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REVEALING THE MEDICINAL SIGNIFICANCE, INNOVATIVE ASPECTS, CURRENT EXISTING CHALLENGES, AND PHARMACOLOGICAL ATTRIBUTES OF MURRAYA KOENIGI

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Abstract

Murraya koenigii has been used as a traditional medicinal plant due to the presence of bioactive compounds makes them effective for therapeutic applications. It belongs to family Rutaceae and widely found in tropical and sub-tropical regions. It is commonly known as "Meethi Neem" or "Curry Tree" with small deciduous shrub reaching up to 2.5 to 6 meters of height. It is a rich source of bioactive compounds such as alkaloids, sesquiterpenes, flavonioids, koenine, β-sitosterol, carbazole, koenidine, koenidine, girinimbine, girinimbiol, and terpenes. It has been used in the treatment of various diseases such as piles, itching, inflammation, edema, dysentery, and fresh wounds. It also has high medicinal potentials such as antipyretic, anti-obesity, anticarcinogenic, antifungal, antibacterial, antioxidant, hypolipidemic, antihypertensive, larvicidal activities and hepatoprotective, gastroprotective, cardioprotective effects. Moreover, this plant had not any toxicological or adverse effects on the health. Therefore, it can be used for treatment a number of different infectious diseases. This review illustrated the medicinal significance, pharmacological applications, and novel therapeutic aspects of Murraya koenigii.

1. INTRODUCTION

Murraya koenigii is commonly known as "Meethi Neem" or "Curry Tree". It is small deciduous shrub reaching up to 2.5 to 6 meters of height. It belongs to family Rutaceae and widely found in tropical and sub-tropical regions [1]. It can widely be found throughout the sub-continent Asia. It is native to Pakistan, India, Sri Lanka, Bhutan, Nepal, and Thailand. It can be easily grown in any fertile yard with surplus availability of shade, naturally grows

well in temperate in the range about 18-25°C. Cultivation of curry plant is easy, and eco-friendly [2]. Due to adverse side effects and high cost, synthetic medicines and traditional methods of medications such as chemotherapy, immunotherapy, surgery, health practitioners as well as general public now mostly adopting herbal medicines because these are safe to use and pocket friendly [3]. A large proportion of population in developing countries approximately 70-90% rely on herbal remedies for the treatment of various diseases, wounds, venomous bite, poisons, and surgeries. Particularly, the poorest nations of Africa account for a large number in this sense. Even third biggest world economy-Germany could produce about 90% of medical drugs using natural products. Another example of herbal products user is China that 40% of healthcare units are structured based on green herbal products. In Fresh as well as dried leaves retain a significant level of aroma which enables it to be imparted in several flavoring and seasoning dishes. Several ointments such as soaps, perfume, and bruises, seem to be incomplete without the fragrance of its oil [2,3].

The major bioactive compounds that found in the M. *koenigii* are Gurjunene, P-elemene, O-phellandrene, and P-caryophyllene [4]. From roots to the shoot tips, every part of this plant is used in synthesizing numerous traditional medicines (Ayurveda). Beyond its application as taste enhancing ingredient, curry leaves retain potential of a medicinal use. It is cultivated usually for its green leaves which are characterized to possess blood purifying, antiemetic, antidiarrheal, dysentery inhibition, febrifuge, and tonic properties. Ethnobotanically, it has been used as raw drugs in the treatment of various diseases such as piles, itching, inflammation, edema, dysentery, and fresh wounds. The roots reserve several chemical compounds which resemble with the paracetamol and is helpful in curing body aches. Its bark acts as antidote to snakebites [5]. Recently, several phytochemicals have been extracted from its leaves including alkaloids such as mahanine, O-methyl murrayanine A, O-methyl mahanine, isomahanine, bismahanine, bispyrayafoline, koenine, koenigine, koenidine, koenidine, girinimbine, and girinimbiol. In addition to it, other phytoconstituents included the riboflavin, niacin, scopotin, thiamine, 6', 6' dimethyl 5-hexene, 5,8-dimethyl furanocoumarin, β-sitosterol, carbazole, vitamin C, iron, phosphorous, calcium, oxalic acid, and carotene [6]. Dipentene, caryophyllene, D-sabinene, D-α-terpinol, D-α-pinene and di-α-phellandrene are essential oils in Murraya [7,8]. These phytochemicals have shown antipyretic, anti-obesity, immunomodulatory, anticarcinogenic, antifungal, antibacterial, antioxidant, antilipo peroxidative, hypolipidemic, antihypertensive, larvicidal activities and retain cholesterol lowering, hepatoprotective, gastroprotective, cardioprotective, cardioprotective effects. Figure 1 shows the pharmacological properties of *Murraya koenigii* L. Moreover, this plant had not any toxicological or adverse effects on the health of experimental animals [9].

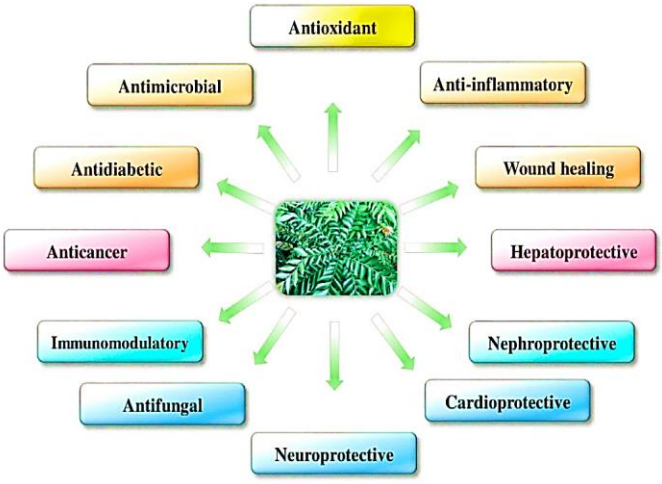

Fig 1. Pharmacological properties of *Murraya koenigii* L bioactive compounds.

Furthermore, extensive investigations are needed to explore it's *in vivo* and *in vitro* screenings, bioavailability and mechanism of drug delivery and optimization. This review article offers detailed discussion about pharmacological applications of *Murraya koenigii* based upon different. Scientific researchers and medical practitioners may get new insights and recommendations about developing and utilizing new medicines from active biomolecules present in this medicinally important plant [10].

2. Potential for Revealing Morphological Features

The main stem is identified as greenish to brownish with many dark spots. Its thin bark on subject to eruption in longitudinal direction exposing out the white wood beneath. The morphological features of *M. koenigii* is shown in Figure 2 (A-D). Compound leaf is extipulate, contain about 24 individual leaflets pinnately extending up to 30 cm length [9]. Reticulate venation expands about 4.9 cm long lanceolate, and 1.8 cm broad holed by 0.5 cm long petiole. Floral characteristics comprised of the white, complete, embrocated, regular, actinomorphic, pentamerous, hypogenous, bisexual, funnel-shaped flowers with sweet scents. Average diameter of a fully opened flower is 1.12 cm. A bunch of flowers are stalked on a large inflorescence, a terminal cyme, bearing a green persistent, 5-lobed calyx alongside an inferior pentapetalous white corolla (lanceolate, about 5mm long). Reproductive parts consist of inferior, dorsifixed polyandrous androecium with 10 stamens arranged into circles of five each. Smaller stamens extend up to 4 mm while longer ones reach up to 5-6 mm [10]. Gynoecium is 5 to 6 mm long with sticky bright stigma and short style enrooted by superior ovary which turns into black shining surface, round to oblong fruit which varies in length from 1.4 to 1.6 cm and 1 to 1.2 cm in diameter. One fruit bear one seed which is a tiny granule of 11 mm length and 8 mm in diameter. Flowering and fruiting season is between December to July. The growth and development of this plant depends upon the available external conditions such as may gain height as much as 6 feet in warm but humid regions while it may also be grown in a pot as a small plant. Pinnate leaves are arranged in opposite slender branchlets and release a pungent smell. Fragrant flowers are succeeded by blackish berries in summer [11].

Fig 2. Morphological features of *M. koenigii* (A=Shoot, B=Fruits, C=Leaves, D=Seeds).

3. Potential for Revealing Anatomical features:

Murraya koenigii L. is characterized by distinguished unicellular appendages originated from obliterated lumen, petiole is filled with parenchymatous pith, midrib is supported by long pericycle fibers and a matrix of calcium oxalate crystals [12]. Large cruciferous stomata exist throughout the lamina. The extract of *M. koenigii* fluoresces brownish black but turns into yellowish white on treatment with the methanolic sodium hydroxide and emits chocolate fluorescence mounted on nitrocellulose. The vascular system in roots includes tetrarch or pentarch stele with concentric grains of parenchyma. Steam distillation of fresh leaves under high pressure yields significant number of volatile oils which can be used as fixative. The edible oil yields 0.76 % yellow volatile

oils which emits neroli-like smell. In transverse section, it exhibits dorsi-ventral structure. Epidermal cells vary in shape from cubic to tangentially elongated form. In the upper epidermis, cells are mostly polyhedral. Midrib bears unicellular trichomes [13]. Two palisade layers are surrounded by anomocytic stomata placed irregularly while inner spongy parenchymatous tissue contains irregularly arranged rectangular or isodiametric cells. Ground tissue consists of 1 to 3 layers of thin, polygonal collenchyma cells submerged in prism-shaped calcium oxalate crystals and large, circular secretory canals. An arc of xylem is prominently set around the phloem which is further aligned with the fibers of pericycle. These features are the main identifying microscopic structures [14].

4. Botanical and bioactive illustrations

The nutritional composition of *Murraya koenigii* leaves is shown in Table 1. Its leaves extract comprised of carbohydrates (39%), proteins (8%), fats (6%), crude fibers (6%), moisture content (23%), and ash (15%) [15]. In addition to primary macromolecules, *M. koenigii* is a huge source of secondary metabolites. All major classes of secondary molecules have been screened out in leaf samples (mg per 100 g) including alkaloids (1.9), flavonoids (7.43), phenols (4.25), saponins (2.50), tannins (0.86) and glycosides (0.11). Further microanalysis revealed the presence of multivitamins and other essential minerals such as ascorbic acid (vitamin C, 0.04), β-carotene (vitamin A 6.04), thiamin (vitamin B1, 0.89), riboflavin (vitamin B2, 0.09), niacin (vitamin B3, 2.73), and α-tocopherol (vitamin E, 0.03). Among minerals, calcium, magnesium, iron, phosphorous, potassium, sodium and zinc exist as predominant elements [16].

Table 1. Nutritional composition of *Murraya koenigii* leaves

Energy	**423 kcal**
Proteins	14 g
Carbohydrates	54 g
Fats	15g
Vitamin A	30 mg
Vitamin C	8 mg
Calcium	626 mg
Iron	32 mg

Chromatographic and spectroscopic techniques assisted in the identification of several biologically active compounds viz: alkaloids, flavonoids, terpenoids, polyphenols, coumarins, and essential oils [17]. Figure 3 shows the structure of some bioactive compounds from of *Murraya koenigii* L. Hydro distilled extracts subsequently subjected to GC-Mass chromatography resulted in the isolation of about 100 chemical compounds from the essential oil of Murraya, few main of these are allocimene, α-terpinene, β-ocimene, elemol, linalool, geranyl acetate, neryl acetate, limonene, bornyl acetate, terpinene-4-ol, γ-terpinene, α-humulene, aromadendrene, β-elemene, juniper camphor, 2-nephtalenemethanol, spathulenol, viridiflorol, and trivertal. The composition of the essential oil varied on different geographical locations and climatic conditions [18].

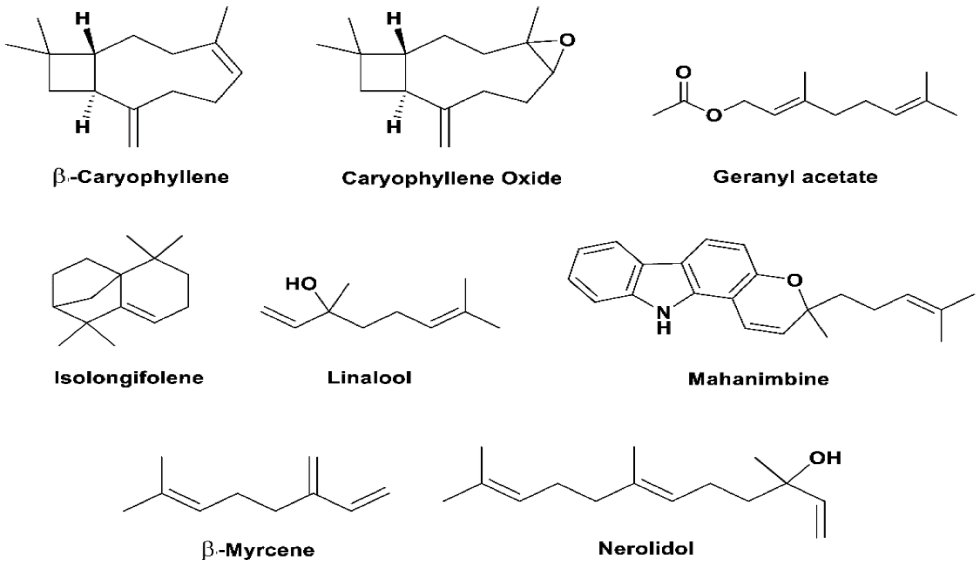

Fig 3. Shows the structure of some bioactive compounds from of *Murraya koenigii* L [18].

Particularly, more than fifty pharmacologically active carbazole-type alkaloids have been obtained from *Murraya koenigii* L. Polyphenols inhibit the growth of harmful bacteria in the elementary canal and maintain blood sugar levels in an optimum range [17,18]. A carbazole alkaloid, mahenine, isolated from the leaves of *M. koenigii* and was reported in down regulation of cell survival factors by activating caspases-3 through mitochondrial dependent pathway and disruption of cell cycle inducing apoptosis in human myeloid cancer cells (HL-60). Koenigine along with its monomer koenigine were obtained from its dry leaves. Girinimbiol and girinimbine exhibiting hypoglycemic and hepaprotective effects have been derived from the methanolic extracts of *M. koenigii* leaves. Underground parts (roots) have depository of an alkaloid such as murrastifoline. Stem bark also yields a numerous concentration of benzisofuranone and steroids which were evaluated for antimicrobial activity with a minimum inhibitory concentration about 3.13 to 100 µg/ml. Seeds of *M. koenigii* are rich source of xanthotoxin, isobyakangelicol, and minor furocoumarins [18]. Its essential oil is a rich source of monoterpene and sesquiterpenes including α-terpinene, β-ocimene, linolol, and terpinene-4-ol. Mahanimbinine, another terpenoid alkaloid has been isolated from this medicinal plant. Few novel terpenoids extracted are Mahanimbicine and bicyclomahanimbicine. The extract of Spreng II reported to contain mahanimbimbidine, cyclomahanimbicine, and bicyclomahanimbicine. The roots of *M. koenigii* reserve the important secondary metabolites such as 9-formyl-3-methylcarbazole and 9-carbethoxy-3-methylcarbazole which showed cytotoxic effects against Adriamycin resistant P388 leukemia cell lines and melanoma B16 in mouse [15,17]. The root extracts provide a bioactive agent, 2-methoxy-3-methyl-9H carbazole that is used to cure infections of dermatophytes, against Tinea infections. Several bioactive compounds such as aromadendranol and selimen-4-α-7-β-ol. Dichloromethane extraction of the leaves furnished the availability of antioxidants such as O-methyl mahanine, O-methyl murrayamine, koenimbine, bispyrayafoline, bismahanine, isomahanine, and bi pyrano 9,9'-dihydroxy bis, retaining scavenging activity against 1,1-diphenyl-2 picryl hydrazyl [DPPH] free radicals and these compounds characterized for oil stability index. A prolonged oil stability index equivalent to α-tocopherol and BHT33 has been observed by another carbazole alkaloid, bismurrayafoline-E extracted from the ethyl acetate soluble fraction and methylene chloride extract [18].

5. Nanotechnology role

In addition to producing single metallic nanoparticles, a number of studies were reported using different plant extracts to produce bi-metallic

NPs. For instance, a recent study reported the environmentally friendly synthesis of Ag/ZnO bimetallic NPs. After cleaning, following filtering, 300 mL of water was used to boil 10 g of dried leaves for 15 minutes at 100 °C. After that, extract was stored for later use in a chilly place [19]. To make NPs, 30 mL of plant extract was dissolved in 80 mL of ethanol while being continuously agitated. A solid product was made by mixing 0.47 g (0.025 mol) of zinc hexahydrate. The Ag/ZnO NPs were created following two hours of drying at 80 °C in a hot oven. TEM which confirmed that the average particle size was between 13 and 18 nm, SEM which confirmed that the synthesized NPs were spherical, EDX, and XPS which confirmed the presence of Ag, Zn, and O in synthesized NPs were among the characterization techniques to describe the NPs [20].

Different studies were reported about the silver nanoparticles and their several uses, including heavy metal ion detection, photocatalytic degradation, and antibacterial [21]. Because they contain several phytochemicals that stabilize the NPs, the leaves are essential for the synthesis. In order to create the NPs, leaf extract was first made. The leaves were cleaned using tap water or double-distilled water and then let to dry in the shade. The dried leaves were crushed into a powder, and 100 milliliters of distilled water was combined with 10 grams of the powdered leaves. After that, this solution was heated to 60°C for almost two hours while being constantly stirred. After cooling and filtering the heated solution, 5 mL of plant extract was gradually added to the 1 mM silver nitrate solution precursor solution. The formation of silver nanoparticles was confirmed when the mixture's vivid yellow color became reddish brown. The NPs were centrifuged at 1000 rpm for around 15 minutes in order to get a pure result [19, 20, 21]. The NPs were also washed with distilled water before being dried at 80 °C for a few hours. The process that produces silver nanoparticles is shown in Fig. 4. The synthesized NPs were characterized using a variety of analytical techniques. The average size of spherical silver nanoparticles was determined by TEM to be around 18 nm. UV spectroscopy confirmed the formation of silver nanoparticles by showing a peak at 419 nm. The stability of NPs was further reinforced by the negative value of the zeta potential [22].

Using the disc diffusion approach, the antibacterial efficacy of Ag NPs against both gram positive and gram negative microorganisms can be investigated. The antibacterial activity is influenced by the NPs' size and concentration. NPs can more easily enter bacterial cell walls and kill cells when they are smaller in size. Likewise, a greater antibacterial impact with higher NP concentrations. The nanoparticle exhibited greater antibacterial action against *S. aureus* and other gram-positive bacteria [23,24].

6. Pharmacological applications of *Murraya koenigii* L

It is used for treatment of different diseases such gastric cancer by inhibiting the growth of proliferating cancerous cells [25]. It is helpful for improving the eyesight, and diarrhea [26]. It is also beneficial for hair growth by stimulating the formation of follicles [27].

Methanol, chloroform and hexane extracts have been reported to exhibit antimicrobial activities against gram positive, gram negative bacteria. Distinctive inhibition zones of Murraya extracts against *Escherichia coli*, *Staphylococcus*, *Proteus*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Streptococcus* were shown comparable to antibiotics The carbazole alkaloid and benzisofuranone derivatives obtained from the bark of *Murraya koenigii* possess antibacterial activity [28]. The essential oil obtained from the leaves of M. *koenigii* reported to show some antibiotic effects against several bacterial strains like *Pasteurella multicide, Staphylococcus aureus, Bacillus subtilis, Corynebacterium pyogenes, and Proteus vulgaris*. The refined oil is highly potent against these germs even at dilution of 1:500. The fresh leaves extract in acetone gives fractions of carbazole alkaloids known as mahanine, mahanimbinine, and murrayanol retain the antimicrobial, topoisomerase I and II inhibition, and mosquitocidal activities. The roots of *Murraya koenigii* showed substantial antimicrobial activity against *Staphylococcus aureus* [29].

The essential oil, obtained from ethanolic extracts of leaves showed antifungal effects against *Colletotrichum falcatum*, *Candida albicans*, *Aspergillus fumigatus*, and *Aspergillus niger*. It is used in making various medicines for curing the skin infection due to antimicrobial properties of leaves [30]. A concentration of 250 ppm

to 900 ppm petroleum ether and acetone extracts of leaf have been tested positive for activity against *Microsporum gypseum*, and *Rhizoctonia solani* [31].

The leaf extract of *M. koenigii* exerts a protective effect in streptozotocin induced diabetic rats by inhibiting antioxidant defense system of pancreas and plasma β-cells [32]. The leaf extracts can be served along with spices as a potential antidiabetic diet as these were proved to retain the some hypoglycemic effects. The antihyperglycemic activity was assessed in a study in which the leaf extracts demonstrated a significant reduction in glucose levels of blood by 13.1%, 16.3%, 21.4%, and 3.2%, 5.58%, 8.21% for mild and moderate diabetes caused by administration the alloxan in rats [33]. Moreover, oral administration of ethanolic extract for a month proved to lower the concentration of sugar, urea, uric acid, creatinine, and glycosylated hemoglobin in the treatment groups of mice [34, 35].

Various extracts of *M. koenigii* leaves in different solvents provided significant amounts of radical scavengers along with prolonged oil stability index [36]. Mass spectral lines and 1H and 13C NMR depicts the presence of five carbazole alkaloids Mahanimbine, Mahanine, Mahanimbicine, Bismurrayafoline, and Euchrestine in the methylene chloride (CH2Cl2) solution. The extract of *M. koenigii* proved to be potent therapeutic agent by eliminating over concentration of nitric oxide (NO) and 1-1-diphenyl 1-2-picrylhydrazyl (DPPH) [37, 38]. The aqueous solution of Murraya leaves mitigates the toxicity of cadmium. Among various leaf extracts, oleoresin gave maximum antioxidant activity of 83.2% at 100 ppm concentration, while methanol and aqueous extracts rated 16.7% and 11.3%, respectively. A significant scavenging activity were also observed by ethanolic extracts in DPPH assays [39].

Table 2. Sources, bioactive compounds and clinical findings of *Murraya koenigii* L. Spreng.

Plant organ	Extraction method	Extracted compound	Bioactivity	Findings	References
Leaves	Solvent extraction using ethanol or methanol	Murrayanine, quercetin and kaempferol, gallic acid	Anti-inflammatory activity	Treat arthritis and muscle pain and reduce pro-inflammatory cytokines.	[40]
Leaves, bark	Steam distillation for essential oils and solvent	Mahanine, murrayanol, girinimbine, linalool	Antimicrobial activity	Significant inhibition of growth against *S. aureus*, and *E. coli*.	[41]
Leaves	Ethanolic or methanolic extraction	Curine, murrayanine, limonene, chlorogenic acid	Neuroprotective activity	Protect neuronal cell death and improve cognitive function in animal models.	[42]
Leaves, stem	Methanol extraction	Koenimbine	Antidiabetic activity	Regulate blood sugar levels, management of hypertension and insulin-resistant diabetes.	[43]
Leaves, Bark	Methanolic extraction	Mahanine, quercetin, β-caryophyllene	Anti-cancer effects	Inhibit cancer cell's growth, induce apoptosis, reduce metastasis	[44]
Leaves	Methanolic extraction	B-Sitosterol	Cholesterol-lowering properties	Contribute to cardiovascular health by lowering LDL cholesterol and increasing HDL cholesterol	[45]

The leaf extract of Murraya sustained with specific metabolites play substantial role against neurodegenerative disorders (ND). Aluminium stress in rats was counteracted by the oral administration

of aqueous extract of curry leaves (100, 200, 400 mg/kg of body mass) and it proved reduce oxidative damage by ameliorating Catalase efficiency (Glutathione reduced) and lipid peroxidation [46]. Ethanolic leaf extract improves memory in rats with chronic partial global cerebral ischemia and prevents aging in diabetic rats. Mahanimbinine present in leaf extract assists in reducing lipopolysaccharide-induced inflammation [47].

Several clinical trials have elaborated potential of bioactive compounds in leaf extracts of *Murraya koenigii* as competent anticancer agents against colorectal cancer and HeLa cells [44]. The active constituents such as koenimbine, mahanimbine, girinimbine obtained from the leaves and stem of curry tree retain the ability to modulate many dysregulated oncogenic signaling pathways evidenced through a couple of scientific investigations [45]. Figure 4 shows the mechanism of apoptosis induced by *Murraya koenigii* L in cancer. Suppression of cancer is done by controlling activation and inhibition factor of cell divisions, growth and apoptosis. These herbal remedies reported to inhibit proliferations in breast cancer cells with IC_{50} 14.4 µg/ml. Cytotoxicity of HL-60 cells was significantly decreased on bioavailability of mahanine, murrafoline-I, and pyrafoline-D [46, 47]. Girinimbine demonstrated higher IC_{50} rate of 19.01µM against hepatocellular and lung cancer cells revealed through microtetrazolium assays. Downregulation of Akt/mTOR and inhibition of glycoprotein in colorectal and lung cancer are key steps in context to anticancer activity which are assisted through active participation of murrayazoline and methenamine, respectively [48].

The administration of normal dose, equivalent to human routine consumption, of curry leaves could not showed any adverse actions in rats [49]. No severe alterations observed in physiological and histopathological processes in the liver of rats during that herbivorous mode of nutrition. All the blood constituents like red blood cells (RBC), white blood cells (WBC), differential counts, total counts, concentration of blood constituents such as serum electrolytes, hemoglobin, blood urea, alkaline phosphatase, fibrin, serum proteins, albumin-globulin ratio, glycosylated hemoglobin, glutamic oxaloacetic transaminase, and glutamic pyruvic transaminase were tested to be in normal range [49].

A controlled experiment conducted for 90 days in standard laboratory environment evinced that addition of curry leave spice in the feed of albino rats regulated biochemical mechanisms leading to substantial health benefits including reduction in total serum cholesterol, LDL and VLDL, control over lipoproteins secretion, and upregulation of Lecithin Cholesterol Acyl Transferase activity and optimized HDL secretion [50]. A sharp increase the activity of Catalase (CAT), Superoxide dismutase (SOD), Glutathione peroxidase (G-POD), Glutathione reductase, and Glutathione-S transferase significantly checked the lipid peroxidation damage by lowering the levels of malondialdehyde and glutathione in kidney, liver and heart [50].

The leaves of curry plant also show anti-inflammatory activity against *Trichomonas gallinae*. The root cause of this has been indicated as antihistaminic activity as well as mast cell stabilization [51]. In another trial, carrageenan-induced paw edema in rats was mitigated by the molecular action of ethanolic extract of curry leaf. Furthermore, a concentration of 300 mg/kg to 400 mg/kg acts like antihistamines and stabilizes mast cells. The leaf extract also possesses analgesic properties as it relieves pain induced by intraperitoneal acetic acid and subplantar formalin injection in rats. Methanol extract regulates adenosine triphosphate sensitive K+ channels and hence reduces glutamate-induced pain. In another scientific discovery murrayakonine-A and O-methylmurrayamine revealed their potential as anti-inflammatory agents by blocking the release of tumor necrosis factor alpha (TNF-α) and interleukin-6 [51].

In another study, male Wistar rats fed ethanol extract for 30 days observed to lose body weight, control over cholesterol, triglycerides, and glycemic levels. Aqueous extract of leaves (at a dose of 250 & 400 mg/kg) prevents gastric ulcers induced by pylorus ligation models and non-steroidal anti-inflammatory drugs [52].

The chronic liver complications have been tested to be remediated through herbal treatment by administration of water extracts of curry leaves. That kind of medication proved to be as effective as standard drug L-aspartate and L-ornithine. Carbazole alkaloids such as mahanimbinine, girinimbine, isomahanimbine, mahanine, and murrayazoline present in the plant extracts are major counterparts to

ethanolic liver toxicity [53]. Ethanol extract of *Murraya koenigii* applicated in incision and excision rat models evidenced to reported to inhibit proliferations in hepatic cancer cells [54].

7. Current challenges and opportunities

There are some challenges still exist in the formation of herbal plants. Develop the precise formulations and SOPs to enhance the safety and efficacy in commercial and clinical applications [55]. Create guidelines and protocols for good manufacturing practices (GMP), quality control and export standards for synthetic drugs obtained from *Murraya koenigii*. Use computational machines for screening the bioactive compounds for the purpose of incorporation in drug development. A detailed profiling of chemical ingredients, pathways of metabolic reactions and mechanism of action should be investigated in order to completely harness the health benefits of active compounds [56]. Mix the curry leaf extracts with the raw materials of other herbs to prepare powders, tinctures, capsules and teas targeting specific health issues such as cardiovascular adjustments and blood glucose regulation. Promote and encourage the large-scale cultivation and organic farming practices of this plant to maintain the potency and purity of the leaves and preserve genetic variability. Educate societies about adopting holistic approaches to add the curry leaves into daily diets for their nutritional and medicinal health [57].

8. CONCLUSION AND FUTURE PERSPECTIVES

Murraya koenigii L. holds a significant ethnobotanical and advanced pharmacological importance. It has long primitive history of application as a culinary herb and making of traditional medicines for therapeutic properties including, anti-inflammatory, anti-diabetic, anti-microbial, and antioxidant effects. Discovery of bioactive compounds including carbazole alkaloids, flavonoids, and essential oils through advanced laboratory procedures has revealed its medicinal value as a potential source of combating chronic disorders such as cardiovascular problems, diabetes, obesity, hypertension and cancer. The recent studies uplift the biological status of this plant in terms of pharmacological, nutraceutical and nutritional applications. There is limited in vitro and in vivo studies about utilization of this plant that needed to address in future studies. The formulation of new medicines from active biomolecules presents in this medicinally important strategy for therapeutic applications. Nevertheless, the historically recognized identity and rapidly growing support and evidence of medicinal properties, there still remains a need to bridge the gap between traditional homeopathic knowledge and current scientific validation. So, it is crucial to integrate its full capacity into discovery and development of new standardized drugs.

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