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Pharmacological effects & quality parameters of *Morus* species: A review

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Abstract
The present review provides a comprehensive summary on the quality parameters and pharmacological effects of mulberry species. It has a unique nutritional profile that makes it a promising natural functional tonic. Mulberry fruits possess properties such as antioxidant, anti-atherosclerotic, anti-obesity, hypolipidimic and anti-hypertensive. Mulberry extracts or components especially flavonoids scavenge free radicals showing potential against oxidative stress. Presence of anthocyanins further strengthens its antioxidant claims. Likewise, some other components such as 1-deoxynojirimycin (DNJ) have been reported to be effective against hyperglycemia and lipid peroxidation in diabetics. Therefore, *Morus spp.* is a multi-functional plant with promising pharmacological properties.

Keywords: mulberry, quality parameters, pharmacological effects

Introduction
Mulberry, genus *Morus* L., family *Moraceae* and *Urticales,* is a perennial, fast growing deep rooted plant, cultivated extensively in countries where sericulture is practiced. Mulberry, also known as saint fruit, is a fast-growing deciduous plant that grows under different climatic conditions i.e., tropical, subtropical and temperate (Srivastava *et al.*, 2003) [35]. Mulberry flowers in January, bear fruits in January to February, and can be harvested from March to April. In many species, the plant grows white but then changes to pale yellow with pink edges and then becomes red after ripening. Their color further turn dark purple to black when fully ripened. The genus *Morus* contains approximately nineteen members (The Plant List, 2017) [36], and the most commonly grown species are white mulberry (*M. alba* L.), black mulberry (*M. nigra* L.), and red mulberry (*M. rubra* L.) (Ercisli & Orhan, 2007) [11]. Amongst the three species, *M. alba* is dominant one.

Turkey is the major source of mulberry fruits. In Turkey, this fruit is also used in manufacturing of medicine, juice, natural dyes and for manufacturing cosmetic products on industrial scale (Ercisli & Orhan, 2008) [12]. China has the largest area under mulberry cultivation, which is above 626,000 ha, followed by India. (Sanchez, 2000) [30]. Most of the countries grow mulberry plants (*Morus* species) for different purposes like production of silk worm (Vijayan *et al.*, 1997) [38]. In other countries like Europe, mulberry plants are grown for the production of mulberry fruits (Zafar *et al.*, 2013) [42]. It is also used as silkworms and as sericulture-related materials.

Mulberry is mainly grown for its leaves, the main source of food to the silk worm, but few species of mulberry like *Morus alba, Morus indica, Morus laevigata* are also cultivated for their edible fruit (Aswathi *et al.*, 2004) [2]. In most mulberry-growing countries, mulberry fruit is commonly eaten fresh, dried, or processed into wine, fruit juice, and jam for its delicious taste, pleasing color, low calorie content, and high nutrient content (Huang *et al.*, 2017) [19]. Apart from being a food item, mulberry fruit has been used in the folk medicine for thousands of years, especially in China, for treating sore throat, anemia, and tonsillitis (Singh, 1997) [34]. To date, different parts of mulberry, from the root bark to the leaves, have been extensively investigated for their health benefits, including hypoglycemic, hypolipidemic and antioxidant effects (Chan *et al.*, 2009) [5]. Therefore, the mulberry fruit could be a type of potential functional food to protect against many types of diseases.

Quality Parameters
Mulberry leaves and fruits contained many bioactive components such as alkaloids, anthocyanins and flavonoids (Hasimoto *et al.*, 2008) [17]. Mulberry leaves are rich in alkaloids including 1-deoxynojirimycin (DNJ), the most potent glycosidase inhibitor that decreases blood-sugar levels (Nakagawa *et al.*, 2010) [29]. Resveratrol (trans-3,41,5-trihydroxystilbene) and Oxyresveratrol (trans-2,31,4,51-tetrahydroxy stilbene) are hydroxystilbenes found in mulberry (Bae & Suh, 2007) [3]. This bioactive substance is a potent neuroprotectant and has cardioprotective effect (Chao *et al.*, 2009) [6]. Anthocyanins are mainly responsible for the color of mulberry fruits (60%) (Gerasopoulos & Stavroulakis, 1997) [14], and also greatly contributed to its health-promoting effects. Specifically, cyanidin 3-O-glucoside (C3G), cyanidin 3-O-rutinoside (C3R), pelargonidin 3-O-glucoside, and pelargonidin 3-O-rutinoside are the main anthocyanins in mulberry fruits (Jin *et al.*, 2015) [20]. Mulberry contains both rutin and querecetin, the content of rutin being the higher (Zhishen *et al.*, 1999) [44]. Phenolic acids of mulberries range from 29.52 (*M. alba* Linn.) to 175.64 mg kg^{-1} fw (*M.*

atropurpurea Roxb) (Zhang *et al.,* 2008) [43], with hydroxybenzoic and hydroxycinnamic acids derivatives being the main components (Sánchez-Salcedo *et al.,* 2015) [31].

Mulberry plants also include nutritive compounds like proteins, carbohydrates, fats, fibers, minerals and some vitamins or their precursors (Table 1). The principal sugars found in mulberry are glucose and fructose (Mahmood *et al.,* 2012) [28]. Malic acid is the most predominant organic acid found in mulberry with a range of 123–218 mg/g followed by citric acid (21–41 mg/g) (Ercisli & Orhan, 2008) [12]. Linoleic acid (18:2) is the dominant fatty acid (53.57– 64.41%) in all black mulberry genotypes, and followed by palmitic acid (16:0) (11.36–16.41%) (Le *et al.,* 2013) [25]. A total of 18 amino acids, including all nine essential amino acids required by humans, are found in mulberry fruit. The essential amino acid (EAA)/total amino acid (TAA) ratio is 42%, which is close to those of some high quality protein foods such as milk and fish (Jiang & Nie, 2015) [21]. Furthermore, Long chain fatty acids, fatty acid esters, fatty alcohols, aromatic alcohols, fatty aldehydes and fatty ketones were reported to be the major aromatic components in mulberry (Chen *et al.,* 2010) [7].

Table 1: Chemical composition of *Morus* species

Type	Content	Type	Content
Fruit weight	1.25–4.75 g	Minerals	
Moisture	85.57–91.00%	N	0.83 %
pH	3.52–5.60	P	235 mg/100 g
TSS	15.9-20.4%	K	1141 mg/100 g
Protein	0.88–1.38%	Ca	139 mg/100 g
Ascorbic acid	19.4- 22.4 mg/100 g	Mg	109 mg/100 g
Total fat	0.14-0.40%	Na	60 mg/100 g
Total sugars	13.11–15.03%	Fe	4.3 mg/100 g
Reducing sugars	6.33–8.18%	Cu	0.4 mg/100 g
Crude fiber	0.43–0.65%	Mn	4.0 mg/100 g
Total ash	0.56–6.75%	Zn	3.1 mg/100 g

***Sources*: (**Han *et al.,* 2012; Ercisli & Orhan, 2007) [16, 11].

Pharmacological Effects

Mulberry has higher content of polyphenols including flavonoids, anthocyanins, and carotenoids (Bae & Suh, 2007) [3]. Extracts of mulberry fruits posse a wide scope of biochemical activities such as scavenging free radicals, anti-hyperlipidemia and anti-atherogenic (Bae & Suh, 2007) [3].

i) Antioxidant Activity

The antioxidant capacity of fruit is correlated well with the level of oxygen radical scavengers, such as phenolic compounds (Giampieri *et al.,* 2012) [15]. Researchers have shown that mulberry fruits have higher polyphenols as compared to other berries (Lee *et al.,* 2009) [26].

Mature fruits are rich in anthocyanins, which are excellent antioxidant agents with stronger free radical scavenging activity than vitamin C (Du *et al.,* 2008) [9]. The highest anti-oxidant activity is found in developing leaves of mulberry followed by young leaves and then matures fruits (Chan *et al.,* 2016) [4].

ii) Anti-diabetic Activity

Mulberry leaves are also used in treatment of diabetes mellitus worldwide mostly in the form of soft drinks, carbonated beverages and tranquilizers. From the root bark of the mulberry tree, a very active medicinal compound, 1-deoxynojirimycin (DNJ) has been isolated, which is also known as moranoline.

Mulberry 1-deoxynojirimycin (DNJ) is a glucose analogue with an NH group. DNJ is a naturally occurring alkaloid from the mulberry tree (Yagi *et al.,* 1976) [40]. In the subsequent decades, DNJ has gained increasing attention as one of the most potent α-glycosidase inhibitors (Watson *et al.,* 2001) [39]. DNJ inhibits α-glucosidase in the small intestine by binding to its active site, resulting in a decrease of glucose absorption and blood sugar levels (Junge *et al.,* 1996) [22]. In vivo studies have supported the administration of mulberry containing DNJ to suppress the postprandial increase of blood glucose levels (Kong *et al.,* 2008) [24].

iii) Hypolipidimic and Anti-obesity Activity

Morus alba is traditionally used for hypolipidemic activities. Six compounds have been identified in mulberry which possesses hypolipidemic effects (Ahmad *et al.,* 2013) [1]. Seventy percent alcohol extract obtained from root bark of mulberry acts as potent hypocholesterolemic nutrient and inhibits lipid peroxidase formation in hypocholesterolemic rats (El-Beshbishy *et al.,* 2006) [10]. Moracin present in mulberry leaves are capable of inhibiting lipid peroxidation that strongly indicates their role as scavenger (Sharma *et al.,* 2001) [33]. Also, in vivo studies of DNJ reported anti-obesity effect of mulberry (Tsuduki *et al.,* 2013) [37].

iv) Anti-hypertensive effect

Hypertension is an important worldwide public health challenge, and is a leading cause of cardiovascular, retinal and kidney diseases (Savica *et al.,* 2010) [32]. γ-Aminobutyric acid (GABA) is a four-carbon amino acid that acts as one of the major inhibitory neurotransmitters in the central nervous system (Kimura *et al.,* 2002) [23].

Mulberry leaves (ML) exert their antihypertensive activity because leaves of *M. alba* L. contain considerable levels of γ-aminobutyric acid (GABA) It has been reported that single administration of a water extract from mulberry leaves (WEML) lowers systolic blood pressure (SBP) transiently (Yang *et al.,* 2012) [41].

v) Anti-atherosclerotic effects

Atherosclerosis, a chronic inflammatory disease characterized by the accumulation of lipids in the arterial intima, is widely accepted as a main cause of cardiovascular disease (Libby, 2002) [27]. Oxidative low-density lipoprotein (oxLDL) is an important atherogenic factor (Hertog, 1993) [18]. Consumption of a diet rich in natural antioxidants is associated with attenuation of the development of atherosclerosis (Gendron *et al.,* 2010) [13].

The studies have reported that feeding mulberry water extracts reduces severe artherosclerosis in the aorta by 42-63%. The levels of triglyceride, cholesterol and low-density lipoprotein cholesterol (LDL-C) decreases due to consumption of mulberry (Chen *et al.,* 2005) [8].

Conclusion

The present review concludes the pharmacological importance of Morus species and their nutritional compounds. A thorough analysis of the literature revealed that Morus species and their medicinally active phytochemicals exhibit broad range of biomedical activities including antioxidant, anti-diabetic, hypolipidimic, anti-obesity, anti-hypertensive and anti-arthrosclerosis. These plants have also shown remarkable role in food, textile, and pharmaceutical industries. It was observed that they possess strong antioxidant activity due to the presence of phenolic compounds especially flavonoids and anthocyanins that have vigor to eradicate free radical production. These broad ranges of activities of mulberry plants appeal for further research and inspection of their pharmaceutical and medicinal potential.

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