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Review Article

MYRICA NAGI: A REVIEW ON ACTIVE CONSTITUENTS, BIOLOGICAL AND THERAPEUTIC EFFECTS

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ABSTRACT

Myrica nagi, an endangered tree with wide medicinal applications in Indian subcontinent has rich amount of anti-oxidants along with other classes of chemicals. The utilization of leaves and fruits, of the tree as medicine is a highly sustainable source of natural medicines. The utilization of roots, and stem barks for different remedies is also in practice. High tannin content on woody tissues provides the longevity to the timber, commercial noun of the tree 'box berry' named after edible berries of this tree. During the last one decade, apart from the chemistry of the *Myrica nagi* compounds, considerable progress has been achieved regarding its biological activity and medicinal applications. The present review is an effort to consolidate information available on *Myrica nagi* in the last one decade.

Keywords: *Myrica nagi*, Anti-oxidants, Medicinal application, Biological activity

INTRODUCTION

Myrica nagi F. syn. *Myrica esculenta* Buch.-Ham. (Myricaceae), commonly known as box berry, Kaiphal, Katphala is an important medicinal tree distributed all along outer Himalaya from Ravi (Punjab) eastwards to Assam, in Khasia, Jaintia, Shimla, Bengal, Naga and Lushai hills at altitudes of 900-2100m. The fruits of the tree are edible and are used in the preparation of a refreshing drink. The tree can grow up from 3m to 15m. Pulp constitutes 75.4% of whole fruit and is edible with juice content of 40 %. The juice possesses 3.68% acidity, 12.65 % total sugars, which are mostly reducing sugars. The bark found to constitute 10.5% moisture, 32.1% tannins, soluble nontans 2.9% while in the juice of the fruit tannin content was found to be 1.05% on pulp basis whereas vitamin C only 4.12 mg per 100 ml. The mineral content of the fruit pulp is 0.387% by its ash. The fruit pulp contains 0.97% protein, 0.007% phosphorus, 0.194 % potassium, 0.039% calcium, 0.013% magnesium and 0.004% iron[1, 2]. The tree is a popular remedy for different ailments and is documented for the same[3, 4]. It is widely known for marketing of its berries globally. In Western Himalayan forests it is common in the canopy of *Pinus roxburghii*, *Quercus leucotrichophora* and mixed *oak* forests[5]. Due to wide application, it is being extensively utilized for its medicinal applications, hence regeneration is a necessity pertaining to this tree, a study has been done for the collection of seeds at the time of its maturity to define seed maturity indicators[6]. In a study, the seeds soaked in hot water for the duration of 48hours showed best results for scarification method[7]. This tree is threatened and endangered. In the northeast, its overexploitation may cause threat to extinction from wild[8]. The present review highlights traditional uses and recent studies on the active compounds isolated from *Myrica nagi,* their biological activities and therapeutic effects. The fruits may be potential source for the formulation of nutraceuticals or natural foods[9]. This review bridges the gap between traditional claims and modern therapy on *Myrica nagi*.

Vernacular names

Box myrtle, bay-berry (English), *Kaiphal* (Himachal Pradesh), *kainaryamy* (Andhra Pradesh), *nagatenga* (Assam*), kaiphal, satsarila* (Bengal), *kariphal* (Gujrat), *kapha, kaiphal* (Hindi), *kaphal* (jaunsar), *kirishivani* (Karnataka), *maruta* (Kerala), *sohphi* (Khasi), *kaphal* (Kumaon), *keiphang* (Lushai), *kayaphala* (Maharashtra), *kobuli, katphala* (Nepal), *kaiphal, kahela, kahi* (Punjab) *kathphala, aranya, krishnagarbha* (Sanskrit), *masudam* (Tamilnadu)[2].

TRADITIONAL USES

Medicinal properties of different parts of *Myrica nagi* for combating various diseases have its history way back from traditional system of medicine[10]. In Ayurveda and Yunani system of medicines, this tree is utilized for its bark, flowers, fruits and roots. In Ayurvedic system of medicine, the bark is quoted as acrid, bitter, pungent, heating and finds its application in reducing inflammations. This tree is also utilized for its applications such as acting as a great remedy in anemia, asthma, bronchitis, cough, chronic dysentery, fever, liver complaints, nasal catarrh, piles, sores, throat complaints, tumors, ulcers, urinary discharges. However, Ayurvedic Samhita mentions *Myrica esculenta* to be harmful to liver and spleen. In contrary to this, oil extracted from the flowers acts as a tonic, and has been used useful in earache, headache, diarrhea and paralysis[2, 11, 12, 13]. Even the yellow color extracted from the bark is used as a Medicinal colorant[14, 15]. Fruit constituents exhibit healing properties in case of different ulcers, it also finds application in retention of placenta and bone fracture[16].In present drug manufacturing industry, there is a constant rising demand for herbal drugs[17]. Due to the high medicinal values, the leaves and bark of this medicinally important tree are imported and exported[18]. Traditionally, it was found that the bark of the tree has been used as a fish poison[19]. Fruits are utilized in food industries in Himalayas in different forms like syrups, jam, and squash[20]. Locals in Arunachal Himalaya, India, utilize the tree as timber, for fuel wood and as a wild edible fruit in their diet [21].

PHYTOCHEMISTRY

Fruits

The fruits of *Myrica nagi* are known for their ravishing taste and have been reported for reducing sugars, tannins and Vitamin C[22, 23]. Gallic acid, catechin, chlorogenic acid and *ρ*–coumaric acid in the ethanolic extract of the fruits[24] were examined by HPLC analysis, it scavenge 2,2'-azinobis(3-ethylbenzoline-6-sulphonic acid) radical ($ABTS^{c+}$) and 1,1-diphenyl-2-picrylhydrazyl radical ($DPPH^{c+}$) and reduce ferric ion. It was found that Gallic acid was responsible for the sourness of the fruits. The natural compound Myricetin isolated from the fruit has been studied for the effective matrix metalloproteinase. Its Inhibition activity has been extensively studied and one patent has been filled for the same[25].

The alcoholic extract of fruits was analysed with TLC using silica gel plate with n-butanol: acetic acid: water (4:1:5) as mobile phase, five spots at R_f 0.25, 0.43, 0.57, 0.75 (all grey) and 0.88 (Yellowish green) were observed under visible light. Under 365 nm seven spots at R_f 0.09, 0.18, 0.30 (all light blue), 0.43 (green), 0.49 (blue), 0.65 (blue) and 0.71 (pink) were observed. After exposing to Iodine vapour eleven spots at R_f 0.07, 0.09, 0.12, 0.25, 0.30, 0.35, 0.43, 0.52, 0.57, 0.75 and 0.88 (all yellow) appeared. While when sprayed with 5% methanolic sulphuric acid reagent and heating the plate at 110°C six spots appeared at R_f 0.09 (black), 0.30 (black), 0.57 (light brown), 0.71 (light pink), 0.82 (light pink) and 0.88 (yellowish green)[26].

Bark

The bark constitute gallic acid, myricanol, myricanone, epigallocatechin 3-*O*-gallate, two prodelphinidin dimmers [epigallocatechin-(4β→8)- epigallocatechin 3-*O*-gallate and 3- *O*-galloyl epigallocatechin-(4β→8)-epigallocatechin3-*O*-gallate], hydrolysable tannin castalagin. Prodelphinidin units with 2,3-cis configuration having average of 5000 mean molecular weight (Mr) were found in the higher mean molecular weight (Mr) fractions. The terminal unit of the polymer has epigallocatechin 3-O-gallate, the extender units were also known to have galloyl group at C-3[27]. Proanthocyanidins with water were extracted by ultrasound-assisted technique[28]. The terminal unit of the polymer has epigallocatechin 3-O-gallate, the extender units were also known to have galloyl group at C-3[27]. Gallic acid, lupeol, oleanolic acid and stigmasterol were evaluated by HPTLC in bark extract. Gallic acid at Rf 0.56 with toluene-ethyl acetate- formic acid (5:5:1) as mobile phase, while oleanolic acid, stigmasterol, and lupeol at Rf 0.38, 0.49, 0.62 with toluene-ethyl acetate (8:2) as mobile phase were established[29]. The stem bark constitute flavonol glycosides myricetin-3-*O*-(3''-Ogalloyl)- α-L- rhamnoside, myricitrin-3-O-(2''-*O*-galloyl)- α-Lgalactoside, myricetin, 3-*O*-(2''-*O*-galloyl)- α-L-rhamnoside, myricitrin, diarylheptanoid glycosides characterized as myricanol-5-O-β-Dglucopyranosyl(1→3)-β-D-glucopyranoside and myricanol-5-O-α-Larabinofuranosyl(1→6)-β-D-glucopyranoside, acetone fraction[30,31] of the bark contains proanthocyanidin while the root bark[32] constitutes 13-oxomyricanol. The methanolic extract of root[33] found to exhibit anti-inflammatory effect. In an another study carried out on gallic acid[34]**;** it was found that in free and combined form on a dry weight basis gallic acid present in the stem bark was 0.276% and 0.541% respectively. Separation of gallic acid using silica gel 60F254 with toluene: ethyl acetate: formic acid: methanol (3:3:0.6:0.4), as mobile phase was done, finally confirmed at 280nm using UV detector. In another study, the separation of Myricetin achieved on silica gel 60F254 HPTLC plates with toluene: ethyl acetate: formic acid: methanol (3: 3: 0.6: 0.4) as mobile phase, the quantification done at 268nm gave 0.225% weight by weight value. The hydrodistilled oil extracted from the stem bark[35] with 0.3% was analysed by capillary GC and GC-MS. The constituents found are as: *n*-hexadecanol (25.2%), eudesmol acetate (21.9%), palmitic acid (11.6%), *cis*-*β*-caryophyllene (8.7%), *n*-pentadecanol (7.7%) and *n*-octadecanol (7.6%). In Swiss albino mice ear, anti-inflammatory activity of the extracted oils was found highly significant against the standard drug. The alcoholic extract of the stem bark was analyzed with TLC on Silica gel plate using Toluene: ethyl acetate (7:3) as mobile phase. Under visible light, four spots at R_f 0.08 (grey), 0.32 (yellow), 0.51 (grey) and 0.58 (yellow) were observed while under UV (365 nm) three fluorescent zones appear at R_f 0.49, 0.67 (both light blue) and 0.86 (blue). When plates were sprayed with 5% Methanolic-Sulphuric acid reagent and heated at 110℃ for ten minutes six spots appear at R_f 0.08, 0.21 (both grey), 0.35 (Pink), 0.52, 0.67, and 0.80 (all grey)[26].

Leaves

Leaves are reported to constitute 4-hydroxy-1,8-cineole 4-*O*-*β*-Dapiofuranosyl-(1→6)-*β*-D-glucopyranosie, (1*S*,2*S*,4*R*)-2-hydroxy-1,8-cineole *β*-D-glucopyranoside, corchoionoside C, (6*S*,9*R*)-roseoside, myricanol, 5-*O*-*β*-D-glucopyranosyl myricanol, arjunolic acid, arjunglucoside, 3-*epi*-ursonic acid, 3-*O*-(E)-caffeoylursonic acid, myricetin, myricitrin[36]. On the spectroscopic evidences flavone 4'-hydroxy-3',5,5'-trimethoxy-7-O-*β*-$_D$-glucopyranosyl (1→4)-α-L-rhamnopyranoside and 3', 4'-dihydroxy-6-methoxy-7-O-α-L-rhamnopyranoside, *β*-Sitosterol, *β*-Sitosterol-*β*-$_D$-glucopyranoside and quercetin were elucidated[37]. The volatile oil was extracted by distillation and analyzed by gas chromatography-mass spectrometry. The major constituents were Nerolidol (13.46%), α-pinene (13.46%), α-Selinene (12.28), β-Caryophyllene (11.66%), β-Selinen (9.71%), α-Caryophyllene (8.94%), α-cadinol (5.32%), Linalool (4.06%)[38].

In a study done on the chemical constituents thirteen compounds myricitrin, myricanol, myricanone, gallic acid, ethyl *β*-*D*-glucopyranoside, 3-hydroxybenzaldehyde, isovanillin, 4-methoxybenzoic acid, 4-(hydroxymethyl) phenol, *β*-sitosterol, daucosterol were isolated by silica gel column chromatography and recrystallization. In this study conformation of Myricanol was done by X-ray diffraction for the first time[39].

PHARMACOLOGY

Medicinal plants possess pharmacological actions on animals due to the presence of secondary metabolites. The pharmacological aspect of this tree with immense medicinal applications has been well studied for its efficacy and wide utility. A number of animal models have been used for finding the pharmacological effects. These pharmacological activities prove the traditional utilization of the tree scientifically[40].

Anti-allergic activity

The stem bark of *Myrica esculenta* has been studied for anti-allergic activity and it was concluded that it can be used in the allergic disorders. The ethanolic extract of the stem bark possess potential anti-allergic activity when studied on mice. In the experiment Allergic pleurisy and vascular permeadbility were induced by acetic acid in mice[41].

Anti-inflammatory activity

An experimental study was carried out to find the anti-inflammatory activity in an animal model as rat paw edema. In rat paw edema ethyl acetate and aqueous extracts of bark showed anti-inflammatroy activity. Challenged rats with histamine induced rat paw edema, showed 18-25 % inhibition with the ethyl acetate and aqueous extracts. While the standard drug showed 27%. This study concluded that flavonoids and steroids might be responsible for the activity. The characterization of such phytoconstituents is still to be done[42]. In an another study carried out by group of scientists on the bark, the essential oils were found to possess significant topical anti-inflammatory activity, in comparison to standard drug in Swiss albino mice ear[35].

Antioxidant activity

The fruits of the tree were studied[24, 43] for the antioxidant activities and it was found that they can be utilized as natural antioxidants. The study also revealed that Phenolics and Flavonoid contents were higher in *Myrica esculenta* fruits than *Myrica rubra*, another species of the same genus found in China. The same study proved that *Myrica esculenta* fruits possess strong antioxidant activity than *Myrica rubra*[24].

Antihelmintic Activity

Aqueous ethanolic extract of bark showed anti-helmintic activity on Indian earthworm. The effects were found more than reference. The extract caused paralysis followed by the death of the worms at all tested dose levels. It was proved through this study that extract effects were dose dependent[22].

Anti-microbial activity

The essential oil of the stem bark was found to be a potent antimicrobial agent against the various bacterias with average zone of inhibition as 17.9mm with 17.6mm, 19.5mm, 26.9mm, 9.5mm and 15.9mm. The aqueous extract of the stem possess strong activity against brine shrimp (*Artemia salina)* while organic extract do not[20, 43]. While in an another *in vitro* antimicrobial activiy analysis done on the ethanolic fruit extracts, potent activity was found against *Escherichia coli*, *Streptococcus pyogenes* against food poisoning bacteria[9].

Anxiolytic effect

The ethanolic extract of the bark was subjected for anxiolytic study, positive results were obtained for the same while negative results were attained for antidepressant effects. Results showed that the ethanolic extract possess dose dependent anxiolytic activity, when the oral administration of the ethanol extract at dosage of 100, 200, and 400 mg/kg was conducted[44].

Chemopreventive effect

Myrica nagi is an effective chemopreventive agent in skin and capable of ameliorating cumene hydroperoxide induced cutaneous

oxidative stress and toxicity. It was found that the protective effect was dose-dependent[45].

Hypertension

A study focused on the megastigmanes of *Myrica esculenta* for the management of hypertension revealed that the compound corchoionoside C and (6*S*,9*R*)-roseoside isolated from the leaves of the tree were potent ACE inhibitors with rates 29.97% and 25.63% at the concentration of 100μM, while myricanol, 5-*O*-*β*-D-glucopyranosyl myricanol and myricetin show weak activity with inhibitory rates of 0.07-1.41% at concentration of 100μM[36].

Mast cell stabilizing effect

Ethyl acetate and water extracts of the bark at the dose of 100mg/kg, 200mg/kg were analyzed for Mast cell stabilizing activity. The studies with egg albumin model showed better protection of mast cell degranulation (45-62%) in comparison to that of the standard drug: prednisolone (65%). When the peritoneal mast cells treated with compound, extracts showed better mast cell stabilizing activity. For the extracts the percentage of advanced results was in the range of 70-78% while for the standard drug it was found 65%[46].

***Myrica nagi* as a herbitar**

Myrica nagi as a herbitar a poly herbal formulation against CCl4 induced hepatotoxicity in rats using albino Wistar rats as animal model. It was found that *Myrica nagi* as herbitar reverse the alterations in lipid peroxidation and antioxidants status during CCl_4 induced hepatotoxicity in rats[47].

APPLICATION IN NANOSCIENCES FIELD

From Bark Tanin (BT)

The homogenous Palladium (Pd) nanoparticles were prepared from the bark of *Myrica esculenta* tannin (BT) and later on were immobilized onto γ-Al_2O_3 for the preparation of heterogeneous γ-Al_2O_3-BT-Pd catalysts. Fourier Transformation Infrared Spectrum and X-ray Photoelectron Spectroscopy were employed to find out the stability of phenolic hydroxyl groups, it was found that Pd NPs were stabilized by the phenolic hydroxyl groups of *Myrica esculenta*. Even after using γ-Al_2O_3-BT-Pd for five times for the hydration of olefins no significant loss of the catalytic activity were recorded. This proves its superior usability over conventionally prepared γ-Al_2O_3-Pd catalysts[48].

From Leaf Extract

Silver (Ag) nanoparticles were prepared from the plant extract of *Myrica esculenta*. The spherical silver nanoparticles with 55nm average size were prepared by the extract of *Myrica esculenta* after the bio-reduction of aqueous Ag^+ ion in six hours. The characterization was done with UV-Vis spectroscopy, X-ray diffractometer and transmission electron microscope[49].

MYRICETIN: AN IMPORTANT PHYTOCONSTITUENT

Myricetin[50], yellow-beige powder crystalline powder, a flavonol, consisting of 3-hydroxyflavone backbone and 6 hydroxyl groups has been extracted from the leaves and fruits of the species. Through literature survey, it is found that there are a lot of benefits of Myricetin to health as it possess wide variety of biological effects, as antioxidant and free radical scavenging activities. Myricetin has anti-cancer, antimutagenic and anti-inflammatory properties. Myricetin application in diabetes, heart problems, and in brain health are well known[51], in an *in-vitro* study on epidermal growth factor-activated mouse epidermal cells found that myricetin might directly target Janus kinase 1 (JAK1) and thereby inhibiting cell transformation. Anti-inflammatory properties were proved as it inhibit the expression of tumor necrosis factor-alpha, which is a cytokine responsible for promoting the inflammatory response. Myricetin is also involved in inflammatory diseases. Leaves of *Myrica rubra*[52] another species of the genus found in China were examined with different *in vivo* models, for both acute and chronic inflammations. The study also proved that Myricetin inhibited the increase in capillary permeability induced by the production of acetic acid in the human body. While on the other hand, Myricetin significantly decreased the serum levels of Malonyldialdehyde (MDA) and, in turn, increased the serum levels of increased superoxide dismutase (SOD) in the carrageenan-induced paw edema model. The significant decreased leukocyte count was also recorded. The granuloma tissue was inhibited during chronic inflammation by Myricetin. The study proves that Myricetin possesses a potent anti-inflammatory function on acute and chronic inflammation. Its anti-inflammatory mechanisms are associated with the inhibition of antioxidant activity. No such study has been done on *Myrica nagi*.

Role of Myricetin In Various Health Issues

Myricetin can improve heart health[53] by preventing Low-density lipoprotein (LDL) oxidation and reducing the uptake of oxidized LDL by macrophages. It is known that Myricetin along with preventing LDL from oxidation block oxLDL uptake by macrophages also that is too at least in part through reducing CD36 gene expression on macrophages. Scientists have a strong opininion that atherosclerosis can be ameliorated by Myricetin use. Diabetic rats[54] were taken for a study and it was found that Myricetin inhibits the uptake of methylglucose by adipocytes and reduces oxidative injury in diabetes related bone diseases, it also reduces glucose plasma level in diabetic rats. It inhibits ROS production caused by glutamate and reduces glutamate-induced activation of caspase-3. Myricetin restored dopamine level in the animals induced with Parkinsonism models[55]**.** Myricetin also inhibit beta-amyloid fibril formation in Alzheimer patients.

FUTURE PROSPECTS

Through literature survey, it was found that the nano particles were already prepared from the leaf extract and bark tannin of the tree but the other parts (roots, fruits) of the tree are yet to be explored in the nanoparticle field. The fruits of the tree have already been quoted for the antioxidant activity. But the most important compound Myricetin found in the fruit of the species has been studied only for effective matrix metalloproteinase Inhibition activity for cancer. This naturally occurring compound can be further studied for diabetes, brain diseases, etc. The compound and its derivatives can be synthesized in the laboratory. The need of hour is to utilize this compound by working on other pharmacological studies because medicinal herbs as the potential source of therapeutics aids has attained a significant role in health system all over the world for both humans and animals not only in the diseased condition but also as a potential material for maintaining proper health. As *Myria nagi* is endangered, a prompt attention needs to be given to protect the tree from extinction.

CONCLUSION

Myrica nagi is an important medicinal tree, which is safely and effectively used to treat various disorders in Ayurvedic system of medicines since ancient times. Bioactive compounds of the tree have several pharmacological activities such as; anti-inflammatory, antioxidant, antihelmintic, anti-microbial, anxiolytic, chemopreventive, mast cell stabilizing, hypertension which itself speaks about the wide scope for the utilization of this species. There are strong prospects for the commercial utilization of the species. Most pharmacological work has been done on bark, fruits, flowers but the pharmacological potential of the other part of the trees constitute a potential area for research in future. Efforts should be made to standardize a technique for its utilization of all the parts which will lead to wider commercial applicability.

REFERENCES

1. Annonymous. The Wealth of India: Raw Material. 6th ed. CSIR (New Delhi) Publications and Information Directorate; 1962. p. 472.
2. Parmar C, Kaushal M K: *Myrica nagi*. In: Wild fruits. New Delhi (India): Kalyani publishers; 1982. p. 49-53.
3. Nadkarni KM. Indian Materia Medica, 1st ed. Bombay: Popular book depot; 1954. p. 828-829.

4. Seal T Antioxidant Activity of some wild edible fruits of Meghalaya state in India. Advan Biol Res 2011;5 :155-160.
5. Bhatt ID, Dhar U Factors controlling micropropagation of *Myrica esculenta* buch.-Ham. ex D. Don: A high value wild edible of Kumaun Himalaya. Afr J Biotechnol 2004;3 :534-540
6. Shah S, Tewari A, Tewari B, Singh R P Seed maturity indicators in *Myrica esculenta*, Buch-Ham. Ex. D.Don.: A multipurpose tree species of subtropical temperate Himalayan region. Springer New forests 2010;40 : 9-18.
7. Rawat JMS, Tomar YK, Rawat V Effects of pretreatments on *Myrica esculenta* D.Don (Kaphal) seed germination and seedling performance. Forests, Trees and Livelihoods 2009;19 **:**193-197.
8. Jeeva S, Lyndem FG, Sawian JT, Laloo RC, Mishra BP *Myrica esculenta* Buch.-Ham. ex D. Don.- A potential ethnomedicinal species in a subtropical forest of Meghalaya, northeast India. Asian Pac J Trop Biomed 2011: S174-177.
9. Saklani S, Chandra S, Mishra AP, Badoni PP Nutritional evaluation, antimicrobial activity and phytochemical screening of wild edible fruit of *Myrica nagi* pulp. Int J Pharm Pharm Sci 2012; 4 Suppl:407-501.
10. Bhatt ID, Rawal RS, Dhar U The availability, fruit yield, and harvest of *Myrica esculenta* in Kumaun (West Himalaya), India. Mt Res Dev 2000;20 :146-153.
11. Kirtikar K R, Basu B D Indian Medicianl Trees. 3rd vol. Allahabad (India): Lalit Mohan Basu publishers; 1988. p. 2350-2351.
12. Chatterjee A, Pakrashi SC The Treatise on Indian Medicinal Plants, Reprinted Edition, 1st vol. New Delhi: Publications and Information Directorate; 1994. p.32-33.
13. Kumari P, Joshi GC, Tewari LM: Diversity and status of ethno-medicinal trees of Almora district in Uttarakhand, India. Int J Biodvers conserv 2011;3 p. 298-326.
14. Kumar JK, Sinha AK Resurgence of natural colourants: A Holistic view. Nat Prod Lett 2004;18 :59-84.
15. Semwal RB, Semwal DK, Kapoor P Dyeing Properties of *Berberis aristata* DC with Natural and Synthetic Mordants. Trends Applied Sci Res 2012;7 Suppl 5 :392-99.
16. Nadkarni KM Indian Materia Medica, Bombay; Popular book depot; 1954. p. 828-829.
17. Maiti B, Nagori BP, Singh R, Kumar P, Upadhyay N Recent trends in herbal drugs: A review. Int J Drug Res Technol 2011;1 Suppl 1:17-25.
18. Verma S, Singh SP Current and future status of herbal medicines. Vet. world 2008;1 :347-50.
19. Pala NA, Negi AK, Todaria NP Traditional uses of medicinal plants of Pauri Garhwal, Uttrakhand. Nat Sci 2010;8 Suppl 6 :57-61.
20. Dhyani PP, Dhar U Box Myrtle (*Myrica esculenta*, Kaiphal)- A promising underexploited tree crop of Himalaya. Himavikas occasional publication .3rd ed. GB Pant Institute of Himalayan Environment and Development, Almora; 1994. p.33.
21. Dollo M, Samal PK, Sundriyal RC, Kumar K Environmentally sustainable traditional natural resource management and conservation in Ziro valley, Arunachal Himalaya India. J Amer Sci 2009;5 :41-52.
22. Jain VK, Jain B Anthihelmintic Activity of ethanolic extract of bark of *Myrica esculenta*. J Pharm Sci 2010;1: 129-131.
23. Patel T, Dudhpejjya A, Sheath N Anti inflammatory activity of *Myrica nagi* Linn. Bark. Ancient Sci Life 2011;30 :100-103.
24. Rawat S, Jugran A, Giri L, Bhatt ID, Rawal RS Assessment of antioxidant properties in fruits of *Myrica esculenta*: A popular wild edible species in Indian Himalayan Region. ECAM 2010:1-8.
25. Mannello F Natural Bio-Drugs as matrix metalloproteinase inhibitors: New perspectives on the horizon. Recent Patents on Anti-Cancer Drug Discovery 2006;1: 91-103.
26. Anonymous: The Ayurvedic Pharmacopoeia of India, Min. of Health and Family Welfare, Department of ISM and H, Govt. of India, Part I. vol. III: New Delhi; 2001.p.90-91.
27. Dawang S, Zhao Z, Wong H, Foo LY Tannins and other phenolics from *myrica esculenta* bark, Phytochem 1988;27 :579-583.
28. Mei WD, Hong CJ, Mei WY, Man X, Song WZ: Study on ultrasound-assisted extraction of proanthocyanidins from *Myrica esculenta* Bark. Conference paper. Chem Indus Forest Prod 2009;29 :105-9.
29. Singh N, Khatoon S, Srivastava N, Rawat AKS, Mehrotra S Qualitative and quantitative standardization of *Myrica esculenta* Buch.-Ham. Stem bark by use of HPTLC. J Planar Chromat 2009;22 :287-291.
30. Patel KG, Patel VG, Patel KV, Gandhi TR Validated HPTLC method for quantification of myricetin in the stem bark of *Myrica esculenta* Buch. Ham. Ex D. Don, myricaceae. J Planar Chromat. 2010;23 :326-31.
31. Krishnamoorthy V, Seshadri TR A new Proanthocyanidin from the stem bark of *Myrica nagi* thumb. Tetrahedron 2001;22 :2367-2371
32. Malterud KE, Anthonsen T 13-oxomyricanol, a new [7.0]-metacyclophane from M*yrica nagi,* Phytochem.1980;19 :705-7.
33. Kunwar R, Shrestha K, Bussmann R Traditional herbal medicine in Far-west Nepal: a pharmacological appraisal. J Ethnobiol Ethnomedicine. 2010;6 :35.
34. Patel KG, Patel VG, Patel KV, Gandhi TR Validated HPTLC method for quantitative determination of gallic acid in stem bark of *Myrica esculenta* Buch-Ham. ex D. Don, myricaceae. J. AOAC Int 2010;93 :1422-7.
35. Agnihotri S, Wakode S, Ali M Essential oil of *Myrica esculenta* Buch. Ham: composition, antimicrobial and topical anti-inflammatory activities. Nat. Prod. Res. 2012; DOI. 10.1080/14786419.2011.652959.
36. Nhiem NX, Kiem PV, Minh CV, Tai BH, Cuong NX, Thu VK, et al A new monoterpenoid glycoside from *Myrica esculenta* and the inhibition of Angiotensis I-Converting Enzyme. Chem Pharm Bull. 2010;58 :1408-1410.
37. Bamola A, Semwal DK, Semwal S, Rawat U Flavonoid glycosides from *Myrica esculenta* leaves. J. Indian Chem. Soc. 2009;86 :535-6.
38. Hui-fen MA, Zheng-liang Y, Sang-zi ZE, Yong-jie Li, De-lul N, Zhen Y U GC/MS analysis of volatile components from leaf of *Myrica esculenta* Buch.-Ham; DOI. CNKI:SUN:GDNY.0.2011-16-035.
39. Wei Y, Chang-ming T, Xian L, Ya Z, Li W, Liang L: Study on the chemical constituents of *Myrica esculenta*. J Yunnan University (Nat Sci) 2011;33 Suppl 4 :453-7.
40. Sarwar M, Attitalla HI, Abdollahi M A review on the Recent Advances in Pharmacological Studies on Medicinal Plants; Animal Studies are Done but Clinical Studies Needs Completing. Asian J Anim Vet Adv 2011; 6 Suppl 8: 867-883.
41. Patel KG, Rao NJ, Gajera VG, Bhatt PA, Patel KV, Gandhi TR Anti-allergic activity of stem bark of *Myrica esculenta* Buch.-Ham. (Myricaceae). J Young Pharmacists 2010;2:74-78.
42. Patel T, Rajshekar C, Parmar R Mast cell stabilizing activity of bark of *Myrica nagi*. J Pharm Stud Res 2011;2 :1-6.
43. Shan B, Cai YZ, Brooks JD, Corke H The in vitro antibacterial activity of dietary spice and medicinal herb extracts. Int. J. Food. Microbiol 2007; 117 :112-9.
44. Khan MY, Sagrawat H, Upmanyu N, Siddique S Anxiolytic properties of *Myrica nagi* bark extract. Informa Healthcare 2008;46 :757-1.
45. Alam A, Iabal M, Saleem M, Ahmed SU, Sultana S *Myrica nagi* Attenuates cumene hydroperoxide-induced cutaneous oxidative stress and toxicity in swiss albino mice. Pharmaco Toxicol 2000;86 :209-4.
46. Rastogi RP, Mehrotra BN Compendium of Indian medicinal trees, 4th ed. New Delhi: CSIR Publication; 1995.p.490-492.
47. Samundeeswari C, Rajadurai M, Periasami R, Kanchana G Hepatoprotective effect of Herbitars, A polyherbal against CCl_4 induced hepatotoxicity in rats. J Pharm Res 2011;4 :676-9.
48. Chen C, Lv G, Huang X, Liao XP, Zhang WH, Shi B Bayberry Tannin as Stabilizer for the Synthesis of Highly Active and Reusable Heterogeneous Pd Catalysts and Their Application in the Catalytic Hydrogenation of Olefins. Bull Korean Chem Soc 2012; 33(Suppl 2):403-408.
49. Phanjom P, Zoremi E, Mazumder J, Saha M, Baruah BS Green Synthesis of Silver Nanoparticles using Leaf Extract of *Myrica esculenta* Int J NanoSci Nanotech 2012; 3 Suppl 2 :73-79.
50. Sharma S, Hullatti KK, Prasanna SM, Sharma P Comparative Morpho-Anatomical and Preliminary Phytochemcial Studies of

Cuscuta reflexa and *Cassytha filiformis*. Int J Pharm Pharmaceutic Sci 2010; 2 Suppl 1 : 59-64.

51. Lett C Myricetin directly targets JAK1 to inhibit cell transformation. Cancer Lett. Mar 2009;8275 :17-26.
52. Wang SJ, Tong Y, Lu S, Yang R, Liao X, Xu YF, et al Anti-inflammatory activity of myricetin isolated from *Myrica rubra* Sieb. et Zucc. Leaves. Treea Med 2010;76 :1492-6.
53. Lian TW, Wang L, Lo YH, Huang IJ, Wu, MJ. Fisetin Morin and Myricetin attenuates CD36 expression and oxLDL uptake in U937-derived macrophages. Biochim Biophys Acta 2008;1781 :601-9.
54. Pandey KB, Mishra N, Rizvi SI Myricetin may provide protection against oxidative stress in type 2 diabetic erythrocytes, Z. Naturforsch C 2009;64 :626-30.
55. Shimmyo Y, Kihara T, Akaike A, Niidome T, Sugimoto H Multifunction of myricetin on A beta: neuroprotection via a conformational change of A beta and reduction of A beta via the interference of secretases. J Neurosci Res 2008;86 :368-77.