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CARBAZOLE ALKALOID: *MURRAYA KOENIGII* A VALUABLE MEDICINAL PLANT

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ABSTRACT

Herbal remedies have been used to cure human aliments in every possible condition. About 80% of world's population relies upon natural products. The use of medicinal plants in therapeutics utmost probably exist in the earliest documented history. *Murraya koenigii* (Curry leaves) is one of most significant medicinal plant used as Herb, spice and condiments. It is rich source of carbazole alkaloids. Almost whole part of plant contains varied phytoconstituents and is used to cure various types of disorder. Extensive research work has been reported in last few decades on this valuable plant. Recent studies, have thrown light on anti-diabetic and anthelmintic activities of aqueous and chloroform extract of *Murraya koenigii* plant. The present review, discusses Ethanobotanical properties, Pharmacognostic, Phytochemical and Pharmacological activity on *Murraya koenigii* (*M. koenigii*).

KEYWORDS: Herbal medicines, *M Koenigii,* Volatile oils

INTRODUCTION

Dried leaves of *Murraya Koenigii* (Curry leaf), belongs to family Rutaceae is one of the most significant plant, found almost everywhere in the Indian subcontinent. Commonly, it is known as curry-leaf tree and is a native of India, Sri Lanka and other South asian countries.[1]

It has distinct aroma due to the presence of volatile oil and have ability to improve digestion. It has been used in many traditional system of medicines namely Ayurvedic system of medicines and Unani prescriptions.[2] It has great therapeutic potential and is used for the treatment of night blindness, dysentery, diarrhoea, vomiting, and bites of poisonous animals, bruises and eruption. These phytochemical compounds possess antioxidant, antimicrobial, anthelmintic, analgesic, anti-inflammatory, hepatoprotective and antitumor activities.[3]

Botanical Classification

Kingdom- Plantae

Sub-kingdom- Tracheobionta

Superdivision- Spermatophyta

Division- Magnoliophyta

Class- Magnoliospida

Subclass- Rosidae

Order- Sapindales

Family- Rutaceae

Genus- Murraya J.Koenig ex L.

Species- *Murraya Koenigii* L. Spreng[1]

Vernacular Name

Bengali: Barsunga

Gujarati: Mitho limdo

Hindi: Meetha neem, Karipatta, Kathnim, Bursunga

Kannada: Karibevu

Malayalam: Kariveppilei, Kareapela

Marathi: Karipat, Karhipatta, Karhinimb, Jhirang

Oriya: Bansago.[3]

Habitat: Distribute and cultivated throughout India. It is found wild from Uttarakhand, Sikkim to Garhwal, Bengal, Assam, Western Ghats and Travancore- Cochin. The Propagation is done by seeds, which grow freely under partial shade. It is also available in other part of Asian region like in moist forests of 500-1600 m height in Guangdong, Bhutan, Nepal, Pakistan, Sri Lanka, Thailand, and Vietnam together with South Indian immigrants, curry leaves reached Malaysia, South Africa and Reunion island. Outside the Indian sphere of influence, they are rarely found.[5]

Botanical Description

It is a small spreading shrub, about 2.5 metres high, the main stem, dark green to brownish, with numerous dots on it. Its bark can be peeled off longitudinally, showing the white wood underneath; the thickness of the main stem is 16 cm.

Leaves: Leaves are exstipulate, bipinnate compound, 30 cm long, and each bearing 24 leaflets **(Fig: 1).**

Flowers: Bisexual, white, funnel-shaped, sweetly scented, stalked, complete and regular.

Fruits: are round to oblong, 1.4 to 1.6 cm long, 1 to 1.2 cm in width, fully ripe fruits, and black with a very shining surface.

Seeds: are spinach green in colour in each fruit, with 11 mm long, 8 mm in diameter.

Plant generally flowers and fruiting during December to July. This suckering plant can raise to a tree up to 6m tall in warm, humid climates. It can also be grown very successfully in a pot as a much smaller plant. It will also generally be smaller if grown out of its normal climate zone.[4]

Part Used Are Leaves, Stem, Bark, Roots and fruits.[3]

Fig.1. Fresh leaves of *Murraya koenigii.*

Phytoconstituents: It consist 63.2% of moisture, 14.6% carbohydrates and 13.06% total ash. The main constituent of curry leaves are oxalic acid, resin, carbazole alkaloids, koenigin,

bicyclomahanimbicine, cyclomahanimbine, murrayastine, Coumarine and koenidine has significant pharmacological activities.

- **Leaves** (Volatile oils): The major portion of volatile oil consist of bicyclomahanimbicine and mahanimbicine. The composition of volatile compounds found in leaves are Linalool (0.56%), *trans*-Sabinene hydrate (0.53%), *trans*-2-Cyclohexen-1-ol (0.48%), *cis*-2-Cyclohexen-1-ol (0.54%), *para*-Cymen-8-ol (10.31%), *β*-Terpinol (2.52%), *trans*-Piperitol (0.40%), Chrysanthenyl acetate (0.39%), Lavandulyl acetate (1.67%), Bornyl acetate (1.68%), α-Copaene (0.82%),β- Elemene (0.35%), (Z)-Jasmone (0.11%),β-Caryophyllene (19.50%), Aromadendrene (0.72%), α- Humulene (15.24%), Butanedioic acid (2.18%), β-Selinene (3.81%), Naphthalene (1.90%), α-Selinene (6.10%), δ-Cadinene (2.03%), Nerolidol (2.64%), *trans*-Nerolidol (1.32%), Cycloheptane (0.13%), Spathulenol (1.98%), Caryophyllene oxide and Phytol (10.07%).

- **Root** It contains murrayanol, murrayagetin, marmesin-1”-O-rutinoside. The benzene extract of roots consist of mukoline and mukolidine.
- **Fruit** Mahanimbine and koenimbine. The pulp of fruit also contains trace amounts of minerals, 1.97% phosphorus, 0.082% potassium, 0.811% calcium, 0.166% magnesium, 0.007% iron and remarkable amount of protein.
- **Seeds** Carbazole alkaloids such as murrayacine, murrayazolidine, murrayazoline, girinimbine, and xynthyletin, it also contain girinimbine, mahanine and isomahanine.
- **Others constituents** Fibre, carotene, vitamin C and nicotinic acid.[6,7]

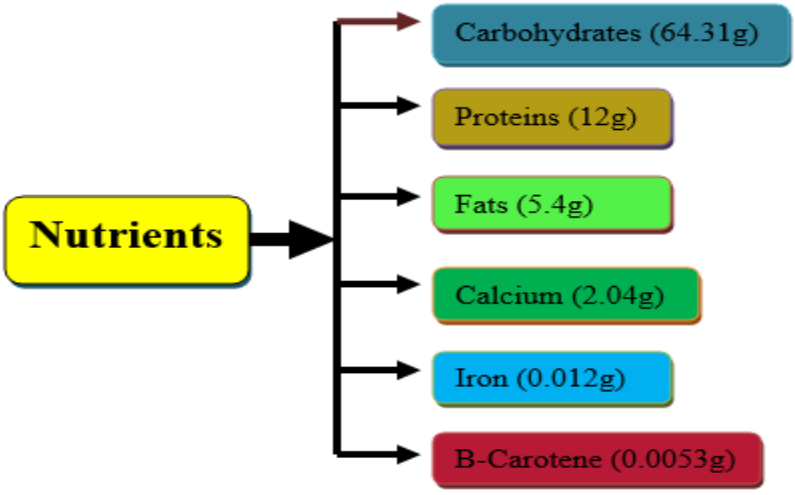

Fig. 2: Nutrient content of dried Curry leaves (100gm).

Traditional Uses

whole plant along with its essential oil are widely used for flavouring soups, non-veg dishes, traditional curry powder blends, seasoning and other food preparations. It also has application in cosmetic aromatherapy industry. Curry leaves blend with coconut oil is used as an excellent hair tonic for retaining natural hair tone and stimulating hair growth. Traditionally, it is used as a whole or in parts as antiemetic, antidiarrheal, febrifuge, blood purifier, antifungal, depressant, anti-inflammatory, body aches, for kidney pain. Furthermore, it is used in osteoporosis due to enrichment of calcium. Fresh juice of Curry leaves with lime juice and sugar is helpful to treat morning sickness.[5,8]

Pharmacology Activities

Antifungal activity

Antifungul activity of aqueous and organic extracts of *Murraya koenigii* were determined against *Candida albicans, Penicillium funiculosum, Penicillium camemberti, Aspergillus niger* as test organisms. Aqueous and organic extracts of the plants were obtained using standard techniques. The extracts were Cold aqueous extract, hot aqueous extract and Ethanol extract. Sensitivity test was carried out using Agar well diffusion method; the set up was incubated at 37°c for 24 hours. Development of zones of inhibition was observed and measured. This showed that some of the tested extracts demonstrated antifungal activities against the test organisms. Comparison of the extracts showed that ethanol extract of *Murraya koenigii* had high activity against all test organisms. The Minimum Inhibitory Concentration of Cold, Hot and Ethanol extracts of *Murraya koenigii* was 20g/ml for all the test organisms. Since the Cold and Hot extracts did not demonstrate high activity on the test organism, it could be concluded that the activity demonstrated by both cold and hot aqueous extract was due to the effect of the extracts. These results indicate that *Murraya koenigii* can be used as an antifungal agent in the treatment of infections.[9] The ethanolic, methanolic and acetonic extract of *Murraya koenigii* were determined against selected fungi i.e. *Aspergillus niger*, *Fusarium oxysporum*, *Penicillium notatum* and *Trichoderma viride* using well diffusion method. In case of *Aspergillus niger*, maximum activity was shown by methanolic extract than ethanolic and acetonic extract of *Murraya koenigii* and Zone of inhibitions (ZOI) were found to be 20±1.0mm, 18±1.0mm and 11±1.0mm respectively. For *Trichoderma viride*, ZOI were 22±1.0mm, 20±1.0mm and 18±1.0mm by methanolic, ethanolic and acetonic extract of *Murraya koenigii* respectively. Furthermore against *Fusarium oxysporum*, methanolic and acetonic extracts showed similar activity with ZOI of 18±1.0mm whereas

ethanolic extract shows 16±1.0mm. Antifungal potential of acetonic extract of plant was maximum against *Penicillium notatum* with ZOI of 22±1.0mm whereas methanolic and ethanolic extracts showed ZOI of 20±1.0 and 15±1.0mm respectively.[10]

Antibacterial activity: Antibacterial activity of plant extract, *M. koenigii* was determined against selected bacteria i.e. *Bacillus cereus*, *Escherichia coli*, *Staphylococcus aureus* and *Salmonella typhi* cultures using well diffusion method. The ethanolic, methanolic and acetonic extract showed Zone of inhibition against bacteria strain and acetonic extract showed maximum potential against *Bacillus aureus* whereas methanolic extract showed highest ZOI as camparison to ethanolic extract respectively. Furthermore, methanolic extract showed lowest ZOI against *Escherichia coli*, whereas acetonic extract highest ZOI as comparable to methanolic extract. The study also obtained the total flavonoid content in crude methanol, ethanol and acetonic extracts *M. koenigii* leaves.[10]

Antioxidant activity: Antioxidant activity of water and ethanol extracts of the *M. koenigii* were determined and extract was obtained by hot continuous extraction. In-vitro activity, ferric reducing power and hydrogen peroxide scavenging assays, the total flavonoid and flavonol level were determined and in vivo activity was evaluated using albino wistar rats which were treated with 100mg/kg of aqueous and ethanol leaf extracts. Ascorbic acid used as positive control for six repeated days after which a single dose (2.5ml/kg body) of CCl_4 was administered except for the normal control group 24hrs later. Aqueous and ethanol extracts showed ferric reducing activity with dose dependent manner. The hydrogen peroxide scavenging potential was very high at various concentrations for both extracts (between 81.2 to 99.9%) comparable to ascorbic acid. The study showed that aqueous and ethanol extracts of *M. koenigii* possess antioxidant activity due to high amounts of flavonoid and flavonol.[11]

Antiulcer activity

Anti-ulcer activity of aqueous extract of the leaves of *M. koenigii* was evaluated by using models of acute gastric lesions induced by ethanol induced, aspirin induced, cold restrain stress and pylorus ligation in rats. Animals pre-treated with doses of 200 mg/kg and 400 mg/kg of Aqueous extract showed significant reduction in lesion index, total affected area and % of lesion in comparison with control group in the ethanol induced, aspirin induced, cold restraint stress-induced ulcer and pylorus ligation models. These results showed that aqueous extract of the leaves of *M. koenigii* shows good antiulcer activity.[12]

Anti-diabetic activity: Antihyperglycemic effect of aqueous extract of *M. koenigii was studied* during five consective days after Single dose streptozotocin (STZ) administration and immediately followed by daily treatment with graded dose (200 & 400 mg/kg) for 30 days. There was a significant blood glucose lowering effect in diabetic treated rats as compared to normal controls. The maximum fall of 85% for the rats treated with *Murraya koenigii* (MK) - 200 mg/kg on the 30th day was slightly above that of MK-400 mg/kg treated rats (83%). The study showed considerable loss of body weight and increase in blood glucose levels and degeneration of the glomeruli and renal convoluted tubules and atrophied islets with disintegration of β-cells. Treatment of diabetic rats with MK extract showed significant (p <0.001) improvement in blood glucose levels and body weight gain. The MK extract also caused an improvement in tissue injury induced by STZ injection in the kidney and islets of Langerhans.[13]

Vasodilating activity: The aqueous leaf extract of *M. koenigii* was determined which showed a dose dependent negative chronotropic effect on cardiovascular system of frog heart preparations which might be due to its direct actions on the heart and blood vessels. Potassium ion concentration was also found to be very negligible by flame photometry, indicating no involvement of potassium ions. The aqueous leaf extract possesses vasodilatory effect which is independent of muscarinic, histaminergic and ß-adrenergic receptor as it increased the number of drops/minute in frog hind limb perfusion experiment and also does not possess α- adrenergic receptor antagonistic activity. The aqueous leaf extract showed significant effect at concentration of 1 mg/ml.[14] Furthermore, Crude ethanol extract of fresh leaves of *M. koenigii* showed dose dependent positive ionotropic effect on an isolated frog heart. The response to *M. koenigii* 62.5 - 1000 µg was not affected in either way by theophylline, imidazole, propanolol and sildenafil. The changes in potassium and sodium concentration did not alter. The result suggested that *M. koenigii* induced positive ionotropic effect possibly by increasing availability of calcium from extra cellular sites.[15]

Antianthelmintic activity

Anthelmentic activity of methanol, n-hexane, chloroform, n-butanol and water fractions of *M. koenigii* were determined in vitro method using egg hatch assay and larval motility assay on *Haemonchus contortus* eggs. Different sub fractions of chloroform showed better ovicidal activity whereas another sub fractions showed best larvicidal activity. The larvae that were used for testing the larvicidal activity, were found to be slowly motile after half an hour

incubation with the extract and were progressively dead on a dose dependent manner. The chloroform extract of *M. koenigii* and its sub fractions exhibit good anthelmintic activity and the isolation of active molecules is required for development of a novel Anthelmentic.[16]

Wound Healing effect

The ethanol extract of leaves of *M. koenigii* was evaluated for wound healing activity using Male albino rates. The rats were sacrificed and the wound healing model reveals that three groups which were taken for wound healing activity showed a decrease in wound area from day to day. Incision model showed a significant increase in tensile strength of the 12-day old wound due to treatment with *M. koenigii*. Thus, the leaves of *M. koenigii* were proved to possess significant wound healing capacity.[17]

Analgesic activity

The methanol extract of leaves of *M. koenigii* showed analgesic effect by using hot plate model and formalin induced paw licking response in mice. The activity might be linked to the processes involved in the prevention of sensitization of nociceptors, down regulation of the sensitized nociceptors or blockade of the nociceptors at peripheral and central levels. Different concentrations of methanolic extract were taken i.e. 100mg/ml, 200mg/ml and 400 mg/ml. Among these 400 mg/ml showed positive results.[18]

Anti-inflammatory: The leaves of *M. koenigii* was subjected to extraction with three various solvents; petroleum ether, chloroform and ethanol. A dose of 250mg/kg was selected which is a 1/10th of 2500mg/kg which was considered as LD50, the dose was administrated via oral route. Compared to the three solvents, it was found that ethanol extract shows significant reduction in carrageenan induced paw edema in the Albino rats of the wistar strain.[19] Another study reported, that the methanol and aqueous extract of *M. koenigii* leaves is effective against carrageenan- induced edema in male albino rats at the dose of 400mg/kg, compared to petroleum ether and hexane extracts which has no decrease in the inflammation. The methanol extract was found to have maximum anti-inflammatory activity compared to aqueous extract.[20]

Inotropic activity: The ethanol extract of the fresh leaves of *M. koenigii* showed a positive inotropic effect on the isolated frog heart in a dose dependent manner. It was suggested that the positive inotropic activity is achieved by an increase in the availability of calcium from the extracellular sites by the *M. koenigii.*[21]

Antiobesity

The dichloromethane and ethyl acetate extracts of leaves of *M. koenigii* significantly reduced the body weight gain, plasma total cholesterol and triglyceride levels when given orally at a dose of 300 mg/kg/day to the high fat diet induced obese rats for 2 weeks. The observed antiobesity and antihyperlipidemic activities of these extract are correlated with the carbazole alkaloids present in them. Mahanimbine when given orally (30 mg/kg/day) also significantly lowered the body weight gain as well as plasma TC and TG levels. These findings exhibit the excellent pharmacological potential of mahanimbine to prevent obesity.[22]

Anticancer activity

In three location (Malaysia), the studied were carried out by taking different concentration of leaves of *M. koenigi*. The highest total phenolic (TP) contents were observed in the extracts from Kelantan (3.771 and 14.371 mg/g DW), followed by Selangor (3.146 and 12.272 mg/g DW) and Johor (2.801 and 12.02 mg/g DW), respectively. High quercetin (0.350 mg/g DW), catechin (0.325 mg/g DW), epicatechin (0.678 mg/g DW), naringin (0.203 mg/g DW), and myricetin (0.703 mg/g DW) levels were observed in the extracts from Kelantan, while the highest rutin content (0.082 mg/g DW) was detected in the leaves from Selangor. The curry leaf extract from Kelantan exhibited higher concentration of gallic acid (0.933 mg/g DW) than that from Selangor (0.904 mg/g DW) and Johor (0.813 mg/g DW). Among the studied samples, the ones from Kelantan exhibited the highest radical scavenging activity (DPPH, 66.41%) and ferric reduction activity potential (FRAP, 644.25 µm of Fe(II)/g) followed by those from Selangor (60.237% and 598.37 µm of Fe(II)/g) and Johor (50.76% and 563.42 µm of Fe(II)/g), respectively. A preliminary screening showed that the curry leaf extracts from all the locations showed significant anticarcinogenic effects inhibiting the growth of breast cancer cell line was observed with the curry leaf extract from Kelantan. Based on these results, it is concluded that Malaysian curry leaf collected from the North (Kelantan) might be potential source of potent natural antioxidant and beneficial chemotherapy agents.[23]

Hepatoprotective activity

The hydro-ethanolic extract of *M. koenigii* treated with CCl_4 induced hepatotoxic rats and its result showed histopathological changes in control and treated rats. The extract pretreated rats with different doses (200, 400 and 600 mg/kg body weight) showed significant decrement in activity levels of enzymes such as alanine aminotransferase, aspartate aminotransferase,

alkaline phosphatase, total protein, and bilirubin. Furthermore, leaf extract treated rats recorded a dose dependent increment in hepatic super oxide dismutase, catalase, reduced glutathione and ascorbic acid and, a decrement in lipid peroxidation. Microscopic evaluations of liver revealed CCl_4-induced lesions and related toxic manifestations that were minimal in liver of rats pretreated with plant extract. The reported results showed that hydro-ethanolic leaf extract possesses hepatoprotective potential due presence of rich polyphenol content in *M. koenigii* extract.[24]

Reduce blood cholesterol level

The curry leaf (*Murraya koenigii*) extract exhibit the property to decline blood cholesterol and blood glucose levels in diabetic mice. Mice received daily intraperitoneal injections of 80 mg/kg curry leaf extract for 10 consecutive days. The extract significantly decreased blood cholesterol level from 277.6 ± 16.6 mg/dl (day 0) to 182.0 ± 15.3 mg/dl (day 10, $p < 0.01$ compared with the change in vehicle group). Our data suggest that curry leaf may be proved to be of clinical importance in improving the management of high cholesterol level.[25]

Memory enhancing

It was reported that ethanol extract of curry leaves lowered serum cholesterol in mice, inhibited brain acetylcholinesterase enzyme and thereby raised the acetylcholine concentration in brain homogenate and ultimately improved memory in aged mice. Two different concentrations were used to carried out in-vivo activity i.e. 300mg/ml and 400mg/ml. Thus, a combination of anticholinesterase and cholesterol lowering effect exhibited by leaves extract may be the factors responsible for this memory improving effect observed in the study.[26]

Other uses

Mosquitocidal activity

Petroleum ether and acetone extracts of leaves of *M. koenigii* act as larvacide for *Aedes aegypti* at the concentration range from 250ppm -900ppm.[27]

CONCLUSION

M koenigii (Curry leaves) is one of most significant medicinal plant used as Herb, spice and condiments. Essential oil, Carbazole alkaloids, mineral, carotenoids and fibers are the dominant phytoconstituents of the plant. The plant validates nearly all traditional uses, clinical trials and formulation development could be taken as future scope. From this review

we conclude that curry leaves are used as a whole or in parts as antiemetic, antidiarrheal, febrifuge, blood purifier, antifungal, depressant, anti-inflammatory, body aches, and for kidney pain. Furthermore, it is used in osteoporosis due to enrichment of calcium. Fresh juice of Curry leaves with lime juice and sugar is helpful to treat morning sickness.

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