Review of Hypoglycemic Activity of *Murraya paniculata* Linn.

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**ABSTRACT**

Background: Diabetes mellitus, one of the non-communicable diseases, is still the seriously problem due to leading the causes of death in the developed countries. The newer anti-hyperglycemic drugs are continued searching because the existing synthetic drugs have several limitations. Traditional medicinal plants are used in the treatment of diabetes mellitus more than century, but only a few of these have proved their safe and efficacy. Aim of this review article is focused *Murraya paniculata* one of the medicinal plants used for antioxidant activities. It contains several kinds of coumarins and derivative, alkaloids, flavonoids, phenolic compounds and essential oil. Many researches have evaluated that these phytochemical substances have the major impact on diabetes mellitus. Conclusion: This review focuses on the hypoglycemic activity of this plant and clears that it has the potential to be considered as a candidate for preparing the new treatment of diabetes mellitus.

**INTRODUCTION**

In 2014, WHO reported the global prevalence of diabetes mellitus was estimated 9% among adult and 1.5 million deaths [51]. The currently anti-hyperglycemic drugs include sulfonylureas, biguanides, and thiazolidinediones, have limited use because of undesirable pathological conditions and high rates of organ failure [47]. There are the ethnobotanical studies of medicinal plants used in the management of diabetes mellitus in many countries. Abo *et al.* [1] identified 31 medicinal plant species in South Western Nigeria belonging to 20 families, mostly from the Rutaceae, Leguminosae and Cucurbitaceae, and *Cassia alata* and *Vernonia amygdalina* are exclusively used. Bahmani *et al.* [6] identified 30 medicinal plant species in Iran from 17 families for the treatment of diabetes. The families with most antidiabetic plants were Lamiaceae (6%), Fabaceae (4%) and Rosaceae (4%), and *Citrus* *colocynthis* has the most frequency of use. Kadir *et al.* [18] identified 83 medicinal plant species in Bangladesh belonging to 38 families, mostly from the Fabaceae, Euphorbiaceae, Liliaceae, and Moraceae, and *Asparagus racemosus* and *Azadirachta indica* are exclusively used. Katemo *et al.* [19] identified 31 medicinal plant species in Democratic Republic of Congo belonging to 24 families, mostly from the Magnoliophyta and *Cathartanus roseus*, *Aloe vera*, *Morinda lucida*, *Morinda morindodes* and *Cassia occidentalis* are exclusively used. Manosroi *et al.* [24] reported the hypoglycemic activity of five Thai medicinal plants including *Anogeissus acuminata* (Combretaceae), *Catunaregam tormentosa* (Rubiaceae), *Diocrescis erythroclada* (Rubiaceae), *Mimoso pudica* (Fabaceae), and *Rauwolfia serpentina* (Apocynaceae), which have been traditionally used in the Northern part of Thailand. Semenya *et al.* [43] identified 24 medicinal plant species in South Africa belonging to 20 families, mostly from the Asteraceae (13%), Cucurbitaceae (8%), Sapotaceae (8%), and *Plumeria obtuse* and *Momordica balsamina* are exclusively used. Tarafdar *et al.* [48] conducted field surveys in 39 medicinal plant species in India belonging to 28 families, mostly from the Acanthaceae, Apocynaceae, Caesalpiniaeae and Euphorbiaceae, and *Scoparia dulcis*, *Syzygium cumini*, and *Cicca acida* are establish the anti-diabetic plants. From these previous surveys, *Murraya paniculata*, one of the medicinal plants has been used in ethnomedicine [32]. It synonym with *M*. *exotica*, *Chalca exotica*, and *C. paniculata*, has been widely used as “Traditional Medicinal Plant” in Southeast Asia to relief symptoms of various diseases [14]. It is commonly known as satinwood, or orange jasmine, it belongs to

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the family Rutaceae. The Rutaceae is a large family, comprised about 150 genera and 1200 species distributed in the world [7, 44].

**Nomenclature:**

There are around 10 global species belonging to the genus Murraya i.e., *M. alata*; *M. crenulata*; *M. euchrestifolia*; *M. koenigii*; *M. kwangsiensis*; *M. microphylla*; *M. ovatifoliata*; *M. stenocarpa*; and *M. paniculata*. The vernacular name of *M. paniculata* is also known as Kamini (Bengali), Thanaka (Burmes), Chiu li xiang, Kau lei heung (Chinese), Kuningning (Filipino/Tagalog), Buis de Chine (French), Gacharisha, Marchula (Hindi), Gekkitsu, Inutsuge (Japanese), Falscher jasmin, Orangenraute (German), Angara gida, Konji (India), Kemuning (Indonesian), Sarika keo (Khmer), Keo (Lao), Kemuning (Malay), Kunti (Marathi), Kemoening (Nederland), Etteriya (Singhalese), Naranjo jazmín (Spanish), Keo (Thai), Satinwood, Simai-konji (Tamil), Nguyet quat (Vietnamese), and Banati (Visayan) [42].

**Morphological characters:**

*M. paniculata* is a pantropical, evergreen plant that grows in small shrubs, usually 2 to 3 m in height but reaching 7.5 m [15]. It is an upright and spreading, compact habit and dense crown of glossy green leaves (Figure 1A). **Stem:** This plant has multiple stems from the ground level. The diameter is around 9-13 cm. The stems are supported by taproots with lateral roots and abundant fine roots. The stem bark is gray, becoming fissured and rough. The branches and twigs are slender and abundant at all heights (Figure 1B). **Leaf:** The alternate leaves, 6-11 cm long, are pinnately compound with three to nine leaflets alternating on the rachis. The 1 to 5 cm leaflets are dark-green, stiff, ovate, and smell of citrus when crushed. Unlike many other citrus family shrubs, this plant does not have thorns (Figure 1E). **Flower:** The white to ivory flowers are about 12 mm in diameter and borne in small round clusters 5-10 cm, near the branch ends. They are very aromatic with a sweet fragrance reminiscent of orange and jasmine blossoms. The 5-petaled flowers are followed by fruits (Figure 1C).

**Fruit:** The fruit is green to red elliptic shape about 1-2 cm long, edible, but rather tasteless (Figure 1D). **Seed:** One or two light green seeds in tear-drop shaped are embedded in the bitter, watery pulp. It is native to southern China, Taiwan, and the sub-continent, southeastern Asia including Thailand and Malaysia, and northern Australia [31]. However, now it is cultivated and can be easily found in many countries in the tropics.

**Phytochemical substances:**

*M. paniculata* contains several kinds of coumarins and derivative [4, 17, 40], alkaloids [14, 37], flavonoids [56, 58], phenolic compounds [11] and essential oil [8, 36, 44]. The coumarins extracted from *M. paniculata* leave as meranzin hydrate, murrangatin and murpanidin were reported by Yang and Du [55] and more additional coumarins derivatives including omphamurrayone, murralongin, isomurrallygnol isovalerate, coummurayin, toddalenone, auraptene and toddasin were reported by Kinoshita et al. [21]. According to Wu et al. [53] another coumarins were extracted from root of this plant known as coummurayin, murragein, omphamarin, muraol, murracarpin, murypadin, mexoticin, ferulyl esters, 3-formylindole, omphalocarpin, 5,7-dimethoxy-8-(3-methyl-2-oxobutyl) coumarin. The new coumarins as gleinadiene [4], murraxocin [20], and murramarin [30] were extracted from leave. The alkaloids extracted from *M. paniculata* as yuehcukene [22], murrayacarine [53], murrayaculatine [54] were reported. The flavonoids extracted from *M. paniculata* as hexamethoxyflavone and heptamethoxyflavone [45, 55], pentamethoxyflavone [9], and polymethoxyflavone [58] were reported.

**Traditional uses:**

*M. paniculata* is traditionally used for analgesic activity [34, 37], anti-inflammation [27, 38, 52], antimicrobial activity [11, 26, 46], antidiabetic [10, 12], and antioxidant activities [12, 20, 39], and associated diseases such as dermatological [25] and gastrointestinal diseases [35]. The acute oral administration in mice with 2000 mg kg$^{-1}$ single dose of *M. paniculata* did not show any mortality and nervous system toxicity whereas the sub-acute oral administration in rat with 100, 200 and 400 mg kg$^{-1}$ of *M. paniculata* for 28 days did not show any change in body weight, food consumption, water intake and biochemical, hematological and histopathological parameters. Those results indicated that *M. paniculata* is safe in its oral effective dose [13].
Hypoglycemic activity:

Medicinal plants have gained huge interests from researches around the world because of their positive bioactivity effects [16]. However, there are still not many data available about the hypoglycemic activity of this medical plant. Zou et al. [59] studied the effects of total flavonoids extracted from the leaves of *M. paniculata* on diabetic nephropathy. They designed the experiment using high fat diet and streptozotocin induced diabetic rats and treated with 35 and 75 mg kg$^{-1}$ of *M. paniculata* for 13 weeks. The results showed total flavonoids significantly decreased the levels of serum blood urea nitrogen, serum creatinine, creatinine clearance, interleukin-6, urinary albumin, 24h-urinary albumin excretion rate, and fasting blood glucose in diabetic rats. They also showed the decrease in triglyceride, total and LDL cholesterol levels. Gautam et al. [12] studied the effects of *M. paniculata* leave. They designed the experiment using alloxan induced diabetic rats and treated with 100, 200 and 400 mg kg$^{-1}$ *M. paniculata* leave for 14 days. The results showed *M. paniculata* leave extract included hypoglycemic agents such as sulfonylures significantly decreased the levels of blood glucose,
cholesterol, triglyceride and lipid. Lipid peroxidation significantly reduced and superoxide dismutase, catalase and reduced glutathione peroxidase antioxidants significantly increase. In addition, they mentioned *M. paniculata* leaves extract can augment β-cell structure, cell membrane and nucleus in pancreas. Hypoglycemic action can be potentiating the insulin by enhancing the pancreatic secretion of it from β-cell of Langerhans islets or emancipating insulin from the bound form [12].

The other species from the same genus *Murraya* have been reported for hypoglycemic or anti-hyperglycemic activity. Arulselven and Subramanian [2] studied the effects of *M. koenigii* leave. They designed the experiment using streptozotocin induced diabetic rats and treated with 200 mg kg$^{-1}$ *M. koenigii* leave for 30 days. The results showed *M. koenigii* significantly decreased the levels of blood glucose and glycosylated hemoglobin and increase the levels of insulin and liver glycogen. Moreover, it decreased activities of lactate dehydrogenase, glucose-6-phosphatase, fructose-1,6-diphosphatase and glycogen phosphorylase but increase activities of hexokinase and pyruvate kinase. Tembhurne and Sakarkar [49] studied the effects of *M. koenigii* fruit juice. They designed the experiment using alloxan induced diabetic mice and treated with 2.5 and 5.0 ml/kg *M. koenigii* fruit juice for 15 days. The results showed *M. koenigii* significantly decreased the levels of blood glucose. Many researchers [3, 5, 41] reviewed the most phytochemical substances with anti-diabetes activity as following flavonoids [59], quercin [50], metformin [28], quinolizidine, anthocyanin, catechin, flavone [29], phenylpropanoids, lipoic acid [23] and coumarin [33].

Apart from the conventional medicines, traditional or alternative therapy plays a significant role in treating diabetes mellitus. It needs to know how to use and what the phytochemical constituents are. This review article has attempted to compile the new medicinal plant, *M. paniculata*, to be the one of choice in the treatment. All of this information will help researchers to explore its scientific evidence.

In conclusion, it has been suggested that oxidative stress can play an important role in tissue damage associated with diabetic complications. Oxidative stress in diabetes and increased of free radicals are generated which cause injury or destruction of pancreatic β cells which can repaired or regenerated by using potent antioxidant. The hypoglycemic activity of *M. paniculata* based on the antioxidant phytochemical constituents thus is the aim of the present review.

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