Review Article

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A REVIEW ON *MURRAYA KOENIGII* AND MAHANIMBINE ACTIVITY AGAINST OBESITY

Shikha Kumari *
M. Pharm Pharmaceutics, Chandigarh Group of Colleges, Landran, Mohali, Punjab, India

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***Corresponding author**
E-mail: siyasinghshikha249@gmail.com

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ABSTRACT

Murraya koenigii, commonly known as curry leaf, is a medicinal plant widely recognized for its diverse pharmacological properties. Among its bioactive constituents, mahanimbine, a carbazole alkaloid has garnered significant attention for its potential anti-obesity effects. Obesity, a global health concern, is associated with metabolic disorders, including diabetes, cardiovascular diseases, and inflammation. Recent studies highlight mahanimbine's ability to regulate lipid metabolism, suppress adipogenesis, and enhance energy expenditure, making it a promising candidate for obesity management. Additionally, *Murraya koenigii* extracts exhibit antioxidant, anti-inflammatory, and hypolipidemic properties, further contributing to metabolic health. This review provides a comprehensive analysis of *Murraya koenigii*, with a specific focus on mahanimbine's molecular mechanisms in combating obesity. It explores its role in modulating key signaling pathways, including AMPK activation, adipocyte differentiation, and thermogenesis. Furthermore, we discuss preclinical and in vivo findings that support mahanimbine's efficacy as a natural anti-obesity agent. While the therapeutic potential of *Murraya koenigii* and its alkaloids is promising, challenges such as bioavailability, dosage optimization, and clinical validation remain crucial areas for future research. Understanding these aspects may pave the way for the development of novel nutraceuticals or pharmacological interventions targeting obesity and metabolic disorders. This review aims to bridge the gap between traditional knowledge and modern scientific advancements, emphasizing the need for further studies to establish the clinical relevance of *Murraya koenigii* -derived compounds in obesity management.

Keywords: *Murraya koenigii*, Mahanimbine, Obesity, Lipid metabolism and Adipogenesis

INTRODUCTION

Obesity is a medical condition characterized by an increase in both the size and number of fat cells in the body. It is a long-term disorder that has been officially recognized as a disease by the World Health Organization (WHO) and various other national and international health organizations. While obesity is easily identifiable by both medical professionals and the general public, there is still no universally accepted clinical definition. The Obesity Medicine Association defines it as a chronic, relapsing, and multifaceted neurobehavioral disease, where excessive body fat leads to dysfunction in adipose tissue and abnormal physical forces from fat mass, resulting in metabolic, biomechanical, and psychosocial health issues. The World Health Organization (WHO) defines overweight as having a Body Mass Index (BMI) of 25 kg/m² or higher, while obesity is classified as a BMI of 30 kg/m² or above. Over the years, the prevalence of overweight and obesity has been on the rise, with a significant increase among children and adolescents (ages 5–19), growing from 4% in 1975 to 18% in 2016 [1-3]. Data from the National Family Health Survey (2019–21) indicates that 13.85% of the population is obese, while 57.71% experience abdominal obesity [4]. The NFHS-5 study revealed that abdominal obesity is prevalent among 40% of women and 12% of men in India. The data further indicates that among individuals aged 30 to 49, approximately 5 to 6 out of every 10 women exhibit abdominal obesity [5]. Abdominal obesity is typically measured using waist circumference, with values exceeding a certain threshold signaling a higher risk of health complications due to visceral fat accumulation. Research suggests that individuals of Asian descent have a genetic tendency to store more fat in the abdominal region [6]. Globally, obesity has reached alarming levels, with its prevalence escalating to the point of being considered a public health crisis [7]. While obesity was once considered a major concern in Western nations, it has now become a widespread global health issue, particularly affecting regions such as South Asia [8]. The WHO identifies obesity as a significant risk factor for numerous noncommunicable diseases, including cardiovascular conditions, stroke, type 2 diabetes, and various forms of cancer, such as those affecting the endometrium, breast, ovaries, prostate, liver, gallbladder, kidneys, and colon. Additionally, obesity is linked to osteoarthritis, unemployment, social disadvantages, and decreased economic productivity [3]. Studies indicate that individuals from the Indian subcontinent face a greater risk of NCDs compared to their European counterparts. This surge in obesity has been attributed to factors such as economic growth, urbanization, and dietary shifts from traditional foods to Western-style diets rich in saturated fats and refined sugars. Additionally, excessive consumption of white rice and a lack of physical activity contribute to the accumulation of abdominal fat among South Asians [9-10]. With a population exceeding 1.2 billion, India is estimated to have approximately 350 million people affected by obesity [11]. Effective management strategies for obesity include reducing calorie intake, engaging in regular physical activity, adopting behavioral changes, and, in some cases, utilizing pharmacological treatments or bariatric surgery [12]. Traditional medical systems such as Unani, Chinese, and Ayurveda rely extensively on plants, utilizing various parts like roots, stems, leaves, fruits, and seeds. These plants undergo thorough evaluation before being incorporated into Ayurvedic pharmacopeia. In India, food including vegetables, fruits, spices, and medicinal plants is considered essential for supporting the body's healing mechanisms. This aligns with Hippocrates' ancient principle: "Let food be thy medicine and medicine be thy food." Beyond medicinal applications, plants serve diverse purposes, including natural dyes, pest control, teas, perfumes, and timber. Among these, *Murraya koenigii* (Linn.) Spreng, commonly known as the curry leaf tree, holds significant ethnomedicinal value and has been a key component of Ayurvedic medicine for centuries. The botanical name *Murraya koenigii* honors two notable figures in botany. The genus Murraya is named after Swedish physician and botanist Johann Andreas Murray, who passed away in 1791, while the species name koenigii pays tribute to botanist Johann König. *Murraya koenigii* belongs to the Rutaceae family, which comprises approximately 150 genera and 1,600 species, this plant is widely recognized by different names across India. It is native to Sri Lanka and India, thriving at elevations up to 900 meters, and is cultivated extensively across the country. Additionally, it has been reported in Nepal, Pakistan, Thailand, Bhutan, and Vietnam, and has also spread to regions like Malaysia, South Africa, and Reunion Island through South Indian migration [13-14]. This review aims to provide insights into *Murraya koenigii* plants and Mahanimbine activity against obesity.

Synonyms

Curry leaf, known by various names across different Indian states and global languages, holds cultural and culinary significance.[15-16]

In India, it is referred to as Karepaku in Andhra Pradesh, Narasingha in Assam, Barsanga or Kartaphulli in Bengal, Gorenimb in Gujarat, Mitha Neem in Himachal Pradesh, Kathnim or Kurry Patta in Hindi-speaking regions, Karibeva in Karnataka, Kariveppilei in Kerala, Gandhela, Gandla, or Gani in Kumaon, Bhursanga in Odisha, Mahanimb in Sanskrit, and Karivempu in Tamil Nadu.

Beyond India, it is recognized under various names: Pindosine in Burmese, Karrry bald in Danish, Kerriebladeren in Dutch, Curry leaves in English, Feuilles de curry in French, Curryblätter in German, Daun kari in Indonesian, Fogli de Cari in Italian, and Hoja… in Spanish.

Taxonomy of plant Kingdom

Kingdom - Plantae
Sub-kingdom - Tracheobionta
Superdivision - Spermatophyta
Division - Magnoliophyta
Class - Magnoliospida
Subclass - Rosidae
Order - Sapindales
Family - Rutaceae
Genus - Murraya J. Koenig ex L
Species - *Murraya koenigii* L. Spreng[15]

Morphology

Murraya koenigii is a small, spreading shrub or tree, typically reaching heights of 2.5 to 6 meters in warm, humid climates. It exhibits a dark green to brownish main stem, speckled with numerous tiny dots.

Bark - The bark can be peeled off in strips, revealing the white wood underneath. The girth of the main stem measures approximately 16 cm, while the trunk diameter can expand up to 40 cm in mature trees. The plant develops dense, dark green foliage with closely spaced, spreading branches.

Leaf Structure - The leaves are exstipulate, bipinnately compound, and grow up to 30 cm in length. Each compound leaf consists of 11 to 21 lanceolate leaflets, each measuring 2–4 cm long and 1–2 cm wide. The leaves are smooth, shiny, with a paler underside, and emit a distinct, pungent aroma. They are borne on opposite slender branchlets, often exhibiting a drooping or pendant growth habit.

Flowers - The plant produces small, fragrant, white flowers, which are bisexual and actinomorphic. The flowers are complete, hypogynous, and pentamerous, growing in terminal cymes, each inflorescence bearing between 60 and 90 blossoms. The calyx is green, five-lobed, and persistent, while the corolla consists of five lanceolate, polypetalous white petals, each measuring approximately 5 mm in length. The androecium comprises 10 dorsifixed stamens arranged in two whorls of five, with the smaller stamens reaching a length of 4 mm, and the larger ones extending between 5 and 6 mm. The gynoecium is about 5 to 6 mm long, featuring a short style and a bright, sticky stigma. The ovary is superior, leading to self-pollination. The average diameter of a fully opened flower is approximately 1.12 cm. [16-22]

Figure 1: *Murraya koenigii* (L.) Spreng flower and leaf (Courtesy- India Biodiversity Portal)

Fruiting and Seeds - Following pollination, the plant produces small, round to oblong fruits that measure 1.4–1.6 cm in length and 1–1.2 cm in diameter. These fruits ripen to a glossy black color and are clustered closely together. Each fruit typically contains one or two seeds that are approximately 11 mm long and 8 mm in diameter, exhibiting a spinach-green hue. Despite the fruits being edible, the seeds are considered toxic and are not used for culinary purposes.

Figure 2: *Murraya koenigii* (L.) Spreng fruits (Courtesy – Anthropogen, *Murraya koenigii*)

Phenology and Growth Conditions - The flowering period varies depending on the region, occurring from mid-April to mid-May, while fruiting takes place between late July and early August. In other climatic zones, flowering and fruiting can extend from December to July. This plant thrives in warm, humid conditions and can grow successfully in containers, maintaining a smaller size when cultivated outside its native environment.

Extraction methods for active chemical constituent

Various techniques have been employed for the preparation of *Murraya koenigii* extracts, including the following:

Ethanolic Extraction - *Murraya koenigii* powder was subjected to extraction using 100 mL of ethanol and placed on a rotary shaker operating at 190–220 rpm for 24 hours. The resulting extract was then collected, and the solvent was evaporated to achieve the desired final volume. The extract was subsequently stored in airtight bottles at a temperature of 40 °C [23].

Essential Oil Extraction via Hydro-Distillation - The essential oil was obtained using the hydro-distillation method with a Clevenger apparatus. After distillation, the oil was separated from water using a separating funnel and preserved under refrigeration to maintain its stability and quality [24].

Extraction and Isolation of Carbazole Alkaloids - Fractionation of hexane, chloroform, and methanol extracts from the stem bark and roots of *Murraya koenigii* facilitated the isolation and characterization of carbazole alkaloids. The concentrated extracts yielded distinct viscous syrups: the crude hexane extract appeared as a brownish-yellow syrup (22.5g and 33.0g), while the crude chloroform extract formed a dark brown viscous syrup (14.0g and 24.0g). These crude extracts were further processed using column vacuum chromatography over silica gel and sequentially eluted with mixtures of hexane, hexane/ethyl acetate, ethyl acetate, ethyl acetate/methanol, and methanol. This approach resulted in approximately 75 different fractions [25-26].

Hydro-Methanolic Extraction via Soxhlet Apparatus - The dried leaf powder of *Murraya koenigii* underwent a preliminary defatting process using petroleum ether for 24 hours. Following this, extraction was performed using a Soxhlet apparatus with a hydro-methanolic solvent system in a 30:70 ratio to optimize the yield of bioactive compounds [27-28].

Chemical Constituents

Murraya koenigii is a rich source of diverse organic compounds, including alkaloids, flavonoids, carbohydrates, and sterols. These bioactive constituents have been identified in plant extracts prepared using various solvents such as petroleum ether, ethyl acetate, chloroform, ethanol, and water. To confirm the presence of these phytochemicals, several qualitative tests were conducted:

Alkaloids – The presence of alkaloids was verified using Mayer's reagent, which resulted in the formation of white or cream-colored precipitates.

Phenolic Compounds – A white precipitate formed upon adding a few drops of 5% lead acetate solution to the alcoholic extract, confirming the presence of phenolic compounds.

Flavonoids – A yellow coloration was observed on filter paper dipped in ammoniated alcoholic extract, indicating the presence of flavonoids.

Saponins – The formation of honeycomb-like frothing after shaking the extract with sodium bicarbonate confirmed the presence of saponins.

Proteins and Free Amino Acids – These were identified using Millon's, Biuret, and Ninhydrin tests.

Sterols and Triterpenes – The presence of sterols and triterpenes was confirmed when the alcoholic extract, after being mixed with chloroform, acetic anhydride, and concentrated sulfuric acid, exhibited a color change from blue to brick red.

Furthermore, the essential oil composition of *Murraya koenigii* has been analyzed, revealing key constituents such as D-sabinene, D-α-terpinol, di-α-phellandrene, D-α-pinene, caryophyllene, and dipentene [29-33].

Chemical constituents in leaves

The fresh leaves of *Murraya koenigii* contain a moisture content ranging from 61.77% to 66.2%, with protein levels varying between 2.1% and 12.5%. Total sugar content falls within 14.6% to 18.97%, while total ash is present in amounts of 9.7% to 13.06%. Additionally, the leaves contain 1.35% to 1.82% acid-insoluble ash and a similar proportion of alcohol-soluble extractives. The water extractive value has been reported to range from 27.33% to 33.45%. Extraction of bioactive compounds from *Murraya koenigii* leaves has been carried out using various solvents, including ethyl acetate, ethanol, petroleum ether, water, and chloroform. These extracts have yielded a diverse range of phytochemicals such as alkaloids, flavonoids, and sterols. Specifically, acetone extraction has led to the isolation of koenigine, koenine, koenidine, and (-)-mahanine. Hexane extracts have been found to contain mahanimbine, isomahanimbine, koenimbidine, and murrayacine, while petroleum ether extraction has resulted in the isolation of isomahanimbicine [34-36].

Chemical constituents in seeds

The seeds of *Murraya koenigii* are composed of various bioactive compounds, including furocoumarin lactone, carbazole alkaloids, glycolipids, phospholipids, and terpinene. These seeds contain approximately 4.4% total lipids, of which 85.4% are neutral lipids, 5.1% are glycolipids, and 9.5% are phospholipids. Among the neutral lipids, triacylglycerol constitutes 73.9%, followed by 10.2% free fatty acids, along with smaller quantities of diacylglycerols, monoacylglycerols, and sterols. Additionally, the seeds contain terpenoid compounds, including terpinene, terpinen-4-ol, linalool, ocimene, limblee, limbolee, and simbolee[37-39].

Chemical constituents in fruits

The fruit pulp exhibits a high moisture content of 64.9% and contains 16.8% total soluble solids. It also comprises 9.76% total sugars, including 9.58% reducing sugars and 0.17% non-reducing sugars. Furthermore, the fruit is a valuable source of vitamin C (13.35%), total ash (2.162%), protein (1.97%), phosphorus (0.082%), potassium (0.811%), calcium (0.166%), magnesium (0.216%), iron (0.007%), and tannins (0.00057%) [40-43].

Literature review of mahanimbine activity in obesity

Okafor *et al.* (2023) investigated the anti-obesity effects of ethanol extract of *Murraya koenigii* (EEMC) in Wistar rats with high-fat diet (HFD)-induced obesity. Thirty adult male Wistar rats (average weight: 183g) were divided into five groups (n=6). Group A served as the normal control and received standard feed, while Group B was the obese control, receiving only an HFD without treatment. Groups C and D were treated with 200 mg/kg and 400 mg/kg of EEMC, respectively, whereas Group E received 150 mg/kg of Xenical as a standard control. The results showed a statistically significant ($P<0.05$) dose-dependent reduction in body weight and body mass indices in the treatment and standard control groups (C, D, and E). Total cholesterol (TC) was elevated in the normal and obese control groups but significantly reduced in the treatment groups. Triglycerides (TG) and low-density lipoprotein cholesterol (LDL-C) levels also decreased significantly ($P<0.05$) in all treated groups in a dose-dependent manner. Conversely, high-density lipoprotein cholesterol (HDL-C) levels increased significantly ($P<0.05$), particularly in the EEMC-treated groups. Histopathological analysis of liver tissue indicated normal cellular architecture in the treatment groups, suggesting no adverse effects. These findings highlight the potential of EEMC as an anti-obesity agent, exerting its effects through weight reduction, improved lipid profile, and overall metabolic modulation. The study suggests that EEMC could serve as a promising therapeutic option for obesity management [44].

Analava Mitra *et al.* (2010) conducted a study to evaluate the effects of mahanimbine, a carbazole alkaloid derived from *Murraya koenigii* leaves, on blood glucose and serum lipid profiles in streptozotocin-induced diabetic rats. Diabetes was induced in adult male Wistar rats through an intraperitoneal injection of streptozotocin (45 mg/kg). The diabetic rats were administered mahanimbine at doses of 50 and 100 mg/kg once weekly for 30 days, while the control group received 0.3% w/v sodium carboxymethyl cellulose. Fasting blood glucose levels and serum lipid profiles were assessed in both diabetic and non-diabetic rats. Additionally, the in vitro inhibitory effects of mahanimbine on alpha-amylase and alpha-glucosidase were evaluated. The findings revealed that mahanimbine significantly reduced elevated fasting blood glucose, triglycerides, low-density lipoprotein (LDL), and very-low-density lipoprotein (VLDL) levels in diabetic rats while increasing high-density lipoprotein (HDL) levels. Furthermore, mahanimbine exhibited a notable inhibitory effect on alpha-amylase but showed comparatively weaker inhibition of alpha-glucosidase relative to acarbose. These results suggest that mahanimbine possesses potential anti-hyperglycemic and anti-lipidemic properties [45].

Birari *et al.* (2010) investigated the anti-obesity and lipid-lowering properties of *Murraya koenigii* (L.) Spreng leaf extracts and mahanimbine in high-fat diet (HFD)-induced obese rats. The study found that oral administration of dichloromethane (MKD) and ethyl acetate (MKE) extracts at a dose of 300 mg/kg/day for two weeks significantly reduced body weight gain, plasma total cholesterol (TC), and triglyceride (TG) levels. These effects were attributed to the presence of carbazole alkaloids in the extracts. Additionally, mahanimbine (30 mg/kg/day) demonstrated a similar pharmacological effect, significantly lowering body weight gain and plasma lipid levels. The findings highlight the potential of mahanimbine as a promising therapeutic agent for obesity and hyperlipidemia management [46].

Jagtap *et al.* (2016) investigated the impact of mahanimbine, a primary carbazole alkaloid from *Murraya koenigii* (curry leaves), on metabolic complications induced by a high-fat diet (HFD) in male and female mice. Mice were administered mahanimbine at 2 mg/kg (HFD 1 LD) or 4 mg/kg (HFD 1 HD) daily alongside HFD feeding for 12 weeks. By the end of the study, male mice in the HFD 1 LD and HFD 1 HD groups exhibited weight gains of 51.70 ± 3.59% and 47.37 ± 3.73%, respectively, compared to 71.02 ± 6.04% in the untreated HFD group. Female mice in the HFD 1 LD and HFD 1 HD groups showed 24.31 ± 1.68% and 25.10 ± 2.61% weight gain, respectively, versus 36.69 ± 3.60% in the HFD control group. Mahanimbine supplementation effectively mitigated HFD-induced hyperlipidemia, fat accumulation in adipose tissue and liver, systemic inflammation, and oxidative stress. Additionally, it enhanced glucose clearance and upregulated insulin-responsive gene expression in the liver and adipose tissue. While male and female mice displayed distinct metabolic responses to HFD, mahanimbine exerted comparable protective effects in both sexes. The study also found that mahanimbine reduced dietary fat absorption, leading to increased fat excretion. These findings suggest that regular consumption of mahanimbine, and by extension curry leaves, may help prevent HFD-induced metabolic disturbances [47].

CONCLUSION

Murraya koenigii (curry leaf) and its bioactive alkaloid, mahanimbine, have demonstrated significant potential in combating obesity through various pharmacological mechanisms. Studies highlight their role in modulating lipid metabolism, reducing adipogenesis, enhancing thermogenesis, and improving insulin sensitivity. Mahanimbine, in particular, exhibits anti-obesity effects by regulating key molecular pathways associated with fat accumulation and energy expenditure. While preclinical research is promising, further clinical studies are essential to validate its therapeutic efficacy and safety in humans. Future investigations should focus on optimizing formulations, bioavailability, and potential synergistic effects with other natural compounds to establish *Murraya koenigii* as a viable anti-obesity agent.

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