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Comprehensive review: *Murraya koenigii Linn*

Ajay S[1]*, Rahul S[3], Sumit G [5], Paras M[2], Mishra A[4], Gaurav A[1]

1. Himalayan Institute of Pharmacy, Kala Amb (HP)
2. Venkateshwara College of Pharmacy, Meerut (U.P.)
3. Faculty of Pharmacy, Amity University, Lucknow (U.P.)
4. AND College of Pharmacy, Babnan, Gonda (U.P)
5. Faculty of Pharmacy, RPETGI, Karnal (HR)

ABSTRACT

Plants have been used in traditional medicine for several thousand years. India is perhaps the largest producer of medicinal herbs and is rightly called the "Botanical garden of the World". Murraya koenigii Linn commonly known as Meethi neem, belongs to the family Rutaceae. The curry tree is native to India and it is found almost everywhere in the Indian subcontinent excluding the higher levels of Himalayas. Curry leaves used traditionally as antiemetic, antidiarrhoeal, 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.

KEY WORDS*: Murraya koenigii (L.), Antioxidant, Antidiabetic, Antibacterial, Pharmacognostical, Phytochemical, Pharmacological activities.*

Corresponding Author: Mr**.** Ajay Sharma **M-**09355655304 **E-mail-** ajaybipkkr@yahoo.co.in

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INTRODUCTION

Murraya koenigii Linn (Rutaceae)commonly known as Meethi neem, is an aromatic more or less deciduous shrub or a small tree up to 6 m in height found throughout India up to an altitude of 1500 m and are cultivated for ite aromatic leaves[1]. 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[2]. The phytoconstituents isolated so far from the leaves are alkaloids viz., mahanine[3], koenine, koenigine, koenidine4, girinimbiol, girinimibine[5], koenimbine, O-methyl murrayamine A, O-methyl mahanine, isomahanine, bismahanine, bispyrayafoline[6] and other phytoconstituents such as coumarin glycoside viz., scopotin, murrayanine[7], calcium, phosphorus, iron, thiamine, riboflavin, niacin, vitamin C, carotene and oxalic acid. The essential oil from leaves yielded di-α-phellandrene, D-sabinene, D-α-pinene, dipentene, D-α-terpinol and caryophyllene[8]. It is reported to possess antioxiant, antibacterial, antifungal, larvicidal, anticarcinogenic, hypoglycemic, anti-lipid peroxidative, hypolipidemic and antihypertensive activity[9]. It is also reported to contain 5,8-dimethyl furanocoumarin, 1-al, 3[6', 6' dimethyl 5-hexene] carbazole and β-sitosterol[10].

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,

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exposing the white wood underneath; the girth of the main stem is 16 cm. Leaves, exstipulate, 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 (11). Flowers, bisexual, white, funnel-shaped, sweetly scented, stalked, complete, ebracteate, regular, actinomorphic, pentamerous, 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(12). 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 (11-13). 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 (13,14).

Microscopical features:

Murraya koenigii is characterised by the presence of unicellular trichomes with obliterated lumen at the basal region, parenchymatous pith in petiole, long pericyclic fibres in the midrib, large cruciferous stomata and prismatic calcium oxalate crystals. The powder of Murraya koenigii leaves fluoresces brownish black. The powder when treated with 1 N methanolic sodium hydroxide shows yellowish white colour and when mounted in nitrocellulose emits chocolate fluorescence (13). The root shows tetrarch to pentarch stele, phelloderm fibres are absent and concentric grains of parenchyma are present. Fresh leaves on steam distillation under pressure yield 206% of volatile oil that may find use as a fixative (15, 16). The fruit is edible. It yields 0.76% of a yellow volatile oil with neroli like odour (17). TS shows a dorsi ventral structure. Epidermis is composed of cubical to slightly tangentially elongated cells. The upper epidermal cells in surface view are polyhedral and straight walled. Trichomes are rare unicellular and found mainly on midrib. Stomata anomocytic; palisade of two layers; irregularly arranged isodiametrical or rectangular cells constitute the spongy parenchyma. Calcium oxalate crystals present in the form of prisms. Secretory canals are large and circular. The midrib shows an arc of radiating xylem with phloem below. Pericyclic fibers appear in patches below the phloem. The fibers measure 2000µ in length. Inner to the lower epidermis is present 1 to 3 layers of collenchyma. Ground tissue is composed of thin parenchymatous polygonal cells.

Powder

Green in color with no distinct odour or taste, unicellular, bent or curved trichomes, two layered palisade, portion of secretory canals, well developed pericyclic fibers and a few prismatic crystals of calcium oxalate are the important identifying characters[18].

Phytochemical Studies

- Mahenine, a carbazole alkaloid was isolated from *Murraya koenigiii* leafs & reported to induce apoptosis in human myeloid cancer cell (HL-60) and mahenine down regulates cell survival factors and disrupts cell cycle progression[19].

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- Girinimbiol and Girinimbine, the most active carbazole alkaloids were isolated from the methanolic extract of *M. koenigii* leafs and have shown to posses hypoglycaemic and hepatoprotective effect[20].
- A benzisofuranone derivative along with six known carbazole alkaloid and three known steroids were isolated from the stem bark of *M. koenigii*. They were evaluated for anti microbial activity and showed significant minimum inhibitory concentration in the range of 3.13-100µg/ml[21].
- Xanthotoxin, isobyakangelicol and other minor Furocoumarines were isolated from *M. koenigii* seeds[22].
- Monoterpene and sesquiterpenes such as α terpinene, terpinen-4-ol, linolol & β-ocimene were isolated from the essential oil of *M. koenigii* seeds[23].
- Mahanimbinine were isolated from the *M. koenigii* & characterized as a terpenoid alkaloid[24].
- Mahanimbicine and bicyclomahanimbicine, two novel alkaloids were isolated and reported from the extracts of *M. koenigii* Spreng[25].
- Three terpenoid alkaloids were isolated from *M. koenigii* Spreng II and identified as a cyclomahanimbicine, bicyclomahanimbicine, and mahanimbimbidine[26].
- 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 B_{16} and adriamycin resistant P_{388} mouse leukemia cell lines[27].
- Murrastifoline-F, an alkaloid was isolated from the root extract of the curry leaf plant *M. koenigii*[28].
- 11-selimen-4-α-7-β-ol and 10 aromadendranol were isolated and identified from the essential oil of *M.* koenigii[29].
- 8,8'-bis koenigine, along with its monomer koenigine were isolated from the dried leaves of *M. koenigii*[30].
- 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[31].
- 8-10`-[3,3`,11,11`-tetrahydro 9,9`-dihydroxy-3,3`,5,8`-tetramethyl-3,3` bis (4-methyl-3-pentyl)] bi pyrano [3-2α] carbazole, koenimbine, O-methyl murrayamine A, O-methyl 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 scaveneging ability against 1,1-diphenyl-2-picryl hydrazyl [DPPH] radical[32].
- 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 α-tocopherol and BHT[33].

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[34].
- The acetone extract of the fresh leaves of *M. koenigii* on fractionation gives three bioactive carbazole alkaloids named as mahanimbine,

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murrayanol and mahanine, which has shown mosquitocidal, antimicrobial and topisomerase I and II inhibition activities[35].

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*[36].
- 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*[37,38,39].
- 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[40].

Larvicidal activity

- Larvicidal activity against *A.aegypti* larvae have been showed by the acetone and petroleum ether extracts of *M. koenigii* leafs at a concentration range 250 ppm-900 ppm[41].

Hypoglycaemic activity

- The possible protective effect of *M. koenigii* leaf extract against β-cell damage and anti-oxidant 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 β-Cell damage[42].
- 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[43].
- *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[44].
- 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[45].
- Curry leaf extract posseses the property to decrease blood cholesterol and blood glucose levels in diabetic mice and reduces the body weight after its treatment[46].
- 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[47].
- 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[48].

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,*

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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[49].

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 (CH_2Cl_2) extract and the ethyl acetate (EtOAc) soluble fraction of the 70 % acetone extract was prolonged the OSI values significantly compared to those of α-tocopherol and BHT. Five carbazole alkaloids were isolated from the CH_2Cl_2 extract and their structures were identified to be euchrestine, bismurrayafoline, mahanine, mahanimbicine and mahanimbine based on ^1H and ^{13}C NMR and mass (MS) spectral data[50].
- 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[51].

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[52].

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[53].
- 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 [54].
- 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

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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[55].

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 [56].

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[57].
- 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[58].

Respiratory disorders

- An herbal composition of *M. koenigii* and piper betel extracts for the treatment and remedy of bronchial respiratory difficulties[59].

Cytotoxic activity

- Carbazole alkalolids Mahenine, pyrayafoline-D and murrafoline-1 showed significant cytotoxicity against HL-60 cells. Fluorescence microscopy with Hoechst 33342 staining revealed that the percentage of apoptotic cells with fragmented nuclei and condensed chromatin was increased in a time dependent manner after treatment with each alkaloid[60].

Trypsin inhibitor

- Structure function studies of *M. koenigii* trypsin inhibitor revealed a compact structure made of central beta sheet surrounded by α-helices with difference in structural functional stability and showed correlating decrease in inhibitory activity and helical content at increasing temperature suggest a possible role for α-helical structure in inhibitory function of the protein[61].

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