A Comprehensive Review on Therapeutic Perspectives of *Morinda citrifolia* (Indian Noni) to Combat Cancer

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Authors’ contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

**Background:** Indian Noni (*Morinda citrifolia* L.) is a large shrub or small evergreen tree, also known as Indian mulberry. It is a medicinal plant that has been used as conventional medicine and food additives for a long time. As a drug, plant bioactivity is attributed to its secondary metabolites. *M. citrifolia* has very rich nutrients and consists of over 100 varieties of chemical compounds which have been isolated so far from the plant. In disorders such as skin ailments, respiratory infections, gastritis, menstrual, abortion, diabetes, and venereal diseases, it also shows beneficial effects.

**Materials and Methods:** The relation of noni juice or its extract (fruit, leaves or root) to anticancer and/or immunostimulant properties was investigated in this study. A Medline quest was performed along with cross-referencing using the main search terms ‘*Morinda citrifolia* and cancer’.

**Results:** According to our search results for scientific study *M. citrifolia* is used in literature for more than 40 forms of ailments. Crude extract is recorded from various plant and fruit juice components. There are records of amino acids, anthraquinones, fatty acids, flavonoids, iridoids, lignans, polysaccharides, sterols, carbohydrates, terpenoids, etc. in the crude extract of different sections of plant and fruit juice that are therapeutically beneficial for a wide range of pathological conditions.

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Conclusion: Literature indicates that Nonii pharmacologically active and used in various cancer types (Colon, breast, esophageal, colorectal Cancers, cardiovascular disorders, diabetes, hypertension, arthritis). This plant's high potential classifies the compounds as the noteworthy medication of the future, and clinical trials are needed to demonstrate their effect on life-threatening diseases such as cancer. Further analysis warrants the isolation of the active components. These properties can be substantiated by the preclinical or/and clinical investigations.

Keywords: M. citrifolia; Indian Noni; antioxidants; anticancer activity; therapeutic perspectives.

1. INTRODUCTION

Modern principles of health assistance, such as dietary therapy and phytotherapy, have arisen as guidelines for the ingestion of nutraceuticals of plant origin. Nutraceutical provides the user with prescription or nutritional benefits by supplying ways to preserve health and protect against illness [1]. A functional plant diet, on the other side, supplies the body with the essential quantities of vitamins, fats, proteins, carbohydrates and several other compounds necessary for its existence. Botanicals are however, commonly used as synonyms for herbal products. Then, a legal distinction between plant nutraceuticals and pharmacologically active herbs or botanicals is required [2]. In every community of the world, herbal and natural products of folk medicine have been used for centuries [3]. India is rich with herbs and medicinal plants and it has been documented that a significant number of plant extracts are of great value against various tropical diseases and physiological disorders such as cancers and tumours. Due to their low toxic effects and costs, usability and great utility as complementary therapies, natural medicines are gaining great popularity [4].

M. citrifolia L. (Rubiaceae)(MC), usually known to as noni [5] commonly referred to as famine fruit, plays an important role in everyday dietary intakes, as it contains a variety of vitamins, phytochemicals, and electrolytes. These constituents have many biological functions that perform a role in the immune system and are anti-tumor, antibacterial, antiviral, antifungal. In all seasons, this plant produces fruit [6]. With circular veins, these fruits are thick and ovoid in form. When unripe, they are green and when fully mature, yellowish-white. During the ripening process, the fruits have a tender, watery flesh, and a cheese scent that becomes more and more pronounced and pungent [7]. In treating parasitic, tumorous, anthelmintic, analgesic, microbial, fungal, coronary, hypotensive diseases, more than 160 phytochemicals have been isolated from the plant M. citrifolia, making it an herbal cure. In disorders such as skin diseases, respiratory infections, gastritis, menstrual diseases, diabetes and venereal diseases, it also shows beneficial effects. About 80 species are included in the genus Morinda, mainly of old-world origin M. citrifolia. In the Pacific and even in tropical America, citrifolia is spread [8]. Many portions of the M. citrifoliane are attributed to their proposed cancer consequences [9], dyslipidemia [10], inflammation [11] and immunostimulant properties [12]. In narcotics, including the stems, leaves, fruit, and seeds, citrifolia tree is used. The aim of this review is to analyze the anticancer property update associated with M. citrifolia L. (Noni Indian).

2. SCIENTIFIC CLASSIFICATION

Botanical name: Morinda citrifolia
Domain: Eukarya
Kingdom: Plantae
Phylum: Magnoliophyta
Class: Magnoliopsida (dicot)
Order: Rubiales
Family: Rubiaceae (coffee family)
Genus: Morinda
Species: Morinda citrifolia

3. BACK GROUND OF M. citrifolia L.

M. citrifolia is one of the most important fruits widely used for its restorative health properties, diminishing its popularity over the years due to the ripened fruit's unpleasant odour. M. citrifolia is also called as Indian Mulberry or Indian Noni [13]. M. citrifolia is often eaten in the form of juice. It is also often preferred for individuals to take M. citrifolia in the form of capsules containing dehydrated M. citrifolia berries. Throughout the year, the M. citrifolia plant blooms. The colour of the flower is white. M. citrifolia plant is evergreen plant [14].
4. MORPHOLOGY AND PHYSIOLOGY

In South-East Asian countries, Australia and the Pacific Islands, there are 80 distinctive species of the genus Morinda. *M. citrifolia* is a small evergreen tree that grows to a height of up to 3-10 m before it matures. The arrangement of the leaves is pinnate, glossy, 5-17 cm long and 10-40 cm broad, opposite each other. It is distinguished by its straight trunk, bright green and elliptical leaves, its unusual ovoid, grenade like yellowish fruit-the development of the fruit seen is up to 12 cm consisting of a lumpy surface while the polygonal shaped parts are hidden. It gives a foul taste and odour to fruit when ripe [15]. In order to insert a peduncle, flowers are clustered together. The peduncles are 5 lobed corollas and the taunted rim calyx of up to 10-30 cm in length [14]. Root structures are a significant lateral compromise of a tap root. Yellowish wood and roots yielding yellow coloured dye are the species' most characteristic feature [16].

5. *M. Citrifolia* L. PHYTOCHEMISTRY

*M. citrifolia* has very rich nutrients and consists of more than 100 chemical compound varieties that have been isolated from the plant so far. Based on the drying process, harvesting method and time, location of cultivation and development and climatic conditions, the variation in their chemistry [17]. Phenols, polysaccharides, anthraquinones, carotenes, lavonoids, steroids and lactone moieties are among other compounds identified from the fruit. Many volatile elements, such as terpenoid aldehydes and ketones [18], have also been isolated from the plant. Some experiments have also extracted fatty acids and esters from the fruit, containing sulphur compounds such as linalool and methanethicol etc. Hexanoic acid and octanoic acids, present in the mature fruits, were isolated from the plant [19]. While lipids are macronutrients, they are present in a much smaller quantity in the fruit. Eicosanoic acid has been isolated from caprylic acid. Higher seeds such as Nonioside A, B, C, D and E were successfully isolated from the plant's seeds. Saturated fatty acids have been identified from the seeds, such as palmitic acid, lauric acid, stearic acid and arachidic acid. Carotenoids and saponins are isolated from roots and fruits, primarily from beta carotene, present in higher concentrations in plant fruits and bark [20].
Flavonoids are primarily from roots derived from plants and tannins are also present along with flavonoids that belong to the polyphenols class. Fruits also contain flavonoids, although they are relatively smaller than the roots. The volume of the plant content ranges from 180-350 mg/100 g, and compounds such as kaempferol, quercetin, narcissoside, and rutin have been isolated. There is a community of tannins from the seeds and stems of the plant that are isolated. With the variance of the plant's growth stage, the phenolic content of the seeds was checked. The more mature and ripe the fruit, the lower the polyphenol level in the plant has been identified [21].

![Anthraquinone glycosides and Other glycosides](image)

**Fig. 5. Bioactive compounds of M.citrifolia [18]**

**Table 1. Chemical composition of Noni [18]**

| Description          | Content | Unit     |
|----------------------|---------|----------|
| Moisture             | 89-90   | g/100 g  |
| Protein              | 0.2-0.5 | g/100 g  |
| Ash                  | 0.2-0.3 | g/100 g  |
| Total fat            | 0.1-0.2 | g/100 g  |
| Total carbohydrate   | 9.0-11.0| g/100 g  |
| Glucose              | 3.0-4.0 | g/100g   |
| Sucrose              | <0.1    | g/100 g  |
| Energy               | 163-197 | kJ/100 g |
| Dietary fiber        | 0.5-1.0 | g/100 g  |
| Vitamin C            | 3-25    | mg/100 g |
| Vitamin B1           | 0.003-0.01| mg/100 g |
| Vitamin B2           | 0.003-0.01| mg/100 g |
| Vitamin B6           | 0.04-0.13| mg/100 g |
| Vitamin B12          | 0.1-0.3 | mcg/100g |
| Folic acid           | 7.0-25.0| mcg/100 g|
| Biotin               | 1.5-5.0 | mcg/100 g|
| Niacin               | 0.1-0.5 | mg/100 g |
| Vitamin E            | 0.25-1.0| IU/100 g |
| Total carotene       | 18-22   | IU/100 g |
6. ANTI-CANCER ACTIVITY OF Morinda citrifolia

As cancer cells have a lower growth factor than normal cells, cancer is a condition caused by abnormal cell division. Anti-cancer compounds are however, usually compounds that can prevent growth or kill cancer cells but do not damage normal cells. Morinda citrifolia fruit juice has long been used by people to cure cancer in the Hawaii and Tahiti islands [22]. Depending on the form, Morinda citrifolia fruit juice activates the immune system to help the body against cancer, and destroys a small portion of cancer cells (0-36 percent). Components will activate the immune system in Morinda citrifolia juice [23]. In MMTC transgenic mice, which were models for mammary cancer, MC juice was examined for anti-tumour activity. There was no evidence of any activity or decline in breast cancer. It should also be advocated that fruit juice has little effects on the probability of occurrence of female breast cancer, but only has supplementation benefits [24]. A research to test the anti-cancer effect of fruit juice on the cell lines of Hela and Siha was performed and compared with the normal drug, Cisplatin. And a sample was also tested with the combination of both, and the findings showed greater behaviour than individual groups in the combination [25].

Endophytic fungi are also associated with the capacity of Morinda citrifolia as an anti-cancer. As many as twelve distinct species of endophytic fungi isolated from leaves and three from Morinda citrifolia have been found by [26]. The development of human LU-1 (lung), PC-3 (prostate), and MCF-7 (breast) cell line carcinomas with IC50 values of around 10μg/mL was inhibited by all (3) Morinda citrifolia leaf endophytic fungi [26]. The dichloromethane leaf extract was tested in cell lines for its anti-cancer efficacy. As responsible for the antineoplastic activity, chemical constituents such as damnacanthal, scopoletin and rutin were hypothesised. Epidermoid carcinoma, vaginal cancer cell lines, breast cell lines, and liver cells were tested. Compared to isolated lead molecules, the extract was powerful in inhibiting cell growth in a better efficacy. The potential of Morinda citrifolia as an anti-cancer is also attributed to the content of anthraquinone essential oil [27] and anthraquinone [28]. Morinda citrifolia fruit essential oil had an IC50 value of 91.46 and 78.15μg/mL for human colorectal carcinoma line cells (HCT-116) and human breast carcinoma cells (MCF-7) respectively [27]. The plant's fermented exudate has been tested for its anti-cancer potency at a dose of 500 microlitres per day. The 180-ascites rat model of sarcoma was studied. It was observed that 80% of mice were less tumorous and 45 days after tumour induction, and those mice that were not treated were dead after 30 days of cancer induction [29]. There was also a research report that was performed on heavy tobacco smoking. After intake of the juice at 1 ounce, these subjects were assessed for the amount of DNA adducts relative to women who are higher in males. The method was proposed to stop the binding of DNA to the carcinogen [30]. An important inhibitory effect on the proliferation of human lung and colon cancer cells [28] is demonstrated by anthraquinone compounds isolated from Morinda citrifolia roots.

7. CONCLUSION

The plant of choice for food or medicine is Morinda citrifolia. It is well known that nearly all the disorders associated with all the body's organ systems are treated. Toxicity was still very low and mortality was seen at higher doses. Further research has been required to determine the plant's anti-cancer mechanisms. These properties can be substantiated by the preclinical or/and clinical investigations. In order to determine a potential role of Morinda citrifolia, further in vitro and in vivo animal studies are needed if any of the relevant bioactivities suggest the presence of unknown anticancer activity.
CONSENT
It is not applicable.

ETHICAL APPROVAL
It is not applicable.

COMPETING INTERESTS
Authors have declared that no competing interests exist.

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