

WNRF Technical Bulletin : 08

Studies on anti-inflammatory, antibacterial and immunomodulatory activity of Noni (*Morinda citrifolia* L.) in experimental animals

by

Department of Veterinary Pharmacology and Toxicology
College of Veterinary Science and Animal Husbandary, Jabalpur (M.P)
&

World Noni Research Foundation
12, Rajiva Gandhi Road, Perungudi, Chennai - 600 096, India

Published by	Edited by	Author (s)	Year of Publication
Prof. P. I. Peter Chairman Noni BioTech, Chennai, India	Dr. P. Rethinam Dr. T. Marimuthu Dr. K.V. Peter	Dr. R. K. Sharma Dr. (Mrs.) Varshs Sharma	September, 2011

Citation :

Sharma, R. K. and Varshs Sharma, 2011. Studies on anti-inflammatory, antibacterial and immunomodulatory activity of Noni (*Morinda citrifolia* L.) in experimental animals. WNRF Technical Bulletin 08, College of Veterinary Science and Animal Husbandary, Jabalpur (M.P) and World Noni Research Foundation, Chennai, India, p. .

Summary and Conclusion

This experimental investigation was carried out in albino rats of either sex weighing 120-150 g. The alcoholic and aqueous extracts of *Morinda citrifolia* (Noni) were prepared and used to find out the chemical constituents. The extractability of Noni was recorded more in water as compared to alcohol. The phyto chemical test revealed the presence of alkaloid, amino acid, reducing sugar, glycosides, tannin and steroid in aqueous extracts of Noni fruit and alkaloid, protein, amino acid, reducing sugar, tannin, anthraquinone and steroid in alcoholic extracts of Noni fruit.

Morinda citrifolia (Noni) has been found to be safe drug as the oral LD50 was found to be more than 2000 mg/kg body weight. Moreover it did not show any significant toxic symptoms. However on chronic exposure for three months the alcoholic extract administered, orally, at the dose rate of 1000 mg/kg body weight produced significant increase in TEC, haemoglobin and PCV. A significant increase in blood clotting time in both aqueous and alcoholic extracts of Noni was produced.

The histopathological study of liver and kidney on chronic exposure for three months showed swollen hepatocytes and mild fatty changes. There was congestion and degeneration in hepatic cells. The histopathological studies of kidney from group of rats treated with alcoholic extract of Noni produced leucocytic infiltration and mild congestion in glomerulus of kidney whereas aqueous extract showed degenerative changes with slight haemorrhages in interstitial tissue. Aqueous extract of Noni produced more degenerative changes in kidney and liver as compared to alcoholic extracts suggesting that aqueous extract is more toxic.

The interpretations of results suggest that though, Noni is a quite safe drug, it produces toxicity during its metabolism and elimination.

This experimental investigation was carried out in albino rats of either sex weighing 120-150g, to elucidate the mechanism of action of *Morinda citrifolia* (Noni). In this study, the aqueous and alcoholic extracts of Noni were used for study on inflammation, pain and pyrexia.

The anti-inflammatory activity was studied against acute and chronic inflammations by using carrageenin induced hind paw edema model and cotton pellet induced granuloma model respectively. Analgesic activity was studied by hot plate method and antipyretic activity was studied against yeast induced pyrexia.

The results of the present experimental investigation are summarized as follows: The alcoholic extract of Noni has been found to produce significant anti-inflammatory activity after 2nd, 3rd and 4th hours of administration on carrageenin induced rat paw edema. Phenylbutazone has been found to significantly increase the anti-inflammatory activity of both aqueous and alcoholic extracts of Noni in acute and chronic process, suggesting similar mechanism of action of these drugs. The anti-inflammatory action is more significant with alcoholic extract and phenylbutazone.

The possible role of mediators of inflammation in anti-inflammatory activity of Noni was studied by pretreating the animals with number of antagonist of mediators namely, cyproheptadine, promethazine, cimetidine and paracetamol both on acute and chronic inflammatory models.

The results of the study showed that during 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 promethazine. Aqueous extract of Noni showed significant anti-inflammatory

activity with cimetidine, paracetamol and promethazine but not with cyproheptadine. Thus anti-inflammatory effect of aqueous extract of Noni might be due to the inhibition of endogenous histamine which increased by pretreatment with cimetidine. The results further revealed that besides histamine, prostaglandins also play a role in controlling anti-inflammatory activity of Noni. Thus anti-inflammatory activity of Noni on transudative and proliferative stages of inflammation may be due to its blocking effects on H1 receptors, H2 receptors and prostaglandins.

The results of the study showed that the maximum increase in anti-inflammatory activity of alcoholic extract of Noni was produced by promethazine during acute phase which was found to persist for 4 hours followed by paracetamol, cyproheptadine and cimetidine. Thus anti-inflammatory effect of alcoholic extract of Noni might be due to the inhibition of endogenous histamine, prostaglandins and 5 HT.

The alcoholic extract of Noni was more effective as compared to its aqueous extract on chronic inflammatory process. The maximum increase in anti-inflammatory activity of aqueous extract on cotton pellet induced granuloma was produced by paracetamol. These results indicate that prostaglandins mainly are responsible for anti-inflammatory action of aqueous extract of Noni in chronic process against proliferative phase of inflammation and this activity may be due to blockade of endogenous prostaglandins. Noni has also been found to produce anti-inflammatory activity on chronic proliferative stage by its antihistaminic effect as it is potentiated by administration of cimetidine.

The maximum increase in anti-inflammatory activity of alcoholic extract on cotton pellet induced granuloma was produced by paracetamol. These results indicate that prostaglandins mainly are responsible for anti-inflammatory action of alcoholic extract of Noni in chronic process against proliferative phase of inflammation and this activity may be due to blockade of endogenous prostaglandins. Noni has also been found to produce anti-inflammatory activity on chronic proliferative stage by blocking 5-hydroxytryptamine.

The aqueous and alcoholic extracts of Noni have also shown dose related antipyretic and analgesic activity. The percent analgesic score of both extracts persisted up to 3 hour of administration. The alcoholic extract @ 1000 mg/kg produced better analgesic action as compared to aqueous extract at the same dose rate.

Both the aqueous and alcoholic extracts of Noni significantly reduced the yeast induced pyrexia starting from 1 hour post administration and it was completely brought back to normal within 4 hour post administration . The alcoholic extract @ 1000 mg/kg produced better antipyretic action as compared to aqueous extract at the same dose rate up to 3 rdhr of administration.

The present study was aimed to elucidate the usefulness of Aqueous extract of Noni, Alcoholic extract Noni, as antibacterial and immunomodulatory agent, affecting haematological and sero biochemical profile in albino rats.

Antibacterial activity of above treatments (*in vitro*) against *Bacillus subtilis*, *Escherichia coli*, *Klebsiella pneumoniae*, *L.monocytogens*, *Salmonella typhimurium*, *Staphylococcus aureus* and *Bacillus cerius* was assessed as compared to Ciprofloxacin, (Ci) the standard drug.

It was interesting to note that aqueous extract of Noni and alcoholic extract of Noni alone did not reveal growth of any bacteria at 40% dilution. This indicates similar antibacterial effect of aqueous extract of Noni and alcoholic extract of Noni at higher concentration.

Antibacterial activity of above treatments (*in vivo*) against *E. coli* was also studied following oral administration of one ml broth culture containing 3×10^9 cfu/ ml. The clinical symptoms noticed were dull, depression, anorexia, diarrhoea, pyrexia, increased pulse dyspnoea and prostration in later stage of infection. The overt clinical symptoms in rats of group I (Control) were most severe than other treatment groups. The mortality rate in group I (50%), other groups did not shown any mortality.

The DTH response, which has a direct correlation of cell mediated immunity (CMI), showed highly significant ($P < 0.01$) increase in mean paw volume .The order of significance of mean paw volume was as follows group IV (IP), group III (Alc), group II(Aq) and group I (C) rats.

The humoral immune response was evaluated by Haemagglutination inhibition (HI) titre against Newcastle disease virus. HI titre showed highly significant increase in group IV (IP) followed by group III (Alc), group II (Aq) and group I (C) rats ($P < 0.01$). Increase in both, HI titre and DTH response indicated that the use of Alcoholic and aqueous extract of Noni has humoral as well as cellular immunity.

In recent years, there has been an upsurge in the clinical use of natural and indigenous drugs. Side effects and operating cost associated with allopathic

drugs have forced the need for research into drugs, which are without the side effects. There is an increasing interest in the search for potential drugs, especially of plant origin, that are capable of masking the untoward side effects of steroidal and non-steroidal drugs. Medicinal plants have many traditional claims including the treatment of ailments of infectious origin. In the evaluation of traditional claims, scientific research is important. The objectives of the study were to determine the presence of antibacterial and immuno modulatory activity in the extracts of Noni fruits.

Looking to all parameters that were envisaged to study the herbal plant, *Morinda citrifolia* (Noni), it can be concluded that both aqueous and alcoholic extracts of Noni fruit contain several phytochemicals viz., alkaloid, amino acid, reducing sugar, glycosides, tannin, steroid, anthraquinone and protein. All these components are responsible for its pharmacological activity.

The chronic intake of both aqueous and alcoholic extracts of Noni fruit did not produce much damage to vital organs but in turn the alcoholic extract showed a increase in TEC, haemoglobin and PCV indicating its stimulating effect on the haemopoietic system.

Further studies concluded that alcoholic extract was better as anti-inflammatory, analgesic and antipyretic agent with no side effects. Noni interact well with other anti-inflammatory drugs such as phenylbutazone. In acute phase of inflammation Noni mainly works via blocking histamine, 5-HT and prostaglandins and in chronic phase of inflammation Noni mainly works via blocking prostaglandins, histamine and 5 HT. Noni besides these functions is also useful in diabetes, hypertension, arthritis, asthma and stones. All parts of Noni plant whether roots, barks, leaves and fruits can be utilized in medication.

A logical conclusion from the present study indicates with certainty that Aqueous extract of Noni, Alcoholic extract Noni distinctly have both antibacterial and immunomodulatory action. Based on scientific deduction and accessible literature indicates that there may be certain metabolites or bio-molecules present in Noni, which possess protective properties i.e. antibacterial action. Aqueous extract of Noni and Alcoholic extract Noni are found to consist of certain alkaloids and resins which are responsible for their antibacterial and immunomodulatory action.

HI titre and DTH response indicates that aqueous and alcoholic extract of Noni are potent immuno-modulatory agents enhancing the humoral and cell mediated immune response. One of the explanations forwarded to justify the

beneficial effect of aqueous and alcoholic extract of Noni, is non specific enhancement of immune status. In summation, aqueous and alcoholic extract of Noni are natural medicinal agents and God's gift to Mankind.

-----End of statement-----