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Review Article

AN ETHANOPHARMACOLOGICAL REVIEW OF FOUR O' CLOCK FLOWER PLANT (*MIRABILIS JALAPA* LINN.)

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ABSTRACT

Mirabilis jalapa Linn. (Nyctaginaceae) is a popular ornamental plant grown worldwide for the beauty of its flowers, sweet fragrance and folklore remedies around the world for treating a variety of conditions. It is commonly called as four o'clock. It has been well characterized with respect to its chemical components. It is extensively using for muscular pain, diarrhea, abdominal colic, in boils, inflammations, aphrodisiac, genitourinary disorders and others by people from different countries. This plant contains several compounds and some are have been isolated from its parts, such as contains alkaloids, glycosides, carbohydrates, flavonoids, phytosterols (beta-sitosterol and stigmasterol), ursolic acid, oleanolic acid, brassicasterol, trigonelline and others. Regarding its biological activity, this plant expored for its cytotoxic, hypoglycaemic, anti-hyperlipodemia, anti-nociceptive, anti-inflammatory, anti-histamine, anti-oxidant, antimicrobial (antiviral, antibacterial and antifungal), and anti-spasmodic activities and also used as a reductant (reducing agent) for the production of gold nanoparticles. The present review article focused on ethano-pharmacological and other important aspects of four o'clock flower plant.

Keywords: *Mirabilis, Mirabilis jalapa* Linn., Nyctaginaceae, traditional herb, anti inflammatory.

INTRODUCTION

The herbs are indispensible sources of medicine since time immemorial. Studies on natural product are aimed to establish medicinal values of plants by exploration of existing scientific knowledge, traditional uses and discovery of potential therapeutic agents. The phytochemicals are used as templates for lead optimization programs, which are intended to make safe and effective drugs[1,2]. A number of modern drugs like aspirin, digoxin, atropine, ephedrine, morphine, quinine, reserpine, tubocurarine and others are examples, which were originally discovered from the source of herbs[3]. The Nyctaginaceae is a relatively small family (there are 30 genus and 400 species) that occurs mainly in tropical and subtropical regions of the world[4] with a few species in India, the Mascarene and Pacific Islands, and Africa[5]. It is commonly known as the Four-O' Clock family, as most of the species have flowers that open in the late afternoon or early evening[6]. The family is best known to South Africans by the variety of Bougainvillas that are widely cultivated in gardens. Species of the introduced genus *Mirabilis* are erect, perennial herbs. The leaves are thin, opposite, ovate to ovate-cordate and the lower leaves have petioles, while the upper leaves are sessile. Flowers are subtended by a calyx-like involucre. The flowers are purple, red, yellow or white, open in the late afternoon and are fragrant at night. The anthocarp is black, hard and ribbed[5]. *Mirabilis jalapa* Linn. (*M. jalapa* Linn.) is a popular ornamental plant grown worldwide for the beauty of its flowers (which can be white, red, pink, purple, or multicolored) and their sweet fragrance[7]. It is using in almost all folklore remedies around the world for treating a variety of conditions. The present article includes the detailed exploration of pharmacological and phytochemical properties of *M. jalapa* Linn. as an attempt to provide a direction for further research.

Synonyms

The synonyms of *M. jalapa* Linn. are; *M. dichotoma* Linn. (in Brazil), *M. dichotoma* Linn. and *M. longiflora* Linn. (in tropical America), *M. lindheimeri* Linn., and *M. odorata* Linn[7].

Vernacular Names

Clavillia, four-o'clocks (in English); gulabas, sanjemallige (in Kannada); gulabbas (in Hindi and Marathi); krishnakeli, sandhykali (in Sanskrit); bathrachi, chandramalli (in Telagu); antinaralu, patharachi (in Tamil); don diego de noche (in Spanish); beauty of the night, belle de nuit (in French); vieruurbom (in Africa); shahelliilli (in Arabia); and tche kia hoa (in Chinese)[7,8].

Description and Distribution

It was officially botanically recorded in 1753 although it already had long been distributed as an ornamental plant throughout the tropics of the world. There is some disagreement about where it came from originally: Mexico, Chile, or India. Today, clavillia is naturalized throughout the tropics of South America, Latin America, France and India. In Brazil the plant is known as clavillia, maravilha, or bonina; in Peru it is known as jalapa or maravilla. Hybrids of clavillia can be found in nurseries throughout the U.S. where they are sold as ornamental landscape plants[7,8]. The detailed taxonomy and

morphology of *M. jalapa* Linn., are discussed in Table 1 and 2 respectively[8,9].

Traditional uses

It has been extensively used in almost all folklore remedies around the world for treating a variety of conditions. It has been reported that indigenous Mexican people uses various decoctions and preparations of *M. jalapa* Linn. for the treatment of dysentery[10,11]. It is extensively using for muscular pain, diarrhea, and abdominal colic by people from other different countries[12]. Leaves are having sharp taste, maturant and generally used in inflammations. Leaves are also used to apply on boils, phlegmons, and whitlow as a maturant. Roots are used as aphrodisiac and good for syphilitic sores[8]. In China, has been used as traditional Chinese medicine and ethnic drug to treat diabetes[13], constipation[14], genitourinary system disorders, and injuries[15]. Apart from its medicinal uses, the flowers of *M. jalapa* Linn. are steeped in water to provide a crimson dye used in China for tinting cakes and jellies prepared from seaweed. A cosmetic powder is made in Japan from the powered seeds[16].

Toxicity

Poisoning of children has been reported after consumption of roots, seeds or fruits of *M. jalapa* Linn[17].

Phytochemical Constituents

Roots of *M. jalapa* Linn. contains alkaloids, glycosides, carbohydrates, and phytosterols by phytochemical analysis[18]. According to literatures, trigonelline is one of the components of *M. jalapa* Linn. root[19]. Trigonelline has been shown to reduce blood glucose concentrations in rats[20] and in human[21]. The preliminary phytochemical investigation indicates the presence of flavonoids, tannic acid and phenolics in the plant[22]. The aerial parts of plants having beta-sitosterol, stigmasterol, ursolic acid, oleanolic acid and brassicasterol[23,24].

Pharmacological Activities

In the recent years, the use of herbal products has been increasing in developing countries. Plants have always been an attractive source of drugs. On the other hand, intricate ways of molecular interactions and bioactivity mechanisms of the extracts or their bioactive constituents provide a challenge to the scientists[25]. The *M. jalapa* Linn. displays a wide range of pharmacological activities with correlate to mechanistic possibilities over respective disorders and overview of its pharmacological activities, has been presented in Table 3.

Pharmaceutical Uses

Reductant (reducing agent) for the production of gold nanoparticles

Generally, nanoparticles are prepared by a variety of chemical methods which are not environmentally friendly. A rapid and convenient method to reductively prepare gold nanoparticles from auric chloride using aqueous extract of *M. jalapa* Linn. flowers. The flower extract acts as a reducing agent and encapsulating cage for the gold nanoparticles. The production of gold nanoparticles has been done by the controlled reduction of the Au^{3+} ion to Au^{0}. The formation of gold nanoparticles has been established by FT-IR and UV-Vis spectroscopy. The study suggests that *M. jalapa* Linn. flowers can be a cheap source as a reductant for the production of gold nanoparticles[37].

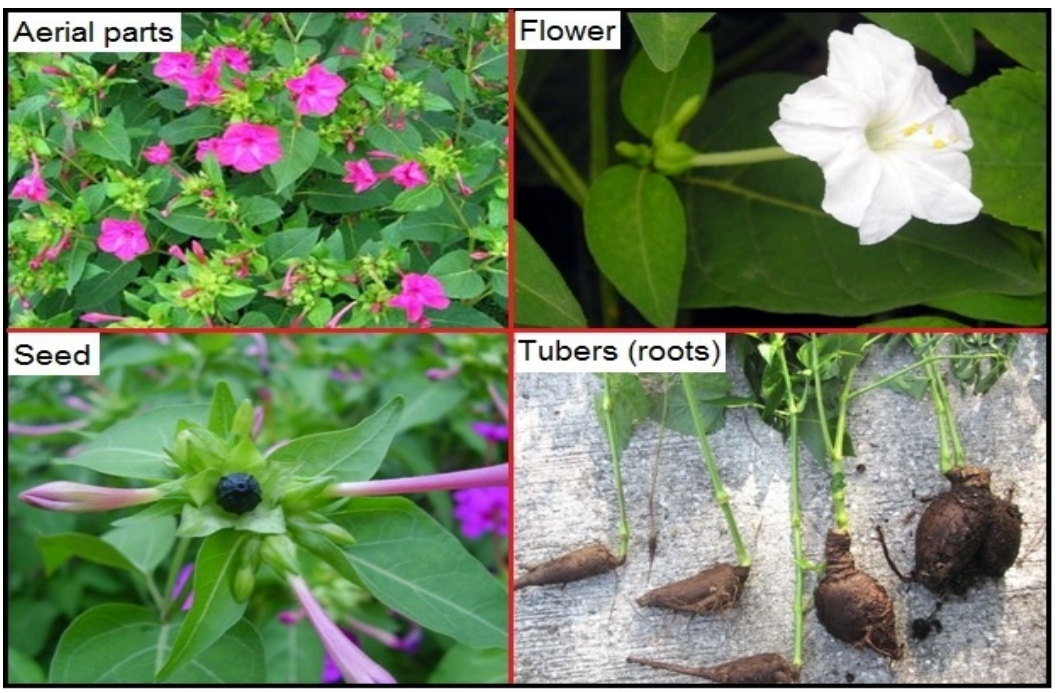

Figure 1: *M. jalapa* Linn. plant and its parts

Table 1: Taxonomy of *M. jalapa* Linn.

Kingdom	Plantae
Sub kingdom	Trcheobionta
Division	Angiosperms
Class	Dicotyledons
Subclass	Caryophylidae
Order	Caryophyllales
Family	Nyctaginaceae
Genus	*Mirabilis*
Species	*jalapa*

Table 2: The morphological features of *M. jalapa* Linn.

Part	Macroscopic features
Herb	Herbaceous, perennial plant grows 30-75 cm high with fleshy stems.
Leaves	Opposite, 3.5-7.5 cm wide, 5-10 cm long, unequal, ovate to sub cordate.
Flowers	Tubular, cluster, funnel-shaped, simple or double, fragrant, colour usually purple and white, yellow or pink, arranged in group of three flowers with five green bracteoles, surrounding the perianth, usually yellow crimson, white or variegated and opening in the evening.
Roots	Perennial tuberous roots, fairly thickened, stem swollen at nodes.
Seeds	Olive, brown or black in colour.

Table 3: Details of pharmacological activities of *M. jalapa* Linn.

Pharmaco-logical activity	Parts	Extract/chemical constituents	Screening method employed	Possible mechanistic action
Cytotoxic activity	Leaves and bark	Petroleum ether, chloroform and methanol extracts	Brine shrimp lethality bioassay	Methanol extract shows potential cytotoxic activity, further mechanistic study is required[9].
	Leaves	Ethanol extract	Cytotoxicity was assayed using the HeLa cell line by microtitration cytotoxicity assay	The results of this preliminary study scientifically substantiate to a certain extent the anticancer activities[26].
Anti-viral activity	Leaves	Ethanol extract	Antiviral activity was tested against the *HSV-1* and *VSV* by simplified plaque reduction assay	The results of this preliminary study scientifically demonstrate to a certain extent the pharmacological activities[26].
Hypoglycemic activity	Root	Ethanol extract	Streptozotocin induced diabetes in rats	The study suggests consumption of *M. jalapa* Linn. root may prevent the complication of hyperglycemia associated with diabetes and still need to be determined in addition to toxicological studies in further experiments[27].
Anti- hyperlipidemia activity	Root	Ethanol extract	Anti- hyperlipidemia effect on normal mice and Streptozotocin induced diabetes in rats by estimating various biomarkers.	Study demonstrates that *M. jalapa* Linn. root can be used to treat diabetes (type 2) with hyperlipidemia[27].
Antinociceptive activity	Leaves and stem	Hydroalcoholic extract of leaves and decoction of stem	Acetic acid induced writhing mice model, Thermal pain model by tail-flick hot water bath.	*M. jalapa* Linn. presents antinociceptive activity in mice, which supports its folkloric use as an analgesic[18].
	Leaves	Hydroalcoholic extract of leaves and ethyl acetate fraction	Chronic inflammation (FCA induced), postoperative (paw surgical incision) and neuropathic (partial sciatic nerve ligation) pain model	Study confirmed the antinociceptive property is clinically relevant pain models. Also its effect on the FCA - induced chronic inflammation seems to be related to AchE inhibition and cholinergic system[28].
Anti-inflammatory activity	Leaves	Alcohol, aqueous and petroleum ether extracts	Carrageenan- induced paw edema , formalin-induced paw edema, cotton pellet induced granuloma models in wistar albino rats	All extracts shows potential anti-inflammatory activity, further mechanistic study is required[29].
	Leaves	Total alcoholic extract and successive petroleum ether fractions	Carageenan induced rat paw edema and cotton pellet induced granuloma models	Both test samples inhibit the increase in number of fibroblasts and synthesis of collagen and mucopolysaccharides during granuloma tissue formation during the chronic inflammation. These experimental results have established a pharmacological evidence for the folklore claim of the drug to be used as an anti inflammatory agent[30].
Anti-histamine activity	Roots	Ethanol:acetone (1:1) extract	Antihistaminic activity using a guinea pig tracheal chain preparation and clonidine-induced mast cell granulation in mice	The study justified the folkloric use of this plant in the treatment of allergic diseases and asthma[31].

Anti-oxidant activity	Aerial parts and roots	Methanol extract	ABTS+ and DPPH free radical scavenging assay	The study reveal the immense potential of the plant for further research that aims at identifying the bioactive components responsible for the anti-oxidant activity and elucidating their tentative mechanisms of action[22].
	Bark	Methanol extract	DPPH free radical scavenging assay	Methanol extract shows potential anti-oxidant activity, further mechanistic study is required[9].
	Aerial parts	Methanol extract	Reducing power assay method, Hydrogen peroxide scavenging activity	This activity is due to presence of flavonoids, polyphenols like phenolic compounds and tannins[32].
	Tubers	Petroleum ether, acetone, water, methanol, and Dichloromethane extracts	DPPH radical-scavenging activity, Lipid peroxidation by TBA assay, beta- Carotene bleaching by linoleic acid assay	Water extract shows significant antioxidant activity and free radical-scavenging activity followed by methanol and dichloromethane extracts, due to high content of flavonoids and beta-Sitosterol identified for the first time by LC/MS and GC/MS, respectively[33].
Antispasmodic activity	Flower	Methanol extract	Antispasmodic effect using Rabbit jejunum, thoracic aorta, and guinea pig ileum (*In vitro*)	These effects were not due to either Ach or His receptors blockage, IP3, cAMP, cGMP, Ca^{2+} release from intracellular storage, or protein kinase mediated contraction– relaxation mechanisms. The effects inducted by this extract may involve a serotoninergic mechanism, which, in turn, interacts with other adrenergic systems. Further studies are necessary to identify the active compounds to elucidate the mechanism of action[34].
Antibacterial activity	Seed	Aqueous and methanol extract	Screening against Gram-positive and Gram-negative bacteria respectively isolated from infected wounds and diarrhoeic faeces by the disk-diffusion method.	Further investigations are required to identify the active principles in seeds of *M. jalapa* Linn [35].
	Leaf	Ethanol extract	The agar ditch-diffusion method against *E. coli, S. aureus, S. typhi, B. cereus,* and *K. pneumoniae*	The plant extract possesses antibacterial activity, thus this plant be a good source of agents for the bio-control and chemotherapy[36].
	Aerial parts	Methanol extract	Agar well diffusion assay against pathogenic *S. aureus, Pseudomonas sp., Bacillus sp.*	Anti bacterial activity have been confirmed as the methanol extract displayed activity against the micro organism used[32].
	Tubers	Petroleum ether, acetone, water, methanol, and Dichloromethane extracts	Agar diffusion method against eight strains of bacteria: *S. aureus, S. epidermidis, M. luteus , E. coli , P. aeruginosa, K. pneumonia, B. cereus* and *E. faecalis*	All extracts had moderate antibacterial activity could be attributed to high content of flavonoids and _-Sitosterol identified for the first time by LC/MS and GC/MS, respectively[37].
Antifungal activity	Tubers	Petroleum ether, acetone, water, methanol, and Dichloromethane extracts	Antifungal activities were tested using Agar diffusion method against *A. niger, F. solani, F. oxysporium* and *F. granularium.*	Water extract had a fungal toxicity could be attributed to high content of flavonoids and Sitosterol identified for the first time by LC/MS and GC/MS, respectively[33].

ROS, reactive oxygen species; NO, nitric oxide; COX-2, cyclooxygenase-2; TNF-alpha, tumor necrosis factor-alpha; IL-1 beta, interleukin-1 beta; NO, nitric oxide; IFN-gamma, gamma interferon; Th1, T-helper cell 1; ABTS+, 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid; DPPH, 1,1-diphenyl-2-picrylhydrazyl; MIC, minimum inhibitory concentration; PGE2, Prostaglandin E2; *M. tuberculosis, Mycobacterium tuberculosis; M. avium, Mycobacterium avium; M. kanasii, Mycobacterium kansasii; M. malmoense, Mycobacterium malmoense; M.* intracellulare, *Mycobacterium intracellulare;* COX, cyclooxygenase; DNFB, 2,4-dinitrofluorobenzene; HSC-3, human oral squamous carcinoma-3; HUVECs, human umbilical vein endothelial cells; *S. aureus, Staphylococcus aureus*; *P.aeruginosa*, *Pseudomonas aeruginosa*; *L. amazonensis*, *Leishmania amazonensis; L. major*, *Leishmania major*; *L. amazonensis*, *Leishmania amazonensis*; *P. berghei, Plasmodium berghei; S. epidermidis, Staphylococcus epidermidis; M. luteus, Micrococcus luteus; K. pneumonia, Klebsiella pneumonia; B. cereus, Bacillus cereus; E. faecalis, Enterococcus faecalis; A. niger, Aspergillus niger; F. solani, Fusarium solani; F. oxysporium, Fusarium oxysporium ; F. granularium, Fusarium granularium;* AchE, acetylcholinesterase; Ach, Acetylcholine, His, Histamine, IP3, Inositiol triphsphate; cAMP, cyclic adenosine monophosphate; cGMP, cyclic guanosine monophsphate; HSV-1, herpes *simplex virus type-1*; *VSV, vesicular stomatitis virus*

CONCLUSION

The plant *M. jalapa* Linn., is widely available as weed and also it is cultivated for various purposes including, medicinal and ornamental usages. The scientific research on *M. jalapa* Linn. suggests a huge biological potential of this plant. It is strongly believed that detailed information as presented in this review on the phytochemical and various biological properties of the plant might provide detailed evidence for the use of this plant in different diseases. It has various traditional uses that differ from one country to another. A variety of phytoconstituents has been isolated from the different parts of it. Thus, there remains a tremendous scope for further scientific exploration of *M. jalapa* Linn. to establish their therapeutic efficacy and commercial exploitation.

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