (change of teeth colour, vomiting, diarrhoea, low immunity) [22].

Mulberry as a medicine

The main use of mulberry globally is as feed for the silkworm, but depending on the location it is very often appreciated for its fruit which can be consumed fresh, as juice or jam, as a delicious vegetable (young leaves and petioles) and for its medical properties (leaf tea) [26].

Mulberry fruit can be used for various medical purposes because it feeds the skin and blood and as a remedy in case of liver and kidney diseases. Also, it can be used in curing urinary infections, tinnitus, dizziness, constipation in the elderly, anemia, sour throat, fever and depression [27]. The juice obtained from mulberry fruit has delicious taste and smell. Wine can be obtained from mulberry fruit; it is sweet and sour, and is used for purification of blood. Many believe that one glass of this wine per day improves health by cleaning the organism from impurities and enables the ejection of fecal residues in the intestines. Besides, mulberry fruits are rich in anthocyanins, the primary source of antioxidant activities [28-34]. Active biomolecules of different mulberry species are kuwanon I, kuwanon I hexamethyl ether, kuwanon I octamethyl ether, 2'-hydroxy-2,4,4'-trimethoxychalcon and 2'-hydroxy-3'-prenyl-2,4,4'-trimethoxychalcone III, mulberrofuran T and kuwanon E, morusin, mulberrofuran D, G, K, kuwanon H, mulberroside A, *cis*-mulberroside A, oxyresveratrol, isoquercetin, moracin E, F, G and kuwanon D, E, F, deoxynojirimycin-1 etc. from fruits, leaves, roots and barks of white mulberry [35]. These molecules possess healing properties like adstringent, anti-HIV, anti-inflammatory, the purgative effect etc. [30-33]. Rubraflavones A, B, C, D, which act as laxatives, purgatives, against urinary infections and weakness, were isolated from the root of red mulberry. Deoxynojirimycin, which can be used in the treatment of diabetes, HIV, cancer and high blood pressure, was isolated from the root, leaves and fruit of the black mulberry. Also, it can be used as a purgative [23, 35-39].

Black, white and red mulberry from the area of south-east Serbia have a high content of natural phenolic compounds. Red and black mulberry have a high content of anthocyanins and showed a significant antioxidant activity [40-43].

The researches of the mineral composition showed that mulberry is a rich source of macro and microelements, especially iron [44].

Mulberry in different cultures and through centuries

Today mulberry is mainly in use as animal food. Besides leaves, mulberry possesses sweet fruit of good taste and smell with nutritious elements which are of vital importance for the human metabolism. Mulberry fruit can be used for the preparation of jam, juice, jelly, cellulose, fruit sauces, and cakes. On the Chinese market, mulberry can be consumed in the form of "sangshengao" paste. This paste can be mixed with hot water in order to make tea which improves the functioning of liver and kidneys [45]. Mulberry fruit can be dried and stored as a powder. About 10 g of dried fruit can give 100 mg of anthocyanins [46]. Because of the presence of resveratrol, mulberry fruit has an antimutagen effect and can inhibit the mutation of healthy and normal cells into cancer cells. It is believed that it can inhibit heart disease, cancer and other diseases connected with chronic inflammation. Fruit as a powder possesses the anti-aging effect. Also, it keeps a normal level of cholesterol and carbohydrates in the human body [38].

In middle ages it was used as a part of the mixture for anesthesia. Hugh of Lucca, the leading surgeon of his period (the 13th century), prepared the sleeping sponge consisting of opium, the juice of the unripe mulberry, hyoscyamus, the juice of hemlock, the juice of the leaves of mandragora, the juice of the wood-ivy, the juice of the forest mulberry, the seeds of lettuce, the seeds of the dock, and the water hemlock [47]. Also, in the middle ages (11th-14th centuries), pharmacists of the Jewish community of medieval Cairo (according to the lists of *materia medica* found in Taylor-Schechter Genizah collection, Cambridge) used drugs of the plant origin. Among twenty-eight plants, mulberry was also mentioned [48].

Overripe fruit and sour can be converted into wine with sweet and sour taste. It can be used for the improvement of general vitality of the organism. In Azerbaijan, Georgia and Armenia it is a very popular liqueur "tut araghi" which is consumed to increase potency. It is one of Azerbaijan forms of vodka. It is believed that a small dose of this drink protects the stomach and heart from diseases. In Greece, mulberry fruit is used for the production of traditional, aromatic drink "mouro distillate". In Europe, it is popular for ladies to consume the wine made from mulberry fruit. Because mulberry fruit is rich in anthocyanins, it deserves to be exploited for the production of natural colours which are used in the food industry. Specifically, mulberry fruit contains cyanin which is red pigment and gives the red to purple colour to fruits. The main found anthocyanins are cyanidin-3-glucoside and cyanidin-3-rutinoside. These pigments can be used as dietary modulators of the mechanism in case of various diseases and as natural coloured food because there is a need for natural colorants in the food industry [39]. Mulberry fruit can be used as ruminant animal feed [45]

and in the pharmaceutical industry [49]. The only use of mulberry in modern medicine is for the syrup preparation, added as a natural colour to drugs [46].

Conclusions

Mulberry is a widespread plant species, very useful in pharmacy and as food. Its health properties have been known from ancient times in old, traditional medicine of India, China, Middle East, etc. The healing properties of mulberry range from depression to the obesity treatment. As fresh food, it gives a pleasant taste and smell, and as processed it serves as a sweet or alcoholic beverage on numerous occasions. In modern medicine, its use is predominantly limited as an additive in syrups and as natural colours.

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Izvod

MORUS VRSTA KROZ VEKOVE U FARMACIJI I KAO HRANA

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Upotreba različitih vrsta *Morus* u farmaciji kao i u tradicionalnoj medicini je dobro poznata širom sveta. U Srbiji postoji izreka koja kaže: „Zdravlje na usta ulazi“. Zato je cilj ovog rada bio da da pregled upotreba vrsta *Morus* koje se primenjuju kroz vekove u različitim kulturama, kao lek, ali i kao važan deo ishrane.

Ključne reči: dud, farmacija, hrana