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Comparative efficacy of Telakucha (*Coccinia indica*) leaves and Amaryl(R) Tablet (Glimepiride) in induced diabetes mellitus in rat

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Abstract

Thirty healthy rats of both sexes weighing between 150 to 200 gm were selected from among the offspring and randomly divided into six equal groups and rats of Group A and Group B were kept as non hypoglycemic control and hypoglycemic control, respectively. After acclimatization hyperglycemia was induced in five groups of rats (B,C,D,E and F) by administering streptozotocin (STZ) intraperitoneally at a dose of 55 mg/kg body weight. After fifteen days of STZ injection, four groups of rats (C,D,E and F) were administered with Telakucha (*Coccinia indica*) and Amaryl(R) (Glimepiride) as per schedule dose and all the control and treated rats were closely observed during 14 days of treatment.The oral administration over 14 days of Telakucha (*Coccinia indica*) leaves extract significantly lowered blood glucose level but was not so potent as patent drug Amaryl(R) (Glimepiride). The herbal preparation also increased body weight but not to the extent caused by the patent drug Amaryl(R) . The Telakucha leaves at 750mg/kg body weight significantly reduced (30.73%) the blood glucose level from 31.24±0.36 mmol/L to 21.64±0.17 mmol/L and significantly increased (5.45%) the body weight from 181.96±21.10g to 191.87±12.42 g.

Keywords: Glimepiride, streptozotocin, Telakucha and Diabetes

Introduction

Bangladesh is one of the poorest countries in the world and has lowest health care spending per capita. Statistical data in Bangladesh showed the gradual increase in the number of diabetic patients. The Diabetic Association of Bangladesh was founded in 1956, only 39 patients were registered, but by the 31st December 1985, the figure was increased to 49,510. 1,12,295 diabetic patients registered in Bangladesh Institute of Research and Rehabilitation in Diabetes Endocrine and Metabolic Disorder (BIRDEM) 28th August, 1992, (BIRDEM, 1992). According to an estimate, 336 million of the world's population will be diabetic by 2030 as against 171 million in 2000. While most of the 40 countries studied will have their diabetic population more than twice, the diabetic population in Bangladesh will be increased to 3.6 times during the period (Manning, 2004). The prevalence of diabetes in Bangladesh is estimated to be 5.2% among the adult population. It is estimated that almost 5 million peoples have diabetes in Bangladesh (Journal of Diabetes, BIRDEM, 1999). In a survey in Bangladesh the prevalence of impaired glucose tolerance (IGT) was found to be 11.8% and 4.8% in rural and urban population, respectively. Bangladesh has an estimated prevalence of 4% in the adult population (Sgapiro and Gong 2002).

Because of the indigenous availability of certain herbs with hypoglycemic effects, treatment of hyperglycemics according to the traditional system of medicine is often easier, cheaper and less costly. Many herbal agents like garlic oil (*Allium sativum*), neem (*Azadirachta* spp), black berry seed extract (*Eugenia jambolana*), onion (A*llium cepa*), buckwheat (*Fagopyrum esculantum*), *Catharanthus roseus*, fenugreek (*Trigonella foenum-graecum*), karela (*Mamordica charatia*), *Mucuna puriens*, *Gynura procumbens,* olive leaf (*Olea europea*) etc are known to have hypoglycemic properties (Zaman *et al.,* 1981 Zhang and Tan, 2000). Traditional medicinal plants are used throughout the world for a range of diabetic presentations. Anti-diabetic drugs available in Bangladesh are imported, expensive and are

not presumably derived of side effects. Telakucha available in the rural areas and also along the road side of urban areas, is known for its hypoglycemic have properties. This work has been undertaken to see the effects of aqueous Telakucha leave extracts on blood glucose level and body weight of rat in comparison with that of Amaryl$^{(R)}$ as a reference standard.

Materials and Materials

The experiment was conducted in the Department of Pharmacology, Bangladesh Agricultural University, Mymensingh from October/2006 to May/2007.

Ten Long Evan's strains (*Ratus norvegicus*), aged 5 weeks and weighing between 100 to 150 gm were collected from International Center of Diarrhoea Disease Research, Bangladesh (ICDDRB). The rats were reared for 30 days and then the males and females were kept together at the ratio of 1:4 for reproductive purpose. After 3 weeks the female gave birth and then the offspring were reared for 2 months. In this experiment, 30 healthy rats of both sexes weighing between 150 to 200 gm were selected from the offspring.

The rats were grouped into six, each containing 5 individuals. Each group of rats was housed in screen bottomed wire cages arranged in rows and kept in the departmental (Pharmacology, BAU) animal house. The rats were fed pellet at a recommended dose of 100gm/kg per day as advised by and purchased from ICDDRB. Drinking water was supplied ad libitum. The rats were maintained in this condition for a period of 21 days to acclimatize prior to their experimental uses.

The rats were fed normal diet and given water ad libitum and then their body weight and blood glucose were recorded after acclimatization. This group of rats served as normal control rats. Body weights and blood glucose level were measured at the same time when that of other groups was measured. This group was served as normal control group.

Body weights and blood glucose level were measured after 18 hours of starvation. Then streptozotocin injection was given at a dose rat of 55 mg/kg in intraperitoneal route to each rat to induce diabetes. The rats were fed normal diet and given water ad libitum from Day 1-15 on 15th day blood glucose level and the body weight were again measured to ensure diabetic condition. Then all the rats of this group were kept for 14 days without any treatment. During that period on Day 0, 7 & 14 the body weight and blood glucose level were measured. This group served as diabetic control group. Following the procedure the aqueous solution of Telakucha leaves were fed at a dose of 250 mg/kg body weight/day for 14 days. During treatment of Telakucha leaves extract, body weight and blood glucose were recorded on Day 0 (Pre-treatment) and Day 7 & 14 (during treatment). This group served to find the effect of aqueous solution of Telakucha leaves extract as antidiabetic drug.

Accordingly, STZ induced group F diabetic rats were administered with Amaryl$^{(R)}$ at the rate of 800 µg/kg body weight/day 14 days. During treatment of Amaryl$^{(R)}$ body weight and blood glucose were recorded on Day 0 (pre-treatment) and day 7 & 14 (during treatment). This group was used to compare the anti-diabetic effect of Amaryl$^{(R)}$ with that of other groups treated with herbal drug. Streptozotocin was dissolved in citrate buffer solution having pH 4.5. This solution was injected intraperitonealy to rats maintained under fasting condition for 18 hours. To induce diabetic condition in rat a dose of 50 mg STZ per kg of body weight was chosen following the recommendation of works done previously. For injection repuisite puantity of STZ for each individual rat was contained in 200 µl of buffer. Fresh Telakucha leaves and Tablets Amaryl$^{(R)}$ were collected locally. Each Amaryl$^{(R)}$ tablet contain 1mg glimepiride. Water extract was made from 1000 gm fresh Telakucha leaves by blending it in

blender machine with 1000 ml distilled water. Then the water extract was lyophilized and the herbal drug was finally collected as powder form by Freeze drying in Central Laboratory, BAU. Oral antidiabetic drug Amaryl$^{(R)}$ (glimepiride) was ground and dissolved in distilled water to make the concentration 800 µg/ml. Telakucha leaves extract and Amaryl$^{(R)}$ were fed orally after solution being made in distilled water to the experimental rats with the help of a micropipette.

The blood samples were collected from the tip of the tail vein of each rat as a drop which was used in an Accu-Check Advantage (strip method) machine to read the glucose concentration.

Statistical analysis

Data was expressed as Mean ± Standard error of Means. Statistical analysis was made by using student's unpaired t-test.

Results and Discussion

From the beginning to end, the blood glucose concentration of normal control rats (Group A, n=5) were 5.43±0.23 to 5.59±0.18 mmol/L. In the diabetic control rats (Group B, n=5) after Streptozotocin administration, the blood glucose concentration were 30.70±0.44 to 32.26±0.52 mmol/L. Due to administration of Telakucha (*Coccinia indica*) leaves extract @ 250 mg/kg 500 mg/kg and 750 mg/kg body weight, the blood glucose concentration was 30.93±0.11, 31.58±0.25 31.24±0.36 and 31.58±0.25 on 0 day (per treatment) mmol/L, on 7th day (post treatment) 29.33±0.43, 27.74±0.49 and 25.68±0.12 on 7th day and 28.95±0.38 26.68±0.30 and 21.64±0.17 mmol/L on 14th day (post treatment)in the Group C,D and E respectively. And also in diabetic rats (Group F,) treated with Amaryl® (Glimepiride) tablet@ 800Mg/kg b.wt. for 14days, the blood glucose concentration was 31.12±0.35 mmol/L, 22.66±0.30 mmol/L and 16.07±0.21 mmol/L. on 0 day (pre treatment) on 7th day (post treatment) and 14th day (post treatment), respectively (Table 1).

Table 1. Effects of Telakucha leaves and Amaryl$^{(R)}$ (Glimepiride) tablet on Blood Glucose (m mol/L, mean±SE) in Normal and STZ treated Diabetic Rat (n=5)

Groups	Drug, dose and route	Pre-treatment Day 0	Post-treatment		% changed in Blood Glucose over 14 days
			Day 7	Day 14	
A	Normal control	5.43±0.23	5.51±0.14 NS	5.59±0.18 NS	+ 2.95
B	Diabetic control	30.70±0.44	31.79±0.71^{b} NS	32.26±0.52^{b} NS	+ 5.08
C	Telakucha leaves extract 250 mg/kg, orally	30.93±0.11	29.33±0.43^{a}*	28.95±0.38^{a} **	- 6.40
D	Telakucha leaves extract 500 mg/kg, orally	31.58±0.25	27.74±0.49^{a}**	26.68±0.30^{a} ***	- 15.51
E	Telakucha leaves extract 750 mg/kg, orally	31.24±0.36	25.68±0.12^{a} ***	21.64±0.17^{a} ***	- 30.73
F	Amaryl$^{(R)}$ (Glimepiride) tablet 800 µg/kg, p.o.	31.12±0.35	22.66±0.30^{a} ***	16.07±0.21^{a} ***	- 48.36

Values given above represent the Mean ± Standard Error (SE) of blood glucose of five animals
Values expressed in parentheses denotes maximum percentage of increase^{b}/ decrease^{a}
SE = Standard Error
*** = Significant increase/decrease. (P=>0.000-0.001)=0.1%
** = Significant increase /decrease. (P=>0.001-0.01)=1%
* = Significant increase/decrease. (P=>0.01-0.05)=5%
NS = Non Significant increase/decrease. (P=>0.5-∞)

The percent increased in body weight gain over 14 days in normal control rats (Group A, n=5) was 0.64 percent. On the contrary, In diabetic control group (Group B, n=5), the percentage of body weight loss was 2.17. In Group C, D and E (n=5) following administration of Telakucha (*Coccinia indica*)leaves extract @ 250, 500 and 750 mg/kg for 14 days the percentage of body weight gain was 1.96%, 3.34%. and 5.45%., respectively. The percentage of body weight was gain 10.95% in Group F (n=5) after treated with Amaryl® (Glimepiride) tablet @ 800µg/kg b.wt. for 14 days. After 14 days of treatment with Telakucha (*Coccinia indica*) and Amaryl® Glimepiride the body weight increased significantly (P<0.01) to the extent of 1.96 to 10.95 percent in comparison with pretreatment period. In this study among the three different dosages of Tilakucha, 750mg/kg b, wt was most effective (5.45%) in comparison with other dosages used. Amaryl® also increased the body weight (Table 2).

Table 2. Effects of Telakucha leaves extract and Amaryl(R) (Glimepiride) tablet on Body Weight gain (%) in normal and STZ treated Diabetic Rat (n=5)

Groups	Drug, dose and route	Pre-treatment Day 0	Post-treatment		% changed in b.wt. over 14 days
			Day 7	Day 14	
A	Normal control	188.63±15.14	189.38 ± 14.87 *	189.83±13.72 *	+ 0.64
B	Diabetic control	172.31±17.09	170.89±18.54***	168.57±14.05***	- 2.17
C	Telakucha leaves extract 250 mg/kg, orally	170.82±19.13	172.57±10.41[b] ***	174.16±23.06[b] ***	+ 1.96
D	Telakucha leaves extract 500 mg/kg, orally	168.73±18.05	172.31±22.11[b] ***	174.37±18.01[b] ***	+ 3.34
E	Telakucha leaves extract 750 mg/kg, orally	181.96±21.10	187.06±13.33[b] **	191.87±12.42[b] ***	+ 5.45
F	Amaryl® (Glimepiride) tablet 800 µg/kg, p.o.	176.18±5.72	185.31±5.99[b] ***	195.48±5.88[b] ***	+ 10.95

Values expressed in parentheses denotes maximum percentage of increase[b]/ decrease[a]
SE = Standard Error
*** = Significant increase/decrease. (P=>0.000-0.001)=0.1%
** = Significant increase /decrease. (P=>0.001-0.01)=1%
* = Significant increase/decrease. (P=>0.01-0.05)=5%
NS = Non Significant increase/decrease.(P=>0.5-∞)

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