

Review of Phytochemical and Pharmacological Activities of Noni (*Morinda citrifolia* L.)

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Abstract

Review Article

Indonesia is a country rich in herbal plants. One of them is noni. Noni (*Morinda citrifolia* L.) is a plant that has long been known to have many properties for treatment and disease prevention. This article aims to review the phytochemical content and pharmacological activity of noni. The way to find information is through Google Scholar with the keywords "*Morinda citrifolia*," "phytochemicals," "pharmacological activity." Phytochemically, this plant has been reported to contain alkaloids, terpenoids, saponins, carbohydrates, proteins, tannins, flavonoids, steroids, scopoletin, anthraquinones, and ascorbic acid. Pharmacologically, this plant has been reported to have antioxidant, antiinflammatory, antifungal, antidiabetic, immunostimulant, anaphylactic, antiulcer, antihypertensive, and antibacterial properties. The conclusion is that the noni plant contains chemical compounds that are efficacious in treating various diseases. Because of that, the noni plant can be developed into phytopharmaca.

Keywords: *Morinda citrifolia* L, noni, phytochemicals, pharmacological activity, phytopharmaca.

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INTRODUCTION

Plants are generally useful as medicine, one of which is the noni plant. Noni or pace (*Morinda citrifolia* L.) is a medicinal plant that has been in demand in recent years. Noni is a tropical and wild plant. Noni can grow on the beach to an altitude of 1500 masl (above sea level), both infertile and marginal lands. Its distribution is broad, covering the entire South Pacific archipelago, Malaysia, Indonesia, Taiwan, the Philippines, Vietnam, India, Africa, and the West Indies

[1]. Noni (*Morinda citrifolia* L.) or pace, kudu (Java), cangkudu (Sundanese), koddhu (Madura), tibah (Bali) originated from Southeast Asia. Other names for this plant are noni (Betawi, Hawaii), nono (Tahiti), nonu (Tonga), ungoikan (Myanmar), and ach (Hindi). Noni tree reaches 3–8 m high, has white hump flowers. The fruit is a compound fruit, which is still young, shiny green, and has spots, and when it is old, it is white with black spots [2]. The noni fruit is shown in Figure 1, and the noni plant is shown in Figure-2.



Fig-1: Fruits of *Morinda citrifolia* L [3]



Fig-2: Plants of *Morinda citrifolia* L [4]

Scientific classification [1]

Kingdom: Plantae
 Subdivision: Angiosperms
 Class: eudicots
 Clade: Asteridae
 Order: Gentianales
 Family: Rubiaceae
 Genus: *Morinda*
 Species: *M. citrifolia*
 Binomial name: *Morinda citrifolia*

DATA COLLECTION

In compiling this review article, the technique used is to use the literature study by finding sources or

literature in primary data or international journals in the last 20 years (2000-2020). In making this review article, the search for data used online media with the keywords *Morinda citrifolia*, phytochemical and pharmacological activities. Search for the primary references used in this review article through trusted websites such as Mendeley, NCBI, ResearchGate, Google Scholar, and other published and reliable journals.

PHYTOCHEMICAL REVIEW

The phytochemical content of noni plants is presented in Table-1 and Table-2 below.

Table-1: The results of the qualitative analysis of phytochemical compounds in noni and their benefits [5]

Plant parts	Types of compounds	Benefits
Fruit	Alkaloids (xeronin)	Increase enzyme activity and protein structure, activate the immune function.
	Polysaccharides (glucuronic acid, glycosides) Scopoletin	Immunostimulant, anticancer, antibacterial Dilates blood vessels, analgesic, antibacterial, antifungal, antiinflammatory, antihistamine
	Vitamin C	Antioxidants
	Dietary fiber	Lowering cholesterol, binding fat, regulating blood sugar levels
Leaf	Glycosides (flavonol glycosides)	Deworming, tuberculosis
Root	Anthraquinone (damnachantal)	Anticancer, antibacterial, antiseptic

Table-2: Results of quantitative analysis of the phytochemical content of *Morinda citrifolia* L

Plant parts	Solvent	Compound	Wavelength	Concentration	Test method	Ref.
Callus	Ethanol	Alkaloids	-	-	Gas chromatography-mass spectrometry	[6]
Fruit	Ethanol	Alkaloids, flavonoids, phenols, and terpenoids.	764 nm	17.191 (mg/L)	Folin -Ciocalteu	[7]
	Ethyl acetate	Alkaloids, flavonoids, phenols, and steroids				
Leaf	n-hexane, methanol	Alkaloids, flavonoids, and saponins.	-	-	Thin-layer chromatography	[8]

Other research discusses the medicinal plant *Morinda citrifolia* L containing various phytochemical

compounds and their pharmacological activities. Phytochemical compounds such as alkaloids,

carbohydrates, proteins, flavonoids, glycosides, fats, steroids, triterpenoids, and tannins have been identified from various parts noni plant (*Morinda citrifolia* L) [9]. Another study showed that flavonoids were present in the ethanol extract of noni (*Morinda citrifolia* L) using thin-layer chromatography (TLC) with a mobile phase

system of butanol-acetic acid glacial-water (3: 1: 1 v/v/v). TLC test results showed the presence of flavonoids in the extract of noni (*Morinda citrifolia* L) [10]. Some of the structures of the noni fruit extract's flavonoid compounds are shown in Figure-3.

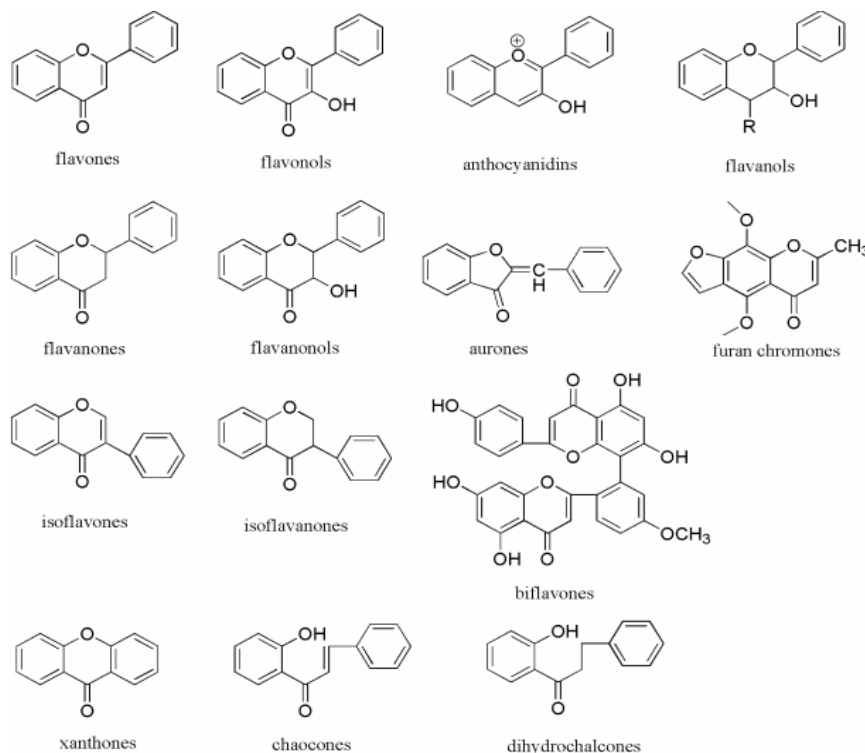


Fig-3: Chemical structure and classification of flavonoids contained in noni fruit extract [11]

Phytochemical compounds that have been isolated from noni fruit can be seen in Table 3 below.

Table-3: Compounds isolated from the fruit of *Morinda citrifolia*

No.	Structural class	Name of the compound	Ref.	
1.	Anthraquinones	Anthragallol 1,3-di-O-methyl ether	[12]	
		6-Hydroxyanthragallol-1,3-di-O-methyl ether		
		Morindone-5-O-methyl ether		
		Anthragallol 1,3-di-O-methyl ether		
2.	Esther	2-Methoxy-1,3,6-trihydroxyanthraquinone	[13]	
		1-n-Butyl-4-(5'-formyl-2'-furyl) methyl	[14]	
		1-n-Butyl-4-methyl-2-hydroxysuccinate		
3.	Flavonoids	1-n-Butyl-4-methyl-3-hydroxysuccinate	[15]	
		Kaempferol		
		Quercetin		
4.	Iridoid	Nicotifloroside	[16]	
		Rutin		
		Asperuloside		[17]
		Borreriagenin (previously morindacin)		
		Deacetylasperuloside		
Dehydromethoxygaertneroside				
6 β ,7 β -Epoxy-8-epi-splendoside				
		6 α -Hydroxyadoxoside		

PHARMACOLOGICAL ACTIVITY REVIEW

Antidiabetic Activity

Diabetes mellitus is a hyperglycemia disease characterized by absolute insulin deficiency or decreased cell sensitivity to insulin [18]. Diabetes is a metabolic disorder due to insulin failure. This study

aimed to observe the antidiabetic effect of *Morinda citrifolia* fruit juice. The research was conducted on Wistar rats consisting of 48 tails from four groups taken for examination. Three groups of 36 mice induced diabetes by administering a single i / p 5% w / v alloxan monohydrate in normal saline. One group as a healthy

control (Group-I), and one as a diabetes control (Group-II), the comparison of the effects of noni juice 2 mg/kg BW (Group-IV), with the usual standard drug, metformin 100 mg/kg (Group -III). The drug is given by oral route. The parameters studied were serum glucose levels, triglycerides, total cholesterol, HDL, LDL, and hemoglobin on days 1, 14, 28 after starting treatment. After the induction of diabetic serum glucose and elevated triglyceride concentration and total cholesterol, HDL, LDL concentration decreased statistically significantly where there was no statistical change in the hemoglobin level. The group given noni juice showed better results, but the best results were obtained with standard antidiabetic drugs [19].

Other researchers also conducted experiments by giving noni juice to Sprague-Dawley rats. Twenty adult male Sprague-Dawley mice weighing from 145 to 230 g were used for the investigation. They were randomly divided into four groups consisting of five mice, each mouse. The first group (Group A) served as control and received standard rat food and water for the study duration. The second group (Group B) received pre-treatment with noni juice for four weeks before introducing diabetes. This group continued treatment with noni juice for the next four weeks of diabetes induction. Group C received noni juice treatment after diabetes induction for four weeks. Group D was given distilled water at a dose of 1 mL/150 mg body weight for four weeks before induction of diabetes with alloxan and distilled water at a quantity of 1 mL/150 mg body weight for four weeks after induction of diabetes with alloxan and distilled water at a dose of 1 mL/150 mg body weight for four weeks afterward induction of diabetes with alloxan. Animal glycemia levels in all four groups were monitored and compared. Mice that received prophylactic noni juice (group B) before induction of diabetes with alloxan had the best glycemic control and the best treatment results. However, discontinuation of treatment with noni juice resulted in the reversal of hyperglycemia. This study demonstrated that noni juice had blood-glucose-lowering activity after trial-induced diabetes in Sprague-Dawley rats [20].

In another study, an evaluation of the effect of noni (*Morinda citrifolia* L.) fruit extract in diabetic rats using glucose tolerance method in rats and alloxan-induced diabetic mice. Glucose tolerance test in mice showed a decrease in serum glucose levels 30, 60, and 90 minutes after giving the extract at a dose of 500 mg/kg BW, respectively 37.0 %, 27.4%, and 25.4%; and at a dose of 1000 mg/kg each of 28.8 %, 19.6 %, and 21.8 %. This study's results were noni fruit extract reduced serum glucose levels in rats by glucose tolerance method, but it was not statistically significant. In the diabetic mice test with alloxan, noni fruit extract showed significant antidiabetic activity at 500 and 1000 mg/kg BW [21].

Antiinflammatory Activity

Utilization of the fruit of the noni (*Morinda citrifolia* L.) plant to treat inflammatory diseases such as arthritis was common in the ancient South Pacific [22]. Another study was also conducted by someone with noni juice experiments on people with gingivitis. This inflammatory process is caused by several species of bacteria in the dental plaque. In vivo and in vitro experiments were prepared. Patients from the in vivo group were divided into noni and control groups. Both groups consisted of patients suffering from gingivitis/periodontitis who were introduced to excellent and standardized oral hygiene practices. Patients in the noni group also used noni juice to wash their mouths with their mouths twice a day. The Papillae-Bleeding-Index (PBI) was evaluated by comparing the inflammation status in the two groups. Bacterial probes were isolated from the patient's gingival pouch for species identification and performed in vitro experiments for possible antimicrobial effects of noni juice. Papillae-Bleeding-Index (PBI) noni group experienced a very significant increase from a mean of 2.25 at the start of the observation period (t_0) to 1.01 after four weeks of noni treatment (t_1), compared with a change of 2.11 at t_0 to 1.95 in t_1 in the control group. Comparing the difference in PBI values (t_0-t_1) between the noni group and the control group was very significant using the t-test at the level of $p = 0.01$. Only small zones of inhibition were observed in agar diffusion tests on agar plates coated with aerobic, anaerobic, and *Candida* cultures isolated from the patient's gingival pouch after treatment with real or neutralized noni juice in different concentrations. The weak bacteriostatic effect occurred in the agar dilution experiment with noni juice in higher concentrations (original and balanced noni juice). This study has shown that a combination of good oral hygiene and noni juice administration is a promising treatment for gingivitis and periodontitis. Additional therapy with noni juice significantly reduced gingival inflammation [23].

Antifungal Activity

Morinda citrifolia juice extract was used in the antifungal test. The antifungal properties of *Morinda citrifolia* fruit extract against *Candida albicans* were tested in vitro at various concentrations and at different times. The inhibitory effect of *Morinda citrifolia* extract on *Candida albicans* was determined by culture and broth dilution test. Using culture was that the growth of *Candida albicans* was not detected with 50 mg/mL extract at 30 minutes contact time or with 60 mg/mL extract at 15 minutes contact time. With the broth dilution test, the minimum fungicide concentration of the extract against *Candida albicans* was 40 mg/mL at a contact time of 90 minutes or with 50 mg/mL at 15 minutes. This study indicated that the *Morinda citrifolia* fruit extract had an antifungal effect against *Candida albicans* and the inhibitory effect varied in concentration and contact time [24].

Antioxidant Activity

One of the antioxidant activity of noni fruit ethanol extract is the presence of flavonoids and phenolic compounds. Antioxidants are electron-giving compounds (electron donors) that play a role in inhibiting oxygen-mediated oxidation. Antioxidant compounds can prevent the harmful effects caused by free radical compounds, so they play an essential role in the body's defense against disease. In this experiment, the antiradical activity test used the DPPH (1,1-diphenyl-2-picrylhydrazyl) method. The DPPH method is an effective and fast colorimetric method for estimating antiradical activity. Antioxidant activity is expressed by IC₅₀, which is the concentration required to produce a 50% decrease in DPPH activity. The smaller the IC₅₀, the stronger the antioxidant activity. From the calculation, it was obtained that the IC₅₀ value for comparison was 10.56 ± 0.42 µg/mL and the IC₅₀ for the ethanol extract of noni fruit was 104.73 ± 4.56 µg/mL. Based on the level of antioxidant strength, Rutin has extreme antioxidant activity (IC₅₀ < 50 µg/mL), while the ethanol extract of noni fruit has moderate antioxidant activity (IC₅₀ 101 - 250 µg/mL). One of the antioxidant activity of noni fruit ethanol extract is the presence of flavonoids and phenolic compounds. As an antioxidant, these compounds can stabilize free radicals by complementing the lack of electrons that free radicals have, and inhibiting chain reactions from forming free radicals [25].

Other studies were also conducted to evaluate noni (*Morinda citrifolia* L.) fruit extracts' antioxidant activity, including leaves, fruits, and roots. The solvents used were methanol and ethyl acetate, and the antioxidant effect was measured by the Ferric thiocyanate method (FTC) and thiobarbituric acid test (TBA). The methanol extract of noni root showed high antioxidant activity, which was not significantly different ($P < 0.05$) with α -tocopherol or butylated hydroxyl toluene (BHT). In contrast, the methanol extract of fruit and leaves showed negligible activity. On the other hand, the ethyl acetate extract from all noni parts showed significant antioxidant activity, comparable to α -tocopherol and BHT. Antioxidant activity was observed using the FTC or TBA method. The highest antioxidant activity is found in the roots. The results showed that several compounds contributed to the antioxidant activity in various parts of noni. Training in the seeds may be due to polar and non-polar compounds but, in leaves and fruit, only to non-polar compounds [26].

Immunostimulant Activity

The alkaloid fraction from the dried noni fruit was known to have immunostimulant activity at all test concentrations [27]. Another study was designed to verify the stimulating effect of the *Morinda citrifolia* fruit extract and fraction on the adaptive immune system's important components such as T lymphocytes and B lymphocytes. The effect of plant extracts on

lymphocytes was tested using in vitro (MTT test) and in vivo (cell response) methods. The results of the MTT study showed that hydroalcoholic extracts (0.5 and 1.0 mg/mL) and water extracts (0.5 and 1.0 mg/mL) significantly ($p < 0.05$) increased the extent of splenocyte proliferation in vitro 43.6, 54.5, 32.7, and 36.4 % respectively. In addition, hydroalcoholic extract (200 mg / kg) and aqueous extract (200 mg/kg) significantly ($p < 0.05$) enhanced cell-mediated immune response to levels of 33.52 and 18.56 %, respectively. Fraction I, Fraction II, and Fraction III failed to obtain lymphocyte stimulating effect in vitro and in vivo studies. The effect of *Morinda citrifolia* fruit extraction on B cells was measured by the delayed-type hypersensitivity method. Thus, this study shows that *Morinda citrifolia* L. fruit stimulates the adaptive immune system's main components, namely T cells, and B cells [28].

Anaphylactic Activity

This study aims to prove that the n-hexane extract of noni fruit can inhibit anaphylactic reactions in male Wistar rats induced by the hepatitis B vaccine. This study used an active cutaneous anaphylaxis method, followed by histopathological observations. A functional cutaneous anaphylaxis test was performed for two weeks. The test animals were divided into five groups, namely the control group without treatment, treatment with n-hexane extract of noni fruit at a dose of 50 mg, 100 mg, and 200 mg/kg BW rats. The group was given chromolin at a dose of 2.16 mg/kg BW rats as control positive. The test animals were sensitized twice (once per week) with hepatitis B vaccine (dose 145 µg/kg BW rats) subcutaneously on the back. In the second week, four animals were taken randomly from each group to be sacrificed, and their skin tissue and liver tissue were taken. The tissue was made as a histopathological preparation with hematoxylin-eosin staining. The results showed that administering n-hexane extract of noni fruit at a dose of 50 mg, 100 mg, and 200 mg/kg BW to Wistar male rats induced by the hepatitis B vaccine could inhibit active cutaneous anaphylactic reactions [29].

Antiulcer Activity

This study aims to analyze ethyl acetate extract's antiulcer activity from the fruit extract of *Morinda citrifolia* Linn (Rubiaceae) using different gastric and duodenal ulceration models in rats. The work was carried out by inducing gastric ulcers with oral administration of ethanol, aspirin by pyloric ligation, and duodenal ulcers caused by oral cysteine HCl. The extract was administered at 200 and 400 mg/kg orally 30 minutes before ulcer induction. The reference standard used is ranitidine (50 mg/kg). The antiulcer activity was tested by determining and comparing the test group's ulcer index with the standard drug treatment group. Gastric volume, total acid, and free acid were estimated in pylorus-bound mice. *Morinda citrifolia* (400 mg/kg) showed maximum

inhibition of gastric acid, free acid, and total acid to 53.54 %, 52.55 %, and 30.30 %, respectively. The ulcer index in the animals treated with *Morinda citrifolia* was much less than the standard cases treated with the drug. The results showed that *Morinda citrifolia* has significant antiulcer properties, which could be due to the drug's cytoprotective action or strengthening of the gastric and duodenal mucosa by increasing mucosal defences [30].

Antihypertensive activity

This study aims to examine the effect of *Morinda citrifolia* on hypertension in the elderly group. The noni fruit from generation to generation has been known as a traditional medicine to treat hypertension. This research is an experimental study with a pretest-posttest randomized control group design. The research subjects were 30 people. The statistical analysis test for systolic blood pressure is that there is a decrease in systolic blood pressure before and after drinking *Morinda citrifolia* extract capsules. Likewise, with diastolic blood pressure, there was decreased diastolic blood pressure before and after drinking *Morinda citrifolia* extract capsules. The results showed a decrease in systolic and diastolic blood pressure in the elderly who routinely took *Morinda citrifolia* extract capsules regularly [31].

Other researchers also revealed a decrease in blood pressure by consuming processed noni fruit and the effect of back massage in patients with hypertension aged 60-74 years. The average reduction in systolic area was 10.46 mmHg with p-value = 0.001, diastolic 3.23 mmHg with p-value = 0.003. Both treatments are known to have the same effect as vasodilation of blood vessels [32].

Antibacterial Activity

This study studied the antibacterial activity of noni leaf, fruit, and seed extracts in vitro using the diffusion disc method. Five different accessions of the *Morinda citrifolia* plant were randomly selected and screened for antibacterial activity against five other bacterial pathogens. The overall analysis of the various extracts' antibacterial activity revealed that the best inhibitory activity was produced by seed extracts (12.23 mm) compared to leaf and fruit extracts. All extracts inhibited *E. coli* and *Pseudomonas*. However, *Salmonella*, *Staphylococcus aureus*, and *Klebsiella* were not deterred by all extracts. The antibacterial activity analysis in all accessions showed the best antibacterial activity was produced by acquisitions 5, followed by accessions 1, 2, 3, and 4, respectively [33].

Other studies have also revealed that noni leaf processing has antibacterial effects. Noni leaf processing is carried out using flour, blending, juicing, and decoction. However, it did not show any inhibition against *Escherichia coli* and *Salmonella typhimurium* using the diffusion well test (negative). Liquid extract

of noni leaf flour is obtained by extracting flour using different solvents, namely water, ethanol, ethyl acetate, and hexane, then macerated for 24 hours, used for well testing. The liquid extract of noni leaf meal, which was macerated for 24 hours, was unable to inhibit the pathogenic bacteria *Escherichia coli* and *Salmonella typhimurium* but macerated using ethanol and ethyl acetate for 48 hours. There was an inhibitory power against the growth of *Salmonella typhimurium* bacteria [34].

CONCLUSION

Noni (*Morinda citrifolia* L.) has several bioactive components related to health benefits such as alkaloids, saponins, carbohydrates, proteins, tannins, flavonoids, steroids, and glycosides. Therefore, noni has biological activities such as analgesic, antipyretic, antiinflammatory, antioxidant, antifungal, antimicrobial, antiulcer, anaphylaxis, immunostimulant, and antidiabetic. Noni (*Morinda citrifolia* L.) has also been shown to have vigorous antihypertensive activity and may help develop new antihypertensive therapies. Because of that, the noni plant can be grown into phytopharmaca.

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