Mulberry

Subjects: Plant Sciences

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Mulberry has acquired a special importance due to its phytochemical composition and its beneficial effects on human health, including antioxidant, anticancer, antidiabetic and immunomodulatory effects. Botanical parts of *Morus* sp. (fruits, leaves, twigs, roots) are considered rich source of nutrients and secondary metabolites. Various mulberry-based foods have been developed and marketed around the world.

Morus sp. anthocyanins flavonols chlorogenic acid morusin

health benefits

1. Introduction

Morus tree is considered a medicinal plant. All of its botanical parts (fruits, leaves, twigs, root bark) have their own special effects on the human body, which is why they are used in traditional Chinese and Indian medicine [1][2][3].

2. Mulberry Fruits

There are multiple *Morus* sp. fruits (about 2 to 3 cm long); they form together and are arranged longitudinally around the central axis, similar to blackberries, and are low in calories, but rich in nutrients and antioxidants, so they can ensure good overall health ^[4]. The fruits contain a high-water content (over 70%), and the pH values differ between species: *M. alba* presents the highest value of pH (5.6), while the *M. rubra* and *M. nigra* have values of 4.04 and 3.52, respectively ^[5]. Based on values of pH, total soluble solid and total dry weight, the *M. alba* could be recommended for processing, while *M nigra* may be recommended for fresh fruit production ^{[5][6]}.

The taste is better in the case of black fruits, which is due to the lower pH value compared to white fruits, which are sometimes characterized as tasteless. All these own connections, together with the nutritional and medicinal ones, make the black mulberry fruits increasingly sought after and studied ^{[2][5][3][7][8][9][10][11]}.

The mineral content of mulberry fruits depends on the species, fruit maturity and composition of soil and environmental conditions (light, humidity, temperature, altitude) ^{[5][12][13][14]}. In the study of Ercisli & Orhan, 2007 ^[5], ten elements were determined from mulberry fruits collected from Turkey, where potassium was predominant.

Iron, an essential mineral and very rare in berry fruits, has a high value of 4.2 mg/100 g in *M. alba* and *M. nigra*. In another study ^[12] of the macroelements, N, K and P are found in large levels, while sodium is present in a very low concentration (0.01 mg) in *M. alba* and *M. nigra* grown in Spain. The levels of iron varied between 28.20 to 46.74 mg/kg and 23.92 to 37.09 mg/kg in *M. alba* and *M. nigra*, respectively, demonstrating good sources of non-heme

iron. In the black mulberry, grown in Western Serbia at different altitudes, the highest amount of minerals was determined for phosphorus and potassium, with a significant difference depending on altitude. Additionally, the authors showed that black mulberries are a good source of iron, with the highest content (1.95 mg/100 g) found at 187 m altitude ^[13]. The form of iron in foods is ferric iron (Fe³⁺), which is less bioavailable than ferrous iron (Fe²⁺). *In vivo*, the increase in iron bioavailability was attributed to ascorbic acid's chelating and reducing properties ^[15]. The high content of vitamin C and iron from mulberry resulted in the better bioavailability of iron and can be used to treat anemia ^[16].

In the mulberries fruits grown in Xinjiang region, China, potassium was the dominant macronutrient, followed by calcium and magnesium. Due to the high Fe content of Russian mulberry and black mulberry from China (11.4–11.9 mg/100 g fw), they can be used as dietary supplements to treat the iron deficiency, anemia ^[16].

In terms of the fatty acids profile of mulberry fruits, linoleic acid is dominant, followed by palmitic acid and oleic acid, the latter being detected only in *M. alba* and *M. nigra* [5][6][17]. Additionally, the high level of linoleic acid (52.3%) was found in white mulberry cultivated from Xinjiang region, China [16].

Regarding protein content, the mulberry fruits grown in southeastern Spain are a good source of protein; *M. alba* had a higher protein content than *M. nigra* ^[12]. In the mulberries cultivated in China, the ratio between essential amino acids (EAA) and total amino acid (TAA) was 44%, 42% and 29% for Russian, white and black mulberries, respectively. Foods with EAA/TAA ratio 40% are an ideal protein source, suggesting that the Russian and white mulberries cultivated in China could be used as an important quality protein source ^[16].

Ascorbic acid (vitamin C), a powerful water-soluble antioxidant compound, was quantified with the reflectometer in the mulberry fruits (n = 30); the highest value was recorded in *M. alba* (22.4 mg/100 mL), followed by *M. nigra* and *M. rubra* with 21.8 and 19.4 mg/100 mL, respectively ^[5]. Black mulberries had the highest content in ascorbic acid (48.4 mg/100 g fw), compared with Russian and white mulberry fruits (5.64 mg/100 g fw and 6.01 mg/100 g fw, respectively) grown in China ^[16].

Figura 1 summarizes the nutrients in mulberry fruits with huge importance in human metabolism.



Figura 1. The nutrients components of mulberry fruits.

Nguyen et al., 2008, mentioned that unripe mulberry, i.e., the green parts of fruits, contain a white sap that may be toxic, stimulating, or mildly hallucinogenic ^[3].

3. Morus Leaves

The leaves of mulberry are just as valuable as the fruits, not only because they are the only known source of food for the development of silkworms (*Bombyx mori*), but also because they contain, in addition to bioactive compounds, vitamins (C, B_1 , D), organic acids, minerals and proteins [18][7][19][20].

The proximate compositions of three different varieties of mulberry leaves were investigated by Iqubal, 2012 ^[21]. The high ash content was found in *M. rubra*, followed by *M. nigra* and *M. alba*, indicates the presence of considerable amounts of inorganic nutrients in leaves. Among the three varieties of mulberry, *M. alba* had the highest lipid content, the *M. rubra* had the highest protein level, while *M. nigra* contained high amounts of fiber. Based on their chemical composition, mulberry leaves can present dietary sources with promising nutritional values ^[21].

The leaves of *M. alba* and *M. nigra* possess a high iron content (119.3–241.8 mg/kg), while the other minerals are found in low concentrations. Among the macronutrients, Ca was found to be predominant, followed by N, K and Mg [6][12].

The protein content in mulberry leaves varied between mulberry species grown in Spain. The leaves of *M. alba* had a higher protein content (ranging from 14.1 ± 0.4 to 19.4 ± 0.7 % dw) than the leaves of *M. nigra* (from 13.4 ± 0.3 to 18.7 ± 0.7 % dw) ^[22].

Mulberry foliage is especially used to feed silkworms, but also other animals such as cattle, goats, and pigs ^{[6][23]} ^[24]. New studies showed that *M. nigra* leaves can be introduced into pig feed in controlled concentrations as an alternative source of protein, without adversely affecting the animals. Mulberry leaves, reporting beneficial effects on the quality of the meat and the chemical composition of the muscles, the growth and finishing performance of their carcass, reduce the thickness of back fat (longissimus dorsi muscle) and increase the fat deposition in the muscles, crude protein levels and amino acids in muscle tissue ^{[23][24]}.

4. Mulberry Twig and Root Bark

Mulberry twigs contains arabinosis, glucose, fructose, maltose, stachyose, tannin, and are also used in medicine, with a series of beneficial effects on serious diseases that affect the human body ^{[25][26]}. So far, no data are available on the content of minerals, carbohydrates, lipids, or root bark proteins, but bioactive compounds were identified.

5. Applications of Mulberry in the Food Industry

Epidemiological studies suggest the role of oxidative stress in the generation and propagation of many chronic diseases. Therefore, to counteract the unwanted effects of oxidative stress exogenous antioxidants in the form of dietary supplements or even functional foods are necessary for the human body ^[21].

Black mulberry fruits are considered functional foods that, when ripe, have a black–purple color and can be eaten fresh or dehydrated ^{[27][28][29]}. Baked mulberries are very perishable fruits, mainly due to their smooth texture, high softening and breathing rate, and susceptibility to fungal attacks. After harvesting, their aroma and appearance change, decomposition processes increase, and synthesis processes are reduced in intensity, which is why an optimal method of preservation is recommended ^{[28][30]}. In order to satisfy the requirements of consumers by ensuring that products are both healthy and delicious, and since mulberries are famous all over the world, they have started to be processed in different forms, so that they can be stored and consumed in the long term ^{[28][31]}. Due to the anthocyanin pigments responsible for their dark color, mulberry fruits are also used as color or flavor additives in the food industry for the production of healthy foods without synthetic food additives ^{[27][32]}.

In recent years, the *Morus* plant species began to occupy an important position in the food industry, due to its health benefits. Recently, various mulberry-based foods were developed and marketed in Asian regions ^[22]. As a

food, in addition to being consumed fresh, but also dried, mulberry is suitable for the preparation of several foods, such as juices, syrups, wine, vinegar, brandy, jellies, marmalades or jams ^{[7][23]}.

Mulberry fruits can be eaten ripe or can be found in the market in various forms as nutritional supplements, as a tonic and sedative. The only official medicinal product in the British Pharmacopoeia is *Siropus mori*, used mainly as an adjunct to its slightly laxative and expectorant qualities ^{[33][34][35]}.

The water-soluble anthocyanin pigments responsible for the color of mulberry fruits are also used as color or flavoring additives in the food industry, a practice increasingly used to create foods that contain natural additives [27][32].

Taking into account the requirements of consumers, the nutritional value and bioactive compounds that provide a number of beneficial effects on the human body, the mulberry plant is becoming increasingly studied or even exploited for the production of food or food supplements. It is also used as a main ingredient in the production of foods, such as jams ^[36], lollipops and jellies ^[37], wines ^{[38][39]}, syrups ^[40] and other functional beverages and foods ^{[41][42][43][44][45][46]} (**Table 1**).

Product Foodstuff	Major Findings	Reference
Black mulberry food colorants	Three formulations of solid natural colorants based on black mulberry anthocyanins (cyanidin-3-O-glucoside and cyanidin-O-rhamnoside), obtained through the spray-drying technique, were developed. These natural additives have a good stability in time and a variation of anthocyanin content and color parameters during the 12 weeks of storage, at room and refrigerated temperatures.	[<u>32</u>]
Mulberry gummy candies	Gummy candies obtained from 5, 7.5 and 10 g of mulberry molasses/100 g gelatin illustrate the potential for using molasses in a healthier development of confectionery products. These candies contain natural sugars, thus replacing sugar syrup or artificial sweeteners.	[<u>37</u>]
Mulberry leaf powder drink	The effect on adults of consuming of biscuits with a beverage of powdered mulberry leaves in the afternoon on postprandial glucose levels at dinner was a significant reduction in postprandial increases in glucose.	[<u>42]</u>
Mulberry leaf tea	The quercetin 3-O-malonylglucoside and kaempferol 3-O-malonylglucoside found in white mulberry leaves can be used as ingredients for a functional food to improve the health benefits, such as controlling blood glucose, preventing aging-related diseases and regulating glycolipid metabolic abnormalities.	[<u>43][47]</u>
Black mulberry dietary syrup	Administered in different concentrations in the diet of fish, the syrup, increased activities of serum lysozyme, myeloperoxidase, superoxide dismutase and catalase, and increased the expression levels of immune-related genes in the spleen and antioxidant-related genes in the liver of fish fed.	[<u>40]</u>

Table 1. Product foodstuffs, their compositions and health benefits (2016–2021).

Product Foodstuff	Major Findings	Reference
Rapeseed honey with mulberry leaves and fruits	The addition of dried leaves and freeze-dried fruits (4%, w/v) to rapeseed honey added value to the product by increasing the content of flavonoids and phenolic acids and antioxidant capacity.	[<u>44]</u>
Black mulberry- aged wines	The non-thermal processing applied at wine maturation point can be a potential method of improving the maturation process by modifying the chromatic properties of the wine.	[<u>38]</u>
	In the volatile composition of the non-thermal, accelerated, aged wines, many volatile compounds were found that are grouped into nine chemical families: alcohols (32), esters (53), acids (14), volatile phenols (11), aldehydes (16), ketones (15), terpenes (11), lactones (11) and furans (3).	[<u>39]</u>
Black mulberry jam	Black mulberries were processed into jam on an industrialized scale. The total phenols, flavonoids, anthocyanins and antioxidant capacity was significantly decreased but % recovery of bioaccessible the natural compounds increased after jam processing.	[<u>36]</u>
Dark chocolate with black mulberry	Dark chocolate was fortified with dry black mulberry waste extract, encapsulated in chitosan-coated liposomes. This formula was shown to protect the anthocyanin content and increase the bioavailability of these pigments in vitro.	[<u>46]</u>

(RO 135033 A2) that implements different processes for obtaining jams from black, white or red mulberry fruit by gelling with the addition of pectin ^[48]. An ethnobotanical study conducted by Li et al., 2017, on white mulberry leaf tea, showed that teas could be included in the category of functional foods, having a detoxifying effect, treating coughs and sore throats, colds, etc. ^[49]. Lin et al., 2020 ^[47], confirmed that drinks obtained from mulberry leaves are functional products that prevent diseases related to aging and Meng et al., 2020, mention that white mulberry leaf tea is used in Asian countries in order to control diabetes ^[50].

Application No.	Species/Part	Sample Type	Results/Mechanism	Ref.
US 11,090,349 B2	Morus alba L.; Morus alba var. multicaulis L.; Morus nigra; Morus australis Poir.	Raw material, dry leaves	Inhibits α-glucosidase. It has the ability to control blood glucose levels and reduce melanin production for the treatment of conditions caused by pigmentation, such as freckles, chloasma, striae gravidarum, sensitive plaque and melanoma.	[<u>51</u>]
AU 2019201188 B2	<i>M. alba</i> root bark; acacia barks; <i>Uncaria</i> <i>gambir</i> , leaves; <i>Curcuma</i> <i>longa</i> L.	Mixture extract	The compound mixture, demonstrated beneficial synergistic effects with improved anti-inflammatory and anti-	[<u>52</u>]

Table 2. List of patents based on the therapeutic and functional applications of *Morus* (2017–2021).

Application No.	Species/Part	Sample Type	Results/Mechanism	Ref.
			nociceptive efficacy, but also the attenuation of joint stiffness.	
US 10,588,927 B2	Mulberry (<i>M. alba</i>) and poria cocos peel	Mixed extract	Used either as a food product or as a pharmaceutical composition with the aim of preventing or treating degenerative neurological diseases, having the ability to improve memory and protection on neurons.	[<u>53</u>]
US 2020/0360457 A1	<i>M. alba</i> and <i>M.</i> <i>nigra</i> root	Macerate extract	As an active ingredient, at least one extract from the root of the plant is used, according to the invention. It is rich in moracenine A, moracenin B, kuwanon C, wittiorumin F and mulberrofuran T, also used in cosmetic composition and a pharmaceutical or nutraceutical composition.	[<u>54]</u>
US 2020/0178585 A1	Morus sp. fruits	Savory concentrate/seasoning, with vegetable fat.	Used as a cooking aid in the preparation of starch-rich food.	[<u>55</u>]
US 2020/0197429 A1	Astragalus root; phlorizin; <i>M. alba</i> root bark; olive leaf and bitter melon.	[<mark>56</mark> Standardized extracts	Dietary supplement with the aim of controlling postprandial blood sugar.	[<u>40</u>]

Yimam et al., 2017, studied the effect of UP1306, a composition based on a patented mixture of heartwood of *Acacia catechu* and the root bark of *Morus alba*, with beneficial effect on joints, evidenced by the attenuation of symptoms associated with osteoarthritis in monosodium–iodoacetate-induced rats, reducing pain sensitivity, significantly improving the integrity of the articular cartilage matrix and causing minimal subchondral bone damage [57].

An aqueous and ethanolic extract of *M. alba* was developed (US7815949 B2) with estrogenic effects, and used for the treatment of climatic symptoms, osteoporosis and breast or uterine cancer ^[58]. Another product (US2010/0166898 A1) from the bark of *Morus australis* Poir, containing kiwanon H, was used as an antimicrobial agent ^[59]. An ethanolic extract of white mulberry branches, which has a whitening effect, is the basis of another patent (US2006/0216253 A1) ^[60].

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