Effect of D-400, a Herbomineral Preparation on Lipid Profile, Glycated Haemoglobin and Glucose Tolerance in Streptozotocin induced Diabetes in Rats

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This study was undertaken to investigate D-400 a herbomineral formulation in streptozotocin induced diabetes in rats. Glycated haemoglobin, lipid profile and glucose tolerance test were studied. D-400 has an established hypoglycaemic effect in alloxan-induced diabetes in rats as well in non-insulin dependent diabetes mellitus patients D-400 treated group showed lower glycated haemoglobin, triglycerides and higher HDL levels. The hyperglycaemic response was blunted after administration of oral glucose in the same group.

Insulin deficiency can be produced in experimental animals by administering streptozotocin. The condition closely resembles insulin dependent diabetes mellitus or non-insulin dependent diabetes mellitus depending on the dosage. Very high blood sugar levels are reached in a short time and a stable diabetic state is reached within 24 hr when treated with streptozotocin. It also causes dyslipidaemia as seen by raised triglyceride, LDL and VLDL levels. Insulin deficiency can interfere with lipid metabolism. Hence, high plasma triglyceride levels and lowered HDL cholesterol are common findings in diabetes.

D-400 is an Ayurvedic herbomineral, formulation which contains herbal extracts and minerals of known antidiabetic effects. Its constituents include Shilajeet, Gymnema sylvestre, Momordica charantia, Tinospora cordifolia, Pterocarpus marsupium, Casearia esculanta, Eugenia jambolana, Ocimum sanctum and Balsamodendron mukul (Guggul).

Gymnemic acid from Gymnema sylvestre has proven efficacy in adrenaline and growth hormone induced hyperglycaemia. Tinospora cordifolia inhibits adrenaline induced hepatic glucose release. Pterocarpus marsupium extract has been reported to promote beta cell regeneration in pancreas. Along with Casearia esculanta, it also blocks glucose absorption from the gut. Momordica charantia potentiates tolbutamide action and promotes peripheral glucose utilisation.

A crystalline fraction extracted from the fruit of Momordica charantia causes hypoglycaemic effect similar to that of insulin in insulin dependent diabetes mellitus. Shilajeet has pancreatotrophic action and promotes weight gain. Eugenia jambolana has also been shown to have hypoglycaemic action. Ocimum sanctum potentiates insulin effects. It also contains Guggul, which is a known lipid lowering agent. D-400 contains in addition many other herbs and minerals which have a blood sugar lowering effects as mentioned in the texts of Ayurveda.

It has been seen in previous studies that D-400 has hypoglycaemic action both in animal and human studies, as well as beneficial effects in alloxan induced renal damage. It potentiates the effect of tolbutamide and is a safe preparation.

In this study the effects of D-400 on lipid profile and glucose tolerance test was studied.
Fifty inbred female Wistar rats of 2.5-3.0 months age and weighing 180 to 220 g were maintained at a room temperature of 22°C±2°C with 12 hr light and dark cycle. They were fed with synthetic diet and water *ad libitum*.

All rats received streptozotocin 50 mg/kg iv (via tail vein) after overnight fast on day 0 and blood sugar was evaluated on day 10. Among the surviving 41 rats, 36 with fasting blood sugar above 250 mg were selected for the study. They were divided into two equally matched groups of 8 each. One group received D-400 (1g/kg body wt.) once daily orally for 26 days and the other group received water and served as a control.

Table 1 shows the constituents of D-400, along with proportion of each ingredient and parts of the plant from which it is available.

<table>
<thead>
<tr>
<th>Table 1: Constituents of D-400 and proportion of each ingredient</th>
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<tbody>
<tr>
<td>Botanical name</td>
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<tr>
<td>----------------</td>
</tr>
<tr>
<td>Gymnema sylvestre</td>
</tr>
<tr>
<td>Momordica charantia</td>
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<tr>
<td>Tinospora cordifolia</td>
</tr>
<tr>
<td>Pterocarpus marsupium</td>
</tr>
<tr>
<td>Casearia esculanta</td>
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<tr>
<td>Eugenia jambolana</td>
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<tr>
<td>Ocimum sanctum</td>
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<tr>
<td>Balsamodendron mukul</td>
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<tr>
<td>Shilajeet (Purified)</td>
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After 21 days of the start of D-400, six rats from the trial group and 6 from the control group were sacrificed after collecting blood for laboratory investigations. Estimation was carried out for serum triglycerides, total cholesterol, HDL cholesterol and glycated haemoglobin.

After 26 days of treatment, glucose tolerance test was done in the remaining rats. At the end of the experiment, the results were analysed using unpaired Student’s ‘t’ test.

There was a significant reduction in glycated haemoglobin levels. HDL cholesterol level was significantly raised in the D-400 treated group as compared to the control group. However, the total cholesterol levels did not show significant difference. Triglyceride levels were significantly low (Table 2). D-400 also blunted the hyperglycaemic response to glucose challenge in streptozotocin treated rats as compared to the control group (Fig. 1).

<table>
<thead>
<tr>
<th>Table 2: Effect of D-400 on glycated haemoglobin, serum triglycerides and HDL-cholesterol in streptozotocin-induced diabetic rats</th>
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<tbody>
<tr>
<td>Parameters</td>
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<tr>
<td>Glycated haemoglobin (%)</td>
</tr>
<tr>
<td>Serum triglycerides (mg/dl)</td>
</tr>
<tr>
<td>HDL-cholesterol (mg/dl)</td>
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</table>

*p<0.05, **p<0.01 as compared to diabetic control
Oral hypoglycaemic agents and insulin have been used in the treatment of non-insulin dependent diabetes mellitus and insulin dependent diabetes mellitus. While these drugs reduce blood sugar levels, maintenance of euglycaemia for 24 hr and prevention of diabetic complications have not been achieved so far. Long-term use of oral hypoglycaemic agents can also have toxic effects on various organs.\textsuperscript{27}

Diabetes is associated with increased incidence of dyslipidaemia.\textsuperscript{28,29} While there have been drugs for both the conditions under trial and usage none is highly effective.

While sulphonylurea therapy is effective in lowering blood sugar levels, the accompanying elevated lipid levels are not significantly reduced as compared to the control subjects. Tolbutamide also decreased HDL-cholesterol levels.\textsuperscript{30} Some studies have suggested that administration of exogenous insulin aggravates the hyperinsulinaemia of NIDDM and may accelerate the progression of atherosclerosis. However, insulin therapy in NIDDM patients with significant dyslipidaemia helps controlling the accompanying lipid abnormalities.\textsuperscript{31,32} Plasma cholesterol and triglycerides are elevated in patients on conventional drugs confirming that the efficacy of these drugs decreases over a period of time.\textsuperscript{33} Oral hypoglycaemic therapy did not show any significant fall in glycated haemoglobin levels in diabetic patients.\textsuperscript{34}

D-400 is a herbomineral formulation with known hypoglycaemic action.\textsuperscript{19} It also protects the kidney in alloxan induced renal damage in rats.\textsuperscript{20} While the effect of D-400 on blood sugar levels has been established, there was need to establish its effects on other metabolic parameters. In this study, D-400 was found to be beneficial in dyslipidaemia and in addition, it effected improvement in GTT and glycated haemoglobin levels.

By this study we can conclusively state that D-400 has definite beneficial effects on blood sugar levels as well as in improving dyslipidaemia due to diabetes. It can serve as a good adjuvant in the present armamentarium of antidiabetic drugs. A number of multicentric trials have proved its hypoglycaemic action either alone or in combination with other hypoglycaemic agent and insulin. Thus, this drug proves to be a safe hypoglycaemic agent and might help in preventing diabetic complications.

REFERENCES
33. Goldberg M F, in *Diabetic retinopathy* edited by J R Lynn, Snyder, & A Vaiser (Grune and Stratton, New York) 1974, 47.