# Blood sugar lowering effect of Momordica charantia L. fruit (Kyethingha thee) in rabbit model

*Aye-Than, Win-Myint, Tin-Myint, Mu-Mu-Sein-Myint, & Mya-Bwin*

Pharmacology Research Division,
Department of Medical Research

In Myanmar, diabetes mellitus can be counted as a single health problem occuring at all ages as reported by various workers. Momordica charantia L. fruit (Kyethingha thee) has been reported to possess anti-diabetic activity in experimental animal model by various workers. The plant is widely distributed and also cultivated in Myanmar for its edible fruits. Therefore, it was thought that, if it will be worthwhile to investigate and confirm experimentally, whether the fruit grown in Myanmar possess similar hypoglycemic activity. Blood glucose levels of adrenaline-induced diabetic rabbits were determined after oral administration of expressed fruit juice (10 ml/kg) which was approximately equivalent to 400 mg/kg of the substance significantly inhibited the hyperglycemic blood glucose level on adrenaline-diabetic rabbits at 2 hr.

## INTRODUCTION

In Myanmar, diabetes mellitus can be counted as a single health problem occuring at all ages as reported by various workers. Many of the plants had been claimed in relieving diabetes mellitus, and even attaining radical cure. Mya Bwin and Sein Gwan [1] and Oliver [2] mentioned a large number of herbal drugs which are reputed for the treatment of diabetes mellitus. Farnsworth [3] stated that "One of the prerequisite for the success of primary health care is the availability and use of suitable drugs. Plants have always been a common source of medicaments either in the form of traditional medicine formulations or as pure active principles".

Myanmar is rich in plants many of which are of medicinal values. But, so far, there has not been full and systematic exploitation of these natural resources with regard to hypoglycaemic effect, So, it is rational to screen the plant extracts preliminarily on laboratory test models. As Momordica charantia Linn. fruit (Kyethingha thee) has been reported to possess anti-diabetic activity in experimental animal model by various workers, it was thought that, if it will be worthwhile to investigate and confirm experimentally, whether the fruit grown in Myanmar possess similar hypoglycaemic activity.

Kyethingha, commonly known as "Bitter gourd" is a climbing or spreading shrub, with alternately arranged, five to seven deeply divided rounded sinuses with sharp-pointed notched lobed, roundish, cordate base leaves, and bright orange ovoid fruit bearing numerous triangular tubercules. Its flowering and fruiting period is during the rainy months. It is widely distributed and cultivated in Myanmar Naingngan for its edible fruits.

## MATERIALS AND METHODS

### *(a) Preparation of the fruit juice and watery extract*

The fruits used for the experiment were purchased from the markets of Yangon area. The fresh fruits were weighed, sliced into small pieces and homogenized in a homogenizer (Polytron Homogenizer, Kinematica, Switzerland). The homogenized material was squeezed through cheese cloth to remove fabric materials. The expressed fruit juice was partitioned into solid and liquid layers by means of centrifuge (IEC International Centrifuge, International Equipment Company, U.S.A.). Thus the turbid supernatant was decanted and pooled in a 500 ml conical flask.

Crude watery extracts were prepared by refluxing 50 g of air-dried fruit powder in a round bottomed flask on a boiling water bath using 500 ml of distilled water for about 6 hrs. It was filtered using cheese cloth and the filtrate was evaporated to dryness on a boiling water bath. The aqueous extract obtained was dissolved in 1% methyl cellulose before administration to respective animals.

### *(b) Qualitative test for the fresh fruit juice and the watery extract*

Qualitative identification tests of the chemical constituents present in the tested samples were conducted according to the standard procedure as stated in Trease and Evans [4] and Pharmacopaeia [5].

### *(c) Inhibitory effect of fruit juice and water soluble substance on adrenaline-induced hyperglycaemia in rabbits*

Adult healthy rabbits of JB strain weighing 2.6 ± 0.20 kg were used in these experiments. The rabbits were made diabetic by injecting them subcutaneously with 0.1 mg/kg of adrenaline tartrate injection using the method of Gupta, Verma, Garg and Mahesh Rai [6]. This study was conducted on rabbits which had been divided into 4 groups of 3 rabbits each. Group I (Control) was given 1% methyl cellulose as the placebo; Group II, the expressed fruit juice (10 ml/kg at 0h and 1h); Group III, the standard drug, glibenclamide (8 mg/kg) and Group IV, the aqueous extract (3 g/kg) respectively. Fasting blood samples were collected at 0h after which adrenaline tartrate was immediately administered subcutaneously to all the rabbits following the oral administration. The serial blood samples were again collected at 1h, 2h and 4h respectively for estimation of blood sugar levels which were determined by the 0-toluidine method [7]. Cross over tests were done after a week's interval so that all the rabbits remained as control at one time and they had treatment with other test drugs at another time.

### *(d) Test for fresh fruit juice on oral glucose tolerance test (OGTT) in rabbits*

The glucose tolerance test on rabbit was performed as the above stated method. The only difference was the first 3 rabbits was given glucose (3 g/kg) only and the second group was given glucose (3 g/kg) dissolved in expressed fruit juice (10 ml/kg) according to the method stated by Mukherjee, Ghosh and Datta [8]. For a time course of peak interaction, 1h, 2h and 4h later, blood samples were taken from each individual animal and the blood sugar levels were estimated. Cross over tests were done as the previous test.

## RESULTS

### *(a) Qualitative test for the fruit juice and watery extract*

It was found that (100 g) of fruit produced (40-50) ml of liquid juice, after centrifuging and soluble solid in this juice was approximately 4 g/100 ml. The yield of water soluble extracts from dried powder of fruit was 28 g/100 g. The results from the qualitative identification tests on the fresh fruit juice and water soluble extracts were shown in Table 1.

**Table 1.** Qualitative tests of fruit juice and water soluble extracts of Momordica charantia L. (Kyethingha thee)

| Samples | Alkaloids | Flavonoids | Amino acid | Tanninoids | Steroids | Triterpene | Saponins | Reducing sugar | Glycoside | Chloride | Sulphate | Nitrate | Phosphate |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Fruit juice | + | - | + | - | - | + | - | + | - | + | - | + | - |
| Water soluble extract | - | - | + | - | - | + | - | + | + | - | - | + | - |

### *(b) Effect of fruit juice, watery extract and glibenclamide on glucose levels in diabetic rabbits*

The mean blood glucose of control and treated animals after oral administration of fruit juice, watery extract and glibenclamide at various time intervals were shown in Fig. 1. These figures showed that the injection of adrenaline significantly induced hyperglycaemia ($p<0.005$) in the rabbits reaching its maximum in 1-2 h. Administration of 10 ml/kg of fruit juice produced a significant inhibition ($p<0.05$) in blood glucose at 2h period when compared with that of the control group. But rabbits treated with 3.0 g/kg of dry fruit watery extract which was equivalent to 12 g/kg dry fruit powder did not show blood sugar levels inhibition throughout the 4h period. The standard test-agent glibenclamide significantly inhibited the blood glucose level when comparison was made between the test and control group at 2h ($p<0.05$) and at 4 h ($p<0.025$).

### *(c) Effect of fresh fruit juice on glucose levels in glucose loaded rabbits*

The mean blood glucose control and treated animals after oral administration of fruit juice at various time intervals were shown in Fig. 2. These figures showed that the administration of glucose significantly induced hyperglycaemia ($p<0.005$) reaching its maximum at 2 h. In the case of animal which received fruit juice along with the sugar, no such rise in blood sugar level at 2 h and 4 h respectively. There was a significant inhibition of hyperglycaemia at 2 h ($p<0.05$) and at 4 h ($p<0.025$).

## DISCUSSION

A preliminary dose finding study of the fresh fruit juice on the adrenaline-induced model indicated that a dose of 10 ml/kg (400 mg/kg)

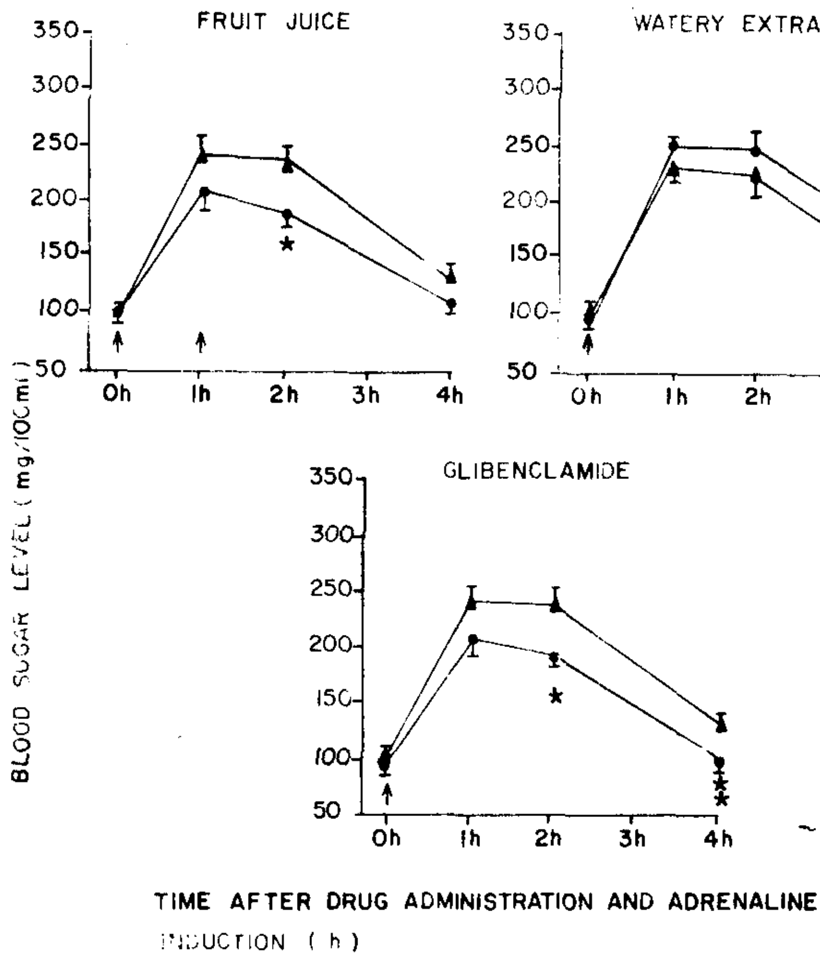


Fig. 1. Time course of the effects of M. charantia fruit juice, its watery extract and *glibenclamide on adrenaline-induced* hyperglycaemia rabbit model.

Each point represents the mean of observations and veritcal bars indicate standard errors of the means. The groups tested were; ▾——▾ , placebo and ●——● , the test agents respectively. ↑ arrow shows the point for oral administration of drug.

* denotes p<0.05

** denotes p<0.025

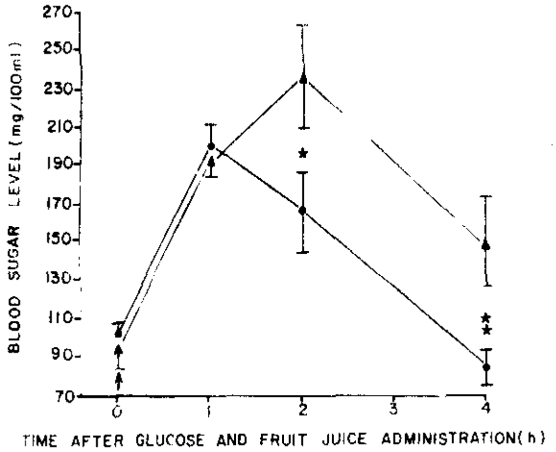


**Fig. 2. Time course of the effect of M. charantia fruit juice on glucose loaded hyperglycaemia rabbit model**

**Each point represents the mean of observations and vertical bars indicate standard errors of the means. The groups tested were; ▼—▼, placebo and o—o , the test fruit juice respectively. ↑ arrow shows the point for oral administration of glucose and fruit juice.**

*** denotes $p<0.05$**

**⁑ denotes $p<0.025$**

which was the maximum practical amount that could be administered to a rabbit model, showed a decreasing trend in blood glucose level. But the effect was not statistically significant. A double dose of the above dose which was 20 ml/kg (800 mg/kg) was then tried out, but since the bulk of the juice was more than that which the animal could tolerate, the dose was administered in two divided doses at 1 hour interval (i.e. 10 ml/kg or 400 mg/kg at a time). In this investigation, the juice caused a significant inhibition ($p<0.05$) of the hyperglycaemic response to the induction of adrenaline. Similarly, glibenclamide (8 mg/kg) caused a significant inhibition ($p<0.025$) of the hyperglycaemic response. With the fruit juice, the peak of action was found to be at 2 h. But the aqueous extract (3 g/kg) did not produce inhibition of the hyperglycaemic response to the induction of adrenaline. There was also a significant inhibition of the fresh fruit juice in blood sugar level at 2 h and 4 h in Oral Glucose Tolerance Test (OGTT).

So it can be concluded that fresh fruit juice possesses an active principle with definite decrease of blood sugar level. Presence of alkaloid like material was also detected in fresh juice of Kyethingha thee. Karunanayake et al. [9] stated the effect of Kyethingha thee juice on streptozotocin-induced diabetes in rats. Chatterjee [10] stated that the fruit contains antidiabetic principle and the centrifuged juice was more active than the alcoholic extract. Diaz [11] reported that powdered drug of the plant contains alkaloid.

Singh et al. [12] also reported the effect of long term feeding of acetone extract of whole fruit powder on alloxan diabetic albino rats. Rivera [13] and Welihinda et al. [14] mentioned that there is some hypoglycaemic action on the sugar tolerance of normal rabbits.

Lotlikar and Rao [15] stated the beneficial clinical results reported from using daily 50-60 ml of the juice of fresh fruits. Akhtar [16] reported the trial of powder in patients with maturity onset diabetes. Day et al. [17] also stated the presence of at least two types of orally active hypoglycaemic principles in Kyethingha thee a more rapidly effective water soluble component, and a more slowly acting component possibly an alkaloid. Akhtar et al. [16] hypothesized that the Kyethingha thee containe more than one type of hypoglycaemic components which may include an alkaloid and an orally active insulin-like compounds. According to our chemical investigation, the significant difference between the juice and watery extract is the presence of alkaloid in the juice. Therefore, further chemical investigation needs to be pursued regarding the active principle.

Hyperglycaemia due to adrenaline was known to be effected partly through release of adreno-corticoids as stated by Gupta et al. [18] and partly through stimulation of the adreno-hypoglyceal axis as stated by Voght [19]. Thus, the action of the fruit juice may probably be effective through either direct glycogenolysis or indirectly through action on the adrenocortico-hypoglyceal axis by inhibiting the gluconeogenesis. Further comprehensive chemical and pharmacological investigations are needed to elucidate the exact mechanism of hypoglycaemic effect of Kyethingha thee.


## ACKNOWLEDGEMENTS

The authors are grateful to Director U Hla Pe for his valuable comments and criticisms.


## REFERENCES


1. Mya-Bwin & Sein-Gwan. Burmese Indigenous Medicinal Plants. Plants with reputed hypoglycaemic action. Burma Medical Research Institute, Rangoon, Burma, 1967.
2. Oliver, B. Plants with oral hypoglycaemic action. Quarterly Journal of Crude Drug Research 1979; 17: 139-196.
3. Fransworth, N.R. Medicinal Plants in Therapy. Bulletin of World Health Organization 1985; 63: 965-981.
4. Trease, G.E. & Evans, W.C. A Text Book of Pharmacognosy, 11th Edn., Bailliers, Tindall & Cassed, London, 1978.
5. The United States Pharmacopoeia. Prepared by the Committee of Revision and published by the Board of Trustees, 20th revision, Mark Publishing Company, Easton, Pa, U.S.A., 1980.
6. Gupta, S.S., Verma, S.C.L., Garg, V.P. & Mahesh Rai. Anti-diabetic effects of Tinospora cardifolia. Indian Journal of Medical Research, 1967; 55: 733-745.
7. Manual of basic techniques for a health laboratory. World Health Organization, Geneva, 1980; 429-431.
8. Mukherjee, K., Ghosh, N.C. & Datta, T. Coccinia indica Linn. as potential hypoglycaemic agent. Indian Journal of Experimental Biology, 1972; 10: 347-349.
9. Karunanayake, E.H., Jeevathayaparan, S. & Tennekoon, K.H. Effect of Momordica charantia fruit juice on streptozotocin-induced diabetws in rate. Journal of Ethnopharmacology 1990; 30: 199-204.
10. Chatterjee, K.P. On the presence of an anti-diabetic principle in Momordica charantia L. Indian Journal of Physiology and Pharmacology 1963; 7: 240-244.
11. Diaz, L.T. Preliminary study of an alkaloid like material obtained from cunderamor or M. charantia L. Puerto Rico Journal of Public Health and Tropical Medicine 11, 812-816. In: Chemical Abstract 1936; 30: 6133.
12. Singh, N., Tyagi, S.D. & Agarwal, S.C. Effects of long term feeding of acetone extract of Momordica charantia (whole fruit powder) on alloxan diabetic albino rats. Indian Journal of Physiology and Pharmacology 1989; 33: 97-100.
13. Rivera, G. Preliminary chemical and pharmacological studie on "Cundeamor" or M. charantia L. II. American Journal of Pharmacology 114, 72-87. In: Chemical Abstract 1942; 36: 3874.
14. Welihinda, J., Karunanayake, E.H., Sheriff, M.H. & Jayasinghe, K.S. Effect of Momordica charantia on the glucose tolerance in maturity onset diabetes. Journal of Ethnopharmacology 1986; 17: 277-282.
15. Lotlikar, M.N. & Rajarama Rao, M.R. Pharmacology of a hypoglycaemic principle isolated from the fruits of

*Momordica charantia* L. *Indian Journal of Pharmacology* 28: 129-133. In: *International Pharmaceutical Abstracts* 1966; 3: 1.8, 1293.

16. Akhtar, M.S., Athar, M.A. & Yaqub, M. Effect of *Momordica charantia* on blood glucose level of normal and alloxan-diabetic rabbits. *Planta Medica* 1981: 42: 205-212.
17. Day, C., Cartwright, T., Provost, J. & Bailey, C.J. Hypoglycaemic of *Momordica charantia* extracts. *Planta Medica* 1990; 56: 1331-1341.
18. Gupta, S.S., Seth, C.B. & Variyar, M.C. Experimental studies on pituitary diabetes I. Inhibitory effect of a Ayurvedic antidiabetic remedies on anterior pituitary extract-induced hyperglycaemia in albino rats. *Indian Journal of Medical Research* 1962; 50: 73-81.
19. Voght, M. Observation on some conditions effecting rats of hormonal output by adrenal cortex. *Journal of Physiology* 1944; 103: 317-332.

*Accepted for publication 26 Aug 1993*