A REVIEW ON RECENT RESEARCHES OF MORINDA CITRIFOLIA, L. (NONI) AS FUNCTIONAL FOODS AND MEDICAL HERBS

TINJAUAN PENELITIAN TERBARU MORINDA CITRIFOLIA, L. (MENGKUDU) SEBAGAI PANGAN FUNGSIONAL DAN REMPAH MEDIS

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ABSTRACT

Morinda Citrifolia, L. known as Noni or Mengkudu is planting belonging to the family of Rubiaceae. A number of major components have been identified in leaves, roots, fruits of Noni plant, such as scopoletin, octanoic acid, vitamin C, iridoid, terpenoids, alkaloids, anthraquinones, beta-sitosterol, carotene, vitamin A, flavone glycosides, alizarin, amino acids, acubin, austin, caproic acid, caprylic acid and putative procynone. Its use as a botanical dietary supplement has grown tremendously in recent years. The results of epidemiological studies suggest that the Noni consumption may help prevent several chronic diseases, including cancer disease, cardiovascular disease, type 2 diabetes mellitus, heart disease, artherosclerosis, blood vessel problem, gastric ulcer, drug addiction, muscle ached and pein. Several studies have also demonstrated anti-inflammatory, antioxidant, antimicrobial, analgesic, and immunological activity. Based on a toxicological assessment, Noni juice was considered as safe. Although, a large number of in vitro and to a certain extent, and in vivo studies demonstrated a range potentially beneficial effects, clinical information data are still lacking completely. Therefore, to what extent the information findings from experimental pharmacological studies is not complete at present, so this article reviews potential health benefits for consumptions, its biological effects and looking for a new information that needs to be explored in detail before a recommendation can be made.

Key words: Noni (Morinda Citrifolia, L), functional food, medical herbs.

ABSTRAK


Kata kunci: Mengkudu (Morinda citrifolia, L), pangan fungsional, rempah medis.
INTRODUCTION

M. citrifolia, L. commonly called Noni from the family Rubiaceae is reported to have been used by Polynesians for over 200 years for two main purposes. First, the roots and the barks have been used as a dye for traditional and ceremonial clothes. Second, every part of the plant has been used medicinally in treating a variety of ailments (Palu et al., 2008).

A number of major components have explored by some researches and identified in the Noni plant such as scopoletin, octanoic acid, potassium, vitamin C, terpenoids, alkaloids, anthraquinones (such as nordamena-canthal, morindane, rubiadiene, and subadiin-1-methyl ether, anthraquinon glyco-side), beta-sitosterol, carotene, vitamin A, flavon glycosides, linoleic acids, alizarin, amino acids, acubin, L-asperuloside, caproic acid, caprylic acid, ursolic acid, rutin and protective proxeroneine (Wang et al., 2002).

Based on a literature review and recent advances in Noni research by Wang et al. (2002) is reported also that a research group led by Chi-Teng Ho at Rutgers University in the US is searching for a new novel compounds in the Noni plant. They have successfully identified several new flavanol glycosides, an iridoid glycoside from the Noni leaves, a trisaccharide fatty acid ester, rutine and asperulosidic acid from the fruit. Recently, phytochemical screenings of different commercial Nigerian Morinda citrifolia juice $1.3 billion in annual sales (Potterat and Humberger, 2007).

Many of Morinda citrifolia commercial juice parameters should be fixed including its concentrations variations, the prevalent bioactive component in the fermented products, pasteurization impact on these bioactive compounds, and the specification regarding the juice source for being fermented, and for how long, and pasteurized or unpasteurized (Brown, 2012).

Concerns have recently been raised about the safety of the Noni fruit juice for consumption (Mustafa et al., 2011). However, the sketchy details and a limited number of cases reported are inadequate to draw any conclusion (West et al., 2006b). The purpose of this article is to review and interpret relatively recent research on the benefits and biological activity of Noni fruit for its extensive utilization in health.

CHEMICAL COMPOSITION AND NUTRITIONAL VALUE OF NONI

Chemical Constituents of Noni

Approximately 160 phytochemical compounds have been identified and isolated from different parts of Noni plant (Singh, 2012). The micro nutrients are phenolic compounds, organic acids and alkaloids. Anthraquinones are the major phenolic compounds that have identified and contains dammcanthal, molindone, morindin, etc. and also aucubin, eserulloside and scopoletin (Krishnaiah et al., 2012). Among the reported, anthraquinones, dammcanthal appear quite unique with respect to their function for its anti-cancer and anti-HIV activity (Brett et al., 2011).

According to Blanco et al. (2006), it was said that the complete physiochemical composition of the fruit has not yet been reported and only partial information is available on Noni juice (Table 1.)

Yang et al. (2009) in their research reported that there are about 51 volatile compounds have been successfully identified in the ripe fruit using gas chromatography-mass spectrometry (GC-MS) including organic acids (mainly octanoic and hexanoic acids), alcohols (3-methyl-3-butene-1-ol), esters (methyl-octanoate, methyl decanoate), ketones (2-heptanone) and lactones.

Fatty acid glycosides and alcohols are one of the classes of phytochemicals
that have been reported in the fruits also by Samoylenko et al. (2006). Due to their structure, they possess more or less pronounced amphiphilic properties and may be the region responsible for the soapy taste of ripenfruits.

Table 1. Physico-chemical composition of Noni Juice (*)

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<tr>
<td>pH value</td>
<td>3.72</td>
<td>3.4</td>
<td>3.6</td>
</tr>
<tr>
<td>Dry matter</td>
<td>9.8 % ± 0.4 %</td>
<td>-</td>
<td>10.0</td>
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<tr>
<td>Total soluble solid (brix)</td>
<td>8</td>
<td>-</td>
<td>10.0</td>
</tr>
<tr>
<td>Protein content</td>
<td>2.5%</td>
<td>0.40 g/100 g</td>
<td>0.2</td>
</tr>
<tr>
<td>Lipid</td>
<td>0.15%</td>
<td>0.30 g/100 g</td>
<td>0.2</td>
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<tr>
<td>Glucose</td>
<td>11.9 ± 0.2 g/l</td>
<td>-</td>
<td>4.0 g/100 g</td>
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<tr>
<td>Fructose</td>
<td>8.2 ± 0.2 g/l</td>
<td>-</td>
<td>4.0 g/100 g</td>
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<tr>
<td>Pottassium</td>
<td>3,900 mg/l</td>
<td>188 mg/100 g</td>
<td>150 mg/100 g</td>
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<tr>
<td>Sodium</td>
<td>214 mg/l</td>
<td>21 mg/100 g</td>
<td>40 mg/100 g</td>
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<tr>
<td>Magnesium</td>
<td>14 mg/l</td>
<td>14.5 mg/100 g</td>
<td>12 mg/100 g</td>
</tr>
<tr>
<td>Calcium</td>
<td>28 mg/l</td>
<td>41.7 mg/100 g</td>
<td>25 mg/100 g</td>
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<tr>
<td>Vitamin C</td>
<td>155 mg/100 g</td>
<td>3 - 25 mg/100 g</td>
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</table>

(*) Source : Blanco et al. (2006).
Note: (a) Noni fruit
     (b) Tahitian Noni Juice (Commercial Noni juice that contains 89% Noni juice, 11% common grape juice concentrate)

Nutritional Value of Noni

Basically, the fruit contains 90% of water and the main components of the dry matter appear to be soluble solids, dietary fibers, and proteins. The fruit protein content is surprisingly high, representing 11.3% of the juice dry matter, and the amino acids are aspartic acid, glutamic acid and isoleucine (Chunhieng, 2003). While, vitamin have been reported in the fruit, mainly ascorbic acid about 24 158 mg/100 g dry matter (Potterat et al., 2007) and pro-vitamin A (Krishnaiah et al., 2012).

Minerals account for 8.4% of dry matter and are mainly potassium, sulfur, calcium and phosphorous, and also traces of selenium have been reported in the juice (Chunhieng, 2003). A phytochemical screening for the presence of secondary on the Indian Morinda citrifolia was detecting steroids, cardiac glycosides, phenols, tannins, terpenoids, alkaloids, carbohydrates, reducing sugar, lipids and fats, saponins and acidic compounds (Nagalingam et al., 2012).

POTENTIAL HEALTH BENEFITS OF NONI FRUIT CONSUMPTION
Prevention of Cancer Disease

In general, cancer is the second leading cause of death in the United States (US). According to the American Cancer Society/ACS (2007), 1,500 people per day die from cancer in the United States of America. Fighting against cancer is the great task for the Scientist engaged in this field. The etiology of most cases human cancer remains unknown (ACS, 2007). Although some cancers are preventable, a means to prevent most cancers is not yetknown. So, seeking a natural way to prevent human cancer is an urgent task for cancer prevention investigators (Wang et al., 2002).

The studies of food , diet, and cancer indicate that lifestyle changes include eating more fruits and vegetables, and quitting smoking will benefits cancer prevention. The phyto-chemicals present in some food have a wide range of
therapeutic effect against a number of diseases like diabetes mellitus, heart disease, common cold, arthritis, cancer, hypertension, dys-lipidemia, inflammatory bowel disease, depression etc. (Dahiya, 2013).

It has been reported that methanol extract of the Noni fruit at a concentration of 0.1 mg/mL exhibited cytotoxic activity against breast cancer and neuroblastoma cell lines at 29% and 36% respectively in 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide assay (Apornsuwan and Punjanon, 2006).

Meanwhile, Scientists extracted and scanned 18 different anthraquinones from the air dried powders of Hawaiian M. citrifolia roots for its anti-cancer activity using MTT cell proliferation assay. All the anthraquinones showed an anti-proliferation activity in both human lung cancer and colon cancer cells, specifically, 1,3-dihydroxy-2-formyl-anthraquinone had the highest effects (Lv et al., 2011).

Subsequently, another antitumor study was conducted on three groups of eight mice was induced with Ehrlich ascites tumor. The first, second, and third groups were given oral Morinda citrifolia juice, doxorubicin (a potent anticancer drug), and a combination of both, respectively. The results suggested that oral Morinda citrifolia fruit juice may be useful in the treatment of breast cancer, either alone or in combination with doxorubicin (Taskin et al., 2009).

Potential Mechanisms for Inverse Associations between Noni Fruit and Cancer Disease

Several mechanisms have been proposed to explain the inverse association between Noni juice consumption and colectal cancer risk observed in case-control studies. The mechanisms have been explained as follows: Inhibition of Both lipid peroxide (LPO) and superoxide anion radicals (SAR). Noni juice showed a dose-dependent inhibition of both LPO and SAR. The SAR scavenging activity of Noni juice compared to that of three known antioxidants: vitamin C, grape seed powder, and pycnogenol at the daily dose per serving level recommended by US RDAs or manufactures recommendations. Under the experimental conditions, the SAR scavenging activity of Noni juice was shown to be 2.8 times higher than that of vitamin C; 1.4 times that of pycnogenol and almost of the same (1.1 times) order as that grape seed powder. Therefore, Noni juice has great potential to scavenge reactive oxygen radicals (Su et al., 2005).

Reduced the liver LPO and SAR or protect the liver from an extrinsic carcinogenesis CCl₄ exposure. It is known that carbon tetrachloride (CCl₄) is liver carcinogen and lipid hydroperoxidation induces. To further confirm the antioxidant activity of Noni juice in vivo; a carbon tetrachloride induced liver injury model in female Sprague-Dawley (SD) rats was selected. In the experiment show that ten percent of Noni juice in drinking water for 12 days was able to reduce the liver LPO and SAR levels to 20% and 50% of that observed in the placebo group 3 hours after CCl₄ administration. In conclusion, Noni juice consumption may protect the liver from extrinsic carcinogenic CCl₄ exposure (Wang et al., 2002).

Protect individuals from oxidative damage induced by tobacco smoke.

It was hypothesized that antioxidants in Noni juice may protect individuals from cigarette smoke by scavenging oxygen free radicals and quenching lipid peroxides. In order to examine this hypothesis a one-month double-blinded, randomized, and placebo - controlled clinical trial was design to test the protective affect of Noni juice on plasma SAR dan LPO in current smokers. There was no effect observed on plasma SAR (0.23 ± 0.15 versus 0.21 ± 0.17 µmol/mL) and LPO (0.58 ± 0.22 versus
059 ± 0.21 μmol/mL) in the placebo group.

Prevention of Cardiovascular Disease

Cardiovascular diseases (DVDs) is the primary chronic diseases afflicting industrialized societies today. Development of atherosclerosis, thrombosis and hypertension is multifactorial process in which endothelial days function, inflammatory response, modified lipids and lipoprotein, and activated platelets; all play significant role in the process (Al-Faris, 2008). While, dyslipidemia is an independent and modifiable risk factors for cardiovascular diseases and treatment of dyslipidemia reduces cardiovascular events (Saf-Ur et al., 2010).

The results indicate that Noni juice may protect individuals from oxidative damage induced by tobacco smoke (Wang et al., 2002). Morinda citrifolia, L. (Noni) has considered in cardio-vascular diseases particularly related to hypertension, atherosclerosis and dyslipidemia. In this study, Saf-Ur and his colleagues (2010) used different animals models to evaluate the possible mode of action(s) of anti-dyslipidemic of the different part of Morinda citrifolia. It caused drastic increase in serum triglycerides and cholesterol synthesis particularly by the increase in HMG-Co-A (3-hydroxy-3-methyl-glutaryl-Co-A) activity and by inhibition of lipoprotein lipase responsible for hydrolysis of plasma lipids. Significant inhibition of rising in lipid level by extracts of various part of Morinda citrifolia in this model is indicative of inhibition of cholesterol biosynthesis by inhibition of HMG-Co-A.

Recent research has shown the role of 5-lipoxygenase in cardiovascular and neuro-psychiatric illness (Radmila and Hari, 2004). Based on the Radmila and Hari experiment, Deng and his colleagues isolated two new lignans, i.e. (+) - 3,4,3,4-tetrahydroxy-9,7-alpha xylic nan-7-alpha; 9-lactone and (+) 3,3-bisdimethyl-tanegaol as well as seven known compounds from the fruits which are responsible for inhibition of 5- or 15-lipoxygenase (Deng et al., 2007).

Another study, Lin et al., (2007) was reported has found two new anthraquinone, i.e. : 1,6-dihydroxy-5-methoxy-2-methoxy-methyl-anthraquinone and 1,5,7-trihydroxy-6-methoxy-2-me-thoxy-methyl-anthraquinone and one new lignan iso americanos acid A that isolated from the fruits of the Morinda citrifolia along with 11 known compounds which potential medicine for cardiovascular diseases.

Potential Mechanisms for Inverse Associations between Noni Fruit and Cardiovascular Disease

Although the results of epidemiological studies suggest that Noni fruit consumption decrease risk of cardiovascular disease, other explanations for the reverse association between Noni fruit consumption and cardio-vascular disease risk have been proposed. For example, serum chole-sterol levels, triglycerides, homocysteine and LDL, have been reported to be lowered while HDL increases by ingestion of commercial Noni fruit juice; in the double blind, placebo control human clinical trial involving 38 current smokers. But there is no significant changes in the placebo group, however, significant changes occurred in the commercial Noni fruit juice group. In fact, total cholesterol and triglycerides levels were lowered by 7.22% and 10.54% respectively (Palu et al., 2012).

In contrast, the HDL levels were increased by 16% in the commercial Noni fruit juice group compared to the placebo group (Wang et al., 2002). Commercial Noni fruit juice cholesterol-lowering effects were shown in the clinical trial involving current smokers but its cholesterol lowering effects in the non-smoking subject has been studied and the cholesterol lowering mechanisms have not been fully elucidated. To this end, a series of in-vitro bioassays were
done to evaluate the inhibitory effect of commercial Noni juice fruit, Noni juice concentrates and a methanol fraction of Noni fruit juice on HMG-Co-A reductase and the ACAT (Acyl-Co-A-Cholesterol-Acyltransferase) enzymes to elucidate its possible mechanisms of action. Nevertheless, Palu et al., (2012), were able to show that Commercial Noni fruit juice and Noni juice concentrates have inhibitory effects on HMG-Co-A reductase and ACAT enzymes. However, Noni juice concentrate inhibitory effects on HMG-Co-A reductase enzymes was more pronounced with < 1.0 mg/mL (IC50) than the inhibition of HMG-Co A reductase enzymes by commercial Noni juice at the 1.5 and 10.0 mg/mL concentrations.

Based on the studies on anti-dyslidelmic of Morinda citrifolia (Noni) fruit that has been done by Safur et al., (2010) it was conclusion the present study provides mechanisms of antidyslipidemic activities of various part of Morinda citrifolia through multiple pathways i.e. inhibition of bio-synthesis, absorption and secretion of lipids. This may be due to the presence of multiple potent antioxidant constituents in this plant, though additional mechanism(s) can not be ruled out.

Prevention of Type 2 Diabetes Mellitus

Diabetes mellitus is a chronic metabolic disorder that effect human body in terms of physical, psychological and social health. It is defined as a group of disorders characterized by hyperglycemia, altered metabolism of lipids, carbohydrates and protein (Warjest, 2011). It is becoming the third killer of the health of mankind along with cancer, cardiovascular and cerebrovascular diseases (Chauhan et al., 2010).

In Malaysia and Indonesia, one of the popular herbs that has been traditionally used to treat diabetic patients without much scientific evidence for its efficacy is Morinda citrifolia or locally known as mengkudu. A growing number of pharmalogu studies on Morinda citrifolia (Noni) have been published in recent years, but many of the reports are only accessible as Congress abstracts. In addition, few peer-reviewed research manuscripts are available that discuss the antidiabetic activity of Morinda citrifolia, even though Morinda citrifolia has customarily used to treat diabetes (Lee et al., 2012).

In fact, only a single study has presented evidence, limited at best, for the antidiabetic effect of Morinda citrifolia fruit juice in animal model of T2DM (Nayak et al., 2011). According to Hadijah and her colleagues, studies showed that an aqueous extract of Morinda citrifolia reduces the blood glucose level in diabetic rats (Hadijah et al., 2008).

It has been reported that the plasma triglyceride levels was increased significantly (p<0.05) in diabetic control rats (2.17 ± 0.61 m mol/liter) as compared to normal control rats (0.56 ± 0.06 m mol/litre). The administration of Morinda citrifolia extract at all dosages reduced the plasma triglyceride levels significantly in diabetic rats, whereas only the highest dose of Morinda citrifolia extract (1.00 mg/kg) managed reduce the liver triglyceride content (Hadijah et al., 2008). The increment in triglyceride was due to the impairment of insulin secretion that occurs in diabetes (Puranik et al., 2013).

Another study that have been conducted by Lee et al. (2012) showed clearly indicate that the antidiabetic effects of Morinda citrifolia (Fermented Morinda citrifolia/FMC) were stronger than those of the commercially available functional health food, Barba (Lagerstroemia speciosa). For example, fermented Morinda citrifolia base diet was more effective in reducing blood and serum glucose levels in KK-Ay mice than a normal diet.
As reported findings by Nayak and his colleagues (2011), *Morinda citrifolia* also gradually reduced blood glucose levels after 40 days of experimentation; however, Fermented *Morinda citrifolia* (FMC) was more efficient in this regard compared with *Morinda citrifolia* (MC). It can be presumed that the antidiabetic activity of *Morinda citrifolia* was markedly improved through solid substrate fermentation, a bioconversion technique employed to increased the function of natural products. This results would be in agreement with recent studies (Lim et al., 2010). Demonstrating that the pharmalogic effects of medical plants are increasing through solid substance fermentation.

**Potential Mechanisms for Inverse Association between Noni Fruit and Type 2 Diabetes**

The aim the treatment of diabetes is to reduce the blood glucose level. Antidiabetic drug can act in different ways such as stimulation of beta cell of pancreatic islet to release insulin, to resist the hormone which rises blood glucose, increase the number and sensitivity of insulin receptors, increase the glycogen content, enhance the use of organ glucose in the tissue; free radical scavenging, resist lipid peroxidation, correct the metabolic disorder of lipid and protein, and promote microcirculation in the body. Free radicals damage cellular molecules, DNA, protein and lipids leading to altered cellular functions and anti-oxidant levels (Patel et al., 2011).

From the scientific research, it was found that several plant species have proven efficacy to reduce the sugar level. By screening of antidiabetic drugs, a large number of plant materials including phyto-constituents were found to possess potent antidiabetic activity (Jerald et al., 2008). There are various types phytoconstituents present in the plant materials belonging to different chemical classes. Phytoconstituent like alkaloids inhibit alpha-glucosidase and decrease glucose transport through the intestinal epithelium. Imidazoline compounds stimulate insulin secretion in a glucose manner (Mustafa et al., 2011).

The mechanism of hypolipidemic effects of *Morinda citrifolia* as shown in the Khadijahs study is yet to be established. Based on Phytochemistry studies found that *Morinda citrifolia* has some chemical constituents such as alkaloids, flavonoids, flavone glycoside and citrifolin in a form of glycoside (Yang et al., 2009).

Flavonoids are plant polyphenols frequently found in fruits, vegetables and grains. The hypolipidemic activity of flavo-oids from various sources has been reported by several studies (Jung et al., 2006). This compound also has been identified as antidiabetic components a number of traditional ethics remedies. Additionally, some flavonoids and polyphenols as well as sugar derivates found to be effective against the inhibitory activities of alpha-glucosidase and aldose reductase (Saf-ur et al., 2010). Most of the plants extracts exhibiting hypoglycemic, hypolipidemic and antioxidant effects in animals may be helpful to treat diabetes and associated complications in human (Brett et al., 2011). Thus, it is possible that these active compounds are responsible for the hypolipidemic activities observed in *Morinda citrifolia*.

Recently, many types of research have reported that various plant-derived flavonoids, anthraquinones and terpenes stimulate glucose uptake in cells (Zhang et al., 2010) reducing insulin resistance. Consequently, the compound as flavonoids and lignans which possess powerful anti-inflammatory and anti-oxidant properties, may be useful in control of T2DM (Type 2 Diabetes Mellitus). It has been reported that *Morinda citrifolia* contains numerous anthra-quinones, flavonol glycosides, and terpenoids, which possess antioxidants, inflammatory and anti-dyslipidemic
effects (Okusada et al., 2011). Therefore, these compounds were likely increased in FMC by fermentation of FMC, leading to at least some of the antidiabetic actions of FMC.

**BIOLOGICAL ACTIVITIES OF NONI PRODUCTS**

The World Health Organization (WHO) estimates that about 80% population living in the developing countries relies on traditional medicine for their primary health care needs (Rajat et al., 2012). In almost all the traditional systems of medicine, the medicinal plants play a major role and constitute their backbone. Widespread claims of the therapeutical effectiveness have encouraged the researchers worldwide to further investigate some of these possibilities. By virtue of this one can easily find out several research articles on the biological activities and pharmacological actions of *Morinda citrifolia* based on a modern scientific investigation. Generally, there are some numerous biological activities of Noni products, i.e. antioxidant properties, antimicrobial effects, analgesic activities, immunological activity, anti-inflammatory activity and wound-healing activity.

**Antioxidant Properties**

Antioxidants are the substance that when present in low concentrations compared to those of an oxidizable substance significantly delays or prevent oxidation of that substance. Recently, the antioxidant potential of medical herbs has been reported (Krishnahia et al., 2012). They absorb the suns radiation and generate high levels of oxygen as secondary metabolites of photosynthesis. Oxygen is easily activated by ultraviolet (UV) radiation and the heat from sunlight to produce toxic, reactive oxygen species (ROS).

Research has revealed that potential of *Morinda citrifolia*, L. as a source of anti-oxidants in roots, fruits and leaves. The extract from leaf, fruit and root from *Morinda citrifolia* or Mengkudu exhibited a promising activity in 2,2-diphenyl-1-picrylhydrazyl (DPPH) scavenging and total phenolic content (Dieridane et al., 2005). The results of the studies showed that the highest activity, total phenolic content and total flavonoid content were exhibited by the extracts obtained by high-pressure extraction with ethyl acetate as solvent. It has been reported also that *Morinda citrifolia* fruit contains relatively larger quantity of non-polar antioxidant compounds.

Chemical studies of Noni fruit have revealed that iridoids are the main phytochemical constituents, with *diacetyl asperulosidic acid* (DAA) comprising the majority of the iridoid content (Potterat et al., 2007). The result of the current study by Ma et al. (2013) has demonstrated that DAA harms on antioxidant effect by increasing superoxide dismutase (SOD) activity. This effect may be responsible at least in part, for the antioxidant properties of Noni juice as demonstrated in human trials and *in vivo*.

**Anti-Microbial Effects**

Varies part of the Noni plants extracts have been reported to have significant antimicrobial and immune enhancing effects (Paul et al., 2008). Due to the pharmaceutical values, *Morinda citrifolia* has gained a great deal of interest. Therefore, information and chemical constituents of plants help for the discovery of novel drugs. The quantitative phytochemical investigation revealed that the extract of *Morinda citrifolia* contain phytoconstituents viz. phenols, alkaloids, flavonoids, glycosides, tannins, saponins and steroid at various levels (Sibi et al., 2013).

The antibacterial activity of *Morinda citrifolia* (Noni fruits) or Mengkudu has evidenced by many reports and is due to the presence of phenolic compounds (Basar et al., 2010). It has been reported that Noni inhibits the growth of certain
bacteria in different strains such as Staphylococcus aureus, Pseudomonas aureuginosa, Proteus morgaii, Bacillus subtilis, Salmonella, Shigella and Escherichia coli. Another study that has been conducted by Lee et al., (2008) showed that an acetonitrile extract of the dried fruit inhibited the growth of Pseudomonas aureuginosa, Bacillus subtilis, E. Coli, Streptococcus pyrogenes, Vibrio alginolyticus and Vibrio harveyi.

Meanwhile, Sharma and Smita (2010) reported that ethyl acetate extract of Morinda citrifolia exhibited broad spectrum of inhibition against gram-negative bacteria; whereas alcohol extract of Morinda citrifolia has exhibited potent antimicrobial activity.

Based on The Sibi and his colleagues study (2013) showed that all concentrations of the Morinda citrifolia extract inhibited the fungal species with varying degree sensitivity. The stronger and broader spectrum of antifungal activity was observed in root extract Against Penicillium and Fusarium follow by leaf extract (Sibi et al., 2013).

Analgesic Activity
Recent researchers have examined and tested the analgesic properties of commercial juice in rats or mice. The results showed that rats fed with 10% and 20% Noni juice had greater point tolerance (162% and 212%, respectively). Compared with the placebo group, Punjanon and Nandhasri (2005) has also studied the analgesic and sedative effects of Noni lyophilized aqueous extract on mice through writhing and hot plate tests. The data from this experiment showed that analgesic efficacy of the extract is 75% as strong as morphine, yet non addictive and also proved to be non-toxic.

Other studies have reported that analgesic activity of Noni fruit puree on mice using the hot plate test was also investigated. A 10% solution of freeze concentrated Noni fruit puree in the drinking water of mice reduced the pain sensitivity comparable to the central analgesic drug tramadol. This affects was only partly reversed by the application of morphine antagonist naloxone (Basar et al., 2010).

Immunological Activity
The immunological activity of an ethanol extract from Tahitian Noni juice (TNJ) and Noni fruit juice concentration (NFJC) was observed by Radioligand binding assay for cannabinoid receptors (CB1) and CB2, and also ELISA analysis of IL-4, IFN-gamma and IL-12 p70 in splenocytes and exudate cells. The results showed that both modulate the immune system via the activation of the CB2 receptors and suppression of the IL-4, but increasing the production of IFN-gamma cytokines (Palu et al., 2008).

The molecular mechanisms of action of Morinda citrifolia, L. on the immune system has been reported and described by Palu et al. (2008) also in detail as follows. Concomitantly, the cannabinoid receptors, specifically CB2 are involved in : (1) Mediating the protective signals that counter act the proinflammatory response , (2) Inhibiting neuropathic pain without psycho active effects, (3) Suppressing microbial activation and (4) Protecting hippocampal neuron from excitotoxicity.

Anti-inflammatory Activity
Morinda citrifolia, L (Noni), an indigenous medical plant has been reported to possess anti-inflammatory, analgesic and antiulcerogenic properties. The anti-inflammatory potency of both orally and intra-peritoneal injected extract of Noni fruit juice has well documented. Therefore, in the present study, the interrelationship of 5-hydroxy tryptamine (5-HT), histamine and prostaglandinewith the anti-inflammatory activity of aqueous and alcoholic extracts of Morinda citrifolia was studied (Jethani et al., 2013).

The conclusion of the study showed that during the acute phase, the
maximum increase in anti-inflammatory activity of aqueous extract of Noni was produced by cimetidine which was found to persist for 4 hours followed by paracetamol and pro-methazine but not with cyproheptadine. Thus antiinflammatory effect aqueous extract of Noni might be due to the inhibition of endogenous histamine which was increased by pretreatment with cimetidine. The results further-revealed that besides histamine, prostaglandins also play a role in controlling anti-inflammatory of Noni (Palu et al., 2012). Anti-inflammatory activity of Noni on transudate and proliferative stages of inflammation may due to its blocking H1 receptors, H2 receptors and prostaglandin.

**Wound-Healing Activity**

Wound-healing is processed by which damaged tissue is restored as closely as possible to its normal state. Wound-healing occurs in three stages: inflammation, proliferation and remodeling. The proliferative phase is characterized by angiogenesis, collagen deposition, granulation tissue formation, epithelialization and wound contraction (Nayak et al., 2007). The results study of evaluation of the wound-healing activity of ethanolic extract of *Morinda citrifolia, L* leaf showed that a significant increase in the wound-healing activity was observed in the animals treated with the Noni extract compared with those who received the placebo control treatments.

**SAFETY AND FUTURE STRATEGY**

It was reported that products derived from Noni fruit (*Morinda citrifolia, L*) have been commercialized in the USA since the 1990s and are increasingly distributed all over the world. Even, a large number of beneficial effects have been claimed for Noni (Gupta and Patel, 2013). Fruit juice of Noni has been approved as a Novel Food by the European Commission in 2003, one anti cell reviewed current knowledge on the phytochemistry, pharmacology and safety aspects of Noni fruit and Noni derived products, and health-related claims and benefits (Potterat and Humberger, 2007).

The knowledge on the chemical composition of Noni fruit has considerably increased over recent years. A number of in vitro and to a certain extent in vivo studies are potential clinical relevance is not clear at present. However, based on a toxico-logical assessment, Noni juice was considered as safe (Gupta and Patel, 2013). Therefore, due to recent reports of cases of hepatotoxicity, the safety issue has been re-examined in Europe. While the European Food Safety Authority sees no link between adverse affects on liver and consumption of Noni juice, so a continuing monitoring of the situation is desirable and some vigilance advised (Potterat and Humberger, 2007).

Nevertheless, new compounds with high levels of pharmacological activity are urgently required for a wide range of human disorders and diseases. A number of scientific publications showed that this plant contains several nutritional and functional compounds, but the current state of knowledge is still far from satisfactory. The most important compounds identified are damn acanthial and some other phenolic compounds. However, its activity as chemo-preventive and anti-HIV needs further investigation (Singh, 2012). Considerably, a drug development pro-gramme should be undertaken to develop modern drugs with the compounds isolated, but before that, a comprehensive investigation of its bioactivity, mechanism of action, pharmacotherapeutics, toxicity and clinical trials are needed to provide sufficient data.

**CONCLUSION**

The *Morinda citrifolia, L* plant, and especially its fruit and product-derived has been in great used in alternative
medicine for various illness such as diabetes mellitus, high blood pressure, heart diseases, various cancers, gastric ulcer, arteriosclerosis, arthritis, blood vessel problems, headache and drug addiction, skin inflammation and wounds.

The most important compounds identified in Noni fruit are phenolics, such as damn acanthal, iridoid and scopoletin, organic acids (caproic and caprylic acid), vitamins (ascorbic acid and provitamin A), amino acids (such as aspartic acid), and mineral. In vitro research and limited experiments with lab animals have shown that Noni has anti-oxidant, anticancer, anti-microbial, antidiabetic, anti-inflammatory, analgesic and cardiovascular activity. Though a large number of in vitro, and to a certain extent in vivo studies demonstrated a range of potentially beneficial effects, clinical data are essentially lacking.

REFERENCES


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