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A COMPERATIVE STUDY OF VANADIUM PENTOXIDE AND CHROMIUM OXIDE IN STREPTOZOTOCIN INDUCED DIABETES IN ALBINO RATS

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ABSTRACT: Objectives: The present study was conducted to evaluate and compare the effect of vanadium pentoxide and chromium oxide in normal and streptozotocin induced diabetic albino rats. **Methods:** Diabetes was experimentally induced by injecting intraperitoneally with a single dose of 60mg/kg. The animals were considered as diabetic, if their blood glucose values were above 300 mg/dl on the 10th day after injection. The blood glucose estimation was done by glucose oxidase method. Glibenclamide was taken as standard drug. The one-way ANOVA followed by Dunnett's 't' test was used for statistical analysis. **Results:** The blood glucose levels were found to be significantly ($p<0.05$) decreased in vanadium pentoxide and chromium oxide treated groups. **Conclusion**: This study suggests that vanadium pentoxide and chromium oxide have antidiabetic effect in a dose dependent manner.

INTRODUCTION: Despite the availability of insulin and many oral hypoglycaemic drugs, Diabetes mellitus still remains a major health concern for human being. Therefore, new therapeutic approaches are needed to treat diabetes more efficiently. Use of 'alternative therapies' must be taken into account by health care providers in order to attain the best metabolic control for their patients [1, 2]. Vanadium belongs to the first transition series of elements, is ubiquitously distributed and represents the 21st most abundant element in the earth's crust [3]. While the vanadium requirement of lower organisms has been established, it's essential value in humans remains to be proven [4, 5].

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Daily vanadium intake has been estimated to be 10–160 µg, mainly from black pepper, mushrooms, parsley, shellfish and spinach, which contain between 0.05 and 1.8µg vanadium per gram. Analysis of body fluids, organs and tissues has estimated that the total body pool of vanadium in humans is between 100 and 200 µg, and it ranges from 0.014 to 7.2 µM in mammalian cells [3, 5].

Chromium is an essential trace element required for the maintenance of normal glucose and fat metabolism [6, 7]. Chromium is present in many foods, especially in liver, Brewer's yeast, American cheese, wheat germ, vegetables such as carrots, potatoes, broccoli, and spinach, and is also present in molasses, dried beans, nuts, seeds, mushrooms, and animal fats [8].

The results of few previous studies on these two compounds are encouraging but comparative studies are still lacking. The present study aims to evaluate the anti-diabetic effect of two trace elements Vanadium and Chromium compounds in

albino rats. The significance of their anti-diabetic effect was compared with Glibenclamide [9].

MATERIALS AND METHODS:

Experimental Animals

Healthy albino rat of either sex with 200-250 gm were procured from intuitional animal house. During the period of experiment, the animals were fed with rat's chaws diet and water *ad libitum*. Animals were maintained under controlled condition with 12 hours light and 12 hours dark cycles at temperature 22±3^{0}C and humidity 55%. The animals were randomized into control and experimental groups and housed in separate cages.

Chemicals and Drugs:

Vanadium Pentoxide and Streptozotocin procured from Himedia, Mumbai. Chromium Oxide and Glibenclamide obtained from Central Drug House, New Delhi and Sigma Aldrich India, Bangalore respectively[10, 11].

Ethical Review:

The protocol was submitted to the institutional animal ethics committee and the study was conducted after due approval (MC/32/2012/6) of the committee (CPCSEA Registration number: 351; 3/1/2001). The study was conducted in Department of Pharmacology, Gauhati Medical College and Hospital.

Acute toxicity test for testing vanadium pentoxide and chromium oxide:

The acute toxicity test was carried out as per the 18th paragraph of OECD guidelines 423 for testing chemicals adopted on 17th December 2001[12]. The fixed dose levels of vanadium pentoxide and chromium oxide, starting from 5, 50, 300, 2000 mg/kg body weight were orally administered to two separate groups containing 3 non-pregnant albino female rats in each group. The rats were observed individually after dosing at least once during first 30 minutes, with special attention given during the first 4 hours, periodically during 24 hours, and daily thereafter, for a total of 14 days for any toxic symptoms and mortality.

Induction of Diabetes in rats:

The animals were fasted for overnight prior to the induction of diabetes. Streptozotocin (STZ) was freshly dissolved in citrate buffer (3mM, pH 4.5). It was immediately injected intraperitoneally with a single dose of 60mg/kg. The animals were considered as diabetic, if their blood glucose values were above 300 mg/dl on the 10th day after STZ injection[13].

Experimental design for estimation of blood glucose:

Blood glucose estimation was done by glucose oxidase method using glucose estimation kit [14].

Each group containing 6 animals (n=6) and were divided as follows:

Group-A: Normal control group: Received normal saline 5ml/kg per orally (p.o.) for 10 days.

Group-B: Diabetic control group: Received normal saline 5ml/kg p.o. for 10 days.

Group-C: Diabetic test group for Vanadium pentoxide

Group C (i): Received vanadium pentoxide 5mg/kg per oral (p.o.) for 10 days.

Group C (ii): Received vanadium pentoxide 10 mg/kg p.o. for 10 days.

Group C (iii): Received vanadium pentoxide 20 mg/kg p.o. for 10 days.

Group-D: Diabetic test group for Chromium oxide

Group D (i): Received chromium oxide 10 mg/kg p.o. for 10 days.

Group D (ii): Received chromium oxide 20 mg/kg p.o. for 10 days

Group D (iii): Received chromium oxide 40 mg/kg p.o. for 10 days

Group-E: Diabetic standard group: Received glibenclamide 0.5 mg/kg p.o. for 10 days.

Statistical Analysis:

The values of blood glucose level were expressed in mg/100 ml as mentioned in the tables. Results were presented as mean ± standard error mean (SEM) for 6 animals (n=6) in each group. The data were statistically analyzed by using one-way analysis of variance (ANOVA) test followed by Dunnett's 't' test. The 'p' value less than 0.05 was considered significant.

RESULTS:

(A) Acute Toxicity Test:

There was no mortality recorded in the rats upto the maximum dose of 2000mg/kg. Hence, the LD_{50} said to be above 2000mg/kg.

(B) Effect of Vanadium Pentoxide and Chromium Oxide on Blood Glucose Level:

As shown in Table 1, on the 10th day it was observed that the blood glucose levels were high in all the groups (except normal control group) as compared to 1st day. In contrast to this, on 20th day the blood glucose levels were significantly decreased in vanadium pentoxide treated C(i), C(ii) and C(iii) groups, chromium oxide treated D(ii) and D(iii) groups and standard drug group.

The results of ANOVA test has not shown any intergroup difference ($p>0.05$) in blood glucose levels among all the groups before the drug treatment i.e. on 1st day, but there was significant difference ($p<0.05$) after the treatment i.e. on 20th days. The results of Dunnett's t test revealed that both the test drugs and standard drug (glibenclamide 0.5mg/kg p.o.) had significant ($p<0.05$) effect on lowering the blood glucose level except blood glucose level of the chromium oxide (10mg/kg) treated group when compared to diabetic control group. The blood glucose level was less on 20th day in vanadium pentoxide treated group C(i), C(ii) and C(iii) as compared to chromium oxide treated group D(i), D(ii) and D(iii) as shown in **Table 1**.

TABLE 1: EFFECT OF VANADIUM PENTOXIDE AND CHROMIUM OXIDE IN STREPTOZOTOCIN INDUCED DIABETIC RATS.

Group	1st days	10th days	20th days
A (Normal control)	81.05±0.867	82.16±2.142	82.19±2.232
B (Diabetic control)	80.24±0.662	303.16±0.631	315.09±1.194[a]
C(i) [Vanadium pentoxide 5mg/kg]	82.41±0.568	304.32±1.258	196.46±3.608[b]
C(ii) [Vanadium pentoxide 10mg/kg]	80.81±0.719	302.58±0.638	172.24±6.861[b]
C(iii) [Vanadium pentoxide 20mg/kg]	81.36±0.644	303.97±1.753	160.75±0.665[b]
D(i) [Chromium oxide10mg/kg]	81.93±0.696	307.66±1.398	297.94±1.164
D(ii) [Chromium oxide 20mg/kg]	82.24±0.617	307.48±2.497	222.75±6.568[b]
D(iii) [Chromium oxide 40mg/kg]	80.91±0.762	304.60±1.546	195.75±0.502[b]
E (Standard drug)	82.98±2.210	309.34±2.377	138.30±8.941[b]

Here values are expressed as mean ± SEM and n=6 for each group. ANOVA followed by Dunnett t test is done. [a]$p<0.05$ when compared to the Normal control group. [b]$p<0.05$ when compared to the Diabetic control group.

DISCUSSION: The inability of the modern therapy to provide a satisfactory treatment in diabetes has led to a shift in focus to alternative forms of therapy based on drugs derived from plants and minerals. Estimation of blood glucose in this study was done by glucose oxidase method as described by Trinder, this method has adequate sensitivity with the advantage that small amount (0.1ml) can be used for analysis of blood glucose[14].

The present study demonstrated that after administration of vanadium pentoxide and

chromium oxide, the hyperglycemic status was improved significantly ($p<0.05$) in STZ-induced diabetic rats by lowering the blood glucose level. The anti-diabetic activity of vanadium pentoxide in this study was probably due to insulino-mimetic effects of vanadium compounds *in vitro* and *in vivo*, including the stimulation of glucose transport and glucose oxidation, glycogen synthesis, lipogenesis as well as the inhibition of lipolysis and gluconeogenesis [15, 16, 17]. While the actions of the chromium compounds in this study can be implicated to the potentiating action on insulin with impaired glucose tolerance, presumably by activation of insulin receptor kinase activity and the inhibition of insulin receptor tyrosine phosphatase leading to increased phosphorylation of the insulin receptor, which is associated with increased insulin sensitivity[18, 19, 20].

CONCLUSION: Vanadium pentoxide and chromium oxide produced significant reduction of blood glucose levels in STZ-induced diabetic albino rats in a dose dependent manner. However, blood glucose levels were lower in vanadium pentoxide treated groups as compared to chromium oxide groups. Thus, it can be concluded that Vanadium pentoxide and chromium oxide has the beneficial effect in diabetes mellitus and these two compounds hold the hope to play a promising role in the treatment of diabetes.

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