Myrica esculenta

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Myrica esculenta (Myricaceae) is a popular medicinal plant most commonly found in the sub-tropical Himalayas. It is widely used in folk medicine to treat several ailments such as asthma, cough, chronic bronchitis, ulcers, inflammation, anemia, fever, diarrhea, and ear, nose, and throat disorders. Due to its multidimensional pharmacological and therapeutic effects, it is well recognized in the ayurvedic pharmacopeia.

Keywords: Myrica esculenta ; ethnomedicinal ; phytoconstituents

1. Introduction

Genus *Myrica* is a large group comprising more than 97 species in the Myricaceae family. This family contains woody plants native to the subtropical and temperate zones of the earth [1]. Plant species of this genus are distributed in China, Taiwan, Japan, Western Highland of Cameroon, North America, South Africa, Australia, Brazil, Ethiopia, Nepal, and India [2][3][4][5]. Specifically, *Myrica esculenta* Buch.-Ham. ex. D. Don named 'Hairy Bayberry' and widely known as Kaiphal or Kataphala in the Indian subcontinent, is broadly used in Ayurveda (traditional Indian system of medicine) [6][7][8]. But this plant also has other synonyms, such as *Myrica sapida* Wall. and *Myrica farqhariana* Wall. [5][9][10]. *Myrica* plants grow well in nitrogen-depleted soils, mixed forests, agricultural and marginal lands [1][11]. *Morella esculenta* (Buch.-Ham. ex. D. Don) I.M. Turner is the newly accepted name for *Myrica esculenta* Buch.-Ham. ex.D. Don, and the later name is treated as a basionym of *Morella esculenta*. Taxonomical classification of *Myrica esculenta* is Kingdom: Plantae; Phylum: Tracheophyta; Class: Magnoliopsida; Order: Fagales; Family: Myricaceae; Genus: *Morella* [12].

M. esculenta is known for its edible fruits and other by-products. Indeed, its fruits have been a potential income generating source for the local tribes of the Meghalaya and sub-Himalayan region [13][14]. It is likewise known by a variety of names, such as "Katphal" in Sanskrit, "Kaiphal" in Urdu, "Nagatenga" in Assam, 'Soh-phi' in Khasi and 'Box myrtle' in English [1][15][16][17]. All the parts of the *M. esculenta* plant have huge nutritional and therapeutic importance. Fruits are used for syrups, jams, pickles, and preparation for refreshing drinks [14]. Traditionally, its bark, roots, and leaves are used for the treatment of various ailments and disorders [3][5]. Besides its traditional uses, bark is also used for making paper and ropes [18]. In addition, *M. esculenta* fruits and roots are used as an active botanical ingredient in numerous ayurvedic formulations (**Table 1**).

Table 1. Ayurvedic formulations of the plant with their uses and manufacturers.

Formulation	Uses	Manufacturers	References
"Chwayanprash"	**Improved digestion and strength and enhanced energy**	**Dabur, Patanjali, Nature & Nurture Healthcare**	**[19][20]**
"Katphaladi Churna"	**Treatment of fever, throat infection, respiratory disorders, and abdominal pain**	**VHCA Ayurveda**	**[19][20]**
"Pushyanuga Churna"	**Treatment for bleeding disorders and candidiasis**	**AVN Ayurveda,Baidyanat-h**	**[19][20]**
"Katphala Taila"	**Treatment of joint pain**	**VHCA Ayurveda**	**[19][20]**
"Arimedadi Taila"	**Helps to relieve tooth decay and breath problem**	**IMIS Pharmaceuticals**	**[19][20]**
"Mahavisagarbha Taila"	**Used for vata imbalance, neuromuscular conditions**	**VHCA Ayurveda**	**[19][20]**
"Bala Taila"	**Treatment of vata disorders, respiratory infections and weakness**	**Patanjali**	**[19][20]**
"Khadiradi Gutika"	**Treatment of dental, oral, throat and tonsillar infections**	**Zandu**	**[19][20]**

Formulation	Uses	Manufacturers	References
“Maha Vatagajankusa Rasa”	Rheumatoid arthritis, Migraine, Paralysis, Cough, Cold, Asthma	Dabur, Baidyanath, Shree Dhootapapeshwar	[19][20]
“Brihat Phala Ghrta”	Treatment of infertility	SN Pandit Ayurvedic	[19][20]

More recently, its numerous ethnomedicinal uses led researchers to explore *M. esculenta* phytochemistry further. For instance, tannins extracted from its bark are used as a dyeing agent [6]. Indeed, the presence of distinct bioactive compounds, such as alkaloids, flavonoids, glycosides, tannins, terpenoids, saponins, and volatile oils [8][21], has been increasingly reported as related to its pharmacological effects. For example, crude extracts and isolated compounds from *M. esculenta* exhibit both in vivo and in vitro pharmacological activities. Local tribes use the tree for timber, fuel, fodder, wood, likewise as used for tanning and getting yellow colored dye [22][23][24][25]. In spite of being a useful tree, the cultivation of the plant is incredibly restricted, and most of the traditional and commercial uses of *M. esculenta* rely solely on collections from the wild sources by endemic people [26]. Thus, wild sources of the species are underneath impending danger of extinction due to the increase in urbanization, overharvesting, negligence of sustainable use, and over-exploitation of forests and wastelands for industrial uses [27]. Due to the over-exploitation of the natural habitat, limited geographical prevalence and the unresolved problems inherent in seed vitality and germination, alternative propagation and conservation approaches are desperately needed to avoid the possible extinction of this vital species [8]. This species is fundamentally the same as *M. rubra*, which is ordinarily found in China and Japan. However, *M. esculenta* contains fruits smaller than about 4–5 mm compared to the *M. rubra* fruits (12–15 mm) [28]. Although information on phenolic content and antioxidant activity of the fruit extract, juice, jam and marc of *M. rubra* [19][20][29][30][31][32] is available, this information is lacking for *M. esculenta*. Previous reviews have suggested that myricetin is obtained mainly by members of the Myricaceae family [33][34] and is a key ingredient in many foods, besides to be used as a food additive due to its antioxidant activity and ability to protect lipids from oxidative damage [35]. It is one of the key ingredients of various foods and beverages. The compound has a wide range of potentialities that include strong antioxidant, anticancer, antidiabetic and anti-inflammatory effects, and can protect a wide variety of cells from in-vitro and in vivo lesions [36]. It was first isolated in the late eighteenth century from the bark of *Myrica nagi* Thunb. (Myricaceae), harvested in India, as light-yellow crystals [37].

2. Ethnomedicinal Uses

M. esculenta, a conventional ayurvedic plant, is used by different native population groups in multiple ways because of the various therapeutic uses of its bark, roots, fruits, leaves and flowers (**Table 2**) [20][38][39][40].

Table 2. Ethomedicinal uses of *M. esculenta.*

Plant Part Used	Uses	Region/Tribe	References
Leaf, fruit, root, bark	Jaundice	Meghalaya, India	[23]
Leaf	Inflammation of vocal cord	Meghalaya, India	[24]
Bark	Antiseptic	Meghalaya, India Khasi tribe	[24]
Fruit, bark, leaf	Fever	Meghalaya, India Vietnam, South China	[24]
Bark	Anemia	Meghalaya, India Khasi tribe	[24]
Fruit	Refreshing drink “Um Soh-Phi”	Meghalaya, India Khasi tribe	[24]
Bark	Sore	Nagaland, India Zeliang tribe	[41]
Bark	Toothache	Meghalaya, India Khasi tribe Almora, Uttarakhand, India	[24][42][43]
Bark	Sprain	Far-flung village, Jajarkot, Nepal	[44]
Flower, bark, leaf	Inflammation, paralysis	Meghalaya, India Khasi tribe Vietnam, South China	[24][45]

Plant Part Used	Uses	Region/Tribe	References
Unripe fruit	Anthelmintic	Himachal Pradesh, India	[45]
Fruit	Bronchitis, dysentery	Nepalese community, Nepal	[46]
Bark	Mental illness	Orissa, India	[47]
Bark	Skin disorder	Vietnam, South China	[48]
Bark	Cholera	Mizoram, India	[49][50]
Bark	Cardiac debility, cardiac edema	Meghalaya, India	[50]
Bark	Carminative	Meghalaya, India Khasi tribe Mizoram, India	[22][50]
Bark, leaf	Asthma, chronic bronchitis, lung infection	Meghalaya, India Khasi tribe Vietnam, South China Chaubas and Syabru, Nepal	[23][49][51]
Flower	Earache	Meghalaya, India Khasi tribe Almor, Uttarakhand, India Himachal Pradesh, India	[24][42][38][52]
Bark, flower, leaf, fruit	Diarrhea, dysentery, stomach problem	Meghalaya, India Khasi tribe Almora, Uttarakhand, India Chungtia village, Nagaland, India	[24][52][53]
Leaf	Redness of mucosa	Chungtia village, Nagaland, India	[53]
Fruit	Body ache	Ukhimath block, Uttarakhand, India	[54]
Bark, fruit	Headache	Mizoram, India Ukhimath block, Uttarakhand. India	[50][54]
Fruit	Ulcer	Himalaya, India	[55]

Apart from these ethnomedicinal uses, various fruit industries in Himalaya used its fruits for making syrup, jam, and squash [56]. The Khasi tribe of Meghalaya uses its bark as fish poison while the extracted tannin from its bark is use as a tanning and dyeing agent [57]. Local peoples in Arunachal Pradesh use this tree for timber and fuel [22].

3. Phytochemistry

Phytochemical screening performed on leaves, stem bark, bark, fruits and fine branches of *M. esculenta* revealed several active phytoconstituents such as tannins, phenolic acids, flavonoids, terpenes, glycosides, steroids, volatile oils, and amino acids [8][21]. These phytoconstituents have shown a wide variety of pharmacological effects. HPTLC profiles of various extracts from different *M. esculenta* plant parts are presented in **Table 3**. The mobile phase used to develop the HPTLC chromatogram for n-hexane, ethyl acetate and ethanol extracts of stem bark and fine branches were toluene: ethyl acetate (5:5 *v*/*v*), toluene: ethyl acetate (7:3 *v*/*v*) and toluene: ethyl acetate: formic acid (5:5:0.5 *v*/*v*) [8] respectively, while for leaves, ethyl acetate, methanol and aqueous extracts of leaves toluene: ethyl acetate (7:3) was used [21].

Table 3. HPTLC profile of various extracts of different parts of *M. esculenta.*

Extract	Wavelength (nm)	Rf Value			References
		Stem Bark	Small Branches	Leaves	
n-hexane	254	0.49, 0.69, 0.88	0.49, 0.78	NR	[8]
	366	0.42, 0.51, 0.59, 0.74, 0.83,0.91	0.42, 0.51, 0.74,0.83,0.91		
Ethyl acetate	254	0.07, 0.12, 0.36, 0.47, 0.61, 0.67, 0.84	0.47, 0.67	0.15, 0.6, 0.8	[8][21]
	366	0.11, 0.15, 0.18, 0.33, 0.38, 0.55, 0.49, 0.65, 0.75, 0.85, 0.90	0.18, 0.30, 0.49, 0.65, 0.75, 0.85, 0.90	0.11, 0.22, 0.38, 0.53, 0.69, 0.82, 0.93	

Extract	Wavelength (nm)	Rf Value			References
		Stem Bark	Small Branches	Leaves	
Ethanol	254	0.23, 0.54	0.23, 0.54	NR	[8]
	366	0.54, 0.73, 0.84	0.25, 0.45, 0.54, 0.73, 0.84		
Methanol	254	NR	NR	0.625, 0.875	[21]
	366			0.46, 0.58, 0.81, 0.86, 0.93	
Aqueous	254	NR	NR	0.1, 0.63	[21]
	366			0.093, 0.65, 0.81	

3.1. Tannins and Phenolic Acids

M. esculenta bark present gallic acid; epigallocatechin 3-*O*-gallate; epigallocatechin-(4β→8)-epigallocatechin3-*O*-gallate;3-*O*-galloyl-epigallocatechin-(4β→8)-epigalloc-atechin3-*O*-gallate along with the hydrolyzable tannin castalagin [6][58]. Reversed-phase high-performance liquid chromatography analysis of fruit extract showed the presence of catechin;gallic acid; chlorogenic acid and *ρ*-coumaric acids [59]. Ethyl-β-D-glucopyranoside; 3-hydroxybenzaldehyde; isovanillin; 4-(hydroxymethyl)-phenol; 4-methoxybenzoic acid have been identified in leaves [60]. LC-MS analysis of fruit extract also indicated the presence of bioactive compounds, such as gallic acid and ferulic acids [61].

3.2. Flavonoids

Myricetin was also reported in leaves, fruits, and stem bark [8][62][40], whereas quercetin was found only in leaves [63].

Two flavonoid glycosides flavone 4′-hydroxy-3′,5,5′-trimethoxy-7-*O*-β-D-glucopyranosyl(1→4) -α-L-rhamnopyranoside and flavone 3′,4′-dihydroxy-6-methoxy-7-*O*-α-L-rhamnopyranoside were found in the leaves [63], while myricetin-3-*O*-(2″-*O*galloyl)-α-L-rhamnopyranoside and myricetin 3-*O*-(2″-*O*-galloyl)-α-L-rhamnopyranoside were revealed in bark [61]. Myricetin 3-*O*-rhamnoside (myricitrin) was accounted in both *M. esculenta* bark, and leaves [62][60][63][64].

3.3. Terpenes

Monoterpenoid

Myresculoside (4-hydroxy-1,8-cineole 4-O-β-dapiofuranosyl (1→6)-β-D-glucopyranoside) were reported in the leaves of *M. esculenta* [62].

3.4. Triterpenoids

Numerous triterpenoids such as lupeol; Oleanolic acid;trihydroxytaraxaranoic acid; dihydroxytaraxerane; dihydroxytaraxaranoic acid; tetrahydroxytaraxenoic aci; 3-epi-ursonic acid; arjunolic acid were reported in bark and leaves of *M. esculenta* [62][58][65][66].

3.5. Volatile Compounds

The volatile compounds identified in leaves [67] were nerolidol; α-pinene; α-selinene; β-caryophyllene; β-selinen; α-caryophyllene; α-cadinol; linalool; whereas in bark were n-hexadecanol; eudesmol acetate and n-octadecanol [66].

3.6. Proanthocyanidins

M. esculenta bark revealed the presence of proanthocyanidins, such as proanthocyanidin acetate; proanthocyanidin methyl-ether and prodelhinidin [68][69].

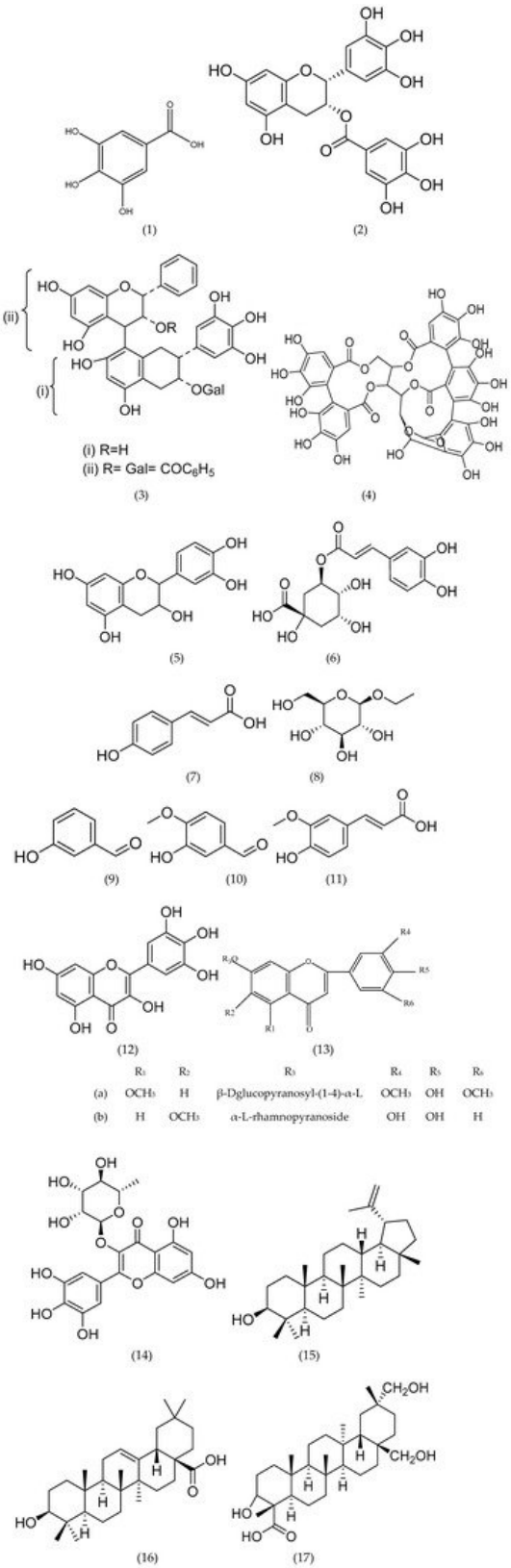
3.7. Diarylheptanoids

M. esculenta bark, leaves and root exhibited the presence of diaylheptanoids. Myricanol and myricnone were reported in bark [6][68][70] and leaves, whereas 13-oxomyricanolwas reported in root [70], 5-*O*-β-D-glucopyranosylmyricanol was accounted in leaves [71], and 16-bromomyricanol was identified in bark [70].

3.8. Steroids

β-rosasterol; daucosterol; β-sitosterol-β-D-glucopyranoside were identified in leaves [60][64] where as taraxerol, stigmasterol were found in bark [72][64][73]. β-sitosterol was identified in both *M. esculenta* leaves [60][64] and bark [65][74]. Other miscellaneous compounds, such as amino acids; 1-ethyl-4-methylcyclohexane, myo-inositol, methyl-d-lyxofuranoside, 2-furancarboxyaldehyde, 2,5-furandionedihydro-3-methylene, furfural, oxirane were also reported in *M. esculenta* fruits [75][61].

The structures of some important bioactive phytoconstituents reported in *M. esculenta* plant are presented in **Figure 1**.



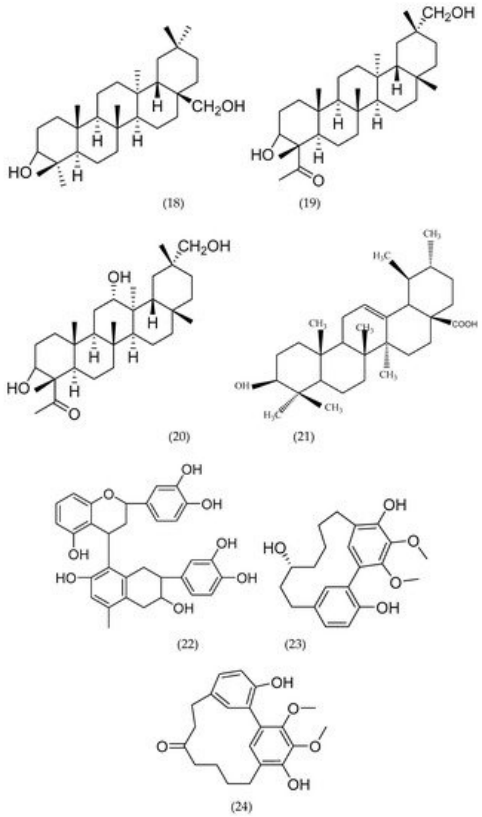


Figure 1. Structure of some isolated bioactive compounds from different parts of *M. esculenta.* (**1**) Gallic acid, (**2**) Epigallocatechin 3-O-gallate, (**3**) i) Epigallocatechin-(4β→8)-epigallocatechin-3-O-gallate, ii) 3-O-galloyl-epigallocatechin-(4β→8)-epigallocatechin-3-O-gallate, (**4**) Castalagin, (**5**) Catechin, (**6**) Chlorogenic acid, (**7**) *p*-coumaric acid, (**8**) Ethyl-β-D-glucopyranoside, (**9**) 3-hydroxybenzaldehyde, (**10**) Isovanillin, (**11**) Ferulic acid, (**12**) Myricetin, (**13**) i) Flavone 4′-hydroxy-3′,5,5′-trimethoxy-7-*O*-β-D-glucopyranosyl(1→4)-α-L-rhamnopyranoside, ii) flavone 3′,4′-dihydroxy-6-methoxy-7-*O*-α-L-rhamnopyranoside, (**14**) Myricitrin, (**15**) Lupeol, (**16**) Oleanolic acid, (**17**) Trihydroxytaraxaranoic acid, (**18**) Dihydroxytaraxerane, (**19**) Dihydroxytaraxaranoic acid, (**20**) Tetrahydroxytaraxenoic acid, (**21**) 3-epi-ursonic acid, (**22**) Prodelphinidin dimer, (**23**) Myricanol, (**24**) Myricanone.

4. Pharmacological Profile

Extracts from *M. esculenta* possess a broad spectrum of pharmacological activities. Previous research revealed that phenolic compounds are highly active antioxidants, and such antioxidant-rich botanicals offer promising potential in the management of degenerative ailments. Phenolic compounds are secondary metabolites synthesized in plants in response to environmental stresses such as attacks from pathogens and insects, UV radiation, and injuries [5][6][7]. These phytochemicals have the ability to eliminate hydroxyl radicals [76], superoxide anion radicals [77], lipid peroxyl radicals [78] and even to chelate metals, besides to play a vital role in the stability of food products, as well as in the defense mechanisms of biological systems [4][8]. These molecules also prevent oxidative losses and have cytoprotective, anti-inflammatory, and adaptogenic properties. It was found that relatively high amounts of phenolic compounds are present in *M. esculenta* fruits than *M. rubra* [59]. The antioxidant activity of *M. esculenta* fruits and bark has been reported by using different antioxidant assays.

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