A REVIEW ON TRADITIONAL INDIAN FOLK MEDICINAL HERB:

MURRAYA KOENIGII

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ABSTRACT

Murraya koenigii (L.) Spreng (Rutaceae) (Curry leaf tree) is a spicy traditional Indian medicinal plant native to Indo-China but grown mostly in the tropics for the medicinal and flavourant properties of the leaves. The family includes plants throughout tropical zones on most continents and includes approximately 1500 genera and 1500 species. It has been used for centuries in the Ayurvedic system of medicine. Leaves are used as a condiment in the preparation of curry powder, pickle, chutney, sausages and seasonings. Curry leaves used traditionally as antiemetic, anti-diarrhoeal, febrifuge and blood purifier. The whole plant is considered to be a tonic and stomachic. Curry leaves is found to be effective as antioxidant, antidiabetic, antibacterial, antihypertensive, cytotoxic and also in the treatment of bronchial respiratory difficulties. The leaves are used traditionally as spice in curry and other eatables. The aim of the present review study is to update information about pharmacognostical, phytochemical and pharmacological studies of Murraya koenigii.

KEYWORDS: Murraya koenigii (MK), Rutaceae, Diabetic wound healing, Hypolipidemic, Hypoglycemic.
INTRODUCTION
Ayurveda is a traditional Indian medicinal system practiced for thousands of years. Herbal medicines are being used by nearly 80% of the world population primarily in developing country for primary healthcare\(^1\). Medicinal plants or bioactive constituents from one of the major sources of raw material for drugs in preventive and curative applications\(^2\). Public, academic and government interest in traditional medicine is growing exponentially due to the increased evidence of the adverse drug reactions and economic burden of the modern system of medicine\(^3\). Crude drugs in many cases are found to be more potent than the pure drugs, the reason may be due to the synergistic action of the other component present which not only enhance biological activity of the drugs but simultaneously lower the toxic effect.

Selection of scientific and systemic approach for the biological evaluation of herbal formulations based on their use in traditional system of medicine forms the basis for the ideal approach in the development of the new drugs from plants. One such plant is *Murraya koenigii* Spreng (Rutaceae)\(^4,5\)

*Murraya koenigii* Spreng (Family: Rutaceae) is commonly known as Curry-leaf tree and is a native of India, Sri Lanka and other South Asian countries. Leaves of *Murraya koenigii* are rich in minerals, Vitamin A, Vitamin B and are a rich source of carbohydrates, proteins, amino acids and alkaloids.\(^4,5\)

Of the 14\(^{th}\) global species belonging to the genus *Murraya*, only two are available in India namely *M. koenigii* (L.) Spreng and *M. Paniculata* (L.) Jack\(^6\). Of the two, the former is more popular due to its large spectrum of medicinal properties and also because of use of its leaves for centuries as natural flavoring agent in various curries and food items\(^7\).

In traditional system of Medicine, it is used as antiemetic, antidiarrhoeal, dysentery, febrifuge, blood purifier, tonic, stomachic, flavoring agent in curries and chetneys. The oil is used externally for bruises, eruption, in soap and perfume industry\(^8\). The phytoconstituents isolated so far from the leaves are alkaloids viz., mahanine\(^9\), koenine, koenigine, koenidine\(^10\), girinimbol, girinimibine\(^11\), koenimbine, O-methyl murrayamine A, O-methyl mahanine, isomahanine, bismahanine, bispyrayafoline\(^12\) and other phytoconstituents such as coumarin glycoside viz., scopatin, murrayanine\(^13\), calcium, phosphorus, iron, thiamine, riboflavin, niacin, vitamin C, carotene and oxalic acid. The essential oil from leaves yielded di-pellandrene, D-sabinene, D--pinene, dipentene, D--terpinol and caryophyllene\(^14\). It is
reported to possess antioxidant, antibacterial, antifungal, larvicidal, anticarcinogenic, hypoglycemic, anti-lipid peroxidative, hypolipidemic and antihypertensive activity\textsuperscript{15}. It is also reported to contain 5,8-dimethyl furanocoumarin, 1-al, 3[6’, 6’ dimethyl 5-hexene] carbazole and –sitosterol\textsuperscript{16}.

**MORPHOLOGICAL CHARACTERS**

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, exposing the white wood underneath; the girth of the main stem is 16 cm. Leaves, extipulate, bipinnately compound, 30 cm long, each bearing 24 leaflets, having reticulate venation; leaflets, lanceolate, 4.9 cm long, 1.8 cm broad, having 0.5-cm-long petiole\textsuperscript{157}. Flowers, bisexual, white, funnel-shaped, sweetly scented, stalked, complete, ebracteate, regular, actinomorphic, pentameres, hypogynous, the average diameter of a fully opened flower being 1.12 cm; inflorescence, a terminal cyme, each bearing 60 to 90 flowers; calyx, 5-lobed, persistent, inferior, green; corolla, white, polypetalous, inferior, with 5 petals, lanceolate, length, 5 mm; androecium, polyandrous, inferior, with 10 stamens, dorsiﬁxed, arranged into circles of ﬁve each; smaller stamens, 4 mm. long whereas the longer ones, 5 to 6 mm; gynoecium, 5 to 6 mm long; stigma, bright, sticky; style, short; ovary, superior\textsuperscript{158}. Fruits, round to oblong, 1.4 to 1.6 cm long, 1 to 1.2 cm in diameter; fully ripe fruits, black with a very shining surface. Seed, one in each fruit, 11 mm long, 8 mm in diameter, colour spinach green. Flowering and fruiting occurs between December to July. This suckering plant can grow to a tree up to 6m tall in warm, humid climates, but it can also be grown very successfully in a pot as a much smaller plant\textsuperscript{17}-\textsuperscript{19}. It will also generally be smaller if grown out of its normal climate zone. The pungently - flavoured pinnate leaves are borne on opposite slender branchlets and have an unusual pendant habit. The leaves themselves are smooth and shiny with paler undersides. Blackish berries follow white, perfumed flowers in summer\textsuperscript{19,20}.

**PHYTOCHEMICAL STUDIES**

- Mahenine, a carbazole alkaloid was isolated from Murraya koenigii leaves & reported to induce apoptosis in human myeloid cancer cell (HL-60) and mahenine down regulates cell survival factors and disrupts cell cycle progression\textsuperscript{21}.
- Girinimbol and Girinimbine, the most active carbazole alkaloids were isolated from the methanolic extract of M. koenigii leaves and have shown to posses hypoglycaemic and hepatoprotective effect\textsuperscript{22}.
A benzisofuranone derivative along with six known carbazole alkaloids and three known steroids were isolated from the stem bark of M. koenigii. They were evaluated for antimicrobial activity and showed significant minimum inhibitory concentration in the range of 3.13-100µg/ml.

Xanthotoxin, isobyakangelicol and other minor Furocoumarines were isolated from M. koenigii Seeds.

Monoterpene and sesquiterpenes such as terpinene, terpinen-4-ol, linolol & -ocimene were isolated from the essential oil of M. koenigii seeds.

Mahanimbinine were isolated from the M. koenigii & characterized as a terpenoid alkaloid.

Mahanimbicine and bicyclomahanimbicine, two novel alkaloids were isolated and reported from the extracts of M. koenigii Spreng.

Three terpenoid alkaloids were isolated from M. koenigii Spreng II and identified as a cyclomahanimbicine, bicyclomahanimbicine, and mahanimbimbidine.

9-carbethoxy-3-methylcarbazole and a 9- formyl-3-methylcarbazole, and a known metabolite, 3-methyl carbazole were isolated from the roots of M. koenigii. 9-formyl compound showed weak cytotoxicity against both mouse melanoma B16 and adriamycin resistant P388 mouse leukemia cell lines.

Murrastifoline-F, an alkaloid was isolated from the root extract of the curry leaf plant M. koenigii.

11-selimen-4--7--ol and 10 aromadendranol were isolated and identified from the essential oil of M. koenigii.

8,8'-bis koenigine, along with its monomer koenigine were isolated from the dried leaves of M. koenigii.

2-methoxy-3-methyl-9H carbazole isolated from the roots extract of the M. koenigii, reported as a bioactive agent for the treatment of infections caused by dermatophytes, particularly Tinea infections.

8-10'-[3,3`,11,11`-tetrahydro 9,9`-dihydroxy- 3,3`,5,8`-tetramethyl-3,3` bis (4-methyl-3-pentyl)] bi pyrano [3-2] carbazole, koenimbine, O-methyl murrayamine A, Omethyl mahanine, isomahanine, bismahanine & bispyrayafoline was isolated from the dichloromethane extract of the M. koenigii leaves were evaluated on the basis of the oil stability index together with their radical scavenging ability against 1,1-diphenyl-2-picryl hydrazyl [DPPH] radical.
Bismurrayafoline E, a carbazole alkaloid was isolated from the methylene chloride extract and the ethyl acetate soluble fraction of the 70% acetone extract significantly prolonged the oil stability index value comparable to those of - tocopherol and BHT.

**PHARMACOLOGICAL STUDIES**

**Antibacterial activity**
- The essential oil from M. koenigii leaves showed antibacterial effect against B. subtilis, Staph. aureus, C. pyogenes, P. vulgaris and Pasteurella multicida. The pure oil was active against the first three organisms even at a dilution of 1: 500.
- The acetone extract of the fresh leaves of M. koenigii on fractionation gives three bioactive carbazole alkaloids named as mahanimbine, murrayanol and mahanine, which has shown mosquitocidal, antimicrobial and topoisomerase I and II inhibition activities.

**Antifungal activity**
- The essential oil from leaves of M. koenigii showed antifungal activity against C. albicans, C. tropicalis, A. niger, A. fumigatus and Microsporum gypseum. It was effective against C. albicans even at a dilution of 1:500. The ethanolic extract of the leaves showed fungitoxicity against Colletotrichum falcatum and Rhizoctonia solani.
- The ethanolic extract of the roots and also the whole plant excluding roots of M. koenigii, however, did not show any antifungal activity against Cryptococcus neoformans, Trichophyton mentagrophytes and Microsporum canis.
- Aqueous and ethanolic extracts of M. koenigii were evaluated for the anti candidal activity against the 30 candida albicans, in that no extract exhibited any anticandidal activity.

**Hypoglycaemic activity**
- The possible protective effect of M. koenigii leaf extract against -cell damage and antioxidant defense system of plasma and pancreas in streptozotocin induced diabetic rats was carried out and suggested that M. koenigii treatment exerts a protective effect in diabetes by decreasing oxidative stress and pancreatic -Cell damage.
- Hypoglycaemic effect of extracts of M. koenigii leafs along with the number of the spices were studied which proved that they can be used as potent antidiabetic diet.
- M. koenigii leaf extract showed reduction in blood glucose level by 13.1, 16.3, and 21.4% and 3.2, 5.58, 8.21% respectively for mild and moderate diabetes induced by alloxan in rats on feeding with extract as diet, proving its potential as antihyperglycaemic activity.
The aqueous extract of the M. koenigii leaves has been taken to evaluate the hypoglycaemic activity in normal and alloxan induced diabetic rabbits with the effect of a standard hypoglycaemic drug, tolbutamide. A single of variable administration of variable dose levels (200, 300, & 400 mg/Kg) of aqueous extract led to lowering of blood glucose level in normal as well as in diabetic rats\textsuperscript{46}.

Curry leaf extract possesses the property to decrease blood cholesterol and blood glucose levels in diabetic mice and reduces the body weight after its treatment\textsuperscript{47}.

Oral administration of ethanolic extract of M. koenigii in Streptozotocin induced diabetic rats for a period of 30 days significantly decrease the levels of blood glucose, glycosylated haemoglobin, urea, uric acid and creatinine in diabetic treated group of animals\textsuperscript{48}.

The aqueous extract of M. koenigii has favourable effect in bringing down the severity of the diabetes in alloxan and normal induced diabetic rabbits for a short duration of 6 hrs\textsuperscript{49}.

**Antiprotozoal activity**

Ethanolic extracts (50 %) of Murraya koenigii whole plant excluding roots (extract A) and roots alone (extract B) were screened for their pharmacological actions. Extract A showed antiprotozoal action against Ent. Histolytica, antispasmodic effect on isolated guinea pig ileum, whereas extract B showed antiprotozoal activity against Ent. Histolytica and as well as antihypertensive activity in cat/dog\textsuperscript{50}.

**Antioxidant activity**

The literature showed that the antioxidative properties of the extract of M.koenigii leaves were done using different solvents. They were evaluated on the basis of oil stability index (OSI) together with their radical scavenging ability against 1-1-diphenyl-2-picrylhydrazyl (DPPH). The methylene chloride (CH2Cl2) extract and the ethyl acetate (EtOAc) soluble fraction of the 70 % acetone extract was prolonged the OSI values significantly compared to those of -tocopherol and BHT. Five carbazole alkaloids were isolated from the CH2Cl2 extract and their structures were identified to be euchrestine, bismurrayafoline, mahanine, mahanimbicine and mahanimbine based on 1H and 13C NMR and mass (MS) spectral data\textsuperscript{51}.

The plant extract of M. koenigii was examined for its possible regulatory effect on nitric oxide (NO) levels using sodium nitroprusside as a NO donor in vitro. The extract had shown direct scavenging of NO and exhibited significant activity. The result showed that
M. koenigii might be potent and novel therapeutic agents for scavenging of NO, the regulation of pathological conditions caused by excessive generation of NO and its oxidation product, peroxynitrite\(^5\). 

**Haematological studies**

- The whole curry leaf was screened for haematological studies. In this study the rats were fed at doses equal to normal human intake. It did not cause any adverse effect on food efficiency ratio (FER), red blood cell count (RBC), white blood cells (WBC), 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 glutamic oxaloacetic transaminase (GOT), glutamic pyruvic transaminase (GPT) and alkaline phosphatase in serum. No histopathological changes were observed in the liver of rats administered curry leaf\(^5\). 

**Hypolipidemic activity**

- Biochemical response in rats was studied by supplementation of curry leaf (M. koenigii) to the diet. Albino rats were fed for 90 days on a standard laboratory rat diet plus 20% coconut oil either with the addition of 10% curry leaf. Feed was offered at a level of 10% body weight. The spice resulted in the reduction in total serum cholesterol and LDL + VLDL, an increase in the HDL, lower release of lipoproteins into the circulation and an increase in the LCAT (Lecithin Cholesterol Acyl Transferase) activity\(^5\).

- Studies on the effect of curry leaves supplementation on lipid profile, glycated proteins and amino acids were also done in non-insulin diabetic patients. The results indicated a transient reduction in fasting and post-prandial blood sugar levels at 15 days period with no appreciable changes in serum glycosylated protein levels, glycosylated low density lipoprotein cholesterol fraction, serum lipids, lipoprotein cholesterol levels. \(^5\)

- Two spices M. koenigii and Brassica juncea seeds were studied on the levels of lipids, fecal bile acids and neutral sterol in rats administered with 1,2 dimethyl hydrazine & showed decrease in the levels of cholesterol and phospholipids in the experimental groups when compared with the control. Morphological and histological studies revealed that the mean number of neoplasms in the colon and intestine were significantly low in the spices fed groups. \(^5\)
Anti-lipid peroxidative activity

- The status of lipid peroxidation was investigated in rats fed M. koenigii. The concentration of malondialdehyde showed a significant decrease, while hydroperoxides and conjugated dienes were significantly increased in liver and heart. Glutathione levels in liver, heart and kidney were lowered in rats administered these spices. Glutathione reductase, Glutathione peroxidase and Glutathione-S Transferase, SOD and catalase activity showed a sharp increase.

Anti-Hypertensive activity

- The angiotensin converting enzyme inhibitor and the antihypertension food, having activities for preventing or ameliorating one or more kind selected from a shell of a seed of jatoba (Hymenaea courbaril), a leaf of guava, M. koenigii, Tomarix chinensis Lour, a leaf of Morus bombycis, an extract of Mimusops elengi and a product of the conshiolin with succinic anhydride.

- Ethanolic extract of fresh leaves of M. koenigii showed a dose dependent positive inotropic effect on isolated frog heart by increasing availability of calcium from extracellular sites.

Respiratory disorders

- An herbal composition of M. koenigii and piper betel extracts for the treatment and remedy of bronchial respiratory difficulties.

Hepatoprotective and anti-ulcer activity

- The tannin and the carbazole from the aqueous extract exhibited hepatoprotective activity with respect to the different parameters studied and maintained normal morphology even after ethanolic challenge to the cells which was comparable to the protection offered by the standard drug L-ornithine-L-aspartate.

- The acetone extract of dry bark powder showed prominent protection of liver cell as compared with the control group and other solvent in CCl₄-induced liver damage. The aqueous extract at dosage of 200 and 400 mg/kg produced significant of gastric laison 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 result obtained suggested that the extract possesses significant anti-ulcer activity.
Anti-inflammatory activity

- Ethanolic extract of M. koenigii (EEMK) (300 and 400 mg/kg) showed anti-histaminic action in the histamine-aerosol protocol. The mast cell stabilization and anti-histaminic effect of EEMK were suggested to be probable mechanism for its anti-inflammatory action\(^6\).
- The ethanolic extract (250mg/kg) showed significant anti-inflammatory effect as compared with petroleum ether and chloroform extract in acute carrageenan-induced paw edema method and yeast induced hyperpyrexia method respectively\(^6\).

Anti-pyretic activity

- The ethanolic extract of leaves M. koenigii was investigated for anti-pyretic activity in rats using yeast induced pyrexia model. Ethanolic extract at a single dose of 300mg/kg produced significant activity in albino rats as compared with the standard drug paracetamol\(^6\).

Immunomodulatory activity

- The methanolic extract of M. koenigii showed significant increase in phagocytic index by rapid removal of carbon particles from blood stream. The extract also increase the antibody titre against ovalbumin and protection towards cyclophosphamide-induced myelo-suppression in albino mice\(^6\).
- Oral administration of the aqueous extract of leaves at dosage of 250 and 500 mg/kg significantly enhance the delayed typed hypersensitivity reaction induced by ovalbumin. The extract also potentiated the production of circulating antibody titre significantly in response to ovalbumin\(^6\).

Anthelmintic activity

- Ethanolic and aqueous extract from M. koenigii leaves were investigated for their anthemintic activity against *Pheretima posthuma*. Both the extract exhibited significant anthemintic activity at concentration of 100 mg/mL\(^6\).

Nephroprotective activity

- Aqueous extract of leaves produce a significant dose dependent decrease in serum urea and creatinine levels (P<0.001), and marked increased in the level of plasma anti-oxidant capacity(P<0.01) in diabetic rats, compared with the control subjects. Histological studies
of the kidney of these animals showed comparable tissue regeneration by the aqueous extract.\textsuperscript{70}

Wound healing activity

- The methanol extract of Murraya koenigii leaves was found to possess significant wound healing activity, which was evidenced by decrease in the period of epithelialization, increase in the rate of wound contraction and skin breaking strength.\textsuperscript{71}
- The aqueous of leaves showed marked reduction in wound area in the comparison with the control group from 4\textsuperscript{th} day onward in albino rats by excision wound model. The result obtained indicated that aqueous extract of M.koenigii accelerate the wound healing process by decreasing the surface area of wound.\textsuperscript{72}

Anti-cancer activity

- The effect of column (SU-I, SU-II, SU-III) extract of M. koenigii in in-vitro (short term incubation method SU-I, SU-II, SU-III) and in-vivo (Dalton’s ascetic lymphoma DAL, SU-II) anticancer model have been evaluated in male Swiss Albino mice. DAL cell were injected i.p. (10\textsuperscript{6} cells) to the mice. After treatment with SU-II, a significant decrease in the cancer cell number and tumor weight was observed in tumor bearing mice. These observations are suggestive of the protective effect of extract in DAL.\textsuperscript{73}

Diabetic wound healing activity

- Wound healing activity of aqueous extract of leaves of Murraya koenigii was studied by excision and incision wound model in high fat diet and streptozotocin treated type-2 diabetic rats (diabetic in hyperlipidemic rats). In the excision wound models, animals treated with Murraya koenigii (oral administration of variable dosage level 200mg/kg, 300mg/kg and 400mg/kg) leaves aqueous extract showed significant reduction in period of epithelisation and wound contraction 50\% when compared to the diabetic hyperlipidemic control group rats. In the Incision wound models, animals treated with Murraya koenigii (oral administration of variable dosage level 200mg/kg, 300mg/kg and 400mg/kg) leaves aqueous extract showed significant increasing the breaking strength of the wound when compared to the diabetic hyperlipidemic control group rats. In both excision and incision wound model very significant(p<0.001) result was found with 300mg/kg dose level because the effect was dose dependent up to 300mg equivalent of extract. The results suggested that aqueous extract of Murraya koenigii possess significant wound healing potential in diabetic hyperlipidemic rats.\textsuperscript{74}
The effect of *Murraya koenigii* leaves aqueous extract on biophysical and biochemical parameters of wound were studied by dead space wound model in diabetic hyperlipidemic rats. **In dead space** wound model animals treated with *Murraya koenigii* (oral administration of variable dosage level 200mg/kg, 300mg/kg and 400mg/kg) leaves aqueous extract showed significant increase in Wet & Dry granulations tissue weight (biophysical parameter) and hydroxyprolin content (biochemical parameter) when compared to the diabetic hyperlipidemic control group rats. In this study very significant (p<0.001) result was found with 300mg/kg dose level because the effect was dose dependent up to 300mg equivalent of extract. The results suggested that aqueous extract of *Murraya koenigii* possess significant wound healing potential in diabetic hyperlipidemic rats.

**Comparative Study of Hypoglycemic and Hypolipidemic Potency of Murraya Koenigii for Wound Healing Activity in high fat diet and low dose streptozotocin treated type-2 diabetic rats:**

**In blood parameter study** *Murraya koenigii* aqueous extract showed significant (p<0.001) anti-hyperglycemic activity and anti-hyperlipidemic activity in diabetic hyperlipidemic rats when compared to the diabetic hyperlipidemic control group. *Murraya koenigii* was found to be more potent for its hypolipidemic activity as compare to hypoglycemic activity because the *Murraya koenigii* showed no significant (p>0.05) difference for its hypoglycemic activity (decreasing fasting blood glucose level) at dose level 400mg/kg in diabetic hyperlipidemic rats when compared to the normal control group rats and in the case of its hypolipidemic activity (decreasing lipid level) it showed no significant difference at dose level 300 mg/kg only.

**In the excision** wound model, animals treated with *Murraya koenigii* (200mg/kg, 300mg/kg and 400mg/kg) leaves aqueous extract showed significant reduction in period of epithelisation and wound contraction 50% when compared to the diabetic hyperlipidemic control group rats.

In this wound model very significant (p<0.001) result was found with 300mg/kg dose level because the effect was dose dependent up to 300mg equivalent of extract. The groups treated with *Murraya koenigii* and Pravastatin showed more significant effect for excision wound healing than Glibenclamide treated group. These results clearly indicate that the hypolipidemic property of *Murraya koenigii* and Pravastatin may promote the epithelization and rate of wound contraction.
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