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Review on potential therapeutic effect of *Morinda citrifolia* L.

Aziatul Natasha Ahmad, Zulfitri 'Azuan Mat Daud and Amin Ismail

Morinda citrifolia L. is traditionally being used as medicinal herb in Polynesia. Previous studies have reported that this plant can be used as a medicinal plant to prevent and cure several diseases. In this paper, recent research regarding the potential therapeutic effect of *M. citrifolia* is reviewed. This plant includes broad range of therapeutic effect such as anti-diabetic effects, antibacterial activity, anti-cancer and antioxidant activity. The presence of antioxidant properties and phenolic compound in *M. citrifolia* were demonstrated as anti-diabetic effects and antibacterial agents, respectively. Besides, *M. citrifolia* act as anti-cancer properties because it enhanced the host of immune system. The primary aim of this paper is to review available information on potential therapeutic effects and nutritional advances related to *M. citrifolia.*

Address
Department of Nutrition and Dietetics, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 Serdang, Selangor, Malaysia

Corresponding author: Mat Daud, Zulfitri 'Azuan (zulfitri@upm.edu.my)

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Introduction

Morinda citrifolia L., commercially known as 'Noni' grows widely throughout the pacific and is one of the most important traditional Polynesian medicinal plants. There are several specific names including 'Indian mulberry', 'nuna' or 'arch' in Indian subcontinent, while it is known as 'mengkudu' in Malaysia or 'nhau' in South-east Asia [1]. The plants belong to family Rubiaceae (coffee family) and the subfamily Rubioideae [2]. The fruit is about 3–10 cm long and 3–6 cm wide in an oval shape and fleshy with an embossed appearance. It is a bit wrinkly, semi-transparent, and range in color from green to yellow, to almost white when ripened [2]. The Polynesians have been using *M. citrifolia* plant for medical purposes and foodstuffs over 2000 years. The fruit of this plant is commonly used and consumed as a juice, although leaves, flower, bark and root also can be used in traditional medicine preparation [3].

Recently, the health claims related to this plant include a broad range of health benefits including cancer, infections, arthritis, diabetes, asthma, hypertension and for relieving pain [4]. Nevertheless, there are only a few scientific research works related to nutritional and functional properties of *M. citrifolia* plants to support these claims [4,5].

Phytochemical properties of *M. citrifolia*

According to Wang and Su [6], *M. citrifolia* contained about 160 phytochemical compounds that have been identified, and the major macronutrients are phenolic compounds, organic acids, and alkaloids [4,7]. Up to date, there are several metabolites that have been described including polysaccharides, fatty acid, glycosides, iridoids, triterpenoid, anthraquinones, coumarins, flavonoids, lignans, phytosterols, carotenoids and a range of volatile constituents including monoterpenes, short chain fatty acids and fatty acid esters [8–10]. The main organic acids found in *M. citrifolia* are caproic and caprylic acids, whereas the principal reported alkaloid is xeronine [6]. *M. citrifolia* fruit also contains proxeronine, which is converted to xeronine in the body by the enzyme proxeroninase. It was hypothesized that xeronine is able to modify the molecular structure of proteins, allowing the protein to fold into its proper conformation and function properly [1]. In addition, xeronine also has a wide range of biological activities. Moreover, phenolic compounds that have been found to be the major group of functional micronutrients in *M. citrifolia* juice include damnacanthal, scopoletin, morindone, alizarin, aucubin, nordamnacanthal, rubiadin, rubiadin-1-methyl ether and other anthraquinone glycosides that have been identified in *M. citrifolia* [5,11].

Potential therapeutic effects of *M. citrifolia*

Different parts of *M. citrifolia* plant have been the subject of medical research aimed at investigating the plant's effects on health. Few published in *in vivo* and *in vitro* studies indicate that this plant exhibit the great use in alternative medicine for various illnesses such as arthritis, diabetes, high blood pressure, muscle aches and pains, menstrual difficulties, headache, heart diseases, AIDS, gastric ulcer, sprains, mental depression, senility, poor digestion, arteriosclerosis, blood vessel problems, drug addiction, and various cancers [12,13•,14,15].

Anti-diabetic effects

The fact that *M. citrifolia* is traditionally being used to treat diabetes mellitus and diabetes complication represents a valuable alternative for controlling this disease [16]. In fact, Sabitha *et al.* [17] reported that there is increased in demand for *M. citrifolia* fruit as alternative medicine for diabetes mellitus. The anti-diabetic agents of traditional medicinal plant extract are normally reliant on the degree of β-cell destruction [18]. The anti-diabetic effects of *M. citrifolia* fruits are due to stimulatory effect on the surviving β-cells to secrete more insulin or from regenerated β-cell [19]. Research on diabetic rats showed that *M. citrifolia* juice had synergistic action with injected insulin in reducing blood glucose [20]. In a clinical survey that involved more than 10 000 *M. citrifolia* juice users, it was reported that 83% of patients with type 1 and type 2 diabetes mellitus experienced an apparent improvement in their disease condition [1].

According to Rao and Subramaniam [19], an ethanolic extract of *M. citrifolia* fruit administered to streptozocin (STZ) induced diabetic rats for a period of 30 days reverted the elevated levels of blood glucose, glycosylated hemoglobin, blood urea and serum creatinine back to normal after the treatment. Moreover, a study by Horsfal *et al.* [20] reported that consumption of *M. citrifolia* fruit juice may reduce blood glucose levels. Similarly, Nayak *et al.* [21] reported a positive result in controlling blood glucose by consuming fermented juice of *M. citrifolia*. The Tahitan Noni Juice was used for the treatment and it showed that the juice had the best glycemic control as compared to normal group, diabetic standard group and diabetic untreated group. Literally, reduction of blood glucose activity takes effect because of the existence of antioxidant properties which are flavonoids, triterpenoid, triterpenes and saponin in *M. citrifolia* [22]. One of antioxidant properties which is saponin may stimulates insulin release from the pancreas [23•]. Flavonoids such as rutin that are present in *M. citrifolia* fruit may act as substances that cause another substance to be secreted, which stimulates insulin secretion by a mechanism related to that of sucrose [22] (Table 1).

Table 1

***In vitro, in vivo* and clinical studies related to anti-diabetic effects of *Morinda citrifolia*.**

Subject — type and number	Treatment	Measurable outcomes	Discussions	Ref
Albino rats of the Wistar strain were used Normal: $n = 6$ Diabetic control: $n = 6$ Diabetic control, fruit extract of *M. citrifolia* and *C. indica* (300 mg/kg/b. wt.): $n = 6$	Oral administration of combined aqueous fruit extract of *M. citrifolia* and *C. indica* at a concentration of 300 mg/kg body weight to Alloxon induced diabetic rats for a period of 7, 15 and 30 days	(1) Blood glucose of diabetic rats returned to normal (2) Significant antidiabetic and antihyperlipidemic effect on diabetic rats	These plants extract preserved the islets of Langerhans β-cells functions, which result in a significant increase in insulin activity	Kumar and Verma [24••]
Human diabetic subjects ($n = 4$)	(1) Subjects were divided into two groups: *M. citrifolia* versus placebo treated group. Treatment last for 21 days	Fasting and postprandial blood glucose were measured (glycemic control) (1) The *M. citrifolia* treated group showed reduction in fructosamine levels while placebo treated group showed increased in fructosamine levels	This study did not reveal the possible blood glucose lowering effects of *M. citrifolia* juice	Sabitha *et al.* [17]
Sprague-Dawley male rats (200–220 g body weight), $n = 24$	There were four groups of animal undergoing treatment for 20 days Normal group: received only food and water Diabetic experimental group: food, water + noni juice Diabetic standard group: food, water + glibenclamide Diabetic untreated group: food and water only	Fasting and postprandial blood glucose were measured (glycemic control)	Both treatment groups (diabetic experimental and diabetic standard) revealed a significant difference reduction in blood glucose level. Meanwhile, there was no significant difference in blood glucose for the diabetic untreated group (1) The presence of triterpenes and saponins may act as substances that lower blood glucose activity	Nayak *et al.* [21]