PHARMACOLOGICAL ASPECTS ON MURRAYA KOENIGII-A REVIEW

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ABSTRACT

The present study has been restricted to the Pharmacological review on Murraya koenigii. The plant grows in forests of 500-1600 m height. M. koenigii is an unarmed, semi deciduous aromatic shrub or small tree with slender but strong woody stem and branches covered with dark grey bark, leaves are imparipinnate, glabrous, and very strongly aromatic. The plant has gained good reputation traditional medicinal system to overcome several ailments like diabetes, diarrhea, anti-infective, anti-inflammatory and so many. The plant exists from ancient time in the Ayurvedic therapy system for several ailments. Leaves of plants are frequently used in cooking of “curry” so called the curry leaves. The literature survey studied here includes reported traditional uses, phytochemical aspects and pharmacological activities on the plant.

KEYWORDS: Murraya koenigii, Pharmacological, Curry leaves, Traditional medicine.

INTRODUCTION

The Curry Tree, also known as Karivepallai or Kadipatta is a tropical to sub-tropical tree in the family Rutaceae. Curry Tree is native to India and produces the leaves known as Curry leaves or Sweet Neem lea Taj Agro Kadippattaves. Curry leaves are cultivated in different parts of extreme north and south India. Murraya koenigii, commonly known as curry leaf or kari patta in Indian dialects, belonging to Family Rutaceae which represent more than 150 genera and 1600 species.[1] Murraya Koenigii is a highly values plant for its characteristic aroma and medicinal value. It is an important export commodity from India as it fetches good foreign revenue. A number of chemical constituents from every part of the plant have been extracted. The most important chemical constituents responsible for its intense...
characteristic aroma are P-gurjunene, P-caryophyllene, P-elemene and O-phellandrene. The plant is rich source of carbazole alkaloids. The plant is distributed and cultivated throughout India. It is found wild from Sikkim to Garhwal, Bengal, Assam, Western Ghats and Travancore- Cochin. Propagation is done by seeds, which germinate freely under partial shade. Is also available in other part of Asian region like in moist forests of 500-1600 m height in Guangdong, S Hainan, S Yunnan (Xishuangbanna), Bhutan, Laos, Nepal, Pakistan, Sri Lanka, Thailand Vietnam. Together with South Indian immigrants, curry leaves reached, South Africa and Réunion island. Outside the Indian sphere of influence, they are rarely found. M. koenigii is an unarmed, semi deciduous aromatic shrub or small tree with slender but strong woody stem and branches covered with dark grey bark, leaves are imparipinnate, glabrous, and very strongly aromatic.

The stem of M. koenigii is an aromatic and more or less deciduous shrub or small tree upto 6 meters in height and 15 to 40 cm in diameter. The main stem is dark green to brownish. The bark of the stem can be peeled off longitudinally which exposes the white wood underneath. Flowers are small, white fragrant ebracteate, calyx deeply five cleft, pubescent. Petals five, free, whitish, glabrous and with dotted glands. Fruits occur in close clusters, small ovoid or sub-globose, glandular, thin pericarp enclosing one or two seeds having spinach green color.

Murraya koenigii leaves

3. TRADITIONAL USES

Fresh leaves, dried leaf powder, and essential oil are widely used for flavouring soups, curries, fish and meat dishes, eggs dishes, traditional curry powder blends, seasoning and ready to use other food preparations. The essential oil is also utilized by soap and cosmetic
aromatherapy industry.\textsuperscript{[5]} Curry leaves are boiled with coconut oil till they are reduced to blanked residue which is then used as an excellent hair tonic for retaining natural hair tone and stimulating hair growth. It is traditionally used as a whole or in parts as antiemetics, antidiarrheal, febrifuge, blood purifier, antifungal, depressant, anti-inflammatory, body aches, for kidney pain and vomiting.\textsuperscript{[6-18]}

**Carotenoids**

14570-μg/100 g of total carotenoids in leaves has been reported as measured by HPLC. Out of total carotenoids, lutein content was 5252 and β-carotene content was 9328 μg /g.\textsuperscript{33}

**Leaves**

Tachibana et.al has isolated 8, 10’-{3,3’,11, 11’-tetrahydro-9,9’ dihydroxy- 3,3’,5, 8’-tetra methyl –3,3’-bis (4-methyl-3-pentenyl)}bis pyrano\textsuperscript{[19-20]} a carbazole (a dimeric carbazole alkaloid) from methylene chloride extract of M. koenigii leaves together with six known alkaloids; koenimbine, O- methyl murrayamine, O- methyl mahanine, isomahanine and bismahanine and bispyrayafoline.\textsuperscript{[20-21]} From dried leaves glycozoline,\textsuperscript{[22]} 1-formyl –3 methoxy- 6-methyl carbazole and 6, 7- dimethoxy- 1- hydroxy- 3-methyl carbazole\textsuperscript{[23]} was isolated. Koenigine, koenine, koenidine and (-) mahanine were isolated from acetone extract of leaves.\textsuperscript{[24]} Form the hexane extract of leaves Joshi et.al has isolated mahanimbine, isomahanimbine, koenimididine and murrayacine.\textsuperscript{[25]} Isomahanimbicine was isolated from petroleum ether extract of leaves of M. koenigii specifically collected in the month of February.\textsuperscript{[26]} Euchrestine B, mahanine, mahanimbicincine, mahanimbine\textsuperscript{[27]}, bismurrayafoline E\textsuperscript{[27,28]} mahanimbicincine, bicyclomahanimbicine\textsuperscript{[29]} cyclomahanimbincine bicyclomahanimbincine, mahanimbidine\textsuperscript{[30]}, mukonicine 9 (43), 8, 8”- bis koenigine, new binary carbazole alkaloid along with its monomer koenigine\textsuperscript{[31]} and a minor alkaloid mahanine\textsuperscript{[32]} were identified and isolated from leaves of M. koenigii.

![Mahanimbine](image-url)
It has been reported that presence of murrayanine (0.32%), glycoside scopolin (0.25%), free glucose (3.5%) and ash (10.4%).[33] Aerial part is reported to contain murrayanine and 8,8” bis koenigine.[34] Petroleum ether extract of leaves was used to isolate carbazole alkaloids, mahanimbine (3,5- dimethyl-3-(4-methylpent-3-enyl)-11H-pyran)[5,6-a] carbazole).[35] Methanolic extract of M. Koenigii was subjected to qualitative thin-layer chromatography and HPLC using different solvent system by Gupta et.al. Spectral analysis (IR, 1H NMR, 13C NMR and MS) was carried out to establish the structure. The structures of these 6-bioactive compounds confirmed as carbazole alkaloids- Mahanimbine, Girinimbine, Isomahanimbine, Murrayazoline, Murrayazolidine, and Mahanine, by the spectrometric data.[36]

**Stem:** From alcohol extract of stem bark Saha et.al has isolated koenigine- quinone A and koenigine quinone B, structures were established as 7- methoxy- 3 methyl carbazole- 1,4-quinone and 6, 7-dimethoxy-3-methyl carbazole-1, 4- quinone respectively.[37] 9- carbethoxy-3-methyl carbazole and 9- formyl –3- methyl carbazole were identified form M. koenigii by Chakraborty et. Al.[38] Me- 2- methoxy carbazole –3- carboxylate and 1- hydroxy –3- methyl carbazole were isolated from stem bark,[39] Mukonal, a probable biogenetic intermediate of pyrano carbazole alkaloid was detected in stem bark.[40] From stem bark Murrayazolinol (a minor carbazole alkaloid)[41], mahanimbino[42], murrayazolidine[43,44] urrayacinine[45] Mukonidine[46], murrayazoline[47] murrayanine, girinimbine and mahanimbine[48], girinimbinol and manahimbilol[49] (possible biogenetic precursors of girinimbine and mahanimbine) has also been identified and isolated. Roots: Murrayanol, murrayagetin, marmesin- 1”- O- rutinoside were isolated from root extract.[50] Three monomeric and five binary carbazole alkaloids named mukoenine- A, -B and C and murrastifoline –F. bis – 2-hydroxy- 3- methyl carbazole, bismahanine, bi koeniquinone- A and bismurrayquinone A were isolated from root and stem bark.[51] Koenoline (1- methoxy-3- hydroxy methyl carbazole) was isolated from the root bark.[52] Mukoline, mukolidine were isolated form the benzene extract of roots63. Roots were also found to contain girinimbine.[53] Seeds: Mahanimbine, girinimbine, koenimbine, isomahanine and mahane were isolated form seeds of M. koenigii from Marassana, Sri Lanka.[54] 2- methoxy-3- methyl carbazole was isolated form petroleum ether extract of seeds.[55] Mandal et.al isolated three bioactive carbazole alkaloids, kurryam (I), Koenimbine (II) and koenie (III) with structural confirmation with 2D-NMR spectra Fruits: Mahanimbine and koenimbine were isolated from petroleum ether extract of fruits. Isomahanine and murrayanol were isolated form fruits by Reisch et. al along
with five previously reported carbazole alkaloids mahanimbine, murrayazolidine, girinimbine, koenimbine and mahanine.\cite{56}

![Girinimbine](image)

**Lipids:** Lipid composition of seeds were reported as 4.4% of total lipids of which 85.4% neutral lipids, 5.1% glycolipids and 9.5% phospho-lipids. Neutral lipids consisted of 73.9% triacylglycerol, 10.2% free fatty acids and small amounts of diacylglycerols, monoacylglycerols and sterols. Steryl glucoside and acylated sterylglucoside are major glycolipids.\cite{56}

**Pharmacological Activity:** Several pharmacological activities and medicinal properties of various parts of M. koenigii are well known. Biological activity of M. koenigii is reported with the crude extracts and their different fraction form leaf, bark, roots, seed and oil.

**Antioxidant and free radical-scavenging activity:** Antioxidant activity of carbazole alkaloids, one of the potential bioactives, has been reported by a number of workers. The antioxidative properties of 12 carbazole alkaloids isolated form M. koenigii leaves were evaluated on the basis of Oil Stability Index (OSI) together with their radical scavenging ability against 1, 1-diphenyl, 2-picryl hydrazyl (DPPH).\cite{57}

**Hypoglycemic activity:**\cite{57} Administration of mahanimbine at doses of 50 and 100 mg/kg intraperitoneally reduced fasting blood sugar, triglycerides, low-density lipoprotein, very low-density lipoprotein levels and increased high-density lipoprotein level were noted on.\cite{63} Fruit juice decreased blood glucose level significantly at the 10th and 15th days of administration in alloxan-induced diabetic mice.

**Hepatoprotective activity:** The acetone extract of dried bark powder showed prominent protection of liver cells as compared with the control group and other solvents in CCl4-induced liver damage.\cite{58}
Antimicrobial and anti-fungal activity: The crude extract of M. koenigii roots showed strong antibacterial activity. Extract containing murrayanol and or isomahanine is used as microbicide in variety of industries due to high safety, strong activity, little odor and without coloring effect.[58]

Pancreatic lipase inhibitory effect: Effect on dental caries: Feeding of murraya leaf extract in golden hamsters showed lower caries scores compared to control group.[58]

Anticancer activity: Koenoline isolated form root bark exhibited cytotoxic activity against the KB cell culture test system[58] 9- formyl-3 methyl carbazole displayed weak cytotoxic activity against both mouse melanoma B 16 and adriamycin resistant P 388 mouse leukemia cell lines.

Effect on bronchial disorders: Herbal composition containing organic extract of any plant part of murraya (leaves, bark, roots and seeds) is useful in the treatment and remedy of bronchial respiratory troubles by blocking 5- lipooxygenase activity.[58]

Cardioprotective activity: The studies indicated that the aqueous extract of Curry leaf protects the rat cardiac tissue against cadmium- induced oxidative stress possibly through its antioxidant activity. Treatment of rats with cadmium also caused alterations in the activities of mitochondrial Kreb’s cycle as well as respiratory chain enzymes. All these changes were ameliorated when the rats were pre-treated with an aqueous extract of Curryleaf (Murraya koenigii).[59]

Antiobesity and antihyperlipidemic activities: The dichloromethane and ethyl acetate extracts of Murraya koenigii leaves significantly reduced the body weight gain, plasma total cholesterol and triglyceride levels significantly. The observed antiobesity and antihyperlipidemic activities of these extract are correlated with the carbazole alkaloids, Mahanimbine. When it was given orally (30 mg/kg/day) significantly lowered the body weight gain as well as plasma TC and TG levels. These findings demonstrate the excellent pharmacological potential of mahanimbine to prevent obesity.[59] Antiamnesic and wound-healing activity Antiamnesic potential of Murraya koenigii leaves was also studied.[60] Aqueous extract of M. koenigii accelerates the wound-healing process by decreasing the surface area of the wound. Aqueous extract of leaves showed marked reduction in wound
area in comparison with the control group from 4th day onwards in albino rats by excision wound model.

12 Kidney protective activity: Aqueous extract of leaves produced a significant dose-dependant decrease in serum urea and creatinine levels (P<0.001), and a marked increase in the levels of plasma antioxidant capacity (P<0.01) in diabetic rats, compared with the control (non-diabetic) subjects. Histological studies of the kidneys of these animals showed comparable tissue regeneration by the aqueous extract.\textsuperscript{[60]}

5.13 Antipyretic activity: The ethanolic extract of leaves of M. koenigii was investigated for antipyretic activity in rats using yeast-induced pyrexia model. Ethanolic extract at a single dose of 300 mg/kg produced significant antipyretic activity (P<0.01) in albino rats as compared with the standard drug paracetamol.\textsuperscript{[61]}

5.14 Histopathological activity: When whole curry leaves with mustard was given to rat at normal human intake, it did not show any histopathological changes. It did not cause any adverse effect on food efficiency ratio, red blood cell count, white blood cells, total count, differential counts or on the levels of blood constituents, like serum electrolytes, blood urea, haemoglobin, total serum protein, albumin-globulin ratio, fibrin level, glycosylated haemoglobin and the activity of aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase in serum.\textsuperscript{[61]}

Radiation protection activity: The effect of 4 Gy gamma radiation 30 min after the last injection of 100 mg/kg of methanolic extract of M. koenigii for 5 consecutive days was observed on adult Swiss albino mice. The extract itself increased the glutathione and enzymes levels, whereas radiation significantly reduced all values. Pretreatment with the extract reduced lipid peroxidation rate induced by radiation. The result demonstrated that M. koenigii leaves possess good antioxidant activity in vitro and are able to protect against radiation-induced depletion in cellular antioxidants.\textsuperscript{[62]} The methanolic extract showed protection against gamma radiation and cyclophosphamide-induced chromosomal damage in Swiss albino mice at a single dose of 100 mg/kg body weight.\textsuperscript{[63]}

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Anti ulcer activity: Anti ulcer activity was observed using aqueous extract at doses of 200 and 400 mg/kg. It produced significant inhibition of gastric lesion induced by non-steroidal anti-inflammatory drugs and pylorus ligation-induced ulcer. The extract reduced ulcerative lesion, gastric volume and free and total acidity but raised the pH value of gastric juice in pylorus ligation model. The results obtained suggested that the extract possesses significant antiulcer activity.\textsuperscript{[68]}

5.17 Antitrichomonal activity: Carbazole alkaloids and their derivatives from M. koenigii leaves showed antitrichomonal activity against Trichomonas gallinae. Girinimbine and
girinimbilol with IC50 values of 1.08 and 1.20 mg/mL were the most active. Acetylation of
girinimbilol and mahanimbilol improved their activities to 0.60 and 1.08 mg/mL.\cite{69}

5.18 Antidiarrhoeal activity: Two bioactive carbazole alkaloids, namely, kurryam and
koenimbine obtained from fractionated n-hexane extract of the seeds of M. koenigii exhibited
significant inhibitory activity against castor oil-induced diarrhoea and prostaglandin E2-
induced enteropooling in rats. These compounds also produced a significant reduction in
gastrointestinal motility in the charcoal meal test in Wistar rats\cite{27} Das et.al has reported
mahanimbine toxicity against the larvae of Culex quinquefasciatus.\cite{70}

5.19 Anthelmintic activity: Ethanolic and aqueous extracts from M. koenigii leaves were
investigated for their anthelmintic activity against Pheretima posthuma. Both the extracts
exhibited significant anthelmintic activity at concentration of 100 mg/mL.\cite{71} The alcoholic
extract produced more significant anthelmintic activity than petroleum ether extract.

Cosmetic use: Hyaluronidase inhibitors are extracted from M. koenigii and are formulated in
a cream base by Tsuneo et.al. M. koenigii extract is included in a skin-lightening cosmetic
for its moisturizing, antioxidant and hyaluronidase inhibitory activity. Herbal composition
containing M. koenigii stem extract as one of the ingredient showed skin lightening and
rough skin improving effect.\cite{72} M. koenigii was studied for sun protection. On the basis of
this study it was suggested that it can be used to maintain the natural pigmentation of the skin
or can be used as an adjuvent in other formulations to enhance the activity.

CONCLUSION
From the available literature on M. koenigii reveals that the plant may be utilized to alleviate
the symptoms of variety of diseases as evident form the pre-clinical data. Although crude
extract from various parts of curry neem have numerous medical applications, modern drugs
can be developed after extensive investigation of its bioactivity, mechanism of action,
pharmacotherapeutics, toxicity and after proper standardization and clinical trials. The
available literature and wide spread availability of M. koenigii in India thus makes it an
attractive candidate for further pre-clinical and clinical research. Murraya koenigi is a
multipotential medicinal plant. Almost each and every part of the plant has numerous medical
applications. Thus it can be consider being a most suitable candidate for new drug discovery.
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