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Bioactive constituents and pharmacological activities of mulberry (*Morus* spp.) fruit: A review

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Abstract
This study examines poor diet, urbanization and other modern styles of life have resulted in the increase in diseases around the world. These factors are a major risk to human health. Among fruits, mulberry is the most appreciated for its nutritional and economic significance. It has been investigated for various health benefits. Mulberry is rich in bioactive compounds that bolster the body's immune system and contribute to preventing hyperlipidaemia, hyperglycemia, liver disorders, microbial infections and abnormal cell growths. There remains a lack of credible and unified evidence regarding the bioactive components in mulberry and their mechanisms of action, although they show promising potential. More and intensified research on mulberry based-products is required to improve the value of the product. It highlights the therapeutic activity of mulberry, discusses how it can prevent and treat chronic diseases, and describe potential applications in functional foods as well as laboratory studies. The discoveries reported in this review form an essential basis for future investigations, novel strategies and successful application of mulberry and its components including prevention of diseases.

Keywords: Mulberry fruit, *Morus* spp, bioactive compounds, nutraceuticals, functional foods

Introduction

The World Health Organization (WHO) defines chronic health condition as long-term illnesses develop gradually and do not spread from person to person. These conditions have complex etiologies and, once established, often result in permanent potential health risks and significant expenses for patients. Poor eating habits and inadequate exercise have been identified as the primary reasons for the increased incidence of these chronic conditions [1]. The mulberry tree's fruits, or mulberries, have additional health advantages because they contain antioxidants called phenolic compounds. Red, purple, and/or blue hues are caused by flavonoids and anthocyanins. A 2020 edition of Mulberry *(Morus alba)* is listed in the Chinese Pharmacopoeia. The Moraceae family's dried fruit spike is known for its capacity to produce fluids, moisten, and nourish Yin and blood dryness. Mulberries are incredibly nutrient-dense and multipurpose. Popular choice for food and medicine all over the world. Its fruit is high in fatty acids (potassium, organic acids), calcium, proteins, carbohydrates, and amino acids (including fiber and sugars). Furthermore, mulberry displays significant biological processes like blood sugar and antioxidant activity decrease, antibacterial, anticancer, and lipid-lowering impacts [2]. Despite early indications that mulberries are healthy and beneficial, there are not many thorough summaries of the structures, physicochemical characteristics, and scientific discoveries of their nutritive elements. The mechanism of action and the human bioavailability of its active ingredients are still poorly understood, and the possibilities and their clinical applications' safety have not been thoroughly evaluated. Filling in these gaps is essential to improving the mulberry's medicinal and economic value. Consequently, the purpose of the review is to go over and summarize the nutritional value, advantages for health, and uses of mulberry fruit in food, bio-supplies, as well as medication. Supporting the development is the aim of novel medications, functional foods, biomaterials, supplements, and treatments, as well as offering fresh approaches for public health and the avoidance of illness [3].

Material and Methods

Cultivation and Propagation

Mulberries come in over 500 types and over 15 species; the most important ones for either fruit or foliage production are the mulberry. Certain mulberry plants bear exclusively male flowers, whereas others produce only female ones, as the species generally exhibits dioecy. Furthermore, unisexual monoecious plants those which produce the same plant that bears both male and female flowers, can be found. Mulberries are a highly cross-pollinated, seed-propagated plant that may grow in an infinite number of shapes and variants, each with unique fruit and leaf characteristics. Numerous soil compositions and landform circumstances with inappropriate in most cultivated plant species can be used to grow mulberries. But it is well understood that mulberries usually grow when in contact with temperatures between 13 and 37.7 degrees celsius. The maximum number of buds that can sprout occurs when the temperature is between 24 and 28 degrees celsius, with a relative humidity of 65 to 80% and about 4 to 12 hours of daylight per day. Mulberries develop readily within rainfed environments. An additional soil watering system is installed if the water quality is poor because of inadequate rainfall. Although mulberries capable of thriving in diverse soil types, they typically do best in sandy loam soils with high levels of *in vitro* organic carbon and pH values between 6.2 and 6.8, which vary from slightly acidic to neutral.

A mulberry plantation requires general maintenance, which includes nutrient application, watering, and highly efficient control. Furthermore, propagation has proven to be an effective method for producing mulberry seedlings under any environmental circumstances. When applied to mulberry explants, the Murashige and Skoog medium with growth regulators promotes cell growth, shoot formation, and enhances flowering and seed germination [4]. Even while the micropropagation method makes it possible to have seedlings that can grow throughout the winter, this only addresses a portion of the issue. For nations with temperate

climates, regions in acidic or saline soils, as well as those with inadequate light and precipitation, achieving large-scale production of leaves and fruits remains a significant issue. As a result, the potential applications of vertical farming technology have been examined. Vertical farming may give results while consuming less water and land than traditional agriculture and may eliminate the need for pesticides. VFT can assist to make in meeting the anticipated give throughout the annual period so that resilient crop-producing systems can be built, especially in crowded areas. VFT already makes different kinds of products, including plants and edible crops, employing multi-layer indoor crop growth techniques like hydroponic, aquaponic, and aeroponic systems. As well as the potential for mulberry cultivation using more environmentally friendly substitute techniques, like vertical farming.

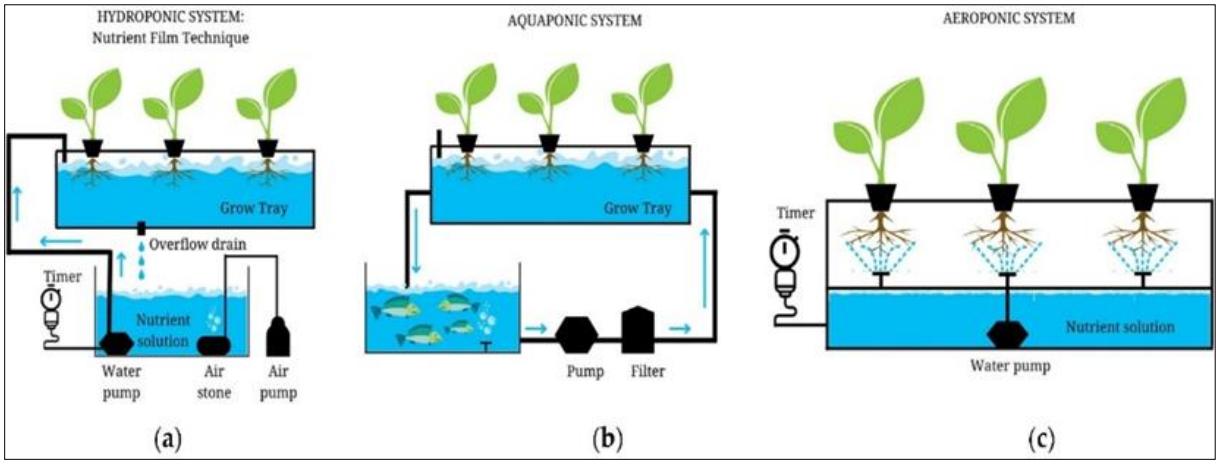

Fig 1: Basic forms of single-layer cultivation techniques [5]. Hydroponic (a), aquaponic (b), and aeroponic (c)

Mulberry Species

Mulberry is a multipurpose fruit that grows in temperate, subtropical, and tropical climates. It is a member of the moraceae family. There are more than 150 mulberry species in the world, but *M. alba, M. nigra,* and *M. rubra* have been identified having the most potential due to their highest level of medicinal qualities. Because of their remarkable therapeutic qualities, the different vegetative parts of mulberries are currently the focus of tremendous interest [6]. The fruits of mulberries contain different kinds of physicochemical materials that add to their pharmacological and nutritional value. Their flavor and stability are affected by the high concentrations of water, proteins, carbohydrates (mostly glucose and fructose), and organic acids such as citric and malic acids. Mulberries act as also a great source of bioactive substances with strong antioxidant qualities, such as anthocyanins, flavonoids, phenolic acids, and ascorbic acid. Different species and cultivars have different total phenolic and flavonoid contents, which have an immediate impact on their color intensity, antioxidant capacity, and possible health advantages. Their nutritional profile is further improved by the inclusion of minerals like potassium, calcium, magnesium, and iron [7].

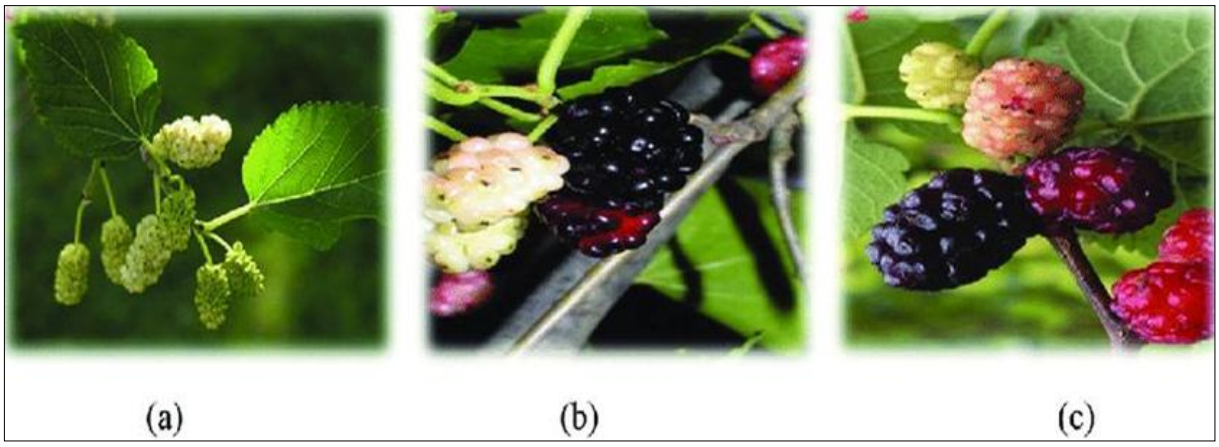

Fig 2: Different species of Mulberry fruit [8]. (a) *Morus alba*, (b) *Morus nigra*, and (c) *Morus rubra*

White mulberry *(M. alba)*

Other names for the *M. alba* plant include Malbari in Malayalam, Tutam in Sanskrit, and Tut in Hindi. This plant, which ranges in height from 4-5m, is classified as either a bush or a tree. The fruit of the *M. alba* plant is commonly used to treat anemia, exhaustion, and early graying of the hair. The plant is known for its numerous types of medicinal benefits in Chinese medicine. In addition to its fruit, all its parts have therapeutic uses for bronchitis, asthma, edema, coughing, etc. The indigenous system possesses anthelmintic, purgative, antimicrobial, provide diuretic qualities [9].

Red mulberry *(M. rubra)*

The words for fruit & red are *Morus* and rubra, respectively. Trees of this species can be Present in floodplains, prefers

damp and moist environments, with distinct plant parts employed for various medicinal purposes. For example, the Rappahannock community uses its juice applied externally to treat ringworm on the epidermis. Among the Cherokee, the bark was steeped in water, and the liquid consumed to eliminate intestinal worms, and the Meskwaki use its root bark to treat a variety of illnesses [10].

Black mulberry *(M. nigra)*

M. nigra is a plant species that grows naturally in moist, mild, and subtropical climates regions of Worldwide [11]. Among the most significant species in the *Morus* genus, its sensory evaluation shows that it contains woody, fresh scent physiognomies, as well as different flavors. The fruit's dark black color is caused by anthocyanins. Fortunately, this plant's berries, bark, and leaves all have therapeutic qualities. The berries are used to heal inflammation and blood loss. The outer layer is used to treat toothaches, and leaf tissues are used as an antidote. This plant is produced in many places without any special protection. Thankfully, it's extremely tolerant to pests and other pathogenic organisms, which means it may produce goods with high nutrient content that promote an ecologically friendly, organic, and healthy lifestyle [12]. In persons with diabetes mellitus, *M. nigra* leaves serve to increase pancreatic hormone in Europe [13].

Bioactive Constituents of Mulberry

High-value components found in mulberries include flavonoids, phenols, anthocyanins, and other bioactive substances that can be utilized as useful components in nutraceuticals. Polyphenol, bioflavonoids are present in it. Phenolics extracted from various mulberry species are shown to have a number of protective health effects, including anti-inflammatory, anti-diabetic, cholesterol-lowering, antioxidant, and anti-proliferative properties. Another common flavonoid found in mulberry fruit is anthocyanins, which give the fruit its inherent color and antioxidant qualities. Apart from providing color, anthocyanins have well-established pharmacological qualities and particular health-promoting traits, like anti-inflammatory, antioxidant, and anti-cancer effects, which help treat chronic illnesses. The main phenolic substances found in mulberries are rutin, 3,4,5-trihydroxybenzoic acid, and 3,4-dihydroxycinnamic acid. Black mulberries had increased levels of these polyphenols than white and red mulberries. In addition to these primary phenolic compounds, mulberries also contain smaller amounts of quercetin, hydroxycinnamic acids, phenolic acids, plant polyphenols, sringic acid, catechin. The three main anthocyanins found are chrysanthemin, kerin, callistephin in black mulberries were between 127.15 - 959.56 milligrams per gram, while 0.33 to 19.51 mg/g were found in other mulberries. For kerin, callistephin black mulberries had the highest proportion, at 573.1 and 28.8 mg/g, while white mulberries had the least values, at 0.19 to 8.65 and 0.04 to 0.51 mg/g. Other anthocyanins, such as pelargonidin-3-O-rutinoside, are also present, although in smaller quantities [14].

Polysaccharides

Polysaccharides are biomolecules with high levels of biological activity, composed of more than ten monosaccharide units connected by glycosidic linkages. They serve as the main source of energy storage. Polysaccharides from mulberries exhibit significant reducing power and hydroxyl radical scavenging ability, with mulberries containing more than 10% polysaccharides [15]. Currently, the proportions of protein and carbohydrates in mulberries are approximately 0.79% and 84.67%, respectively. The major components of these polysaccharides include galactose (25.75%), glucose (19.18%), galacturonic acid (13.03%), and mannose (10.31%) [16]. Three varieties of mulberry-derived polysaccharides, namely Mulberry Fruit Powder- 1,2,3 respectively and arabinose-based galacturonic acid, mannose, xylose, glucose, and galactose. Among them, mulberry fruit powder-1 has the greatest molecular weight than mulberry fruit powder-2, whereas mulberry fruit powder-2 shows greatest capacity to decrease how fast and how much lipid is digested, making it a potentially useful supplement in high-fat foods to support health. The primary linkages in these polysaccharides are mannans connected by (1→3) bonds, with galactose and glucose residues branching at the O-6 position of mannose residues [17].

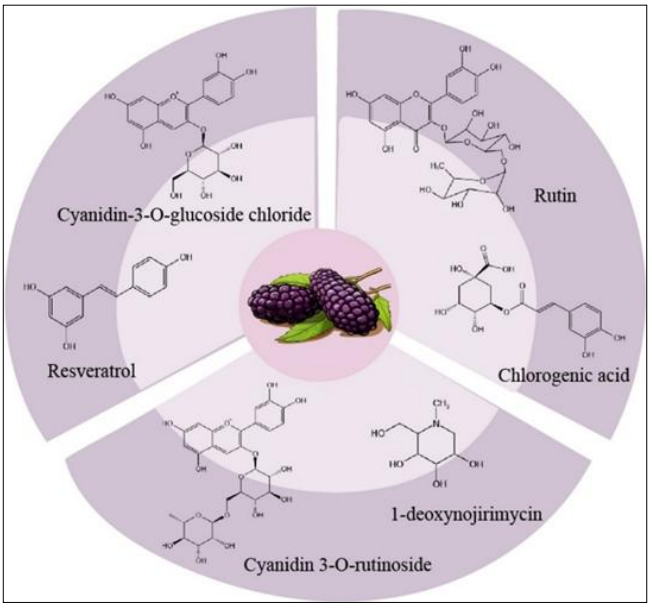

Fig 3: Bioactive constituents from Mulberry fruit [3].

Polyphenols

Polyphenolic compounds promote benefits chiefly attributed to their antioxidant activity. They function as radical-scavenging and metal-binding chelators, thereby exerting diverse biological effects. Consequently, determining the polyphenol content in plant extracts is essential for evaluating their role in antioxidant potential. In the present study, mulberry fruit powder was subjected to ultrasonic-assisted ethanol extraction. Following centrifugation and filtration to eliminate lipids, fatty acids and total polyphenols. Polyphenolic content of fruit is considerably higher than that of many other berries [18].

Alkaloids

Alkaloid substances extracted from mulberry trees frequently coexist with betaine, amino acids, and other substances, and are categorized as glycosides of polyhydroxy alkaloids. Polyhydroxy-pyrrolidine, polyhydroxypiperidine, and polyhydroxytropane are the three main categories into which they fall. One such

compound is 1-deoxynojirimycin a special alkaloid that is only present in the genus *Morus*. Only mulberry twigs, leaves, and fruits contain it [19]. It has been established that the primary bioactive ingredient in mulberries for the treatment of diabetes is 1-deoxynojirimycin, and its alkylated derivatives are employed as therapeutic drugs in clinical settings [20].

Flavonoids

Fruits' color and scent are attributed to flavonoids, which are also essential for improving pollinator productivity and fruit quality. A branched pathway produces both colorless compounds (flavonols) and pigmented compounds (anthocyanins, a key group of flavonoids) when flavonoids are synthesized. The flavonoid group also includes flavanol [21].

Anthocyanin compounds

Anthocyanins, a type of flavonoid compound, give blossoms and berries their different colours. It has antioxidant activity; it is being used in a variety of studies [22]. Mulberry species are primarily composed of monomeric anthocyanins, according to reports. The study also revealed that the largest concentrations of total monomeric anthocyanins are found in black mulberry (*M. nigra)* species, which are superior to russian mulberry (*M. alba*) and other barriers in addition [23].

Pharmacological Action of Mulberry

Antioxidant

Natural free radical scavengers found in mulberries can neutralize different types of free radicals, such as superoxide anions, hydrogen peroxide, alkyl radicals, and hydroxyl radicals. Several researchers have extensively studied the pharmacological potential of mice and have shown that mulberry extract dramatically raises hyaluronic acid and moisture levels, and hydroxyproline content in the skin, lowers levels of AGEs, and lessens damage brought on by oxidative stress. These results imply that mulberries have significant cosmetic benefits [24]. Earlier studies have provided substantial evidence supporting the role of mulberries in antioxidant capacity, and phenolic substance content is positively correlated. Particularly, resveratrol and resveratrol glucoside have demonstrated strong antioxidant properties by improving the functions of glutathione, catalase, and superoxide dismutase, while reducing the production of ROS. Human hepatocellular carcinoma cells are successfully shielded from oxidative damage by this mechanism [25]. Mulberry fruit's antioxidant capacity is inextricably related to its quality; it is a key indicator of quality that aids in the fruit's response to the outside stressors & lessens quality decline brought with them. Mulberry fruit has a high total phenol and flavonoid content, which adds to its strong antioxidant properties. Previous investigations demonstrated that it is crucial to keep the antioxidative activity to reduce the phenolic compounds' deterioration over time in barriers. Also, there is a strong link between stress resistance as well as fruit's antioxidative activity. Fruit's antioxidant capacity can help it fend off harmful Fungi [26].

Anticancer

It is becoming increasingly clear that eating a diet having significant polyphenol content likely reduces the incidence of malignant tumors. Several studies have reported similar findings, indicating that a thorough analysis of polyphenolic constituents and their chemopreventive potential has recently demonstrated substantial anticancer and other health-promoting benefits. Numerous investigations using preclinical models, clinical studies, and cultured cell systems have demonstrated the protective function of dietary polyphenolic compounds against various cancers. Their capacity to halt or reverse carcinogenesis is one of several mechanistic explanations for their chemopreventive effectiveness. Act on cell signaling molecules that are implicated in the development of *in vivo* respreads related to cancer, or their ability to halt or counteract the cancer's development stage [27]. Cyanidin-3-O-glucoside, Cyanidin-3-O-rutinoside mulberry anthocyanins, demonstrated a suppressive effect on the invasion as well as migration of a lung cancer cells of human origin by controlling Nuclear Factor kappa-light-chain-enhancer of activated B cells and Cellular Jun activation. Earlier studies have provided substantial evidence supporting the role of mulberry fruit extracts cause human glioma cells to die by producing mitochondrial pathway dependent on ROS and the growth of glial tumor through the triggering of apoptosis and the inhibition of tumor cell growth. By focusing on the c-jun and p38/p53 pathways, mulberry anthocyanin caused apoptosis and suppressed the growth and survival from gastric tumor cells both *in vivo* and *in vitro*. Several researchers have extensively studied the B16-F1 could be mediated by monocyte-derived macrophages cell metastasis through the inhibition activities of MMP-2 and MMP-9 pathway of Ras/phosphoinositide 3-kinase (PI3K) signaling pathway. Additionally, C57BL/6 mice were given MACs concurrently with an injection of B16-F1 melanoma cells were injected into the right groin. Hematoxylin and eosin staining was performed. Immunohistochemistry stain demonstrated that the monocyte-derived macrophages cell prevented B16-F1 cells from metastasizing *in vivo* [28].

Several studies have reported that mulberry extract influences cancer development through multiple mechanisms. Numerous investigations have summarized the effects of mulberry extract on immune regulation, anti-angiogenesis, and tumor microenvironment modulation, although several of these findings have been completed but not yet published. The multidrug resistance phenomenon remains a major obstacle in anticancer chemotherapy, and traditional Chinese medicines have long been recognized for their role in multi-drug therapeutic approaches [29]. According to earlier findings, human fetal fibroblast cells treated with single anticancer drugs and various concentrations of mulberry extract combined with doxorubicin showed that the IC_{50} values of doxorubicin alone were significantly lower than those observed in the combinational treatments [30]. Furthermore, it has been documented that mulberry extract may function as a chemopreventive agent by inhibiting angiogenesis, suppressing tissue metastasis, preventing apoptosis evasion, and reducing insensitivity to antigrowth signals. Additionally, previous reports have emphasized the potential application of mulberry extract in combination drug therapy by modulating the immune status of the tumor microenvironment [31].

Lipid lowering Effect

Mulberry's ability to lower cholesterol has been widely studied mostly *in vivo* using models of mice, rats, and

hamsters. As per recent study, used mice in a controlled clinical trial to clarify relationship between mulberry and its lipid-reducing benefits. Any significant decrease in TG levels and an increase in high-density lipoprotein cholesterol above control levels were shown after a powder [32]. At the same time, other researchers confirmed that moderate and high doses of mulberry fruit polysaccharides (500 mg/kg and 800 mg/kg) had a lipid-modulating effect. After administering mulberry fruit polysaccharides, mice showed marked decreases in circulating lipid and lipoprotein levels. In contrast to the control model group, which demonstrated notable reductions in high-density lipoprotein cholesterol and increases in triacylglycerol levels. In contrast to the typical control group [33]. According to recent study showed that this mulberry fruit therapy for six weeks elicited significant changes in high-density lipoprotein cholesterol were not elicited by ethanol extract. Levels in a high-fat diet, even though noticeable improvements were noted in the group receiving a lower dose of mulberry extract. Triglyceride levels in plasma stayed largely unchanged throughout the various treatment groups that received a high dose of mulberry ethanol extract show showing reduced levels compared to the group that followed a high-fat diet [34].

The effectiveness of mulberry water extracts was highlighted in recent research. Mulberry water extracts in carefully *in vivo* investigation of serum lipid profiles. 1% and 2% Mulberry water extracts doses completely offset the increase in triglycerides brought on by a diet heavy in fat, at the same time Raising HDL levels [35]. Wattanathorn and colleagues confirmed these results, proving that different dosages of mulberry fruit extract in capsules produced notable drops in cholesterol and triglycerides, while concurrently raising HDL cholesterol levels compared to rats that were only given a diet rich in carbohydrates and fats [36]. Recent data showed that the impact of mulberry on the lipid profile of the serum. There were no appreciable differences between the groups that underwent a 4-week regular diet with freeze-dried mulberry powder added, except for a significant 17.6% drop in TG levels of the high-fat diet group supplemented with5% mulberry fruit powder. On the other hand, the 10% mulberry fruit powder added to a high-fat diet group showed a noticeable 33.1 percent enhancement of high-density lipoprotein cholesterol and 35.7% reductions triglycerides [37].

Hepatoprotective

The body's most metabolically adaptable organ is the liver. Controlling protein synthesis and secretion, glycogen storage, metabolism, and detoxification [38]. Earlier studies have provided substantial evidence supporting the role of bioactive substances in mulberry water extracts reduce liver damage, with early findings showing a decrease in liver fibrosis. This hepatoprotective effect might also be connected to the control of lipid metabolism and fatty liver degeneration.as the inhibition of inflammatory reactions and oxidative stress [39]. Earlier studies have demonstrated that micro RNAs which regulate gene expression, play a crucial role in modulating physiological and pathological processes in the liver by influencing mRNA expression and translation efficiency" [40]. Additionally, Wei46 found that by triggering the nuclear factor erythroid signaling pathway, mulberry water extracts prevent liver oxidative stress, ferroptosis, and inflammation, providing substantial protection against fibrosis of the liver caused by CCl_4. Interestingly, studies have shown that by increasing protein levels, white mulberry extract can prevent apoptosis brought on by iron overload of polymerase, and caspase-3. Additionally, this treatment reduces liver damage by influencing the levels of MAPKs like extracellular signal-regulated kinase, c-Jun N-terminal kinase, p38 mitogen-activated protein kinase. As well as fibrosis. Furthermore, mulberroside exhibits significant promise in halting the progression in hepatic fibrosis by blocking stimulation of macrophages and a decrease in pro-inflammatory factor production [41].

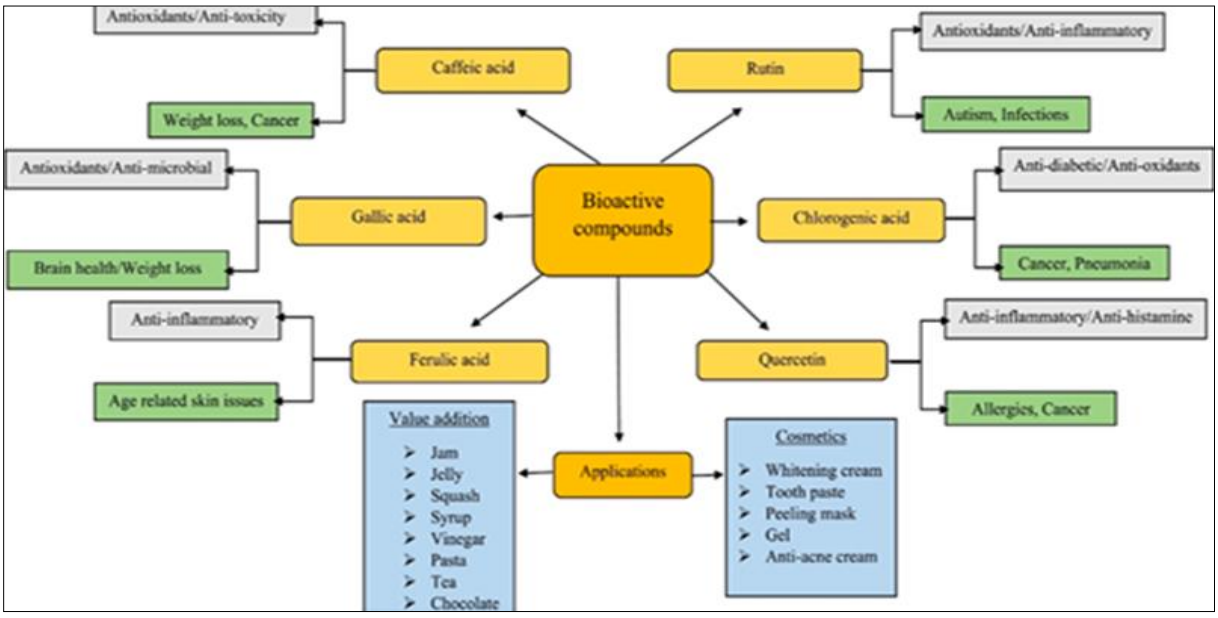

Fig 4: Bioactive constituents from Mulberry fruit and its uses [14].

Antimicrobial

Several studies have reported that the rise of antimicrobial resistance poses a major global public health concern, thereby emphasizing the essential role of medicinal plants in combating bacterial infections. Previous investigations have shown that berry water extracts exhibit strong antibacterial

activity against Vibrio cholerae, Salmonella typhi, Shigella dysenteriae, Staphylococcus aureus, and Escherichia coli. Earlier reports have further demonstrated through time-kill and adhesion inhibition assays that berry water extracts can suppress bacterial growth and prevent harmful intestinal pathogens from adhering to intestinal epithelial cells. These findings have highlighted the therapeutic importance of mulberries, confirming their significant antimicrobial potential in managing gastrointestinal infections [42].

Anti-obesity

Several studies have reported that obesity raises the risk of diabetes, cancer, and cardiovascular disease; it is turning into a major issue in modern times. Mulberry fruits have shown the most effective anti-obesity properties in a number of innovative studies. Demonstrated that when mulberry fruit powder was given to rats given fat, the serum and hepatic triglycerides, Total cholesterol, LDL, and atherogenic index were reduced. Furthermore, serum HDL cholesterol increased considerably [43]. An independent group's lower cholesterol level significantly decreased after hypercholesterolemic individuals were given 40 g of a six-week intervention with freeze-dried mulberry fruits. According to these studies, mulberry fruits have the potential to be used as therapeutic agents to lower hyperlipidemia [44]. Treatment with a fermented *M. alba* (mulberry) leaf extract significantly inhibited weight gain, reduced fat cell size, lowered serum triglycerides and Low-Density Lipoprotein, increased High-Density Lipoprotein, and decreased accumulation of fat droplets in the liver of high-fat diet–induced obese subjects' mice [45].

Value-added goods made from various mulberry varieties

Mulberry fruits have thin flesh and over 70% water content, making them extremely perishable [46]. Mulberry leaves are not used as food because their many nutritional benefits are intended to enhance the foliage, which aids in the rearing of silkworms. All things considered, mulberries are the best antioxidant source, particularly phenolic compounds and flavonoids. Which may be applied to this creation from different products with added value [47].

Table 1: Use of various Mulberry fruit [14].

variety	Part used	Product made
Black mulberry	Black mulberry juice	Food colorants
White mulberry	White mulberry juice	Jelly
White mulberry	Dry fruit	Pastry
Black mulberry	Dry fruit	Chocolate
Black mulberry	Fruit extract	Pasta
Red mulberry	Red mulberry juice	Food colorants in yogurt
White mulberry	Fruit extract	Vinegar
White mulberry	Fruit paste	Cup cake

Applications of Mulberry

Mulberries in natural product

Their rich phytochemical content, mulberries known for their delicious flavor, thin skins, and popularity as a fruit, have long been used as functional foods. Fresh mulberries must be processed into a variety of goods, including dried fruits, jams, health yogurts, mulberry juice, mulberry vinegar, mulberry wine, and others, because they are not storage-resistant. The bioavailability and bioaccessibility of mulberries polyphenols and other bioactive ingredients are critical to their effectiveness. For example, mulberry syrup, which is high in anthocyanins, flavonoids, and phenols, keeps its component levels steady for up to 30 days [48]. Fruit pomace's phenolic chemicals have the ability to attach to cell walls during fermentation, feeing them from the matrix and increasing their bioaccessibility. Therefore, utilizing the fermentative release of free phenolic compounds by lactic acid bacteria and incorporating phenolic-rich fruit pomace into the yogurt production process increase the antioxidant activity of the final product [49]. Mulberry wine maximizes the use of mulberry fruits by demonstrating improved free radical scavenging capabilities [50]. Furthermore, it has been demonstrated that mulberry vinegar, which is made from fermented mulberries, lowers pro-inflammatory factors and stops neuroinflammation via modulating the NF-κB pathway and neuroglial activity [51]. The food industry reduces the loss of antioxidants and improves the quality of the finished product by processing mulberry juice and jam. Mulberry jelly has been transformed into possible functional jelly formulations by including prebiotics like agar-agar and inulin as gelling agent's antioxidant qualities [52].

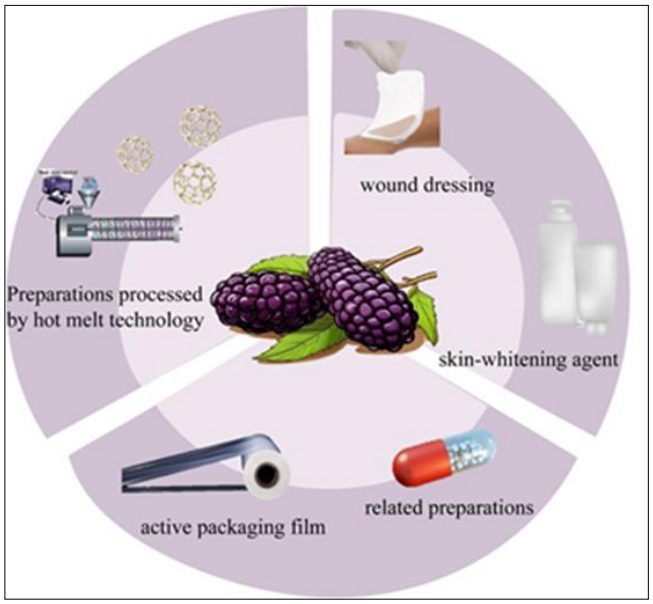

Fig 5: Application of mulberry fruit [3].

Mulberries in Biomaterials

From "artificial non-living materials that integrate with the living body" to "materials used for the diagnosis, treatment, rehabilitation, and prevention of diseases, as well as for replacing, enhancing, or restoring the function of biological tissues and organs when in contact with biological systems," the definition of biomaterials, also known as biomedical materials, has changed. Mulberries are praised for their divine virtues and wide range of applications in human existence in the compendium of materia medica, a classic reference on Eastern medicine. Mulberries, a traditional Chinese medicine with a similar origin to food, are frequently used as supplemental treatments for cancer, anemia, diabetes, high blood pressure, and high cholesterol, coronary cardiac disease, and neurasthenia. The potential of natural products as biomaterials has attracted a lot of research interest in addition to these medical applications. Numerous anticancer drugs utilized in clinical settings are derived from plants. Recent research has shown that silk fibroin, a protein derived from silkworms, can be

successfully used as a drug carrier to accomplish prolonged or controlled drug release as well as targeted delivery of cytotoxic drugs to different cancer cell types [53]. Successfully created an active food packaging film by adding lauroyl arginate and mulberry anthocyanins to a polyvinyl alcohol/tapioca starch matrix as colorants and antimicrobials. This film can prolong the storage life of packaged food and track changes in its quality. Nevertheless, antimicrobial polymer technologies are still required despite the several established methods for coating antimicrobial drug delivery devices [54]. Technologies for antibacterial polymers are still required. By adding antimicrobial compounds to polymer matrices, new packaging materials can more successfully inhibit the activity of microbial foodborne pathogens and target bacteria, increasing the storage life of a variety of foods and decreasing food waste [55]. New therapeutic alternatives for wound areas are made possible by the mixing of natural and synthetic polymers with plant-based chemicals. Because of their potent anti-inflammatory qualities, polyphenolic chemicals found in mulberries can be quite effective at reducing microbial infections and hastening the healing of wounds. Mulberries can also be used as whitening agents because they have antioxidant properties and hinder the creation of melanin [56].

Result and Discussion

Mulberries (*Morus* spp.) are widely used functional fruits in tropical, subtropical and temperate regions. Have attracted scientific attention for their high nutritional value and diversity of bioactive compounds. Mulberries are famous for their powerful antioxidant, anti-inflammatory, antidiabetic, anticancer, hepatoprotective, neuroprotective and cardioprotective properties. They have been used for thousands of years in Ayurvedic, Chinese and Korean medicine. Mulberries especially offer vitamins: C, E, K and B-complex, as well as minerals: iron, calcium, potassium and magnesium; fibers; proteins and amino acids all because of its essential content. Black Mulberries are generally considered to have the highest antioxidant levels as they contain many phenolic compounds and flavonoids, such as anthocyanins, quercetin, rutin, kaempferol and morin. One of the effective substances used in curing diabetes is 1-deoxynojirimycin that inhibits the degradation of carbohydrates and keeps blood sugar stable. Other bioactive compounds aid in cardioprotection, lipidaemia modulation, inflammation regulation, and oxidative stress reduction. Mulberries also have anticancer properties with their ability to prevent DNA damage and induce apoptosis in malignant cells. Their antioxidants could protect against neurodegenerative diseases, safeguard brain tissue, improve cognition and support liver function. It is rich in fiber which is good for the gut, digestion and weight control. Mulberries also enhance blood circulation, slow down the aging process, and promote collagen all good for both skin and hair.

Future Prospects

Mulberries are becoming increasingly important in food and health industries because of their rich nutrient and antioxidant profile. They offer a lot of scope for creating new functional foods things like enriched drinks, nutraceutical gummies, detox blends, and even natural sweeteners. Their clean, natural composition makes them attractive for companies trying to develop “clean-label” products. On the medicinal and pharmaceutical side, some sites of components from mulberry trees that fit partially or all these therapeutic properties include anthocyanins, DNJ and resveratrol. There are also studies that suggest they may be useful for managing diabetes, promoting heart health and protecting the brain, and even demonstrate anticancer benefits. Possibly with more clinical research, standard mulberry-based treatments or supplements will eventually be established. And also, there is an increasing demand for mulberry plants improvement. Found in mulberries such a help with diabetes manage potential. With more clinical research, it is possible modern tools, including advanced breeding methods and CRISPR, could help produce varieties with higher anthocyanin levels, better nutritional value, greater yield, and stronger resistance to environmental stress. Because mulberries naturally contain strong pigments, they can be used as natural food colorants in bakery items, dairy products, sweets, and beverages.

Conclusion

Mulberries (*Morus* spp.) are nutrient-rich fruits that contain a variety of beneficial compounds, including phenolics, anthocyanins, alkaloids, and polysaccharides. Studies have shown that these fruits have strong antioxidant, antidiabetic, anticancer, liver-protective, antibacterial, and anti-obesity effects 1-Deoxynojirimycin. Another mechanism of substances like DNJ is blocking carbohydrate digestive enzymes to regulate blood glucose levels, and the treatment of diabetes. It has also proven that bioactive anthocyanins such as cyanidin-3-glucoside and cyanidin-3-rutinoside can induce apoptosis and arrest the growth of cancer cells, representing natural anticancer drugs. Mulberry also exhibits hepatoprotective effects through decreasing inflammation and hepatic fibrosis by modulating the oxidative and inflammatory pathways. These byproducts are employed in functional foods and added value products, for example vinegar, marmalades and juices that maintain their bioactive and antioxidant properties as well as medicinal uses. Due to their antibacterial and biocompatible nature, many of the recent advances have studied their applications in biomaterials and active packaging. After all, mulberries are an army knife of wellness. Importance of underutilized medicinal crops in pharmaceutical, biomedical and nutraceutical industries may be enhanced with further investigation on their modes of action, safety, efficacy.

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