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Phyto-pharmacology of *Murraya koenigii* (L.)

Deepa Iyer [1] * and P. Uma Devi [2]

[1] *Faculty, Shri Ram Institute of Technology, Near I.T.I., Madhotal, Jabalpur-482002, M.P., India*

[2] *Jawahar Lal Nehru Cancer Hospital & Research Centre, Idgah Hills, Bhopal- 462001, M.P., India*

*** Author for Correspondence**: *deepa2183@yahoo.com*

ABSTRACT

Herbs have always been the principal form of medicine in India. Medicinal plants have curative properties due to the presence of various complex chemical substances of different composition, which are found as secondary plant metabolites in one or more parts of these plants. *Murraya koenigii* (L.) commonly known as Meethi neem, family Rutaceae, is used traditionally as antiemetic, antidiarrhoeal, febrifuge and blood purifier. The whole plant is considered to be a tonic and stomachic. The leaves are used extensively as a flavoring agent in curries and chutneys. The oil derived from the leaves is also applied externally to bruises and eruptions. The oil is also used in the perfume and soap industries. Studies indicate that it possesses antioxidant, antibacterial, anticarcinogenic, anti-lipid peroxidative, hypoglycemic and hypolipidemic properties. The present review aims to update information on its phytochemistry and pharmacological activities.

KEY WORDS - *Murraya koenigii* (L.), Antioxidant, Antibacterial, Anticarcinogenic, Phytochemistry, Pharmacological activities.

INTRODUCTION

Murraya koenigii (L.) is an aromatic more or less deciduous shrub or a small tree up to 6m. in height found throughout India up to an altitude of 1,500m. commonly in forest often as gregarious under-growths. It is cultivated for its aromatic leaves (1). The plants grow best in tropical and sub-tropical climates in sunny to semi-shaded locations, though they can be sustained in other climates by moving pots to warm protected areas in winter and maintaining humid conditions in areas where summers are hot and dry. They are very frost sensitive. Soil needs to be enriched with lots of organic material and be well drained. Water well when the weather is dry but don't over-water. The plants require very little in the way of fertilizer. Seeds germinate fairly readily (2).

Almost every part of this plant has a strong characteristic odour. The people of the plains, particularly of southern India, use the leaves of this plant as a spice in different curry preparations (3).

Murraya koenigii contains carbazole alkaloids namely murrayanine (4), mahanimbine (5), girinimbine (6), murrayacine (7), isomurrayazoline (8), mahanine, koenine, koenigine, koenidine, koenimbine, 8,8'-biskoenigine.Other alkaloids are O-methylmurrayamine, O-methylmahanine, isomahanine, bismahanine and bispyrayafoline (9,10). The leaves are fair sources of vitamin A. They are also a rich source of calcium, but due to presence of oxalic acid in high concentration its nutritional availability is affected. The free amino acids present in leaves are: asparagine, glycine, serine, aspartic acid, glutamic acid, theonine, alanine, proline, tyrosine, and tryptophan. It contains 0.8% potash. The major constituents of curry leaf are monoterpenes [70%]; seed cotyledons [86%], constituting -pinene [52%] and *cis*-ß-ocimene [34%] (1,3).

The plant has been used in traditional Indian medicine for a range of ailments. The whole plant is considered to be a tonic and stomachic. Roots and bark are stimulant and are applied externally for skin eruptions and poisonous bites. Green leaves are febrifuge and used in dysentery (1,2,3).

Botanical Description

Taxonamy

Kingdom:	*Plantae*
Division:	*Magnoliophyta*
Class:	*Magnoliopsida*
Order:	*Sapindales*
Family:	*Rutaceae*
Genus:	*Murraya*
Species:	***M. koenigii***
Synonyms	
Assamese	*: Narsinghs, Bisharhari*
Hindi	*: Kathnim, Mitha neem, Curry patta*
Bengali	*: Barsanga, Kariphulli*
Gujarati	*: Goranimb, Kadhilimbdo*
Kannada	*: Karibevu*
Malayalam	*: Karriveppilei*
Marathi	*: Karhinimb, Poospala, Gandla,*
Oriya	*: Barsan, Basango, Bhuraunga*
Punjabi	*: Curry patta*
Sanskrit	*: Krishna nimba*
Tamil	*: Karivempu, Karuveppilei*
Telugu	*: Karepaku*

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, 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).

PHYTOCHEMISTRY

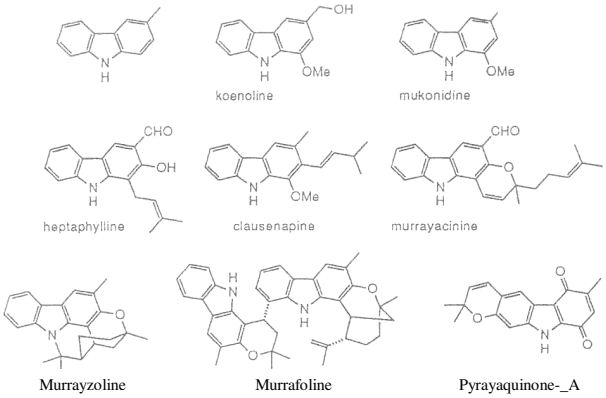
The leaves of *Murraya koenigii* are reported to yield a number of alkaloids *viz.*, mahanine, koenine, koenigine and koenidine (9,10,18,19). The hexane extract yielded mahanimbine, girinimbine, isomahanimbine and koenimbidine (20-24). The structures of mahanine (25), koenine, koenimbine (26), isomahanimbine and koenigicine (27) were confirmed by synthetic studies. The other constituents isolated from the leaves were a coumarinic glucoside (16,28), scopolin (16,29,30) and murrayanine. The leaves have been reported to contain calcium, phosphorus, iron, thiamine, riboflavin, niacin, vitamin C, carotene and oxalic acid. The essential oil from leaves yielded dl-α-phellandrene, d-sabinene, d-α-pinene, dipentene, d-α-terpinol and caryophyllene (31).

The stem barks of *Murraya koenigii* on extraction with petroleum were reported to yield a number of carbazole alkaloid *viz.*, girinimbine (32), murrayanine (33) and mahanimbine (34). Optically inactive mahanimbine was also isolated from the extract (35). Murrayacine was the other alkaloid isolated (36,37). Spectroscopic, degradative and synthetic evidences have been documented for girinimbine (38), cyclomahanimbine, mahanimbidine (39), mahanimbinine (40), murrayanine, mahanimbicine (41), murrayacine, murrayacinine (42), mahanimboline (43) and mukanol (44).

The other carbazole alkaloids isolated from the stem bark were murrayazolidine (45, 46), murrayacinine (47), cyclomahanimbine (48), murrayazoline (49), murrayazolinine, isomurrayazoline, curryanin and curryangin (50,51). Eventually curryangin, murrayazoline and mahanimbidine were reported to have the same structure.

The alcoholic extract of the *Murraya koenigii* stem yielded mukoenic acid (52) i.e., 1-methoxy-carbazole-3-carboxylic acid. The methyl ester of mukoenic acid – mukonine (53) was isolated from the petrol extract of the stem bark.

The roots of *Murraya koenigii*, on extraction with light petroleum, yielded a carbazole alkaloid, mahanimboline. The hexane extract of roots yielded girinimbine. The benzene extract yielded two alkaloids mukoline and mukolinidine and assigned the structures 6- hydroxymethyl-1-methoxy carbazole and 6-formyl-1-methoxy carbazole respectively (54). *Murraya koenigii* fruits yielded an alkaloid namely koenimbine, murrayazoline, murrafoline and pyrayaquinone-A



PHARMACOLOGY

Antibacterial activity

The essential oil from *Murraya 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 (55). The leaf extract was tested against *A. aerogens, B. polymyxa, Ps. aeruginosa, Serratia marcensce, Sar. lutea* (56) and the root extract and also the extract of whole plant excluding roots was tested against *Sal. typhi, A. tumefaciens* and *M. tuberculosis* (57), but found to be inactive.

Antifungal activity

The essential oil from leaves of *Murraya 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* (58). The ethanolic extract of the roots and also the whole plant excluding roots of Murraya koenigii, however, did not show

any antifungal activity against *Cryptococcus neoformans*, *Trichophyton mentagrophytes* and *Microsporum canis* (59,60,61).

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* and antispasmodic effect on isolated guinea pig ileum, whereas extract B showed antiprotozoal activity against *Ent. Histolytica* as well as hypertensive activity in cat/dog (57).

Hypoglycaemic activity

Significant hypoglycaemic action of *Murraya koenigii* also has been reported. Feeding of diet containing various doses of curry leaves (5, 10 and 15%) to normal rats for 7 days as well as mild diabetic (blood glucose levels >175 mg/dl induced by alloxan 35 mg/kg i.p.) and moderate diabetic rats (blood glucose levels >250 mg/dl induced by STZ 60 mg/kg i.p.) for 5 weeks showed varying hypoglycemic and anti-hyperglycemic effect. In normal rats, reduction in blood glucose was almost negligible (approximately 4% with 10 and 15% diet). In mild and moderate diabetic rats, feeding of 5, 10 and 15% diet caused a maximal reduction in blood sugar by 13.1, 16.3 and 21.4% and 3.2, 5.58, 8.21% respectively (62).

Another study reported that *Murraya koenigii* showed anti-hyperglycemic activity in STZ-induced diabetic rats. Oral administration of ethanolic extract of *Murraya koenigii* at a dose of 200 mg/kg/ b.w. /day for a period of 30 days significantly decreased the levels of blood glucose, glycosylated hemoglobin, urea, uric acid and creatinine in diabetic treated group of animals. Determination of plasma insulin level revealed the insulin stimulatory effect of the extract. The results suggest that *Murraya koenigii* possesses statistically significant hypoglycemic potential in STZ-induced diabetic rats. The *Murraya koenigii* extract appeared to be more effective than glibenclamide, a known antidiabetic drug (63).

Another study postulates the effect of daily oral administration of aqueous extract (600 mg/kg b.wt.) and methanol extract (200 mg/kg b.wt.) of *Murraya koenigii* leaves for a period of eight weeks on blood glucose and plasma insulin level in alloxan-induced diabetic rats. Blood glucose levels of diabetic rats treated with aqueous and methanol extracts of *Murraya koenigii* showed significant reduction as compared to diabetic control groups. Plasma insulin showed significantly high on 43rd and 58th days of treatment in aqueous and methanol extracts of *Murraya koenigii* treated groups. This suggests that the hypoglycemic effect may be mediated through stimulating insulin synthesis and/or secretion from the beta cells of pancreatic islets of Langerhans (64).

The findings also suggest that the aqueous extract of *Murraya koenigii* leaves showed hypoglycemic activity in normal and alloxan induced diabetic rabbits. The scientific evaluation of its hypoglycemic activity was explored and compared with the effect of a standard hypoglycemic drug, tolbutamide. A single oral administration of variable dose levels (200, 300 and 400 mg/kg) of aqueous extract led to lowering of blood glucose level in normal as well as in diabetic rabbits. The maximum fall of 14.68% in normal and 27.96% in mild diabetic was observed after 4 h of oral administration of 300 mg/kg. The same dose also showed a marked improvement in glucose tolerance of 46.25% in sub-diabetic and 38.5% in mild diabetic rabbits in glucose tolerance test after 2 h. the aqueous extract of these leaves may be prescribed as adjunct to dietary therapy and drug treatment for controlling diabetes mellitus (65).

Antioxidant activity

The literature showed that the antioxidative properties of the extract of *Murraya 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 -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 (66).

The plant extract of *Murraya 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 *Murraya 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 (67).

In another study, the antioxidant potential of curry leaves in rats, treated with a known chemical carcinogen - dimethylhydrazine hydrochloride (DMH), was investigated. Vitamin A content in the liver was significantly increased whereas glutathione (GSH) content was not altered. The results indicated that curry leaves have high potential as reducer of the toxicity of DMH (68).

Oxidative stress and oxidative damage to tissues are common end points of chronic diseases such as atherosclerosis, diabetes, and rheumatoid arthritis. Oxidative stress in diabetes coexists with a reduction in the antioxidant status, which can further increase the deleterious effects of free radicals. Another study was done to evaluate the possible protective effects of *Murraya koenigii* leaves extract against beta-cell damage and antioxidant defense systems of plasma and pancreas in streptozotocin induced diabetes in rats. The levels of glucose and glycosylated hemoglobin in blood and insulin, Vitamin C, Vitamin E, ceruloplasmin, reduced glutathione and TBARS were estimated in plasma of control and experimental groups of rats. To assess the changes in the cellular antioxidant defense system such as the level of reduced glutathione and activities of superoxide dismutase, catalase and glutathione peroxidase were assayed in pancreatic tissue homogenate. The levels of glucose, glycosylated hemoglobin, insulin, TBARS, enzymatic and non-enzymatic antioxidants were altered in diabetic rats. These

alterations were reverted back to near control levels after the treatment of *Murraya koenigii* leaves extract. Transmission electron microscopic studies also revealed the protective nature of *Murraya koenigii* leaves on pancreatic beta cells. These findings suggest that *Murraya koenigii* treatment exerts a therapeutic protective nature in diabetes by decreasing oxidative stress and pancreatic beta-cell damage (69).

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 (70).

Hypolipidemic activity

Biochemical response in rats was studied by supplementation of curry leaf (*Murraya 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 (71).

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 (72).

Anti-lipid peroxidative activity

The status of lipid peroxidation was investigated in rats fed *Murraya koenigii*. The concentration of melondialdehyde 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 (73).

CONCLUSION

Medicinal plants are the local heritage with the global importance. World is endowed with a rich wealth of medicinal plants. Medicinal plants also play an important role in the lives of rural people, particularly in remote parts of developing countries with few health facilities. The present review reveals that *Murraya koenigii* is utilized as spice, for the treatment of some common disease. The carbazole alkaloids are the most searched chemical constituents of *Murraya koenigii*. The plant has been studied for their various pharmacological activities like antioxidant, antibacterial, antifungal, antiprotozoal, anti-lipid peroxidative, hypoglycemic and hypolipidemic activity. Haematological studies have also been studied. Therefore it is necessary to exploit its maximum potential in the field of medicinal and pharmaceutical sciences for novel and fruitful application.

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