Evaluation of anti hyperglycaemic activity of *Zingiber officinale* (Ginger) in albino rats

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ABSTRACT

*Zingiber officinale* (commonly known as ginger) is widely used in traditional medicine. The juice of *Z. Officinale* has shown hypoglycemic activity in STZ induced diabetic rats. The present study was designed to compare the anti hyperglycemic activity of juice of *Z. Officinale* with standard glibenclamide and metformin in alloxan induced diabetic rats. 30 albino rats were randomly divided into 5 equal groups. Four groups of six animals each were induced diabetes by giving alloxan. Group I: Normal control, Group II: Diabetic control receiving normal saline (0.5 ml), Group III: Standard control 1 receiving glibenclamide (5 mg/kg body weight), Group IV: Standard control 2 receiving metformin (10 mg/kg body weight) and Group V: Test group receiving *Z. officinale* juice (4 ml/kg body weight). Fasting blood sugar level was estimated on day 1,3,7,14,21,28,35 and 42 from rat tail vein using glucometer. Data was statistically analyzed by New Mann Keul’s Post Hoc test and ANOVA. Fresh juice of *Z. Officinale* produced a time dependent decrease in blood glucose level significantly compared to both glibenclamide and metformin. The earlier study has showed *Z. officinale* juice increases insulin sensitivity. However this study shows hypoglycemic action inspite of insulin depletion by alloxan and additional non insulin related hypoglycemic action could be inferred. Further studies are needed to explore this property.

**Key words:** Alloxan, Diabetes, Glibenclamide, Metformin, *Zingiber officinale*.

INTRODUCTION

Diabetes mellitus is a metabolic disorder due to relative or absolute lack of insulin, resulting in elevated blood glucose levels in association with long term vascular and neurological complications.[1] The number of diabetic patients in the world had been estimated at 110 million by 1994. This figure has drastically raised to 175 million by the end of the year 2000.[2] The picture in India is much more alarming. The current estimation shows that there are 3.5 crore
people with diabetes and this number is likely to raise up to 5.72 crore by 2025. India has now
been declared by WHO as the ‘Diabetes capital of the world’. [3]

The currently used hypoglycemic drugs in the treatment of diabetes are not completely effective
and are associated with adverse effects both in the short and long run. [4] Several herbs have
been tried in various studies with the aim to prevent or delay type 2 diabetes. Aegle marmelose,
Aloe vera, Artemisia pallens, Coccinia indica & many others have been shown to have
antidiabetic activity. [5, 6, 7]

Therefore there is a need to continue the search for more effective and safer drugs for the
treatment of diabetes. An important area of this search is to screen plant extracts for potential
hypoglycemic properties.

The fresh and dried rhizome of Zingiber officinale (commonly known as ginger) is widely used
in traditional medicine for its anti-emetic, anti-inflammatory anti oxidant, anxiolytic and
hypoglycemic effect. [8] Studies done with extract of Zingiber officinale has been shown to
possess hypoglycemic activity both in vivo & in vitro. [8, 9] The present study aims at
investigating the effect of juice of Zingiber officinale on the blood sugar level of alloxan induced
diabetic rat-model and compare with standard drugs.

**EXPERIMENTAL SECTION**

**Materials and Methods**

The study was undertaken at the department of pharmacology, J.J.M.Medical College after
obtaining the approval from Institutional Ethics Committee (Registration Number
57/1a/CPCSEA). Albino rats, of wistar strain, weighing between 150-200gm of either sex were
used for the study. The animals were fed with standard laboratory food and water. Freshly
prepared solution of Alloxan monohydrate 2% (dissolved in normal saline) was used as single
dose (150mg/kg i.p, pH-4.0) to induce Diabetes in rats. Rats with fasting blood sugar of more
than 200mg/dL were selected for the study. The animals were divided into 5 groups of six
animals each.

*Group I: Non diabetic rats treated with normal saline*
*Group II: Diabetic rats treated with normal saline.*
*Group III: Diabetic rats treated with glibenclamide (Aventis, Mumbai) 5mg/kg.*
*Group IV: Diabetic rats treated with metformin (Sanofi Aventis, Mumbai) 10mg/kg*
*Group V: Diabetic rats treated with Z.Officinale 4ml/kg (local market and authenticated by botanist fr om DRM
Science College, Davangere).*

All animal Handling and animal care was done as per the guidelines set by Indian National
Science Academy, New Delhi, India. Animals had free access for food, water and ad libitum.
The polythene infant feeding tube was used for oral administration of all drugs as single dose in
morning. Fasting Blood Sugar (FBS) was recorded on day 1, 3, 7, 14, 21, 35 and 42 days. After
42 days of treatment Oral Glucose Tolerance Test (OGTT) was performed after overnight fast in
order to assess the effects of Z.officinale on alloxan induced diabetes. On the day of the OGTT,
animals were given an oral dose of glucose (3g/kg body weight) [10] after collecting sample for
blood glucose estimation. Blood samples were collected at 45 min intervals for 3 readings, with
the first sampling commencing after 45 min of glucose load. Oral glucose was given 30 min after
administration of the drug to facilitate absorption. [10] In all groups on day 1, blood glucose was
estimated at every half hour interval from the time of administration of the drug, for 3 hours to
know the peak time of action.
Method of blood collection: Blood samples were obtained from rat tail vein, after applying xylene to make veins prominent. Blood glucose was estimated by using glucometer (Accu-Chek sensor from Roche diagnostic corporation).

Statistical analysis: One way ANOVA was used for multiple group comparisons followed by Newmann Keul’s Post Hoc Test for statistical significance between groups. P values less than 0.05 were considered to be significant.

RESULTS

Mean blood glucose levels in non-diabetic control group varied from 53.33 to 61 mg/dl, without much of variation during the study. In diabetic control group, there was a gradual increase in blood glucose levels from mean value of 266.33 mg/dl on day 1 to 287.33 mg/dl on day 42. In test group, there was gradually increasing reduction in blood glucose level from day 1 till the end of experiment. Which was statistically significant compared to control. However with respect to standard control it was statistically significant from day 14.

<table>
<thead>
<tr>
<th>Groups</th>
<th>0 MIN</th>
<th>45 MIN</th>
<th>90 MIN</th>
<th>135 MIN</th>
</tr>
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<tbody>
<tr>
<td>NDCG</td>
<td>54.67 +/- 5.01</td>
<td>78.5 +/- 5.21</td>
<td>88.67 +/- 3.5</td>
<td>85.67 +/- 3.67</td>
</tr>
<tr>
<td>DCG</td>
<td>287.33 +/- 7.33</td>
<td>320.0 +/- 12.45</td>
<td>357.66 +/- 9.5</td>
<td>403.33 +/- 122.02</td>
</tr>
<tr>
<td>SC-1</td>
<td>97.66 +/- 8.71</td>
<td>175.83 +/- 36.38</td>
<td>206.66 +/- 29.68</td>
<td>230.0 +/- 31.64</td>
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<tr>
<td>SC-2</td>
<td>81.66 +/- 7.31</td>
<td>210.33 +/- 56.04</td>
<td>230.0 +/- 31.7</td>
<td>206.33 +/- 35.33</td>
</tr>
<tr>
<td>DTG</td>
<td>67.33 +/- 4.5</td>
<td>165.16 +/- 8.68</td>
<td>147.952</td>
<td>123.67 +/- 10.8</td>
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<td>F* Value</td>
<td>1213.81</td>
<td>47.64</td>
<td>146.82</td>
<td>26.38</td>
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<tr>
<td>Significance</td>
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<td>P&lt;0.001</td>
<td>P&lt;0.001</td>
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NDCG-Non Diabetic Control Glucose, DCG- Diabetic Control Glucose, SC-1- Standard Control 1(Glibenclamide), SC-2- Standard Control 2(Metformin), DTG- Diabetic Test Drug.

Table :1 the effect of each drug on oral glucose tolerance test in each group after 42 days treatment (mean +/-SD ) n=6
The percentage of blood glucose reduction on day 1 was 10.6%. This steadily increased to 77.1% on day 42. This was better than the standard control (glibenclamide) and standard control 2 (metformin) which showed 64.6% and 67.4% reduction respectively [Graph 1]. Similarly the overall mean percentage reduction of glucose was higher with test group (43.68%) compared to standard control 1 (29.91%) and standard control 2 (38.68%). The effect of test drug on oral glucose tolerance test (OGTT) after completion of treatment is better than the standard group [Table 1].

DISCUSSION AND CONCLUSION

The current study shows that fresh juice of Z. officinale produces a marked decrease in blood glucose levels in alloxan induced diabetic rats. Z. officinale has been shown to possess hypoglycemic activity in some previous studies, both in vivo [4] and in vitro. [9] These studies were conducted using both ethanolic and aqueous extract of Z. officinale. [10] The present study goes in accordance with the previous studies of Akhani SP et al and Al – Amin et al, with respect to the outcome on day 42. [11] It shows that Z. officinale has hypoglycemic activity, with its peak effect at the end of 6 weeks. But in the intervening periods of the study particularly on day 28, 35 and 42, Zingiber has showed better glycemic control than the standard drug glibenclamide and metformin, which is statistically significant (p < 0.05). Kar A et al study showed significant reduction of blood glucose level within 2 weeks, which supports our study. [12] In our study decrease in blood glucose level is significant with respect to glibenclamide but not with metformin.

In present study oral glucose tolerance test was performed after completion of 42 days treatment. It shows that glibenclamide, metformin and ginger extract reduced the blood glucose levels and the effect of ginger extract was significantly more efficacious than that of both glibenclamide and metformin. The exact mechanism of action is still unclear. Z.officinale decrease blood glucose level by inhibiting 5- HT receptor. The inhibition of 5 – HT induced hyperglycemia by Z. officinale suggests the presence of a 5 – HT 2A or 5-HT3 receptor antagonist in the juice of Z.officinale. Another study shows that ginger extracts were found to enhance the adipocyte differentiation. [9] Active constituent was identified as gingerol, which increases insulin sensitive glucose uptake. It is expected that ginger enhances the insulin – sensitivity and improves chronic disease, such as diabetes. However the exact mode of action still needs to be elucidated and requires further studies in both animal models and in human trials.

The present study has several draw backs. The study is very primitive in the parameters used. The study has been carried out only in one species of animals viz “rats” and needs to be extended to other animals as well. The effect on serum lipid levels, reactive oxygen species, atherogenesis β-cell pathology etc needs to be evaluated. Chronic toxicity studied to evaluate the effect of extract of Z. officinale on various hematological parameters, lipid profile, electrolyte profile, teratogenic and carcinogenic potential etc. have to be under taken for further evaluation.

At the end of the study it can be concluded that Z. officinale extract has hypoglycemic effect better than glibenclamide and metformin in diabetic rats with improved oral glucose tolerance. Thus Z. officinale could be used as an oral hypoglycemic agent in diabetes. However further extensive studies need to be done to confirm this activity in animal models as well as human trials.
REFERENCES