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Research Article

Hypoglycemic Effect of *Polyalthia longifolia* on Glucose Tolerance in Glucose-Induced Hyperglycemic Mice and Analgesic Effect of *Polyalthia longifolia* in acetic acid-induced writhing model Mice

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Abstract

The high level of blood glucose causes the diabetes and many of the diseases are concerned with the symptom of acute or chronic pain. The present study showed the hypoglycemic and analgesic effect of ethanolic extract of *Polyalthia Longifolia* leaf was investigated. Oral glucose tolerance test was performed in the present study to find the hypoglycemic effect and acetic acid-induced writhing method was used to test the analgesic effect of the leaves. The hypoglycemic effect was found from 16.25 mM to 6.22 mM ± SEM at the dose of 500 mg extract ($p<0.05$). The analgesic activity was observed 69.46 % and 58.08% at the rate of 500 mg and 250 mg ($p<0.05$) respectively compared to writhing inhibition of standard drug Diclofenac 78.16%. The presence of Alkaloid, Flavonoid, Gum, Tannin and Saponin in the extract of leaves may be the reason of these effects. *Polyalthia Longifolia* has much potential in the medicine of diabetic and pain.

Key Words: Blood Glucose, Hypoglycemic, Mice, Analgesic, Diabetic, *Polyalthia Longifolia*

1.Introduction

Diabetes mellitus (DM) is a group of metabolic diseases characterized by high blood sugar (glucose) levels that result from defects in insulin secretion. Diabetes can lead to blindness, kidney failure, nerve damage, kidney failure (nephropathy), lesions of the eye (retinopathy) and atrophy of the peripheral nerves (neuropathy). Hyperglycemia is an important factor in the development and progression of long-term complications of DM affecting kidney, retina, heart and nervous system.[1] Diabetes is a global disease with a huge adverse impact on health and mortality. Despite the introduction of hypoglycemic agents from natural and synthetic sources, diabetes and its secondary complications continue to be a major medical problem in the world population. It is important to administer a safe analgesic in postoperative pain, palliative care and chronic pain due to demand of safety margin of the painkiller drugs. *Polyalthia longifolia* is tall bushy evergreen tree, (family *Annonaceae)* with smooth, dark bark and undulate leaves. It was reported that Ethanolic Extract of the leaves has significant anti-ulcer properties.[2] Methanolic extracts of *Polyalthia longifolia* showed cytotoxic properties.[3-4] The hexane extract of the seeds of *Polyalthia longifolia* demonstrated significant antibacterial and antifungal activities.[5-7] Some author proved it as hypoglycemic[8] function and hypotensive

activity[9]. *Polyalthia longifolia* is used as folk medicine for the treatment of fever, pain, skin diseases, hypertension, diabetes, helminthiasis, and febrifuge[10-11].

The objective of this study was to evaluate the hypoglycemic effect of *Polyalthia longifolia* leaves extract in normal and alloxan-induced diabetic mice and analgesic effect in acetic acid induced writhing model mice.

2. Materials

2.1 Plant Materials: *Polyalthia longifolia* leaves were collected from National Parliament House, Bangladesh on January, 2011 under the Accession Number# DACB-35392 of the Bangladesh National Herbarium, Mirpur-Dhaka.

2.2 Drugs and Chemicals: The standard drug, Metformin hydrochloride was collected from Beximco Pharmaceuticals Ltd, Bangladesh. Alloxan monohydrate was purchased from Merck Schuchardt OHG, Germany. Blood samples analyzed for blood glucose content using EZ Smart-168 glucose test meter (Tyson, Taiwan). Acetic acid was collected from laboratory of Bangladesh University. The standard drug Diclofenac-Na was purchased from Square Pharmaceuticals Limited, Bangladesh.

2.3 Experimental Animals: Eight weeks old Swice albino mice (27-30g) purchased from ICDDR'B, Dhaka, Bangladesh and kept in animals cages under standard environmental conditions (22-25°C, humidity 60-70%, 12 hr light: 12 hr dark cycle). The mice were feed with standard pellet diet taken from ICDDR'B, Dhaka. The animals used in this study were cared according to international animal experimentation guideline of National Institute of Health, USA and appropriate permissions obtained from the ethical review committee of Department of Pharmacy, Bangladesh University (ID no. 200631208004) before commencing the experiments.

2.4 Preparation of Extract: *Polyalthia longifolia* leaves were dried in shade for fifteen days at room temperature to ensure the active constituents free from decomposition. The dried leaves were dried at the temperature of 50°C and powdered using electrical grinder. The powder was extracted with 96% ethanol at room temperature. The extract was kept at room temperature for 10 days with occasional stirring. Then the liquid alcohol contents were filtered with filter paper (Whatman Fitter Paper#1). A highly concentrated ethanolic crude extract were obtained and preserved.

2.5 Oral Glucose Tolerance Test (OGTT) in Aloxen induced diabetic mice: After fasting of 16hr, diabetes was induced into mice by in intra-peritoneal injection (i. p.) of alloxan monohydrade (100 mg/kg), dissolved in saline (100 ml/mice, ip.). Plasma glucose levels were measured by glucometer (Tyson, Taiwan) after 48hr using a blood sample withdrawn from tail-vein of mice. Mice with blood sugar level higher than 8.5-11.5 mmol/l were considered as diabetic. Healthy mice were used to examine the effects of extract on normal mice.

The diabetic 25 mice were divided into five groups for the oral administration of the leaves extract. The mice were fasted over-night and blood samples were taken from all groups of animals after 24 hr. After 1 hour of feeding of 1gm/kg glucose; extract and drug blood samples were collected at 0, 30, 90 and 120 minutes intervals to determine the blood glucose level using glucometer.

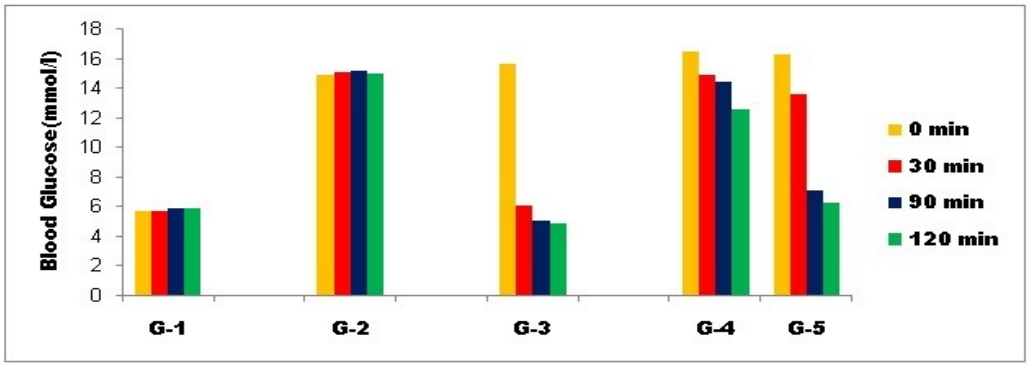
2.6 Acetic acid-induced writhing test for Analgesic activity: All mice were divided into four groups for analgesic test. Each group contained four mice. Control group (received 0.5% methyl cellulose), Standard Group (received Diclofenac-Na 75mg, 1ml), 250mg Group (received 250mg/kg extract) and 500mg Group (received 500mg/kg extract). The analgesic activity of the samples was studied using acetic acid-induced writhing test. 1% acetic acid was administered intra-peritoneal after 30 min of oral administration of test samples. Diclofenac-Na was administered intra-peritoneal after 15 min. Then the mice were observed for specific contraction of body referred to as "writhing" for the next 10 min.

2.7 Statistical analysis: All values were expressed as mean ± Standard error of mean (SEM). Statistical comparison were performed by One-way analysis of variance (ANOVA), followed by using Tukeys test. Results were considered as significant when p values less than 0.05 ($p<0.05$).

3. Results

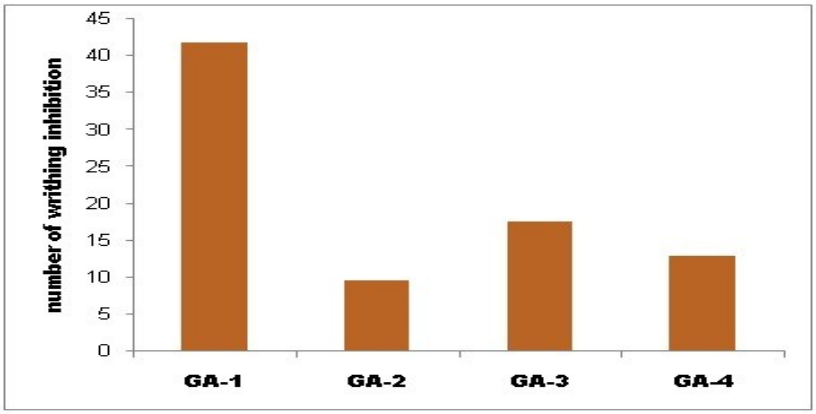
Blood glucose levels of experimental groups showed in Fig. 1. The blood glucose levels were high after oral administration of glucose. The decreased level was found in G-3, G-4 and G-5.

Fig. 1: Effect of the ethanolic extract of *Polyalthia longifolia* leaves on oral glucose tolerance test in G-1(normal), G-2(control, 0.5% methyl cellulose), G-3(Standard Metformin), G-4(250mg/kg extract), G-5(500mg/kg extract)



The effect of extract on acetic acid-induced writhing in mice showed in the fig. 2. The oral administration of both doses of *Polyalthia longifolia* extract decreased writhing response. The effect was dose dependent and 500mg Group (500 mg/kg) was very close to the standard group.

Fig. 2: Effect of the ethanolic extract of *Polyalthia longifolia* leaves on acetic acid-induced writhing in GA-1(control, 1% tween80), GA-2(standard, 75mg/kg Diclofenac), GA-3(250mg/kg extract), GA-4(500mg/kg extract)



4. Discussion

Hyperglycemia and Hyperlipidemia are the two metabolic complications of both clinical and experimental diabetes.[12] In the present study hypoglycemic effect was found 16.25 mM to 6.22 mM at the dose of 500 mg/kg *Polyalthia longifolia* leaves extract ($p<0.05$). Nair R et al, 2007 showed the hypoglycemic effect using Dioxan extract, methanol extract, acetone extract and crude extract at the dose of 300 mg/kg body weight[8] while the present study showed the hypoglycemic effect using ethanolic extract. The dose of 250 mg/kg did not show hypoglycemic effect. This result showed that, the *Polyalthia longifolia* leaves extract had the properties to stimulate or regenerate the ß-cell for the secretion of insulin and is most effective for controlling diabetes by various mechanisms due to presence of hypoglycemic alkaloids, saponins and flavonoids. Oral Glucose Tolerance Test (OGTT) can measure the body ability to use glucose, the body's main source of energy.[13] It can be used to diagnose pre-diabetes and diabetes. In this study, it was found that various fractions (extract) had hypoglycemic effect in glucose induced hyperglycemic mice. The effects of extract on blood sugar levels are dose dependent. Induction of diabetes with alloxan was associated with decrease in hepatic glycogen, which could be attributed to the decrease in the availability of the active form of enzyme glycogen synthetase because of low levels of insulin.[14-15] In the present study, *Polyalthia longifolia* may restore the depressed hepatic glycogen levels possibly by increasing the level of insulin. This study showed that supplementation of diabetic mice with plant extract resulted in significant elevation in hepatic glycogen content.

Satisfactory analgesic activity was found at the dose of 500 mg and 250 mg with 69.46% and 58.08% inhibition of writhing reflex respectively while standard drug Diclofenac showed 78.16% writhing inhibition. The present study indicates significant hypoglycemic and analgesic effects of *Polyalthia longifolia* leaves extract. Acetic acid-induced writhing model presented pain sensation by triggering localized inflammatory response. Such pain stimulus leads to the release of free arachidonic acid from phospholipids**.** The acetic acid-induced writhing model response is a sensitive procedure to evaluate peripherally acting analgesic. The response is thought to be mediated by

peritoneal mast cells, acid sensing ion channels and the prostaglandin pathway.[16-17]The plant extract may contain flavonoid, alkaloids, tannins and saponins that might cause for analgesic activity.

Polyalthia longifolia extract might be useful in the diabetes and analgesic treatment. It is needed to investigate the mechanism of action of anti-diabetic and analgesic effects of *Polyalthia longifolia* Extract.

Acknowledgement and Conflict of interest

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