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Review Article

ADVANCE REVIEW ON PHYTOCHEMISTRY, PHARMACOLOGY, ANTIMICROBIAL, AND CLINICAL ACTIVITIES OF AN ANTIDIABETIC PLANT (*MURRAYA KOEINGII* L.)

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ABSTRACT
Murraya Koeingii is a valuable medicinal plant which has been used in traditional system of medicine since long time. Leaves and roots are also used traditionally as bitter, anthelmintic, analgesic, curing piles, inflammation, itching and are useful in leucoderma and blood disorders. The branches of *M. koenigii* are very popular for cleaning the teeth used as datun. It is traditionally used as a whole or in parts as antiemetics, antidiarrheal, febrifuge, bloodpurifier, antifungal, depressant, anti-inflammatory, bod aches, for kidney pain and vomiting. The anticarcinogenic potential of curry leaf using benzo (a) pyrene induced fore stomach and 7, 12 dimethyl Benz (a) anthracene (DMBA) induced skin papillomas was studied. Chemo protective responses were measured as decrease in tumor burden of tumor bearing animals in both the models. This review paper incorporates the description of *M. Koenigii*, its phytochemical constituents and various pharmacological activitites of isolated compounds as well as bioactivity of extract studies carried out by many laboratories.

Keywords: *Kari Patta, Antidiabetic, Antimicrobial, Phytochemistry, Pharmacology*

INTRODUCTION
Murraya koenigii, commonly known as curry leaf or Kari patta in Indian dialects, belongingto Family Rutaceae which represent more than 150 genera and 1600 species (Satyavati *et al.*, 1987). *Murraya Koenigii* is a highly values plant for its characteristic aroma and medicinal value. It is an important export commondity from India as it fetches good foreign revenue. A number of chemical constituents from every part of the plant have been extracted. The most important chemical constitutents responsible for its intense characteristic aroma are P-gurjunene, P-caryophyllene, P-elemene and O-phellandrene. The plant is rich source fof carbazole alkaloids (Kumar *et al*., 1999). *M. koenigii* is widely used in Indian cookery for centuries and have a versatile role to play in traditional medicine. The plant is credited with tonic and stomachic properties. Bark and roots are used as stimulant and externally to cure eruptions and bites of poisonous animals. Green leaves are eaten raw for cure of dysentery, diarrhoea and for checking vomiting. Leaves and roots are also used traditionally as bitter, anthelmintic, analgesic, curing piles, inflammation, itching and are useful in leucoderma and blood disorders (Nadkarni, 1976; Kirtikar and Basu, 1981). The branches of *M. koenigii* are very popular for cleaning the teeth used as datun. It is also said that the branches of *M. koenigii* are used to strengthen gums and teeth's (The Wealth of India 2003) the juice of the root is good for pain associated with d kidney.

Various Names- English- Curry leaves; Kannada- Karibevu; Hindi- Karipatta, Mitha nim; Tamil- Kariveppilai; Malayalam- Kariveppu; Marathi- Kadhilimb; Sanskrit- Girinimba; Telugu- Karepeku; Tulu- Bevusoppu; Portuguese- Folhas de caril; Russian- Listya karri; Spanish- Hojas de curry; Italian- Fogli di Cari; French- Feuilles de Cari; German- Curryblatter; Guajarati- Mitho limado

Habitat-he plant is distributed and cultivated throughout India. It is found wild from Sikkim toGarhwal, Bengal, Assam, Western Ghats and Travancore- Cochin. Propagation is done by seeds, which germinate freely under partial shade.

Plant description- Curry leaves reached Malaysia, South Africa and Reunion Island. Outside the Indian sphere of influence, they are rarely found. *M. koenigii* is an unarmed, semi deciduous aromatic shrub or small tree with slender but strong woody stem and branches covered with dark grey bark, leaves are imparipinnate, glabrous, and very strongly aromatic. Leaflets 9-25 or more, short stalked, alternate, gland

dotted and strongly aromatic. The stem of *M. koenigii* is an aromatic and more or less deciduous shrub or small tree upto 6 meters in height and 15 to 40 cm in diameter, the main stem is dark green to brownish. The bark of the stem can be peeled off longitudinally which exposes the white wood underneath. Flowers are small, white fragrant ebracteate, calyx deeply five cleft, pubescent. Petal five, free, whitish, glabrous and with dotted glands. Fruits occur in close clusters, small ovoid or sub-globose, glandular, thin pericarp enclosing one or two seeds having spinach green color (Raghunathan and Mitra, 2012).

Traditional Uses- Fresh leaves, dried leaf powder, and essential oil are widely used for flavouring soups, curries, fish and meat dishes, eggs dishes, traditional curry powder blends, seasoning and ready to use other food preparations. The essential oil is also utilized by soap and cosmetic aromatherapy industry (Rao *et al.*, 2011). It is traditionally used as a whole or in parts as antiemetics, antidiarrheal, febrifuge, bloodpurifier, antifungal, depressant, anti-inflammatory, bod aches, for kidney pain and vomiting (Rao *et al.*, 2011; Rana *et al*., 2004; Kumar *et al.*, 1999; Purohit *et al.*, 2004; Iyer and Mani, 1990; Nutan *et al.*, 1998; Chakrabarty *et al.*, 1997; Ponnusamy *et al.*, 2010; Adebajo *et al.*, 2004; Gandhi *et al*., 2010; Manda *et al.*, 2010; Ningappaa *et al.*, 2010; Khuntia and Panda, 2011).

Antidiabetic Property

Mahanimbine a chemical constituent of *M. koenigii* was isolated from column chromatography of the petroleum ether extract of dried plant. The anti-diabetic activity was performed on the streptrozotocin induced wistar rats by using pure compound at a dose of 50 mg/kg and 100 mg/kg. The possible mechanism by which the mahanimbine 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. Mahanimbine showed appreciable alpha amylase inhibitory effect as compared with acarbose (Dineshkumar *et al.*, 2010).

Antiulcer Activity

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 (Annie *et al.*, 2006), Crude aqueous extract of leaves showed anti-ulcer activity which was evaluated by using models of acute gastric lesions induced by ethanol induced, aspirin induced, cold restrain stress and pylorus ligation in rats. Animals were pretreated with doses of 200 mg/kg and 400 mg/kg of aqueous extract which showed efficient reduction in lesion index, total affected area and percentage of lesion in comparison with control group in the ethanol induced, aspirin induced, cold restrain stress induced ulcer and pylorus ligation models. These observations provide a confirmation about aqueous extract of leaves of *M. koenigii* can act as good anti- ulcer drug (Praveen *et al.*, 2011)

Antidiarrhoeal Activity

Two bioactive carbazole alkaloids, namely, kurryam and koenimbine obtained from fractionated n-hexane extract of the seeds of *M. koenigii* exhibited significant inhibitory activity against castor oil-induced diarrhoea and prostaglandin E2-induced enteropooling in rats. These compounds also produced a significant reduction in gastrointestinal motility in the charcoal meal test in Wistar rats (Mandal *et al.*, 2010). Das *et.al* has reported mahanimbine toxicity against the larvae of Culex quinquefasciatus (Das *et al*., 1996).

Anticancer Activity

Koenoline isolated form root bark exhibited cytotoxic activity against the KB cell culture test system (Bandyopadhyaya *et al.*, 2002) 9- formyl-3 methyl carbazole displayed weak cytotoxic activity against both mouse melanoma B 16 and adriamycin resistant P 388 mouse leukemia cell lines. The effects of extracts of *M. koenigii* in in-vitro (short term incubation method and in-vivo (Dalton's ascitic lymphoma (DAL) anticancer models have been evaluated in male Swiss albino mice. DAL cells were injected intraperitoneally (106 cells) to the mice (Nutan *et al.*, 1998). The anticarcinogenic potential of curry leaf using benzo (a) pyrene induced fore stomach and 7, 12 dimethyl Benz (a) anthracene (DMBA) induced skin papillomas was studied. Chemo protective responses were measured as decrease in tumor burden (papillomas/mouse) and % of tumor bearing animals in both the models. Increase in level of acid soluble sulphydral compounds, glutathione S- transferase and DT- diaphorases were also measured. Antioxidant

parameters (reduced glutathione, Super Oxide dismutase, catalases, and glutathione peroxidase and glutathione reductase) were also elevated (Khan *et al.,* 1997) al19the in-vitro anti-tumour promoting activity and antioxidant properties of Girinimbine isolated from the stem bark of *Murraya koenigii* was studied by Yih *et al.,* The in vitro anti-tumour promoting activity of girinimbine was determined by measuring the percentage inhibition of induced early antigen (EA) of EBV on the surface of Raji cells (Yih *et al*., 2012). *M. koenigii* has been found to induce apoptosis in human myeloid cancer cell (HL-60). Results shows that mahanine down-regulates cell survival factors by activation of caspase-3 through mitochondrion-dependent pathway, and disrupts cell cycle progression (Roy *et al.,* 2004). Another study reported that mahanine, purified from the leaves of *M. koenigii*, has a dose- and time-dependent antiproliferative activity in acute lymphoid (MOLT- 3) and chronic myeloid (K562) leukemic cell lines and in the primary cells of leukemic and myeloid patients, with minimal effect on normal immune cells including CD(+) cells (Roy *et al.,* 2010).

Antimicrobial and Anti-fungal Activity

Murrayanine, girinimbine and mahanimbine isolated form stem bark showed anti fungal activity against human pathogenic fungi (Das *et al.,* 1965). 1- formyl-3 methoxy-6- methyl carbazole and 6,7-dimethoxy-1- hydroxy-3- methyl carbazole were reported to possess antibacterial and anti fungal property by Choudhury *et al.,* (2001) Mahanimbine, murrayanol and mahanine from fresh leaves showed anti microbial and topoisomerase I and II inhibitory activity (Ramsewak *et al.,* 1999). Marmesin- 1'-O-β-D-galactopyranoside from stem bark showed anti bacterial, anti viral and anti fungal activity 48 (Kumar *et al.,* 2010). Essential oil was found to be effective against Rhizoctania batiticola (ED 50 0.112 %) and Helminthosporium oryza (0.1214%), and the effect is possibly due to presence of β- caryophyllene and gurjunene Essential oil and aqueous extract of leaf were found active against Staphylococcus epidermidis, S. aureus and streptococcus species. Crude extract and chloroform soluble fraction and petroleum ether soluble fraction showed a promising antibacterial activity against all the tested bacteria (Shimomura and Hattori, 2010; Srivastava and Singh, 2001; Akerel and Ayinde, 1998) the crude extract of M. koenigii roots showed strong antibacterial activity 64 (Chihiro *et al.,* 1993). Extract containing murrayanol and or isomahanine are used as microbicide in variety of industries due to high safety, strong activity, and little odor and without coloring effect (Tanaka *et al.,* 1988).

Antioxidative Property

Isolated carbazole alkaloids from dichloromethane extract of leaves of *M. koenigii* were evaluated on the basis of oil stability index together with their radical scavenging ability against DPPH radical on the basis of lag time to reach a steady state.

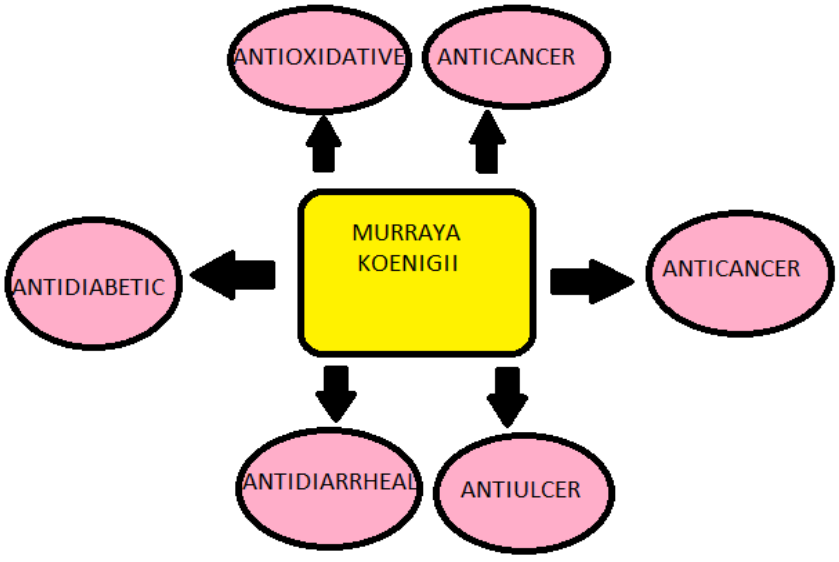

Figure 1: Biological properties of murraya koeingii.

The 12 carbazole were classified in to 3 groups. It suggested that an aryl hydroxyl substituent on the carbazole ring plays a role in stabilizing the thermal oxidation and rate of reaction against DPPH radicals (Yukari *et al*., 2001). The antioxidative properties of the leaf extracts of *Murraya Koenigii* using differesnt solvents were evaluated based on the oil stability index OSI together with their radical scavenging ability against 1, 1- diphenyl-2-picrylhydrazyl (Yukari *et al*., 1969). Mahanimbine and koenigine, two carbazole alkaloids, isolated from the leaves of *M. koenigii* showed antioxidant activity. Koenigine also showed a high degree of radical- scavenging properties (Rao *et al*., 2006).

Clinical & Pharmacological Properties

In vitro antibiofilm activity of *Murraya koenigii* essential oil extracted using supercritical fluid CO2 method against Pseudomonas aeruginosa PAO1. The antibiofilm activity of *Murraya koenigii* essential oil (EO) against Pseudomonas aeruginosa PAO1 was investigated in this study. A decrease in the production of rhamnolipid, extracellular polymeric substance and swarming motility was observed by the EO treatment (0.3% v/v). The static microtitre plate assay revealed 80% reduction in biofilm formation by P. aeruginosa PAO1 on *M.koenigii* EO treatment. Fluorescence microscopy and scanning electron microscopy pnalyses confirmed the reduction of biofilm formation in P. aeruginosa PAO1 when treated with *M. koenigii* EO. Gas chromatography-mass spectrometry analysis of the EO revealed the presence of well-known antibiofilm agents such as spathulenol (5.85%), cinnamaldehyde (0.37%) and linalool (0.04%). Cinnamaldehyde has not been previously reported in *M. koenigii* EO. The potent antibiofilm properties of *M. koenigii* EO may be effectively exploited in food and pharmaceutical industries as well as in controlling Pseudomonas biofilms on indwelling medical devices (Sankar and Rai, 2015).

Larval packet test was used for detection of resistance status against cypermethrin and deltamethrin, the most commonly used synthetic pyrethroids in Rhipicephalus (Boophilus) microplus collected from Faridkot district, Punjab (India). The slope of mortality, lethal concentration for 50 % (LC50) and resistance levels were determined from the regression graphs of probit mortality of ticks plotted against log values of increasing concentrations of cypermethrin and deltamethrin. Results indicated presence of resistance of levels I and II against cypermethrin (resistance factor (RF) = 2.82) and deltamethrin (RF = 8.44), respectively. Adult immersion test was used to assess the acaricidal activity of aqueous (MLAq), ethanol (MLE), chloroform (MLC), acetone (MLA) and hexane (MLH) extracts of leaves of *Murraya koenigii* against these synthetic pyrethroid (SP)-resistant engorged adult females of R. (B.) microplus by determination of per cent adult mortality, reproductive index (RI), per cent inhibition of oviposition (%IO) and hatching rate. The per cent mortality caused by various extracts at concentrations ranging from 0.625 to 10.0 % varied from 0.0 to 100.0 % with maximum per cent mortality of 10.0, 100.0, 70.0, 40.0 and 10.0 recorded against MLAq, MLE, MLC, MLA and MLH, respectively. Among all extracts, the highest acaricidal property against SP-resistant R. (B.) microplus was exhibited by the MLE as it showed the minimum LC50 [95 % confidence limit (CL)] values of 2.97 % (2.82-3.12 %), followed by MLC as 10.26 % (8.84-11.91 %) and MLA as 18.22 % (16.18-20.52 %). The average egg mass weight recorded in live ticks treated with various concentrations of different extracts was lower than the respective control group ticks and was significantly ($p < 0.01$) lower in ticks treated with MLH extract. However, no significant effect on hatchability of eggs of treated groups when compared to control was recorded. A significant $p < 0.05$) decrease in the RI was recorded in MLH extract-treated ticks, and the %IO varied from 0.07 to 34.73 % with various extracts and was recorded maximum with highest concentration of MLH. The results of the current study indicate that the extracts of *M. koenigii* can be used for control of SP-resistant ticks (Singh *et al*., 2015).

Optimization of ultrasound-assisted extraction of flavonoid compounds and their pharmaceutical activity from curry leaf *(Murraya koenigii* L.) using response surface methodology: Extraction prior to component analysis is the primary step in the recovery and isolation of bioactive phytochemicals from plant materials. Response surface methodology was applied to optimize ultrasound-assisted extraction conditions followed by ultra high performance liquid chromatography (UHPLC) to achieve high catechin, myricetin, and quercetin contents, and high antioxidant and anticancer activities in the curry leaf extracts. The antioxidant and anticancer activities of the leaf extracts were determined by the 1, 1-diphenyl-2-

picryl-hydrazyl (DPPH) and 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assays, respectively. The central composite experimental design (3-level, 3-factorial) was employed to consider the effects of ultrasonic power (80-150 W), temperature (40-80°C), and methanol dilution (40-80%) on the properties of the curry leaf extracts. : It was found that ultrasonic power of 145.49 W at 55.9°C with 80% methanol was the most appropriate set of conditions for the extraction of catechin, myricetin, and quercetin from curry leaves with the consequent high antioxidant activity. Using the optimum extraction conditions, the extraction yields of catechin, myricetin, and quercetin were 0.482, 0.517, and 0.394 mg/g DW, respectively, and the antioxidant activity was enhanced to 83%. The optimized extract showed more distinct anticancer activity against HeLa cancer cells in a concentration of 67.2µg/mL ($P < 0.01$) swithout toxicity to normal cells. The results indicated that the pharmaceutical quality of curry leaves could be improved significantly by optimizing the extraction process using response surface methodology (Ghasemzadeh *et al.*, 2014).

Evaluation of aqueous extract of *Murraya koenigii* in unilateral renal ischemic reperfusion injury in rats. AIM. The aqueous extract of leaves of *Murraya koenigii* was studied for its renoprotective potential against unilateral renal ischemia reperfusion (RIR) injury in male Wistar rats. Healthy adult male Wistar rats were divided into five groups (n = 8) and were treated with 200 mg/kg., p.o. of aqueous extract of *M. koenigii* (AEMK) for 30 days to assess both preventive and curative effects of AEMK. Except Group I, RIR was induced to all the groups by clamping the left renal artery using artery clamp for 1 h followed by reperfusion by removing the clamp. Groups II and III underwent RIR at 30 (Th) days whereas RIR was induced in Groups IV and V at 1(st) day of treatment schedule. Biochemical parameters (serumcreatinine, blood urea nitrogen, serum total protein and serum Na (+) urinary parameters (urine output, urinary creatinine, urinary urea, urinary total protein, urinary Na (+)), in vivo anti-oxidants, renal myeloperoxidase (MPO) activity and histopathology of kidneys were monitored. Statistical significance was set at $P < 0.05$. Rats were treated with AEMK significantly ($P < 0.05$) restored the serum and urinary parameters with significant ($P < 0.05$) improvement in endogenous anti-oxidants such as superoxide dismutase, catalase and reduced glutathione and decreased levels of malondialdehyde and renal MPO when compared with the control groups. Histopathological examination also supported the biochemical and urinary tests. : Aqueous extract of *M. koenigii* possesses both preventive and curative effects against RIR injur (Punuru *et al.*, 2014).

Modifying santi sinflammatory effect of Diclofenac with *Murraya koenigii*.*Murraya koenigii* (Curry leaves) has been widely used in Asian countries for the treatment of some ailments such as diabetes and hypertension. In the present study, leaves of *Murraya koenigii* were extracted with ethanol and evaluated for anti-inflammatory activity in rats using carrageenan induced paw edema method. Ethanolic extract showed a potent anti-inflammatory activity at third hour after carrageenan administration when compared with the standard drug, Diclofenac. The percent inhibition of paw volume was found to be 84.75% for 50 mg/kg of extract whereas it was found to be 80.86% for 50 mg/kg extract in combination with Diclofenac 10 mg/kg. Thus, the present study suggests that the combination therapy potentiates the anti-inflammatory effect of diclofenac and may help in reducing the dose of the synthetic drug. Some relevant patents are also outlined in this article (Kaur *et al.*, 2014).

Augmented primary humoral immune response and decreased cell-mediated immunity by *Murraya koenigii* in rats. *Murraya koenigii* (Rutaceae) (curry patta: Hindi) of the family Rutaceae is used in the traditional Indian system of medicine for its immunomodulatory properties. The essential oil of the leaves of *M. koenigii* possesses antimicrobial, antifungal, and pesticidal activities and is used for the treatment of amebiasis, diabetes, and hepatitis. The present study was performed to evaluate the effect of *M. koenigii* on humoral and cell-mediated immune responses in rats. : Aqueous extract of *M. koenigii* leaves was administered orally in a dose of 350 mg/kg. Cell-mediated immunity was assessed by measuring foot pad thickness following sensitization by injection of keyhole limpet hemocyanin and subsequent challenge by the same. Humoral immunity was assessed by measurement of hemagglutination titer to sheep red blood cells (SRBCs). In the humoral immune response, the administration of *M. koenigii* [350mg/kg per os (p.o.)] from day 1 to day 7 after sensitization with SRBC on day 0 caused a significant increase in the

primary anti-SRBC titer. However, the secondary immune response was decreased significantly ($p<0.05$) as shown by a decrease in secondary anti-SRBC titer measured on day 11 following a booster dose of antigen on day 8. In the delayed-type hypersensitivity test, *M. koenigii* (350 mg/kg, p.o.), when administered for 14 days, produced a significant ($p<0.05$) decrease in foot pad thickness when compared with the control group. Thus, these results suggest that oral administration of *M. koenigii* augments primary humoral immune response and decreases cell-mediated immunity (Kaur *et al.*, 2014).

Evaluation of in vitro aldose reductase inhibitory potential of alkaloidal fractions of Piper nigrum, *Murraya koenigii*, Argemone mexicana, and Nelumbo nucifera. Aldose reductase is primarily involved in development of long-term diabetic complications due to increased polyol pathway activity. The synthetic aldose reductase inhibitors are not very successful clinically. Therefore, the natural sources may be exploited for safer and effective aldose reductase inhibitors. In the present study, the aldose reductase inhibitory potential of hydroalcoholic and alkaloidal extracts of Piper nigrum, *Murraya koenigii*, Argemone mexicana, and Nelumbo nucifera was evaluated. The hydroalcoholic and alkaloidal extracts of the selected plants were prepared. The different concentrations of hydroalcoholic and alkaloidal extracts of these plants were evaluated for their goat lens aldose reductase inhibitory activity using dl-glyceraldehyde as substrate. The aldose reductase inhibitory potential of extracts was assessed in terms of their IC50 value. Amongst the hydroalcoholic extracts, the highest aldose reductase inhibitory activity was shown by P. nigrum (IC50 value 35.64±2.7 µg/mL) followed by *M. koenigii* (IC50 value 45.67±2.57 µg/mL), A. mexicana (IC50 value 56.66±1.3 µg/mL), and N. nucifera (IC50 value 59.78±1.32 µg/mL). Among the alkaloidal extracts, highest inhibitory activity was shown by A. mexicana (IC50 value25.67±1.25 µg/mL), followed by N. nucifera (IC50 value 28.82±1.85 µg/mL), P. nigrum (IC50 value 30.21±1.63 µg/mL), and *M. koenigii* (IC50 value 35.66±1.64µg/mL). It may be concluded that the alkaloidal extracts of these plants possess potent aldose reductase inhibitory activity and may be therapeutically exploited in diabetes-related complications associated with increased activity of aldose reductase (Gupta *et al.*, 2014).

Naloxone blocks the beneficial effects of aqueous extract of *Murraya koenigii* (L.) Spreng leaves in models of pain. AIM: This study investigated the antinociceptive effects of aqueous extract of *Murraya koenigii* (AEMK) leaves (200, 400 and 800 mg/kg, orally) on animal models of acute and persistent pain and its modulation by naloxone. Antinociceptive effects were assessed using tail-flick, hot plate and formalin tests in mice. To differentiate between central and peripheral antinociceptive effect of AEMK, naloxone (2 mg/kg) was administered along with the 800 mg/kg dose of extract. Morphine was used as a standard drug. AEMK and morphine significantly increased the tail-flick latency (tfl) and paw licking/jumping latency in tail-flick and hot plate tests, respectively, in comparison to control. Also, in both the tests AEMK and morphine significantly increased the AUC0-120 min. In formalin test, AEMK (400 mg/kg and 800 mg/kg) and morphine significantly reduced licking time in both early and late phases in comparison to control. : Thus, in all three pain models AEMK showed antinociceptive effect, which was blocked by naloxone suggesting the involvement of opioidergic central mechanism (Gupta *et al.*, 2013).

Antioxidants and anti-glycation activities correlates with phenolic composition of tropical medicinal herbs. To determine the contribution of total phenolic content (TPC) in glycation inhibitory activity of common tropical medicinal food and spices with potential antioxidative properties In vitro glucose-bovine serum albumin (BSA) assay was used. Ethanolic extracts of ten common household condiments/herbs (Allium sativum, Zingiber officinale, Thymus vulgaris, Petroselinum crispum, *Murraya koenigii* Spreng, Mentha piperita L., Curcuma longa L., Allium cepa L., Allium fistulosum and Coriandrum sativum L.) were evaluated for antioxidative activity by 2,2-diphenyl-2-picrylhydrazyl (DPPH), and ferric reducing antioxidant power (FRAP) and the TPC, flavonoid and tannins content were determined. Findings showed good correlation between TPC/DPPH (r = 0.8), TPC/FRAP (r= 0.8), TPC/anti-glycation (r = 0.9), DPPH/anti-glycation (r = 0.6), FRAP/anti-glycation (r = 0.9), Flavonoid/anti-glycation (r = 0.7) and Tannins/anti-glycation (r = 0.8) and relatively fair correlation for TPC/Flavonoids (r = 0.5) and TPC/Tannins (r = 0.5). Results imply that these plants are potential sources of natural antioxidants which

have free radical scavenging activity and might be used for reducing oxidative stress. The positive glycation inhibitory and antioxidative activities of these tropical herbs suggest a possible role in targeting ageing, diabetic complications and oxidative stress related diseases (Ramkissoon *et al.*, 2013).

Effect of Mangiferin and Mahanimbine on Glucose Utilization in 3T3-L1 cells. Stem barks of Mangifera indica contain a rich content of mangiferin (xanthone glucoside), whereas *Murraya koenigii* leaves contain rich sources of mahanimbine (carbazole alkaloid) and used traditionally for the treatment of diabetes. To investigate the effects of mangiferin (xanthone glucoside) and mahanimbine (carbazole alkaloid) on glucose utilization in 3T3-L1 cells. Mangiferin was isolated from stem barks of Mangifera indica and mahanimbine was isolated from *Murraya koenigii* leaves. These isolated compounds were subjected to MTT assay and glucose utilization test with 3T3-L1 cells. Treatment of the 3T3-L1 cells with mangiferin and mahanimbine increased the glucose utilization in a dose-dependent manner. At a concentration of 1 mM, mangniferin showed 2-fold increase in glucose utilization compared with untreated control. In case of mahanimbine, the observed effect at 1 mM was almost equivalent to positive control (insulin at 1 μM). Moreover, MTT assay showed that both of these compounds were less toxic at a concentration of 1 mM (nearly 75%cells are viable). The present results indicated that these natural products (mangiferinand mahanimbine) exhibited potential ethnomedical uses in management of diabetes (Kumar *et al.*, 2013).

Ethnopharmacology guided screening of traditional Indian herbs for selective inhibition of Plasmodium specific lactate dehydrogenase. Keluskar P (1), Ingle S. Medicinal plants traditionally used to treat malaria can provide quality leads towards identifying novel anti-malarial drugs. Here we combined this approach with target based drug discovery and explored Plasmodium specific lactate dehydrogenase (LDH) inhibitory activity of 8 Indian plants which are ethnically used to treat malaria. LDH from Indian Plasmodium falciparum and Plasmodium vivax strains, were cloned and expressed in Escherichia coli, followed by purification of recombinant enzymes (rPfLDH and rPvLDH respectively). Extracts of 8 plants in different organic and aqueous solvents, were screened for their inhibitory activity on rPfLDH, rPvLDH and mammalian LDHs. Phyllanthus amarus aqueous extract was further tested for in vitro parasiticidal activity. Aqueous extract of Phyllanthus amarus Schum.and Thonn.and chloroform extract of *Murraya koenigii* (L.) Sprengs Exhibited profound and exclusive inhibitory effect on Plasmodium falciparum LDH (IC (50)11.2 μg/ml ±.4) and Plasmodium vivax LDH (IC (50) =6.0 μg/ml ± 0.6) respectively. Moreover, Phyllanthus amarus aqueous extract also demonstrated antiplasmodial activity in vitro, on Chloroquine sensitive and resistant strains of Plasmodium falciparum (IC(50)=7.1 μg/ml ± 0.5 and 6.9 μg/ml ± 0.7 respectively). Target specific screening of traditional herbs used in malaria treatment has proffered Phyllanthus amarus and *Murraya koenigii* extracts as hits which can optimistically provide novel antimalarial drugs (Keluskar and Ingle, 2012).

Protective Effect of Leaves of *Murraya koenigii* on Reserpine-Induced rofacial *Murraya koenigii* L. (Rutaceae), commonly known as curry leaf tree, closely associated with south India where the word "curry" originates from the Tamil "kari" for spiced sauces. Curry leaves are a rich source of carbazole alkaloids which possess various biological activities such as antitumor, antioxidant andAnti-inflammatory. Curry leaf has a potential role in the treatment of diabetes. Reserpine-induced orofacial dyskinesia in rats is an animal model of tardive dyskinesia that has been linked with free radical generation and oxidative stress. In this study, neuroprotective potential and in-vivo antioxidant status of methanol extract of the leaves of *Murraya koenigii* (MEMK) in reserpine-induced orofacial dyskinesia are investigated. Reserpine was used to induce orofacial dyskinesia. The effect of MEMK on locomotion and catalepsy was studied using Open-field apparatus and Bar-test, respectively. The effect of MEMK on the levels of protective anti-oxidant enzymes i.e. superoxide dismutase (SOD), catalase (CAT), glutathione reductase (GSH) and inhibited lipid peroxidation (LPO) in forebrain region were investigated in reserpine-treated animals. Results demonstrated that the MEMK significantly inhibited the reserpine-induced vacuous chewing movements (VCM), tongue protrusion (TP), orofacial burst (OB) and catalepsy. MEMK significantly increased the number of squares traversed and rearing in open field apparatus. Treatment with MEMK significantly restored the levels of protective anti-oxidant enzymes i.e.

SOD, CAT, GSH and inhibited LPO in forebrain region when compared with reserpine. It also inhibited haloperidol-induced catalepsy. The present study concludes that the oxidative stress might play an important role in reserpine-induced abnormal oral movements, and *Murraya koenigii* may have great potential in the treatment of neuroleptic-induced orofacial dyskinesia (Patil *et al.,* 2012).

Antinociceptive activity of acute and chronic administration of *Murraya koenigii* L. leaves in experimental animal models. AIM: To evaluate the antinociceptive activity of acute and chronic administration of petroleum ether extract of *Murraya koenigii* L. leaves (PMK) and total alkaloids separated from petroleum ether extract of *Murraya koenigii* leaves (AMK) in mice. PMK was subjected for isolation of total alkaloid fraction AMK. The antinociceptive activity of PMK (100 and 300 mg/kg, p.o.) and AMK (100and 300 mg/kg, p.o.), after acute and chronic administration (for 15 days), was evaluated using peripheral model like acetic acid-induced writhing method and central model like hot plate method and tail immersion method. Statistical analysis was carried out by one-way ANOVA followed by Dunnett's test. : In acute studies, PMK and AMK significantly and dose-dependently reduced the number of acetic acid-induced writhing, significantly increased the latency of paw licking in hot plate method, and significantly increased the basal reaction time in tail immersion method. With chronic administration of PMK and AMK, highest activity was observed on day 9 in acetic acid-induced writhing model. In hot plate and tail immersion method, chronic administration of PMK and AMK initially showed fluctuating responses but produced highest degree of antinociception on day 9 of the study. : The degree of antinociception produced by PMK and AMK at the end of 15 days study suggest that *Murraya koenigii* (Patil *et al.,* 2012).

Efficacy of carbazole alkaloids, essential oil and extract of *Murraya koenigii* in enhancing subcutaneous wound healing in rats. The traditional use of *Murraya koenigii* as Asian folk medicine prompted us to investigate its wound healing ability. Three carbazole alkaloids (mahanine (1), mahanimbicine (2), mahanimbine (3) essential oil and ethanol extract of *Murraya koenigii* were investigated for their efficacy in healing subcutaneous wounds. Topical application of the three alkaloids, essential oil and crude extract on 8 mm wounds created on the dorsal skin of rats was monitored for 18 days. Wound contraction rate and epithelialization duration were calculated, while wound granulation and collagen deposition were evaluated via histological method. Wound contraction rates were obvious by day 4 for the group treated with extract (19.25%) and the group treated with mahanimbicine (2) (12.60%), while complete epithelialization was achieved on day 18 for all treatment groups. Wounds treated with mahanimbicine (2) (88.54%) and extract of *M. koenigii* (91.78%) showed the highest rate of collagen deposition with well-organized collagen bands, formation of fibroblasts, hair follicle buds and with reduced inflammatory cells compared to wounds treated with mahanine (1), mahanimbine (3) and essential oil. The study revealed the potential of mahanimbicine (2) and crude extract of *M. koenigii* in facilitation and acceleration of wound healing (Nagappan *et al.,* 2012). Comparison of *Murraya koenigii*- and Tribulus terrestris-based oral formulation versus tamsulosin in the treatment of benign prostatic hyperplasia in men aged >50 years: a double-blind, double-dummy, randomized controlled trial. Comment in J Urol. 2012 Oct; 188(4):1236-7. Drug treatment can defer surgical intervention in benign prostatic hyperplasia (BPH), a common disorder in elderly men, and is widely practiced. Various herbal formulations have been used for the treatment of BPH, but few have been compared with established modern medicines in head-to-head clinical trials. We compared the effectiveness and tolerability of an oral formulation, comprising standardized extracts of *Murraya koenigii* and Tribulus terrestris leaves being marketed in India under Ayurvedic license, versus tamsulosin in the treatment of symptomatic BPH. A double-blind, double-dummy, parallel-group, randomized controlled trial was conducted with treatment-naive ambulatory patients with BPH aged >50years. Patients received either the plant drug in a dose of 2 capsules BID or tamsulosin 400 µg once daily for 12 weeks with 2 interim follow-up visits at the end of 4 and 8 weeks. The double-dummy technique was used to ensure double-blinding. The primary effectiveness measure was reduction in the International Prostate Symptom Score (IPSS). Proportion of patients becoming completely or relatively symptom free (IPSS <8), change in prostate volume (assessed by using ultrasonography conducted by a radiologist blinded to the nature or duration of treatment), and peak

urinary flow rate (assessed by using uroflowmetry) were secondary measures. Treatment-emergent adverse events, changes in weight, vital signs, and routine laboratory safety parameters were recorded. Forty-six patients were randomized (23 per group); 19 completed all study visits in the plant drug group and 21 in the tamsulosin group. However, applying modified intention-to-treat criterion, 23 and 21 patients, respectively, were considered for effectiveness analysis. Mean (SD) age and baseline weight were 58.5 (14.0) years and 57.5 (10.5) kg in the plant drug arm, and 62.9 (6.3) years and 59.8 (9.9) kg in the tamsulosin arm, respectively. Median (interquartile range) symptom duration was 12.0 (12.0-24.0) months and 15.0 (12.0-24.0) months, respectively, in the 2 arms. These differences were not statistically significant. IPSS (median [interquartile range]) declined from 17.0 (12.0-19.0) to 9.0 (5.0-13.0) with the plant drug and from 14.0 (11.0-18.0) to 8.0 (6.0-13.0) with tamsulosin after 12 weeks of treatment. The decline was individually significant in both groups (both, $P < 0.001$), but intergroup values showed no statistically significant difference at any point of time. IPSS <8 at study end was achieved by 10 and 7 patients, respectively, in the 2 arms ($P = 0.548$). The plant drug reduced prostate volume from 33.5 (26.2-45.9) mL to 31.6 (26.1-37.5) mL ($P = 0.040$). The corresponding reduction with tamsulosin, from 41.3 (29.4-51.3) mL to 39.9 (32.6-52.3) mL, was not statistically significant. Peak urinary flow rate did not change appreciably. Mild joint pain was the most common adverse event in both arms. No serious events were encountered. Compliance was satisfactory. : These findings suggest that the *M koenigii*- and T terrestris-based formulation significantly lowered IPSS scores in the initial treatment of symptomatic BPH. Further trials are needed to determine if the beneficial effect is sustained beyond the 12-week observation period of this trial (Sengupta *et al.,* 2011). Reversal of haloperidol-induced orofacial dyskinesia by *Murraya koenigii* leaves in experimental animals. Orofacial dyskinesia (OD) is a late complication of prolonged neuroleptic treatment characterized by involuntary movements of the oral region. Chronic treatment with neuroleptics leads to development of vacuous chewing movements (VCMs). VCMs in rats are widely accepted as an animal model of OD. To study the effect of *Murraya koenigii* L. (Rutaceae) leaves on aloperidol-induced OD. Effect of alcohol extract of *M. koenigii* leaves (EEMK) and its alkaloid fraction (AMK) on body weight, locomotor activity, behavioral parameters, such as VCMs, tongue protrusions (TPs), orofacial bursts (OBs), and biochemical parameters such as antioxidant defense enzymes levels [superoxide dismutase (SOD) and catalase (CAT)], glutathione (GSH) levels, and lipid peroxidation (LPO) in the forebrain region was studied in haloperidol-treated rats. Rats chronically treated with haloperidol (1 mg/kg, i.p., and 21 days) significantly decreased locomotion and developed VCMs, OBs, and TPs. Biochemical analysis reveals that chronic haloperidol-treated rats also showed decreased levels of SOD and CAT. Chronic haloperidol treatment significantly induced LPO and decreased the forebrain GSH levels in the rats. Co-administration of EEMK (100 and 300 mg/kg, p.o.) and AMK (30 and 100 mg/kg, p.o.) along with haloperidol significantly reversed the effect on locomotion. EEMK and AMK significantly reversed the haloperidol-induced decrease in forebrain SOD and CAT levels in rats and significantly reduced the LPO and restored the decreased GSH levels by chronic haloperidol treatment. The study concludes that *M. koenigii* could be screened as a potential drug for the prevention or treatment of neuroleptic-induced OD (Patil *et al.,* 2012).

Food & Nutrietional Aspect

Antioxidant potential of curry *(Murraya koenigii* L.) and mint (Mentha spicata) leaf extracts and their effect on colour and oxidative stability of raw ground pork meat during refrigeration storage. Biswas (1), Chatli (2), Sahoo (2). The aim of this study was to investigate the antioxidant activity of different solvent extracts of curry and mint leaf and their effect on colour and oxidative stability of raw ground pork meat stored at 4±1°C. The results indicated that among the two individual leaf categories, the ethanol extract of curry leaf (EHEC) and the water extract of mint leaf (WEM) showed higher DPPH and ABTS(+) activity. EHEC also exhibited the highest total phenolic contents while these were the lowest for WEM. WEM showed the highest superoxide anionic scavenging activity (%). The pork meat samples treated with EHEC and WEM showed a decrease in the Hunter L- and a-values and a increase in b-value during storage at 4°C. However, the pH and TBARS values were higher in control samples irrespective of storage periods. In conclusion, EHEC and WEM have the potential to be used as atural antioxidants to

minimise lipid oxidation of pork products (Biswas *et al.*, 2012). Hepatoprotective Sesquiterpenes and Rutinosides from *Murraya koenigii* (L) Spreng.Three new sesquiterpenes (1-3) and two new rutinosides (4 and 5) along with 17 known compounds (6-22) were isolated from the leaves of *Murraya koenigii* (L.) Spreng.The new compounds were elucidated as (3R,5S,6R)-3,5,6-trihydroxy-1,1,5-trimethylcyclohexyl-8-butyn-9-one(1),(8E,9R)-ethyl-7-(3S,5R,6S)-3,6-dihydroxy-1,1,5-methylcyclohexyl-9-hydroxybut-8 -enoate (2), (3R)-3-O-β-d-glucoside-6'-d-apiose-β-ionone (3), 4-O-β-d-rutinosyl-3-methoxyphenyl-1-propanone (4), and 1-O-β-d-rutinosyl-2(R)-ethyl-1-pentanol (5) based on their spectroscopic data. Compounds 1, 4, 5, 18, and 21 (10 μM) exhibited moderate hepatoprotective activitiy (Ma *et al.*, 2014).
Murrayas koenigii (L) Spreng ameliorates insulin resistance in dexamethasone-treated mice by enhancing peripheral insulin sensitivity. *Murraya koenigii* (L) Spreng.is an important medicinal plant used traditionally as an antiemetic s,antidiarrhoeal agent and blood purifier and as a medicine for a variety of ailments.This study investigated the effects of ethanolic extract of *M. koenigii* (MK) on diabetes-associated insulin resistance induced in mice by chronic low-dose injection of dexamethasone. : Mice treated with dexamethasone exhibited hyperglycaemia and impaired glucose tolerance. Treatment with MK reduced the extent of dexamethasone-induced hyperglycaemia and decreased insulin resistance as indicated by improved glucose tolerance and increased insulin-stimulated AKT phosphorylation in skeletal muscle tissue. Further evaluation in clonal skeletal muscle cell lines suggested that MK increased glucose uptake in L6 skeletal muscle cells by increasing cell surface GLUT4 density via an AKT-mediated pathway. : MK can ameliorate dexamethasone-induced hyperglycaemia and insulin resistance in part by increasing glucose disposal into skeletal muscle (Pandey *et al.*, 2014).
Comparative antioxidant effect of aqueous extracts of curry leaves, fenugreek leaves and butylated hydroxytoluene in raw chicken patties. Antioxidant properties and use of aqueous extracts of curry leaves *(Murrayakoenigii*) and fenugreek leaves (Trigonella foenum-graecum) as source of natural antioxidant in raw chicken meat were evaluated. Four treatments viz. sI Control (meat +2% salt), II.BHT (meat +2% salt +0.1% BHT)III CLE (meat +2% salt +2% curry leaves extract) and IV. FLE (meat +2% salts +2% fenugreek leaves extract) were compared for lipid oxidation during eight days refrigerated storage. The average phenolic content was 59.2 and 52.8 mg/g gallic acid equivalent in CLE and FLE respectively. Free radical scavenging activity was 61.4 and 64.2% in CLE and FLE, respectively. CLE had significantly ($P < 0.05$) higher reducing activity (2.4) as compared to FLE (2.2). Observation on lipid oxidation showed a significant ($p < 0.05$) higher TBARS values in control patties than other patties containing BHT, CLE and FLE. Overall percent increase during storage period was highest in control followed by BHT, CLE and FLE. Both synthetic antioxidants and natural extracts significantly ($p < 0.05$) decreased the TBARS values. The average percent decrease in TBARS values during storage was 18, 25.5 and 27.5 in BHT, CLE and FLE treatments, respectively. Therefore, it was concluded that water extracts obtained from curry leaves and fenugreek leaves could be explored as natural antioxidants in poultry meat and meat products (Devatkal *et al.*, 2012).
Biguanide relatad compounds in traditional antidiabetic functional foods. Biguanides such as metformin are widely used worldwide for the treatment of type-2 diabetes. The identification of guanidine and related compounds in French lilac plant (*Galega officinalis* L.) led to the development of biguanides. Despite of their plant origin, biguanides have not been reported in plants. The objective of this study was to quantify biguanide related compounds (BRCs) in experimentally or clinically substantiated antidiabetic functional plant foods and potatoes. The corrected results of the Voges-Proskauer (V-P) assay suggest that the highest amounts of BRCs are present in green curry leaves *(Murrayakoenigii* (L.) Sprengel) followed by fenugreek seeds (*Trigonella foenum-graecum*L.), green bitter gourd (*Momordica charantia* Descourt.), and potato (*Solanum tuberosum* L.). Whereas, garlic (*Allium sativum* L.), and sweet potato (*Ipomea batatas* (L.) Lam) contain negligible amounts of BRCs. In addition, the possible biosynthetic routes of biguanide in these plant foods are discussed (Perla and Jayanty, 2013). Anti-inflammatory, analgesic and anti-ulcerogenic effect of total alkaloidal extract from *Murraya koenigii* leaves in animal models. The fresh leaves of *Murraya koenigii* are often added to various dishes in Asian countries due to the delicious taste and flavour that they impart. In the present study, the effect of the total alkaloidal

extract from *Murraya koenigii* leaves (MKA) with respect to anti-inflammatory, analgesic and anti-ulcerogenic effects were evaluated using different experimental animal models. Oral supplementation of MKA at 10, 20 and 40 mg skg (-1) body weight successfully and dose-dependently reduced the formation of oedema induced by carrageenan, histamine and serotonin as well as formaldehyde-induced arthritis. In addition, the extract (10, 20 and40 mg kg(-1), p.o.) attenuated the writhing responses induced by an intraperitoneal injection of acetic acid and late phase of pain response induced by a subplantar injection of formalin in mice. MKA at higher doses (20 and 40 mg kg (-1), p.o) reduced the early phase response induced by formalin as well as reaction time on hot plate models. Interestingly, there was no ulcer score with the ulcerogenic effect of MKA. Moreover, all the doses of MKA (10, 20 and 40 mg kg(-1), p.o) showed promising anti-ulcerogenic activity with protection against acute gastric ulcers induced by ethanol plus hydrochloric acid and aspirin models in a dose dependent manner (Mani *et al.*, 2013).

An aqueous extract of *Murraya koenigii* leaves induces paraoxonase 1 activity in streptozotocin induced diabetic mice. *Murraya koenigii* (Mk) leaves possess a hypoglycemic effect. Activity of paraoxonase 1 (PON1), a HDL-associated antioxidant enzyme, was found to be decreased during hyperglycemia. The present study explored the effect of *Murraya koenigii* leaves (MkL) on paraoxonase 1 activity in order to control the oxidative stress in diabetes. Hyperglycemia was induced in mice by a single dose of streptozotocin (200 mg kg (-1) body weight). Diabetic mice were treated with the aqueous extract of MkL orally once daily for 15 days. Doses of 75 and 150 mg g (-1) body weight of the aqueous MkL extract decreased the blood sugar level significantly in a dose dependant manner. MkL administration significantly reduced oxidative stress by decreasing the MDA level and by increasing GSH level, SOD as well as catalase activity. However, PON1 activity was found to be increased after administration of aqueous MkL extract. MkL treatment also possesses a hypolipidemic effect as inferred from the decrease in total cholesterol, triglyceride level and increase in HDL-C concentration. Here we conclude that after MkL treatment, not only the antioxidant parameters like SOD, CAT, GSH and MDA, but also PON1 may be involved in decreasing the oxidative stress associated with diabetes (Saha and Mazumder, 2013).

Green leafy porridges made with leaf water extracts, rice and coconut milk are common Sri Lankan dietary remedies for diabetes. Though water and ethanolic extracts of most leaves elicit hypoglycaemic effects, data are not available on the efficacy when leaf extracts are incorporated into porridges. Thus, an effort was made to evaluate the proximate compositions and glycaemic index (GI) of some commonly consumed green leafy porridges. The GI of rice porridge and coconut milk porridge were measured to evaluate the effect of other ingredients other than the leaf extracts. Rice was the main contributor to carbohydrate (56-68% on dryweight) and water was the main component in porridges (89-93%). Fat and total dietary fibre contents ranged between 2.5-27% and 5-10%, respectively. The GI of all porridges was low (GI $\leq$ 55), except Cassia auriculata which had a high GI of 77 ± 12. The GIs of coconut milk, Aerva lanata, Hemidesmus indicus, Scoparia dulcis, Asparagus racemosus, Cephalandra indica, Cardiospermum halicacabum, *Murraya koenigii* and Aegle marmelos were 31 ± 5, 32 ± 5, 40 ± 8, 39 ± 8, 37 ± 4, 49 ± 8, 46 ± 8, 44 ± 8 and 50 ± 8, respectively. All porridges had a low or medium glycaemic loads ($\leq$ 19). However, peak blood glucose reductions of $\geq$ 25% were observed in all leafy and coconut milk porridges, except in C. auriculata and Atlantia zeylanica, when compared with the glucose control. Therefore, green leafy porridges, except Cassia, can be recommended as breakfast meals for diabetics due to their low GI, peak blood glucose reduction and presence of other nutrients in green leaves (Anuruddhika and Ekanayake, 2013).

Carotenoids retention in processed curry leaves *(Murraya koenigii* L. Spreng). Lutein content and β-carotene content of dried curry leaves *(Murraya koenigii* L. Spreng) by various methods [microwave, combo, infrared (IR), hot air oven, freeze drying, cross flow tray drying, sun and shade drying] have been evaluated. The dried leaves were treated with ice-cold acetone to get the extracts (0.69-3.64% w/w) on dry weight basis. Lutein content and β-carotene content of all these extracts were determined by high-performance liquid chromatography using an established method and found in the range of 8.2-99.5 mg/100 g and 2.9-19.2 mg/100 g, respectively. The results indicated that the microwave processed leaves contain higher levels of lutein (99.4 mg/100 g) and β-carotene (19.2 mg/100 g) compared with other

drying methods. The cross flow dried (8.2 mg/100 g and 3.5 mg/100 g) and IR dried samples (23 mg/100 g and 2.9 mg/100 g) retained minimum amount of lutein and β-carotene, respectively (Shivanna and Subban, 2013).

Protective effect of aqueous Curry leaf *(Murraya koenigii*) extract against cadmium-induced oxidative stress in rat heart. Treatment of rats with a low dose of cadmium chloride caused a significant damage in the rat cardiac tissue indicated by the increase in the level of serum glutamate oxaloacetate transaminase and lactate dehydrogenase1 activities. Histological studies confirmed the damage due to cadmium. That cadmium-induced tissue damage was caused due to oxidative stress was evident from the changes observed in the levels of lipid peroxidation and reduced glutathione, the protein carbonyl content, and the alterations in the activities of cardiac antioxidant and pro-oxidant enzymes. Treatment of rats with cadmium also caused alterations in the activities of mitochondrial Kreb's cycle as well as respiratory chain enzymes. All these changes were ameliorated when the rats were pre-treated with an aqueous extract of Curry leaf *(Murraya koenigii*). The studies indicated that the aqueous extract of Curry leaf protects the rat cardiac tissue against cadmium-induced oxidative stress possibly through its antioxidant activity. As curry leaf is consumed by people as part of their diet in India and South-East Asian and some European countries as well, and, as it has no reported side-effects, the results seem to have relevance at places where humans are exposed to cadmium environmentally or occupationally (Mitra *et al.*, 2012).

Protective effects of total alkaloidal extract from *Murraya koenigii* leaves on experimentally induced dementia. Dementia is a syndrome of gradual onset and continuous decline of higher cognitive functioning. It is a common disorder in older persons and has become more prevalent today. The fresh leaves of *Murraya koenigii* are often added to various dishes in Asian countries due to the delicious taste and flavor that they impart. These leaves have also been proven to have health benefits. In the present study, the effect of total alkaloidal extract from *M. koenigii* leaves (MKA) on cognitive functions and brain cholinesterase activity in mice were determined. In vitro β-secretase 1 (BACE1) inhibitory activity was also evaluated. The total alkaloidal extract was administered orally in three doses (10, 20 and 30 mg/kg) for 15 days to different groups of young and aged mice. Elevated plus maze and passive avoidance apparatus served as the exteroceptive behavioral models for testing memory. Diazepam-, scopolamine-, and ageing-induced amnesia served as the interoceptive behavioral models MKA (20 and 30 mg/kg, p.o) showed significant improvement in memory scores of young and aged mice. Furthermore, the same doses of MKA reversed the amnesia induced by scopolamine (0.4 mg/kg, i.p.) and diazepam (1 mg/kg, i.p.). Interestingly, the brain cholinesterase activity was also reduced significantly by total alkaloidal extract of *M. koenigii* leaves. The IC50 value of MKA against BACE1 was 1.7 µg/mL.In conclusions, this study indicates MKA to be a useful remedy in the management of Alzheimer's disease and dementia (Mani *et al.*, 2012).

Dietary agents in the prevention of alcohol-induced hepatotoxicty: preclinical observations. Long term alcohol consumption is one of the important causes for liver failure and death. To complicate the existing problem there are no dependable hepatoprotective rugs and a large number of patients prefer using complementary and alternative medicines for treating and managing hepatic complications. Almost 25 centuries ago, Hippocrates, the father of medicine, proclaimed "Let food be thy medicine and medicine be thy food." Exploring the association between diet and health continues even today. Preclinical studies carried out in the recent past have shown that the commonly used dietary agents like *Allium sativum* (garlic), *Camellia sinensis* (tea), *Curcuma longa* (turmeric), Emblica officinalis (Indian gooseberry), Ferula asafoetida (asafoetida), Garcinia cambogia (Malabar tamarind), Glycine max (soyabean), *Murraya koenigii* (curry leaves), Piper betle (beetle leaf), Prunus armeniaca (apricot), Ocimum gratissimum (wild basil), Theobroma cacao (cocoa), Trigonella foenum-graecum (fenugreek) and Vitis vinifera (grapes) protect against ethanol-induced hepatotoxicity. Mechanistic studies have shown that the beneficial effects of these phytochemicals in preventing the ethanol-induced hepatotoxicity are mediated by the antioxidant, free radical scavenging, anti-inflammatory and anti-fibrotic effects. The present review for the first time collates the hepatoprotective effects of these agents and also emphasizes on aspects that need future research to establish their utility inHumans (Shivashankara *et al.*, 2012).

Hepatoprotective potential of polyphenol rich extract of *Murraya koenigii* L.: an in vivo study.The present study investigates hepatoprotective effects of polyphenol rich *Murraya koenigii* L. (MK) hydro-ethanolic leaf extract in CCl (4) treated hepatotoxic rats. Plasma markers of hepatic damage, lipid peroxidation levels, enzymatic, and non-enzymatic antioxidants in liver and histopathological changes were investigated in control and treated rats. MK pretreated rats with different doses (200, 400 and 600mg/kg body weight) showed significant decrement in activity levels of alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, total protein, and bilirubin. Also, MK treated rats recorded a dose dependent increment in hepatic super oxide dismutase, catalase, reduced glutathione and ascorbic acid and, a decrement in lipid peroxidation. Microscopic evaluations of liver revealed CCl (4)-induced lesions and related toxicManifestations that were minimal in liver of rats pretreated with MK extract. These results demonstrate that hydro-ethanolic leaf extract of MK possesses hepatoprotective potentials (Desai *et al.*,).

Antioxident & Antimicrobial Activity

Antimicrobial efficacy of the combinations of Acacia nilotica, *Murraya koenigii* L sprengel, Eucalyptus hybrid and Psidium guajava on primary plaque colonizers There is an urgent need for innovative strategies to combat the two most common dental diseases of mankind namely dental caries and periodontitis. The aim was to assess the antimicrobial efficacy of the double combinations of Acacia nilotica (AN), *Murraya koenigii* L. Sprengel (MKL), Eucalyptus hybrid and Psidium guajava on primary plaque colonizers. : The plant extracts of AN, MKL. Sprengel, Eucalyptus hybrid and P. guajava were prepared using Soxhlet apparatus. The stock solutions of individual plant extracts (100 mg/ml) were prepared. Equal quantities of stock solutions were mixed to obtain six double combinations of herbal extracts. The antimicrobial efficacy testing was done against three primary plaque colonizers using agar well-diffusion method. 0.2% chlorhexidine and dimethyl sulfoxide were used as positive and as negative controls. The mean inhibition zone between the categories was compared using one-way Analysis of Variance and Tukey's post hoc test. The combination of AN and P guajava produced the highest mean diameter of inhibition zone (21.08 mm ± 2.11) against Streptococcus mutans. The chlorhexidine produced the least inhibition zone against S. mutans (14.50 ±2.07). The combination of an andPs guajava produced the maximum antimicrobial efficacy against Streptococcus sanguis (19.67 ± 1.03) and Streptococcus salivarius (20.33 ± 1.86). All the combinations of plant extracts have the potential to be used as antiplaque and anticaries agents. The combinations of herbal extracts offer enhanced antimicrobial efficacy due to the synergistic effects besides slowing the development of resistance (Chandra *et al.,* 2014).

In vivo antiplasmodial potentials of the combinations of four Nigerian antimalarial plants. Various combinations of Nauclea latifolia root, Artocarpus altilis stem bark, *Murraya koenigii* leaf and Enantia chlorantha stem bark used in African ethnomedicine as decoctions for malaria and fevers, and combinations with standard drugs, were investigated for antiplasmodial activities using Plasmodium berghei berghei-infected mice. The respective prophylactic and curative ED50 values of 189.4 and 174.5 mg/kg for N. latifolia and chemosuppressive ED50 value of 227.2 mg/kg for A. altilis showed that they were the best antimalarial herbal drugs. A 1.6-fold increase of the survival time given by the negative control was elicited by *M. koenigii*, thereby confirming its curative activity. Pyrimethamine with an ED50 of 0.5 ± 0.1 mg/kg for the prophylactic, and chloroquine with ED50 = 2.2 ± 0.1 and 2.2 ± 0.0 mg/kg for the chemosuppressive and curative tests, respectively, were significantly ($p < 0.05$) more active. Co-administrations of N. latifolia with the standard drugs significantly reduced their prophylactic, chemosuppressive and curative actions, possibly increasing the parasites' resistance. Binary combinations of N. latifolia or *M. koenigii* with any of the other plants significantly increased the prophylactic and suppressive activities of their individual plants, respectively. Also, E. chlorantha with A. altilis or N. latifolia enhanced their respective prophylactic or curative activities, making these combinations most beneficial against malaria infections. Combinations of three and four extracts gave varied activities. Hence, the results justified the combinations of ethnomedicinal plants in antimalarial herbal remedies and showed the importance of the three in vivo models in establishing antimalarial activity (Adebajo *et al.,* 2014).

Review Article

Chemical composition, antibacterial and antioxidant profile of essential oil from *murraya koenigii* (L.) leaves. This study is designed to extract and examine hemical composition, antimicrobial and antioxidant activity of the hydro-distillated essential oil of *Murraya koenigii* leaves from the south region of Tamilnadu, India. Matherials and Methods: Gas Chromatography (GC) and Gas Chromatography-Mass Spectrometry (GC-MS) analysis of the essential oil result was indicates the 33different compounds representing 97.56 % of the total oil. Major compounds detected in the oil were Linalool (32.83%), Elemol (7.44%), Geranyl acetate (6.18%), Myrcene (6.12%), Allo-Ocimene (5.02), α-Terpinene (4.9%), and (E)-β-Ocimene (3.68%) and Neryl acetate (3.45%). From the identified compounds, they were classified into four groups that are oxygenated monoterpenes (72.15%), monoterpene hydrocarbons (11.81%), oxygenated sesquiterpenes (10.48%) and sesquiterpenes hydrocarbons (03.12%). The antibacterial activity of essential oil has pronounced by Disc Diffusion Method against various pathogenic microbes. The oil has a maximum zone of nhibition ability against Corynebacterium tuberculosis, Pseudomonas aeruginosa, Streptococcus pyogenes, Klebsiella pneumonia and Enterobacter aerogenes. The antioxidant profile of the sample was determined by different test systems. In all the systems, essential oil showed astrongest activity profile within the concentration range (Rajendran *et al.*, 2014).
Antiplasmodial activity of certain medicinal plants against chloroquine resistant Plasmodium berghei infected white albino BALB/c mice. In the present study of antimalarial efficacy, aqueous extracts of leaves and unripe fruits of Psidium guajava, leaves of Ocimum sanctum and leaves of *Murraya koenigii* are evaluated against Plasmodium berghei (chloroquine resistant NK65 strain) infected white albino BALB/c mice. A 7 days oral administration was adopted with different dosage viz., 350 mg, 750 mg and 1,000 mg/kg body weight as treatment schedule along with parasite (Group I) and drug control with Chloroquine, 50 mg/kg body weight (Group II). All the parts were extracted based on the decoction method, which is commonly seen among the villagers/tribes as their usual method of preparation of decoction for most of the ailments. The antimalarial activities were evaluated from the giemsa stained blood smears collected from different treated groups of mice used in this experiment. The antiplasmodial effect that is percent parasitaemia and percent suppression (values in parenthesis) showed by the treated groups of mice at 350 mg/kg b. wt. by the aqueous extracts of P. guajava leaves (Group III) was 19.8 ± 1.22 (73.7 %), *P. guajava* unripe fruits (Group IV) was 52.7 ± 2.19 (30.0 %), leaves of O. sanctum (Group V) was 64.0 ± 0.73 (15.1 %) and leaves of *M. koenigii* (GroupVI) was 28.9 ± 0.81 (61.6 %) whereas at 750 mg/kg b. wt., it all showed 10.3 ± 0.7 (80.2 %), 26.3 ± 0.52 (65.1 %), 42.0 ± 0.47 (44.2 %) and 14.9 ± 0.46 (71.5 %) whereas at 1,000 mg/kg b. wt. dose, it all showed 9.2 ± 0.39 (85.8 %), 25.6 ± 0.40 (62.0 %), 41.8 ± 0.29 (35.5 %) and 14.0 ± 0.42 (76.9 %) respectively (Rajendran *et al.*, 2014).
Study on antioxidant potential of *Murraya koenigii* leaves in Wistar rats. The antioxidant activity of *Murraya koenigii* (L) Spreng (Family: Rutaceae), leaves was investigated in male wistar rats. Potassium dichromate was used to induce oxidative stress. The traditional medical literature describes its potential role as a source of many vitamins, flavonoids, phenols and domestic remedy for many human disorders. The whole plant is considered to be tonic, antidiarrhoeal, febrifuge, blood purifier and as stomachic. In the present study animals were divided into four groups Group I (Control), Group II (Potassium dichromate), Group III *(Murraya koenigii* + Potassium dichromate) and Group IV (*Murraya koenigii*). In vivo antioxidant activity of Murraya koenigii inhibited the toxicity of potassium dichromate. The GSH content in liver (1.79 +/- 0.019) and kidney (1.967 +/- 0.013) of Group IV rats significantly ($p < 0.05$) increased whereas, hepatic malondialdehyde content in liver (2.44 +/- 0.29) and kidney (2.34 +/- 0.057) was significantly ($p < 0.05$) reduced as compare to control. However, Chromate significantly ($p < 0.05$) decreased the reduced glutathione (GSH) content and increases hepatic malondialdehyde (MDA) content in both liver and kidney as compared to control. Further post treatment with *Murraya koenigii* (Group III) significantly ($p<0.05$) increase the GSH content in liver (1.54 +/-0.013) and kidney (1.27 +/- 0.011) as compared to Group II whereas, hepatic malondialdehyde content in liver (4.24 +/- 0.71) and kidney (3.86 +/- 0.038) was significantly ($p<0.05$) reduced as compare to Group II(Potassium dichromate). These results clearly indicate that *Murraya koenigii* leaves have significant potential as a natural antioxidant agents (Gill *et al.*, 2014).

Review Article

Bioassay-guided isolation and characterization of active antiplasmodial compounds from *Murraya koenigii* extracts against Plasmodium falciparum and Plasmodium berghei. Malaria is an overwhelming impact in the poorest countries in the world due to their prevalence, virulence and drug resistance ability. Currently, there is inadequate armoury of drugs for the treatment of malaria. This underscores the continuing need for the discovery and development of new effective and safe antimalarial drugs. To evaluate the in vitro and in vivo antimalarial activity of the leaf ethyl acetate extract of *Murraya koenigii*, bioassay-guided chromatographic fractionation was employed for the isolation and purification of antimalarial compounds. The in vitro antimalarial activity was assayed by the erythrocytic stages of chloroquine-sensitive strain of Plasmodium falciparum (3D7) in culture using the fluorescence-based SYBR Green I assay. The in vivo assay was done by administering mice infected with Plasmodium berghei (NK65) four consecutive daily doses of the extracts through oral route following Peter's 4-day curative standard test. The percentage suppression of parasitaemia was calculated for each dose level by comparing the parasitaemia in untreated control with those of treated mice. Cytotoxicity was determined against HeLa cells using MTT assay. Histopathology was studied in kidney, liver and spleen of isolated compound-treated Swiss albino mice. The leaf crude ethyl acetate extract of *M. koenigii* showed good in vitro antiplasmodial activity against P. falciparum. The in vivo test of the leaf crude ethyl acetate extract (600 mg/kg) showed reduced malaria parasitaemia by 86.6% against P. berghei in mice. Bioassay-guided fractionation of the leaf ethyl acetate extract of *M. koenigii* led to the isolation of two purified fractions C3B2 (2.84 g) and C3B4 (1.97 g). The purified fractions C3B2 and C3B4 were found to be active with IC50 values of 10.5 ± 0.8 and 8.25 ± 0.2 µg/mL against P. falciparum, and in vivo activity significantly reduced parasitaemia by 82.6 and 88.2% at 100 mg/kg/body weight on day 4 against P. berghei, respectively. The isolated fractions C3B2 and C3B4 were monitored by thin-layer chromatography until a single spot was obtained with R f values of 0.36 and 0.52, respectively. The pure compounds obtained in the present investigation were subjected to UV-visible spectroscopy, Fourier transformer infrared spectroscopy, 1D and 2D (1) H-Nuclear magnetic resonance (NMR), (13) C NMR, DEPT, COSY and Mass spectral analysis. Based on the spectral analysis, it is concluded that the isolated compounds were myristic acid (C3B2) and β-caryophyllene (C3B4). The cytotoxic effect of myristic acid and β-caryophyllene showed the TC50 values of >100 and 80.5 µg/mL, respectively against HeLa cell line. The histopathology study showed that protection against nephrotoxicity of kidney, hepatic damage of liver and splenocytes protection in spleen was achieved with the highest dose tested at 100 mg/kg/body weight. The present study provides evidence of antiplasmodial compounds from *murraya koenigii* and is reported for the first time (Kamaraj *et al.*, 2014).

Evaluation of antibacterial and cytotoxic activity of Artemisia nilagirica and *Murraya koenigii* leaf extracts against mycobacteria and macrophages. Artemisia nilagirica (Asteraceae) and *Murraya koenigii* (Rutaceae) are widely distributed in eastern region of India. Leaves of Artemisia nilagirica plant are used to treat cold and cough by the local tribal population in east India. *Murraya koenigii* is an edible plant previously reported to have an antibacterial activity. Pathogenic strains of mycobacteria are resistant to most of the conventional antibiotics. Therefore, it is imperative to identify novel antimycobacterial molecules to treat mycobacterial infection. In this study, ethanol, petroleum ether and water extracts of Artemisias nilagirica and *Murraya koenigii* were tested for antibacterial activity against Mycobacterium smegmatis and Mycobacterium bovis BCG in synergy with first line anti-tuberculosis (TB) drugs, and for cytotoxic activities on mouse macrophage RA264.7 cells. Antibacterial activity was determined by colony forming unit (CFU) assay. Intracellular survival assay was performed by infecting RAW264.7 cells with M. smegmatis before and after treatment with plant extracts. Cytotoxity was checked by MTT [3-(4s, 5-Dimethylthiazol-2-yl)-2, 5-Diphenyltetrazolium Bromide] assay. Genotoxicity was studied by DAPI staining and COMET assay using mouse macrophage RAW264.7 cell line. Cell apoptosis was checked by Annexin-V/FITC dual staining method. Reactive oxygen species and nitric oxide production was checked by DCFH staining and Griess reagent, respectively. Results: Ethanol extracts of A. nilagirica (IC50 300 µg/ml) and M. koenigii (IC50400 µg/ml) were found to be more effective against Mycobacterium smegmatis as compared to petroleum ether and water extracts. *M. koenigii* extract showed maximum

activity against M. bovis BCG in combination with a first line anti-TB drug rifampicin. *M. koenigii* leaf extract also exerted more cytototoxic (IC50 20µg/ml), genotoxic and apoptosis in mouse macrophage RAW 264.7 cell line. Treatment of mouse macrophages with A. nilagirica extract increased intracellular killing of M.smegmatis by inducing production of reactive oxygen species and nitric oxide. : Ethanol extracts of A. nilagirica and *M. koenigii* were found to be more effective against mycobacteria. As compared to A. nilagirica, *M. koenigii* ethanol extract exhibited significant synergistic antibacterial activity against M. smegmatis and M. bovis BCG in combination with anti-tuberculosis drug rifampicin, and also showed increased cytotoxicity, DNA damage and apoptosis in mouse macrophages (Naik *et al.,* 2014).

Axially chiral biscarbazoles and biological evaluation of the constituents from *Murraya koenigii* Chemical investigation of the fruit pulp of *Murraya koenigii* resulted in the identification of two new dimeric carbazole alkaloids, bisgerayafoline D (1) and bismahanimbinol (2) along with four known alkaloids, bispyrayafoline (3), O-methyl mahanine (4), O-methyl mukonal (5), and mahanine (6). Structures of 1-6 were determined with the aid of UV, IR, Mass and extensive NMR spectroscopic studies. Absolute configurations of biaryls in 1 and 2 were assigned using a combination of computational Circular Dichroism (CD) and experimental electronic CD spectroscopic data. Compounds 1-6 were evaluated for anti-oxidant, anti-α-glucosidase, DNA binding, protein interactions and cytotoxic activities. Among all the isolates, mahanine (6) was found to exhibit significant radical scavenging and α-glucosidase inhibitory activities. Compound 6 was also found to be active in cytotoxicity assay against three human cancer cell lines HeLa, HCT116, AGS and this compound was weakly active against normal mouse embryonic fibroblasts (NIH3T3) (Uvarani *et al.,* 2014).

Antiplasmodial potential of selected medicinal plants from Eastern Ghats of South India Malaria caused by the protozoan parasite Plasmodium falciparum is a major health problem of the developing world. In the present study medicinal plants from Eastern Ghats of South India have been extracted with ethyl acetate and assayed for growth inhibition of asexual erythrocytic stages of chloroquine (CQ)-sensitive (3D7) and (CQ)-resistant (INDO) strains of P. falciparum in culture using the fluorescence-based SYBR Green I assay. Studied extracts showed a spectrum of antiplasmodial activities ranging from (a) very good (IC(50)<10-10 µg/mL: Cyperus rotundus and Zingiber officinale); (b) good (IC(50), >10-15 µg/mL: Ficus religiosa and *Murraya koenigii*); (c) moderate (IC(50)>15-25 µg/mL: Ficus benghalensis); (d) poor activity (IC(50)>25-60 µg/mL) and (e) inactive (IC(50)>60 µg/mL). Resistance indices ranging from 0.78 to 1.28 suggest that some of these extracts had equal promise against the CQ resistant INDO strain of P. falciparum. Cytotoxicity assessment of the extracts against HeLa cell line using MTT assay revealed that the selectivity indices in the range of 3-15 suggesting a good margin of safety (Kaushik *et al.,* 2013).

Green synthesis of silver nanoparticles using *Murraya koenigii l*eaf extract against Anopheles stephensi and Aedes aegypti.Mosquitoes transmit serious human diseases, causing millions of deaths every year. The use of synthetic insecticides to control vector mosquitoes has caused physiological resistance and adverse environmental effects in addition to high operational cost. Insecticides of synthesized natural products for vector control have been a priority in this area. In the present study, the activity of silver nanoparticles (AgNPs) synthesized using *Murraya koenigii* plant leaf extract against first to fourth instars larvae and pupae of nopheles stephensi and Aedes aegypti was determined. Range of concentrations of synthesized AgNPs (5, 10, 20, 30, and 40 ppm) and ethanol leaf extract (50, 200, 350, 500, and 650 ppm) were tested against the larvae of A. stephensi and A. aegypti. The synthesized AgNPs from *M. koenigii* leaf were highly toxic than crude leaf ethanol extract in both mosquito species. The results were recorded from UV-Vis spectrum, Fourier transform infrared spectroscopy, scanning electron microscopy, and energy-dispersive X-ray spectroscopy analysis. Larvae were exposed to varying concentrations of aqueous extract of synthesized AgNPs for 24 h. The maximum mortality was observed in synthesized AgNPs, and ethanol leaf extract of *M. koenigii* against A. stephensi had LC50 values of 10.82, 14.67, 19.13, 24.35, and 32.09 ppm and 279.33, 334.61, 406.95, 536.11, and 700.16 ppm and LC90 values of 32.38, 42.52, 53.65, 63.51, and 75.26 ppm and 737.37, 843.84, 907.67, 1,187.62, and 1,421.13 ppm. A. aegypti had LC50 values of 13.34, 17.19, 22.03, 27.57, and 34.84 ppm and 314.29, 374.95, 461.01,

606.50, and 774.01 ppm and LC90 values of 36.98, 47.67, 55.95, 67.36, and 77.72 ppm and 777.32, 891.16, 1,021.90, 1,273.06, and 1,509.18 ppm, respectively. These results suggest that the use of *M. koenigii* synthesized silver nanoparticles can be a rapid, environmentally safer biopesticide which can form a novel approach to develop effective biocides for controlling the target vector mosquitoes (Suganya *et al.*, 2013).

Larvicidal efficacy of Sphaeranthus indicus, Cleistanthus collinus and *Murraya koenigii* leaf extracts against filarial vector, Culex quinquefasciatus Say (Diptera: Culicidae). Sphaeranthus indicus, Cleistanthus collinus and *Murraya koenigii* leaf extracts were tested against the third instar larvae of Culex quinquefasciatus. The plant material was shade dried at room temperature and powdered coarsely. From each plant, 500 g powder was macerated with 1.5 L of hexane, chloroform and ethyl acetate sequentially for a period of 72 h each and filtered. The yield of the S. indicus, C. collinus and *M. koenigii* crude extracts by hexane, chloroform and ethyl acetate was 9.16, 11.71 and 10.83 g for S. indicus; 8.17, 10.69 and 9.85 g for C. collinus; and 10.11, 11.92 and 9.87 g for *M. koenigii*, respectively. The extracts were concentrated at reduced temperature on a rotary vacuum evaporator and stored at a temperature of 4°C. The S. indicus, C. collinus and *M. koenigi*i leaf extracts at 250, 500, 750 and 1,000 ppm caused a significant mortality of C. quinquefasciatus. The LC(50) and LC(90) valuesof S. indicus, C. collinus and *M. koenigii* against third instar larvae at 24, 48 and 2 h (hexane, chloroform and ethyl acetate) were the following: S. indicus LC(50) values were 544.93, 377.86 and 274.79 ppm and LC(90) values were 1,325.32, 1,572.55 and 1,081.29 ppm at 24 h; C. collinus LC(50) values were 375.34, 318.29 and 226.10 ppm and LC(90) values were 699.65, 1,577.62 and 1,024.92 ppm at 24 h; and *M. koenigii* LC(50) values were 963.53, 924.85 and 857.62 ppm and LC(90) values were 1,665.12, 1,624.68 and 1,564.37 ppm at 24 h, respectively. However, the highest larval mortality was observed in C. collinus followed by S. indicus and *M. koenigii* of various concentrations at 24, 48 and 72 h. The study proved that S. indicus, C. scollinus and *M. koenigii* leaf extracts had larvicidal property against species of C. quinquefasciatus. This is an ideal ecofriendly approach for the control of vector control programmes (Kovendan *et al.*, 2012).

Antibacterial activities of essential oils extracted from leaves of *Murraya koenigii* by solvent-free microwave extraction and hydro-distillation.

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 300microg/mL provided 92% inhibition, indicating its potential as a natural antimicrobial agent (Erkan *et al.*, 2012).

Phytochemical $ Biochemical Analysis

Volatile constituents of *Murraya koenigii* fresh leaves using headspace solid phase microextraction--gas chromatography-mass spectrometry.The volatile components of *Murraya koenigii* fresh leaves, collected from Surat Thani province, Thailand were studied by using headspace (HS) solid-phase microextraction (SPME) coupled with gas chromatography-mass spectrometry (GC-MS). The four fibers employed to extract the volatiles were polydimethylsiloxane (PDMS), polydimethylsiloxane-divinylbenzene (PDMS-DVB), carboxane-polydimethylsiloxane (CAR-PDMS) \polydimethylsiloxane-divinylbenzene-carboxane (PDMS-DVB-CAR). The volatile constituents of *M. koenigii* fresh leaves were also extracted by hydrodistillation and analyzed by GC-MS. Fifty-one compounds were identified by these fibers. Five major compounds, γ-terpinene, β-caryophyllene, β-phellandrene, a-selinene and a-pinene, were detected

in all fibers. The PDMS-DVB-CAR fiber was considered as the best for trapping key volatiles of *M. koenigii* fresh leaves (Sukkaew *et al.*, 2014).

Three new carbazole alkaloids and biological activities of *Murraya koenigii* spectral analysis including UV, IR, MS, and 2D NMR spectroscopy.The antimicrobial activity of different fractions of plant extract was also determined (Naz *et al.*, 2015).

Green synthesized iron oxide nanoparticles effect on fermentative hydrogen production by Clostridium acetobutylicum. A green synthesis of iron oxide nanoparticles (FeNPs) was developed using *Murraya koenigii* leaf extract as reducing and stabilizing agent. UV-vis spectra show that the absorption band centred at a wavelength of 277 nm which corresponds to the surface plasmon resonances of synthesized FeNPs. Fourier transform infrared spectroscopy spectrum exhibits that the characteristic band at 580 cm (-1) is assigned to Fe-O of γ-Fe2O3. Transmission electron microscopy image confirms that the spherical with irregular shaped aggregates and average size of nanoparticles was found to be ∼59 nm. The effect of synthesized FeNPs on fermentative hydrogen production was evaluated from glucose by Clostridium acetobutylicum NCIM 2337. The hydrogen yield in control experiment was obtained as 1.74 ± 0.08 mol H2/mol glucose whereas the highest hydrogen yield in FeNPs supplemented experiment was achievedas 2.33 ± 0.09 mol H2/mol glucose at 175 mg/L of FeNPs. In addition, the hydrogen content and hydrogen production rate were also increased from 34 ± 0.8 to 52 ± 0.8 % and 23 to 25.3 mL/h, respectively. The effect of FeNPs was compared with supplementation of FeSO4 on fermentative process. The supplementation of FeNPs enhanced the hydrogen production in comparison with control and FeSO4. The supplementation of FeNPs led to the change of the metabolic pathway towards high hydrogen production due to the enhancement of ferredoxin activity. The fermentation type was shifted from butyrate to acetate/butyrate fermentation type at the addition of FeNPs (Mohanraj *et al.*, 2014).

Structural insights into the aggregation behavior of *Murraya koenigii* miraculin-like protein below pH 7.5*Murraya koenigii* miraculin-like protein (MKMLP) gradually precipitates below pH 7.5. Here, we explore the basis for this aggregation by identifying the aggregation-prone regions via comparative analysis of crystal structures acquired at several pH values. The prediction of aggregation-prone regions showed the presence of four short peptides either in beta sheets or loops on surface of the protein. These peptides were distributed in two patches far apart on the surface. Comparison of crystal structures of MKMLP, determined at 2.2 Å resolutions in pH 7.0 and 4.6 in the present study and determined at 2.9 Å in pH 8.0 in an earlier reported study, reveal subtle conformational differences resulting in gradual exposure of aggregation-prone regions. As the pH is lowered, there are alterations in ionic interactions within the protein interactions of the chain with water molecules and exposure of hydrophobic residues. The analysis of symmetry-related molecular interfaces involving one patch revealed shortening of nonpolar intermolecular contacts as the pH decreased. In particular, a decrease in the intermolecular distance between Trp103 of the aggregation-prone peptide WFITTG (103-108) unique to MLPs was observed. These results demonstrated that aggregation occurs due to the cumulative effect of the changes in interactions in two aggregation-prone defined regions (Mohanraj *et al.*, 2015). Bioactive dimeric carbazole alkaloids from *Murraya koenigii* Phytochemical studies on the CHCl3 extract of the fruit pulp of *Murraya koenigii* afforded three new dimeric carbazole alkaloids, bisgerayafolines A-C (1-3). Bisgerayafolines A-C (1-3) is structurally unique dimeric carbazole alkaloids comprising geranyl moieties incorporated in their structures. Compounds 1-3 exhibited various levels of antioxidant, anti-α-glucosidase, DNA binding, and cytotoxic activities and protein interactions (Uvarani *et al.*, 2015).

Phytochemical diversity of *Murraya koenigii* (L) Spreng fromWestern Himalaya *Murraya koenigii* (L) Spreng (Rutaceae), commonly known as 'curry leaf tree', is a popular spice and condiment of India.To explore the diversity of the essential-oil yield and aroma profile of curry leaf, growing wild in foot and mid hills of north India, 58 populations were collected during spring season. *M. koenigii* populations were found to grow up to an altitude of 1487 m in north India. Comparative results showed considerable variations in the essential-oil yield and composition. The essential-oil yield varied from 0.14 to 0.80% in shade-dried leaves of different populations of *M. koenigii*. Analysis of the essential oils by GC and GC/MS, and the subsequent classification by statistical analysis resulted in four clusters with significant

variations in their terpenoid composition. Major components of the essential oils of investigated populations were α-pinene (2; 4.5-71.5%), sabinene (3; <0.05-66.1%), (E)-caryophyllene (11;1.6-18.0%), β-pinene (4; <0.05-13.6%), terpinen-4-ol (9; 0.0-8.4%), γ-terpinene (8; 0.2-7.4%), limonene (7; 1.1-5.5%), α-terpinene (6; 0.0-4.5%), (E)-nerolidol (14; 0.0-4.1%), α-humulene (12; 0.6-3.5%), α-thujene (1; 0.0-2.5%), β-elemene (10; 0.2-2.4%), β-selinene (13; 0.2-2.3%), and myrcene (5; 0.5-2.1%). Comparison of the present results with those in earlier reports revealed new chemotypes of *M. koenigii* in investigated populations from Western Himalaya. The present study documents *M. koenigii* populations having higher amounts of sabinene (3; up to66.1%) for the first time (Verma *et al.,*). Ioactive carbazole alkaloids from *Murraya koenigii* (L) Spreng Four new carbazole alkaloids (1-4) and fourteen known carbazole alkaloids (5-18) were isolated from *Murraya koenigii*. Their structures were elucidated on the basis of extensive spectroscopic analysis. Compounds 4, 6, 16, and 17 (10 μM) had moderate hepatoprotective activities against d-galactosamine-induced HL-7702 cell damage. Compounds 11, 12 and 18 showed significant PTP1B inhibitory activity with IC50 values of 1.773, 1.875 and 2.286 μM, respectively (Ma *et al.,* 2013).
Alkaloids from Sri Lankan curry-leaf *(Murraya koenigii*) display melanogenesis inhibitory activity: structures of karapinchamines A and B.
A methanolic extract and its ethyl acetate-soluble fraction from Sri Lankan curry-leaf, the leaves of *Murraya koenigii*, inhibited melanogenesis in theophylline-stimulated murine B16 melanoma 4A5 cells Two new carbazole alkaloids, karapinchamines A and B, were isolated from the ethyl acetate-soluble fraction together with 12 known carbazole alkaloids. The structures of karapinchamines A and B were determined by physicochemical analyses. The principal alkaloid constituents were found to display potent melanogenesis inhibitory activity. The structural requirements of the carbazole alkaloids for melanogenesis inhibitory activity were discussed (Ma *et al.*, 2003).
Chemotaxonomical markers in essential oil of *Murraya koenigii* the composition of the essential oils of *Murraya koenigii* (L) Spreng, cultivated at six locations in Peninsula Malaysia and Borneo are presented. The oils were obtained from fresh leaves by hydrodistillation and analyzed by gas chromatography-mass spectrometry (GC-MS); 61 compounds were identified, of which eleven were present in all the specimens analyzed. The two major volatile metabolites were identified as beta-caryophyllene (16.6-26.6%) and alpha-humulene (15.2-26.7%) along with nine minor compounds identified as beta-elemene (0.3-1.3%), aromadendrene (0.5-1.5%), beta-selinene (3.8-6.5%), spathulenol (0.6-2.7%), caryophyllene oxide (0.7-3.6%), viridiflorol (1.5-5.5%), 2-naphthalenemethanol (0.7-4.8%), trivertal (0.1-1.0%) and juniper camphor (2.6-8.3%). The results suggest that beta-caryophyllene and alpha-humulene could be used as chemotaxonomical markers for Malaysian *M. koenigii*; hence these specimens could be of the same stock and different from the ones in India, Thailand and China (Nakamura *et al.*, 2013).
Effects of the total alkaloidal extract of *Murraya koenigii* leaf on oxidative stress and cholinergic transmission in aged mice. Alzheimer's disease (AD) is characterized by signs of major oxidative stress and the loss of cholinergic cells.
The present study was designed to investigate the role of the total alkaloidal extract from *Murraya koenigii* (MKA) leaves on age related oxidative stress and the cholinergic pathway in aged mice. Ascorbic acid (100 mg/kg, p.o.) was used as a standard drug. The MKA improved the level of protective antioxidants such as glutathione peroxidase (GPx), reduced glutathione (GSH), glutathione reductase (GRD), superoxide dismutase (SOD) and catalase (CAT) in brain homogenate at higher doses (20 and 40 mg/kg, p.o.). Moreover, a dose dependent decline was noted in lipid peroxidation (LPO) and the nitric oxide assay (NO) at all doses of MKA (10, 20 and 40 mg/kg, p.o.). Interestingly, significant progress was noted with the supplementation of MKA by an improvement of the acetylcholine (ACh) levels and a reduction in the acetylcholinesterase (AChE) activity in aged mouse brain. In addition, a significant elevation of serum albumin (ALBU), alkaline phosphatase (ALP), alanine transaminase (ALT), aspartate transaminase (AST) and total protein as well as a decline in creatinine, total cholesterol, urea nitrogen and glucose levels with MKA also ameliorated the hepatic and renal functions in normal ageing process. The results showed the possible utility of *Murraya koenigii* leaves in neuroprotection against neurodegenerative disorders such as Alzheimer's disease (Mani *et al.*, 2003).

Review Article

Anticancer

Evaluation of Bioactive Compounds, Pharmaceutical Quality, and Anticancer Activity of Curry Leaf *(Murraya koenigii* (L) in this study, we investigated some bioactive compounds and pharmaceutical qualities of curry leaf *(Murraya koenigii* L.) extracts from three different locations in Malaysia. The highest TF and total phenolic (TP) contents were observed in the extracts from Kelantan (3.771 and 14.371 mg/g DW), followed by Selangor (3.146 and 12.272 mg/g DW) and Johor (2.801 and 12.02 mg/g DW), respectively. High quercetin (0.350 mg/g DW), catechin (0.325 mg/g DW), epicatechin (0.678 mg/g DW), naringin (0.203 mg/g DW), and myricetin (0.703 mg/g DW) levels were observed in the extracts from Kelantan, while the highest rutin content (0.082 mg/g DW) was detected in the leaves from Selangor. The curry leaf extract from Kelantan exhibited higher concentration of gallic acid (0.933 mg/g DW) than that from Selangor (0.904 mg/g DW) and Johor (0.813 mg/g DW). Among the studied samples, the ones from Kelantan exhibited the highest radical scavenging activity (DPPH, 66.41%) and ferric reduction activity potential (FRAP, 644.25 μ m of Fe(II)/g) followed by those from Selangor (60.237% and 598.37 μ m of Fe(II)/g) and Johor (50.76% and 563.42 μ m of Fe(II)/g), respectively. A preliminary screening showed that the curry leaf extracts from all the locations exhibited significant anticarcinogenic effects inhibiting the growth of breast cancer cell line (MDA-MB-231) and maximum inhibition of MDA-MB-231 cell was observed with the curry leaf extract from Kelantan. Based on these results, it is concluded that Malaysian curry leaf collected from the North (Kelantan) might be potential source of potent natural antioxidant and beneficial chemopreventive agents (Ghasemzadeh *et al.*, 2014).

A naturally derived small molecule disrupts ligand-dependent and ligand-independent androgen receptor signaling in human prostate cancer cells. Continued reliance on androgen receptor (AR) signaling is a hallmark of prostate cancer, including the development of castration-resistant prostate cancer (CRPC), making it an attractive therapeutic target for prostate cancer treatment.Mahanine is a novel carbazole alkaloid derived from the leaves of *Murraya koenigii*, commonly known as the curry leaf plant, which grows widely across East-Asia. We show here that mahanine possesses the ability to inhibit ligand-dependent and -independent AR transactivation, leading to a prominent decline in AR target gene expression. Mahanine treatment causes a time- and dose-dependent decline in AR protein levels, including truncated AR splice variants, in a panel of androgen-responsive and -independent prostate cancer cells. The decrease in AR levels induced by mahanine occurs posttranslationally by proteasomal degradation, without any change in the AR gene expression. Mahanine treatment induces an outward movement of the AR from the nucleus to the cytoplasm, leading to an initial increase in cytoplasmic AR levels, followed by a gradual decline in the AR levels in both cellular compartments. Ligand-induced AR phosphorylation at Ser-81, a phospho-site associated with prostate cancer cell growth and AR transactivity, is greatly diminished in the presence of mahanine. The decline in AR phosphorylation at Ser-81 by mahanine occurs via the inactivation of mitotic kinase CDK1. Collectively, our data demonstrate that mahanine strongly disrupts AR signaling and inhibits the growth of androgen-dependent and -independent prostate cancer cells, thereby implicating a therapeutic role of mahanine in prostate cancer treatment (Amin *et al.*, 2004).

Antioxidant capacity and antimutagenic potential of *Murraya koenigii* It is well known that the intake of antioxidants with increased consumption of fruits and vegetables and medicinal herbs contributes towards reduced risk of certain diseases including cancers.This study aims to evaluate the broad-spectrum antioxidant and antimutagenic activities as well as to elucidate phytochemical profile of an Indian medicinal plant *Murraya koenigii* (curry) leaves. Leaves of the plant were successively fractionated in various organic solvents. Benzene fraction demonstrated the highest phenolic content followed by petroleum ether. The benzene fraction showed maximum antioxidant activity in all tested assays, namely, phosphomolybdenum, 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical, ferric reducing antioxidant power (FRAP) and cupric reducing antioxidant capacity (CUPRAC) assays. Based on the promising broad-spectrum antioxidant activity, benzene fraction was further evaluated for antimutagenic activity and showed a dose-dependent antimutagenic response in Ames Salmonella mutagenicity assay. It inhibited

72-86% mutagenicity induced by sodium azide, methyl methanesulfonate, benzo (a) pyrene, and 2-aminoflourene at the maximum tested concentration (100µg/mL) in Salmonella typhimurium tester strains. At least 21 compounds were detected by GC/MS. The findings clearly demonstrated that phenolic-rich benzene fraction has promising broad-spectrum antioxidant and antimutagenic property and needs further evaluation to exploit its therapeutic potential (Zahin *et al*., 2003).

Apoptosis Effect of Girinimbine Isolated from *Murraya koenigii* on Lung Cancer Cells in Vitro.*Murraya koenigii* Spreng has been traditionally claimed as a remedy for cancer. The current study investigated the anticancer effects of girinimbine, a carbazole alkaloid isolated from *Murraya koenigii* Spreng, on A549 lung cancer cells in relation to apoptotic mechanistic pathway. Girinimbine was isolated from *Murraya koenigii* Spreng. The antiproliferative activity was assayed using MTT and the apoptosis detection was done by annexin V and lysosomal stability assays. Multiparameter cytotoxicity assays were performed to investigate the change in mitochondrial membrane potential and cytochrome c translocation. ROS, caspase, and human apoptosis proteome profiler assays were done to investigate the apoptotic mechanism of cell death. The MTT assay revealed that the girinimbine induces cell death with an IC50 of 19.01 µ M. A significant induction of early phase of apoptosis was shown by annexin V and lysosomal stability assays. After 24 h treatment with 19.01 µ M of girinimbine, decrease in the nuclear area and ncrease in mitochondrial membrane potential and plasma membrane permeability were readily visible. Moreover the translocation of cytochrome c also was observed. Girinimbine mediates its antiproliferative and apoptotic effects through up- and downregulation of apoptotic and antiapoptotic proteins. There was a significant involvement of both intrinsic and extrinsic pathways. Moreover, the upregulation of p53 as well as the cell proliferation repressor proteins, p27 and p21, and the significant role of insulin/IGF-1 signaling were also identified. Moreover the caspases 3 and 8 were found to be significantly activated. Our results taken together indicated that girinimbine may be a potential agent for anticancer drug development (Mohan *et al*., 2013).

Murraya koenigii leaf extract inhibits proteasome activity and induces cell death in breast cancer cells. Inhibition of the proteolytic activity of 26S proteasome, the protein-degrading machine, is now considered a novel and promising approach for cancer therapy. Interestingly, proteasome inhibitors have been demonstrated to selectively kill cancer cells and also enhance the sensitivity of tumor cells to chemotherapeutic agents. Recently, polyphenols/flavonoids have been reported to inhibit proteasome activity. *Murraya koenigii* Spreng, a medicinally important herb of Indian origin, has been used for centuries in the Ayurvedic system of medicine. Here we show that *Murraya koenigii* leaves (curry leaves), a rich source of polyphenols, inhibit the proteolytic activity of the cancer cell proteasome, and cause cell death. Hydro-methanolic extract of curry leaves (CLE) was prepared and its total phenolic content [TPC] determined by, the Folin-Ciocalteau's method. Two human breast carcinoma cell lines: MCF-7 and MDA-MB-231 and a normal human lung fibroblast cell line, WI-38 were used for the studies. Cytotoxicity of the CLE was assessed by the MTT assay. We studied the effect of CLE on growth kinetics using colony formation assay. Growth arrest was assessed by cell cycle analysis and apoptosis by Annexin-V binding using flow cytometry. Inhibition of the endogenous 26S proteasome was studied in intact cells and cell extracts using substrates specific to 20S proteasomal enzymes. CLE decreased cell viability and altered the growth kinetics in both the breast cancer cell lines in a dose-dependent manner. It showed a significant arrest of cells in the S phase albeit in cancer cells only. Annexin V binding data suggests that cell death was via the apoptotic pathway in both the cancer cell lines. CLE treatment significantly decreased the activity of the 26S proteasome in the cancer but not normal cells. Our study suggests *M. koenigii* leaves to be a potent source of proteasome inhibitors that lead to cancer cell death. Therefore, identification of active component(s) from the leaf extract could lead to the development of anti-cancer agents which could be useful in the treatment of different types of cancers (Noolu *et al*., 2013).

Comparison of *Murraya koenigii*- and Tribulus terrestris-based oral formulation versus tamsulosin in the treatment of benign prostatic hyperplasia in men aged >50 years: a double-blind, double-dummy, randomized controlled trial (Kaplan, 2012). Anti-tumour promoting activity and antioxidant properties of

girinimbine isolated from the stem bark of *Murraya koenigii*. 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 6.0µg/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 at32.0 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 26.3µg/mL respectively however girinimbine failed to scavenge the stable diphenyl picryl hydrazyl (DPPH)-free radical (Kok *et al.*, 2012).

Biological activity of carbazole alkaloids and essential oil of *Murraya koenigii* against antibiotic resistant microbes and cancer cell lines A total of three carbazole alkaloids and essential oil from the leaves of *Murraya koenigii* (Rutaceae) were obtained and examined for their effects on the growth of five antibiotic resistant pathogenic bacteria and three tumor cell lines (MCF-7, P 388 and Hela). The structures of these carbazoles were elucidated based on spectroscopy data and compared with literature data, hence, were identified as mahanine (1), mahanimbicine (2) and mahanimbine (3). The chemical constituent's ofthe essential oil was identified using Gas Chromatography-Mass Spectroscopy (GCMS). These compounds exhibited potent inhibition against antibiotic resistant bacteria such as Staphylococcus aureus (210P JTU), Psedomonas aeruginosa (ATCC25619), Klebsiella pneumonia (SR1-TU), Escherchia coli (NI23 JTU) and Streptococcus pneumoniae (SR16677-PRSP) with significant minimum inhibition concentration (MIC) values (25.0-175.0 mg/mL) and minimum bacteriacidal concentrations (MBC) (100.0-500.0 mg/mL). The isolated compounds showed significant antitumor activity against MCF-7, Hela and P388 cell lines. Mahanimbine (3) and essential oil in particular showed potent antibacteria and cytotoxic effect with dose dependent trends (≤5.0 µg/mL). The findings from this investigation are the first report of carbazole alkaloids' potential against antibiotic resistant clinical bacteria; MCF-7 and P388 cell lines (Nagappan *et al.*, 2011).

Genetic Analysis

Molecular characterization and analysis of bacterial diversity in Aleurocanthus woglumi (Hemiptera: Aleyrodidae). Aleurocanthus woglumi Ashby (Hemiptera: Aleyrodidae), commonly referred to as citrus blackfly, is a sap-sucking hemipteran insect. Although polyphagous, citrus is its most preferred host plant. Samples of this insect were collected from *Murraya koenigii* (L.). The cytochrome c oxidase subunit I gene (mtCO1)-based analysis by sequencing helped in molecular identification of the insect. Phylogenetic analysis of cytB-nd1-LrDNA showed the coevolution of A. woglumi with its primary bacterial symbiont Portiera. Sequencing a 16S rDNA library from insect DNA revealed three bacterial phylotypes, namely, Portiera, Wolbachia, and Erwinia chrysanthemi Further we used fluorescence in situ hybridization to visualize the endosymbionts in a whole mount of A. woglumi. Culturable bacteria were obtained on different media and were classified on the basis of 16S rDNA. In total, 30 bacterial phylotypes belonging to 14 different genera, namely, Bacillus, Kocuria, Micrococcus, Staphylococcus, Paenibacillus, Rhodococcus, Rummellibacillus, Arthrobacter, Curtobacterium, Psychrobacillus, Listeria, Brevibacillus, Bhargavae, and Pantoea, were isolated by culturable methods (Pandey *et al.*, 2013).

Phylogenetic relationships of citrus and its relatives based on matK gene sequences The genus Citrus includes mandarin, orange, lemon, grapefruit and lime, which have high economic and nutritional value. The family Rutaceae can be divided into 7 subfamilies, including Aurantioideae. The genus Citrus belongs to the subfamily Aurantioideae. In this study, we sequenced the chloroplast matK genes of 135 accessions from 22 genera of Aurantioideae and analyzed them phylogenetically. Our study includes many accessions that have not been examined in other studies. The subfamily Aurantioideae has been classified into 2 tribes, Clauseneae and Citreae, and our current molecular analysis clearly discriminate

Citreae from Clauseneae by using only 1 chloroplast DNA sequence. Our study confirms previous observations on the molecular phylogeny of Aurantioideae in many aspects. However, we have provided novel information on these genetic relationships. For example, inconsistent with the previous observation, and consistent with our preliminary study using the chloroplast rbcL genes, our analysis showed that Feroniella oblata is not nested in Citrus species and is closely related with Feronia limonia. Furthermore, we have shown that *Murraya paniculata* is similar to Merrillia caloxylon and is dissimilar to *Murraya koenigii*. We found that "true citrus fruit trees" could be divided into 2 subclusters. One subcluster included Citrus, Fortunella, and Poncirus, while the other cluster included Microcitrus and Eremocitrus. Compared to previous studies, our current study is the most extensive phylogenetic study of Citrus species since it includes 93 accessions. The results indicate that Citrus species can be classified into 3 clusters: a citron cluster, a pummelo cluster, and a mandarin cluster. Although most mandarin accessions belonged to the mandarin cluster, we found some exceptions. We also obtained the information on the genetic background of various species of acid citrus grown in Japan. Because the genus Citrus contains many important accessions, we have comprehensively discussed the classification of this genus (Verma *et al.*, 2013).

Genetic relationships among wild and cultivated accessions of curry leaf plant *(Murraya koenigii* (L.) Spreng.), as revealed by DNA fingerprinting methodss *Murraya koenigii (*L) Spreng. (Rutaceae), is an aromatic plant and much valued for its flavor, nutritive and medicinal properties. In this study, three DNA fingerprinting methods viz., random amplification of polymorphic DNA (RAPD), directed amplification of minisatellite DNA (DAMD), and inter-simple sequence repeat (ISSR), were used to unravel the genetic variability and relationships across 92 wild and cultivated *M. koenigii* accessions. A total of 310, 102, and 184, DNA fragments were amplified using 20 RAPD, 5 DAMD, and 13 ISSR primers, revealing 95.80, 96.07, and 96.73% polymorphism, respectively, across all accessions. The average polymorphic information content value obtained with RAPD, DAMD, and ISSR markers was 0.244, 0.250, and 0.281, respectively. The UPGMA tree, based on Jaccard's similarity coefficient generated from the cumulative (RAPD, DAMD, and ISSR) band data showed two distinct clusters, clearly separating wild and cultivated accessions in the dendrogram. Percentage polymorphism, gene diversity (H), and Shannon information index (I) estimates were higher in cultivated accessions compared to wild accessions. The overall high level of polymorphism and varied range of genetic distances revealed a wide genetic base in *M. koenigii* accessions. The study suggests that RAPD, DAMD, and ISSR markers are highly useful to unravel the genetic variability in wild and cultivated accessions of *M. Koenigii* (Verma and Rana, 2013).

Antidiabetic

Anti-diabetic effect of *Murraya koenigii* (L) and Olea europaea (L) leaf extracts on streptozotocin induced diabetic rats. Phytotherapy has a promising future in the management of diabetes, considered to be less toxic and free from side effects as compared to the use of synthetic drugs. The aim of the present study was to assess the antidiabetic possible of orally administered aqueous extracts of *Murraya koenigii* (ML) and Olea europaea (OL) leaves (100 and 200 mg/kg doses), in streptozotocin (70 mg/kg) induced diabetic rats. Metformin was used as a standard drug. Blood glucose, cholesterol, triglycerides, creatinine levels and body weight were estimated. ML and OL administration showed significant decrease ($p>0.05$) in cholesterol, triglyceride, and serum glucose levels (range 55.6%-64.6%) compared to the metformin (62.7%); however, there was no significant effect on body weight and serum creatinine. Our results suggest that both the ML and OL possess a potent antihyperglycemic and hypolipidemic effect, which may be due to the presence of antioxidants such as carbazole alkaloids and polyphenols (El-Amin *et al.*, 2013).

Islet protective and insulin secretion property of *Murraya koenigii* and Ocimum tenuflorum in streptozotocin-induced diabetic mice sThe present study investigates the antidiabetogenic effects of *Murraya koenigii* (L.) Spr. and Ocimum tenuflorum L. on streptozotocin-induced diabetic Swiss mice Treatment with extracts of *M. koenigii* (chloroform; MKC) and O. tenuflorum (aqueous; OTA) resulted in proper glucose utilization with an increase in liver glucose-6-phosphate dehydrogenase enzyme activity, and normal glycogenesis in hepatic and muscle tissues. Pancreatic and intestinal glucosidase inhibitory

activity observed with MKC andOTA treatment indicated beneficial effects in reducing postprandial hyperglycemia with concomitant improvement in glucose metabolism. The glucosidase inhibition was prolonged, even after discontinuation of MKC and OTA treatment. Normalization of plasma insulin and C-peptide levels was observed in diabetic mice, indicating endogenous insulin secretion after treatment. The histochemical and immunohistochemical analysis of pancreatic islets suggests the role of MKC and OTA in pancreatic β-cell protection and the functional pancreatic islets that produce insulin. The study demonstrates the significance of MKC and OTA in glucosidase inhibition and islet protection in the murine diabetic model. These findings suggest the potential of the extracts in adjuvant therapy for the treatment of diabetes and the possible development of potential neutraceuticals (Dusane and Joshi, 2013).

CONCLUSION

Murraya Koeingii is a very important medicinal plant which can be used for production of different plant based medicine in recent years; ethnobotanical and traditional uses of natural compounds, especially of plant origin received much attention as they are well tested for their efficacy and generally believed to be safe for human use. It is interesting to note that pure compounds and crude organic extracts of leaves of *Murraya Koenigii* have been screened for some pharmacological activities and found to possess anti-diabetic, cholesterol reducing property, anti-diarrhea activity, cytotoxic activity antioxidant property, antiulcer activity antimicrobial, antibacterial potential and many more useful medicinal properties. *M. koenigii* may be utilized to alleviate the symptoms of variety of diseases as evident form the pre-clinical data. *Murraya koeingii* is a very important plant for various type of disease. The evidence by published literature and wide spread availability of curry leaves in India thus is a strong candidate of recommendation for further pre-clinical and clinical research.

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