

STUDY OF HYPOGLYCEMIC EFFECT OF HERBAL AND HOMEOPATHIC ANTIDIABETIC DRUGS IN NORMAL AND ALLOXAN INDUCED DIABETIC RABBITS

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ABSTRACT:

Commercially available herbal and homeopathic drugs claimed to be used for the treatment of diabetics are evaluated for blood glucose level in normal and alloxan induced diabetic rabbits. The glibenclamide and gliclazide were used as standard drugs. The herbal drugs, dolabi and dawai ajeeb ziabitus, showed the significant ($p < 0.05$) decrease in the blood glucose level in normal rabbits. In alloxan induced diabetic animals the significant decrease was for very short period of time compared with the normal rabbits. The single dose administration of homeopathic drugs, i.e. acid phos, syz jambol and uranium nitricum failed to reduce the blood glucose level both in normal and alloxan induced diabetic rabbits. However, the oral administration of single dose daily of acid phos and syz jambol significantly reduced the blood glucose level on 7th days after 2 h and 4h, respectively, post administration of the drugs.

KEY WORDS: Herbal, homoeopathic, drugs, alloxan induced diabetic rabbits, normal rabbits, Blood glucose level.

INTRODUCTION

Diabetes mellitus is a rising problem all over the world, particularly in developing countries. Diabetes mellitus is characterized by hyperglycemia, glycosuria, polydipsia and ketosis, is caused by relatively or absolutely non-functioning of insulin activity. Many plants have been used for the treatment of the diabetes mellitus. The oral hypoglycemic agents in allopathic treatment are mainly for NIDDM and include sulphonylureas, biguanides and alpha-glucosidase inhibitors.

It is estimated that around 80% of the world's population in the developing world relies on herbal remedies (Khan, 1985). Herbal drugs are considered to be safe due to low amount of active constituent(s) and the presence of several other components that may respond to the side effects of the potent part of the drug. Several plants have been reported to have hypoglycemic activities and are used for treatment of diabetes mellitus (Akhter *et al.*, 1983, Twaij and Al Badr, 1988; Gupta, 1994, Ajsaonkar, 1979; Bailley and Caroline, 1989, Ivorara *et al.*, 1989, Rahman and Zaman, 1989, Karunanayake *et al.*, 1984, Amalraj and Ignacimuthu, 1998, Prince *et al.*, 1998). It has been reported that most of these plants contain glycosides, alkaloids, sulfur oils and flavonoids (Oliver-Bever, 1986, Cheri an *et al.*, 1992, Sarg *et al.*, 1991, Iqbal *et al.*, 2002, Nash *et al.*, 1950).

Homeopathy seeks to cure in accordance with natural laws of healing and uses medicine made from natural substances viz. animal, vegetable and mineral (Bhanja, 1967). Some important homeopathic oral hypoglycemic drugs are Rhus Aromatica (rootbark of Rhus aromatica) Syzygium Jambolinum (dried fruits of syzygium Cumini L.), Urinium Nitricum (Nitrate of Uranium) and Acid Phos.

The aim of the present work is to evaluate the antidiabetic activities of herbal and homeopathic medicine using allopathic drug as a controlled standards.

MATERIALS AND METHOD

Chemicals and drugs were obtained from the following resources:

Glucose (Merck, Germany), Gum Tragacanth (local market), Gliclazide powder drug (Wilson's Pharmaceuticals, Pakistan), Glibenclamide (Efroze Chemical Industries (Pvt.) Ltd., Karachi). The herbal and homeopathic. drugs i.e. Dolabi (Hamdard Laboratories, Karachi), Dawai Ajeeb Ziabitus (Ajmal Dawakhana, Lahore), Syz-Jambol (BM Homeopathic Pharmacy, Lahore), Acid Phos and Uranium Nitricum (from a local homeopathic pharmacy. D.I. Khan). Alloxan monohydrate (Merck, Germany), Blood Glucose determination Kit (Randox Laboratories Ltd. u.K.). .

Table-I
Dose calculations of various drugs for rabbits

Name of drug	Minimum recommended dose for 70 kg body weight/Equivalent dose	Dose per kg body weight
Gliclazide	80mg 1	1.14 mg
Glibenc lamide	5mg 1	0.07 mg
Dolabi	616mg 2 (2 tablets)	8.80 mg
Dawai Ajeeb Ziabetes	1111.60 mg 2 (2 tablets)	15.88 mg
Acid Phos	20 drops 3	4 drops (Minimum required dose)
Syz- Jambol	210 mg 3	3mg
Uranium Nitricum	20 drops 3	4 drops (Minimum required dose)

1 Martindale. The Complete Drug Reference, 32 nd Ed, 1999.

2 Manufacturer's specifications.

3 Clark, 1975.

Composition of the Dugs Used:

Dolabi: Extract of pancreas, Gynnama sylvestre, Acacia Arabica, Calcined iron, Calcined egg shell, Bambusa arundinacea, Opium, Rumix vesicarius, Pearls, Gum acacia (excipient).

Dawai Ajeeb Ziabetes: Tukhm Kharfa Siyah, Tukhm Jaman, Tukhm Kahu, Sandal Sapaidd, Gul Surkh, Qushta Poast Sapaidd, Kashniz Khushk, Gul-eArmani, Gul-e-Anar, Qushta Sadaf, Qushta Zamurrad, Qushta Faulad, Sunaq Dana.

Acid Phos: Phosphoric acid.

Uranium Nitricum: Nitrate of Uranium (made from Pitch-blend; an oxide of Uranium)

Syz-Jambol: Insulin DS, Uranium Nitricum D2, Experimental animals used.

Healthy male rabbits weighing 1000-1500 g were used in these experiments. The animals were kept under

observation - for one week before experimentation in the animal house. The animals were fed the green fodder *ad libitum*. Fresh and whole some water was also supplied *ad libitum*.

Distribution of rabbits:

The rabbits were randomly divided into two groups.
Normal (non-diabetic) group
Alloxan induced diabetic group

Preparation of alloxan diabetic rabbits:

Rabbits were made diabetic by injecting alloxan monohydrate 150 mg/kg body weight in marginal ear vein using turberculin syringe. After eight days of injection the blood glucose levels of the surviving rabbits were determined. Rabbits with blood glucose level of 300-500 mg/100 ml were considered as diabetic and were employed for further study (Butt, 1962, Akhtar *et al.*, 1981).

Calculation of dose:

The doses of the drugs were calculated on body weight as shown in Table-I.

Administration of drug:

Dose of the drug was carefully calculated for each animal according to the data shown in Table-I, then accurately weighed and suspended in gum tragacanth solution (2%). The suspension was then administrated by passing a polythene feeding tube # 6, equipped with a 20 ml syringe containing the prepared dose, through nasal route into the stomach of the rabbit.

Determination of blood glucose level:

Blood glucose levels were determined by the glucose oxidase method (Neese, 1982).

Statistical analysis:

Statistical analysis was carried out using "Minitab" a statistical package. The significant difference was measured using *student-t* test (at 95% confidence interval) and one way ANOV A.

RESULTS AND DISCUSSION

Normal rabbits (Non diabetic)

Control Rabbits treated With gum tragacanth suspension (2%).

The oral administration of gum tragacanth suspension (2%) in rabbits did not alter blood glucose level as

shown in Table 2. The similar results also have been observed elsewhere (Akhtar et al., 1983).

Rabbits treated with gliclazide and glibenclamide

The significantly lower blood glucose level was observed from 2 h post oral administration of gliclazide to the rabbits. It was highly significant ($p < 0.001$) at 2h and 4h and was maintained significantly low ($p < 0.05$) compared with the zero time for 12h (Table-2). The oral administration of the glibenclamide also significantly ($p < 0.001$) reduced the blood glucose level throughout the study as shown in Table 1. After 24h, both of the drugs did not show any effects on blood glucose level.

It is known that sulphonylureas produce hypoglycemia in normal animals by stimulating the pancreatic beta cells to release more insulin. It binds to the receptors on islet cells of langerhans and increases the exchange

of potassium and calcium in the cell and to stimulate the secretion of insulin (Herfmdal, 1988). Both gliclazide and glibenclamide significantly reduced the blood glucose level for about 12h compared with the zero time level.

Effect of herbal drugs on blood glucose level in normal rabbits:

The oral administration of dolabi significantly ($p < 0.001$) reduced the blood glucose level from 2h to 8h. The decrease was highly significant ($p < 0.001$) at 4h and 6h post administration of the drug compared with the zero time (shown in Table 2). The oral administration of the Dawai Ajeeb Ziabetes also significantly ($p < 0.01$) reduced the blood glucose level for 6h., after that i.e. at 8h, 12h and 24 h the decrease was not significant. ($p > 0.05$) compared with the zero time as shown in Table 2. This study shows that the herbal drugs under study also produced consistent

Table 2 Mean (I SEM) Blood Glucose level of Normal Rabbits after oral administration of various drugs (Allopathic, Herbal and Homeopathic)

Time (hours)	Gum tragacanth	Gliclazide	Glibenclamide	Dolabi	Dawai Ajeeb Ziabetes	Acid Phos	Syz Jambol	Uranium Nitricum
0	105.3:t1.3	108.5:t1.5	102.2:t2.0	106.7:t3.2	114.9:t3.2	111.8:t1.5	109.0:t1.4	107.0:t1.5
2	104.3:t1.3	76.0:t1.3**	52.3:t2.6**	84.1:t4.4*	95.3:t2.3*	110.0:t1.7	107.5:t1.08	106.5:t1.8
4	104.5:t1.4	68.5:t1.7**	54.2:t3.8**	62.8:t2.9**	92.2:t3.4**	109.0:t1.2	107.1:t0.7	105.5:t1.5
6	104.0:t1.3	98.0:t1.8*	41.0:t4.4**	68.4:t3.0**	97.9:t0.7**	108.0:t1.2	107.5:t0.9	104.6:t1.6
8	103.8:t1.4	95.5:t1.5*	48.8:t2.7**	91.5:t3.5*	110.0:t2.1	108.5:t1.0	106.0:t2.9	104.0:t1.9
12	103.4:t1.2	94.9:t2.7*	71.3:t3.5**	101.0:t3.6*	114.0:t2.0	107.0:t1.7	104.0:t2.1	102.9:t0.9
24	102.8:t2.1	110.0:t3.1	101.7:t2.3	104.8:t1.9	110.4:t2.3	114.1:t3.1	108.7:t2.6	106.1:t1.5

Table 3 Mean (:f: SEM) Blood Glucose level of Alloxan-induced Diabetic Rabbits after oral administration of various drugs (Allopathic, Herbal and Homeopathic)

Time (hours)	Gum tragacanth	Gliclazide	Glibenclamide	Dolabi	Dawai Ajeeb Ziabetes	Acid Phos	Syz Jambol	Uranium Nitricum
0	365.8:t2.3	373.1:t1.5	397.0:t2.3	394.3:t2.4	377.8:t2.6	365.0:t2.5	389.9:t2.1	371.3:t1.3
2	362.3:t2.0	326.7:t3.2*	354.3:t3.4*	376.7:t2.6*	365.0:t3.9	363.8:t1.8	386.0:t2.1	369.0:t0.8
4	362.0:t1.5	359.0:t1.7*	365.0:t3.3*	366.8:t2.7*	355.2:t3.4*	362.0:t1.8	387.9:t3.0	368.8:t1.3
6	360.2:t1.4	362.0:t1.8	381.7:t3.8	382.1:t1.9	368.7:t1.3	362.1:t2.2	387.6:t3.0	367.0:t1.3
8	359.8:t1.0	367.5:t4.0	380.0:t3.7	380.4:t2.3	367.8:t4.0	361.7:t1.2	385.3:t2.4	366.8:t2.0
12	363.1:t1.7	365.3:t3.5	388.1:t6.2	391.2:t2.9	378.1:t3.1	362.3:t2.1	384.9:t1.8	366.0:t1.5
24	370.1:t3.5	371.4:t2.4	389.7:t5.3	383.6:t3.1	380.0:t3.1	359.6:t2.3	392.4:t2.7	370.3:t1.8

hypoglycaemic effects in nonnal rabbits that may be either by stimulating the release of insulin from beta cells of pancreas or themselves possess some insulin like action or by facilitating glucose uptake by the cells and increasing the rate of phosphorylation of glucose (Baker, 1982).

Effect of homeopathic drugs on blood glucose level in normal rabbits:

In nonnal rabbits the acid phos, uranium nitricum and syz-jambol failed to reduce the blood glucose level as shown in Table 2. The treatment of the animals with a single dose/ day with these homeopathic drugs for 7days showed that only on 7th day syz-jambol significantly reduced ($p<0.05$) the blood glucose level at 2h and 4h and Uranium Nitricum only after 12h, post administration of the drug, while acid phos did not show any effect on blood glucose level. It is possible that the homeopathic way of treatment may require longer time compared to the other way of curing the diseases.

The single dose of homeopathic drugs did not reduce the blood glucose level appreciably even after the oral administration for 7 days. It has been postulated that homeopathic treatment aims to cure the sickness of patients by stimulating the vital dynamics or the power of resistance of the sick person (Dewey, 1960).

Alloxan Induced Diabetic Rabbits

The blood glucose level of the surviving rabbits was determined eight days after the injecting the alloxan. The animals with blood glucose levels 300 mg/100ml or more than 300 mg/100ml were recruited and distributed into various groups, each group was comprised of six animals. The results of these experiments were in good in agreement with others work (Butt, 1962 Akhtar et al., 1981).

Effect on Control Group (gum tragacanth suspension 2%)

The oral administration of gum tragacanth aqueous suspension to the alloxan induced diabetic rabbits did not show any significant changes ($p>0.05$) in the blood glucose level through out the study as shown in table 3.

Diabetic rabbits treated with Gliclazide and Glibenclamide

The diabetic rabbits treated with gliclazide and glibenclamid showed the significant ($p<0.05$)

reduction in blood glucose level only at 2h and for 4h, respectively. Gliclazide and glibenclamide produced only significant decrease in blood glucose level in nonnal rabbits while in alloxan induced diabetic rabbits the effect of the drug was not significant after 4h, respectively. These results shows that sulphonylureas are effective only in the treatment of nonnal rabbits while in alloxan induced diabetic rabbits the Bcells have been destroyed. These results are in compliance with other studies (Goth, 1985; Gilman et al., 1991).

Effect of herbal drugs on blood glucose level in diabetic rabbits

Diabetic rabbits treated with Dolabi and Dawai Ajeeb Ziabetus

Dolabi significantly reduced ($p<0.05$) the blood glucose level at 2h and 4h post administration of the drug. Dawai Ajeeb Ziabetus reduced the blood glucose level significantly ($p<0.05$) only at 4h post administration of the drug; results are shown in Table 3.

The reduction of blood glucose level in alloxan induced diabetic rabbits by herbal drug may follow some extra pancreatic route: Dolabi contains (*Tymnema sylvestre*, which is a potent hypoglycaemic agent. It has been observed that *Gymnema sylvestre* reduced insulin requirement in patients with IDDM (Shanumuga-sunaram et al., 1990). It is possible that this therapy may stimulate the endogenous insulin, possibly by regeneration/revitalization of the residual beta cells. The effect of the herbal drug on lowering the blood glueose level was more potent and longer lasting in nonnal rabbits compared with alloxan induced diabetic animals.

As biguanides produce hypoglycaemia only in diabetic rabbits and not in nonnal rabbits, therefore it would appear that active principals in herbal drugs contains both types of constituents that reduce the blood glucose level in nonnal and alloxan induced diabetic rabbits.

It is known that herbal drugs contain certain trace elements like manganese, magnesium, zinc, calcium and phosphorus. It has been reported that alloxan causes complexation with biologically significant metals in beta cells producing their deficiency (Donsbach, 1982). Therefore, it is also possible that the trace elements present in the herbal drugs may play

an important role in the hypoglycemic action both in normal as well as alloxan diabetic rabbits (Donsbach, 1982).

Effect of homeopathic drugs on blood glucose level in diabetic rabbits

Table 3 shows that acid phos, syz-jambol and uranium nitricum were not found to be effective in reducing the blood glucose level significantly ($p > 0.05$) throughout the study.

The oral administration of the homeopathic drugs even for 7 days with a single dose per day did not bring any substantial changes in blood glucose level. A significant ($p < 0.05$) decrease in blood glucose level was observed only at 2h post administration of the Acid Phos drops for 7 days. While syz-jambol and uranium nitricum significantly ($p < 0.05$) reduced the blood glucose level only at 4h posts administration of the drug. The changes in blood glucose level were not insignificant ($p > 0.05$) during rest of the study.

The exact mode of action of homeopathic hypoglycaemic agents has not been fully elucidated but it is possible that the hypoglycaemic action may be due to the stimulation of beta cells to secrete insulin or may manipulate insulin like effect. A reasonable percentage of beta cells (approximately 30%) must be in good functioning for the hypoglycaemic action of homeopathic drug (Usman, 1996). It is also possible these agents may decrease hepatic gluconeogenesis and glycogenolysis. There is evidence that these agents depress gluconeogenesis (Usman, 1996). However further chemical and pharmacological investigations are required to elucidate the exact mode of hypoglycemic effect of homeopathic drugs.

These studies showed that the herbal drugs Dolabi and Dawai Ajeeb Ziabitus are effective in reduction of the blood glucose level both in normal and alloxan induced diabetic rabbits like glicalazide and glibenclamide, used as control drugs. Therefore the treatment of the diabetics may be acceptable using the herbal medicines subject to the study of the unwanted effects of the drugs. Homeopathic drugs used in this study fails to decrease the blood sugar level significantly and further studies are required for the evaluation of the antidiabetic properties. The standardization and the development of the quality control of the herbal drugs is the other major area of the study.

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