Phytochemical and pharmacological review on *Morinda citrifolia*

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**Abstract**

*Morinda citrifolia* as the names suggests it is generally grown or harvested for fruits and the distribution of chemical constituents are also in other parts of the plants. The plant is native of South Asian countries and Western American lands in the pacific region. This plant has generally been used as a culinary vegetable and an edible fruit too and also considered as a natural immune booster and health enhancers. The plant was extracted to give most of the chemical constituents that possess anti-inflammatory, hypotensive, antimicrobial, antifungal, antiviral and anthelmintic activities. There had been significant uses that industries also employ as insecticidal agents and as chemical agents and catalyst. In this review, the details about the events, applications and studies that are performed on the plant were discussed.

**Introduction**

Man is using herbs and plants for their medical properties to treat diseases and ailments. Though there is no reliable scientific evidence for the herbs to prove their mechanism of action in treating the infections, they had been used in traditional medicine and folklore medicine too [1].

This plant is commonly known as noni, and its scientific name is *Morinda citrifolia* which belongs to the family Rubiaceae. It is locally called in India as Indian Mulberry, in Hawaii as Noni, in Malaysia as Menkudu and in other areas of western pacific as hair and cheese fruit. It overgrows, and the height usually ranges between 4-6 meters. It has large fleshy leaves with lanceolate and ovate shape. The stem is straight and hard. The fruits of the plant are oval in the way and fleshy. They are hard and becomes soft after maturation. The fruit is about 2-3 inches long and 1-2 inches wide. It usually contains a lot of seeds which can vary between 200-300. When the fruits grow mature and ripened, they usually smell foul and unpleasant [2].

This plant had been used as a therapeutic agent to treat various diseases like arthritis, hypertension, burns, Tb, DM and headaches. The juice of the plant had been used industrially not only in the food industry but also in Biotechnology, Nanotechnology and Pharmacy [3]. *M. citrifolia* was given credits for its medical and economic status. Local practitioners use the fruit for various traditional therapies. Considering the different therapeutic properties of the plant as medicinal, industrial and technical applications, this review article updates the information and scientific study of the plant that were performed till now. This article summarizes the phytochemical profile, pharmacological activities and other research that is shown on the plant till now.

**Phytochemistry**

*M. citrifolia* has very rich nutrients and consists of more than 100 varieties of chemical compounds that
had been isolated from the plant till now. The diff in their chemistry based on the drying method, harvesting method and time, place of the cultivation and growth and climatic conditions [4]. The plant is already introduced to harvest for fruits as said earlier, and these are rich in sugars. 85% of the pulp is almost water, and just 10-15% is fibre and solids that contain sugars. It is nearly 5% fructose and glucose and 1% sucrose, which makes the fruits very sweet and sugar. The rest of the solids is proteins, and the nutritional content is as follows. Its contains approximately 70% carbohydrates, 30% Fibres and around 0-5% proteins. The other dietary fats in the fruit are Vitamin C about 0.1-0.5%, Sodium of about 16-200mg/L and potassium up to 3500 ppu’s [5]. Other nutrients like calcium, selenium and iron were also identified in the plant which was enough to meet eh daily required adult doses of the micronutrients. Freeze-dried juice of the fruits showed the presence of copper, cobalt, molybdenum and manganease also [6].

Many other compounds are reported from the plant they are phenols, polysaccharides, anthraquinones, carotenes, flavonoids, steroids and lactone moietyes. There also isolated many volatile components from the plant, like terpenoidal aldehydes and ketones [7]. Sulphur containing compounds like linalool and methanethiol etc. some studies also isolated fatty acids and esters from the plant. Hexasoic acid and octanoic acids were isolated from the plant, which is present in the ripe fruits [8]. Though lipids are macronutrients in the plant, they are found in a very less quantity. Eicosanoic acids, caprylic acid had been isolated. Higher moieties like Nonioside A, B, C, D and E have been successfully isolated from the seeds of the plant. Saturated fatty acids like Palmitic acid, Lauric acid, Stearic acid and arachidic acid have been identified from the seeds. Carotenoids and saponins are isolated from roots and fruits which constituted majorly of beta carotene, which is found in higher amounts in fruits and bark of the plant [9].

Flavonoids are isolated from plants are basically from roots and tannins are also found along with flavonoids which comes under the class polyphenols. Fruits also contain flavonoids but comparatively less than that of roots. The amount varies around 180-350mg/100g of the plant material, and the compounds like kaempferol, Quercetin, Narcissoside and rutin were isolated. There are a group of tannins that are isolated from the seeds and stems of the plant. The phenolic content of the seeds was tested with the variation of the growth stage of the plant. It was found that the more mature and most ripe the fruits, the less is the polyphenol content in the plant [10].

Fermentation of the fruit juice and drying yields in the compounds like anthraquinones lacidine, rubiadine and alizarin compounds [11]. From the plant, other Anthraquinones like Damcanical, which is an anti-cancer agent, was isolated. Researchers isolated Modasima A from the plant that belongs to the same taxa as of citrifolia [12]. Few other works have isolated anthraquinone derivatives like bismethoxymethyl and dihydroxy methoxymethyl derivatives [13]. Amino acids like Aspartic acid, Cysteine, Glutamic acid, Glycine, Histidine, Lysine, Methionine and phenylalanine have been isolated from the plant. There were few other coumarin derivatives also isolated from the fruits they are Scopoletin derivatives. It is significant coumarin present in the edible parts of the plant and is advocated responsible for analgesic properties and regulating the serotonin hormone in the body [14]. Tectoquinone, Rubiadin and lucidin have been isolated from the plant.

Alkaloids are potent and vital components that are isolated from the plant and are claimed responsibility for the structural alteration of proteins and cell signalling protocol. Xerine is on the significant alkaloids that had been separated from the plant. Its precursor is called as proxerine was isolated by Heinicke (1985).

Terpenes that were derived from geraniol are known as Iridoids that were glycosidic derivatives called, citrifolinoside A and asperulosidic acid. They are found to regulate blood pressure [15]. Diacetyl asperulosic acid constitutes almost for about 78% total iridoids in the plant [16].

PHARMACOLOGICAL ACTIVITIES
Anti dementia activity
The fruits of M.citrifolia are dried and extracted with ethanol. This was fractionated using chloroform, ethyl acetate and butanol and was used at a dose of 100microgram/ml. Results showed that the M.citrifolia extracts were increasing the blood circulation to the brain, thereby promoting the memory of the rats [17].

Anti-inflammatory activity
There was a study where the in-vitro anti-inflammatory activity of the fruit juice was estimated on COX-1 and 2 directly and another study where the study was conducted in carrageenan-induced paw edema method which was compared with standard drugs, Aspirin, indomethacin. The oil that is extracted from the seeds was used to test the activity in COX and LOX, which showed the oil was potent at concentration 0.5-1mg/ml.
**Antibacterial activity**

The roots of the plant are used to test the analgesic activity of the plant *M. citrifolia*. The aqueous extract was used to test the analgesic activity in the hot plate method using rats. It showed the activity at a dose of 800mg/kg via injections to the peritoneal cavity. The standard drug used was naloxone in the writhing test, too [18].

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**Anti-parasitic activity**

The aqueous extract of fruits of the *M. citrifolia* plant at a dose of 50mg/ml and ethanol extract at the dose of 25mg/ml were tested for anti-parasitic activity against Ascardiagalli in chickens. The death rate of the parasites was higher in the ethanol extracts and suggested a better activity at higher doses [19].

**Antibacterial activity**

The Iridoids, especially diacetyl aperulodisic acid and aperulodisic acid, were found responsible for the antibacterial activity of the fruits of *M. citrifolia*. The methanol fraction from the n butanol extract was investigated for antibacterial efficacy on *E.coli, Calbicans* and *S.aureus*, which showed a potent efficacy [20].

There was a study where the *M. citrifolia* fruit juice was investigated for the antibacterial activity on the human tooth. The study was designed to estimate the effect of the oral administration of extract on *E.faecalis*. The bacterial culture was inoculated in the teeth, and a smear was formed, and the treatment of the teeth with the juice removed the smear layer under scanning electron microscopy [21].

Another study included to compare the antibacterial activity of methanol extract, hexane and ethyl acetate extracts on various bacterial strains like *B.subtilis, S.aureus, L.lactis, E.coli, K.pneumonia, S.paratyphi, V.cholera* and *E.faecalis*. The results showed methanol extract was potent to kill all the strains of bacteria and hexane extract was not active on any of the above bacteria [22]. The same test was conducted on fungus also. Fungal species included were *Calbicans, A.niger, Fetospermum, Rhizopus* and mucor species. Int his test even methanol and ethyl acetate extracts showed the highest activity compared to the hexane.

**Antiviral activity**

The fruit was investigated for the antiviral activity against HIV-type 1 in Hela cell lines. The results showed that the juice showed better activity in treating HIV and other viruses [23].

**Anti-cancer activity**

Citrifolia juice was investigated for the anti-tumour activity in MMTC transgenic mice which were models for mammary cancer. It did not show any activity on breast cancer and its reduction. So it can be advocated that the fruit juice does not have any effect on the female breast cancer risk of incidence but will give only supplementation advantages only [24].

The fermented exudate of the plant was tested for its anti-cancer activity at a dose of 500 microlitres per day. It was investigated on sarcoma 180 ascites rat model. It was noted that 80% of mice became tumour less and 45 days after tumour induction and those mice which were not treated were dead in 30 days of the cancer induction [25].

A study was conducted to test the anti-cancer activity of the fruit juice on the Hela and Siha cell lines and was compared with standard drug, Cisplatin. And a group with the combination of both was also studied, and the results showed the combination showed better activity than individual groups [26].

The dichloromethane extract of the leaf was tested for its anti-cancer activity in cell lines. Chemical constituents like damnacanthal, scopoletin and rutin were hypothesized as responsible for the antineoplastic activity. The tests were carried on epidermoid carcinoma, cervical cancer cell lines, breast cell lines and liver cells. The extract was potent in inhibiting the growth of cells in a better efficacy when compared with isolated lead molecules [27].

There was a clinical trial also that was conducted on the heavy smokers of cigarette. Those subjects were tested for the DNA adducts level after consumption of the juice at 1 ounce compared to females who are higher in males. The mechanism was suggested by preventing the DNA binding to the carcinogen [28].

**Antioxidant activity**

The free radical scavenging activity of the fruits without seeds was estimated and reported there is a comparably similar activity of the juice with that of standard ascorbic acid [29]. The antioxidant activity of citrifolia was studied, and results showed that the fruit extract is three times more potent than Vitamin C that is ascorbic acid. Neurologin and American were the antioxidant chemicals that were found in the study.

**Anti-arthritic activity**

The anti-arthritic activity was tested with the fruit juice on arthritic rats at a dose of 2ml/kg. The extract reduced the inflammation in the joints and arthritic index also. The results were compared to the standard drug indomethacin. This activity was inferred to the presence of phenols and flavonoids. The reduction in the secondary lesions and mononuclear infiltration also [30].
Anti melanin activity
The anti-pigmentation activity of the various parts of the plant like fruits, leaves, stems and seeds were investigated in tyrosinase inhibitory activity. The ethanol extracts of fruits and seeds showed better activity in controlling the tyrosinase enzyme compared to the leaf. This activity was attributed to the presence of lignans.

Wound healing activity
The leaf juice was extracted with ethanol and further extracted with methanol and hexane were tested for wound healing capacity of the plant. The platelet-derived growth factors and adenosine receptors were taken as the parameters for the study in mice. In the study, methanol extract showed significant wound healing activity by closing the wound, and the times were considerable [31].

Antihyperlipidemic activity
The clinical trial was conducted for weight loss on 22 subjects with the regular diet and exercise and supplementation with the plant-based supplements. The weight loss was observed in all the issues significantly. Interestingly, there were no side effects reported too after a fat loss in the subjects [32].

One study probed the activity of ethanol extract of leaf and fruits on obesity by testing them on lipoprotein lipase. The activity was found to be higher in leaves than fruits. It was attributed to the presence of catechin and rutin that are present in the leaves that caused the activity [33].

Anti hyperlipidemia activity was studied on the ethanol extracts of fruits, leaves and roots of the plant in rats and mice, which showed a reduction in cholesterol, LDL and atherogenic index too. The death of the animals happened at the dose of 10g/kg, which was way safer than any other extract known. So there was lesser toxicity shown in the study [34].

The study included the comparison of methanol, ethanol, aqueous, butanol and chloroform extracts of fruit in inhibiting the LDL’s of the plant. All of the extracts showed better activity in lowering the LDL oxidation, which was hypothesized to the presence of Americanol, morindolin and isoprene [35]. Further studies proved that the fruit juice reduced the obesity that is related to the insulin resistance in invitro muscle cells which was schematized by the inhibition of ROS and damage to the mitochondria.

Anti-diabetic activity
The commercially available fruit juice was tested for the anti-diabetic activity, and the extract was administered orally in the steroid-induced model in Wistar rats. The dose was given at 2ml/kg in rats. The steroid used to produce DM was dexamethasone and compared with the standard drug, Rosiglitazone. It caused liver damage in the rats [36].

Other studies include the investigation of the anti-diabetic activity of the fermented juice in streptozotocin-induced diabetes, and the standard drug was taken as Glibenclamide. The dose was 2ml/kg and which was administered two times a day for twenty days. The juice was proven effective in streptozotocin-induced diabetes.

Other test included the testing of fruit juice in the alloxan-induced diabetes method. The assay was performed in Dawley rats at a dose of 1ml per 150g and was administered orally two times a day for 20 days. The blood glucose was significantly raised with the induction of diabetes, and the administration of the juice significantly lowered the blood glucose levels [37].

Hepatoprotective activity
The hepatoprotective activity of the plant was investigated in hamster which was fed on the high-fat diet and administered the juice daily at 5ml/kg. It showed a significant activity that was attributed to the antioxidant activity of the fermented juice of the fruit

CONCLUSION
Morinda citrifolia is a plant of choice it comes to food or medicine. It is well known to treat almost all the diseases related to all the organ systems of the body. The toxicity was also very low, and at higher doses mortality was seen. Further research was demanding in establishing the anti-cancer mechanisms and antiviral properties of the plant. The industries also should employ the products related to the fruit juice of the plant in view of its chemical composition and nutritional fact.

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Conflict of Interest
Authors declared no conflict of interest.

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