Mechanism of Action of *Azadirachta Indica* Linn. (Neem) Aqueous Leaf Extract as Hypoglycaemic Agent

**Lakshman Das**, Assistant Professor, 
*Department of Pharmacology, Tripura Medical College and Dr. B.R. Ambedker Memorial Teaching Hospital, Hapania, Agartala, Tripura.*

**Ng. Gunindro**, Assistant Professor, 
*Department of Pharmacology, Regional Institute of Medical Sciences, Imphal, Manipur.*

**Ranjib Ghosh**, Associate Professor, *Department of Pharmacology*  
**Mukut Roy**, Assistant Professor, *Department of Medicine* 
— *Tripura Medical College and Dr. B.R. Ambedker Memorial Teaching Hospital, Hapania, Agartala, Tripura.*

**Asis Debbarma**, Tutor, *Department of Biochemistry, Agartala Government Medical College, Agartala, Tripura.*

Abstract

**Objective:** To find out the mechanism of action of *Azadirachta indica* aqueous leaf extract (ALE) as hypoglycaemic agent. **Materials and Methods:** Overnight fasted albino rats of Wister strain of either sex were divided into 3 groups-a) Control (5% aqueous gum acacia suspension 5ml/kg, PO), b) Test (ALE-500mg/kg, PO) and c) Standard (glibenclamide 0.5mg/kg, PO). Blood glucose was estimated before administration of drugs and at 30min, 60min & 120min after the administration of drugs. For glycogen estimation also different animals were taken and divided into similar groups and after 1h of administration of drugs, the animals were killed and glycogen concentration from the liver, skeletal muscle and cardiac muscle were estimated. **Results:** The ALE produces a marked decrease in blood glucose level in normal rats. The glycogen content of liver, skeletal muscle and cardiac muscle was increased significantly (p<0.001) after 1h of administration of ALE as compare to control. **Conclusion:** ALE decreases blood glucose level and increases glycogen concentration in liver, skeletal muscle and cardiac muscle significantly. Increased glycogen synthesis is one of the important mechanisms responsible for its hypoglycemic action.

Keywords  
*azadirachta indica*, glycogen, glibenclamide

Introduction

*Azadirachta indica* (Family-Meliaceae) is an indigenous plant widely available in India and Burma. Different parts of the plant have been reported to possess medicinal properties like hypoglycemic, anti septic, wound-healing, curing of skin diseases and anti ulcer activities. It has been seen that *Azadirachta indica* aqueous leaf extract (ALE) has significant hypoglycemic effect in both IDDM and NIDDM models (Bajaj S and Srinivasan BP, 1999). The present study was conducted to find out the mechanism of action of ALE.

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*Address for correspondence:* Dr Lakshman Das, Assistant Professor, Department of Pharmacology, Tripura Medical College and Dr. B.R. Ambedker Memorial Teaching Hospital, P.O: Hapania – 799 014. Agartala, Tripura (W). E-mail: doctorldas@gmail.com
Materials and Methods

Animals

Albino rats of Wister strain (150-200 g) of either sex were used. Animals were obtained from the animal house of Tripura Medical College and Dr. B.R. Ambedkar Memorial Teaching Hospital and kept in polypropylene cages in the departmental animal house. They were acclimatized for 10 days and fed on standard laboratory diet and water ad libitum. 12 hours light and dark cycle was maintained.

Laboratory practice

The Institutional Animal Ethics Committee of Tripura Medical College and Dr. B.R. Ambedkar Memorial Teaching Hospital, Agartala approved the proposal for the study.

Preparation of the Extract

Fresh neem leaves were collected and authenticated by expert botanist of Tripura University. The aqueous extract of the leaves was obtained by the procedure as described by Khosla P et al., 2000. One kg of freshly collected, shade dried, powdered leaves of A. indica were ground and soaked in 4 litres of distilled water overnight. The suspension was centrifuged at 5000rpm for 20 minutes and filtered through Whatman no. 1 filter paper. The supernatant fluid was allowed to evaporate in sterile glass petridishes. After drying, the extract was collected by scraping and stored. The yield was 12.5%.

The effect of ALE on blood glucose level of normal albino rats was done to reestablish its hypoglycemic effect and to evaluate its mechanism of action as hypoglycemic agent, glycogen concentration of liver, skeletal muscle and cardiac muscle of albino rats was estimated.

Effect of ALE on blood glucose level in normal rats

18 albino rats weighing 150-200g were fasted overnight with free access to water. Care was taken to prevent corpophagy. They were divided into 3 groups containing 6 animals in each group as follows:-

Group I (Control): Aqueous 5% gum acacia (5ml/kg, P.O)
Group II (Test): ALE (500mg/kg, P.O)
Group III (Standard): Glibenclamide (0.5mg/kg, P.O)

All drugs were administered with the help of a stomach tube. No adverse effect or mortality was observed in the albino rats with oral ALE extract (2gm/kg) observed for 24 hours during preliminary toxicity testing. The dose of glibenclamide was calculated from human dose by extrapolation based on the surface area. 1 ml of blood was taken from the orbital sinus of each rat with the help of capillary tubes and serum glucose was estimated by glucose oxidase method (Barham D and Trinder P, 1972). The blood glucose levels of the rats of different groups were estimated before administration of drugs and at 30min, 60min and 120min after administration of drugs.

Effect of ALE on glycogen content in liver, skeletal muscle and cardiac muscle

The effect of ALE on glycogen concentration of liver, skeletal muscle and cardiac muscle was studied in normal albino rats. 18 albino rats weighing 150-200g were fasted overnight (Chattopadhyay R.R. et al., 1993). They were divided into 3 groups containing 6 animals in each group. Then, the animals were treated as follows:

Group I (Control): Aqueous 5% gum acacia (5ml/kg, P.O)
Group II (Test): ALE (500mg/kg, P.O)
Group III (Standard): Glibenclamide (0.5mg/kg, P.O)

After 1 h of administration of drugs, the animals were killed by decapitation and the liver, leg muscle and heart tissues were taken out with care. Glycogen from these tissues was estimated by the method as described by Carroll NV et al., 1956.

Results

Results were analysed by ANOVA followed by ‘t’ test. p<0.05 was considered to be statistically significant.

The effects of ALE on blood glucose level in normal albino rats are shown in Table 1 and the effect of ALE on glycogen concentration in liver, cardiac muscle & skeletal muscle are shown in Table 2.

Discussion

The ALE produces a marked decrease in blood glucose
level in normal rats. This finding is in agreement with those reported by Murty et al. (1978) and Khosla P. et al. (2000). The reduction of blood glucose level by ALE(500mg/kg) at 60 min was statistically highly significant (p< 0.01) as compared to control Group. Maximum reduction of blood glucose was observed at 60 min after the administration of ALE. The hypoglycemic effect of ALE started to decline at 120min of administration of the drug.

Glycogen content of liver was increased after 1 h of administration of ALE (p<0.001). The increased glycogen content in liver may be due to increased release of insulin (Mathew PT et al., 1973).

Glycogen content of skeletal and cardiac muscle also was increased following ALE administration (p<0.001). Increased glycogen content in skeletal and cardiac muscle indicates enhanced cellular transport of glucose.

**Conclusion**

The present study showed that Azadirachta indica Linn. aqueous leaf extract decreased the blood glucose level in albino rats and also increased glycogen content in the liver, skeletal muscle and cardiac muscle. Enhanced cellular transport of glucose into liver, cardiac muscle and skeletal muscle and also increased glycogenesis in these tissues may be responsible for the hypoglycemic effect of A. indica Linn.

**References**


