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# HYPERGLYCEMIC EFFECT OF *ARTOCARPUS HETEROPHYLLUS* SEED METHANOL EXTRACT

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## ABSTRACT

**Background:** The leaves of *Artocarpus heterophyllus* have previously been shown to give hypoglycemic activity in alloxan diabetic rats. Since seeds of the plant are consumed in Bangladesh, it was of interest to evaluate the glucose tolerance effect of methanol extract of seeds (MEAH). **Methods:** Oral glucose tolerance test (OGTT) was done to evaluate glucose tolerance. **Results:** In oral glucose tolerance tests, MEAH at doses of 50, 100, 200 and 400 mg per kg body weight in mice, respectively, caused 0, 3.6, 8.6 and 11.8% increases in blood glucose levels compared to control animals in glucose-loaded mice. By comparison, a standard antihyperglycemic drug, glibenclamide, reduced blood glucose levels by 40.9% at a dose of 10 mg per kg. Thus, the seeds had the opposite effect; it caused a hyperglycemic effect in contrast to previously reported antihyperglycemic effect of leaves. **Conclusion:** Seeds should be consumed by diabetic patients with caution.

**KEYWORDS:** Hyperglycemic, *Artocarpus heterophyllus*, OGTT, diabetes.

## BACKGROUND

An estimated 285 million people in the world lived with diabetes in 2010 and the number has been predicted to double after 2030. The prevalence of Type 2 diabetes is on the rise in Bangladesh.[1] Both urban and rural population of Bangladesh shows an increasing trend of Type 2 diabetes.[2] Diabetes or diabetes mellitus is characterized by high blood glucose levels due to either decreased insulin production or inability to use the produced insulin effectively. Since the disease cannot be cured, the available anti-diabetic medications deal only with

trying to decrease elevated blood glucose levels through various mechanisms or try to ameliorate other complicating symptoms of diabetes like kidney or heart disorders.

We had been screening plants and plant parts of Bangladesh for several years in an effort to find out plants or plant parts that can effectively lower blood glucose and be readily available and affordable to the diabetic patients.[3,20] *Artocarpus heterophyllus* Lam. belongs to the mulberry family (Moraceae) and is known in English as jackfruit and in Bengali as kanthal or kathal. It is a large tree, bearing fruits which are large in size and are actually multiple fruits. Fruits and seeds are edible both in the unripe and the ripe form. The fruits are consumed by the poor during season in lieu of rice and are also known as the poor man's food.

Hot water extract of mature jackfruit leaves have been shown to give hypoglycemic effect in alloxan diabetic rats.[21] Antidiabetic activity has also been observed with rag (yellowish filament like structures present in fruit) extract in streptozotocin diabetic rats.[22] Aqueous extract of leaves also reportedly gave hypoglycemic activity in streptozotocin diabetic rats.[23] As the fruits and seeds are plentifully available during season, it was the objective of the present study to evaluate the glucose tolerance potential through oral glucose tolerance test (OGTT) of methanolic extract of seeds of the plant (MEAH).

## METHODS

### *Plant material collection*

Seeds of *Artocarpus heterophyllus* were collected from Gongapur village I Laxmipur district, Bangladesh. The seeds were brought to Dhaka and identified at the Bangladesh National Herbarium (Accession No. 45405).

### *Preparation of methanolic extract of Artocarpus heterophyllus seeds (MEAH)*

For preparation of methanol extract of seeds of *Artocarpus heterophyllus* (MEAH), seeds were thoroughly sliced, dried in the shade, and pulverized into a fine powder. 100g of the powder was extracted with 500 ml methanol over 48 hours. Methanol was evaporated at 40$^{o}$C and the extract was dissolved in Tween 20 prior to administration to mice by gavaging. The final weight of the extract was 5.28g.

***Chemicals and Drugs***

Glibenclamide and glucose were obtained from Square Pharmaceuticals Ltd., Bangladesh. All other chemicals were of analytical grade. Glucometer and strips were purchased from Lazz Pharma, Bangladesh.

***Animals***

Swiss albino mice, which weighed between 12-15g were used in the present study. The animals were obtained from International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B). The animals were acclimatized for three days prior to actual experiments. During this time, the animals were fed with mice chow (supplied by ICDDR,B) and water *ad libitum*. The study was conducted following approval by the Institutional Animal Ethical Committee of University of Development Alternative, Dhaka, Bangladesh.

***Oral glucose tolerance tests for evaluation of glycemic activity***

Oral glucose tolerance tests (OGTT) were carried out as per the procedure previously described by Joy and Kuttan[24] with minor modifications. Briefly, fasted mice were grouped into six groups of five mice each. The various groups received different treatments like Group 1 received vehicle (1% Tween 20 in water, 10 ml/kg body weight) and served as control, Group 2 received standard drug (glibenclamide, 10 mg/kg body weight). Groups 3-6 received, respectively, MEAH at doses of 50, 100, 200 and 400 mg per kg body weight. All substances were orally administered by gavaging. The amount of Tween 20 administered was same in both control and experimental mice. Following a period of one hour as described earlier[8,14], all mice were orally administered 2g glucose per kg of body weight. Blood samples were collected 120 minutes after the glucose administration through puncturing heart following previously published procedures.[8,14] Blood glucose levels were measured with a glucometer. The percent lowering of blood glucose levels were calculated according to the formula described below.

Percent lowering of blood glucose level = $(1 – W_e/W_c) X 100$,

Where $W_e$ and $W_c$ represents the blood glucose concentration in glibenclamide or MEAH administered mice (Groups 2-6), and control mice (Group 1), respectively. Gavaging was done carefully such that injuries do not happen, and no mice fatalities occurred during gavaging. Mice were handled carefully throughout the experiment so that they did not get subjected to any unnecessary pain.

***Statistical analysis***

Experimental values are expressed as mean ± SEM. Independent Sample t-test was carried out for statistical comparison. Statistical significance was considered to be indicated by a p value < 0.05 in all cases.[10]

## RESULTS

In oral glucose tolerance tests, MEAH at doses of 50, 100, 200 and 400 mg per kg body weight in mice, respectively, caused 0, 3.6, 8.6 and 11.8% increases in blood glucose levels compared to control animals in glucose-loaded mice. By comparison, a standard antihyperglycemic drug, glibenclamide, reduced blood glucose levels by 40.9% at a dose of 10 mg per kg. Thus, the seeds had the opposite effect; it caused a hyperglycemic effect in contrast to previously reported antihyperglycemic effect of leaves.[21,23]

**Table 1: Effect of MEAH on blood glucose levels in oral glucose tolerance tests in glucose-loaded mice following 120 minutes of glucose loading.**

| Treatment | Dose (mg/kg body weight) | Blood glucose level (mmol/l) | % lowering/increase of blood glucose level |
|---|---|---|---|
| Control | 10 ml | 5.58 ± 0.19 | - |
| Glibenclamide | 10 mg | 3.30 ± 0.09 | 40.9*(-) |
| (MEAH) | 50 mg | 5.58 ± 0.11 | No effect |
| (MEAH) | 100 mg | 5.78 ± 0.06 | 3.6(+) |
| (MEAH) | 200 mg | 6.06 ± 0.05 | 8.6(+) |
| (MEAH) | 400 mg | 6.24 ± 0.10 | 11.8(+) |

All administrations were made orally. Values represented as mean ± SEM, (n=5); $^{*}P < 0.05$; significant compared to hyperglycemic control animals. (+) indicates increase, (-) indicates decrease.

## DISCUSSION

Contrary to expectations, the seeds of *Artocarpus heterophyllus* caused an increase in blood glucose levels in oral glucose tolerance tests. To our knowledge, this has been previously unreported. The mechanism(s) for this increase was not elucidated in the present study and awaits further laboratory experiments.

## CONCLUSION

The results suggest that seeds of *Artocarpus heterophyllus* should be consumed with caution by diabetic patients.

**Conflicts of interest**

The author(s) declare that they have no competing interests.

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