Noni Clinical Research Journal

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Communication Address :
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World Noni Research Foundation
64, Third Cross Street, Second Main Road,
Gandhi Nagar, Adyar, Chennai - 600 020.
E-mail : mail@worldnoni.org   Visit : www.worldnoni.org
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Clinical Research on

*Morinda citrifolia* L. – Noni

**Abstract:** Morinda Citrifolia –Noni –family Rubiaceae has been widely used by the people and folk healers for food and other medicinal purposes. Traditional medical manuscripts handed down from generation to generation cite the Noni fruit as the primary ingredient in their health preparation. Decades of ground breaking research reveals a broad range of therapeutic effects, including antibacterial, antiviral, antitumor, antihelminthic, analgesic, hypotensive, anti-inflammatory, immune enhancing and cancer prevention activities. In order to encapsulate the medicinal value and therapeutic effects of the Noni fruit and to summarize scientific evidence that supports the traditional claims a literature review and recent advances in Noni research has been detailed.

**Keywords:** *Morinda citrifolia*, Xeronine, antibacterial, antiviral, antitumor, analgesic, anti-inflammatory, immune enhancing, cancer prevention.

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**Introduction**

*Morinda citrifolia* L., is commonly known as Great morinda, Indian mulberry, Beach mulberry and the (noni) fruit has been used in tropical regions as both food and folk medicine. The recent use of noni as a dietary supplement has increased greatly and is reported to have a broad range of therapeutic effects, including antibacterial, antiviral, antifungal, antitumor, anthelminthetic, analgesic, hypotensive, anti-inflammatory, and immune enhancing effects. *Morinda citrifolia*, L., is native to South East Asia but has been extensively spread by man throughout India and into the Pacific islands as far as the islands of French Polynesia, of which Tahiti is the most prominent. It can also be found in parts of West Indies. Noni is a valuable medicinal plant and the recent discoveries about Noni, looks bright for this plant, but further studies has to be performed to discover its full potential.

In order to reveal the nutritional and medicinal value of the Noni plant, and to summarize scientific evidence that supports the claim, a literature review and recent advances in Noni research are given below.
Pharmacological activity of the active principles in Noni

The presence of phytonutrients and vitamins in Noni can help the body fight microbes, help fight against inflammation, help fight carcinogens, and boost the immune system.

The Pharmacological activity of the active principles being:

- **Oligo- and polysaccharides** – long-chain sugar molecules that serve a probiotic function as dietary fiber fermentable by colonic bacteria, yielding short chain fatty acids with numerous potential health properties.

- **Glycosides** – sugar-phenolic compounds including flavonoids such as rutin and asperulosidic acid, are common in several Rubiaceae plants; specifically named noni isolates called iridoides and morindoides have been reported.

- **Trisaccharide fatty-acid esters, “noniosides”** - resulting from combination of an alcohol and an acid in noni fruit, noniosides are chemicals giving noni its noxious smell and taste.

- **Scopoletin** – may have antibiotic activities; research is preliminary.

- **Beta-sitosterol** – a plant sterol with potential for anti-cholesterol activity.

- **Damnacanthal** – an anthraquinone having potential as an inhibitor of HIV viral proteins.

- **Alkaloids** – naturally occurring amines from plants, often attributed to causing bitter tastes and so may contribute to the foul taste of noni. Some references mention xeronine or proxeronine as important noni constituents.

Other components being octoanoic acid, potassium, vitamin C, terpenoids, alkaloids, anthraquinones (such as nordamnacanthal, morindone, rubiadin, and rubiadin,methyl ether, anthraquinone glycoside), carotene, vitamin A, flavone glycosides, linoleic acid, Alizarin, amino acids, acubin, L-asperuloside, caproic acid, caprylic acid, ursolic acid, rutin, and a putative proxeronine.

**Xeronine system:** Noni fruit contains a natural precursor for Xeronine that was named Proxeronine. Proxeronine is converted to the alkaloid, Xeronine, in the body by an enzyme called Proxeroninase. Xeronine is able to modify the molecular structure of proteins. Thus Xeronine has a wide range of biological activities. Xeronine will interact with the protein and make it fold into its proper conformation.

**Pharmacological Studies and medicinal uses**

Noni is used by some cancer patients for its anti-cancer and tumor-reducing possibilities. Some sufferers from immune-compromised diseases such as AIDS...
and chronic fatigue syndrome use Noni to boost immune system function. In research conducted on mice, Noni has been shown to boost the immune system directly by increasing the activity of macrophages and or lymphocytes in the immune system. In recent studies, the polysaccharides in Noni have shown to exhibit an anti-tumor effect and when taken in conjunction with chemotherapeutic agents it can help improve recovery time. People with diabetes and hypoglycemia have reported that noni helps stabilize blood sugar levels in the body. People with arthritis, joint pain, and inflammatory conditions have used noni. It is also used as a sedative, painkiller, and sleeping aid. Noni juice is recommended to remove parasites, to cleanse the digestive tract and improve digestion, and to control weight. It is used as a general health tonic to improve energy and resistance and to slow the effects of aging. It is also used for asthma; digestive disorders including ulcers; irritable bowel syndrome; constipation and diarrhea; and fibromyalgia, a condition characterized by fatigue and chronic pain.

Noni has been traditionally used as an analgesic pain reliever and sedative. Researchers recently put this to the test with mice in an experiment and found that in fact Noni did demonstrate a non-toxic analgesic pain relieving effect and sedative effect on the mice. The researchers findings did confirm the traditional analgesic properties and uses of the Noni plant.

Scientific Studies

A substance called ursolic acid found in the leaves of the noni plant has been shown to have anti-cancer properties in the body. A Japanese study found that noni fruit contains another substance (damnacanthal) that has some effectiveness against pre-cancerous cells. Some evidence points to noni’s ability to increase immune system activity, due to substances found in the fruit (including a chemical called proxerone). The leaves of the plant contain chemicals that may lower blood sugar levels, as well as reduce pain and inflammation. One study showed that laboratory mice with lung cancer had much longer survival times when given noni juice daily. A French study determined that the roots of the noni plant contain natural sedatives, while another study pointed to a compound that noni leaves may contain that is anti-malarial and anti-parasitic in its effects. Finally, surveys of noni users have indicated testimonial success with the use of noni for cancer, strokes, diabetes, and as a general health and energy improver. Noni has been shown to contain vitamins, minerals, and antioxidants.

Preliminary medical research

Over the years since 1994, noni has increasingly stimulated the interest of medical science, with 114 papers published since then and 36 just in 2006-7. Despite the
large market for juice products and research developments, the nutrient and phytochemical profiles of noni have not been extensively studied.

Furthermore, numerous health claims made in noni juice marketing are gradually supported by scientific research and in human clinical trials. One cancer study completed under NIH peer-review in 2006 has been conducted, the results of which remain unpublished as of August 2007.

Likewise, in a university-based clinical trial funded by the noni juice manufacturer, Tahitian Noni International, Inc., it was shown that noni juice consumption lowered blood cholesterol levels. Completed in 2006, however, the results of this study have not been published under peer-review.

Laboratory studies have investigated noni’s effect on the growth of cancerous tissue in mice. One such study in vitro found that noni reduced growth of capillary vessels sprouting from human breast tumor explants and, at increased concentrations, caused existing vessels to degenerate. It remains unknown whether such effects occur in vivo in other animal models or in cancer patients.

Another study showed noni juice to inhibit formation of cancer cells in rats (using detection methods of biochemical markers called DNA adducts). It further showed a reduced number of DNA adducts in rats induced with a carcinogen. The same study showed effective antioxidant properties of noni juice compared with those of vitamin C, grape seed powder, and pycnogenol. The results indicated reduced carcinogen-DNA adduct formation in this laboratory model and antioxidant activity that may be relevant to anti-cancer mechanisms.

Recent advances in Noni research- Biological activities of Noni

Antibacterial activity

Acubin, L-asperuloside, and alizarin in the Noni fruit, as well as some other anthraquinone compounds in Noni roots, are all proven antibacterial agents. These compounds have been shown to fight against infectious bacteria strains such as Pseudomonas aeruginosa, Proteus morgani, Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Salmonella, and Shigella. These antibacterial elements within Noni are responsible for the treatment of skin infections, colds, fevers, and other bacterial-caused health problems Recently, Duncan demonstrated that scopoletin, a health promoter in Noni, inhibits the activity of E. coli, commonly associated with recent outbreaks resulting in hundreds of serious infections and even death. Noni also helps stomach ulcer through inhibition of the bacteria H pylori.
Antiviral activity

Umezawa and coworkers found a compound isolated from Noni roots named 1-methoxy-2-formyl-3-hydroxyanthraquinone suppressed the cytopathic effect of HIV infected MT-4 cells, without inhibiting cell growth.

Anthelmintic activity

An ethanol extract of the tender Noni leaves induced paralysis and death of the human parasitic nematode worm, Ascaris Lumbricoides, within a day. A botanist via Morton reported that Noni has been used in the Philippines and Hawaii as an effective insecticide.

Analgesic activity

Joseph Betz reported that the Noni fruits possess analgesic and tranquilizing activities. A French research team led by Younos, tested the analgesic and sedative effects of extracts from the Morinda citrifolia plant. The extract did “show a significant, dose-related, central analgesic activity in the treated mice.” They stated that “these findings validate the traditional analgesic properties of this plant.” The analgesic efficacy of the Noni extract is 75% as strong as morphine, yet non-addictive and side effect free. In cooperation between University of Illinois College of Medicine and Henan Medical University, Wang and Fu examined the analgesic properties of noni in animal models. NONI was tested for its analgesic properties by the “twisted method” animal model.

Hypotensive activity

Dang Van Ho of Vietnam demonstrated that a total extract of the Noni roots has a hypotensive effect. Moorthy and coworkers found that an ethanol extract of the Noni roots lowered the blood pressure in an anesthetized dog. Youngken’s research team determined that a hot water extract of Noni roots lowered the blood pressure of an anesthetized dog. A Hawaiian physician reported that Noni fruit juice had a diuretic effect.

Immunological activity

Asahina found that an alcohol extract of Noni fruit at various concentrations inhibited the production of tumor necrosis factor-alpha (TNF-a), which is an endogenous tumor promoters. Therefore the alcohol extract may inhibit the tumor promoting effect of TNF-a. Hirazumi found that noni contains a polysaccharide-rich substance that inhibited tumor growth. It did not exert significant cytotoxic effects in adapted cultures of lung cancer cells, but could activate peritoneal exudates cells to impart profound toxicity when co-cultured with the tumor cells.
Mental health and improved high frequency

A small human clinical trial of the effect of Noni on auditory function and quality of life in the patients with decreased bone mineral density and auditory function has been conducted in UIC College of Medicine, Rockford, IL. This study showed that Noni provided a positive benefit on mental health and improved high frequency hearing. The data suggests that increased amounts or extended duration of Noni intake may be required to affect this disorder.

Anti-inflammatory activity

*Selective inhibition of COX-2 activity of Noni.*

Accumulating evidence indicates that COX-2 inhibitors may be involved in breast, colon, and lung cancer development.

Interest in cancer chemoprevention with COX-2 inhibitors has been stimulated by epidemiological observations that the use of aspirin and other non-steroidal inflammatory drugs (NSAIDs) is associated with the reduced incidence of colon and breast cancer. The main target of NSAID activity is the cyclooxygenase (COX) enzyme. Two isoforms of COX have been identified: COX-1, the constitutive isoform, and COX-2, the inducible form of the enzyme. COX-2 can undergo rapid induction in response to chemical carcinogens. It has been suggested that COX-2 over expression may lead to increased angiogenesis and inflammatory reaction.

Therefore the inhibition of COX-2 might have a general cancer preventive effect via anti-inflammatory activity and decrease angiogenesis. In this study, the selectivity of COX-2 inhibition of Noni versus COX-1 *in vitro* was investigated. The discovery of the selective COX-2 inhibition of Noni is very significant since Noni is a natural fruit juice without side effects. This is the first scientific evidence for a strong anti-inflammatory activity in Noni, which may also be one mechanism of cancer prevention.

Cancer Preventive Effect of *Morinda citrifolia* (Noni)

The hypothesis that *Morinda citrifolia*, L. possesses a cancer preventive effect at the initiation stage of carcinogenesis was studied. One preliminary data indicated that 10% Noni Juice made from *Morinda citrifolia* fruit in drinking water for one week was able to prevent DMBA-DNA adduct formation. The levels of DMBA-DNA adducts were reduced by 30% in the heart, 41% in the lung, 42% in the liver, and 80% in the kidney of female SD rats. Even more dramatic results were obtained in male C57 BL-6 mice: 10% noni was able to reduce DMBA-DNA adduct formation by 60% in the heart, 50% in the lung, 70% in the liver, and 90% in the kidney. In order to explore the mechanism of this preventive effect, the antioxidant activity of
Noni was examined in vitro by lipid hydro peroxide (LPO) and Tetrazolium nitroblue (TNB) assays. The results suggest that prevention of carcinogen-DNA adduct formation and the antioxidant activity of noni may contribute to the cancer preventive effect of *Morinda citrifolia* L.

**Conclusions**

Ancient folk healers used *M. citrifolia* as one of their primary medicinal plants. As folk traditions have been blended with introduced cash economies, modified medicinal systems have evolved. These systems are based upon both commercialized healers and commercialized plant-based remedies. Elements that have contributed to the commercialization of *M. citrifolia* L., includes, key publications and technological introductions from other cultures, and shifts from indications with existing over-the-counter commercial products (eg, topical antibiotics) to indications with few satisfactory over-the-counter commercial products (eg, internal treatment of cancer, diabetes, hypertension, etc). In modern society, which is dominated by a bioscience paradigm, claims of efficacy need to be linked to specific chemical causes and mechanisms of action. Without these supporting "scientific" findings, *M. citrifolia* L fruit products would probably not have developed as rapidly as they have. It is interesting that although the rationale for turning to natural products is to avoid perceived harshness, reduction, and "unnatural" attributes of synthetic medicinal products, people still have a desire to know why a natural product works and expect that rationale to include a bioscience explanation of activity. This research may initially follow the implied indications of the culture that developed the plant's use. Other leads may be followed as they arise from the research process. Although there do not seem to be traditional indications for its use in lifestyle disease, *M. citrifolia* is offering promise in this area.

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The effect of Noni (*Morinda citrifolia* L.) in Type 2 diabetes mellitus in inadequately controlled patients

**Abstract**: The proper management of diabetes mellitus has assumed great importance in recent years in view of the steady increase in its prevalence all over the world including the USA and India. Apart from the suffering it causes to the individual in terms of morbidity, mortality, and decrease in quality of life, the economic costs of treating diabetes and the losses caused by decrease in productivity are a major source of worry to society and organizations concerned with public health. Both genetic and environmental factors are implicated in the causation of Type 2 diabetes. Among environmental factors; over eating decreased physical activity and obesity, cigarette smoking, increased oxidant stress, and inflammatory processes have been associated, either as a cause, or an effect of the developing diabetic state. Patients diagnosed with Type 2 diabetes for at least 5 years, who are currently on insulin and not adequately controlled with current treatment, with HbA1c > 8%. Present study highlights how patients inadequately controlled with an existing insulin treatment and Oral Hypoglycemic Agents (OHIS). By adding Noni as a food supplement significant improvement in HbA1c and FBG is observed after 6 months follow-up.

**Introduction**

World Health Organization states that India and Asia Pacific regions continue to be at the forefront of diabetes mellitus epidemic, with consequences to health which threaten to be devastating. Younger members of our communities are not spared from the disease, with a significant problem emerging in the urbanized young in the most affluent parts of our country. Lifestyle changes and urbanization appear to be the underlying causes of this problem, the current number of people with diabetes in South East Asia is estimated to be 40 million, and this number will increase to at least 81.5 million by 2025.

However, there is irrefutable evidence that diabetes can be prevented or delayed in people at high risk and that the progression of many of the complications associated with diabetes can be halted. Appropriate diet and physical activity,
maintaining a healthy body weight, refraining from tobacco smoking, and proper control of diabetes and blood pressure in people with diabetes will help prevent diabetes and reduce its complications. Each country needs to develop appropriate guidelines for the prevention and control of diabetes, and set up systems to ensure that these guidelines are adhered to. There is a need to establish the diagnostic criteria and classification, followed by target treatment of diabetes.

The United Kingdom prospective diabetes study (UKPDS) showed that intensive treatment can decrease the morbidity and mortality of the disease by decreasing its chronic complications. However, the majority of patients with a longer duration of diabetes remain poorly controlled with oral agents, and the use of insulin, which could improve glyceamic control, is often long delayed and not aggressive enough. There is also limited information regarding next step therapy options for patients with diabetes who fail to achieve or maintain adequate glyceamic control with current treatment.

Materials and Methods

The study was done using randomized design with double blind (OHA’s + Insulin/OHA’s + Noni) and Control - (only OHA’s) for 24 weeks.

A total of 305 patients attending the diabetic clinic for treatment were enrolled for this study. After a running in period of 3 months, the patients were randomized either to the control or to the study groups and followed up for next 6 months from April 2006 to September 2006.

Drugs used : (i) Metformin, Glimiperide, Rosiglitazone and Insulin.
(ii) Noni : Indian Noni 15ml twice a day on empty stomach given.

Results and Discussion

The results are presented in Table 1 & 2 and Figure 1 & 2.

A perfect glyceamic control (fasting plasma glucose), HbA 1c increased insulin sensitivity improve C-peptide levels and improvement in fasting blood lipids, were observed (Heinicke 2001; Schecter S 1999)

G. Sathish Kumar The effect of Noni (Morinda citrifolia L.) in Type 2 diabetes mellitus in inadequately controlled patients
Table. 1 Investigations and blood parameters.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Control (OHA'S)</th>
<th>OHA'S + Insulin</th>
<th>OHA'S + Noni</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting Plasma Glucose (mg/dl)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>223.2</td>
<td>223.2</td>
<td>230.4</td>
</tr>
<tr>
<td>Week 4</td>
<td>248.4</td>
<td>201.6</td>
<td>190.8</td>
</tr>
<tr>
<td>Week 16</td>
<td>248.4</td>
<td>183.6</td>
<td>165.6</td>
</tr>
<tr>
<td>Week 24</td>
<td>237.6</td>
<td>172.8</td>
<td>111.6</td>
</tr>
<tr>
<td>HDL Cholesterol (mg/dl)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>35.20</td>
<td>35.5</td>
<td>30.80</td>
</tr>
<tr>
<td>Week 8</td>
<td>37.10</td>
<td>40.6</td>
<td>40.80</td>
</tr>
<tr>
<td>Week 16</td>
<td>37.10</td>
<td>40.8</td>
<td>40.0</td>
</tr>
<tr>
<td>Week 24</td>
<td>37.10</td>
<td>46.8</td>
<td>50.0</td>
</tr>
<tr>
<td>LDL Cholesterol (mg/dl)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>125.2</td>
<td>121.6</td>
<td>125.4</td>
</tr>
<tr>
<td>Week 8</td>
<td>125.2</td>
<td>118.8</td>
<td>120.4</td>
</tr>
<tr>
<td>Week 16</td>
<td>125.2</td>
<td>116.0</td>
<td>109.0</td>
</tr>
<tr>
<td>Week 24</td>
<td>120.0</td>
<td>112.0</td>
<td>97.0</td>
</tr>
</tbody>
</table>

OHAS : Oral Hypo Glyceamic Agents

Fig. 1. Investigators over all Opinion on Noni Treatment
Table 2. Investigator's overall opinion on Noni Treatment

<table>
<thead>
<tr>
<th>Opinion</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent</td>
<td>55.90%</td>
</tr>
<tr>
<td>Good</td>
<td>34.30%</td>
</tr>
<tr>
<td>Fair</td>
<td>08.70%</td>
</tr>
<tr>
<td>Poor</td>
<td>0.90%</td>
</tr>
</tbody>
</table>

Fig. 2 Percentage of Patients showed 1% or higher A1C reduction.

OHA's and Noni are effective in achieving glycemic goal.

Discussions: The study group showed a statistically significant better compliance than the control group on all parameters, Indian Noni, in patients with type 2 diabetes showed that, when used as a combination therapy (noni), this agent lowers fasting and postprandial glucose in patients with type 2 diabetes. The authors found Noni to be safe and well tolerated. Indian Noni proves definitely improves the quality living of the patients.

Xeronine, the alkaloid of Noni in the presence of insulin activates the peripheral cell membrane insulin receptors and helps for the normal absorption of glucose.

Low Glycemic index - A 3 : 1 ratio of carbohydrate to fibre in Noni juice helps to balance blood glucose levels.

Noni modifies the body immune system to keep the sensitivity of beta cells intact and body develops resistance to many diseases.

Noni helps in reducing anxiety, lessens the stress, response to some extent by elevating serotonin levels in blood.
In this research on diabetic practice, it was learnt that several micronutrients are normally deficient in patients with full blown diabetes.

Noni, rich in antioxidants and micronutrients which are essential for all the diabetic patients. (Anonymous 1990) could meet the demand.

Conclusion

It can be said that Noni helps in type diabetes patients management.

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Studies of Comparative Anti-HIV Activity and cytotoxicity of *Morinda citrifolia* L.

**Keywords** : Anti-HIV Activity, cytotoxicity and *Morinda citrifolia*

**Abstract** : Fruit juice and ethanol, methanolic extract of fruit powder of *Morinda citrifolia* (MC) have been studied against the replication of HIV-1(IIIb) in MT-4 cells. Fruit juice of *Morinda citrifolia* (MC) exhibited a maximum protection of 18% of the cells against the cytopathic effect of HIV-1(IIIb) strain and displayed marked cytotoxic activity in lymphocyte (MT-4) cells (CC50: 0.19 mg/ml). However the ethanol (EMC) and methanol extracts (MMC) displayed cytotoxic activity (CC50) in lymphocyte (MT-4) cells only at higher concentration the CC50 being at 72.34 and 220 µg/ml, respectively.

**Introduction**

Acquired immuno deficiency syndrome (AIDS) is a life threatening and debilitating disease state caused by retrovirus infection, and the etiologic agent is now widely known as the human immunodeficiency virus type 1. Many compounds of plant origin have been identified that inhibit different stages in the replication cycle of HIV (Wu, *et al*., 2004; Sanchez *et al*., 2001; Shahidul *et al*., 2000; Hu *et al*., 2000). *Morinda citrifolia* L (Noni) has been used in folk remedies by Polynesians for over 2000 years, and is reported to have a broad range of therapeutic effects, including antibacterial, antiviral, antifungal, antitumor, antihelmintic, analgesic, hypotensive, anti-inflammatory, and immune enhancing effects (Wang MY *et al*., 2002). The present study is designed to determine the antiviral activity of fruit juice and ethanolic (EMC) and methanolic (MMC) extract of *Morinda citrifolia* (MC) against the replication of HIV-1(IIIb) in MT-4 cells and cytotoxicity in mock-infected MT-4 cells was also assessed by the MTT method.

**Material and Methods**

Extraction : Fruit juice of *Morinda citrifolia* is a gift from Health India Laboratory, Chennai, Tamilnadu, India, and the fruit powder of *Morinda citrifolia* was subjected to hot continuous percolation using methanol and ethanol. The methanol (MMC) and ethanol (EMC) extract of *Morinda citrifolia* were concentrated by distillation and used for screening.
Anti-HIV Assay. *Morinda citrifolia* was tested for its inhibitory effects against the replication of HIV-1(III<sub>b</sub>) in MT-4 cells (Pauwels *et al.*, 1988; Witvrouw *et al.*, 2004). The MT-4 cells were grown and maintained in RPMI 1640 DM Medium supplemented with 10% (v/v) heat-inactivated Fetal Calf Serum (FCS), 2 mM-glutamine, 0.1% Sodium bicarbonate and 20mg/ml gentamicin (culture medium). Inhibitory effect of MC on HIV-1 replication was monitored by inhibition of virus-induced cytopathic effect in MT-4 cells and were estimated by MTT assay. Briefly, 50 ml of HIV-1 and HIV-2 (100-300 CCID<sub>50</sub>) were added to a flat-bottomed microtiter tray with 50 ml of medium containing various concentrations of extracts of MCT. MT-4 cells were added at a final concentration of 6x10<sup>5</sup> cells/ml. After 5 days of incubation at 37°C, the number of viable cells were determined by the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) method. Cytotoxicity of MC against mock-infected MT-4 cells was also assessed by the MTT method.

Results and Discussion

The anti-HIV data are presented in Table 1.

<table>
<thead>
<tr>
<th>Compound</th>
<th>EC&lt;sub&gt;50&lt;/sub&gt; a (µg/ml)</th>
<th>CC&lt;sub&gt;50&lt;/sub&gt; b (µg/ml)</th>
<th>Maximum % Protection</th>
</tr>
</thead>
<tbody>
<tr>
<td>MC</td>
<td>&gt;0.19</td>
<td>0.19</td>
<td>18</td>
</tr>
<tr>
<td>EMC</td>
<td>&gt;72.34</td>
<td>72.34</td>
<td>0</td>
</tr>
<tr>
<td>MMC</td>
<td>&gt;220</td>
<td>220</td>
<td>0</td>
</tr>
<tr>
<td>AZT (STD)</td>
<td>0.0062</td>
<td>65.65</td>
<td>106</td>
</tr>
</tbody>
</table>

a Concentration required to inhibit the cytopathic effect of HIV-1(III<sub>b</sub>) in MT-4 cells by 50%.

b Concentration required to cause cytotoxicity to 50% of the MT-4 cells.

An ethanolic, methanolic extract and fruit juice of *Morinda citrifolia* has been evaluated for its anti-HIV activity and cytotoxicity (Table 1) against HIV-1(III<sub>b</sub>) replication in acutely infected MT-4 cells. *Morinda citrifolia* exhibited a maximum protection of 18% of the MT-4 cells against the cytopathic effect of HIV-1(III<sub>b</sub>) after acute infection. *Morinda citrifolia* displayed marked cytotoxic activity in lymphocyte (MT-4) cells (CC<sub>50</sub> 0.19 mg/ml). Both ethanol (EMC) and methanol extracts (MMC) displayed cytotoxic activity (CC<sub>50</sub>) in lymphocyte (MT-4) cells at 72.34 and 220 µg/ml respectively.
Acknowledgement

We acknowledge A. Nijs and B. Van Remoortel for excellent technical assistance. We thank the NIH AIDS Research and Reference Reagent Programme, Division of AIDS, NIAID for providing the HIV-1(IIIb) strain and MT-4 cells. Work at KULeuven is supported by the European Commission (CSHB-CT-2005-505480). World Noni Research foundation for financial support. Author is grateful to Dept of Science and Technology for award of BOYSCAST fellowship for this research work.

References


Effects of Noni (Morinda citrifolia L.) on Carcinoma of Breast

Authors’ affiliation:
Dr. Rangadhar Satapathy
MIG – II, 6/2, BDA colony,
Chandrasekharapur,
Bhubaneswar, Orissa, India

Abstract: Breast cancer is the fifth most common cause of cancer death (after lung cancer, stomach cancer, liver cancer, and colon cancer). In 2005, breast cancer caused 502,000 deaths (7% of cancer deaths; almost 1% of all deaths) worldwide. Among women, breast cancer is the most common cause of cancer death. The mainstay of breast cancer treatment is surgery when the tumor is localized, with possible adjuvant chemotherapy, and/or radiotherapy. Depending on clinical criteria (age, type of cancer, size, metastasis) patients are roughly divided into high risk and low risk cases, with each risk category following different rules for therapy. Treatment possibilities include radiation therapy, chemotherapy, hormone therapy, and immune therapy. Nothing guarantees that you won’t develop breast cancer. There are lots of side effects of chemotherapy and radiotherapy that makes the patient worse than cancer itself. Indian Noni helps to overcome maximum side effects of all cancer cases including the breast cancer by its immune enhancing and nutritive supplementing property. It also contains many bio anti carcinogenic ingredients that helps by enhancing the efficacy of the cancer treatment too. It acts as a tool for primary prevention, secondary prevention and as an adjuvant immune enhancing supplement with the common line of cancer treatment.

Keywords: Carcinoma, Morinda citrifolia anticarcinogenic agents.

Introduction
Breast cancer, the second-leading cause of cancer deaths in India, is the disease women fear most. Breast cancer can also occur in men. Today, radical mastectomy is rarely performed. Most breast lumps aren’t cancerous. Yet the most common sign of breast cancer for both men and women is a lump or thickening in the breast. Often, the lump is painless. In breast cancer, some of the cells in the breast begin growing abnormally. These cells divide more rapidly than healthy cells do and may spread (metastasize) through the breast, to the lymph nodes or to other parts of the body. The most common type of breast cancer begins in the milk-producing ducts, but cancer may also begin in the lobules or in other breast tissue. In most cases, it’s not clear what causes...
normal breast cells to become cancerous. Doctors do know that only 5 percent to 10 percent of breast cancers are inherited. Treatments exist for every type and stage of breast cancer. Most women will have surgery and an additional (adjuvant) therapy such as radiation, chemotherapy or hormone therapy.

Because breast cancer treatment is likely to damage healthy cells and tissues, unwanted side effects are common. Specific breast cancer side effects depend mainly on the type and extent of the treatment. Side effects of breast cancer radiation therapy—including uncommon side effects that may involve the heart, lungs, and ribs. One of the common side effects of breast cancer radiation treatment is fatigue, especially in the later weeks of treatment and for sometime afterward. The side effects of chemotherapy depend mainly on the drugs the patient receives. As with other types of breast cancer treatment, side effects vary from person to person. In general, anticancer drugs affect rapidly dividing cells. These include blood cells, which fight infection, cause the blood to clot, and carry oxygen to all parts of the body. When blood cells are affected by anticancer drugs, patients are more likely to get infections, bruise or bleed easily, and may have less energy during treatment and for some time afterward. Cells in hair follicles and cells that line the digestive tract also divide rapidly. As a result of chemotherapy, patients may lose their hair and may have other side effects, such as loss of appetite, nausea, vomiting, diarrhea, or mouth sores.

Indian Noni and Cancer

**Noni ppt (The polysaccharide)**

Noni has anti tumor activity by stimulating immune factors like TNF, NK cells etc. to attack the tumor.

Noni ppt (The polysaccharide) is one unique polysaccharide that can be used as a chemo-immunotherapy agent to treat cancer. NONI-ppt present in NONI develops an anti-tumor response by stimulating the release of various cytokines mediator of the immune system of our body like

- Interleukin
- Interferon – gamma
- Nitric oxide
- Tumour necrosis factor
- Natural killer cells

Thus they help in controlling carcinogenesis by inhibiting the growth and mutation of the malignant cells.
Pretreatment with Noni followed by ultraviolet irradiation increased the levels of phosphorylated extra cellular signal-regulated kinases (ERK) and stress-activated protein kinases (SAPK) enzymes in the body. Activation of SARK and ERKs plays an important role in triggering apoptosis. Thus their activation proves the stimulatory effect of Noni on ultraviolet-induced apoptosis. Thus Noni can be used as an immune supplemental therapeutic agent with any cancer therapy.

Noni exhibits antiangiogenesis effects on the malignant cells.

The cancer tumor has the ability to develop its own blood vessels around it to get their nutrition for growth by the process of angiogenesis. About 150+ phytochemicals present in Noni like Damnacanthal, Alcerin, limonene, Epigallocatechin gallate (EGCg) etc, to name a few, exhibit antiangiogenesis effect on the malignant cells thus inhibiting the growth and mutations of these cells and induces program cell death or apoptosis.

Epigallocatechin gallate (EGCg)- EGCg is a polyphenolic flavonoid antioxidant that is found in abundance in Noni. EGCg in Noni inhibits the quinol oxidase (NOX) enzyme including tumor activity, thus helping in antiangiogenesis.

NOX enzymes are found in a variety of cell types and tissues where they react with oxygen to generate reactive oxygen species (ROS), the free radical forms of oxygen that damage the DNA of cell.

The ROS is involved in mutations and tissue damage in diseases such as cancer and rheumatoid arthritis. Normal amounts of NOX production are important to regulate the cell growth. It is generally inactive during the normal cell division process, in response to growth hormone stimulation but it is active in cancerous cells and responsible for the cancerous cell proliferation, cell motility, invasion and angiogenesis process, all of which are prerequisites for tumor metastasis.

EGCg, a primary component of Noni inhibits the NOX activity of cancer cells. According to Dr. Morre's experimental studies it is found that EGCg in Noni inhibits NOX carcinogenesis activity but does not inhibit the NOX activity of healthy cells.

Noni prevents the carcinogen DNA adduct formation on cell

Noni Prevents DNA adduct formation, and hence protects the cell from converting to cancer. Hence Noni can be used for primary and secondary prevention of cancer.

Most chemical carcinogens binds to our genetic DNA to form DNA adducts. Carcinogen DNA adducts formation causes DNA damage. Carcinogen DNA
adducts can be repaired by body enzymes. The unprepared DNA damaged cell will be responsible for mutation and consequent cancer development. Therefore preventing carcinogen-DNA adduct formation is a key step for primary prevention in cancer at the initiation of carcinogenesis.

Noni helps to check the carcinogen DNA adduct formation. Hence it may prevent cancer at the initiation stage of carcinogenesis.

**Role of Antioxidant in Cancer Prevention**

Oxidative stress in our body is the underlying cause of cancer. When excessive free radicals are allowed to exist near the nucleus of cell, significant damage to the DNA of cell can result. Free radicals can also wreak damage on the genetic structure of the DNA, which can then lead to abnormal growth of cell. As these cells continue to replicate, this mutated DNA is carried to each newly developed cell. When there is further oxidative stress to this mutated DNA of the cell, more damage occurs. The cell will then begin to grow out of control. It spreads from one part of the body to other (metastasis), thus becoming a true cancer.

Oxidative stress is indeed the cause of cancer and antioxidants used to bring free radical back into balance would lower the risk of cancer. Therefore the bet strategy is to maximize your own body's immune system and antioxidant defense and this begins by eating a healthy natural supplement that rich with antioxidants. **Noni is the rich source of antioxidants.** The high anti oxidant property of Noni helps to prevent the formation of carcinogen-DNA adducts. It was hypothesized that the antioxidants in Noni may have cancer protective effects by scavenging reactive oxygen free radicals and quenching lipid peroxides. In vitro study shows that the Dammacanthal, one phytochemical present in Noni have anti-carcinogenic effect.

**Glutathione S-transferase (GST)**

The Glutathione S-transferase (GST) is a system which eliminates carcinogens. Limonene, present in Noni juice seems to promote the GST system in the liver and small bowel, thereby decreasing the damaging effects of carcinogens. Animal studies demonstrated that dietary limonene present in Noni reduced mammary tumor growth.

Noni inhibits Matrix metalloproteinases (MMPs) enzyme

Matrix metalloproteinases (MMPs), the enzyme have been identified as key players in tumor invasion and metastasis. Excessive MMPs secretion has been regarded as an index of malignancy which leads to the degradation of extra
cellular matrix. Lysine and proline are building blocks of collagen fibers that stabilize connective tissue by inhibiting the enzymatic digestion of collagen fibers. Vitamin C is essential for production of collagen and acts as a powerful antioxidant by scavenging free radicals and thereby protects cells from damage. Epigallocatechin gallate (EGCG) has antioxidant and anticancerogenic properties. It prevent cancer cell invasion by inhibiting MMPs. The natural amino acid lysine, especially in combination with vitamin C and other selected cellular nutrients, is capable of blocking this ‘collagen digestion’. Noni contains the above two amino acids lysine and proline. Noni is rich with vitamin C. Noni contain the phytochemical Epigallocatechin gallate (EGCG). Hence Noni should help to prevent the cancer tumor invasion and metastasis.

Limonene, the phytochemical present in Noni increases the levels of liver enzymes involved in detoxifying carcinogens.

Many recent studies have shown that elevation of phase II enzymes, such as NAD(P) H : quinone reductase (QR) and GST, correlates with protection against chemical - induced carcinogenesis in animal models, in the stage of promotion as well as initiation. Noni fruits contain an extremely potent quinone reductase inducer, 2 - methoxy - 1,b,6 - trihydroxyanthraquinone. This new anthraquinone was nearly 40 times more potent than any other quinone.

Noni contain many glycosides

Noni contains many glycosides. Asperuloside is a glycoside. Traditionally, this glycoside has been used for diurises. Research has indicated that it is also an anticlastogenic (that is, prevents the breakage of chromosomes). As a result, it is anti-mutagenic or resists mutation within the cell’s DNA.

Three new glycosides as listed below were isolated from Morinda citrifolia (Noni) fruit are :

1. 6-O- (beta-D-glucopyranosy) -1-O-octanoyl-beta-D-glucopyranose,
2. 2. 6-O- (beta-D-glucopyranosy) -1-O-hexanoyl-beta-D-glucopyranose,
3. 3-methylbut-3-enyl6-O-beta-D-glucopyranosyl-beta-D-glucopyranoside.

Noni clinical trail

The patient named Mrs. Lalita pahan from Berhampur, orissa is suffering from carcinoma of breast. Her condition was pretty worse before 4 months. The whole right breast and axillary portion had severe swelling with radiating pain from breast to axial and back. There was a big nodular hard mass inside the right breast. Her treating physician sent her for the FNAC report of that portion and it was detected cancer of breast. She was advised for the operation as the cancer had already spread to the axillary lymph nodes. Due to financial problem
she did not go for operation. Then she started consuming Noni. After taking Noni for three months her hard nodular mass softened and gradually reduced in size. The surrounding swellings of the mammary gland gradually improved. The pain reduced a lot and occasional bleeding was observed for a month. Now the condition has improved more than 70% than before. She is now continuing Noni internally as well as applying Noni externally.

Conclusion

Current treatment protocols with chemotherapy and/or radiation although beneficial, is toxic and has the potential to destroy healthy cells as well. Our approach has been to develop strategies to inhibit cancer development, progression and metastasis using naturally occurring nutrients, which are relatively non-toxic. Indian Noni is one among them. It contains the entire major and most of the micro nutrients. Noni is helpful for cancer patient. Along with all the cancer treatment if Noni is added with their treatment protocol it will cover maximum side effects of chemotherapy or radio therapy; acts as an immune supplemental adjuvant to the current therapy; as it prevents the DNA adduct formation it help in primary prevention and secondary prevention for all cancer patient or those with family history of cancer treatment.

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Wang MY B.J. West; C.J. Nowicki, D.; C.Su; A.K. Palu.; and G. Anderson 2002 Acta Pharmacol Sin Dec; 23 (12): 1127-1141. Morinda citrifolia (Noni): A literature review and recent advances in Noni research. WANG Mian-Ying, Brett J WEST, C Jarakae JENSEN, Diane NOWICKI, SU Chen, Afa K PALU, Gary ANDERSON. University of Illinois College of Medicine, Department of Pathology, 1601 Parkview Avenue, Rockford, IL 61107, USA; Department of R & D, Morinda Inc, Provo, Utah 84606, USA.
**Abstract:** Lymphatic Filariasis is a parasitic and infectious tropical disease, caused by the thread-like parasitic filarial worms, *Wuchereria bancrofti*, *Brugia malayi*, and *Brugia timori*, all transmitted by mosquitoes. The most spectacular symptom of lymphatic filariasis is elephantiasis (thickening of the skin and underlying tissues), which was the first disease discovered to be transmitted by insects. Elephantiasis is caused when the parasites lodge in the lymphatic system. Elephantiasis affects mainly the lower extremities, whereas ears, mucus membranes, and amputation stumps are rarely affected; however, it depends on the species of filaria. *W. bancrofti* can affect the legs, arms, vulva, breasts, while *Brugia timori* rarely affects the genitals. One in vitro study showed that the adult parasite of *Wuchereria bancrofti* died within 20 hours in the culture media mixed with Noni in comparison to the control group which survived for 60 hours without adding Noni. Similarly, extract of Noni induces paralysis and death of parasitic nematode worm of the human *Ascaris Lumbricoides*, within a day. A botanist via Morton, botanist reported that Noni has been used in the Philippines and Hawaii as an effective insecticide. Hence it can be suggested to prescribe Noni along with other medication of the filariasis.

**Introduction**

It has been shown that Noni has anti helminthic effect on Round worm (*Ascaris umbricoids*). Noni has been used in the Philippines and Hawaii as an effective anti-parasitic. On that basis an invitro study of the effects of Noni juice on both adult and microfilaria of cattle parasite *Setaria digitata* has been conducted. Lymphatic Filariasis is a parasitic and infectious tropical disease, caused by three thread-like parasitic filarial worms, *Wuchereria bancrofti*, *Brugia malayi*, and *Brugia timori*, all transmitted by mosquitoes.

The signs and symptoms: lymph adenoma, massive leg swelling, elephantiasis, lymphangitis, fever, pain epididymitis, orchitis, eosinophilia, etc.
With the objective to evaluate the effect of Noni on different stages of filarial parasites, a study was carried out and the details with results are furnished in this paper.

Materials and Method

1. Collection of *Setaria digitata*: Adult female *setaria digitata*, cattle filarial parasites were collected from the local slaughter house.

2. Collection of Microfilaria: Adult parasites were cut into different pieces in the ISCOV medium and kept at 37°C for an hour. Microfilaria were harvested after centrifuging at 10'000 RPM. Microfilaria count was then adjusted to 2000 mf / ml of medium.

100 micron medium = 200 mf +Noni

Medium : Adult *Setaria digitata* parasites were incubated at 37°C in ISCOV medium at antibiotic and antimycotic care with 10% FCS (Foetal calf serum) at 5% CO2.

Different Noni dilutions

Two dilutions of Noni were prepared

1. N: 50 (i.e. one part Noni with 50 parts of medium)
2. N: 25 (i.e. one part Noni with 25 part medium). Both the Noni dilutions were filtered through 25 micron filter before adding to the culture medium.

Control group of parasites were cultured in the medium without Noni that is named C

1. Effects of Noni on adult parasite was studied in vitro in 3 groups of medium.

Medium and groups

1. Control group C ( no dilution of Noni)
2. Group 1 (where N: 50 Noni dilutions were added with the culture medium).
3. Group 2 (where N: 25 Noni dilutions were added with the culture medium).
4. Adult parasites were taken in each group

Observation

The motility of the adult parasites was noted at day 1, 2, and 3.

It was found that

At day1 the motility was almost same in each group

At day 2 (after 24 hrs) the motility of Gr-1 and Gr-2 were sluggish than control.
At day 3 (after 48 hrs) some parasite of Gr-1 and Gr-2 were dead and the rest of them were moving very slowly

**Effects of Noni on Microfilaria - An In Vitro Study**

Medium and group - Same ISCOV medium  
Same 3 groups were prepared  
1. Control group C (no dilution of Noni)  
2. Group 1 (where N: 50 Noni dilutions were added with the culture medium).  
3. Group 2 (where N: 25 Noni dilutions were added with the culture medium).  
About 200 microfilaria were taken in each group.

**Observations**

The motility of the microfilaria was noted at day 1, 2, 3 & 4.

It was found that:

- At day one the motility was almost same in each group
- At day two (after 24 hrs) the motility of Gr-1 and Gr-2 were sluggish than control. Gr-2 motility was more sluggish than Gr-1
- At day three (after 48 hrs) the motility of Gr-1 was remarkably sluggish and Gr-2 were found dead without any movement.
- At day four (after 72 hrs) the microfilaria in both the Gr-1 and Gr-2 were found dead without any movement

**Conclusion**

This study brought out the fact that Noni induces neuromuscular effects (paralysis) and death of the filarial parasite both in adult and microfilaria at higher concentrations within 48 hours.
Anti-fibrotic effect of Noni (Morinda citrifolia. L) on carbon tetrachloride induced liver fibrosis

Authors’ affiliation:
N. Murugesh
A.J.M. Christina
N. Chidambaranathan
Institute for Pharmacology, Madurai Medical College, Madurai, Tamil Nadu, India.
Department of Pharmacology, K.M. College of Pharmacy, Uthangudi, Madurai, Tamil Nadu, India - 625107.

Abstract: A study was carried out to investigate the effect of Noni against carbon tetrachloride (CCl₄), induced liver fibrosis. Liver fibrosis was induced by twice/week administration of CCl₄ at a dose of 1 ml/kg weight mixed with an equal volume of corn oil. The extent of liver fibrosis was assessed by the content of hydroxyproline in liver, serum level of asparate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP) and bilirubin. Treatment with Noni reduced the hydroxyproline content of liver, serum enzyme levels and total bilirubin. These observations confirm the antifibrotic effect of extract.

Keywords: Morinda citrifolia L., Antifibrotic effect liver

Introduction
Fibrosis is seen as a scar formation in liver (Borchers et al., 2000). Hepatic fibrosis is the result of chronic viral, toxic auto immune or cholestatic liver injury (Wasmuth, et al., 2003). Viral infection seems to be a crucial factor in liver fibrosis. Numerous chemicals and drugs can harm the liver (Chojkier and Brenner, 2003). In many experimental fibrotic models, CCl₄ was used to induce hepatic injury (Madro, et. al., 2002). Some workers have used N-nitro dimethyl amine (NMDA) to injure rat liver and have reported that hyaluronic acid plays a role in the pathogenesis of liver fibrosis (George, et. al., 2004). Likewise, bile duct ligation technique was used by many workers to induce fibrosis (Kountouras, J., et. al., 1984; Turkacaper, N., et. al., 2003).

In this study CCl₄ induced liver fibrosis was used as a model to evaluate the antifibrotic effect of Noni.

Materials and Methods

Animals
Male albino Wistar rats (150 –200 g) were purchased from Chellamuthu Trust, Madurai. They were housed in groups of 3 to 4/cage, maintained at 25 ± 2°C under 12 hour light -dark cycle. They were fed with standard pellet diet and water ad libitum.
Induction of liver fibrosis by Carbon Tetrachloride

CCL₄ was given to rats orally twice a week for 28 days at the dose of 1 ml/kg body weight mixed with an equal volume of corn oil (Bickel, et. al., 1991). Three days after the last dose, rats were sacrificed under light anesthesia and blood and liver samples were collected for biochemical studies.

Treatment with Noni

The diluted Noni extract was given orally by gavage for 28 days at a dose of 5 ml. The control group received equal amount of distilled water, given orally for 28 days. For comparison a group of normal rats was used throughout. The body weight of the animals was recorded every day for this study.

Estimation of serum biochemical parameters

After 28 days, the rats were sacrificed under light anesthesia and blood was collected by cardiac puncture. A part of it was used for biochemical estimation and centrifuged at 3000 rpm to obtain serum. The levels of aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP) and total bilirubin were estimated by standard procedures.

Determination of Hydroxyproline content in liver

The hydroxyproline content of liver was determined by the method suggested by Jamall, et. al., (1981). The specimens of liver were weighed and hydrolysed completely in 6 M HCl. A fraction of the sample was derivatised using Chloramine T solution and Erhlich’s reagent. The density was measured at 558 nm.

Statistical analysis

The values are expressed as mean $\pm$ SEM. The data were analysed using one way ANOVA followed by Newman Keul’s multiple range tests. Differences below P < 0.05 implied significance.

Results

The results are presented in Tables 1 and 2.

**Table 1: Effect of Noni on the biochemical parameters of rats treated with CCl₄**

<table>
<thead>
<tr>
<th>Treatments</th>
<th>AST IU/L</th>
<th>ALT IU/L</th>
<th>ALP IU/L</th>
<th>Total Bilirubin mg/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal rats</td>
<td>159 ± 6</td>
<td>47 ± 2.2</td>
<td>215 ± 6.8</td>
<td>0.48 ± 0.01</td>
</tr>
<tr>
<td>CCL₄ treated rats</td>
<td>289 ± 1.1*</td>
<td>102 ± 5*</td>
<td>396 ± 8*</td>
<td>1.6 ± 0.08*</td>
</tr>
<tr>
<td>CCL₄ + Noni treated rats</td>
<td>175 ± 8*</td>
<td>61 ± 4*</td>
<td>235 ± 13.2*</td>
<td>0.7 ± 0.03*</td>
</tr>
</tbody>
</table>

*N. Murugesh et al. Anti-fibrotic effect of Noni (Morinda citrifolia. L) on carbon tetrachloride induced liver fibrosis*
Data are mean + SEM. n=6, Newman Keuls multiple test was used (P<0.05).

* Significantly different from normal rats.
* Significantly different from CCl4 treated rats.

**Table 2: Hydroxyproline content of liver and liver weight following various treatments**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Hydroxyproline Content (mg/g liver)</th>
<th>Liver weight on day 28</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal rats</td>
<td>$53 \pm 3$</td>
<td>$3.5 \pm 0.02$</td>
</tr>
<tr>
<td>CCl4 treated rats</td>
<td>$124 \pm 7$</td>
<td>$4.5 \pm 0.06$</td>
</tr>
<tr>
<td>CCl4 + Noni treated rats</td>
<td>$77 \pm 3,*_a$</td>
<td>$3.8 \pm 0.07,*_a$</td>
</tr>
</tbody>
</table>

Data are mean + SEM. n = 6, Newman Keuls multiple test was used (P<0.05)

* significantly different from normal rats.
* Significantly different from CCl4 treated rats.

**Serum parameters**

Treatment with CCl4 altered various tissue and serum parameters and also the architecture of liver. In CCl4 treated rats, the serum parameters AST, ALT, and ALP were significantly elevated. The bilirubin level was also high. However, in CCl4 + Noni treated rats, the serum levels of these enzymes and bilirubin were significantly low when compared to CCl4 alone treated rats.

**Tissue parameters**

The main tissue parameters assessed were hydroxyproline content and weight of liver. Hydroxyproline was elevated following CCl4 treatment. Treatment with the extract reduced this parameter. Liver weight was increased in CCl4 treated rats which was reduced by Noni.

**Discussion**

Large literature states that collagen content in the extracellular matrix is high in fibrosis, the extent of which could be assessed by the hydroxyproline content (Muriel and Escobar, 2003). Many earlier studies have reported high hydroxyproline content in association with liver fibrosis. Present study showed a high hydroxyproline content in CCl4 treated rats, indicating the development of fibrosis, which was brought down by co-treatment with Noni.

In the present study, CCl4 the toxicant that injures liver is converted to trichloromethyl radical by the enzyme cytochrome P450 which initiates lipid
peroxidation and liver damage. Hence, liver damage was reflected by high levels of serum AST, ALT, ALP and bilirubin in CCl₄ treated rats. The rats treated with CCl₄ + Noni showed low levels of AST, ALT, ALP and bilirubin. These observations suggest that Noni is effective against CCl₄ induced liver fibrosis in rats.

Conclusion

This study has indicated the protective effect of Noni against CCl₄ induced chronic liver injury. This conclusion was based on the correction of serum as well as tissue parameters by Noni.

References


Uricosuric Effect of Indian Noni
(Morinda citrifolia. L)

Abstract : Uricosuric effect of the Indian Noni was studied by an indirect method of phenol red elimination and a direct method of estimating uric acid in serum and urine in Noni fed rats. Plasma level of phenol red shows an increase in Noni fed rats which is an indirect evidence for its uricosuric effect. Direct estimation of uric acid in serum showed a decrease and that in urine showed an increase. All these effects are comparable to that of probenecid, a standard uricosuric agent. These effects are suggestive of a beneficial effect of Indian Noni in gout.

Keywords : Uric acid, gout and Noni

Introduction
Gout is a painful type of arthritis. It attacks large and small joints. Usually it attacks one joint at a time. It is caused by high level of uric acid in blood (hyperuricaemia). Uric acid crystals collect in joints and connective tissues. (Edwards and Bouchin, 1991). Drugs used in the treatment of gout include NSAIDs, corticosteroids, uric acid synthesis inhibitors such as allopurinol, in addition to uricosuric agents like probenecid and sulphinpyrazone (Tripathi, 2003). The use of these drugs involves a variety of drug interactions and adverse effects. Noni has been advocated for a variety of joint disorders such as rheumatoid arthritis, polyarthritis, juvenile arthritis etc.. Also it is much effective in gout and hence a scientific validation for this effect has been sought in this investigation by evaluating the uricosuric effect of Indian Noni.

Materials and Methods
Animals
Male albino rats weighing between 150 and 175g were used. The animals were maintained under standard laboratory conditions with pellet diet and water *ad libitum*.

Phenol red elimination
Uricosuric agents delay the renal excretion of phenol red (Phenol sulphonapthalein). So plasma level of phenol red increases which is an indirect
evidence for its uricosuric effect. (Vogel and Vogel, 1997). Two ml of Indian Noni was administered to a group of 6 rats orally. Thirty minutes later, 2.5ml/kg of a 3% aqueous solution of phenol red was injected through tail vein. It was followed by flushing of 2.5ml/kg of saline by the same route. Blood was collected by retro-orbital puncture at 30, 60, 120 and 180 minutes and phenol red concentration estimated.

Serum uric acid

Serum uric acid concentration was determined by standard procedures (Varley, 1967) at 5, 10, 15 and 20 days of Noni administration at a dose of 2ml daily by oral route for 20 days.

Uric acid in urine

Noni fed animals (2ml daily orally for 20 days) were maintained in a metabolic cage. Urine collected was estimated for uric acid on the 5th, 10th, 15th and 20th day.

All the results were compared with probenecid, a standard uricosuric agent administered at a dose of 10mg/kg body weight by oral route.

Results and Discussion

Indian Noni is a wonderful remedy for gout and hence its uricosuric effects has been investigated for the first time in this report. Increase in phenol red concentration in plasma is an indirect evidence for its uricosuric effect. Noni produces a significant increase in plasma phenol red concentration (Fig. 1). The effect is very much comparable to that of probenecid, a standard uricosuric agent.

![Figure. 1. Phenol red concentration on administration of Noni and Probenecid.](image-url)
Direct estimation of serum uric acid shows a decline in Noni fed rats (Fig. 2) and the decrease is proportional to the days of administration. Again these results are similar to those of probenecid. This decrease in serum uric acid concentration coincides with an increase in urine (Fig. 3). Contrary to phenol red estimation, these two results are direct evidences for the uricosuric effect of Indian Noni. Again, the uricosuric effect of Noni is comparable to that of probenecid. The beneficial effect of Indian Noni in gout is thus evident and it can be safely recommended for these patients since it is a natural product devoid of any adverse effects.

![Figure 2. Serum uric acid level on administration of Noni and Probenecid](image1)

![Figure 3. Uric acid concentration in urine on administration of Noni and Probenecid.](image2)
References


World Noni Research Foundation

With the mission of educating the people, the World Noni Research Foundation, a non-profit organisation dedicates itself to love and care for Morinda citrifolia, through research and development. Learning from the wisdom of the simple people, WNRF aims at working with everyone to conserve and improve Noni towards sustainable human and ecological health. It will share the Noni's past glory, ethnobotany, history, science, benefits and its multiple uses with all. The WNRF also serves as a facilitatory body for all Noni farmers, industries and consumers to establish a sustainable Noni economy network. The WNRF collectively represents the interests of all people in the Noni research and industry. It is an independent body and committed to exclusive Noni research and development. The WNRF website, journals and news letters are established to provide a non-biased forum for the researchers, consumers and industries to publicise their research findings and experiences with Morinda species.

WNRF believes that this synergistic effort of scientists and people of ‘Noni Solidarity’ would empower millions of ordinary masses to find their dignity and economic freedom, more naturally. This will lead to the realization of our vision “Healthy people, Healthy nation” in India and rest of the world.

Our Programmes Focus on

- Conserving the Morinda species in India and rest of the world from its degradation.
- Organising “Noni Biodiversity Action Network” (NBAN) to save endangered (Red listed) Morinda species in the above regions.
- Developing Bioinformatics database on Morinda species existing in India and rest of the world and record all Indigenous Technical Knowledge about it.
- Supporting the research and development programmes on discovering the multiple potential of Morinda species in fields like pharmaceutical, nutraceutical, cosmetology, dye, agriculture, etc.
- Sharing the cutting edge action-programmes and research findings with researchers, farmers, consumers, food industry leaders, health - drug industry leaders, students and masses.
- Connecting the Morinda species researchers in India and rest of the world.
- Promoting the Indian Noni for health regenerative systems and processes through clinical studies & biotechnological research.
- Developing “Noni Villages” for Noni based socio-economic development of people at the grass-root level.
- Monitoring and encouraging quality Morinda products in the Market.
- Regenerating the glory of Indian Noni