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Phytopharmacological potential of different species of *Morus alba* and their bioactive phytochemicals: A review

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ABSTRACT

Medicinal plants of Moraceae family have been well-recognized traditionally due to their versatile applications in various fields including agriculture, cosmetic and food as well as in pharmaceutical industries. Their biomedical and medicinal importance is reflected from their broad range of pharmacological activities for treatment of various inflammatory conditions, cancer, infectious diseases, and gastrointestinal disorders. The present review was aimed to summarize and critically discuss the biomedical implications of *Morus* species, their bioactive compounds, and phytochemicals. Bioactivity guided fractionation of these medicinal plants revealed that different types of bioactive phytochemicals and secondary metabolites such as steroids, saponins, alkaloids, glycosides and phenolic compounds including terpenoids, flavonoids, anthocyanins and tannins were present. The critical analysis of the literature revealed that the aqueous, methanolic, and ethanolic extracts of *Morus* species and their bioactive compounds exhibit remarkable anti-oxidative, anti-diabetic, anti-stress, nephroprotective, antimicrobial, anti-mutagenic, anticancer, anxiolytic, hepatoprotective, anthelmintic, antimicrobial, immune-modulatory and cholesterol lowering effects. Based on the literature review and bioactivity guided investigation of *Morus* species and their phytomedicinal effects, we anticipate that these herbal products hold excellent potential for future research.

1. Introduction

Morus alba (*M. alba*) belongs to the family of Moracea which is a family of flowering plants. The most acceptable species of *Morus* are 10–14. These grow very fast when young, but become slow afterward. 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. They are distributed into the subtropic regions of Asia such as Japan, India, China and Korea. They are also present in other region of world like North America, an Africa. Out of a total of 14 species that have been reported so far, former nine are present in Asia and the last five are newly discovered (Table 1) [1]. Most of these countries grow mulberry plants (*Morus* species) for different purposes like production of silk worm (*Bombys mori* L.) or enhancing the foliage production in India and China [2]. In other countries like Europe, mulberry plants are grown for the production of mulberry fruits [3]. It is also used as silkworms and as sericulture-related materials. Turkey is the major source of mulberry fruits such as mulberry pekmex, mulberry Kestil and mulberry Kome. In Turkey, this fruit is also used in manufacturing of medicine, juice, natural dyes and for manufacturing cosmetic products on industrial scale [4].

Multi growing of mulberry plant by the process of grafting, cutting and tissue culturing is called 'Micro propagation' [5]. Mulberry plants are not only used as nutrition or flavors, but are also used traditionally due to their broad range biomedical activities such as laxatives, odentalic emetic, and toxin-adsorbents. Due to the presence of several essential unsaturated fatty acids such as linnolenic acid, linoleic acid, and oleic acid, mulberry fruits are commonly used as essential

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Table 1
Taxonomic classification of *Morus* L. (Mulberry) and its species.

Kingdom	Plantae-Plant
Subkingdom	Tracheobionta-Vascular plant
Superdivision	Spermatophyta
Division	Magnoliophyta-Flowering plant
Class	Magnoliopsida-Dicotyledons
Subclass	Hamamelididae
Order	Urticales
Family	Moraceae-Mulberry family
Genus	*Morus* L. (mulberry)
Species	1. *Morus alba* 2. *Morus australis* 3. *Morus cathayana* 4. *Morus macroura* 5. *Morus mongolica* 6. *Morus nigra* 7. *Morus notabilis* 8. *Morus serrate* 9. *Morus celtidifolia* 10. *Morus insignis* 11. *Morus microphylla* 12. *Morus rubra* 13. *Morus mesozygia* 14. *Morus indica*

foods. These unsaturated fatty acid play vital roles in the synthesis of cell membrane, normal functioning of brain, secretion and production of hormones, regulation of immune functions and inflammatory responses, and modulation of blood pressure [6]. The mulberry root bark has also been traditionally used as antitussive and anti-asthmatic in China [7]. The medicinal efficacy of mulberry fruits has also been established due to the presence of a large amount of antioxidants that have shown strong anti-inflammatory, anti-diabetic, anti-stress, and antiviral activities [8]. The leave of *Morus* plants can also be used as hypoglycemic, hypotensive, diuretic, and anti-mutagenic tonics. Bioactivity guided fractionation of *Morus* fruits revealed that they contain large number of medicinally active compounds including anthocyanins, flavonoid, and polyphenols [9]. These bioactive compounds, their sources, and biological activities are presented in Table 2. These plant species are also adopted for their protective mechanisms against cellular injuries caused by UV irradiations [10]. Leave of mulberry plants inhibit peroxidation due to the presence of a high amount of linoleic acid, α-tocopherol or vitamin E (approx. 72%). On the other hand, the presence of anthocyanin which is a hydrophilic pigment is directly proportional to its antioxidant activity [11].

2. Habitats

Mulberry tree is *Morus* specie which belongs to Moracea family. The trees grow in Europe, West China, Korea and Japan with very large scale. Their leaves are very commonly utilized as feed of silkworms. *Morus* has more than 14 species including *M. alba* L. (white mulberry), *Morus nigra* (*M. nigra*) (black mulberry), *Morus rubra* (red mulberry). Intercrossed forms exist among *M. alba*, *Morus rubra*, *Morus australis* (Korean Mulberry) and *Morus laevigata* (Himalayan Mulberry). *M. alba* L. and *M. nigra* L. are white and black mulberries. There are a number of compounds which are extracted from both of these plant species. Five compounds that derived from the methanol extract have been discovered throughout HPLC/PDA. And four compounds including Quercetin 3-*O*-rutinoside, Kaempferol 3-*O*-rutinoside and 5-o-caffeoylquinic acid, Quercetin 3-*O*-glucoside have been detached by Sephadex LH-20 column chromatography. Furthermore, red pigments of *M. nigra* fruits show the existence of four anthocyanins accepted as a cyanidin 3-*O*-glucoside, cyanidin 3-*O*-rutinoside, pelargonidin 3-*O*-glucoside and pelargonidin 3-*O*-rutinoside [23,24].

3. Commonly used *Morus* species and their biomedical uses

3.1. Morus mesozygia (M. mesozygia)

M. mesozygia, one of the *Morus* species, is also known as black mulberry. Leaves and fruits of this species are used as food for Guereza and monkey in Africa. Around the globe, a huge number of population use naturally sourced medicines for the treatment of their different types of diseases. *M. mesozygia* is also traditionally used for treatment of many ailments such as arthritis, gastrointestinal disorders, disability, and wound healing. Their pharmacological significance is due to the presence of significant concentration of antioxidants and antimicrobial compounds. There are several bioactive compounds extracted from stem bark of *M. mesozygia* which include Moracin Q, Moracin T, Artocarpesin, cycloartocarpesin, Moracin R, Moracin S, Moracin U, Moracin C, and Moracin These compounds exhibit great antimicrobial potential against various species of microbes [25].

Table 2
Phytochemical constituents of different species of *Morus* L. (Mulberry) and their pharmacological activities.

Phytochemical constituents	Different species of *Morus* L. (Mulberry)														Biological activity	Refs
	1	2	3	4	5	6	7	8	9	10	11	12	13	14		
Steroids	+	+	−	−	−	+	−	−	−	−	−	−	+	−	1. Antidiabetic 2. Immunomodulatory	[12,13]
Glycosides	−	−	+	+	+	−	+	−	−	−	−	−	−	−	1. Antioxidant 2. Hypocholesterolemic	[8,14]
Terpenoids	−	+	+	+	+	−	−	−	−	−	−	−	+	+	1. Anthelmintic 2. Anxiolytic	[15,16]
Saponins	+	+	+	+	−	−	−	−	−	−	−	+	−	−	1. Antimicrobial 2. Hepatoprotective	[17,18]
Alkaloids	+	+	−	+	+	+	−	−	−	+					1. Anti-dopaminergic	[19]
Flavonoids	+	+	−	−	+	+	+	−	−	−	−	−	−	+	1. Anti-mutagenic activity 2. Inhibition of melanin biosynthesis	[20]
Tannins	+	+	+	−	−	−	−	−	−	−	+	+	−	−	1. Anticancer 2. Nephroprotective	[21,22]

3.2. M. nigra

M. nigra, also a species of *Morus*, is also known as black mulberry. Fruits of this species are commonly used as flavoring agent and as herbal medicines due to the presence of a wide range of therapeutically active compounds. The bioactive compounds extracted from this plant are also used as analgesic and anti-inflammatory agents in different animals and human suffering from diabetic mellitus. The reason is that their leaves contain adequate amount of 1-deoxynojirimycin which is well-known and fast inhibitor of α-glycosidase. Recently, their fruits have also been investigated for anti-diabetic, anti-oxidative, anti-inflammatory, and anti-hyperlipidemia activities [8,12–14]. Bioactivity guided fractionation revealed that these biological activities were due to their polyphenolic components such as anthocyanins. Black mulberry also contain cyanidin-based anthocyanins particularly cyanidin-3-*O*-glucoside and cyanidin-3-*O*-rutinoside [26].

3.3. Morus indica (M. indica)

Another species of *Morus* is *M. indica*. Studies revealed that methylene chloride-based extracts of *M. indica* showed promising anti-inflammatory activities. Steroids and terpenoids which are extracted from the mulberry plant have negative effects for the presence of tannins, alkaloids, flavonoids and saponins. *M. indica* has also been used to cure inflammatory conditions (i.e., edema) because of its similar pharmacological properties to indomethacin [27]. Recent studies showed that some new compounds including polyhydroxylated alkaloids, (2R,3R,4R)-2-hydroxymethyl-3,4-dihydroxypyrrolidine-N-propionamide and 4-*O*-α-d-galactopyranosyl-calystegine B2, and 3β,6β-dihydroxynortropane have been extracted from the root extracts of *M. indica* using ion exchange resins technique [28]. Other investigations showed several positive effects (such as cell protection from chemicals) of cyanidin-3-glucoside (C3G) extracted from the fruit of *M. indica* which have shown protective effect against pancreatic β-cell destruction which is caused due to hydrogen peroxide induced oxidative stress.

4. Pharmacological effects

4.1. Effect on diabetes mellitus

Mulberry leaves are also used in treatment of diabetes mellitus worldwide. For the treatment of diabetes mellitus, mulberry fruits are commonly used as soft drinks, carbonated beverages and tranquilizers. From the root bark of the mulberry tree, a very active medicinal compound, 1-deoxynojirimycin has been isolated, which is also known as moranoline. These isolates have shown strong anti-diabetic effects by decreasing blood glucose levels in postprandial states. A total of 18 compounds were extracted from the mulberry plant, some of which showed pronounced pharmacological effects in the management of various diseases. In Korea, the powder form of the extract from mulberry leaves is commonly used as ice cream to decrease or control blood glucose levels. Some of the compounds extracted from the root bark of the plant include N-methy-1-deoxynojirimycin, 2-*O*-α-D-glactopyranosyl-1-deoxynojirimycin, 2-*O*-α-D-glucopyranosyl-1-deoxinojirimycin, 3-*O*-β-D-glucopyranosyl-1-deoxinojirimycin, 4-*O*-β-D-glucopyranosyl-fagomine, 4-*O*-β-D-glucopyranosyl-1-deoxinojirimycin, 6-*O*-β-D-glucopyranosyl-1-deoxinojirimycin, calystegine B1, calystegine B2, fagomine, 3-epi-fagomine, 1,4-deideoxy-1,4-imino-D-arabinitol, 1,4-dideoxy-1,4-imino(2-*O*-β-Dglucopyranosyl)-D-arabinitol, and 1,4-dideoxy-1,4-imino-D-ribitol [28].

The proposed glucose lowering mechanism of *Morus* plants is their promising potential to regenerate or maintain the functioning of β-cells which are responsible to synthesize and secrete insulin in the physiologic feedback mechanism. The regeneration of β-cells control the blood glucose levels effectively [29]. It is evidenced that through various range of experiments including immunofluorescence staining, flow cytometry and western blotting, the death of β-cells is primarily caused by oxidative stress induced by H_2O_2 which initiate apoptosis by the activation of caspase-3, production of intracellular reactive oxygen species, stimulation of lipid peroxidation, and DNA fragmentation. Studies showed that C3G decrease the intracellular production of H_2O_2 which eventually results in decreased apoptosis and destruction to β-cells in the Islets of Langerhans [30]. Studies showed that a significant anti-diabetic effects produced by mulberry fruit extracts is due to the presence of C3G in high amount [30].

4.2. Stress management

The ethyl acetate soluble fraction of *M. alba* also showed promising efficacy for the management of chronic restrain stress (RS)-induced perturbations in behavioral, biochemical and brain oxidative stress status [19]. In this study, they induced stress in animals by restraining them inside an adjustable cylindrical plastic tube for 3 h daily for ten consecutive days. The anti-stress effects of ethyl acetate soluble fraction of *M. alba* were tested by administering different doses (25, 50, 100 mg/kg) of *M. alba* extract and the results were compared with diazepam (1 mg/kg). The anti-stress efficacy was tested by determining the behavioral and biochemical parameters such as open field, cognitive dysfunction, leucocytes count, blood glucose and corticosteroid levels. On day 10, the rats were sacrificed and biochemical assessment of lipid peroxidation, superoxide dismutase (SOD), catalase (CAT), and glutathione reductase (GSH) were performed in whole rat brain. Results showed that all the biochemical parameters including cognitive dysfunction, abnormal leucocytes count, and glucose and corticosterone levels, SOD, lipid peroxidation, CAT and GSH were attenuated in rats treated with *M. alba*. These results evident that *M. alba* has strong effects to alleviate stress induced disorders [19].

4.3. Effect on cardiovascular diseases

Several medicinal compounds have been isolated from various parts of *M. alba* including tree, fruits, and leaves are chlorogenic acid (CA), rutin (RT), quercetin-3-*O*-(6-*O*-malonyl)-β-D-glucoside, isoquercitrin, astragalin, and kaempferol-3-*O*-(6-*O*-malonyl)-β-D-glucoside. All these compounds are phenolic in nature and the structure of these phenolic compounds are identified under UV/visible spectrophotometer, fourier-transform infrared spectroscopy, nuclear magnetic resonance and mass spectrometry. It was observed that the levels of these polyphenols varied in mulberry trees based on their cultivated range.

Studies showed that dietary intake of various plant parts including fruits, leaves and vegetables can significantly lower the cardiovascular risks [31,32]. The cardio-protective effect of methanolic extract of *M. alba* L. against myocardial infarction was investigated using an *in vivo* method in rats [31]. Results showed that the intragastric administration of *M. alba* (500 mg/kg body weight) showed significant cardio-protective effects by decreasing the levels of thiobarbituric acid reactive substances and enhanced antioxidant activities (SOD, CAT, GPx and GSH) in myocardial infarcted rats. These results showed that dietary intake of *M. alba* could significantly reduce the risks of myocardial infarction [31].

In another study, the effect of administration of *M. alba* leaf extracts on the total cholesterol, low-density lipoprotein cholesterol, alanine aminotransferase, aspartate aminotransferase and lactate dehydrogenase were measured in the plasma of mice treated with the mulberry leaf extract [32]. Results showed that the mice administered with mulberry leaf extract showed significant alleviation on this biochemical, physiological and pathological parameters. Additionally, the mulberry extract stimulated both innate and acquired immunity, including the induction of scavenger and Toll-like receptors and the activation of pathways in various lymphocytes, such as macrophages, eosinophils, neutrophils, natural killer cells, B cells, and T cells. These results clearly revealed that the mulberry leaf extract could be a natural herbal medicine for the alleviation of cardiovascular diseases [32].

4.4. Antimicrobial activity

The antimicrobial activity of *Morus* species is mainly associated with the stem bark of the mulberry plant [33]. Several compounds that have isolated from various parts of Morus plant and their crude extracts have been tested for antibacterial and antifungal activities. The analysis of structure-activity relationship revealed that most of the bioactive compounds such as flavonoids and terpenoids exhibit potent antimicrobial activity while arylbenzofurans showed weaker antimicrobial activity coupled with the position of phenyl group. The cyclisation of arylbenzofurans decreased the antimicrobial activity. The arylbenzofurans isolated from *Morus* species including Moracin C and Moracin M showed promising antimicrobial activity against methicillin–resistant *Staphylococcus aureus*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* [17]. On the other hand, prenylated compounds also showed antifungal activity at the concentration range of (6.25–120.00) μg/mL and antibacterial activity at a dose range of (6.25–100.00) μg/mL. The higher antimicrobial activity of the prenylated flavonoids is due to their hydrophobic nature which makes them capable to easily penetrate through the microorganism cell membrane [17].

On the other hand, the crude extracts isolated from different part of species have also shown antifungal and antibacterial activities. Recent study also showed the connection between the antimicrobial and antibiotics. Ampicillin and erythromycin have good antibacterial activity. Amphotericin B and miconazole possess strong antifungal activities [34]. The pharmacological mechanism for the antimicrobial action of different compounds is not clear yet; however, the disruption of cell wall function or damage to the cell membrane function are the most proposed mechanisms.

4.5. Anti-oxidative effects

Several factors are involved in the initiation of stress in plant during the normal process of growth and development. These causative factors include some external factors like drought, light, heat, air pollution, toxins, pathogen attack, water pollution and seasonal changes [35,36]. During these stress conditions, plant adopts many protective mechanisms by increasing antioxidant activity and inhibiting the processes of lipid peroxidation. Several compounds which act as antioxidant agents include phenolic compounds, flavonoids, steroid, glycoside, terpenoids, saponins, alkaloids and tannins [37]. The anti-oxidant activity of flavonol is due to the presence of glycoside and aglycones such as QT, QT-G, QT-GA, rutin [23,38].

4.6. Anti-dopaminergic effects

The effect of methanolic extract of *M. alba* L. has also been evaluated on dopaminergic function. The effect of the methanolic extract of *M. alba* L. was evaluated on foot shock-induced aggression, metoclopramide and haloperidol induced catalepsy, amphetamine-induced stereotyped behavior and phenobarbitone induced sleeping in mice. In each of these tests, the extract was administered in doses of 50, 100 and 200 mg/kg, *i.p.*, 30 min before performing the test in mice [9].

Results showed that the plant extract produced significant dose-dependent synergism in haloperidol (1 mg/kg) and metoclopramide (20 mg/kg) induced catalepsy in mice. The extract significantly reduced the number of fights and increased latency to fight in foot shock-induced aggression. The analysis of amphetamine (1 mg/kg) induced stereotyped behavior revealed that the animals treated with extract showed significant dose-dependent decrease in this behavior. Furthermore, the phenobarbitone (50 mg/kg) induced sleep duration was also extended. These results revealed that methanolic extract of *M. alba* L. holds greater anti-dopaminergic potential and thus can be used as alternative medicine in conjunction with pharmacological agents for the better management of psychotic disorders [9,39].

4.7. Anti-mutagenic effects

Studies showed that *M. alba* and *M. nigra* possess genoprotective properties. These extracts may diminish the mutation level caused by the chemical mutagens such as X-rays and gamma rays [20].

4.8. Anticancer effects

Phytochemical screening of *M. alba* has also shown promising anti-proliferative and anticancer efficacy. Their anti-proliferative effects have been established against various cancer cells lines including Calu-6, breast cancer cells (MCF-7), HCT-116, human gastric carcinoma (SNU-601) cell line [40]. Results showed that the various plants parts showed moderate anti-proliferative activity against human cancer cell lines. It was observed that the anti-proliferative activity of methanol extract of mulberry leaves could be enhanced by the fermentation process only against human gastric carcinoma (SNU-601) cell line in concentration of 1 000 mg/mL. Conclusively, we anticipated that some parts of the plant could be recommended

as anticancer agents due to their moderate anti-proliferative ability [40].

4.9. Immunomodulatory effects

The methanolic extract of *M. alba* L. has also shown promising immunomodulatory activity [41]. In this study, authors have evaluated the immunomodulatory effects of *M. alba* by using different experimental models such as effect on serum immunoglobulins, cyclophosphamide induced neutropenia, carbon clearance test, neutrophil adhesion test, mice lethality test and indirect haemagglutination test. Results showed that the administration of *M. alba* in mice tend to increase serum immunoglobulins levels and prevent the mortality induced by bovine *Pasteurella multocida* in mice. Results have also evidenced that the administration of *M. alba* methanolic extract of leaves significantly reduced neutropenia and significant increased the phagocytic index in carbon clearance assay. These results revealed that *M. alba* may potentiate both cell mediated immunity and humoral immunity [41].

4.10. Hepatoprotective effects

Different species of *Morus* plant have also been established for their heptoprotective effects [18,42,43]. Mallhi *et al.* [42] conducted a study to evaluate the hepatoprotective activity by orally administering two doses (250 mg/kg and 500 mg/kg) of aqueous methanolic extract of *M. nigra* L. against paracetamol induced liver toxicity using mice model. Resulting data showed that the mice treated with plant extract showed significant dose-dependent decrease in the liver enzymes (ALT, AST and ALP) and total bilirubin induced by paracetamol. These results evident that the aqueous methanolic extract of *M. nigra* possesses promising hepatoprotective activity against paracetamol induced hepatotoxicity [42].

The hepatoprotective activity of ethanolic extract of mulberry leaves has also been investigated [43] by *in vitro* (human hepatoma, HepG2 cells) and *in vivo* studies against methotrexate induced liver injury using albino rats. The incubation of HepG2 cells with ethanolic extract of mulberry leaves showed a significant decrease in their cell viability within 48 h with very low IC_{50} value (14.5 μg/mL). Similarly, the administration of ethanolic extract of mulberry leaves in animals predisposed to drug induced liver injury showed significant downregulation in the serum levels of AST, ALT, ALP and LDH as compared to the control group. These results showed that the administration of ethanolic extract of mulberry leaves is hepatoprotective against drug-induced hepatotoxicity [43].

5. Pharmacological activities of phytochemicals isolated/extracted from *Morus* species

Herbal products have large amount of bioactive compounds which are used to cure and heal different human diseases. Phytochemicals have two types, *i.e.*, primary and secondary. The first type of phytochemicals contain huge amount of chlorophyll, carbohydrate proteins and amino acids. Secondary type includes terpenoids and alkaloids. Herbal medicines have anti-inflammatory, antibacterial and anti-inflammation activities. In the industrial bases, phytochemicals analysis is very important commercially, and pharmaceutical companies produce new drugs for the different diseases. Among medicinal plants, phytochemicals are occurring in leaves, vegetables and roots. Alkaloids are found in medicinal plants and are used as anesthetic agents [44]. Phytochemicals are compounds which are naturally present in plants (Phyto means 'plant' in Greek). There are many phytochemicals which are responsible for color and other food taste related function such as the high purple color of blueberries and smell of garlic, as well as flavonoids or carotenoids, but they are not accepted for essential nutrients. Approximately 4000 various phytochemicals are present [45]. Physiological properties of different phytochemicals may be elements rather than organic molecules, for example, our dietary selenium is found in thyroid hormone metabolism and immune function [46]. Phytochemicals food may be breakdown by processing techniques. Thermal decomposition is the main cause of phytochemical loss from cooking. Medicinal processing is food processing techniques can also free carotenoids and other phytochemicals [47].

In the field of phytochemistry, commonly used techniques are extraction, isolation and structural elucidation of natural products. Plants are primarily constructed in simple elements including carbon, oxygen, calcium and phosphorus. Most of the Chinese medicines are made by natural plants which consisted large number of phytochemicals, such as flavonoids, saponins, alkaloids, volatile oils and anthraquinones. These types of phytochemicals are consumed from dietary sources such as vegetables, fruits, beans and grains for good and long health. Different types of phytochemicals are present in plants including polyphenols, anthocyanins, salicylic acid, fibers, ellagic acid, and flavonoids *etc* [48]. Salicylic acid and ellagic acid are main constituents of blackberries and have protective effects against cancer cells [49] especially breast cancer [50].

6. Phytochemicals and their biological activities

Following are the most commonly employed phytochemicals isolated or extracted from *Morus* plant and their biological activities.

6.1. Flavonoids

Flavonoids paly vital roles in biological systems against the various oxidative stresses. *Morus* family contain substantial amount of flavonoid phytochemicals. This type of phytochemicals is taken by plant in the form of nutrition. These phytochemicals can modify or control influence on lipid peroxidation that results in atheroma, plaques in the inner lining of arteries and clotting of the blood in circulatory system. Cancer formation exhibits the properties of flavonoids such as free radical search, collect from discarded waste, strong hydrolytic, antioxidant activity, oxidative enzymes inhibitor (phospholipase A2, cyclooxygenase, lipoxygenase) and anti-inflammatory action. Antioxidant effects of flavonoids on lipid peroxidation may be associated with specific item or process of OH and O_2. During the peroxidation unsaturated fatty acid O_2 plays an important role. Flavonoids can be directly used to discard waste O_2 and OH by transfer of single electron. The phytochemical reduction of riboflavin was firstly used to determine the further change of O_2 mutation by superoxide dismutase (SOD) and other natural compounds. The flavonoids were obtained from fresh leaves,

oven-dried and air dried leaves and its concentration in the leave of mulberry species is different due to the seasonal alteration, higher (11.7 mg/g to 26.6 mg/g) in spring compare to autumn (9.84 mg/g to 23.4 mg/g). Flavonoids extracted from mulberry branches have scavenging activity against superoxide radicals. The discarded waste effects of rutin and quercetin on superoxide radicals were tested by the Electron Spin Resonance method.

6.2. Alkaloids

Alkaloid morphine was individually isolated in 1 804 from the opium poppy for the first time [51]. Alkaloids are chemical compounds, containing basic nitrogen atoms, sulfur, oxygen, phosphate, chlorine *etc*. and large number of drugs activities like anti-cancer, anti-malarial [52].

6.3. Phenolic acids

The most popular bioactive components of phytochemicals in food-polyphenolic constituents derived from plants and may be attributed to the adapted effects *in vivo* while these derived compounds are most efficient antioxidants *in vitro* rather than vitamins E or C. In disease preventions have been ascribed. This plays a major role in fruits, vegetables and red wine. They are aromatic and secondary plant metabolites that are broadly expanded all over the plant kingdom. They have crucial role in food quality and their organoleptic properties.

6.4. Anthocyanins

Anthocyanins have the property to transfer from blood brain barrier to brain for protective effects [53]. Most of vegetables and fruits plant have the plentiful color for attraction like red, blue, orange, yellow etc, in barriers, grapes and juices. This color is directly proportional to the concentration of anthocyanins in the plant or fruit. In animals and cell culture have anti-carcinogenic activity [54]. Those anthocyanins that were not found in sweet potatoes are involved in the reproduction of cancer cell and that leads to cause death [55].

The chromatogram of Anthocyanin extract develop at 515 nm Anthocyanin's in black mulberries from Italian cultivars are an assortment of five different anthocyanidine glycocyadin seen in decades. The total amount of anthocyanin is 27 mg/10 g of fresh berries. *M. nigra* and *M. alba* are applicable source of flavonoids which are famous for having a beneficial effect on human health [56].

7. Summary

The present review summarizes the biomedical and medicinal importance of *Morus* plants and their bioactive compounds. A thorough analysis of the literature revealed that *Morus* species and their medicinally active phytochemicals display broad range of biomedical activities including anti-inflammatory, analgesic, anti-mutagenic, anticancer, antioxidant, antimicrobial, anxiolytic, anti-diabetic gastro-protective, hepato-protective, nephron-protective, and cardio-protective. These plants have also shown significant 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 potency to abolish free radicals production and free-radical induced cellular injuries. These broad ranges of activities of mulberry plants appeal for further exploration and investigation of their pharmaceutical and medicinal potential.

Conflict of interest statement

The authors report no declaration of interest in the present work.

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