

DURING PRACTICE

## Evaluation of D-400 (Diabecon) as Anti-diabetic Agent - A Double Blind Placebo Controlled Trial in NIDDM Patients with Secondary Failure to Oral Drugs

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### Introduction

In patients with non insulin dependent diabetes mellitus (NIDDM) the disease can be usually controlled with diet and oral hypoglycaemic agents (OHA) like sulphonylurea and biguanides for approximately 10-15 years after diagnosis of diabetes. After this period a stage of secondary failure to OHA is reached and most patients require insulin injections. A number of herbal preparations and plant extracts have been used with varying degree of success in the management of NIDDM. Few studies have looked at these alternative therapies in patients with secondary failure to OHA. In this study, we report on the usefulness of an Ayurvedic/herbal preparation, D-400 (Diabecon) in NIDDM patients with secondary failure to OHA.

### Patients and Methods

The study group comprised 40 NIDDM patients with secondary failure to OHA attending the M.V. Diabetes Specialities Centre, Chennai.

### Inclusion criteria

1. NIDDM diagnosed according to WHO Study Group Classification<sup>1</sup>.
2. Age over 30 years.
3. Patients who are not obese ( weight not more than 20% above ideal body weight).
4. Failure to respond to OHA even in maximal doses of combination therapy i.e. Glibenclamide 15 mg plus metformin 1000 mg/day for over 3 months despite good diet control and absence of infections etc.

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***Results of a double blind placebo controlled trial of D-400 (Diabecon) — an Ayurvedic drug — in NIDDM with secondary failure to oral hypoglycemic drugs' show modest improvement in their diabetic control. There occurred a significant decrease in PP blood glucose and glycosylated haemoglobin levels.***

### Protocol and study design

The study was a double blind, placebo controlled trial of D-400 (Diabecon). forty consecutive NIDDM patients attending MVDSC, Chennai who satisfied the inclusion criteria were taken up for the study. The drug and placebo looked identical and were packed in different boxes coded A and B and the investigators did not know which was the drug and which was placebo until the codes were broken at the end of the trial. Patients were randomly allocated to either group A or B. There were equal number of patients in each of the treatment arms. The dose used was 2 tablets three times a day for 6 months. Patients in both groups received similar diet instructions from the dietician. A standard breakfast was provided for all study subjects in order to get reliable post-prandial measurements (taken at 90 minutes) and also to provide a standardized stimulus for the stimulated insulin and C-peptide measurements as de-

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scribed elsewhere<sup>1</sup>.

### Biochemical studies

The fasting and post-prandial plasma glucose measurements were made on a monthly basis while the glycosylated haemoglobin, insulin measurements and C-peptide assay were done at baseline, after 3 and 6 months of the trial.

All biochemical studies were done on Corning Express plus Auto Analyser (Croning, U.S.A.). Fasting and post-prandial plasma glucose (glucose oxidase method) were estimated using kits supplied by Boehringer Mannheim, Germany. Glycosylated haemoglobin (HbA1c) were estimated by HPLC method using the variant machine (Bio Rad, U.S.A.). Insulin and C-peptide assays were done by Elisa technique using Dako kits (Dako Diagnostics Ltd., Ela, UK) by methods described elsewhere.<sup>2-4</sup>

### Statistical analysis

All values are expressed as mean  $\pm$  SD. Differences between means were tested using paired T-tests. P value less than 0.05 was considered significant.

### Results

Of the 40 patients who entered the trial, there were 8 drop outs. The reasons for drop out were non compliance by the patients (n=3, two in placebo group and one in drug treated group), side effects like gastritis and skin rashes (n = 2, both in drug treated group). Three patients had very

high blood sugar values (all in placebo group) and had to be started on insulin and hence were excluded from the study. Thus a total of 32 patients completed the trial (17 in drug treatment group and 15 in placebo group).

Table 1 shows the results of the trial. In the diabecon treated group there was a decrease in both fasting and post prandial plasma glucose levels but only the latter reached statistical significance ( $p = 0.004$ ). There was however an increase in the plasma glucose levels in the placebo group.

There was a significant decrease in the glycosylated haemoglobin levels from  $9.2 \pm 2.1\%$  to  $8.2 \pm 1.2\%$  ( $p = 0.04$ ). In the placebo group there was no decrease in HbA1c levels.

The results of the plasma insulin and C-peptide assays showed interesting results. In the diabecon treated group, the plasma insulin and C-peptide levels (both fasting and stimulated) tended to be maintained, or slightly increased even at the end of 6 months. In the placebo group, however there was a decrease in both plasma insulin and C-peptide levels (both fasting and stimulated) by the end of the study. However due to small study numbers, these differences did not reach statistically significant level.

There were no significant changes in body weight, blood urea, serum creatinine or the haemogram profile in either placebo or drug treated groups.

### Discussion

This study reports on the anti-diabetic effect of D-400 (Diabecon) an Ayurvedic product, in NIDDM patients with

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**Table 1 : Results of the study**

Biochemical Parameters	Group	At Baseline	At end of study	p Value
Fasting plasma glucose (mg/dl)	Drug group	180 ± 44	161 ± 35	0.89 N.S.
	Placebo	170 ± 36	180 ± 50	
Post-prandial glucose (mg/dl)	Drug group	277 ± 43	244 ± 49	.004 S
	Placebo	268 ± 67	280 ± 81	
Glycosylated haemoglobin HbA1c (%)	Drug group	9.2 ± 2.	1 8.2 ± 1.2	.004 S
	Placebo	9.0 ± 1.1	9.2 ± 1.3	
Fasting insulin assay (µm/ml)	Drug group	8.9 ± 6.7	8.6 ± 6.7	.004 N.S.
	Placebo	6.3 ± 2.6	5.0 ± 2.9	
Stimulated insulin assay (µm/ml)	Drug group	24.8 ± 13.0	24.4 ± 13.8	N.S.
	Placebo	3.4 ± 13.8	19.3 ± 7.5	
Fasting C-peptide (pmol/ml)	Drug group	0.62 ± 0.20	0.84 ± .22	N.S.
	Placebo	0.51 ± 0.19	0.46 ± .17	
Stimulated C-peptide (pmol/ml)	Drug group	1.62 ± 0.81	1.82 ± 6.6	N.S.
	Placebo	1.51 ± 0.59	1.42 ± .75	

NS. - Not significant                      S - Significant

utes to the anti-diabetic properties, as all these have been claimed to have hypoglycaemic properties.

Although the improvement of diabetic control in this study is only modest, it must be remembered that all these are patients with secondary failure to OHA who were already receiving maximal doses of OHA. An improvement of HbA1c by 1% even in this group of patients with secondary failure to OHA is therefore encouraging.

The preservation of beta cell function noted in this study after use of Diabecon is also of great interest. Animal studies using D-400 have demonstrated regeneration of rat beta cells<sup>6</sup>. Obviously further studies are needed to establish the mechanism of ac-

secondary failure to OHA. There was a significant reduction in post-prandial plasma glucose levels and glycosylated haemoglobin levels in the drug treated group. Moreover the drug helps to maintain pancreatic beta cell function as measured by plasma C-peptide assay and plasma insulin levels. These results, although preliminary are encouraging.

D-400 contains *Gymnema Sylvester* (Meshashringi), *Eugenia Jambolana* (Jambu), *Tinospora Cordifolia*, *Pterocarups Marsupium*, *Ficus Glomeruta*, *Momordica Charantia* (Karela), *Ocimum Sanctum* (Vishnupriya), as its main ingredients. It is difficult to say which of these contrib-

tion of the drug.

It is also necessary to isolate the individual active principles and determine which of these compounds has the maximum antidiabetic activity, and probably use higher doses of that compound to produce better results.

Except for 1 patient each, who complained of gastritis and skin rash, there were no other side effects of the drug. This study hence confirms the earlier observation regarding the efficacy and safety of D-400 (Diabecon) in the treatment of diabetes<sup>6-8</sup>. However to our knowledge this is the first

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double blind placebo controlled trial and also the first to measure insulin and C-peptide levels to study the mechanism of action of the drug.

In summary, D-400 (Diabecon) an Ayurvedic drug, produces modest improvement in diabetic control in NIDDM patients with secondary failure to OHA.

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