Comparative study of Hypoglycemic activity of gliclazide to its silver complex

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Abstract

Gliclazide, N-(4-Methyl Benzene Sulphonyl)-N-(3-azocyclo (3,3,0-Oct-3-yl) urea trade name Diamicron, an oral hypoglycemic agent was used to synthesize its complex with Ag(I). The hypoglycemic activity of gliclazide was observed on experimental animals (dogs) and then compared with Ag Complex, using Folin-Wu method. Results reveals that the gliclazide Ag-Complex is more effective than that of parent drug. This blood sugar lowering effect of sulfonyleureas seems to be related to the stimulation of insulin secretion. On the other hand many studies have strongly indicated the presence of long term or extra pancreatic action of sulfonyleureas. The interesting observation on metal complex of oral sulfonylurea used as anti-diabetic agent for lowering blood sugar concentration may likely substantiates the use of these complex after extensive clinical studies.

Key words : Silver complex, Hypoglycemic Activity, Diabetes Melitus, Antidiabetics, Insulin.

Introduction

A large number of metals are used as Chemotherapeutic agents in Unani & Ayurveda system of medicine. Iron (Kushta-e-faulad) used in sprue and anaemia.

Nobel metal silver has a powerful ablugo dynamic action, due to which silver vessels are used for various purposes. It is used in the treatment of epilepsy.

Diabetes is a deceptive disease and if not detected at an early stage may cause even death. Diabetes mellitus is characterised by an excess sugar in blood and its excretion in urine also. To avoid daily prick of insulin injection the use of oral anti-diabetics has become more common in recent years.

Looking to the useful effect of silver and its metal complex1-5. An attempt is made to synthesized a gliclazide-Ag complex and to compare its hypoglycemic activity, which is presented in this paper.
Experimental Section

Materials

All the reagents and chemicals employed for the preparation of the ligands and their Ag(I) complexes were of the best grade available (Merck) and used without further purification.

Methods

Four dogs of appropriate body weight 4.00 kg were kept in laboratory condition on experimental diet (milk and bread) for four days and their fasting sugar was estimated for five days (Folin and Wu method) colorimetrically as well as by glucometer to maintain an average blood sugar level. On sixth day animals (dog) were given a dose of gliclazide according to body weight and fall in blood sugar level was noted with increasing duration of time. The maximum decrease in blood sugar was up to 42.35 mg/100ml of blood (an average of four animals). Now the animals (dogs) were again kept on same experimental diet for three days so as to further maintain the normal blood sugar. On Eighth day animals (dogs) are given orally the gliclazide-Ag complex and fasting blood sugar was noted again, on the day of administration of drug and complex, the diet was given to the animals (dogs) after final observations i.e. at 2:00 pm. Result are recorded. Table -2.

Results & Discussion

The hypoglycemic effect of gliclazide, an oral anti-diabetic drug was investigated on the blood sugar level of normal non-diabetic male dogs. Analysis of data reveals the drug caused a marked decrease in blood sugar level to the extent of 42.35% while its Ag-complex reduced sugar level to 49.49%.

These results clearly indicates a better hypoglycemic activity of Ag-gliclazide complex over its parent drug which is in agreement with the earlier finding of Iqbal et al. This increased hypoglycemic activity of parent drug may also be due to smaller particle size of Ag-gliclazide complex than gliclazide, as on complexation size is reduced, which may enhance the rate of absorption of complex in gastro-intestinal tract.

Result of the present work are also in conformity with hypoglycemic effect of Fe-tolazamide

| Test sample | Glucose Standard 1 | Glucose Standard 2 | Blank (without sugar) |
|-------------|--------------------|--------------------|-----------------------|
| 0.05 ml blood + 3.9ml copper reagent + 0.05 ml sodium tungstate (to coagulate protein) and centrifuge the solution. | 0.01% Standard Glucose solution (1) | 0.0025% Standard Glucose solution (2) | |
| 2.0 ml supernatant liquid of the sample + 2 ml Harding’s B- solution (NaHCO₃ + potassium oxalate + sodium tartrate). | 2ml glucose solution + 2 ml Hardings B- solution | 2 ml glucose + 2 ml Harding’s B- solution | 2 ml Cu reagents + 2 ml Harding’s B- solution |
| Sample (a) | Sample (b) | Sample (c) | Sample (d) |

1. \[ \text{Test reading} \times 80 = \frac{\text{Glucose /100 ml of blood in mg}}{100} \]
2. \[ \text{Test reading} \times 200 = \frac{\text{Standard (2) reading}}{100} \]
Table 2
COMPARATIVE HYPOGLYCEMIC EFFECT OF Gliclazide & ITS SILVER COMPLEX

| Average Group of in animals | FASTINGS BLOOD SUGAR LEVEL IN mg/100 ml OF MALE DOGS | Oral Administration of Drug | Least blood sugar values | Fall in blood sugar | % Fall in blood blood |
|-----------------------------|------------------------------------------------------|-----------------------------|--------------------------|-------------------|----------------------|
|                             |                                                      | 8am 10am 12 noon 2 pm 4 pm | 8am 10am 12 noon 2 pm 4 pm | 8am 10am 12 noon 2 pm 4 pm | 8am 10am 12 noon 2 pm 4 pm |
|                             |                                                      |                            |                          |                   |                      |                      |
| A                           |                                                      | 98 97 97 98 97.5           | 83 65 62 69 80           | 62                | 35.5                | 36.41               |
| B                           |                                                      | 94 92 94 92 94             | 77 62 54 67 85           | 54                | 40                  | 42.55               | 42.35               |
| C                           |                                                      | 99 97 98 99 98.25          | 79 64 51 69 86           | 51                | 47.25               | 48.09               |
|                             |                                                      |                            |                          |                   |                      |                      |
| Average Group of in animals |                                                      | 5 Day 6 Day 7 Day 8 Day     | 8am 10am 12 noon 2 pm 4 pm | 8am 10am 12 noon 2 pm 4 pm | 8am 10am 12 noon 2 pm 4 pm |
|                             |                                                      |                            |                          |                   |                      |                      |
| A                           |                                                      | 99 99 100 99 99            | 72 62 58 50 74           | 50                | 49                  | 49.49               |
| B                           |                                                      | 101 102 105 104 103        | 69 60 59 57 77           | 57                | 46                  | 44.46               | 49.49               |
| C                           |                                                      | 100 99 100 103 100.5       | 79 64 57 52 72           | 52                | 48.5                | 48.25               |

*Values without drug or complex diet was given at 6:10 am.
*Values after administration of drug/complex diet was given at 4:00 pm.
complex than tolazamide drug as mentioned by Qureshi et al.\textsuperscript{5}

**Conclusion**

In conclusion, the present study revealed the oral administration of Ag-complex marked blood glucose lowering effect on experimental animals (dogs) which is in agreement of previous work\textsuperscript{9-19}.

Further study is recommended to investigate the hypoglycemic activity of Ag- gliclazide complex on induced diabetes on experimental animals.

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