

A REVIEW ON *MURRAYA KOENIGII*: MULTIPOTENTIAL MEDICINAL PLANTHARISH K HANDRAL<sup>1</sup>, ANUP PANDITH<sup>2</sup> AND SHRUTHI SD<sup>3\*</sup><sup>1</sup>Department of Solid State Crystal Unit SSCU, Indian Institute of Science, Bangalore, Karnataka, India, <sup>2</sup>Department of Organic Chemistry, Indian Institute of Science, Bangalore, Karnataka, India, <sup>3</sup>P.G. Department of Biotechnology, The Oxford College of Science, Bangalore, Karnataka, India ; Email: sdshruthi@gmail.com

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## ABSTRACT

Medicinal plants are used in herbalism and thought to have some medicinal properties. They form the easily available source for healthcare purposes in rural and tribal areas. Ethanobotany is a distinct branch of natural science dealing with various aspects such as anthropology, archaeology, botany, ecology, economics and medicine, religious, cultural and several other disciplines. Recently, great interest in the above given studies of herbal drugs and traditional remedies is indicated worldwide and there has been an upsurge in the scientific investigations in this area. The *Murraya koenigii* plant is widely used as herb, spice, condiments and also used to treat various types of ailments in Indian traditional system. World's about 80% population relies upon herbal products, because they have been considered as safe, effective and economical. The present study was aimed to review the ethanobotanical properties, pharmacognostic, phytochemical and pharmacological properties of *Murraya koenigii* plant. The various parts of this plant are widely used by different tribal communities. The leaves of plant are use as tonic, stomachic, carminative, internally in dysentery, vomiting. Used as anthelmintic, analgesic, cures piles, allays heat of the body, thirst, inflammation and itching. Following various claims for cure of numerous diseases, efforts have been made by researchers to verify the efficacy of the plant through scientific biological screening. A scrutiny of literature reveals some notable pharmacological activities of the plant such as activity on heart, anti diabetic and cholesterol reducing property, antimicrobial activity, antiulcer activity, antioxidative property, cytotoxic activity, anti diarrhea activity, phagocytic activity and many more medicinal values.

**Keywords:** curry leaf, ethanobotany, pharmacognosy, pharmacology, phytochemistry

## INTRODUCTION

Man uses plants in many ways to meet his basic needs food, clothing and shelter. Wild plants supply medicines, crafts and cosmetics to rural and urban communities. In addition, wild plants are the sources of income and employment to the rural areas <sup>1</sup>. Important herbal products are spices, herbal teas, functional food ingredients, medicinal raw materials, aromatic plants, essential oils, flavoring, fragrant products and dietary supplements. Plants have also been used as medicines for thousands of years all over the world. WHO estimates indicate that 80% of the population, mostly in developing countries still relies on plant-based medicines for primary care WHO 1978. The different systems of medicinal usage practiced in India, Ayurveda, Siddha, Unani, Amchi and local health traditions, utilize a large number of plants for treatment of human and animal diseases. Those plants used were called as medicinal plants. India is a country with a vast reserve of natural resources and a rich history of traditional medicine. Medicinal plants contain numerous biologically active compounds which are helpful in improving the life and treatment of disease. Compounds such as carbohydrates, proteins, enzymes, fats, oils, terpenoids, flavonoids, sterols simple phenolic compounds etc. Natural products are the source of synthetic and traditional herbal medicine and are still the primary health care system. The presence of various life sustaining constituents in plants made scientists to investigate these plants for their uses in treating certain infective diseases and management of chronic wounds <sup>2</sup>.

The traditional medicine literature describes the potential role as a source of many vitamins and a domestic remedy for many disorders like diabetes, cancer, arthritis and many others. There is a proportional increase in demand for herbal products both locally and internationally. The demand for herbal products is caused by population increase, poverty, increasing awareness of herbal products, high cost of modern medicine and limited access to trained

doctors. The type of plants and parts removed vary from one locality to another and their use depends on the local indigenous knowledge and experience present over countries. Recent research has focused on the natural plant products alternatively for disease control and cure. Medicinal plants are cheaper, more accessible to the most of the population in the world. Thus, there is need to encourage the use of medicinal plants as potential sources of new drugs. There has been as highly increased interest for herbal remedies in several parts of the world <sup>3</sup>.

Since from the beginning of this century, there has been an increasing interest in the study of medicinal plants and their traditional use in different parts of the world <sup>4</sup>. With the chemically synthesized drugs for number of diseases, natural products of plant origin has its own importance and has maintained the most important resource for developing new drugs to treat various diseases. One of the medicinally important herbs is *Murraya Koenigii*, upon which the presence of Ethanobotany and scientific importance is being reviewed.

## Taxonomy of plant

Kingdom-	Plantae
Sub-kingdom-	Tracheobionta
Superdivision-	Spermatophyta
Division-	Magnoliophyta
Class-	Magnoliopsida
Subclass-	Rosidae
Order-	Sapindales
Family-	Rutaceae
Genus-	<i>Murraya</i> J.Koenig ex L.
Species-	<i>Murraya Koenigii</i> L. Spreng.



Fig 1: Morphology of *Murraya koenigii* plant A, along with Fruits B and Flowers C.

*Murraya Koenigii*, belongs to the family Rutaceae, commonly known as curry-leaf tree, is a native of India, Sri Lanka and other south Asian countries. It is found almost everywhere in the Indian subcontinent, it shares aromatic nature, more or less deciduous shrub or tree up to 6 m in height and 15-40 cm in diameter with short trunk, thin smooth grey or brown bark and dense shady crown<sup>5</sup>. Most part of plant is covered with fine down and has a strong peculiar smell. *M. koenigii* is genus of tree, native to tropical Asia from Himalaya foothill's of India to Srilanka eastward through Myanmar, Indonesia, Southern China and Hainan. The *M. koenigii* is having grey color bark, longitudinal striations on it and beneath it white bark is present. Leaves are bipinnately compound, 15-30 cm long each bearing 11-25 leaflets alternate on rachis, 2.5-3.5 cm long ovate lanceolate with an oblique base. Margins irregularly crenate, petioles 2-3 mm long, flowers are bisexual, white, funnel shaped sweetly scented, stalked, complete, ebracteate, regular with average diameter of fully opened flower being in average 1.12 cm inflorescence, terminal cymes each bearing 60-90 flowers. Fruits are ovoid to subglobose, wrinkled or rough with glands. It is having the size of 2.5 cm long and 0.3 cm in diameter and gets purplish black when ripen. Fruits are generally biseeded. Seeds generally occur in spinach green color, 11 mm long, 8 mm in diameter and weighs up to 445 mg<sup>6</sup>.

#### 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; Gujarathi- Mitho limado.

#### Ethanobotany

*M. koenigii* is a plant which has various important uses in the traditional system of medicine in Eastern Asia<sup>7</sup>. Based on ethanomedicine, *M. koenigii* is used as a stimulant, antidiabetic and for the management of diabetes mellitus<sup>8</sup>. The plant is highly valued for its leaves an important ingredient in an Indian cuisine to promote appetite and digestion. The leaves, root and bark are tonic, stomachic and carminative. Leaves are used internally in dysentery

also checking vomiting<sup>9</sup>. Steam distillate of the leaves can be used as stomachic, purgative, febrifuge and antianemic<sup>8</sup>. Leaves are applied externally to bruises and eruption<sup>10</sup>. The leaves and roots are bitter, acrid, cooling, anti-helminthic, analgesic, it cures piles, allays heat of the body, thirst, inflammation and itching. It is also useful in leucoderma and blood disorders. An infusion of the toasted leaves in used to stop vomiting<sup>5</sup>. The juice of the root is good for pain associated with kidney. Fruits are also considered as astringent in Indo-China. Crushed leaves are applied externally to cure skin eruption and to relieve burns. The pastes of leaves are applied externally to treat the bites of poisonous animals<sup>9</sup>. The plant is credited with tonic and stomachic property<sup>5</sup>. The fruits are known to have very high nutritional values with many medicinal properties. 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<sup>11</sup>. It has also been used as an anti-periodic and many a time the powdered dry leaf, mixed with honey and juice of betel nut, is recommended in the Ayurvedic system of medicine<sup>12</sup>.

#### Pharmacognosy

The presence of important phytochemicals make the plant useful for treating different ailments and have a potential of providing useful drugs of human use. The quantitative determination of pharmacognostic parameters will help for setting standards for crude drugs. The total ash is particularly important in evaluating the purity of drugs. The pharmacognostic constants for the leaves of this plant, the diagnostic microscopic features and the numerical standards are reported, which is useful for the compilation of a suitable monograph for its proper identification. Microscopic and morphological characters were examined by pharmacognostic evaluation, which also includes the determination of leaf content, ash value, powder analysis and extractive values. Phytochemical screenings including qualitative chemical examination were also performed. The leaf had reticulate venation and dentate margin with asymmetrical base. The stomata were distributed on both the sides. Phytochemicals such as carbohydrates, alkaloids, sterols, tannins, volatile oils, saponins, anthroquinone glycosides and flavanoids are reported<sup>13</sup>. The organoleptic characters including colour, odour, taste and external features of bark of *M. Koenigii* were observed<sup>14</sup>.

Powdered leaf material was analyzed for its fluorescence with chemical reagents such as alcohol, sulphuric acid, sodium hydroxide and nitric acid. The fluorescence analysis is explained in **Table 1**.<sup>13</sup>

Treatment	Day light	UV light
Powder as such	Pale Green	Fluorescent pale green
Power in distilled water	Bluish-Green	Fluorescent Bluish-Green
Powder in absolute alcohol	Olive-green	Fluorescent Orange
Powder in 10% NaOH	Light-brown	Fluorescent Dark brown
Powder in 50% HNO <sub>3</sub>	Yellow	Fluorescent Black
Powder in 50% H <sub>2</sub> SO <sub>4</sub>	Dark Green	Fluorescent Yellowish-Green

**Table 1: Fluorescence Analysis of *M. koenigii* leaves.**

### Phytochemistry

The preliminary phytochemical screening of petroleum ether extract, ethyl acetate extract, chloroform extract, ethanol extract and aqueous extract was performed. The presence of alkaloids, flavonoids, carbohydrates, and sterol in various extracts were observed<sup>15</sup>. For the confirmation of the phyto constituents in the plant extract, various numbers of tests were performed. Test for alkaloids was confirmed by using Mayer's reagent, upon which addition to petroleum ether, chloroform, ethyl acetate, alcohol and water extracts separately showed formation of white or cream colored precipitates. Phenolic compounds were confirmed by formation of white precipitate upon addition of few drops of 5% lead acetate solution to alcoholic extracts of root. Yellow coloration of filter paper upon dipping in ammoniated alcoholic and aqueous extract indicated the presence of flavonoids. Saponins were considered to be present when the extract showed honey comb like frothing after giving a shake with sodium bicarbonate. Millon's, Biuret's and Ninhydrin's test were conducted to indicate the presence of proteins and free amino acids. When the hydro-alcoholic extract was shaken with chloroform and few drops of acetic anhydride along with few drops of concentrated sulphuric acid from the side of the tube forms the blue to brick red coloration which indicates presence of sterol and triterpenes<sup>16</sup>. The plant can be used as bitter as its bitterness is found to be 2.5 unit/gm. The plant possesses haemolytic activity. The alcoholic and aqueous extracts were screened for presence of amino acid and carbohydrates. The extracts showed the presence of amino acids viz. phenylalanine and glycine and carbohydrates i.e. galactose, ribose and fructose.

Leaves are aromatic and contain proteins, carbohydrates, fiber, minerals, carotene, nicotinic acid and vitamin C. The leaves contain high amount of oxalic acid, leaves also contains crystalline glycosides, carbazole alkaloids, koenigin and resin. Fresh leaves contain yellow colored volatile oil conversely also rich in vitamin A and calcium<sup>6</sup>. It also contains girinimbin, iso-mahanimbin, koenine, koenigine, koenidine and koenimbine<sup>17</sup>. Mahanimbine, bicyclomahanimbicine, phebalosin, coumarine as Murrayone imperatoxin etc are isolated from leaves<sup>18</sup>. Triterpenoid alkaloids like cyclomahanimbin and tetrahydromahanimbin are also present in the leaves<sup>19</sup>. Murrayastine, murrayaline, pypayafolinecarbazole alkaloids and many other chemical compounds have been reported in the leaves of *M. koenigii*<sup>20</sup>. Bark mainly contains the carbazole alkaloids as murrayacine, murrayazolidine, murrayazoline, mahanimbin, girinimbin, koenioline and xynthyletin<sup>18</sup>. The pulp of fruits generally contain 64.9% moisture, 9.76% total sugar, 9.58% reducing sugar, 0.17% non reducing sugar and negligible amount of tannin and acids. It also contains 13.35% of vitamin C. The pulp of fruits contain trace amount of minerals 1.97% phosphorus, 0.082% potassium, 0.811% calcium, 0.166% magnesium and 0.007% iron. It also contain markable amount of protein<sup>21</sup>.

### Pharmacological activities

#### *In vivo* studies

#### Vasodilating activity

Crude aqueous leaf extract of *M. koenigii* was prepared which showed a dose dependent negative chronotropic effect on cardiovascular system of frog heart preparations which might be due to its direct actions on the heart and blood vessels. Potassium ion concentration was also found to be very negligible by flame photometry, indicating no involvement of potassium ions. The aqueous leaf extract possesses vasodilatory effect which is independent of muscarinic, histaminergic and  $\beta$ -adrenergic receptor as it increased the number of drops/minute in frog hind limb perfusion experiment and also does not possess  $\alpha$ -adrenergic receptor antagonistic activity. The aqueous leaf extract showed significant effect at concentration of 1 mg/ml<sup>22</sup>. Crude ethanolic extract of fresh leaves of *M. koenigii* showed dose dependent positive inotropic effect on an isolated frog heart. The response to *M. koenigii* 62.5 - 1000  $\mu$ g was not affected in either way by theophylline, imidazole, propranolol and sildenafil. The changes in potassium and sodium concentration did not alter. The result suggested that *M. koenigii* induced positive inotropic effect possibly by increasing availability of calcium from extra cellular sites<sup>23</sup>.

#### Antidiabetic property

Mahanimbin 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 streptozotocin induced wistar rats by using pure compound at a dose of 50 mg/kg and 100 mg/kg. The possible mechanism by which the mahanimbin 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. Mahanimbin showed appreciable alpha amylase inhibitory effect as compared with acarbose<sup>24</sup>.

#### Hypocholesterolemic activity-

Hypocholesterolemic activity was checked in aged mice, which was done by using crude ethanol extract of plant leaves of *M. Koenigii*. The experiment was confirmed by observing a decrease in cholesterol level in dose dependent manner in aged mice. The dose of 500 mg/kg was found more efficient than the 300 mg/kg and was comparable with the standard cholesterol reducing agent, Simvastatin. Carbazole alkaloids a major phytochemical constituent of plant found to have various biological activities like anti-oxidant, anti-diabetic, anti-microbial, lipid lowering etc<sup>25</sup>.

#### 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<sup>26</sup>. 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<sup>27</sup>.

#### Anti Diarrheal activity

The bioassay guided fractionation of the *n*-hexane extract of the seeds of *M. koenigii* resulted in the isolation of three pure compounds of bioactive carbazole alkaloids, kurryam, koenimbin and koenine. Of the three compounds kurryam and koenimbin exhibited significant inhibitory activity against castor oil-induced diarrhea and PGE<sub>2</sub>-induced enter pooling in rats. The compounds also produced a significant reduction in gastro-intestinal motility in the charcoal meal test in Wistar rats<sup>28</sup>.

#### Phagocytic activity

The methanol extract of *M. koenigii* leaves was evaluated on human oral and cell mediated immune response to ovalbumin, phagocytic activity by carbon clearance test, nitric oxide NO release from murine peritoneal macrophages and cyclophosphamide induced mycosuppression. Phagocytic nature of macrophages was increased by the increase in production of Nitrite. Extract showed significant increase in NO production from peritoneal macrophage at 416 µg/ml and 834 µg/ml with 24% and 56% respectively. This activity was evidenced by increase in Phagocytic index in carbon clearance test <sup>29</sup>.

#### Analgesic and antinociceptive activity

The methanolic extract of leaves showed analgesic effect in hot plate model and formalin induced paw licking response in mice. The activity might be linked to the processes involved in the prevention of sensitization of nociceptors, down regulation of the sensitized nociceptors or blockade of the nociceptors at peripheral and central levels. Methanol extracts were taken at different concentrations, viz. 100mg/ml, 200mg/ml and 400 mg/ml. Among these 400 mg/ml showed prolific results <sup>30</sup>.

#### Anti-lipid peroxidative activity

The status of lipid peroxidation was investigated in rats fed with *M. Koenigii*. The concentration of melondialdehyde showed a significant decrease, while hydroperoxides and conjugated dienes were significantly increased in liver and heart. Glutathione levels in liver, heart and kidney were lowered in rats after administering this plant. Glutathione reductase, Glutathione peroxidase, Glutathione-S-Transferase, SOD and catalase activity showed a sharp increase <sup>31</sup>.

#### Radioprotective and chemoprotective activity

The study was aimed to investigate the radio protective and chemoprotective effect of *M. koenigii* methanolic extract after irradiation. It has demonstrated protection against radiation RT & cyclophosphamide CP induced chromosomal damage in vivo. Gama Radiation 4Gy produced a significant increase in the percent aberrant metaphases and different types of aberrations compared to same treated control. Radiation increased all types of aberrations like fragment chromatid and chromosome breaks, rings and dicentrics. Quantitatively, methanolic extract pretreated group showed similar aberrations only in one group. But treatment with methanolic extract of *M. koenigii* before radiation significantly reduced percentage aberrant metaphases and different types of aberrations. Thus, the study on leaf extract clearly revealed that a single dose of 100 mg/kg methanolic extract of *M. koenigii* can significantly decrease the chromosomal damage caused by irradiation and cyclophosphamide and also showed bone marrow protection <sup>32</sup>.

#### Antiamnesic activity-

Transfer latency TL was measured using elevated plus model. Standard cholinergic agent, Piracetam 400mg/kg was comparable to the petroleum ether extract of plant leaves 300 and 500 mg/kg in improving the learning and memory of aged mice and was reversed from the effect of scopolamine. A 15days pre-treatment with petroleum ether extract of leaves 300 and 500 mg/kg reversed the effect of sodium nitrite which was comparable with standard Piracetam 400mg/kg. Thus *M. koenigii* leaves extract could be said to improve the learning capabilities of the aged mice in hypoxic condition as indicated by a better performance of animals in the learning task. The results of cholinesterase assay showed that 15 days treatments with petroleum ether 300 and 500mg/kg extract of *M. koenigii* leaves remarkable reduce the brain cholinesterase activity compared with those of their control groups in aged mice. The standard, Donepezil 0.5mg/kg, reduced more cholinesterase activity <sup>25</sup>.

#### Anthelmintic activity

The anthelmintic activity was performed on adult Indian earth worm 'Pheretima posithuma'. The organism was chosen due to its resemblance with the intestine round worm parasites of human

beings. Petroleum ether and alcoholic extracts were selected for the activity and Piperazine citrate as standard. Ether and methanolic extracts were taken at 25 mg/ml, 50mg/ml and 100 mg/ml concentrations. Worms were kept under observation to notice the time taken to paralysis and death in individual worms. Paralysis was said to occur when the worms do not revive even in normal saline. Death was concluded when the worms lost their motility followed by the fading of body color. Among them alcoholic extract of plant leaves at a dose of 100 mg/ml had significant anthelmintic activity where as petroleum ether showed moderate activity <sup>33</sup>.

#### Memory enhancing

It was observed that ethanolic extract of leaves lowered serum cholesterol in mice, inhibited brain acetylcholinesterase enzyme and thereby elevated the acetylcholine concentration in brain homogenate and ultimately improved memory in aged mice. Extract was used in two different concentrations, viz. 300mg/ml and 400mg/ml. Thus, a combination of anticholinesterase and cholesterol lowering effect exhibited by leaves extract may be the factors responsible for this memory improving effect observed in the study <sup>25</sup>.

#### Wound Healing effect

Male albino rates were used to check the wound healing activity by screening with ethanolic extract of leaves of *M. Koenigii*. In the excision, wound healing model reveals that three groups which were taken for wound healing activity showed a decrease in wound area from day to day. Incision model showed a significant increase in tensile strength of the 12-day old wound due to treatment with *M. koenigii*. Thus, the leaves of *Murraya koenigii* were proved to possess significant wound healing capacity <sup>34</sup>.

#### In vitro studies

##### Antimicrobial Activity

Benzoisofuranone derivatives along with six known carbazole alkaloids and three known steroids were isolated from stem bark of *M. Koenigii*. These compounds are found to be effective in range 3.13 - 100 µg/ml concentration <sup>35</sup>. Literature survey revealed that methanolic extract of 21 plant species were screened for *in vitro* anti bacterial activity against multi resistant bacterial isolates including Gram positive and Gram negative strains. Study showed that *M. koenigii* shown maximum antibacterial activity. Staphylococcus *epidermidis* was significantly inhibited by *M. koenigii* <sup>36</sup>. Mahanimbine, murrayanol and mahanine are three carbazole alkaloids isolated from the acetone extract of the fresh leaves of *M. Koenigii*. Of these three, murrayanol showed an IC50 of 109 µg/mL against hPGHS-1 and an IC50 of 218 µg/mL against hPGHS-2 in anti-inflammatory assays, while mahanimbine displayed antioxidant activity at 33.1 µg/ml. All these three carbazole alkaloids were mosquitocidal and antimicrobial and exhibited topoisomerase I and II inhibition activities <sup>19</sup>.

##### 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. 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 <sup>37</sup>. The antioxidative properties of the leaf extracts of *Murraya Koenigii* using different solvents were evaluated based on the oil stability index OSI together with their radical scavenging ability against 1, 1-diphenyl-2-picrylhydrazyl <sup>19</sup>. 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 <sup>38</sup>.

##### Skin pigmenting

The formulation of cream of essential oil of leaf of *M. koenigii* was found to have sun protection factor. It was postulated that cream parameters complied as per official acceptance criteria's but the SPF

sun pigmentation factor for curry leaf oil cream formulation showed minimum sun protection activity for sunlight and erythema. The cream was found useful in maintaining the natural skin pigmentation or it can be used as additives in other formulations to enhance the activity <sup>39</sup>.

#### Cytotoxic Activity

The isolated carbazole alkaloid as Koenoline from root bark of *M. koenigii* exhibited the cytotoxic activity against KB cell culture system <sup>40</sup>. Carbazole alkaloids isolated from the stems of *M. koenigii* have effects on the growth of the human leukemia cell line HL-60. Also the carbazole alkaloids, mahanine, Pyrafoline-D and murrayline-I showed significant cytotoxicity against HL-60 cells and induced the loss of mitochondrial membrane potential <sup>41</sup>.

#### Anti-Tumor assay

The three cell lines were used in this investigation comprised human breast MCF-7, human cervical HeLa and murine leukemia cell lines P388. The MCF-7, HeLa and P388 cells each were cultured as monolayers in RPMI-1640, supplemented with 10.0% v/v heat-inactivated FBS, 100 U/mL penicillin and 100.0 µg/mL streptomycin. All cell cultures were grown in a humidified incubator at 37 °C in 5.0% CO<sub>2</sub> and 95% O<sub>2</sub>. The cytotoxic effects of mahanine, mahanimbicine, mahanimbine and essential oil were determined by

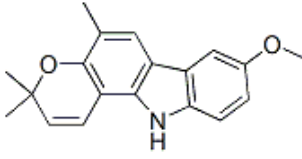
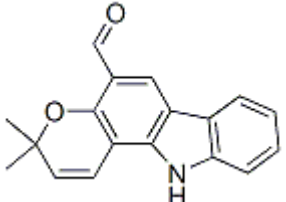
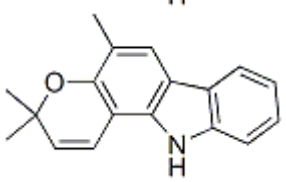
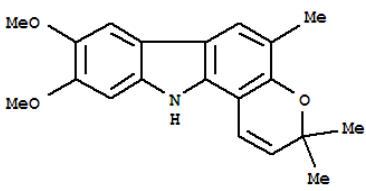
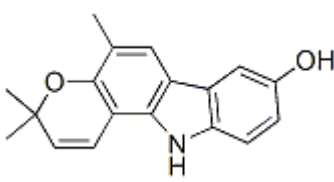
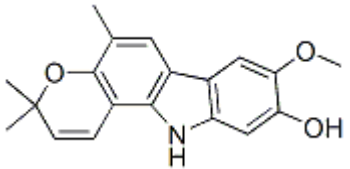
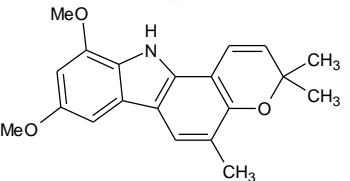
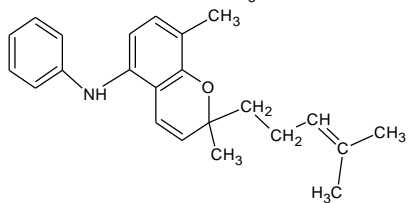
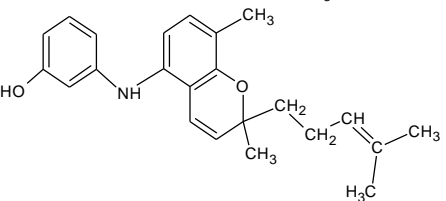
measuring conversion of 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide MTT dye. All pure compounds and essential oil were dissolved in DMSO to a final concentration of 30 µg/ml briefly, 2.0 × 10<sup>4</sup> MCF-7 cells were treated in triplicate with each pure compound and the essential oil. The same treatments were applied on 5.0 × 10<sup>5</sup> HeLa cells and 1.0 × 10<sup>5</sup> P388 cells. MTT reagent was added and cells were incubated in the dark at 37°C. DMSO was added to dissolve purple formazon crystals and a microtiter plate reader was used to measure the absorbance at 570 nm with 630 nm as the reference wavelength <sup>42</sup>.

A pure compound, Girinimbine has been isolated from stem bark of *M. koenigii*, was used to show the in-vitro anti-tumor promoting activity by measuring the percentage inhibition of induced early antigen EA of Epstein Barr virus EBV on the surface of Raji cells. Raji cells are B-human lymphoblastoids latently infected with EBV, in which the early antigen of the virus can be induced by phorbol 12-myristate 13-acetate and n-butyrate to express on the surface of cells which can be detected by immunofluorescence using human antisera of nasopharyngeal carcinoma. The study showed that the girinimbine strongly inhibited the induction of EA of EBV more than 90% when tested at 16.0 and 32.0 µg/ml. The inhibition rate was moderate when tested at 8.0 µg/mL inhibition rate 58% and low at 4.0, 2.0 and 1.0 µg/mL inhibition rates of 46, 35 and 32%, respectively. The inhibition rate at fifty percent of the compound extrapolated from the dose response curve was 6.0 µg/ml <sup>43</sup>.

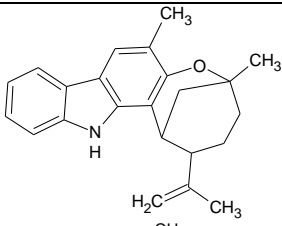
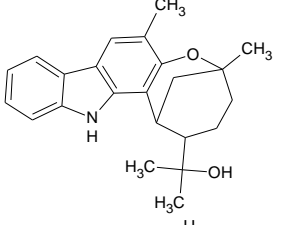
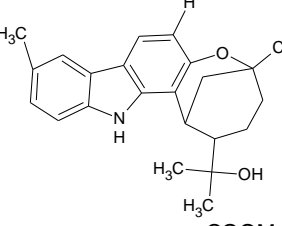
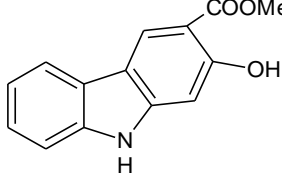
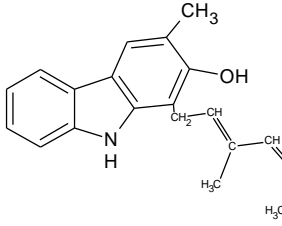
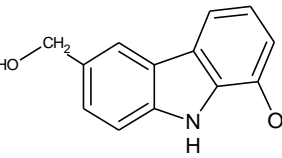
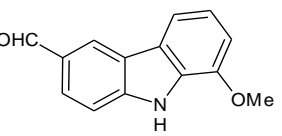
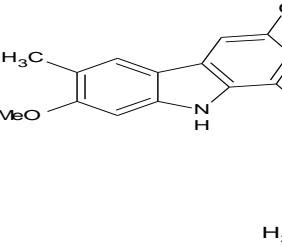
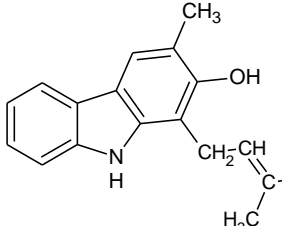
**Table 2: Pharmacological activities done on *Murraya koenigii* plant.**

Sl. No.	Pharmacological Activity	Plant part	Extract
1.	Anti-inflammatory	Leaf	Ethanol, Petroleum ether, Chloroform, methanol
2.	Anti-amnesic	Leaf	Petroleum ether
3.	Hypocholesterolemic	Leaf	Ethanol
4.	Memory enhancer	Leaf	petroleum ether
5.	Anti-helminthic	Leaf	Alcoholic
6.	Anti-bacterial	Bark, Leaf	Petroleum ether, Alcohol
7.	Anti-cancer	Stem bark	Petroleum ether
8.	Anti-diabetic	Whole plant, fresh leaf, fruit.	Aqueous, methanol
10.	Antidiarrhoeal	Seeds	n-hexane
11.	Anti-fungal	Leaf	Petroleum ether, alcohol and acetone
12.	Radioprotective and chemoprotective	Leaf	Methanol
13.	Analgesic and Antinociceptive	Leaf	Methanol
14.	Anti-oxidant	Leaf	Methanol and Aqueous
15.	Cardiovascular	Leaf	Aqueous
16.	Skin pigmentation	Leaf	
17.	Anti-lipid peroxidative	Leaf	Methanol
18.	Anti-tumor	Leaf	Petroleum ether
19.	Anti-ulcer	Leaf	Aqueous
20.	Cytotoxicity	Roots, stem	Aqueous
21.	Wound healing activity	Leaf	Ethanol
22.	Phagocytic activity	Leaf	Methanol

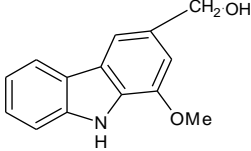
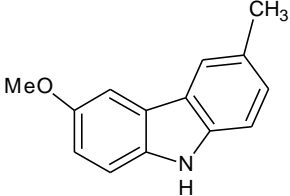
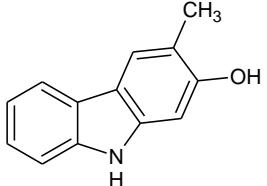
Table 3: Chemical constituents of *M. koenigii* with tested pharmacological activities.

Sr no	Constituent	Constituent structure	Activity
1	Koenimbine		Anti- diarrhea
2	Murrayacine		Anti-microbial
3	Girinimbine		Anti-tumor
4	Koenimbidine/Koenidine/Koenigicine		Anti- diarrhea
5	Koenine		Anti-oxidant
6	Koenigine		Anti-oxidant
7	Mukonicine		Anti-oxidant
8	Mahanimbine		Cytotoxicity, Anti-oxidant, Anti-microbial, Anti- diabetic and Hyperlipidemic
9	Mahanine		Cytotoxicity, Anti- microbial, Anti cancer

10	Mahanimbicine		Anti-oxidant, Anti- microbial, Anti- diabetic and Hyperlipidemic
11	Murrayacinine		Anti-oxidant, Anti- microbial, Anti- diabetic and Hyperlipidemic
12	Isomahanimbicine/ Mahanimbicine		Anti-oxidant, Anti- microbial, Anti- diabetic
13	Mahanimboline		Cytotoxicity, Anti-oxidant, Anti- microbial, Anti- diabetic and Hyperlipidemic
14	Isomahanine		Cytotoxicity, Anti-oxidant, Anti- microbial, Anti- diabetic and Hyperlipidemic
15	Mukoeic acid		Anti-oxidant
16	Murrayanine		Anti-oxidant
17	Mukonine		Anti-oxidant
18	Isomurrayazoline		Anti-amnesic, immunomodulatory

19	Cyclomahanimbine or Curryanine		Anti-inflammatory
20	Murrayazolinine		Anti-leukemial
21	Isomurrayazolinine		Nil
22	Mukonidine		Nil
23	Mahanimbicol		Nil
24	Mukoline		Nil
25	Mukolidine		Nil
26	Murrayanol		Anti-inflammatory, Anti-microbial
27	Girinimbicol		Anti-trichomonal



28	Koenoline		Cytotoxicity
29	Glycozoline		Antifeedant, Antiinflammatory
30	3-methyl carbazole 2-hydroxy-3 methyl carbazole		Anti-oxidant

## CONCLUSION

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. They obviously deserve scrutiny on modern scientific lines such as phytochemical investigation, biological evaluation on experimental animal models, toxicity studies, investigation of molecular mechanism of actions of isolated phytoprinciples and their clinical trials. It is a best classical approach in search of new lead molecules for management of various diseases. Thorough screening of literature available on *Murraya Koenigii* depicted the fact that it is a popular remedy among the various ethnic groups, Vaidyas, Hakims and ayurvedic practitioners for cure of variety of ailments. Following the traditional and folk claims, very little efforts have been made by the researchers to explore the therapeutic potential of this plant. 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. Till other parts of plant such as seeds, leaves and seed oil which are documented to possess important medicinal virtues, are not explored scientifically for their biological potential. In future study, the isolated principles from curry leaf needs to be evaluated in scientific manner using scientific experimental animal models and clinical trials to understand exact molecular mechanism of action, in search of lead molecule from natural resources.

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