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PHYTOCHEMICAL CONSTITUENTS AND PHARMACOLOGICAL ACTIVITIES, PROFILE OF *MORINDA CITRIFOLIA:* A REVIEW

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ABSTRACT

Morinda citrifolia, known as Noni or Indian mulberry have been used in traditional medicine for the treatment various diseases. Noni is an evergreen shrub whose ripe fruit and leave has a strong unpleasant butyric acid odor & flavor and astringent taste. The crude extracts of *M. citrifolia* (Rubiaceae) obtained from the leaves and fruit under different solvents such as methanol, ethanol and aqueous, which that are subjected to phytochemical study. The phytochemical studies of *M. citrifolia* naturalize broad spectrum of secondary metabolites. Saponins, alkaloids, and reducing sugar are predominantly obtain in all these types of tested extract followed by phenol, steroid, terpenoids, tannin, It also cantains cardiac glycoside, flavanoids and carbohydrate are obtain in all the tested solvents and aqueous extract of the fruit. Protein is present in aqueous and ethanolic extract but it is not found in methanolic extract. The compound such as phylobatannin, and resin are not found in *M. citrifolia* fruit extract. It has been posses various therapeutic report to have a broad range of therapeutic effects, including immunostimulatory, antibacterial and antiseptic, antiviral, antifungal, antitumor, neuroprotective, antiallergic, antihelmin, analgesic, anti-obesity, antioxidant, hypotensive, anti-inflammatory, and immune enhancing effects. The goal of this review is to provide updated information of the phytochemical constituents, biological activity and safety found in *Morinda citrifolia* and to provide perspective for its extensive utilization as a major Noni dietary supplement.

KEYWORDS: Dietary supplement, Chemical structures, Biological activity, Phytochemicals.

INTRODUCTION

Morinda citrifolia Linn (family - Rubiaceae) is popular small evergreen tree or shrub. *Morinda citrifolia* is native obtained from Southeast Asia. While is cultivated in India, Malaysia, the Caribbean, Polynesia, Central and also north South America, and in Australia.[1,2] The tree can grow as tall as 6 m and has bright green color, oval-shaped leaves, which measure from 10 to 30 cm. The fruit is ovoid in shape and mature have an unpleasant butyric acid odor with flavor and astringent taste. The seeds have an air sac at one end which allows them to float, partly explaining the wide distribution of Noni trees in the Indo-Pacific islands.[3] Several in *vitro and in vivo* studies already have been performed**.** *M. citrifolia* containing various part such as fruits, leaves, roots and seeds are widely used in some common medicine such as herbal and other remedies, and number of therapeutic effects of *Morinda citrifolia* have already been studied.[4] Applications of *Morinda citrifolia* have been reported for all parts of the plant, like fruit leaves and seeds with the most prevalent traditional and most topically used Responding to Noni's ethnobotanical and popular use a substantial number of biological and.[5] Chemical studies have been performed on this species dating back more than 100 years.[6]

This review paper is attempted to **review of various phytochemical constituent, pharmacological activity and safety of *Morinda citrifolia* (Noni).** The review divided into five sections. The first section of review documented ethnobotanical and common names of *M. citrifolia*. The second section is presenting a compilation of the different phytochemicals constituents. The third section described its current usage such as medicinally and dietary supplement. In the fourth section show the biological activity of Noni extracts and/or pure compounds for prevents various diseases. In the fifth section discussed published data on the safety and toxicity of *morinda citrifolia*. Various aspects of the uses of phytochemical profiles and biological activity of *M. citrifolia* have been reviewed previously.[7,8,9]

Phytochemical Constituents

Morinda citrifolia plant contained more than 160 phytoconstituents of which over 120 constituents have nutraceutical properties with proven biological activity.[10]

Fruit extract of *Morinda citrifolia* have various constituent such as alcohols, phenols, micronutrients, acids, non-volatile and volatile components, beta-carotenoids, ketones, lactones, terpenoids, proxeronine etc.

Morinda citriflia fruit containing physicochemical, phytochemical and antimicrobial properties collected at different maturity levels, while that has been investigated. The results show maximum antibacterial activity in ethanolic extract of mature *M. citrifolia* fruit against K. Pneumonia and maximum antifungal activity in methanolic extract of *M. citrifolia* fruit against A. Flavous. (Samiraj R. 2012).

Morinda citrifolia have also been review of phytochemical constituent consist as amino acid, fatty acid, lignin, anthraquinones, glycosides, sterols, alcohol and phenols, ester, and flavonoids etc. Fruit juice of *M. citrifolia* is a health drink and also has several pharmacological properties. *Morinda citrifolia* juice can be used development of the post-ischemic glucose intolerance known as a cerebral protective mechanism.[11,12,13]

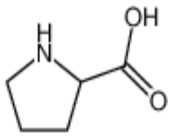
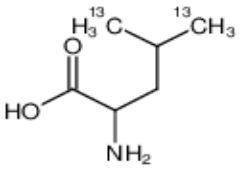
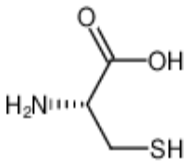
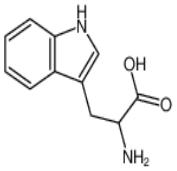
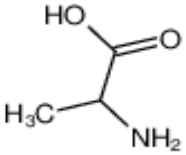
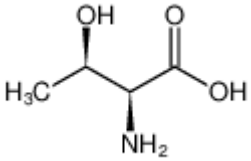
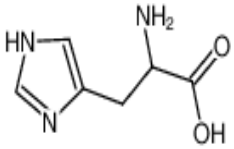
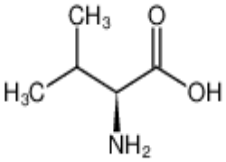
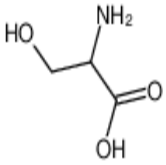
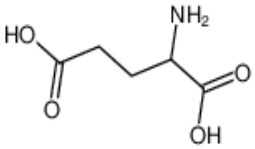
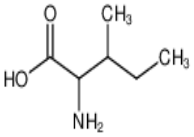
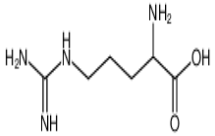
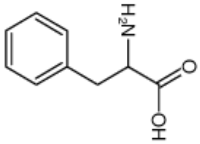
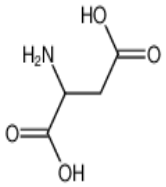
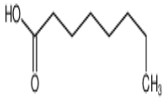
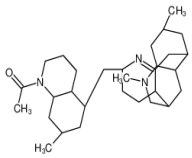
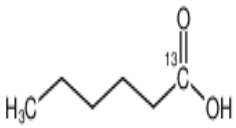
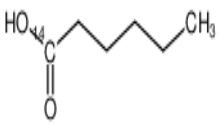
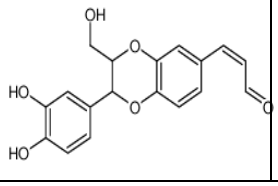
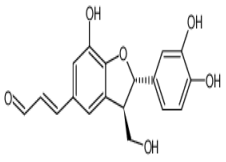
Table 1: Important chemical constituents of *Morinda citrifolia* along with their compounds, locations and references.

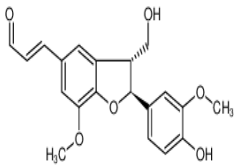
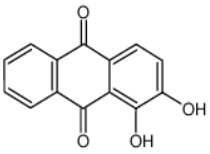
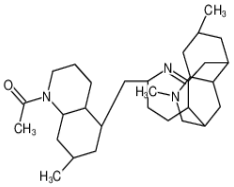
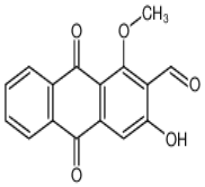
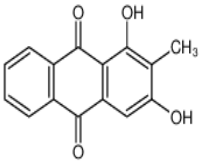
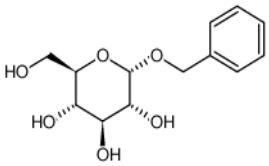
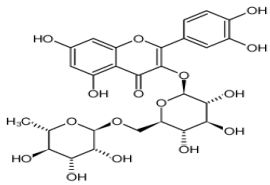
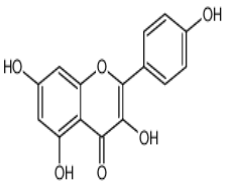
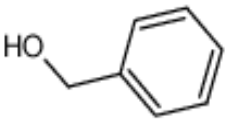
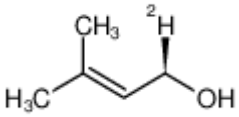
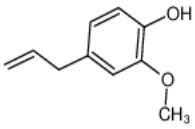
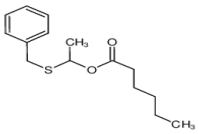
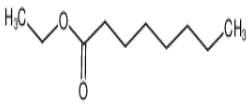
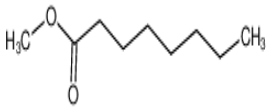
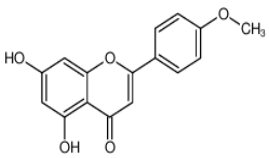
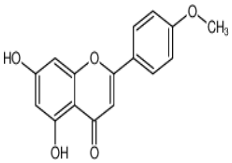
Compounds	Parts of plant	Activities	References
Amino acid		Essential and conditional	
Proline	Leaf	Skin, joint & muscle health support,	[14,15,16]
Leucine	Leaf	Dietary supplement	[14,15,16]
Cystein	Leaf	Antioxidant	[14,15,16]
Tryptophan	Leaf	Insomnia, anxiety & depression	[14,15,16]
Alanine	Leaf	Antidiabetic & liver disease	[14,15,16]
Threonine	Leaf	CNS disorder	[14,15,16]
Histidine	Leaf	Antiulcer, antiallergic & Arthritis	[14,15,16,20]
Valine	Leaf	Nervous & immune system	[14,15,16]
Serine	Leaf	Essential for brain development & metabolism	[14,15,16]
Glutamic acid	Leaf	Central nervous system use	[14,15,16]
Isoleusine	Leaf	Energy production	[14,15,16]
Arginine	Leaf	Heart disease	[14,15,16]
Phenylalanine	Leaf	Skin disease use	[14,15,16]
Mithionine	Leaf	Anti-toxic	[14,15,16]
Aspartic acid	Leaf	Increase size & strength of muscle	[14,15,16]
Fatty acid			
Octanoic (caprylic) acid	Fruit	Antifungal	[14,15,16,20,21]

Hexanoic	Fruit	Antifungal, antioxidant	[14,15,17]
Caproic acid	Fruit	Antifungal	[14,15,16]
Lignin			
Americanin A	Leaf, fruit	Antioxidant	[18,19]
Americanoic acid	Fruit	Antioxidant	[19,21]
Americanol A	Fruit	Antioxidant	[19]
Balanophonin	Fruit	Antioxidant	[19,21]
Anthraquinones			
Alizarine	Cell culture, heartwood	Textile dye	[22]
Alizarin 1-O-methyl ether	Root	Textile dye	[21]
Morenone 1	Root	Anti-cancer	[14,23,24]
Morenone 2	Root	Anti-cancer	[14,23,24]
Lucidin	Root, cell culture	Hypovolemia	[22,23]
Lucidin w-methyl ether	Cell culture, roots		[25,26]
Damnacanthal	Root	Anti-carcinogenic	[13,16,21]
8-hydroxy-8-methoxy-2- methyl-anthraquinone, rubiadin	Root	Antiviral	[14,17,25]
1,3-dihydroxy-6-methyl anthraquinone	Root	Antiviral	[14,17,25,27]
Glycosides			
β-D-glucopyranoside	Leaf	Heart disease	Joseph B. (1997)
Citrifolinoside-B	Leaf	Fixative	[14,15,17]
Citrofolinin-A	Leaf	Fixative	[14]
Asperulosidetetraacetate	Fruit	Antiobesity	[21,22]
Quercetin (Ruin)	Leaf	Antioxidant	[28,29]
Kaempferol	Leaf	Antioxidant	[28,29]
Sterols			
β- sitosterol	Leaf	stimulating immune system & lowering BP	[28,29]
Alcohols and phenols			
Bezyl alcohol	Fruit	Becteriostatic preservative & topical	[13]
1-Butenol (butyl alcohol)	Fruit	Antibiotics & cosmetic	[13]
Eugenol	Fruit	Local anesthetic & antiseptic	[13]
1-Hexanol	Fruit	Topical	[13]
3-Methyl-2-buten-1-ol	Fruit	Flavoring agent	[13]
3-Methyl-3-buten-1-ol	Fruit	Flavoring agent, stress tolerance	[13]
Ester			
Ethyl caproate		Anti hypertensive (metabolic disease)	[25]
Ethyl caprylate		Flavoring agent & scent	[20]

		additives	
Methyl octanoate			[13]
Methyl decanoate		Wetting agent	[13,14]
Flavonoids		Antimicrobial	
Quercetin-3-O-b-Dglucopyranoside	Leaf	Anti-inflammatory and Lipoxygenase inhibitor	[16]
Quercetin-3-O-a-Lrhamnopyranosyl-(1-6)-b-Dglucopyranoside	Leaf	Anti-inflammatory	[16]
Kaempferol	Fruit	Antioxidant	[14,16,17]

Chemical Structures of Constituents in *Morinda Citrifolia*

Proline 	**Leucine** 	**Cystein** 	**Tryptophan** 
Alanine 	**Threonine** 	**Histidine** 	**Valine** 
Serine 	**Glutamic acid** 	**L-Isloleusine** 	**Arginine** 
Phenylalanine 	**Aspartic aci** 	**Octanoic acid** 	**Lucidine B** 
Hexanoic acid 	**Caproic acid** 	**Americanine** 	**Americanol** 

Balanophonin 	**Alizarin** 	**Lucidine** 	**Damnacanthal** 
Rubiadine 	**Bezoyl- β-D-glucopyranoside** 	**Rutin** 	**Kaempferol** 
Benzyl alcohol 	**3-Methyl-2-buten-1-ol** 	**Eugenol** 	**Hexanol** 
Ethyl caproate 	**Ethyl caprylate** 	**Methyl octanoate** 	**Methyl decanoate** 
Acecetine 	**Kaempferol** 		

Pharmacological activities

Anti cancer activity

Morinda citrifolia have been used previous several years for the health problems or various pharmacological activities such as anticancer, antiepileptic, antiinflammatory, antidiabetic, antioxidant and other activity. Noni generally basic constitute polyphenols and flavonoids have been investigated. The phytochemical especially polyphenols studies has suggested such as antioxidant properties, while help to decrease the risk of degenerative diseases, like as cancer.[30]

The medicinally valuable constituent such as anthraquinones in the leaves and roots of Noni plant is damnacanthal, while use for the treatment of several chronic diseases as heart and

cancer disease.[31] Ethanolic extract of Noni fruit and leaves acts on tumor cells and on the pathways involved in immunological response through cyclooxygenase2 (COX2) suppression, it is an important inflammatory marker, and the increase of the tumor (cancer) suppressor gene.[32]

Morinda citrifolia plant was used as medicinally or food supplement in patients with several types of cancer. Lim et al., (2016) has been performed a study, which showed demonstrated that ethanolic extract of *M. citrifolia* fruit or leaves action on tumor cells and on the pathways involved in immunological response via cyclooxygenase 2 (COX2) suppression, an important inflammatory marker and the rise of the tumor(cancer) suppressor gene and concentrated fruit. The injected of 10% TNJ® in laboratory animals also extends to the prevention of gene mutations: carcinogenic compounds tag covalently to the DNA, forming structures known as diffract that, if not repaired, cause mutations. *Morinda citrifolia* may be used to inhibit the formation of these structures.[33]

The methanolic extract of *M. citrifolia* fruit has been delineate in large number of the cell lines to the antiproliferative effect, such as human breast adenocarcinoma cells and neuroblastoma, green monkey kidney (Vero) cells, baby hamster kidney (BHK) cells and African human epithelial type 2 cells (Hep2). Antiproliferative action was exhibited during the ethanolic extract of *Morinda citrifolia* has tested in B16-F10 melanoma cells (LAN5).[34, 35] According to the Hirazumi et al.,(1994) ethanolic extract of Noni leaves also decrease the expression of epidermal growth factor receptor (EGFR) or a lung adenocarcinoma biomarker, in albino mice and acting on Lewis lung carcinoma in synergetic mice.[35]

Antiepileplic Activity

Fruit extract of *M. citrifolia* is a medicinal plant extract administration to the animals use for many neuroprotective effects. Ayurvedic preparation has been evaluated for its protective effect against seizures induced by Maximal Electro Shock (MES) method in rats. A daily dose given such as 200 and 400 mg/kg of the fruit extract was administered to the animals for 15 days, after seizures induced by maximum electro shock method and the duration of various phases of epileptic attacks were recorded and compared with the control group of animals and its possible mechanisms may be due to the inhibition of prostaglandin synthesis and monoamine oxidase enzyme.[36]

Antidiabetic Activity

The increasing number of diabetic patient who support integrative or functional medicine has stimulate a growing number of studies. Nerurkar et al. (2012) has been investigated, the antidiabetic effects of *M. citrifolia* in mice with a high-fat diet.[37,38] The improvement of the glucose metabolism, via phosphorylation of the transcription factor FOXO1, was observed. Similarly was observed the use of the *M. citrifolia* juice on the treatment of induced diabetes in rats led to decrease blood glucose levels. Noni produce a synergistic action when used in combined therapy with insulin.[39] Kamiya et al., (2008) Study has been performed to the hypoglycemic and hepatoprotective properties in diabetes induced rats. Diabetes induced by administered Streptozotocin. Diabetic experimental animals were evaluated and treated with *Morinda citrifolia* juice as (2 ml/kg, twice a day) and diabetic standard with reference hypoglycemic drug, glibenclamide orally for 20 days. Both the groups exhibited a significant reduction in blood glucose level.[40,41]

Immunostimulatory Activity

Largest plants have compounds that present immunomodulatory activity or contain substances that can encourage or terminate the immunological responses of the body, like cytokine production. *Morinda citrifolia* stands out during plants for its immunomodulatory activities, which are related to both cellular and humeral responses. The coadministration of Noni juice and immunosuppressant drugs decrease the immunostimulatory effect in mice, if confirms the action of Noni like an immunomodulating agent which that can interfere in immune response under different pathological conditions. Two types of extract such as aqueous and hydroalcoholic extract of *M. citrifolia* fruit promote *in vitro* splenocyte proliferation and encourage B and T lymphocyte activity.[42]

Antiinflammatory Activity

The *Morinda citrifolia* work against the inflammatory action, that has been demonstrated in *in vitro and in vivo* study models in large number of pathological conditions included with inflammation. The Noni juice decrease paw edema directly inhibitor prevent action of COX 1 & 2 and decrease nitric oxide or prostaglandin E2 production in J774.G8 cells, this process a dose-dependent manner and demonstrating the anti-inflammatory action of *M. citrifolia*.[43] Serafini et al., (2011) Identified aqueous extract of *M. citrifolia* fruit and leaves has an anti-inflammatory potential, significantly decrease leukocyte migration, and also can be used like alternative pain and inflammatory condition, including those related to oxidation.[44]

The root extract of the *Morinda citrifolia* with chloroform fraction has an anti-inflammatory effect, significantly decrease histamine and increase paw edema at known concentration of 3 gram/kg. Damnacanthal, used alone, meantime was decrease edema at known concentrations of 10–100 microgram/kg. Likewise, other isolated anthraquinones from the methanolic fraction of fruit extract of *M. citrifolia* compound exhibited potent antiinflammatory activity during an induced inflammation model in mice.[45,46]

Antioxidant Activity

Morinda citrifolia also be used as a valuable source of natural antioxidants activity.[47] The various part of *Morinda citrifolia* containing fruit juice or leaves juice with or without seeds, are capable of modulating cell mediated immune reaction and antioxidant enzyme activity in vitro.[48]

According to Calzuola et al. (2006), *Morinda citrifolia* hydroalcoholic plant extract demonstrate antioxidant activity and with significant elimination of oxygen superoxide *in vitro.* That treatment was orally for 14 days with 50 microgram per kg of *M. citrifolia* leaf ethanol extract induce activity of antioxidant enzymes like as catalase, glutathione peroxidase and superoxide dismutase on mice with lymphoma.[49,50]

CONCLUSION

The present study indicates that *Morinda citrifolia* have several phytochemical constituents, several *in vitro and in vivo* studies and potent activity with an attractive safety profile for treatment of patients suffering from various disease or disorders. We have found finally that administration of *Morinda citrifolia* fruit and leaves extract and its possible mechanisms may be due to prevent of a number of disease.

Conflicts of Interest: The authors have no conflict of interest.

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