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A comprehensive assessment of the nutritional, phytochemical, volatile components and utilization of Himalayan bayberry as a potential ethnic fruit crop

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Abstract

Myrica esculenta is also known as Kaiphal or Box Myrtle, widely grown in China, Japan, Taiwan, South Africa, Australia, North America, Nepal, Ethiopia, Brazil, and India. The fruit is known to contain high contents of diverse classes of phytochemical compounds including tannins, sugars, and vitamin C, flavonoids, phenolic acids, triterpenoids, alkaloids, tannins, saponins, and essential oils, which are applied to treat various human and livestock health ailments. Among all, the principal compounds present in the fruits are hydroxybenzoic acid, gallic acid, p-coumaric acid, chlorogenic acid and myricetin. However, high moisture content and delicate texture limits its shelf life to 3 days at 20–22 °C and 7–10 days at refrigerated temperature. This review paper presents a preview of the various prospective solutions available for shelf life extension and consumption of this fruits and its by-products. The review also highlights its strong pharmacological activities including antimicrobial, chemo preventive, hepatoprotective, anti-diabetic, anti-inflammatory, antioxidant, anti-allergic, antidiarrheal, anticancer, anti-asthma, and antifungal properties. Various parts of *M. esculenta* has been studied for their potential use in ayurvedic medicines owning to their nutritious and therapeutic properties. The outer bark of the plant and its flowers possess carminative, disinfectant and astringent properties. Its utilization in the treatment of cough, ulcers, inflammation, piles, acute diarrhoea, opthalamia, cancerous tumours and asthma has also been addressed multiple times in the literature. Food processing technologies, such as freezing, drying, juicing, utilization for wine and vinegar have been largely employed to extend its utilization in daily meals. Extraction of its bioactives and essential oil altogether extends its application in the pharmaceutical sector. However, more intensive biological research or clinical interventions are required to examine the potential health benefits of *M. esculenta* plant and its various products so as to ensure its availability to the future generations.

Keywords Ethnic crop, Nutrition, Phytochemical properties, Health benefits

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1 Introduction

Myrica esculenta is also known as "Box Myrtle or Kaiphal, there are about 97 species of the genus Myrica, having small trees (20–25 feet height) and aromatic shrubs which are mainly found in subtropical regions of the world. Plants of this genus are widely distributed around China, Japan, Taiwan, South Africa, Australia, North America, Nepal, Ethiopia, Brazil, and India [35]. *M. esculenta* is also pronounced as Hairy Bayberry which found in the Indian subcontinent region. In India, among the 670 species of edible plants known for their nutritional and health benefits present in the Himalayan region, *M. esculenta* is the principal one. This species is majorly present in the subtropical regions starting from the Himalayas to Assam thriving at attitudes of 900–1200 m above sea level. Different varieties are found in the neighbouring countries Nepal and China as well. Myrica tress are known for their resilience and ability to grow in nitrogen poor soils and often found grown with pine and oak. Different varieties of Myrica are distributed across various nations, for example, *M. rubra* is predominant in China, Japan, Korea and Taiwan and the variant of it M. rubra var. microphylla is present only in China. *M. acuminanta*, *M. nagi* and *M. serrata* are principally found in India and Nepal. The predominant variety of *Myricaceae* family in Bhutan and Nepal and in some parts of north eastern India is *M. salicifolia*, whereas in Northern Europe and Canada has *M. gale* available, highlighting its adaptability to various climates and regions.

The fruit of *M. esculenta* is a small, round berry, typically green when unripe and turning purplish-black upon maturity. The popularity of the fruit was judged based on the revenue earned by people selling it, which was 1,400,000 rupees per season [9, 72]. The species has several applications, including fuelwood, fodder, medicine and crude oil. Its fruits are known for their ravishing taste because of higher sugars, tannins, and vitamin C contents. Many illnesses such as asthma, cough, ulcers, inflammation, bronchitis, fever, diarrhea, and problems in the ear, nose, and throat can be treated with *M. esculenta* berries and their various plant parts. It has several medicinal uses in the ayurvedic pharmacopeia mainly because it has some therapeutic and high pharmacological uses. The outer bark of the plant is known to possess carminative, disinfectant and astringent properties. Literature outlines the effectiveness of the *M. esculenta* bark in the treatment of numerous ailments, such as aching ears, diarrhoea, inflammatory disorders, throat pain, cancerous tumors, iron deficiency, ulcerations and eye sight problems [32, 55]. Oil extracted from its flower petal were found to be beneficial in diarrhoea, inflammatory disorders and paralysis [41]. The waxy substance produced by its berries have been used for the treatment of sores. *M. esculenta*, recognized for its Ayurvedic significance, is utilized by numerous indigenous groups for the healing benefits derived from its bark, roots, fruits, leaves, and flowers [48]. The plant is also used in treating skin diseases [16, 31, 38, 79]. Moreover, it is applied in skin use to relieve itchiness and rashes thus enhancing the health of the skin. Even though modern medicines are advanced, these practices remain valued, and there lies cultural and medicinal significance behind *M. esculenta*.

Nevertheless, *M. esculenta* berries possess limited shelf life and cannot be stored beyond 3 days under uncontrolled temperature thus for prolonged utilization of *M. esculenta* berries processing of it to other forms is highly required. Various technologies for processing berries into dried powdered form, juice, wine, vinegar, jam and preservation through additives are available to attain its long term consumption. In conclusion, Myrica esculenta is a nutritionally rich and phytochemically dense but underutilized

fruit with unrealized potential for value addition via systematic processing interventions. More advancements in post-harvest handling, pulp processing, drying, and extraction techniques will open avenues for its application in functional foods and beverages, while the valorization of by-products such as peels, kernel, and pomace can attract opportunities for the recovery of phenolics, antioxidants, and dietary fiber. Regardless of these benefits, large-scale processing and commercialization are restricted by seasonal availability, high perishability, and the lack of standardized processing technologies. Addressing these challenges through targeted research, process optimization, shelf-life enhancement, and industrial scalability will be critical for unlocking the full potential of *M. esculenta* and its by-products in the food industry.

2 Morphology of *M. esculenta* fruit

M. esculenta grows from 900 to 2100 m in altitude, throughout the Himalayan states of India, which includes separate male and female plants in different places like Jammu & Kashmir, Uttarakhand, Himachal Pradesh, Assam, and Khasi, Naga, Jaintia, and Lushi Hills. Morphological studies categorize the plant as a medium to large woody tree, growing to heights of 12 to 15 m with a trunk diameter of 92.5 cm. The outer bark is grayish-dark and rough with vertical wrinkles, while the inner bark is smooth and dark brown [77]. The bark is tough when broken, has a bitter flavor, and releases a nauseating smell. Pistillate flowers are tiny, attached directly to the stem, and stand alone with bracts. Sepals and petals are almost non-existent. The inflorescence forms a catkin, about 4.2 cm long, located in the axils of leaves, comprising around 25 flowers with a slender style (Fig. 2). In contrast, the inflorescence of staminate flowers is a compound raceme [28]. The fruiting season starts in the first week of May and continues for the entire month [32]. The tree produces a drupe fruit that is red to dark brown, ellipsoidal or oval, and approximately 2–7 mm in diameter (Fig. 3). The fruit has a sweet and sour taste and contains an ovoid, smooth, light brown seed about 1–6 mm in diameter with an oily taste. Fruits appear like deep red raspberries, lacking pulp and one large seed in the center. Fruits are acidic when ripened properly and unripened ones have tangy flavor, available for a brief period.

3 Nutritional composition of *M. esculenta*

The fruit of *M. esculenta* are small berries with 4–5 mm in size. The color of berry depends upon the presence of anthocyanins, and varies from purple to red. Bhatt et al., [10] study shows that the *M. esculenta* contains total sugars of 2.18% -7.68%, reducing sugars of 0.83%-3.57%, with a 72.38% of moisture content and the fruit pulp consist of crude fat of 4.93%, protein of 9.62%, carbohydrates of 78.03%, and fiber of 72.38%, which provides of 395.04 kcal per 100 g of fruits. *M. esculenta* is packed with minerals as mentioned in Table 1. *M. esculenta* mainly originated from India and the chemical analysis of *M. esculenta* fruit shows the presence of ascorbic acids (0.071 mg/100 g DW), phenolics (34.95 mg/g FW), flavonoids (30.16 to 44.55 mg/100 g FW), saponins (8.27% FW), and alkaloids (7.48% FW). Catechin, trans-cinnamic acid, chlorogenic acid, p-coumaric acid, gallic acid, hydroxybenzoic acid, caffeic acid, myricetin, and ellagic acid are the major compounds in the fruits [10]. Myricetin (3,5,7- trihydroxy-2- (3,4,5- trihydroxyphenyl)-4-chromenone) a bioactive flavone, derived from *M. esculenta* berries is known for its potent free radical scavenging activities, cancer preventive, hypoglycemic and

Table 1 Mineral profile of *Myrica esculenta* fruits

Minerals	Fruit (mg/100 g)
Calcium	4.63 ± 0.06
Potassium	7.75 ± 0.11
Sodium	0.81 ± 0.013
Phosphorous	0.24 ± 0.25
Magnesium	8.4 ± 0.20
Manganese	0.032 ± 0.0001
Iron	0.404 ± 0.0021
Zinc	0.216 ± 0.0016
Copper	0.004 ± 0.0002

anti-inflammatory qualities. Additionally, *M. esculenta* contains numerous vital nutrients including antioxidant components, iron, retinol, L-ascorbic acid, tocopherol, thiamine and other B-complex vitamins, especially oligomeric proanthocyanindins [28] Table 2 and 3.

4 Phytoconstituents of *M. esculenta* plant parts

Many studies revealed that the flavanoids, anthocyanins, and phenolics are the bioactive compounds, which is mostly present in *M. esculenta* fruits [11]. These pharmacologically active compounds are also found in other parts of the plant, including the bark, leaves, stem, fruits, and fine branches, which have different pharmacological effects [35, 78]. Persual of Table 2, clearly presents the bioactives present in different parts of *M. esculenta* plant. The plant contains volatile compounds such as, alkaloids, glycosides, diarylheptanoids, ionones, steroids, saponins, and triterpenoids. The polyphenolic compound levels decrease as the fruits ripen; some of the compounds may even be lost completely in fully ripened fruits [8]. Phenolic acids such as caffeic acid and gallic acid increase the plant's antioxidant and anti-inflammatory properties, thereby increasing its medicinal value. Some of the important flavonoids, myricetin, quercetin, and kaempferol are potent antioxidants that scavenge free radicals and reduce oxidative stress. According to Bhatt et al., [10], chemical analysis of fruit of *M. esculenta* reported to contain ascorbic acid (0.071 mg/100 g DW), phenolics (34.95 mg/g FW), flavonoids (30.16 to 44.55 mg/100 g FW), saponins (8.27% FW), and alkaloids (7.48% FW). The major compounds isolated from *M. esculenta* include catechin, trans-cinnamic acid, chlorogenic acid, p-coumaric acid, gallic acid, hydroxybenzoic acid, caffeic acid, myricetin, and ellagic acid [10]. In general, these phenolic compounds are known to have antioxidant capacities that prevent oxidative harm to cells [4]. This makes *M. esculenta* a rich source of natural antioxidants, hence likely to protect organisms against oxidative stress and free radicals damage, which shows its utility in the treatment of many diseases. Rawat et al., [65] reported that the antioxidant activities of *M. esculenta* measured 1.84 mM in ABTS, 2.55 mM in DPPH, and 2.97 mm/AAE/100 g FW. It consists of rich compounds comprising of proanthocyanidin, tannins, glycosides, myricanol, myricanone, epigallocatechin 3-O-gallate, and its two prodelphinidin dimers: epigallocatechin – (4β → 8) epigallocatechin 3-O-gallate and 3-O-galloylepigallocatechin- (-4β → 8 epigallocatechin 3 -gallate, besides having hydrolysable tannin castalagin and myresculoside. Sood and Shri, [77]; also confirmed through their study that the M. esculenta berried contain numerous

Table 3 Biological and pharmacological potential of *Myrica esculenta* fruit and its by product

Health benefits	Matrix	Target organization	Dose frequency and concentration	Impact action	References
Anti inflammatory		Male Wister albino rats (carageenan induced inflammation) (250–300 g). Rats In vitro and in silico	Oral administration @ 100 and 200 mg/kg body weight. MNSBEE (400 mg/kg, p.o.) and diclofenac (5 mg/kg, p.o.) were given 30 min before carrageenan injection. 2 µL 230 and 320 C° 6.6018 psi pressure	Dose dependent inhibition was found with 26.51% and 27.51% reduction in the carageenan induced edema for 100 mg/kg and 200 mg/kg body weight of the rat. Similarly for histamine induced rat paw edema, dose dependent inhibition was observed with reduction of 22.55% and 26/0.82% when administered with 100 mg/kg and 200 mg/kg body weight respectively. Increased pain latency in acetic acid-induced writhing and hot plate tests in mice. Inhibited paw edema volume in carrageenan-induced paw edema. Reduced granuloma weight in the cotton pellet granulomamodel. These effects were observed at doses of 200 and 400 mg/kg when administered orally. The bark extract exhibited the highest antioxidant and anti-inflammatory activity compared to the root extract.	Patel et al. [60]. Patel et al. [59]. Shrivastava et al. [74].
Antidiabetic effect		Swiss albino mice Weighing 20–30 g and age of 8–12 weeks. Male wistar rats (3–4 months old)	Oral administration of 400 mg/kg fasted male rats 150 mg/kg, After 30 min of the STZ injection, the mice were given to feed. 300 mg/kg body weight-daily for 28 days 22 ± 2 °C RH 45 ± 5%.	Highest significant reduction in fasting blood glucose level (BGL) compared to diabetic control in STZ-induced diabetic mice model. The root extract and fractions of M. salicifolia exhibited significant antihyperglycemic, α-amylase inhibitory and antioxidant activity with no sign of toxicity. Treatment with M. esculenta (300 mg/kg) led to a statistically significant reduction in fasting blood glucose levels, with a maximum decrease. Approximately 35.1% observed on day 28 ($p < 0.01$). T2D rats showed significant signs of polyphagia and polydipsia, as evidenced by a marked increase ($p < 0.01$) in food and water intake compared to normal rats. T2D rats exhibited a ~ 0.3- fold reduction in HOMA beta score compared to normal rats, indicating a decrease in beta cell function.	Emiru et al. [21]. Dua et al. [19].
Antiulcer activity		Swiss albino mice weighing 25–30 gm and Wistar rats weighing 180–200 gm.	Dose concentration is 200, 400 mg/kg for 7 days.	Myrica nagi significantly reduced ulcer development in both the pylorus ligated and Aspirin-induced ulcer models. In the pylorus ligation model, both doses of Myrica nagi decreased the ulcer index, gastric volume, free acidity, and total acidity compared to the control group.	Zade et al. [88].
Anticancer activity		MIA PaCa-2 cell line	Concentration of 1 µg/ml for 48 h.	albumin-based nanoparticles loaded with plant extracts hold significant promise in cancer therapy. These nanoparticles exhibit excellent drug delivery capabilities and potent anticancer effects, all while minimizing side effects. By specifically targeting cancer cells, they offer a more selective and efficient approach compared to traditional chemotherapy.	Shukla et al. [75].

Table 2 (continued)

Health benefits	Matrix	Target organization	Dose frequency and concentration	Impact action	References
Anti allergic activity		Male wistar albino rats (egg albumin induced allergy test). Albino Wistar rats (male/female) Passive paw anaphylaxis	(250–300) Temperature of 22 ± 2 °C, and RH of 60 ± 5% for 12-hour light/dark cycle. Oral administration of Methanolic extract of leaves (CLA) 100 mg/kg Methanolic extract of fruits (CFA) 100 mg/kg Centrifuged at 1500 rpm and for 24 h	Dose-dependent shows better mast-cell protection ($p < 0.01$). Allergic symptoms are significantly reduced by prednisolone compared to the control group. Dose-dependent significant($p < 0.05$) shows the reduction of paw volume, which is compared to control in the methanolic extract of leaves and fruits. The fruit was more effective than the leaf extract in reducing paw volume Alkaloid, saponin, steroid, phenolic, flavonoid, and terpenoid are present in leaves. Phenolic compounds, sterols, carbohydrate, saponins, and flavonoids are present in fruit.	Parmar et al. [58]. .
Antipsychotic activity		Male albino rats	(150–200 g) 24 °C ± 2 (60–70%)	Reduce the apmorphine-induced sterotyphed behavior. Increase the symptoms of catalepsy (intensity of the symptoms) in a dose-dependent manner	Sapkota et al. [70].
Anti-diarrheal activity		Wistar Albino rats (weighing 150–180 g). Swiss Albino mice (23–25 g). Albino Wistar rats (weighing 150–200 g) of both sexes.	Dose concentration is 2000 mg/kg. Oral administration is 200 and 400 mg/kg body weight. Oral administration is 250, 500, 1000 mg/kg body weight.	Aqueous extract of stem bark of Myrica nagi (AENN) is effective in managing diarrhea and related problems, particularly at a higher dose of 500 mg/kg. The active compounds likely responsible for this effect are tannins, flavonoids, and terpenoids. Nonetheless, further studies are necessary to determine the precise mechanism behind this activity Dose dependent manner was observed with root bark extract of C. Africana in preventing castor oil-induced diarrhea and reducing intenstinal motility. A significant reduction in diarrheic drops was observed at 200 and 400 mg/kg doses. Loperamide achieved a more significant reduction in both fecal output and diarrheic drops compared to all doses of the extract ($P < 0.001$). The rats showed no mortality or visible signs of general weakness after receiving the extract at doses up to 6000 mg/kg. At doses of 250, 500, and 1000 mg/kg, the extract significantly reduced the number of wet feces ($p < 0.01$) to 12.20 ± 1.06, 7.00 ± 0.94, and 6.20 ± 0.58, respectively, compared to the control group (18.6 ± 0.74).	Kumar et al. [38]. Asrie et al. [5]. Meite et al. [51].

Table 2 Overview of secondary metabolites in *Myrica esculenta* fruit and its parts and their therapeutic significance

Plant parts	Bio-active compounds in *Myrica esculenta*	Significance	Refernc-es
Bark	Gallic acid Myricetin Tannins	It has antimicrobial properties, supports liver health, and has strong antioxidant effects. It functions as a potent antioxidant and anti-inflammatory agent, providing neuroprotective and anti-cancer advantages. Recognized for their astringent, anti-inflammatory, and wound-healing qualities, they are beneficial in treating skin infections and respiratory conditions.	Kabra et al. [35].
Leaves	Quercetin Kaempferol	Quercetin is renowned for its role in diabetes management, heart protection, and inflammation reduction. Additionally, it lowers oxidative stress and boosts immune function. An antioxidant known for its heart health benefits, inflammation reduction, and potential anti-cancer properties.	Bhatt et al. [12].
Fruit	Myricetin Anthocyanins Vitamin C	Promotes brain health and may possess anti-cancer properties. Antioxidants that promote cardiovascular health and provide anti-cancer benefits by reducing oxidative stress. Boosts immune function and acts as a potent antioxidant, supporting collagen synthesis and improving overall skin health.	Mallya et al. [48].
Roots	Tannins Phenolic Acids Saponins	Recognized for their ability to treat diarrhea, fight microbes, and act as astringents. Protect against oxidative damage, decrease inflammation, and enhance overall cellular health. Has the ability to regulate the immune system, fight against microbes, and potentially combat cancer.	Shukla et al. [75].
Flowers	Polyphenols Flavonoids	Powerful antioxidants that protect against UV damage, oxidative stress, and the signs of skin aging. Offer anti-inflammatory and antioxidant benefits, lowering the risk of chronic illnesses like heart disease and cancer.	Bhatt et al. [10].
Seed	Essential Oils Linoleic Acid	Exhibit anti-inflammatory, antimicrobial, and antioxidant effects. Crucial for heart health and enhances the skin's barrier, reducing inflammation and preventing moisture loss.	Lily et al. [64].

other phenolic compounds namely, isovanillin, 4-(hydroxymethyl) phenol, 3-hydroxybenzaldehyde, 4-methoxybenzoic acid, myricitrin myricetin-3-O-(3′′-Ogalloyl)-α-L-rhamnoside, flavone 3′,4′-dihydroxy-6-methoxy-7-O-α-L-rhamnopyranoside, (1→4)-α-L-rhamnopyranoside, myricitrin (myricetin 3-O-rhamnoside), Flavone 4′-hydroxy-3′,5,5′-trimethoxy-7-O-β-D-glucopyranosy), myricetin-3-O- (2′-Ogalloyl)-α-L galactopyranosideside, triterpene diol (3β,28-dihydroxytaraxerane), daucosterol, corchoionoside C, myrecetin 3-O-(2′-Ogalloyl)-α-L-rhamnopyranoside, (6 S,9R)-roseoside, β-sitosterol-β-D-glucopyranoside, β-rosasterol, myricanone, 3-epi-ursolic acid, 3-O-(E)-caffeoylursonic acid, 16bromomyricanol, 5-O-β-D-glucopyranosyl myricanol, 13-Oxomyricanol, 3β,12α,28,30-tetrahydroxytaraxeran-23- oic acid, lupeol, 3β,30-dihydroxy-taraxerane-23-oic acid, myricanol, 3β,28,30-trihydroxy- taraxara-23-oic acid, monoterpinoidal myresculoside (4-hydroxy-1,8-cineole 4-O-β- dapiofuranosyl (1→6)-β-Dglucopyranosie), oleanolic acid, Triterpinoidal glycosides: arjunglucoside, proanthocyanidin acetate, proanthocyanidin methyl-ether, Nerolidol, α-caryophyllene, α-cadinol, (1 S,2 S,4R)– 2-hydroxy-1,8-cineole β-D-glucopyranoside, linalool, palmitic acid, eudesmol acetate, n-Hexadecanol, ci cis-β-caryophellene, α-pinene, α-selinene, β-caryophyllene, n-pentadecanol, n-octadecanol, β-selinen, and various amino acids such as L-hydroxyproline, isoleucine, valine, 2-aminoburytic acid The bark was also reporte to contain rich in essential oil, which contains hexadecanol (25.2%), eudesmol

acetate (21.9%), palmitic acid (11.6%), cis-βcaryophyllene (8.7%), n-pentadecanol (7.7%), and n-octadecanol (7.6%). This bark has been reported to exhibit antimicrobial activity [1].

The leaves of *M. esculenta* contain flavonoid glycosides viz. flavones 4'hydroxy-3',5,5'-trimethoxy-7-O-β-D-glucopyranoside (1→4)—L-rhamnopyranoside and flavone 3',4'-dihydroxy-6-methoxy-7-O—L-rhamnopyranoside, apart from three known compounds as β-sitosterol, β-sitosterol-β-D-glucopyranoside, and quercetin Bamola et al., [6]. The myricetin confers anti-inflammatory, anticancer, and neuroprotective properties. The quercetin has reported antihistamine, anti-inflammatory properties, and kaempferol showed potential to decrease the predisposition towards chronic diseases using antioxidant and anti-inflammatory mechanism [40]. Tannins include ellagitannins and gallotannins that have astringent characteristics in the plant and are characterized with antimicrobial, anti-inflammatory, and anticancer activity, thus useful for gastrointestinal disorders. Triterpenoids, including betulinic acid and ursolic acid, provide various biological benefits. They can induce apoptosis in cancer cells and inhibit viral replication [39].

The volatile compounds such as eugenol and limonene are rich in essential oils of *M. esculenta*, which have antimicrobial and antioxidant properties and thus prove to be very useful in the treatment of respiratory and skin infections. The flower oil is tonic in nature, which is used for treating earaches, diarrhea, inflammation, and paralysis [32]. Phenolic and flavonoid levels are different in cultivars of *M. esculenta*. The physical and biochemical properties of the fruits might be associated with the population levels of *M. esculenta.* Such variations might help in finding appropriate sources for mass production by horticulture and forestry [65]. Fruits of *M. esculenta* are around 4–5 mm in size, while fruits of *M. rubra* are bigger, about 12–15 mm in size [27]. There is good information on the phenolic content and antioxidant properties of *M. rubra's* fruit extract, juice, jam, and residue. However, comparable data for *M. esculenta* were not available. Earlier reviews indicate that myricetin is primarily obtained from plant species of the *Myricaceae* family. It is a crucial component in various foods and is also used as a food additive because of its antioxidant properties, which help protect lipids from oxidative damage [71].

5 Pharmacological activities of *M. esculenta*

M. esculenta exhibits a wide array of pharmacological effects, including anti-inflammatory, antimicrobial, antioxidant, antifungal, antidiabetic, antiulcer, antiasthma, anxiolytic, hepatoprotective, chemo preventive, anticancer, wound healing activity, antihypertensive, and antiallergic [25]. Crude extracts of the plant parts were studied for their biological efficacy utilizing both in vitro and in vivo experimental models. The detailed biological and pharmacological activities associated with *M. esculenta* have been discussed in Table 3 and Fig. 3.

5.1 Antimicrobial potential

The term 'antimicrobial activity' refers to the compound that can destroy or inhibit microorganisms, such as viruses, protozoa, fungi, and bacteria [24]. *M. esculenta* essential oils exhibits antifungal activity due to their interaction with the microbial cells and interference with its vital functions. The essential oils may cause disruption of the

microbial cell membrane because they are lipophilic, and interact with the lipid bilayer of the microbial cells, causing structural changes, leakage of cellular components, and ultimately, death of the cell [20]. In addition, such essential oils contain compounds that inhibit the microbial enzymes vital to their survival. This includes inhibiting bacterial enzymes for cell wall formation or protein synthesis, which are essential for their cellular processes [54]. By doing this, these components can prevent microbes from causing infections and sustaining in host tissues [20]. Essential oils extracted from *M. esculenta* leaves revealed antimicrobial activity. In fact, the volatile components must have been responsible for their use in treating microbial infection since time immemorial [30]. The compounds responsible for the antimicrobial activity of *M. esculenta* include flavonoids, phenolic acids, and terpenes, which are responsible for its antioxidant and antimicrobial activity. Previous studies reported the bioactive compounds namely p-coumaric acid, saponins, oleanolic acid and orstigmasterol responsible for antimicrobial activities of *M. esculenta*.These compounds can exhibit antimicrobial activity on many microorganisms, particularly bacteria and fungi. The antimicrobial activity of *M. esculenta* has been validated through several methods of in vitro and in vivo, that is through agar well diffusion and broth microdilution technique.

Kabra et al., [35] have also demonstrated that *M. esculenta* extract exhibits significant activity against a number of bacterial species, such as *S. aureus*, *E. coli*, *B. subtilis*, and *P. fluorescens*. The volatile oil from *M. esculenta* bark of esculenta shows strong antimicrobial activity against both Gram-negative and Gram-positive bacteria [34]. Such bacterial species can cause infections in tissues, joints, bones, skin, and even heart valves, thereby indicating that *M. esculenta* extract can be helpful in treating various diseases. The compounds 4-H-pyran-4-one, dodecanol, and phytol were found to be responsible for the antimicrobial activity of its extract as determined by a modified diffusion method [35]. Mann et al., [49] screened methanolic extracts of *M. esculenta* against three Gram-positive bacteria (*S. aureus*, *B. subtilis*, and *S. epidermis*) and three Gram-negative bacteria (*E. coli*, *Salmonella enterica*, and *Proteus mirabilis*). The extracts were found to be of quite significant potency against both *S. epidermidis* and *S. aureus*, which was shown by an inhibition zone of 16 ± 0.5 mm, 12 ± 0.2 mm, and 18 ± 0.5 mm, respectively. However, for Gram-negative bacteria, the inhibition zones of the extracts against *E. coli*, *S. enterica*, and *P. mirabilis* were 15.5 ± 0.5 mm, 10 ± 0.1 mm, and 12 ± 0.2 mm, respectively.

Presence of phytochemicals, such as flavonoids and tannins causes the fungal cell membrane to break, increasing its permeability and leakage of content. They also interfere with the synthesis of ergosterol, which is an important constituent element of the fungal cell walls, thus inhibiting its growth and reproduction [56]. Studies demonstrate that various extracts from parts of the plant, such as leaves and fruits, possessed high antifungal activity against strains, including *Aspergillus niger* and *Candida albicans*, thus, *M. esculenta* is a significant natural product for developing potential antifungal agents. Pant et al., [56] demonstrated that the fruits of *M. esculenta* contain antifungal properties by assessing against *Fusarium oxysporium*, *Rhizoctonia solani*, *and Sclerotium rolfsii* with the diffusion method. Agnihotri et al., [1] also reported that oil of *M. esculenta* exhibited anti-inflammatory and antimicrobial action against several microorganisms including *Candida albicans*, *E. coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Saccharomyces cerevisiae*, and *Bacillus epidermidis.* Kabra et al., [35] evaluated

the myricene extract of *M. esculenta* in relation to its antifungal activity against *C. albicans* and *A. niger* .

5.2 Antidiabetic activity

It is the capacity of a compound, which lowers the blood sugar levels and it is crucial for treating diabetes. Nowadays, diabetes is the most common endocrine disorder globally and which affecting approximately 10% of the global population. The ninth edition of the international Diabetes Federation (IDF) Diabetes Atlas, published in 2019 by the IDF, an estimated 373.9 million adults aged 20-79 years (7.5% of the adult population) had impaired glucose tolerance. Most of these adults were under 50 years old. The diabetes prevalence was slightly lower in women (9.0 %) and higher in men (9.6%). The number of diabetes cases is predicted to increase in both women and men by 2045. The anti-diabetic potential of M. esculenta is linked to its effects on molecular pathways that regulate glucose metabolism and enhance insulin sensitivity. Bioactive compounds from M. esculenta can enhance the sensitivity of certain tissues to insulin. This occurs through the modification of the insulin signaling pathway, enhancing glucose uptake and utilization by cells. Glucose production in the liver, called hepatic gluconeogenesis, is further affected by extracts from the plant. The plant extracts inhibit certain enzymes in the pathway that lead to regulating blood sugar levels (Emiru et al., [21]). Some parts of M. esculenta have been reported to protect pancreatic beta cells, which are responsible for the secretion of insulin. These plant extracts help maintain the balance of insulin and glucose in the body by supporting pancreatic health. Methanolic extract of leaves of M. esculenta has exhibited promising anti-diabetic activities against T2D (Kumar et al., [39]). Kabra et al., [35] reported that doses up to 300 mg/kg were nontoxic, while the doses at 2000 mg/kg were toxic for animals. A study conducted on streptozotocin-induced diabetic rats, shows that the M. esculenta methanol extract of leaves reduces the blood sugar levels. Blood sugar ($p<0.05$), blood cholesterol, and body weight were eventually lowered due to the oral treatment of the extract and it has an improvement in dose dependent on lipid profile ($p<0.0.5$) as compared to the vehicle treated groups (Rawat et al.2013). A bio-active compound present in M. esculenta bark called myricitrin, which has the ability to improve the absorption of glucose and have hypoglycemic effects in rats suffering from Type 2 diabetes. Baral et al., [7] proved the antidiabetic effect in the methanol extract of M. esculenta stem bark as it was found exhibiting a strong alpha-amylase inhibitory activity (IC50 value of 0.96 mg/ml). Myricetin plays an important role in lowering the risk of kidney disease caused by high blood sugar by blocking NF- Kb activation, fibrosis, apoptosis, and inflammatory damage. The M. esculenta fruits having certain bioactive compounds have been proven to play a crucial role in managing diabetes and improves the glucose metabolism (Dua et al., [19]; Rahman et al., [63]). Myricitrin compounds of M. esculenta have also been observed to exhibit antihyperglycemic effects. Low to moderate doses of myricitrin, had antioxidant effects on hyperglycemia induced oxidative damage in mouse myoblast (C2C12) (Anhangarpour et al., [2]).

5.3 Antioxidant activity

Antioxidant activity is the capacity of an agent to neutralize the free radicals, and it is unstable molecules that can cause cellular damage through oxidative stress. The antioxidant activity of *M.a esculenta*, which is attributed to its flavonoids and polyphenolic

compounds, functions through several mechanisms that can neutralize ROS and guard against oxidative damage [65]. These include flavonoids such as quercetin and myricetin, which are strongly efficient in scavenging free radicals, neutralize ROS such as superoxide anions and hydroxyl radicals, thereby giving protection to cellular components, such as proteins, lipids, and DNA against oxidative stress-induced damage. Polyphenols in *M. esculenta* may also strengthen natural antioxidant defences in the body Kabra et al., [35]. This process increases the activity of enzymes like superoxide dismutase (SOD) and catalase, which are very important in neutralizing reactive oxygen species and maintaining cellular redox balance reactions, thus strengthening the body's antioxidant defences Liu et al., [45]. The ethanolic bark extract has been shown to decrease lipid peroxidation and improve antioxidant parameters like catalase and glutathione in experimental studies [81]. According to Silva et al., [76], *M. esculenta* exhibits antioxidant activity that is very effective in regulating and preventing oxidative stress, from disorders that occur due to aging up to cardiovascular diseases. It was found to reduce lipid peroxidation and augment antioxidant parameters such as catalase and glutathione in experimental studies [81]. *M. esculenta* showed the strong antioxidant properties. It proved useful in controlling and hindering oxidative stress, including aging related disorders and cardiovascular diseases. The antioxidants present in *M. esculenta* are also a necessity in neutralizing free radicals. Different methods, such as significant antioxidant activity, have been observed to be present and linked to the content of flavonoids, phenols, and flavanols Kumar et al., [39]. Fargere et al., [23]. *M. esculenta* fruit, which is rich in phenolic compounds, exhibited high DPPH radical scavenging activity with acetone extraction. 1,1Diphenyl-2-picrylhydrazyl (DPPH), the 2,2-azinobis (3-ethylbenzothiazoline-6-sulphonic acid), and ferric reducing antioxidant power (FRAP) are three various in vitro methods of scavenging for radicals which are utilized for determining antioxidant potential of *M. esculenta* fruit methanolic extract by Mann et al., [49] and also the methanolic pulp extract by Rawat et al., [65]. The result of the research work which was reported was that it showed potent antioxidant activity on all the methods applied. The reason behind this might be due to bioactive compounds, such as flavonoids, phenols, and flavanols [49, 65].

5.4 Anti-inflammatory activity

Inflammation is a complex biological response that is mediated by blood and the vascular tissues to harmful stimuli, such as irritants, damaged cells, or pathogens. It is of two types: acute and chronic. This process involves the local vascular system, various cell types within the affected tissue, and the immune system. Chlorogenic acid (CGA) has anti-inflammatory properties and it has been found that, it would suppress the production of proinflammatory mediators including prostaglandin (PG2), chemotactic protein-1, interferon-γ, TNF-α, IL-6, monocyte inflammatory protein-1α and reduce cyclooxygenase-2 (COX-2). The anti-inflammatory activity of *M.a esculenta* is mainly due to the triterpenoids in its bark. These exhibit their action on various molecular mechanisms involved in the body's inflammation process.

Identified to be produced from *M. esculenta* as triterpenoids have the ability to inhibit pro-inflammatory mediators such as cytokines and prostaglandins by inhibiting an essential enzyme like cyclooxygenase (COX) and lipoxygenase (LOX) responsible for the synthesis of inflammatory molecules. These triterpenoids may also influence the NF-κB signaling pathway that is an important transcription factor regulating the expression of

genes related to inflammation. These may interfere with this pathway and thereby reduce the transcription of inflammatory genes, decreasing the overall inflammatory response [3]. The scientific use of *M. esculenta* has been confirmed based on its anti-inflammatory activities. Triterpenoids in the bark can potentially inhibit inflammatory pathways and would, therefore, be of interest in the treatment of diseases such as arthritis and inflammatory bowel diseases Shrivastava et al., [74]. Middha et al., [52] conducted a study on the anti-inflammatory effect of methanol extract from *M. esculenta* leaves at a dosage of 200 mg/kg. The outcomes revealed that acute inflammation was reduced by 21.71% in treated animals after 4 h, similar to the 32.75% decrease recorded in the diclofenac-treated group (10 mg/kg). Pundir et al., [62] studied another study on ME-EtAC extract from leaves of the plant significantly reducing carrageenan-induced paw edema at $p < 0.05$; it had efficiency comparable with diclofenac, but at 10 mg/kg dosage. The essential oil obtained from the bark of *Myrica esculenta* has shown remarkable topical anti-inflammatory activity when it was applied topically to the ears of Swiss albino mice and was found more potent than the standard drug used for reference Agnihotri et al., [1]. In addition, aqueous extracts from the roots and bark of M. The activity of Lipoxygenase (LOX) on esculenta was analyzed using a technique similar to that reported by Truong et al., [82]. The extract of acetone from *M. esculenta* had the best DPPH radical scavenging action due to its high concentration of phenolic compounds. Several mediators are present in inflammatory process, some of these compounds are used to find the development of new anti-inflammatory substance.

5.5 Antiulcer activity

An ulcer is a widespread gastro intestinal disorder, that cause discomfort to patients, disturb their daily schedules, and causes emotional distress [50]. Peptic ulcer disease (PUD) had a significant impact on morbidity and mortality until the late 20th century, when its occurrence significantly decreased. This change was attributed to modernization and improved hygiene, which reduced childhood infections and the spread of *H. pylori*. Key factors in this decline included the discovery of effective acid suppressants and treatments for *H. pylori* infection. However, the increased use of NSAIDs led to a reduction in duodenal ulcers (linked to *H. pylori*) and a rise in gastric ulcers (caused by NSAIDs). PUD remains prevalent worldwide, particularly in developing countries with high *H. pylori* prevalence. In these regions, many children are infected with *H. pylori* before age 10, with prevalence peaking over 80% by age 50. Conversely, in developed countries, *H. pylori* infection is uncommon before age 10 but increases with age. The lifetime risk of developing a peptic ulcer is about 10%, though only a minority of *H. pylori* infections result in ulcers. Most people experience nonspecific discomfort, abdominal pain, or gastritis instead. Bioactive flavonoids and phenolic acids were determined in the *M. esculenta* that counts for its antiulcer activity. Ethanolic extracts of the bark in *M. esculenta* were evaluated on rats, and the compound displayed excellent activity against ulcers in a pyloric ligation model [35]. The extract increased the antioxidant status of gastric tissue via the increase in the levels of these enzymes such as SOD, catalase, and glutathione peroxidase [40]. These results further implied that the antiulcer activity of the extract was akin to the standard antiulcer drug, omeprazole in the same model animal.

In the study conducted by [77], it has been proven that oral administration of ethanol extract of *M. esculenta* bark in dosages of 100 mg/kg and 200 mg/kg was shown to

protect against ulcers in a rat model of pylorus ligation with significant reductions in gastric secretions, acidity, lipid peroxidation and myeloperoxidase enzyme in comparison to control. As per the study, it has been identified that bioactive compounds like phenolic acids and flavonoids existing in *M. esculenta* justified its antiulcer activities [39]. Strong antioxidant mechanism of the bark as evidenced from increased levels of catalase activity, nitrite and glutathione supported its antiulcerogenic potential and provided proofs for the traditional utilization of *M. esculenta* in ulcer treatment.

5.6 Anxiolytic activity

Ananxiolytic is a medication used primarily for the treatment of anxiety and other disorders associated with it. Bioactive compounds in *M. esculenta*, like phenolic acids and flavonoids, have shown to be anxiolytic in effect. Anxiety disorders impact around 264 million individuals globally, reflecting a 15% rise since 2005. These conditions often result in considerable absences from work and school and carry a higher financial burden than other psychiatric disorders due to their widespread occurrence. Despite their significant effects, there has been comparatively less research on new medication treatments for anxiety disorders over the past 5–10 years compared to major depressive disorder, bipolar disorder, and schizophrenia. The development of new drug compounds for anxiety disorders is limited partly because there are already effectiveFDA-approved medications and psychotherapies, and it's believed that current treatments manage these disorders adequately. However, research indicates that only 60–85% of patients with anxiety disorders see at least a 50% improvement with existing treatments, and only about half of these patients achieve minimal anxiety symptoms. Additionally, those with anxiety disorders, especially generalized anxiety disorder (GAD) and social anxiety disorder (SAD), often experience high recurrence rates and persistent symptoms, particularly if they also suffer from major depressive disorder (MDD). Factors such as misdiagnosis, poor adherence to treatment, substance use, or other comorbidities may contribute to the difficulty in treating these disorders, suggesting that conventional treatments may not be effective for everyone and that new pharmacotherapies are needed. Unfortunately, most of the developed studies so far are merely derivatives of already approved drugs.

It is through its broad range of phytochemicals that *M. esculenta* exerts its anxiolytic actions, such as flavonoids, tannins, and terpenoids. These compounds interact with the central nervous system, particularly targeting gamma-aminobutyric acid receptors, which are crucial for regulation of anxiety [26]. The active principles of *M. esculenta*, that possess inhibitory activity in GABAergic transmission, reduce the excitability of neurons and confer a soothing effect. The antioxidant activity of these phytocompounds also minimizes oxidative stress, usually implicated in the pathogenesis of anxiety disorders. The two action combined accounts for the potentiality of *M. esculenta* as a natural agent, which might soothe anxiety. The presence of free hydroxyl groups and specific structural features of flavonoids make them essential for reducing anxiety [29]. Khan et al., [37] performed light/dark exploration and elevated plus-maze tests, and the results were that the ethanol extract of *M. nagi* bark exhibited substantial anxiolytic potential at doses of 100, 200, and 400 mg/kg, which was more effective than the standard drug diazepam. Studies have shown that the ethanolic bark extract of *M. esculenta* exhibits anxiolytic activity through the inhibition of anxiety-like behavior in mice.

5.7 Hepatoprotective activity

M. esculenta fruit contains flavonoids, tannins, and terpenes which possesses hepatoprotection. These antioxidant compounds neutralize free radicals and reduce oxidative stress from the liver cells [31]. Beyond that, *M. esculenta* enhances the antioxidant liver defence system and inhibits lipid peroxidation thus protecting the hepatic cells. Another protective mechanism is its anti-inflammatory effect through the inhibition of inflammatory mediators and reduction of liver inflammation. Myricitrin is also shown to prevent toxin-induced liver damage by replenishing antioxidant enzyme levels and reducing inflammation caused by carbon tetrachloride. Another effect that increases the potential of the compound as a liver-protecting agent is its ability to inhibit cell death and fibrosis in the liver cells (Dua et al., In another study conducted by [77], isolated *M. esculenta* (5 mg/g) which was incorporated in a polyherbal Ayurvedic formulation, Herbitars (50 and 100 mg/kg), which has been shown to exert its hepatoprotective effects against carbon tetrachloride (CCL4)-induced liver damage in Wistar rats. The bioactive compounds responsible for the hepatoprotective effects in *M. esculenta* include phenolic acids and flavonoids.

5.8 Chemo-preventive activity

Chemoprevention is the use of naturally occurring or synthetic substances to prevent cancer development. According to the American Academy of Dermatology, one in five Americans will develop skin cancer during his lifetime. Among the deaths due to skin cancer, the most common cause of death in an estimated 7,650 cases due to malignant melanomas is skin cancer. Of the NMSC cases, there are basal cell carcinomas (BCC) and SCC, accounting for approximately 2–3 million cases worldwide in a single year. Ultraviolet radiation is the leading cause of skin cancer. Education on prevention and early detection forms the main basis for controlling and reducing the progression of skin cancer. *M. esculenta* fruit has excellent chemo preventive activity because it contains a high number of bioactive compounds such as flavonoids, phenolic acids, and triterpenoids. These compounds have high antioxidant potential, neutralizing free radicals and reducing the oxidative stress, which forms a major contributing factor in the course of cancer [67]. Furthermore, *M. esculenta* may influence other signaling pathways related to cell growth, apoptosis, and inflammation. It was also observed to inhibit the NF-κB pathway, an important pathway in inflammation and cancer progression, and also activate the p53 pathway leading to inducing the killing of cancer cells through apoptosis. These preventive effects collectively indicate it as a worthwhile chemo preventive agent [42]. Sood et al., [77] found that pretreatment of mice with *M. nagi* ethanol extract at 2.0 and 4.0 mg/kg significantly reduced the repression of cutaneous glutathione and antioxidant enzyme activities including glucose-6-phosphate, catalase, glutathione peroxidase, dehydrogenase, and glutathione reductase by cumene hydroperoxide. For skin, *M. nagi* act as an effective chemo preventive agent.

5.9 Antiasthmatic activity

Asthma is a long-term respiratory disease that affect 155 million people globally. In 2013, the US National Health Interview Survey indicated that 8.3% of children aged 0–17 years had asthma diagnosed by a doctor, based on parent reports. The International Study of Asthma and Allergies in Childhood (ISAAC) from 1999 to 2004, also

using parental reports, showed that asthma prevalence in European children aged 6–7 years ranged from under 5% in Albania to over 20% in the UK, with rates rising annually. Asthma rates differ by age and gender in children, with older children (13–14 years) having higher rates than younger ones (6–7 years). Several studies have screened *M. esculenta* bark for its anti-asthamatic potential. In a study conducted by Patel et al., [61], bark extracts of *M. esculenta* (75 mg/kg and 150 mg/kg) were administered to guinea pig and was observed to exhibit antiallergic activity due to the marked inhibition of eosionophil accumulation in allergic pleurisy test as well as significant decrease were reported in the plasma exudation in acetic acid induced vascular permeability. Further they reported that lower doses (27 mg/kg and 54 mg/kg) of water extracts of the bark exhibited higher antiasthamatic activity than its ethanol extracts by providing protection against histamine aerosol-induced bronchospasm in guinea pigs and by relaxing histamine induced guinea pig tracheal chain contraction.

In a similar study conducted by Sood et al., [77] explained that on administration of ethanol bark extract of *M. esculenta* at a dose of 75 mg/kg showedspasmolytic activity by relaxation of guinea pig smooth muscle (tracheal muscle) in histamine and acetylcholine (Ach) induced contraction, antianaphylactic activity induced by egg albumin and bronchodilatory activity by protecting against acetylcholine and histamine aerosol induced bronchospasm in guinea pigs, which inhibit the total and differential leucocytes in bronchoalveolar lavarage fluid as well as inhibition of histamine release from the chopped lung tissues off egg albumin sensitized guinea pigs.

5.10 Anticancer activity

In 2020, around 9.9 million people succumbed to cancer. This disease is marked by uncontrolled cell growth that forms tumors, which can metastasize to other body parts. The abnormal cell behaviour can stem from genetic factors or epigenetic changes impacting key genes (oncogenes) related to cell cycle regulation and apoptosis. Cancer cells typically exhibit dysregulated apoptosis and abnormal microtubule behaviour. According to the World Health Organization, the main causes of cancer include random somatic mutations, ionizing radiation, reactive oxidative species, and various chemical and biological agents. The FDA states that more than 60% of drugs used in cancer treatment come from natural sources. Moreover, *M. esculenta* can influence the production of pro-inflammatory mediators, such as cytokines and chemokines, which can further enhance its anti-cancer effects. The ethanolic extract of *M. esculenta* bark significantly decreased the build-up of eosinophils and reduced plasma leakage in experimental models of allergic pleurisy and vascular permeability in mice. A study conducted by Sood et al., [77] explained that the fruit *M. esculenta* methanol extract showed a normal level of anticancer activity. In methylthiazolyltetrazolium (MTT) method at a concentration of 5 mg/ml, it reduces the growth of Hela, Hep G2, MDA-MB-231 cancer cell lines by 48.29%, 50%, and 46.19% individually.Another study conducted by Saini et al., [69] demonstrated that acetone and acid methanol extracts of M. esculenta berries exhibits anticancer proliferative activities which resulted in 70–92% reduction in the viability of C33, SiHa and HeLa cancer cells with no cytotoxicity towards normal transformed cell lines. Major bioactives responsible for having dose dependent effects on inhibition of cancer cells were reported to be ferulic acid and gallic acid as determined by LC/MS analysis [49].

5.11 Antihypertensive activity

Antihypertensives are a class of drugs that are used to treat hypertension (high blood pressure). The antihypertensive effects of *M. esculenta* are largely due to its rich phytochemical content, including flavonoids, tannins, and triterpenoids. These compounds help regulate blood pressure through various mechanisms. Flavonoids, like myricetin and quercetin promote vasodilation by increasing the production of nitric oxide (NO), which relaxes blood vessels and enhances blood flow and, their antioxidant properties reduce oxidative stress, a known factor in hypertension. Tannins and triterpenoids regulate blood pressure by inhibiting the angiotensin-converting enzyme (ACE). Blocking ACE prevents the formation of angiotensin II, which constricts blood vessels, thereby lowering blood pressure Yousefi et al., [87]. Studies on related species like Pimenta dioica show a dose-dependent reduction in blood pressure in hypertensive rats, suggesting *M. esculenta* extracts may have similar effects Suárez et al., [79]. Antihypertensive therapy aims to prevent high blood pressure complications like stroke, heart failure, kidney failure, and myocardial infarction. Sood et al., [77] found that *M. esculenta* leaves contain (6 S,9R)-roseoside and corchoionoside, the most effective ACE inhibitors, with inhibition rates of 25.63% and 29.97% at 100 μM. Compounds like myricetin, myricanol, and 5-O-β-D-glucopyranosyl myricanol showed lower hypotensive activity, with inhibition rates of 1.41% and 0.07%.

5.12 Wound healing activity

The wound interrupts the functional and cellular balance of living tissues. The wound healing properties of the plant are derived from the bioactive compounds such as flavonoids, phenolic acids, and terpenes. These compounds exhibit anti-inflammatory, antioxidant, and antibacterial effects [39]. It would reduce inflammation, promote tissue regeneration, and would enhance the overall wound healing process. *M. esculenta* has been ethnobotanically proved to be an old drug in wound treatment and, therefore, selected as the drug to advance in this scenario of herbal drug development in modern herbal medicines [66]. Myricitrin improves glucose metabolism and attenuates oxidative stress, important to enable healing and recovery for the cells through trigger cellular repair pathways; thus, it impacts the healing mechanisms. According to Sood et al., [77] the bark of *M. esculenta* heals wounds by both incision and excision models, establishing its potential. An ointment prepared from its aqueous bark extract increases tensile strength, wound contraction rates, hydroxyproline, and shortens the epithelization period relative to the standard 0.2% w/w nitrofurazone [53]. Medicines from *M. esculenta* bark treat wounds, cuts, and skin infections. Rathna et al., [64] suggest that the bark holds bioactive compounds exhibiting antibacterial and tissue-regenerative properties .

5.13 Antiallergic activity

Antiallergic activity refers to a substance's ability to prevent allergic reactions. Research has shown that the stem bark of *M. esculenta* exhibits antiallergic properties. The crude extract of its stem bark significantly inhibits eosinophil accumulation and plasma exudation in experimental models Shin et al., [73]. This effect likely comes from reduced histamine release, inhibition of mast cell degranulation, and suppression of eosinophil accumulation, preventing cytokine and chemokine release Xu et al., [85]. These

mechanisms make *M. esculenta* a promising candidate for managing allergies. Studies also highlight that *M. nagi* possesses antioxidant properties and medicinal uses, suggesting that other Myrica species may also treat allergic conditions Panthari et al., [57]. *Myrica* extracts lower Th2 chemokine levels, including CCL5, CCL17, and CCL22, in HaCaT cells, indicating potential in managing atopic dermatitis by influencing immune responses [33]. A study conducted by Patel et al., [60] explained the antiallergic effect of *M. esculenta* stem bark in mice. Vascular permeability and allergic pleurisy induced by acetic acid are the two experimental models where study focused on. Researchers found out that initial treatment with 75% mg/kg and 150 mg/kg of *M. esculenta* decrease the amount of plasma exuadation by 59.77% and eosinophil gathering 57.12% in mice.

6 Processing technologies for developing *M. esculenta* based food products

Himalayan bayberry is highly perishable fruit owing to no peel and active respiration makes it impossible to storage it in high quality for more than one day. Its susceptibility to lose freshness with loss in texture, sensitivity to water loss, mechanical damage, physiological deterioration and microbial spoilage increases the challenge of its storage. Postharvest duration is limited to 1–2 days at high temperatures and humid conditions of the marketing storage and transportation challenges. Maintenance of freshness is the prime problem in bayberries industry which largely limits the sales channels and economic benefits [15]. Several technologies have been proposed to enhance its shelf life such as cold storage (0–4 °C), coatings, medicament treatments and modified atmospheric packaging, but these too offer freshness for few days.

Industrial processing of *M. esculenta* primarily focuses on the conversion of the highly perishable fresh berries into value-added products such as juices, squashes, jams, wines, nutraceutical extracts, and natural colorants (Fig. 4). Advanced extraction technologies such as microwave-assisted or ultrasound-assisted extraction are increasingly explored for efficient recovery of phenolic compounds and antioxidants for functional food and pharmaceutical applications. Additionally, drying methods such as freeze-drying and spray drying are employed to produce stable powders rich in bioactive constituents, facilitating their incorporation into functional formulations and nutraceutical products (Fig. 1).

6.1 Freezing

Freezing has been observed to be the least destructive method for preserving the quality of berries but ruins the texture owing to the formation of ice crystals. Quick Freezing Technology (QFT) offers additional advantage of forming small ice crystals and better preservation of flavor, color and nutritive value and better texture over other freezing methods. QFT employs higher local heat transfer coefficient rates in between bayberry and cold medium at freezing temperatures. Zhao et al., [89] conducted QF of bayberry with least thawing losses (1.9%), insignificant in variations pH and textural profile parameters when frozen with liquid nitrogen (LN2) flowing at velocity of 2.0 m/s at -120 C for 2.27 min. Zhao et al., [90], reported insignificant differences in the pH of fresh and quick frozen Chinese bayberry with less moisture loss and cell damage. The study also reported insignificant differences in the textural profile of frozen Chinese Bayberry and fresh berry (Fig. 2).

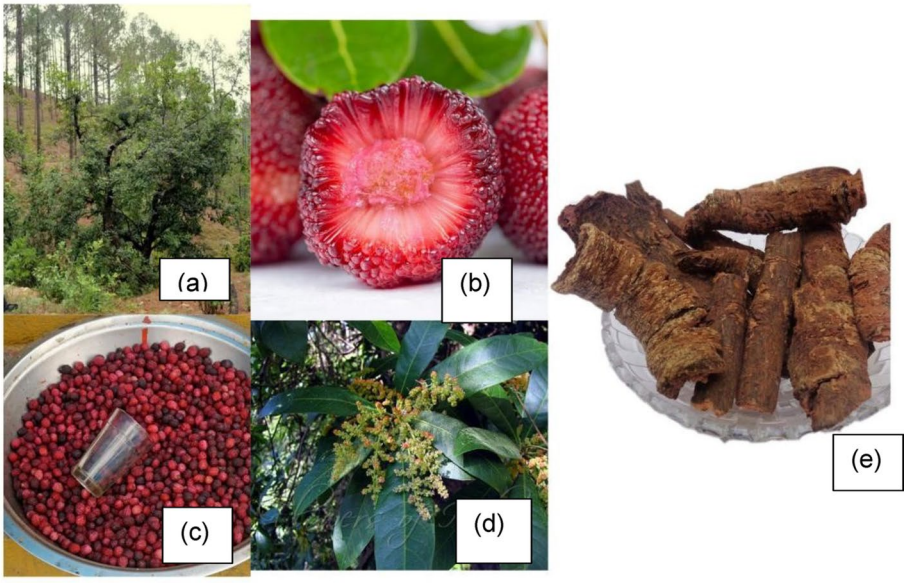


Fig. 1 *Myrica esculenta* tree and its various parts (**a**) fully grown tree, (**b** and **c**) ripened berry fruit, (**d**) leaves with some unripe berries; (**e**) tree bark

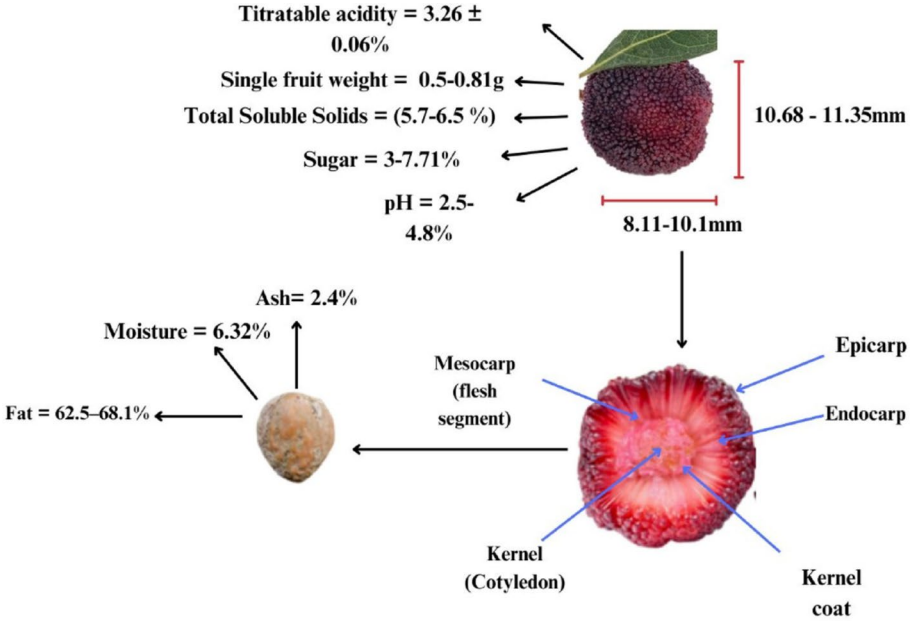


Fig. 2 Morphology and chemical composition of *Myrica esculenta* fruits and its kernel

6.2 Non thermal methods

The pretreatment method such as Vacuum impregnation (VI), has also been observed to be effective in increasing the shelf life of berries. Li et al., [43] carried out the vacuum impregnation of Chinese bayberry by treating it under pressure of 5 kPa for 15 min and impregnation temperature of 20 °C and in combination with isotonic sucrose solution (disodium stannous citrate and calcium ascorbate). They reported significant effects in inhibiting the decrease of firmness and weight loss and delayed decay rate (4–10 days) and microbial growth (2–10 days) with best sensory attributes. Perkins et al., (2017),

studied the impact of acetic acid ultrasonic fog (exposure time 1 h) on the microbial stability of Chinese bayberry (genotype N1MR06) and reported less than 18% decay in berries against 70% decay for untreated control fruit. The acetic acid treatment was also observed to exhibit insignificant effects on the sensorial quality, titrable acidity measures and total soluble solids. Acetic acid (weak acid) possess antibacterial properties which increases the acidity in the cytoplasm due to the passage of undissociated molecules into the cell (Fig. 3).

Another non-thermal method, Pulse light sterilization technology (PL) has also been utilized for the shelf life enhancement of Chinese bayberries when treated with pulses treatments of 9kJ/m^2, (PL1) 18 kJ/m^2, (PL2) 45 kJ/m^2 (PL5) per side for 1 min, 2 min and 5 min with significantly lower decay indices of 13.75%, 11.25% and 8.75% respectively, when compared with control group (22.51%) at 12th day of storage. PL method has also been observed to reduce the activity of PPO within initial few days and also increased the phenylalanine ammonia lyase activity by 96.59% after 9 days. Wang et al., [84]. PL treatment was also proven to be effective in suppressing *Colletotrichum cordylinicota* activity from 13.86% at 0 day to 12.72% on 12th day of storage. However, most of these methods are relatively expensive approaches for extending shelf life of bayberries and required skilled personnel to carry them out. Researchers have suggested processing of bayberries for their effective incorporation directly into food products such as dried fruits, juices, wines or powders etc.

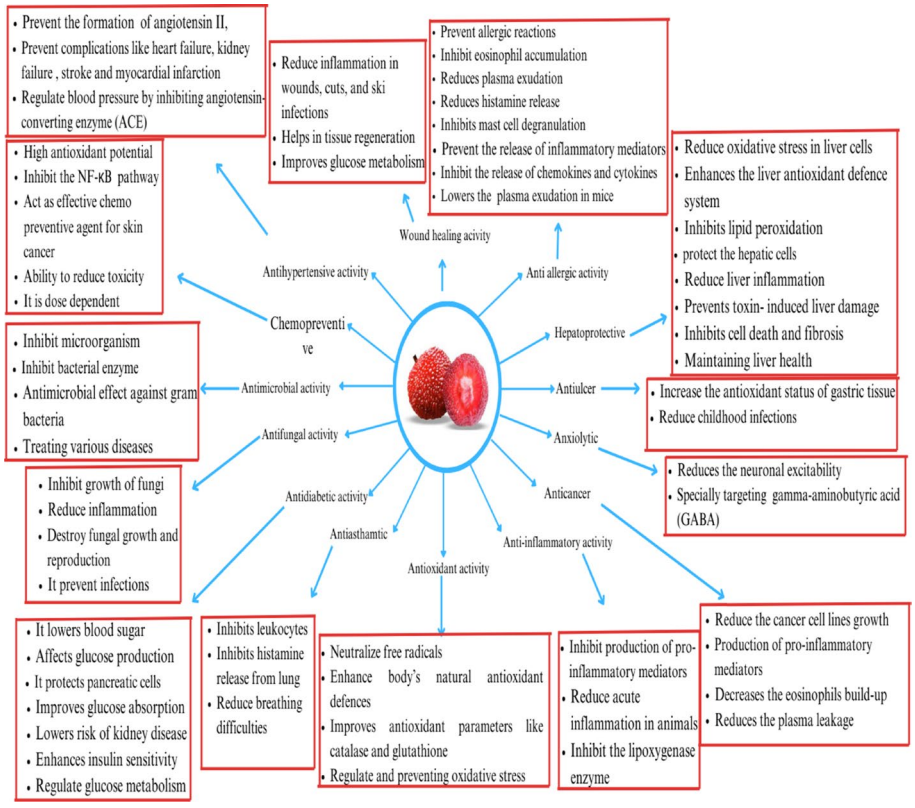


Fig. 3 Potential biological activities of *Myrica esculenta* fruit and its products

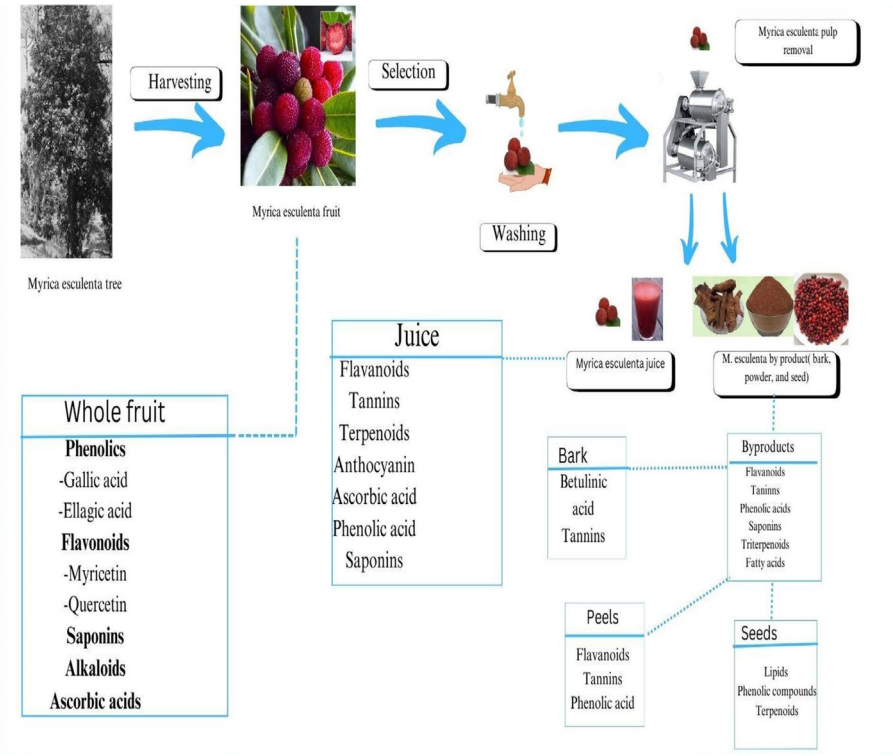


Fig. 4 General scheme of industrial processing of *Myrica esculenta* fruit

6.3 Dehydration

6.3.1 Fruit powder

Removal of moisture from food through drying is the prime objective of food preservation, as it reduces chances of microbial spoilage and prevents enzyme action. Drying techniques such as spray drying (SD), freeze drying (FD), hot air drying (HAD) and vacuum drying (VD) have been employed to prepare dried products as these techniques speed up the drying process without compromising the quality of final products. SD of bayberry has also represented superior results in terms of better preservation of total anthocyanins contents (ACNs) and total phenolic contents by 94 and 95% respectively [22]. Several efforts were made to enhance the recovery rates of bayberry juice powder by incorporating drying substances such as whey protein isolate at level of 1%, which increased the recovery rates by 53%. The obtained bayberry powder was recovered possessing excellent characteristics, 3.14% moisture, 9.5% hygroscopicity, 43.16 °C glass transition temperature, 16.5 total color difference, maximum ACNs retention (92.3%), phenolics retention (79.9%) and excellent antioxidant activity (28.5 Trolox equivalents/g) [46]. Liu et al., [47] also confirmed the appropriateness for freeze drying for bayberries, in terms of its stronger α-glucosidase inhibition and higher concentration of C3G, myricetin – 3-O glucoside, quercetin-3-O-galactoside, quercetin-3-O-glucoside and quercetin-3-O-rhamnoside. Similarly, Saili et al., studied the impact of various dehydration methods on the solubility and bulk density of bayberry powders. The reported solubility and bulk density were 32.98%, 35.84% and 36.50% and 0.63, 0.58 and 0.07 g/mL respectively (Fig. 4).

6.3.2 Fermentation

6.3.2.1 Wine Wines are considered as one of the important products of bayberries. However studies on the production of wines are limited owing to its short shelf life and unstable quality. Whereas little literature is available on the production of wines from Chinese Bayberries. Du et al., [18] produced fine quality wine from CBB by optimizing the fermentation conditions as initial sugar (22.0 Bx), pH (2.9), temperature (26.5 C) and inoculum conc. of *S. cerevisiae* (0.3%), the obtained wine was observed to contain 13.4% final alcohol, 77 mg/L ACNs and residual sugar content of 1 g/L. They also studied the flavor profile of obtained wine and highlighted the contribution of 3-methyl-1-butanol, 2 phenyl-ethanol, ethyl acetate and 2-methylbutyl acetate and acetic acid in the wine. Another group of researchers [93] investigated the changes in wine obtained from CBB when stored at 4, 25 and 37 °C for 70 days. Their findings indicated a significant decrease in the color values, total phenols and total flavonoid contents where polymeric pigment concentration increased significantly, whereas 5-hydroxymethyl furfural and browning index increased only at 37 °C. They also concluded that wines stored at higher temperature showed higher polymeric pigments. Around 40 six volatile flavors have been identified in wine of bayberry, consisting of 19 esters, 3 terpenes, 7 alcohols, 6 acids, 2 aldehydes, 2 ketones and 7 other unidentified compounds and for aroma esters and alcohols were found to be the significant contributors [13]. In berry wines, package oxygen plays a critical role in determining the wine color and volatile composition during its storage. High package oxygen level accelerated the deterioration of color, degradation of anthocyanins and also results in the formation of polymeric pigments along with production of acetaldehyde in wine. Zhang et al., [94] reported increased levels of total volatile esters and acid concentrations by 19.74% and 41.03% with increase in package oxygen levels in Chinese bayberry wine. They attributed this change to higher monomeric anthocyanins degradation rate or more consumption of monomeric anthocyanins in polymerization in wines with higher package oxygen.

6.3.2.2 Vinegar Inclusion of fruits for vinegar preparation has become increasing prominent in the field of nutrition as an approach to boost effectiveness and benefits of these substances. High sugar content, high content of dietary fiber, organic acids, minerals and bioactives complement the fermentation reactions. Researches have confirmed the presence of 8 essential amino acids with 38.78% content and 8 different organic acids, such as acetic acid, citric acid etc. They further reported presence of trace elements such as Ca, Mg, and Se and high vitamin C content of 9.74 mg/kg of vinegar produced. Zhu et al., [92] observed high anthocyanin content ($4.1 \cdot 10^{-5}$ mol/L) in vinegar prepared from *Myrica rubra*. In another study, GC-MS analysis confirmed high alcohol content (40.81%), esters (19.10%) and acids (19.39%) in vinegar produced from CBF [91].

7 Advanced uses of *M. esculenta* in nanotechnology

Various parts of the *M. esculenta* tree namely, stem, bark, fruits and leaves have traditionally been used for the treatment of various diseases, headaches, asthma, cough, fever, bronchitis, inflammation, ulcers, diarrhoea, lung and throat infections. But the advanced uses of it are still limited and have not been explored properly.

M. esculenta bark tannin has been successfully employed for the as a stabilizer for the fabrication of Palladium (Pd) nanoparticles. Tannin-stabilized Pd nanoparticles were immobilized onto γ-Al2O3 with the goal of generating heterogeneous γ-Al2O3-BT-Pd catalysts. Prepared γ-Al2O3-BT-Pd NPs had high initial turnover frequency as 12,804 mol/mol/h in the allyl alcohol hydrogenation with superior reusability after 5th usage cycle. Recently, Chauhan et al. [14] tried utilizing fruit extracts (aqueous and

methanolic) as a capping agent and reducing agent for synthesizing Cu2O nanoparticles. They reported successful formation of uniformly spherical crystal like particles embedded in a sheet with average size of 25.45 and 22.04 nm respectively. The obtained methanol extracted particles were observed to display higher antimicrobial efficacy against *Bacillus subtilis* (15.62 µg/ mL) and Staphylococcus aureus (31.25 µg/ mL) and high antioxidant potential (IC50 of 57.38 µg/ mL).

As *M. esculenta* plant extract known to exhibit anticancer properties. Shukla et al., [75] prepared M. esculenta plant extract based albumin nanoparticles (ME-BSA NPs) to enhance the absorption of phytoconstituents and to improve cancer cell selectivity which causes apoptosis. Molecular docking results confirmed good binding affinity of phytoconstituents to albumin which carried these nanoparticles to target the cancer site to trigger apoptosis confirming the contribution of these NPs in cancer treatment. The NPs were also observed to exhibit excellent drug delivery and anticancer activities with fewer side effects.

Plant extracts have been observed to be an easy and convenient alternative to chemical and physical methods for the preparation of metallic nanoparticles and their composites as these contribute to sustainability and lesser environmental degradation. Yadav et al., [86] assessed the effectiveness of magnetic chitosan composite and nanoparticles produced from leaf extract of *M. esculenta* for removing cadmium from aqueous solutions. The prepared NPs and magnetic composites were observed to possess high adsorption capacities 290 mg/g and 426 mg/g respectively. The prepared NPs and magnetic composites were also observed to exhibit excellent regeneration capabilities (with 80.44% in magnetic composites and 42% NPs) and easy separation from a solution hold a significant potential for application in industrial wastewater and sewage treatment.

8 Conclusion and future perspective

M. esculenta is renowned for its medicinal and nutritional value, and it has been traditionally used in the treatment of various health disorder such as cough, ulcers, asthma, and gastrointestinal issues. The various part of *M. esculenta* including roots, barks flowers, and leaves are used by local peoples for their medicinal value. Phenolic acid, tannins, myricetin, anthocyanin, and flavonoids are the bio-active compounds present in the plant, and it provides a wide range of pharmacological effects including antimicrobial, chemo preventive, hepatoprotective, anti-diabetic, anti-inflammatory, antioxidant, anti-allergic, anti-diarrheal, anticancer, anti-asthma, and antifungal. The traditional uses of *M. esculenta* are still highly valued and indicating its medicinal and cultural significance, even though with the advancements in modern medicine. The *M. esculenta* processing, application, and harvesting are important to maximize its economic potential and health benefits. It is non-climacteric in nature and requires proper care in harvesting and handling, so that fruit quality is maintained. Chemical preservation and controlled atmosphere storage are the various preservation methods that used to increasing the shelf life. Further development and research will enhance its market value and utilization, making it a valuable resource for both trade and health. *M. esculenta* holds vast opportunities for further exploration and usage. Advanced studies could lead to the discovery of more health benefits and uses of its bioactive compounds. The new processing and harvesting methods will enhance its quality and shelf life for wider use in the markets. This will integrate the traditional knowledge with modern scientific methods to enhance

its role in eco-friendly agriculture, nutrition, and medicine and ensure that *M. esculenta* remains an important source for health and wellness.

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