MURRAYA KOENIGII (CURRY LEAVES) - A REVIEW

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ABSTRACT
Murraya Koenigii (meethi neem) member of family Rutaceae is a deciduous to semi evergreen tree traditionally used as a medicinally important herb of Indian origin. Its extract has been found to be useful as an antidiabetic, antimicrobial, antifungal agent. The plant extract also possess antioxidant activity. The presence of phytochemicals, cytotoxicity, and antimicrobial and antioxidant activities were investigated in the extracts of ethanol of Murraya koenigii, Oleoresin of curry leaves (Murraya koenigii Spreng.), obtained using acetone, was evaluated for its antioxidant activity using a β-carotene–linoleic acid model system. Antiulcer activity of aqueous and ether extracts of M. koenigii was studied in reserpine induced gastric ulcer model in albino rats. Extracts were effective in gastric ulceration and suggested as protective as ranitidine.

Keywords: Murraya Koenigii, antioxidant activities, β-carotene–linoleic acid model, antimicrobial.

INTRODUCTION
India is the country which has some of the richest, oldest and diverse cultural tradition associated with the use of medicinal plants since centuries and still persists in living tradition. Herbal Medicines are used in almost 75% over the world with special reference to the developing countries where it is still practiced for the primary health care. Medicinal and aromatic plants are important for the well being of the population, especially of the rural poor who depend on these resources to treat human and livestock ailments and diseases. Murraya koenigii (Rutaceae), a member of family Rutaceae is a deciduous to semi evergreen tree traditionally used as a medicinally important herb of Indian origin. Traditionally it is used as analgesic, stomachic and carminative. The leaves, bark and the roots of the plant are used in indigenous medicine as tonic, stomachic, stimulant and carminative. An infusion of the roasted leaves is used to prevent vomiting. Of the fourteen global species belonging to the genus Murraya, only two are
available in India, viz. Murraya koenigii and Murraya paniculata. It is traditionally used as antibacterial, antihelminthic, antidiabetic, antifungal, antiulcer, and antioxidant agent. An intense review of the literature has revealed that the stems, leaves, roots and seeds are potential sources of carbazole alkaloids apart from this presence of flavinoids, sterols, phenols, saponins has been observed in the plant which grant it various pharmacological properties. In case of livestock and Poultry stress, bacterial infections, parasitic infestations and injury are some of the major constraints which affect their production directly or indirectly. Murraya koenigii plant as a whole proves to be extremely useful in this aspect.

Antidiabetic Properties-
Protective effects of Murraya koenigii leaves extract against β-cell damage and antioxidant defence systems of plasma and pancreas in streptozotocin induced diabetes in rats was evaluated. 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 M. koenigii leaves extract. Transmission electron microscopic studies also showed the shielding nature of M. koenigii leaves on pancreatic β-cells. Therefore it suggests that M. koenigii treatment exerts a therapeutic protective nature in diabetes by lessening oxidative stress and pancreatic β-cell damage. [25] Another study was planned by [34] to investigate the beneficial effect of the leaves of Murraya koenigii (Linn.) on diabetes-induced renal damage in vivo with regard to prove its efficacy by local traditional practitioners in the treatment of kidney dysfunction in diabetics, results of this study scientifically support the traditional belief for using the leaves of Murraya koenigii (Linn.) as adjuvant, in the treatment of pain disorders related to renal impairments among diabetics [34]. Vinuthan et al studied 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 (P<0.05) as compared to diabetic control groups. Plasma insulin showed significantly high level on 43rd and 58th days of treatment in aqueous and methanol extracts of Murraya koenigii treated groups. This suggests that the
hypoglycaemic effect may be mediated through stimulating insulin synthesis and/or secretion from the beta cells of pancreatic islets of Langerhans[33]

Anti-hyperglycemic efficacy of Murraya koenigii in STZ-induced diabetic rats was also evaluated by Adebajo et al and they observed that when ethanolic extract of M. koenigii was given orally at a dose of 200 mg/kg b.w./day for a period of 30 days significantly decreased levels of blood glucose, glycosylated hemoglobin, urea, uric acid and creatinine was seen in diabetic treated group of animals. Determination of plasma insulin level revealed the insulin stimulatory effect of the extract the results suggest that M. koenigii possesses statistically significant hypoglycemic potential in STZ-induced diabetic rats. And it even appeared to be more effective than glibenclamide, a known antidiabetic drug [1]. Another anti-diabetic activity was performed on the streptozotocin induced wistar rats by using pure compound mahanimbine at a dose of 50 mg/kg and 100 mg/kg. The possible mechanism by which it decreases blood sugar level may be by potentiating of insulin effect either by increasing the pancreatic secretion of insulin from beta cells of islets of langerhans or by increasing the peripheral glucose uptake. [8]

Antibacterial Properties-

Methanolic extract of 21 plant species were screened for in vitro anti bacterial activity against multi resistant bacteria isolates including Gram positive and Gram negative strains. Study showed that M. koenigii posses maximum antibacterial activity. Staphylococcus epidermidis was significantly inhibited by M. koenigii [19]

The present study deals with antimicrobial studies of different part of Murraya Koenigii Linn. The antimicrobial studies conformed that the ethanolic extract of leaves was active against S. aureus and B. subtilis at 6.25-12.5 mg/ml with maximum inhibition zone diameter (20mm) and moderate effect against all. Where as the bark extract was found to be more active against the A. niger and C. Albicans at 6.25-12.5 mg/ml with maximum inhibition zone diameter (16-18 mm.) present study might be useful to supplement information in regard to its identification as potent antimicrobial agent [37]

Various solvent extract of Murraya Koenigii plant was evaluated against E coli,Klebsiella,Pseudomonas,Staphylococcus aureus ,and fungus like Aspergillus,Candida,Micrococcus,Cryptococcus species. In this study hot water extract in bacteria and ethanolic extract in fungus showed various degree of inhibition and thus the
The study confirmed the presence of antibacterial activity in the plant [38]. The presence of phytochemicals, cytotoxicity, and antimicrobial and antioxidant activities were investigated in the extracts of Indonesian medicinal plants including *Murraya koenigii*.

Parts of *M. koenigii* were extracted with ethanol. The extracts were evaluated for antimicrobial activity using the disc diffusion method, while antioxidant activity was determined with a 1,1-diphenyl-2-picrylhydrazyl radical scavenging assay. Cytotoxicity was investigated using the brine shrimp lethality test, and phytochemical screening was performed using a standard method. *M. koenigii* leaf extract exhibited the most activity in the test microorganism activity index (AI), 0.38-1.25, when compared with standard drugs. Phytochemical analysis revealed that carbohydrate, tannin, alkaloid, steroid, triterpenoid, and flavonoid were present in the extracts of *M. koenigii* leaves, while saponin was absent. The work revealed that the *M. koenigii* leaves have potential as sources of new antimicrobial, antioxidant, and cytotoxic compounds, respectively.

Solvent-free microwave extraction (SFME) for the isolation of essential oil from leaves of *Murraya koenigii* L. (Rutaceae) has been compared with the conventional hydro-distilled oil (HD) in terms of yield, composition, antioxidant activity, and antibacterial activity against *Listeria innocua*. The yield of essential oil obtained from 30 min of SFME was similar to that of HD for 180 min. By GC-MS analysis, the major compounds of the essential oil extracted by SFME, which were obtained in somewhat lower amounts than in the essential oil obtained by HD, were alpha-copaene (44.3%), beta-gurjunene (25.5%), isocaryophyllene (12.1%), beta-caryophyllene (8.7%) and germacrene D (2.9%). The content of oxygenated terpenes, slightly higher for the SFME-essential oil (2.3%) than the HD-essential oil (1.4%), were much lower than that of nonoxygenated terpenes in both oils. DPPH radical scavenging activities of both essential oils were relatively low (10%-24%). Complete inhibition of growth of *L. innocua* was observed with both SFME and HD essential oils, at 400 and 600 microg/mL (minimum inhibitory concentration), respectively. The SFME-essential oil at 300 microg/mL provided 92% inhibition, indicating its potential as a natural antimicrobial agent. (Antibacterial activities of essential oils extracted from leaves of *Murraya koenigii* by solvent-free microwave extraction and hydro-distillation.[9] Benzoisofuranone derivatives along with six known carbazole alkaloids and three known steroids were
isolated from stem bark of M. Koenigii. These compounds were found to be effective in the range 3.13 - 100 g/ml concentration. Literature survey revealed that methanolic extract of 21 plant species were screened for in vitro anti bacterial activity against multi resistant bacterial isolates including Gram positive and Gram negative strains. Study showed maximum antibacterial activity by M. koenigii. Staphylococcus epidermidis was significantly inhibited by M. koenigii [19,26].

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[10].

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 [7]. 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. [23]. Anti-diarrhoeal activity of aqueous and alcoholic extract of the leaves of Murraya koenigii (M. koenigii) by using models of castor oil induced diarrhoea, charcoal meal test and PGE2 induced diarrhoea was evaluated by Sharma et al. in 2012 and found that it could act centrally and inhibit the PGE2 to give anti-diarrhoeal effects were used for the anti-diarrhoeal activity.

Results: The result suggested that. Result of charcoal meal test also suggested its antimuscarinic activity, aqueous extract of the leaves of M. koenigii displays good anti-diarrhoeal activity, corroborating the folk use of M. koenigii preparations and contributing for its pharmacological validation. [24]. The bioassay guided fractionation of the n-hexane extract of the seeds of M. koenigii resulted in the isolation of three pure compounds of bioactive carbazole alkaloids, kurryam, koenimbine and koenine. Of the three compounds kurryam and koenimbine exhibited significant inhibitory activity against castor oil-induced diarrhea and PGE2-induced enter pooling in rats. The compounds also produced a significant reduction in gastro-intestinal motility in the charcoal meal test in Wister rats [20].
Wound-healing Properties

Wound healing model reveals that aryl hydroxyl substituent on the carbazole ring plays a role in stabilizing the thermal oxidation and rate of reaction against DPPH radicals [35]. The wound healing efficacy of methanol extract of Murraya koenigii was evaluated in excision and incision wound models. The parameters studied include rate of wound contraction, period of complete epithelialization and tensile strength of incision wound.

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. Ethanolic extract of M. koenigii was studied by excision and incision wound models in male Albino rats (in vivo). In excision model, compared to the control group, percent concentration of wound was significantly higher in M. koenigii (5% w/w ointment)-treated group. In incision model, tensile strength of the healing tissue after treatment with M. koenigii was found to be significantly higher compared to the control group, indicating better wound-healing activity of the test plant. These results suggest that ethanolic extract of M. koenigii possesses significant wound healing potential in normal wound. In another study 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 Murraya koenigii were proved to possess significant wound healing capacity [2].

Antioxidant Properties

The antioxidative properties of the leaf extracts of Murraya koenigii using different solvents were evaluated based on the oil stability index (OSI) together with their radical scavenging ability against 1,1-diphenyl-2-picrylhydrazyl (DPPH) [11]. [18]

The status of lipid peroxidation was investigated in rats fed with M. Koenigii. The concentration of melondialdehyde showed a significant decrease, while hydroperoxides and conjugated dienes were significantly increased in liver and heart.[17].

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The presence of natural antioxidant in plants is well known paper reports antioxidative activities of some methanolic plant extracts namely ‘ulam raja’ (Cosmos caudatus), ‘kesum’ (Polygonum minus), ‘selom’ (Oenanthe javanica), ‘pegaga’ (Centella asiatica) and ‘curry leaf’ (Murraya koenigii). The analysis carried out was total phenolic content, ferric reducing power, ferric thiocyanate (FTC) and thiobarbituric acid (TBA) tests. From the analyses, M. koenigii had the highest yield extraction (1.65%), highest total phenolic content (38.60 mg TAE/100 g fresh weight) and antioxidant activity (70.60%) using FTC method. Increasing the concentration of the extracts resulted in increased ferric reducing antioxidant power for all methanolic extracts tested. TBA analysis showed that C. caudatus extract had the highest antioxidant effect. Total phenolic content had positive correlation with antioxidant capacity (r = 0.451). This shows that the plants, especially M. koenigii, may be potent source of natural antioxidants.

Oleoresin of curry leaves (Murraya koenigii Spreng.), obtained using acetone, was evaluated for its antioxidant activity using a β-carotene–linoleic acid model system along with the other extracts obtained using methanol, water and volatile oil. The oleoresin showed maximum activity of 83.2% at 100 ppm among all other extractives in comparison to a synthetic antioxidant, namely, butylated hydroxy anisole which exhibited 90.2% activity at the same concentration. The methanol and water extracts showed activities of 16.7% and 11.3%, respectively, at the same concentration. The volatile oil showed negligible (<10%) activity at 100 ppm concentration. Therefore, the oleoresin was fractionated on a silica gel column to obtain five compounds. Among the five, two compounds with maximum antioxidant activity were identified by 1H and 13C NMR spectra as mahanimbine and koenigine. Koenigine also showed a high degree of radical-scavenging activity.

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. Beneficial effects of Murraya koenigii leaves on antioxidant defense system and ultra structural changes of pancreatic cells in experimental diabetes in rats., [39].

Immunological Properties
The methanolic extract of M. koenigii leaves was evaluated on human oral and cell mediated immune response to ovalbumin, phagocytic activity by carbon clearance test, nitric oxide (NO) release from murine peritoneal macrophages and cyclophosphamide induced mycosuppression[31]. Effect of the leaves of M. koenigii on carbohydrate metabolism has been studied using rats as experimental animals. It showed significant hypoglycemic action. There was increase in the concentration of hepatic glycogen [6]

Antitumor Properties
Carbazole alkaloids isolated from the stems of Murraya koenigii (Rutaceae) have effects on the growth of the human leukemia cell line HL-60. Also the carbazole alkaloids, mahanine, pyrafoline-D and murrafoline-I showed significant cytotoxicity against HL-60 cells and induced the loss of mitochondrial membrane potential [14].

The radio protective and chemoprotective effect of M. koenigii methanolic extract after irradiation has demonstrated protection against radiation RT & cyclophosphamide CP induced chromosomal damage in vivo. Gama Radiation 4Gy produced a significant increase in the percent aberrant metaphases and different types of aberrations compared to same treated control. Single dose of 100 mg/kg methanolic extract of M. koenigii can significantly decrease the chromosomal damage caused by irradiation and cyclophosphamide and also showed bone marrow protection [11]

Girinimbine, a carbazole alkaloid isolated from the stem bark of Murraya koenigii was tested for the in vitro anti-tumour promoting and antioxidant activities. Anti-tumour promoting activity was determined by assaying the capability of this compound to inhibit the expression of early antigen of Epstein-Barr virus (EA-EBV) in Raji cells that was induced by the tumour promoter, phorbol 12-myristate 13-acetate. The concentration of this compound that gave an inhibition rate at fifty percent was 6.0 µg/mL and was not cytotoxic to the cells. Immunoblotting analysis of the expression of EA-EBV showed that girinimbine was able to suppress restricted early antigen (EA-R). However, diffused early
antigen (EA-D) was partially suppressed when used at 32.0 µg/mL. Girinimbine exhibited a very strong antioxidant activity as compared to a-tocopherol and was able to inhibit superoxide generation in the 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced differentiated premyelocytic HL-60 cells more than 95%, when treated with the compound at 5.3 and 26.3 µg/mL, respectively. However girinimbine failed to scavenge the stable diphenyl picryl hydrazyl (DPPH)-free radical Molecules [36]

Analgesic Properties

The methanolic extract of leaves showed analgesic effect in 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. Methanol extracts were taken at different concentrations, viz. 100mg/ml, 200mg/ml and 400 mg/ml. Among these 400 mg/ml showed prolific results [12]

Cardiovascular Properties

Crude aqueous leaf extract of M. koenigii was prepared 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 β-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.[16]

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 [31].

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 [27]. Positive inotropic effect of Murraya koenigii Linn spreng extract on an isolated perfused frog heart.
Structure function studies of *M. koenigii* trypsin inhibitor revealed a compact structure made of central beta sheet surrounded by _-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 _-helical sstructure in inhibitory function of the protein[28]

Hypocholesterolemic activity was checked in aged mice, which was done by using crude ethanol extract of plant leaves of *M. Koenigii*. decrease in cholesterol level in dose dependent manner in aged mice. The dose of 500 mg/kg was found more efficient than the 300 mg/kg and was comparable with the standard cholesterol reducing agent, Simvastatin[32].

Antiulcer activity of aqueous and ether extracts of *M. koenigii* was studied in reserpine induced gastric ulcer model in albino rats. Extracts were effective in gastric ulceration and suggested as protective as ranitidine [3].

The leaves, bark and the root of the plant are used in indigenous medicine as a tonic, stomachic, stimulant and carminative. An infusion of the roasted leaves is used to stop vomiting. The green tender leaves are eaten raw for the cure of dysentery. A decoction of the leaves is sometimes given with bitters as a febrifuge and the leaves have been claimed to be used with mint in the form of “chutney” to check vomiting. It has also been used as an anti-periodic and many a time the powdered dry leaf, mixed with honey and juice of betel nut, is recommended in the Ayurvedic system of medicine [15].

*Murraya koenigii* is a rich source of biologically active carbazole alkaloids which would attract the attention of chemists and pharmacologists and play a significant role in future research in medical science [4].

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**Anthelmintic Properties**

Petroleum ether and alcoholic extracts were selected for the activity and Piperazine citrate as standard. Ether and methanolic extracts were taken at 25 mg/ml, 50mg/ml and 100 mg/ml concentrations. Worms were kept under observation to notice the time taken
to paralysis and death in individual worms. Paralysis was said to occur when the worms do not revive even in normal saline. Death was concluded when the worms lost their motility followed by the fading of body color. Among them alcoholic extract of plant leaves at a dose of 100 mg/ml had significant antihelminthic activity where as petroleum ether showed moderate activity[40].

Ethanolic and aqueous extracts from the Murraya koenigii leaves were investigated for their anthelmintic activity against Pheretima posthuma. Three concentrations (25, 50 and 100 mg/ml) of each extract were studied in activity, which involved the determination of time of paralysis and time of death of the worm. Both the extracts exhibited significant anthelmintic activity at highest concentration of 100 mg/ml. Piperazine citrate in same concentration as that of extracts was included as standard reference and distilled water as control. It was concluded from the present study that the plant revealed significant anthelmintic activity, therefore, in vivo trial may be conducted for further evidence for there use in livestock on scientific basis. Vol.1/issue-3/jul-sep. international journal of pharma and bio sciences 2010

Leaves extracts uma shankar sharma*, umesh kumar sharma, abhishek singh, niranjan sutar, and puspak jyoti singh

The present study of undertaken to perform the evaluation of anthelmintic activity of murraya koenigii belonging to family Rutaceae. Methanolic extract of murraya koenigii was taken for anthelmintic activity against Indian earth worm. A concentration of extract was taken and tasted results were expressed in term of paralysis and death of worms. Piperazine citrate was taken as a reference standard drug. When the dose of extract gradually increased and anthelmintic activity was observed [42].

Development of anthelmintic resistance and high cost of convectional anthelmintic drugs lead to the evaluation of medicinal plants has an alternative source of Anthelmintics. The aim of the present study was to determine the anthelmintic activity of crude ethanolic and aqueous extracts of root of Murraya koenigii (Linn) using Eudrilus eugeniae. Three concentrations (25, 50, 100mg/ml) of each extracts were studied in the activity, which involved the determination of time of paralysis and time of death of the worms. Albendazole was used as standard reference and normal saline as control. The present study proves the potential usefulness of root of Murraya koenigii (Linn) as comparable

Hypocholesterolmic Properties

Ethanolic extract of leaves lowered serum cholesterol in mice, inhibited brain acetylcholinesterase enzyme and thereby elevated the acetylcholine concentration in brain homogenate and ultimately improved memory in aged mice. Extract was used in two different concentrations, viz. 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 [32]

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