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***Murraya koenigii* (L.) (Curry Leaf): A Traditional Indian Plant.**

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ABSTRACT

India is rightfully called as the “Botanical garden of the world”. It is the land of several medicinal plants and herbs that are traditionally used to cure ailments. *Murraya koenigii*, is one such plant, also called the curry leaf. It belongs to the family Rutaceae. It grows throughout the Indian subcontinent. It has wide culinary use and is one of the main components of formulations in the traditional Ayurvedic system. The ethanobotanical, phytochemical, pharmacological and pharmacognostic characteristics of *Murraya* have been studied in great detail over the past years. Carbazol alkaloids are abundantly present in its stem, leaf and root extracts. These have antidiabetic, anticancer, antimicrobial, antioxidant and several other beneficial properties. This review gives a description of the structural features, history, ecology, composition as well as applications of this incredible plant in medicine and therapy.

Keywords: *Murraya koenigii*, Curry leaf, Rutaceae, Carbazol alkaloids, Pharmaceutics.

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INTRODUCTION

Several plants have been beneficial to mankind since ancient times. They play an important role in providing shelter, clothing, food, flavor and medicinal products among many other uses [1]. Ayurveda, Unani, Amchi and Siddha are some of the Indian practices that use medicinal plants for treatment of several human as well as animal diseases [2]. As stated by the World Health Organization, 80% of the population, markedly in the developing countries, banks on traditional plant based medicine for primary health care [2, 3]. Compounds such as proteins, fats, carbohydrates, enzymes, oils, flavonoids and terpenoids are known to be present in plants, out of which several compounds are biologically active and are used in the cure and control of numerous diseases. One such medicinal plant is the *Murraya Koenigii*, known as Kari patta or Meethi neem in the local dialect. It belongs to the family *Rutaceae* (Citrus family) that consists of approximately 150 genera and 1500 species [4]. *Murraya Koenigii* is found to be native mainly to India and Sri Lanka. Additionally, it can be found in some other South Asian countries as well. It is a deciduous, small tree or a shrub which is aromatic in nature and grows up to a height of about 6-9m and up to an altitude of 1500m. It is an important ingredient in Indian curries owing to its fragrance and aroma. This plant is known to be the richest source of carbazole alkaloids. Carbazole alkaloids, present in *M. koenigii* (L.) Spreng, is responsible for its multiple biological properties such as its anti-tumor, anti-mutagenic, anti-oxidative and anti-inflammatory activities.

The oil of *Murraya koenigii* is reported to possess antibacterial, antifungal, hypolipidemic, anti-lipid peroxidative, hypoglycemic, antioxidant and anti-hypertensive properties [5]. The soap and cosmetic aromatherapy industry utilizes this essential oil as an important part in soap making ingredients, bath oils, massage oils, perfume oils, lotions, diffusers, facial steams, potpourri, towel scenting, air fresheners, incense, body fragrance, scent, aromatherapy products and more [6]. Curry leaves, boiled with coconut oil are reduced to blanked residues that are then used as a powerful hair tonic for retaining and maintaining natural hair tone, hair growth stimulation and prevention of premature growing of hair [7].

Thus, *Murraya koenigii* oil has increasing importance in the pharmaceutical industry as well as in aromatherapy besides having a major traditional role in cosmetics and food, as fragrance donor as well as a potent ingredient.

DESCRIPTION, HISTORY AND ECOLOGY

Out of the 14 global species that belong to the genus *Murraya*, only two are known to be found in India, which is *M. koenigii* (L.) Spreng and *M. paniculata* (L.) Jack. Out of these two, the former is more popular as it has potent medicinal properties and its leaf is widely used as a natural flavoring agent in varied food delicacies [5]. The curry leaf tree is indigenous to India, Sri Lanka, Andaman Islands and Bangladesh. It was later spread worldwide by the Indian migrants. These trees are seen growing in forests and waste lands throughout the subcontinent except in the Himalayas. The use of these leaves in curries can be dated back to Tamil literature, around 1st to 4th centuries AD. Its use has been mentioned in some of the Kannada literature also. The word 'curry' originated from the Tamil word 'kari' which means 'spiced sauce' [10]. It is a shrub or a small tree having a main, dark greenish to brown, stem with several dots on it. The bark can be longitudinally peeled off to expose the white wood that lies underneath. Leaves are bipinnately compound having reticulate venation, bearing leaflets. The flowers are small, white in color, bisexual, deeply five cleft calyx, pubescent, having five petals which are free, glabrous, whitish in color and with dotted glands. Fruits are seen to occur in close clusters, small ovoid or sub-globose, glandular with a thin pericarp. They are biseeded, seeds having spinach green colour [7].

COMPOSITION

The curry leaves are a rich source of many carbazole alkaloids with a diverse chemical composition. Solvents like ethyl acetate, ethanol, petroleum ether, water and chloroform have been used by researchers to prepare the plant extracts, and compounds such as alkaloids, flavonoids and sterols have been reported to be present in them.

The curry leaves are rich in various sources such as proteins, fibers, carbohydrates, minerals, nicotinic acid, vitamin C and carotene. They have a great content of oxalic acid and also contain crystalline glycosides, carbazole, alkaloids, resin and koenigin. Girinimbin, koenimbine, koenigine, koenidine, koenine, coumarine

(called murrayone imperotoxin), mahanimbicine, iso-mahanimbicin, bicyclomahanimbicine and phebalosin are also the major phytoconstituents as depicted in Figure 1 [2]. Leaves also contain triterpenoid alkaloids such as cyclomahanimbicine and tetrahydromahanimbicine. Carbazole alkaloids such as girinimbine, murrayacine, koenioline, xynthyletin, murrayazoline, murrayacine and murrayazolidine are the main constituents of the bark [11]. The fruit pulp contains reducing and non reducing sugars along with some negligible amounts of tannins and acids. Trace amounts of phosphorous, potassium, calcium, magnesium and iron are also present along with vitamin C [12]. Xanthotoxin, isobyakangelicol and other minor Furocoumarines have also been isolated from the seeds. The volatile oil that is present in fresh leaves is a rich source of vitamin A and calcium. The essential oil composition, when studied, showed the presence of D-sabinene, D- α -terpinol, di- α -phellandrene, D- α -pinene, caryophyllene and dipentene [13]. Roots contain girinimbine, koenoline (1- methoxy-3- hydroxyl methyl carbazole) [14-17].

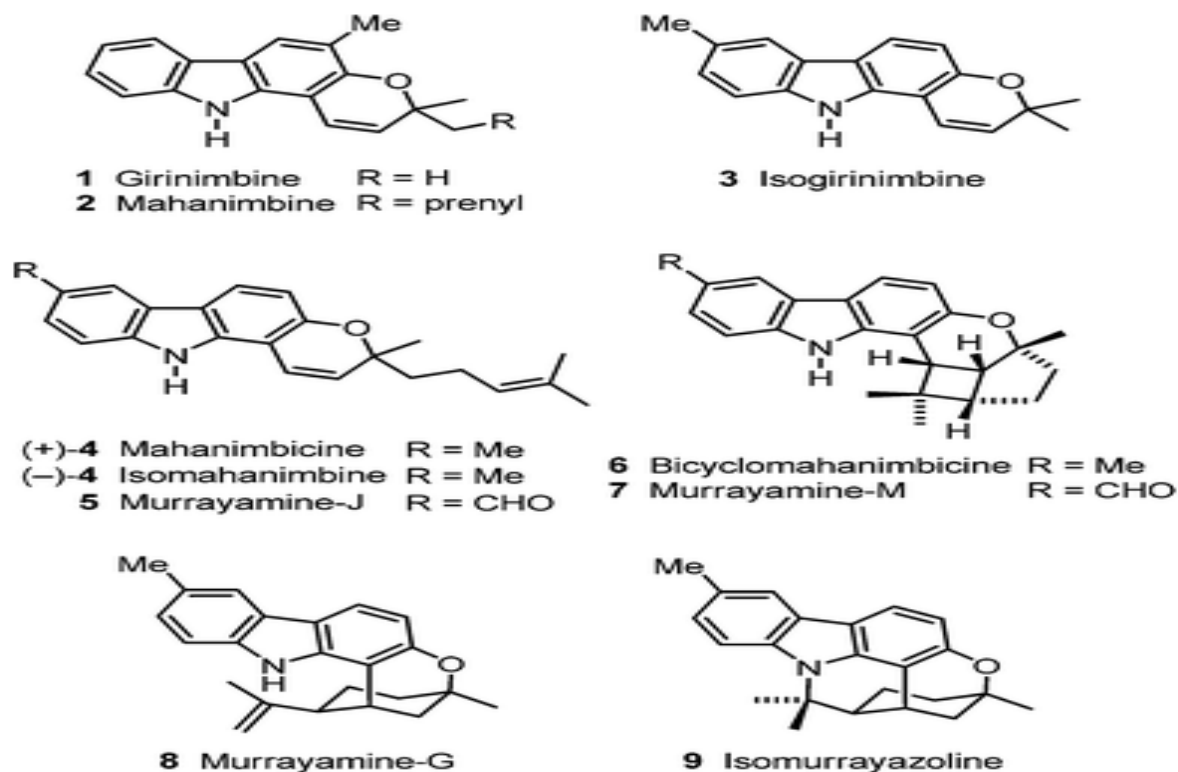


Figure 1: Phytoconstituents present in Curry leaves

BIOACTIVITY OF VARIOUS COMPOUNDS

Various bioactive compounds present in *Murraya koenigii* makes it helpful for treating several diseases and as a potential source for providing useful drugs. As mentioned before, this plant is rich in carbazole alkaloids, and GCMS analysis shows the presence of various compounds that have medicinal properties, making *Murraya koenigii* a pharmacologically important plant.

Different chemical constituents that are obtained from various parts of the plant show versatile properties. Girinimbiol and Girinimbine, the most active carbazole alkaloids that are present in the stem and leaves show anti fungal, antibacterial, anti-cancer, anti tumor, hypoglycaemic as well as hepatoprotective properties. Murrayanine and Murrayacine show anti bacterial and anti fungal properties. Mahanine and Mahanimbicine are topoisomerase I and II inhibitors. Mahenine is also reported to instigate apoptosis in human myeloid cancer cell (HL-60). Down regulation of cell survival factors as well as disruption of cell cycle progression is also brought about by this compound.

Koenimbine, Koenine and Koenigine, that are extracted from the leaves, show antioxidant, anti-diarrheal and radical-scavenging properties. Hepatoprotective nature is inherent in compounds like murrayazolidine, murrayazoline, tocopherol and isomahanimbicine.

Mahanine, bismurrayafoline E, euchrestine, bismahanine, bispyrafoline, isomahanine, O-methyl murrayamine A, O-methyl mahanine, lutein, carotene and tocopherol, that are all leaf extracts, show anti-oxidant properties. Murrayanol is mosquitocidal also [14-19]. 9-formyl-3-methylcarbazole, isolated from the leaf, shows weak cytotoxicity against both adriamycin resistant P388 mouse leukemia cell lines and mouse melanoma B16 [12].

APPLICATIONS OF CURRY LEAF

Traditional Uses

The leaves of this plant are aromatic and have a characteristic taste. They are hence used in various curries, especially in South India. Other parts of the plant such as the stem are used for cleaning the teeth and gums for their strengthening [4]. Ayurvedic system of medicine uses powdered dry curry leaf mixed with honey and betel nut juice as an anti-periodic. The leaves of this plant are used externally for application onto bruises, burns, eruption, and treatment of bites of poisonous animals. Internally, they are used to cure dysentery. For the treatment of diabetes mellitus, *Murraya koenigii* is currently being used as a stimulant and antidysentric [2]. An infusion of the toasted leaves is used as an antiemetic. The steam distillates of the leaves are used as stomachic, carminative, purgative, febrifuge and anti-anemic. The leaves and roots, owing to their bitter and acrid properties, show cooling, anti-helminthic and analgesic actions. They are also used for curing piles, allaying body heat, thirst, itching and inflammation. They have also been helpful in leucoderma and other blood disorders [1]. Influenza and rheumatism can also be treated with these leaves [25]. The juices of the roots have hepatoprotective actions and are proven to be good for kidney related pains. Fruits are highly nutritious with several medicinal properties, astringency being one of them. Furthermore, the plant has anti-tumor, hypoglycaemic and antihypercholesterolemic effects [26, 27].

Pharmacological and medicinal uses

Anti-microbial activities

From the stem bark of *M. koenigii*, a benzoisofuranone derivative, 3ξ-(1ξ-hydroxyethyl)-7-hydroxy-1-isobenzofuranone and a carbazole alkaloid, dimeric in nature, 3,3'-[oxybis(methylene)] bis (9-methoxy-9H-carbazole), along with three known steroids as well as six known alkaloids have been isolated [28]. These compounds were seen to have a minimum inhibitory concentration (MIC) in the range of 3.13-100 µg/ml [29]. According to a literature survey, the methanolic extracts of 21 species of plants were tested for anti bacterial activities for different Gram negative and Gram positive species. It has been observed that maximum anti bacterial activity is shown by *M. Koenigii*. The essential oil of this plant, that consists mainly of α-pinene (39.93%), sabinene (13.31%) and trans-caryophyllene (9.02%), was observed to have anti bacterial effect against *Bacillus subtilis*, *Staphylococcus aureus*, *Corynebacterium pyogenes*, *Pasteurella multocida* and *Proteus vulgaris* [30]. The three bioactive carbazole alkaloids, that are obtained upon acetone extraction of the fresh leaves are mahanine, mahanimbine and murrayanol. These compounds possess remarkable antimicrobial and topoisomerase I and II inhibition activities [5, 31]. *A. fumigates* and *Microsporium gypseum* also show positive results. *Murraya koenigii* is effective, at a dilution of 1:500, against *Candida albicans*. The ethanolic extracts of the roots and the whole plant, excluding roots of *Murraya koenigii*, do not show any significant antifungal activity against *Cryptococcus neoformans*, *Trichophyton mentagrophytes* and *Microsporium canis* [12,32]. 55% ethanolic extract of the whole plant, excluding roots and also the roots alone, have been tested for anti protozoal activity. The whole plant extract shows activity against *Entamoeba histolytica* and an antispasmodic effect on isolated guinea pig ileum, but only the root extract is active against *Entamoeba histolytica*. Antihypertensive activity is also observed in in cats/dogs [30].

Anti-helminthic activity

The petroleum ether and methanolic extracts of *M. koenigii* have been tested against *Pheretima posthuma*, the adult Indian earth worm for its anti helminthic activity. Piperazine citrate served as the standard. The worms were kept in three varied concentrations (25, 50 and 100 mg/ml) of the extract to observe for paralysis and death. It was observed that death occurred followed by fading of body color, thus proving the anti helminthic properties of the leaves [2]. Also, 100 mg/ml of the methanolic extract had significant anti helminthic activity compared to petroleum ether that showed only moderate activity [33].

Anti-oxidative property

The extracts of *M. koenigii* leaves were prepared using dichloromethane that contained carbazole alkaloids. They were been estimated on the basis of their oil stability index (OSI) and radical scavenging ability against the DPPH (1-1-diphenyl-2-picrylhydrazyl) radical, to reach a steady state, on the basis of lag time. The 12 carbazoles isolated were classified into 3 groups. The carbazole ring which contains an aryl hydroxyl substituent plays an important role in stabilizing the thermal oxidation and reaction rate against DPPH radicals. The two carbazole alkaloids, koenigine and mahanimbine, isolated from *M. koenigii* leaves showed antioxidant activities. Koenigine also showed radical-scavenging properties to a great extent. The plant extract of *M. koenigii* has been surveyed for its potential regulatory effect on levels of nitric oxide (NO) using sodium nitroprusside as a NO donor *in vitro*. The result shows that the plant might be a novel and powerful therapeutic agent for radical scavenging of NO, the regulation of pathological conditions due to excessive generation of NO and also peroxynitrite, its oxidation product [2,5, 34, 36-39].

Anti-diabetic property

The chemical constituent, mahanimbine, present in *M. koenigii*, has been checked for anti-diabetic activity by injecting it in streptozotocin induced diabetic Swiss mice. Mahanimbine was shown to decrease the blood sugar levels by enhancing the insulin effect either by increasing the peripheral glucose uptake or by secretion by Islets of Langerhams of the beta cells of the pancreas. Mahanimbine also showed significant alpha amylase inhibitory effect compared to acarbose. Additionally, the level of glucose-6-phosphate dehydrogenase enzyme was increased, and hepatic and muscle glycogenesis was normalized leading to proper utilization of glucose, when the mice were injected with this extract [1, 2].

Anti-lipid peroxidative activity

Rats fed with curry leaf extracts show decreased concentrations of malondialdehyde in the blood while hydroperoxides and conjugated dienes show a considerable increase in the heart and liver. In the kidney, liver and heart, catalase, Glutathione-S Transferase, Glutathione reductase, Glutathione peroxidase and Superoxide dismutase activities show a sharp increase whereas Glutathione levels are lowered, therefore proving its anti-lipid peroxidative activity[12].

Anticancer Activity

Dalton's Ascitic Lymphoma (DAL) cells were intraperitoneally inoculated in mice. This leads to an extensive increase in the count of cancer cells suggesting the progression of cancer in the mice. When the mice were treated with ether extracts of *Murraya koenigii*, there was a decrease in the cancer cells, signifying the inhibitory effect of the test drug on the tumor cells. In some mice, an increase in tumor weight is also observed due to accumulation of peritoneal fluid. As a result, atypical enlargement of peritoneal cavity is also seen. When treated with the extract, it reduces the tumor weight and increases the life span of the animals. Thus curry leaf was proven to have significant anti-tumor activity [34]. Also, Girinimbine significantly induces programmed cell death in HepG2 cells making way for further evaluations in the preclinical human hepatocellular carcinoma models. It is seen that *Murraya koenigii* holds capability as an immune-modulatory agent acting by stimulation of the humoral immunity and phagocytic function as it shows a significant increase in the phagocytic index by the speedy removal of carbon particles from the blood stream. But the extracts are unable to stimulate cellular immunity [1,39,40].

Hepatoprotective activity

Gupta *et.al* has studied the hepatoprotective nature of *M. koenigii* leaves extract. The effect was due to the combined effect of carbazole alkaloids such as Girinimbine, Mahanine, Mahanimbine, Isomahanimbine, Murrayazolidine, Murrayazoline and minerals such as Zinc, Iron, Copper along with α -tocopherol and ascorbic acid, extracted from the leaves. Thus *M. koenigii* is a favorable and a rich source of free radical quencher. The process is mediated through hepatocyte membrane stabilizing activity along with the reduction of fat metabolism. Hydroethanolic leaf extracts of *Murraya koenigii* in doses of 200, 400 and 600mg/kg body weight demonstrates a pronounced decrease in the levels of alanine aminotransferases, aspartate aminotransferases, alkaline phosphatases and total bilirubin in CCl₄ treated hepatotoxic rats. Also there is a dose-dependent

elevation in hepatic superoxide dismutase, ascorbic acid, catalase, reduced glutathione and a decline in lipid peroxidation. Microscopic studies report minimal CCl_4 induced lesions in *Murraya koenigii* treated rats, suggesting the hepatoprotective potential of curry leaf. The carbazole alkaloids and tannins from the aqueous extracts exhibits wonderful hepatoprotective activity against ethanol-induced hepatotoxicity comparable to the standard drug L-ornithine L- aspartate (LOLA). The acetone extract of powdered dry bark shows protection of liver cells in comparison to the control group of rats and other solvents in CCl_4 -induced liver damage [1,13, 35,39,41].

Capability of enhancing memory

Total alkaloid extracts of *Murraya koenigii* leaves, in doses of 20 and 40 mg/kg p.o., improves the values of protective antioxidants like catalase, glutathione peroxidase, glutathione reductase, reduced glutathione and superoxide dismutase in brain homogenates. Furthermore, a reduction in lipid peroxidation and nitric oxide has also been indicated. An increase in the acetylcholine levels and decrease in anticholinesterase activity has also been noticed. Thus, these properties play a beneficial role in protection against neurodegenerative diseases such as Alzheimer's [1]. The leaf extracts also show a significant improvement in cognitive functions in aged mice, such as improvement in memory that could be used in the management of dementia [2].

Capacity to heal wounds

The wound healing capacity of aqueous extracts of *M.koenigii* has been studied by excision and incision wound model in male albino rats. In incision wound model, a significant increase in tensile strength was seen in mice that were treated with the extract, in comparison to the control group of mice. In excision wound model, a marked reduction in wound area was seen. Hence, it was evident that the aqueous extracts of *M. koenigii* accelerated the process of wound healing by aiding a decrease in the surface area of the wound [41,42].

Effect on dental caries

Dental caries are caused by bacterial species such as *Streptococcus mutans* and *Porphyromonas gingivali*. Feeding of curry leaf extract in golden hamsters lowers the number of dental caries. *Murraya* extract, that contains isomahanine, murrayanol and mahanine present in foods such as juices, candies, chewing gums, cakes and biscuits shows a inhibition of 86.2% of methyl sulphhydryl formation by *Fusobacterium nucleatum*. *M. koenigii* leaf extract containing the above mentioned compounds are found to be useful as oral disinfectants to protect against dental caries and periodontal disorders and are thus used as active ingredients in toothpaste formulation [34,43].

Use in cosmeceuticals

M. koenigii contain hyaluronidase inhibitors that are formulated in a cream base. This extract is incorporated in skin-lightening cosmetics for hyaluronidase inhibitory activity as well as for its moisturizing and antioxidant property. Herbal compositions containing *M. koenigii* stem extract as one of the ingredients show rough skin improving, skin-lightening effect and erythema. *M. koenigii* has been studied for its sun protective properties and it has been found that it can also be used to maintain the natural pigmentation of the skin or can be used as an adjuvant in other formulations to intensify the activity. The cream prepared from curry leaf oil shows the sun protection factor (2.04 ± 0.02) and hence can be used to maintain natural skin pigmentation [34, 33].

CONCLUSION

Murraya koenigii is a traditional multipotential plant which has tremendous use in pharmacology. All parts of the plant such as leaf, stem, root, fruits and seeds have medicinal properties and are used to cure various ailments. The oil extracted from the leaves has proven to be useful as well. Thus *Murraya koenigii* can be considered for further research on its bioactive components.

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