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Investigation of Comparative Hypoglycemic Effect of Neem (*Azadirachta indica*), Karala (*Momordica charantea*) and Nayantara (*Cathranthus roseus*) with Glibenclamide on Rat

M.W. Rahman, M. Mostofa, S.A. Sardar, M.R. Sultana, M.M. Haque and M.E. Choudhury
Department of Pharmacology, Bangladesh Agricultural University, Mymensingh, Bangladesh

Abstract: The experiment was conducted to compare the hypoglycemic efficacy of Neem, Karala and Nayantara with that of Glibenclamide on normal rat. In addition to that the experiment was conducted to compare the effects on body weight of rat after administration of those drugs. After 14 days during treatment with those drugs following observation were made (1) Neem when administered orally @ 500 mg kg^{-1} b.wt. significantly ($p>0.01$) decreased blood glucose level (7.52 to 3.98 mol L^{-1}) and body weight also significantly ($p<0.01$) increased (153.20 to 155.80 mg kg^{-1}) (2) Karala when administered orally @ 200 mg kg^{-1} b.wt. significantly ($p>0.01$) decreased blood glucose level (8.96 to 4.82 mol L^{-1}) and body also significantly ($p<0.01$) increased (169.20 to 177.20 mg kg^{-1}) (3) Nayantara when administered orally @ 500 mg kg^{-1} b.wt. significantly ($p>0.01$) decreased blood glucose level (6.80 to 4.44 mol L^{-1}) and body also significantly ($p<0.01$) increased (120.40 to 140.40 mg kg^{-1}) and Glibenclamide when administered orally @ 0.25 mg kg^{-1} b.wt. significantly ($p>0.01$) decreased blood glucose level (7.20 to 6.61 mol L^{-1}) and body also significantly ($p<0.01$) increased (164.00 to 171.40 mg kg^{-1}). From this experiment it is concluded that Neem (*Azadirachta indica*), Karala (*Momordica charantia*) and Nayantara (*Cathranthus roseus*) is potent hypoglycemic agent as Glibenclamide.

Key words: Hypoglycemic, neem, Karala, Nayantara, Glibenclamide, rat

INTRODUCTION

Diabetes mellitus, a malfunction of metabolism of the pancreas and possibly of immune system[1] important debilitating disease at present, leading cause of death in human and animals. Diabetes mellitus is regarded as a syndrome a collection of disorders that have hyperglycemia as hallmark[2]. Diet control, insulin therapy and oral hypoglycemic drug could be the means of treatment of diabetes mellitus but long time insulin therapy may cause resistant, similarly oral hypoglycemic agents may not prevent all the complications of diabetes. Herbal medicine may plays an important role in this aspect in poor because of availability and cheapness.

Herbal medicine has been known to man for centuries. Therapeutic efficacy of many indigenous plants has been described by practitioners of traditional medicine. Antidiabetic medicinal plants were used to treat diabetes before the early 1920s (Roberts). Shipro and Gong[3] listed a number of plants to control the blood glucose level such as Neem (*Azadirachata indica*), Karala (*Mamordica charantea*) which are indigenous plant of Indian subcontinent. Here the hypoglycemic effect of Neem Leaves Extract (NLE), Karala fruit juice and Nayantara leaf extract was evaluated in Animal Models and finally it was compared with Glibenclamide[3]. The present study was planned to reach the aim of finding out a cheapest and effective herbal antidiabetic drug especially for the poor as a substitution of insulin therapy and hypoglycemic drugs.

MATERIALS AND METHODS

The experiment was preformed in the department of Pharmacology, Bangladesh Agricultural University, Mymensingh. The experiment was conducted to evaluate the comparative efficacy of Neem Leaf Extract (NLE), Karala Fruit Juice (KFJ) and Nayantara Leaf Extract (NtLE) with the patent drug Dibenol® (Glibenclamide) on rats. The following procedures were adopted for conducting the experiment:

The animal laboratory house of the Department of Pharmacology was selected for the research. The research was carried out during the period of October to November 2003. Twenty-five apparently healthy adult rats (Mixed albino male rats, long Evan's strain) were collected from the International Centre for Diarrhoeal Diseases Research Bangladesh (ICDDRB), Mohakhali, Dhaka. Prior to the

Corresponding Author: Dr. M. Mostofa, Department of Pharmacology, Bangladesh Agricultural University, Mymensingh, Bangladesh E-mail: mostofa57@yahoo.com

commencement of the experiment all the rats were acclimatized to the new environmental condition for a period of one week. During the experimental period the rats were kept in a well-ventilated animal house at a room temperature of 25°C and were supplied with standard ration collected from ICDDRB, Mohakhali, Dhaka and fresh drinking water *ad libitium*. Twenty-five rats of 60 of 70 days old were used in the experiment. The rats were randomly divided into five groups, each group containing five rats. These groups were designated as Group A: Control (normal rat without any treatment), Group B: Normal rats treated with Dibenol® (Glibenclamide) @ 0.25 mg kg^{-1} b.wt., Group C: Normal rats treated with Neem Leaf Extract (NLE) @ 500 mg kg^{-1} b.wt., Group D: Normal rats treated with Karala Fruit Juice (KFJ) @ 200 mg kg^{-1} b.wt. and Group E: Normal rats treated with Nayantara Leaf Extract (NtLE) @ 500 mg kg^{-1} b.wt. Then rats were placed in separate in separate cages according to group. Each cages was labeled of different groups. Food and water were provided *ad labium* during the whole experimental period. Then Dibenol® (Glibenclamide) manufactured by Scquare Pharmaceutical Ltd, Bangladesh, was collected from the local market. Dibenol® was preserved at room temperature and was used during 14 days treatment period @ 0.25 mg kg^{-1} b.wt. day^{-1}. Fresh Neem leaves was collected from medicinal plants garden of department of Pharmacology, Faculty of veterinary science, Bangladesh Agricultural University, which are taxonomically identified by Botanist Mr. Moniruzzam. The leaves were measured by electronic balance. Then it was grinding with morter and pastle. Finally the leaves extract was mixed with 10 mL distilled water and stirred for homogenous mixture and then filtered with silk cloth. It was then kept in refrigeretor (4°C). Karala was collected from the local market and taxonomically identified by the above botanist @200 mg kg^{-1} b.wt. day^{-1} Karala were measured by electronic balance and then grind with morter and pastle. This mixture was mixed with 5 mL distilled water and then filtered with silk cloth. The prepared juice was collected and preserved in a reagent bottle and kept in refrigerator for further use. This Karala juice were prepared for every alternate days during the whole experimental period then fresh Nayantara leaves were collected from medicinal plants garden of department of Pharmacology, Faculty of veterinary science, Bangladesh Agricultural University which were taxonomically identified by above botanist. The leaves were measured by electronic balance. Then it was grinding with morter and pastle. Finally the leaves extract was mixed with 10 mL distilled water and stirred for homogenous mixture and then filtered with silk cloth. It was then kept in refrigeretor (4°C).

All the parameters i.e. blood glucose and body weight were estimated and recorded before and after administration of different herbal preparation and patent drug.

After administration of patent drug Dibenol® (Glibenclamide) and herbal preparation of NLE, KFJ and NtLE for consecutive 14 days all the rats of treated and control group were closely observed during the whole treatment period and following parameters were studied:

Determination of blood glucose: Blood glucose of all rats of treated (4 Groups) and control groups were carried out before treatment i.e first day 0 and 7th and 14th days of post treatment by Glucotrend Kit machine.

Determination of body weight: Body weight of all rats of treated (4 Groups) and control groups were carried out before treatment i.e first day 0 and 7th and 14th days of post treatment by help of electronic balance.

RESULTS AND DISCUSSION

The experiment was carried out for the study of comparative efficacy of herbal drug preparation i.e. Neem Leaf Extract (NLE), Karala Fruit Juice (KFJ) and Nayantara Leaf Extract (NtLE) with a patent drug Dibenol® (Glibenclamide) as blood glucose lowering agent in rats. Attempts were also made to investigate the effects of those herbal preparation and patent drug on body weights in rats.

To perform the experiment 25 Rats (Mixed albino male rats, long Evan's strain) were randomly divide into 5 equal groups. Group A was kept as control without giving any treatment. Group B, C and D were treated with Dibenol® (Glibenclamide), Neem leaf extract, Karala Fruit Juice (KFJ) and Nayantara Leaf Extract (NtLE), respectively. All the control and treated were closely observed during 14 days of treatment period and above-mentioned parameters were estimated as per schedule.

Effect of blood glucose level: Blood glucose level was significantly ($p<0.01$) decreased following administration of Glibenclamide in Group B at the level of 44.77% on 1st day, 35.50% on 7th day and 44.31% on 14th day, in Group C which treated neem leaf extract, blood glucose level was 26.86, 41.76 and 47.07% on 1st day, 7th day and 14th day and in Group D which treated with Karala Fruit Juice (KFJ) blood glucose level 30.58, 41.96 and 46.20% on 1st day, 7th day and 14th day, respectively and in Group E which treated with Nayantara Leaf Extract (NtLE) blood glucose level was 11.17, 20.06 and 34.70% on 1st day, 7th day and 14th day, respectively.

Table 1: Effects of Glibenclamide, Neem leaf extract, Karala fruit juice and Nayantara leaf extract on blood glucose (mg dL^{-1}) in rat (n=5)

		Pretreatment of blood glucose (mg d L^{-1})	During treatment of blood glucose (mg dL^{-1})		
Groups	Treatment with dose	Day 0	1st Day	7th Day	14th Day
A	Normal rats (Control)	7.20±1.10	6.82±1.01	6.38±0.81	6.61±1.02
B	Glibenclamide @0.25 mg kg^{-1} b.wt.	8.62±0.24	4.76±0.06**	5.56±0.35 **	4.80±0.21**
C	Neem leaf extract @ 500 mg kg^{-1} b.wt.	7.52±0.73	5.50±0.23**	4.34±0.1 6**	3.98±0.13**
D	Karala fmit juice @ 200 mg kg^{-1} b.wt.	8.96±0.22	6.22±0.35**	5.20±0.29**	4.82±0.24**
E	Nayantara leaf extract @ 500 mg kg^{-1} b.wt.	6.80±0.55	6.04±0.63**	5.30±4.02**	4.44±0.39**

Value express are mean±SD of 5 rats, ** = Significant at 1% level (p>0.01)

Table 2: Effects of Glibenclamide, Neem leaf extract, Karala fruit juice and Nayantara leaf extract on body weight (mg) in rat (n=5)

		Pretreatment of body weight (mg)	During treatment of body weight (mg)	
Groups	Treatment with dose	Day 0	7th Day	14th Day
A	Normal rats (Control)	105.80±39.92	113.60±30.03 (+7.37%)	119.20±28.62 (+12.66%)
B	Glibenclamide @0.25 mg kg^{-1} b.wt.	164.00±35.84	168.20±34.54 (+2.56%)	171.40±34.80 (+4.51%)
C	Neem leaf extract @ 500 mg kg^{-1} b.wt.	153.20±41.22	151.60±38.02 (-1.04%)	155.80±38.40 (+3.25%)
D	Karala fmit juice @ 200 mg kg^{-1} b.wt.	169.20±70.27	180.20±76.83 (+6.5%)	177.20±66.12 (+4.73%)
E	Nayantara leaf extract @ 500 mg kg^{-1} b.wt.	120.40±47.83	133.60±40.64 (10.96%)	140.40±37.69 (+16.61%)

+ = increase - = decrease

Among the herbal preparation Neem Leaf Extract (NLE) produced maximum efficacy (47.07%) followed by Karala fruit juice (46.20%) and Nayantara Leaf Extract (34.07%) on 14th day (post treatment). However, there was not significant change on blood glucose level in Group A (control) where mean values of blood glucose was 5.27, 11.38 and 8.33% on 1st day, 7th day and 14th day, respectively indicating negligible change in the parameter (Table 1).

Four hours after treatment the blood glucose level was markly decreased in all treated Groups (B, C, D and E) of rats except the Group A. After 14 days of treatment with Glibenclamide, neem Leaf Extract (NLE), Karala Fruit Juice (KFJ) and nayantara Leaf Extract (NtLE) also decreased which relevance with Ahmed[4]. There were significant ($p<0.01$) reduction of the blood glucose level. The exact mechanism in reducing blood glucose level is not well understood. The mechanism of reducing blood glucose might be due to increased uptake of glucose peripherally and increased sensitivity of insulin receptor in case of NLE. In accordance to the present findings few researchers also reported reduction of blood glucose following administration of insulin and neem extract[5-7]. On the other hand Chattopadhyay *et al.*[8] reported that *Azadirachta indica* alcoholic Leaf Extract significantly lowered the blood sugar level in glucose-fed and adrenaline induced hyperglycemic rats[8]. In case of Karala Fruit Juice (KFJ) the anti -hyperglycemic effect might be derived in part from a decrease in insulin resistance because of increase of GLUT 4 (Glucose transporter isoform 4) protein content in the plasma membrane of the muscle[9]. The active constituents of *Momordica charantea* those might be responsible for anti-hyperglycemic activity is not known clearly. Bitter melon extracts might enhance the secretion of insulin from pancreas. Anunciado and Masangkay[10], Chakravarthy *et al.*[11], Ahmed *et al.*[12], found that the juice of bitter melon fruit might actually help to renew or recover partially dastroyed insulin secreting cells in the pancreas. In dichloromethane-methanol extract of leaves and twigs of nayantara (*Catharanthus roseus*) @ 500 mg kg^{-1} b. wt. day^{-1} given orally for 7 and 15 days showed 48.6 and 57.6% hypoglycemic activity, respectively[13].

Effects on body weights: There was a significant ($p<0.01$) effect of body weight in treated Group B at 2.56 and 4.51% increased on 7th day and 14th day, respectively; in Group C 1.04% decreased and 1.69% increased on 7th day and 14th day in treated Group D 605 and 4.73% increased and in Group E 10.96 and 16.61% increased On 7th day and 14th day, respectively (Table 2). Whereas, in Group A (control) the body weight increase at the level of 7.37 and 12.66% on the 7th day and 14th day, respectively. On the other hand in Group A (control) there was increased in body weight by 7.73 and 12.66% on 7th day and 14th day, respectively which made a support that herbal treatment has significant ($p<0.01$) effect on body weight. Among the herbal treatment Neem Leaf Extracrt (NLE) has maximum effect on body weight at 1.04% decreased on 7th day and 1.69% increased on 14th day and Nayantara Leaf Extract (NtLE) has maxium effect on body weight at 10.96 and 16.61% increased on 7th day and 14th day, respectively in comparison to control Group A at 7.37 and 12.66% on 7th day and 14th day, respectively (Table 2).

During treatment on both 7th day and 14th day with Glibenclamide, NLE, KFJ and NtLE body weight of all the treated groups were increased accept in treated Group C on 7th day in comparison with pre-treatment period,

Among the herbal drugs used in the study NtLE was more effective (16.61%) m comparison with other herbal preparations i.e. NLE (4.51%) and KFJ (4.75%) on 14th day (post-treatment). Results of the present study supports partially the findings of Ponnachan *et al.*[14], Bopanna *et al.*[5] and Srivastava *et al.* .[8] Who also observed significant increase in body weight after treatment with herbal preparations in hyperglycemic animals[14].

REFERENCES

1. Adams, H.R., 1995. Veterinary Pharmacology and Therapeutics. 7th Edn., Iowa State University Press, Ames, USA., pp: 644-652.
2. Zimmet, P., 1997. Diabetes-definition and classification. Med. Intl., 11: 1-9.
3. Shapiro, K. and W.C. Gong, 2002. Natural products used for diabetes. J. Am. Pharmacol., 42: 218-224.
4. Ahmed, S., 2003. Comparative efficacy of neem and Karala with insulin and Glibenclamide on hematoblochemical parameters in rabbit. MS Thesis, Bangladesh Agricultural University, Mymensingh.
5. Bopanna, K.N., J. Kannan, S. Gadgil, R. Balaraman and S.P. Rathod, 1997. Anti-diabetic and anti-hyperlipaemic effects of neem seed kerne powder on alloxan diabetic rabbits. Indian J. Pharmachol., 29: 162-167.
6. Bajaj, S. and B.P. Srinivasan, 1998. Investigations into the anti-diabetic activity of *Azzadirachta indica*. Indian J. Pharmachol., 31: 138141.
7. Kosla, P., S. Bhanwra, J. Singh, S. Seth and R.K. Srivasta, 2000. A study of hypoglycemic effects of *Azadirachta indica* (neem) in normal and allxan diabetic rabbits. Indian J. Physiol. Pharmacol., 44: 69-74.
8. Chattopadhyay, R.R., 1993. A comparative evaluation of some blood sugar lowering agents of plant origin. J. Ethnopharniacol., 67: 367-372.
9. Mirua, T.C.I., N. Iwamoto, M. Kato, M. Kawai and I. Suzuki, 2001. Hypoglycemic activity nof the fruit of the *Momordica charantea* type II diabetic mice. J. Nutr. Sci. Vitaminol (Tokyo), 47: 340-344.
10. Anunciado, R.V.P. and J.S. Masangkay, 2002. Effects of bitter gourd (*Momordica charantea*) administration on alloxan is induced diabetic mice. Philippine. J. Vet. Medicine, 39: 15-20.
11. Chakravarthy, B., K.S. Gupa and K.A. Gode, 1982. Functional beta cell regeneration in the islets of pancreas in alloxan induced diabetic rats by epicatechin. Life Sci., 51: 2693-2697.
12. Ahmed, L., E. Adeghate, A.K. Sharma, D.J. Pallot and J. Singh, 1998. Efffects of *Momordica charantea* fruit juice on islet morphology in the pancreas of the streptozotocm-diabetic rat. Diabetes Res. Clin. Pract., 40: 145-151.
13. Singh, S.N., V. Praveen, S. Shoba, S. Radhey, M.M.L. Kumria, S. Ranganathan, K. Sridharan, P. Vat, S. Suri and R. Shyam, 2001. Effect of an antidiabetic extract of *Catharanthus rosus* in enzymetic activities in streptozotocin induced diabetic rats J. Ethnopharmacol., 76: 269-277.
14. Ponnachan, P.T.C., C.S. Paulose and K.R. Panikkar, 1993. Effects of Leaf extract of Aegle marmelose in diabetic rats. Indian J. Exp. Biol., 31: 345-347.
15. Srivastava, Y., B.H. Venkatakrishna, Y. Varma, K. Venkaiah and B.H. Raval, 1993. Antidiabetic and Adaptogenic properties of *Mamodica charantea* extract: An experimental and clinical evaluation. Phytother. Res., 7: 285-289.