Diabecon® DS (TABLET)

The beacon of hope for diabetics

with 4C advantage
- Offers the **Convenience** of 1 tablet twice daily dosage
- Offers dosage **Compliance** by the patient
- Offers tight **Control** of glycemic levels
- Offers the **Cost** benefit

- Significantly reduces FPG, PPG & Hb A1c levels
- Effectively reduces the risk of micro- & macrovascular complications
- In patients on sulfonylurea therapy:
  - Helps in reducing the dose
  - Prevents development of tolerance
  - Reduces the risk of secondary failure
- In patients on biguanide therapy:
  - Improves peripheral utilization of glucose without GI adverse events
  - Prevents micro- & macrovascular complications
- In patients on insulin therapy:
  - Helps in reducing the dose

Efficacy & safety of Diabecon is proven by a meta-analysis of 15 published clinical studies, wherein 435 patients were studied over a span of 11 years.

Newly detected type II diabetes
Type II diabetes with micro- and macrovascular complications

Dosage
As monotherapy: 1 tablet twice daily before food.
As adjuvant therapy: 1 tablet once daily before food.

The Himalaya Drug Company
Makali, Bangalore 562 123, India
ABSTRACT

The aim of this meta-analysis was to analyze the efficacy and safety of Diabecon tablets in 435 patients with diabetes mellitus (DM) as reported in 15 published clinical study reports, which also includes two double-blind studies, published between 1993 and 2004. Diabecon tablets were given as two tablets b.i.d or t.i.d for 12-60 weeks. Improvement in various parameters including fasting blood sugar (FBS), postprandial blood sugar (PPBS), glycated hemoglobin, plasma insulin levels as well as protective effects on diabetic complications including hyperlipidemia, microalbuminuria and diabetic retinopathy were evaluated. Changes in various study parameters from baseline values and values at the end of the study were pooled and analyzed cumulatively using paired 't' test. Statistical analysis was carried out using GraphPad Prism software (version 4.03). Of the 435 diabetic individuals, 332 received only Diabecon as therapy, 69 patients received Diabecon in addition to insulin/oral hypoglycemic agents (OHAs), and remaining 34 patients received placebo. Results of these studies indicate significant beneficial effects in patients given Diabecon tablets. Significant improvements were observed in FBS, PPBS, glycated hemoglobin, plasma insulin, microalbuminuria, etc. Similar results were observed in studies that used Diabecon along with OHA or insulin in OHA-resistant cases. Diabecon treatment also significantly improved lipid profile [total cholesterol, HDL-cholesterol (HDL-c), LDL-cholesterol (LDL-c)] as well as diabetic retinopathy and microalbuminuria. Adverse effects were seen in only two out of 332 patients treated with Diabecon; these were mild in nature and did not necessitate drug withdrawal. The findings of 15 clinical trials with Diabecon clearly indicated the beneficial effects in DM and related complications with additional advantage of long-term safety.

Key words: Diabecon, meta-analysis, diabetes mellitus

Despite advances in understanding the etiopathogenesis of noninsulin-dependent diabetes mellitus (NIDDM), there is an alarming increase in the number of insulin-resistant cases and failure of oral hypoglycemic agents (OHAs). There has been an explosive global increase in the number of people diagnosed with NIDDM worldwide in the past two decades. In India, an estimated 19.4 million individuals are affected by NIDDM, and is likely to go up to 57.2 million by the year 2025. Today, India leads the world with the largest number of diabetics in any given country. In the 1970s, the prevalence of diabetes among urban Indians was reported to be 2.1%, which has now risen to 12.1%. Also, there is an equally large pool of individuals with impaired glucose tolerance (IGT), many of whom will eventually develop NIDDM in the coming future.1

Diabetes can affect almost every physiological system of the body. The chronic hyperglycemia of diabetes is associated with long-term dysfunction, damage and failure of various organs (such as eyes, kidneys, nerves, heart and blood vessels). Individuals with undiagnosed NIDDM are also at higher risk for cardiovascular disease, coronary artery disease and peripheral vascular disease as compared with nondiabetics.

These individuals also have a greater likelihood of having dyslipidemia, hypertension and obesity. Early diagnosis and control of NIDDM is important in order to reduce the risk of later complications, such as cardiovascular events, visual loss, renal failure and limb amputations.2 Various herbs have also been found beneficial in the management of NIDDM and are gaining considerable recognition worldwide.3 The analysis of available data indicates that the use of herbs has increased during the past several years.4 Diabetes mellitus (DM) type 1 (type 1 diabetes, IDDM or juvenile diabetes) is a form of DM that results from autoimmune destruction of insulin producing β-cells of the pancreas. The subsequent lack of insulin increases blood and urine glucose levels that cause the classical symptoms of polyuria (frequent urination), polydipsia (increased thirst), polyphagia (increased hunger) and weight loss.5

Diabecon is a polyherbal formulation, which contain the extracts of Balsamodendron mukul, Gymnema sylvestre, Pterocarpus marsupium, Glycyrrhiza glabra, Casearia esculenta, Eugenia jambolana, Aphanopus racemosus, Boerhaavia diffusa, Sphaeranthus indicus, Tinospora cordifolia, Swertia chirata, Tribulus terrestris, Phyllanthus amarus, Gilêmera arborea, Gossypium heracleum, Berberis aristata, Aloe vera, Shilajit and powders of Momordica charantia, Piper nigrum, Ocimum sanctum, Abutilon indicum, Curcuma longa, Rumex maritimus and Tribkat as its main constituents.

Fifteen clinical trials conducted with Diabecon tablets in patients with DM between 1993 and 2004, were subjected to meta-analysis to analyze the efficacy as well as short- and
long-term safety. Meta-analysis is a two-stage process; first stage is data extraction from each study and calculation of the result for each study. The second stage involves deciding whether it is appropriate to calculate a pooled average result across studies. This gives greater weightage to the results from the studies that give more information as these are likely to be closer to the truth.7

Aim of the Study

To perform a meta-analysis on the efficacy and short- and long-term safety of Diabecon tablets in individuals with DM, as reported in 15 published clinical trials.

Material and Methods

Study Design: This is a cumulative meta-analysis of 15 published clinical trials of Diabecon in DM. Of these, 13 were open and two double-blind placebo-controlled trials (DBPCT). Details of clinical studies evaluated for the meta-analysis are mentioned in Table 1.8-22 Figure 1 depicts the trial selection process.

Inclusion Criteria: All published studies, which evaluated the role of Diabecon in DM, were included in the meta-analysis. These clinical trials were either controlled or open clinical studies and provided additional information (regarding long-term effects, prognostic factors, adverse effects and generalization). Studies that included at least 20 patients and reporting clinical outcome were considered for meta-analysis. There were no restrictions regarding sex, age or duration of disease.

Exclusion Criteria: Phase I studies were excluded.

Procedure of the Meta-analysis: In this meta-analysis of 15 clinical studies conducted between 1993 and 2004, the efficacy and safety of Diabecon was evaluated in 435 patients with DM at various reputed hospitals in India. Patients were given Diabecon at a dose of two tablets b.i.d or t.i.d. The duration of treatment varied between 12 and 60 weeks (Table 2). Improvement in laboratory results of various parameters viz. FBS, PPBS, glycated hemoglobin and insulin levels as well as its protective effects on diabetic

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Table 1. Clinical Studies Included in the Meta-analysis

<table>
<thead>
<tr>
<th>Investigators</th>
<th>Year</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yajnik VH, et al.</td>
<td>1993</td>
<td>43</td>
</tr>
<tr>
<td>Prasanna Kumar KM, et al.</td>
<td>1995</td>
<td>28</td>
</tr>
<tr>
<td>Dubey GP, et al.</td>
<td>1993</td>
<td>28</td>
</tr>
<tr>
<td>Mitra SK, et al.</td>
<td>1995</td>
<td>17</td>
</tr>
<tr>
<td>Maji D, et al.</td>
<td>1996</td>
<td>20</td>
</tr>
<tr>
<td>Ganguly D, et al.</td>
<td>1995</td>
<td>31</td>
</tr>
<tr>
<td>Maji D, et al.</td>
<td>1995</td>
<td>33</td>
</tr>
<tr>
<td>Yajnik VH, et al NV</td>
<td>1995</td>
<td>19</td>
</tr>
<tr>
<td>Singh AK, et al.</td>
<td>1995</td>
<td>29</td>
</tr>
<tr>
<td>Prasanna Kumar KM, et al</td>
<td>2002</td>
<td>15</td>
</tr>
<tr>
<td>Malhotra AK</td>
<td>1999</td>
<td>22</td>
</tr>
<tr>
<td>Mohan V</td>
<td>1998</td>
<td>40</td>
</tr>
<tr>
<td>Shri Kant, et al</td>
<td>2002</td>
<td>30</td>
</tr>
</tbody>
</table>

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Table 2. Diabecon Meta-analysis (n = 435)

<table>
<thead>
<tr>
<th>Study group</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabecon alone</td>
<td>332</td>
</tr>
<tr>
<td>Diabecon + OHA</td>
<td>69</td>
</tr>
<tr>
<td>Diabecon + Insulin</td>
<td>13</td>
</tr>
<tr>
<td>Placebo</td>
<td>34</td>
</tr>
<tr>
<td>Duration of treatment</td>
<td>15 (13 open and 2 double-blind placebo-controlled trials)</td>
</tr>
</tbody>
</table>

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Figure 1. Flow chart of patients included in the clinical studies

*Open label 13; DBPCT: 2.
complications including hyperlipidemia, microalbuminuria and diabetic retinopathy were evaluated. Incidence of adverse events during the study period and compliance to the drug treatment were also evaluated.

**Primary and Secondary Outcome Measures:** Primary predefined outcomes in most of these studies were laboratory improvement in various parameters including FBS, PPBS, glycated hemoglobin, plasma insulin and microalbuminuria. Secondary end points were safety and compliance to Diabecon therapy.

**Adverse Effects:** Incidence and type of adverse events (AEs) reported by various studies were tabulated separately. All AEs, either reported or observed by patients, were recorded with information about severity, duration, and action taken regarding the study drug. Relation of AEs to study medication was predefined as 'Unrelated' (a reaction that does not follow a reasonable temporal sequence from the administration of the drug), 'Possible' (follows a known response pattern to the suspected drug, but could have been produced by the patient's clinical state or other modes of therapy administered to the patient), 'Probable' (follows a known response pattern to the suspected drug that could not be reasonably explained by the known characteristics of the patient's clinical state), and 'Certain' (the AEs must have definitive relationship to the study drug, which cannot be explained by concurrent disease or any other agent).

**Statistical Analysis:** Statistical analysis was done according to the intention-to-treat principles. Changes in various parameters from baseline and at the end of the study were pooled and analyzed cumulatively using paired 't' test. Values are expressed as mean ± SD or as incidences of patients with or without symptoms. The minimum level of significance was fixed at 95% confidence limit and a two-sided p < 0.05 was considered significant. Statistical analysis was performed using GraphPad Prism, Version 4.03 for Windows, GraphPad Software, San Diego, California, United States (www.graphpad.com).

**Results**

**Effect of Diabecon on Various Laboratory Parameters in Patients with Diabetes Mellitus**

**Comparative Analysis of FBS:** FBS was evaluated in 273 out of 332 patients who were treated with Diabecon alone for a period of 12-60 weeks. The initial mean FBS significantly reduced from 176.10 ± 33.51 mg/dl to 119.70 ± 26.24 mg/dl (p < 0.0001). The mean FBS levels evaluated at the start and end of the treatment in 69 cases (56 cases resistant to OHAs received Diabecon in addition to OHAs and 13 cases received Diabecon in addition to insulin) showed 188.00 ± 59.09 mg/dl and 139.80 ± 54.88 mg/dl, respectively, with statistically significant reduction (p < 0.0241). Thirty-four patients received placebo in two double-blind placebo-controlled studies. The mean FBS analyzed at the start and end of treatment in these patients showed 143.80 ± 46.95 mg/dl and 140.30 ± 56.21 mg/dl, respectively, and was not found to be significant (Tables 3).

**Comparative Analysis of PPBS:** In the 287 cases treated with Diabecon alone, the PPBS levels significantly reduced from 263.40 ± 32.58 mg/dl to 163.10 ± 34.74 mg/dl at the end of treatment (p < 0.0001). Mean PPBS levels evaluated at the start and end of treatment in 69 cases (56 cases resistant to OHAs received Diabecon in addition to OHAs and 13 cases received Diabecon in addition to insulin) showed 258.80 ± 49.11 mg/dl and 198.70 ± 57.57 mg/dl, respectively with statistically significant reduction (p < 0.049). In 34 placebo-treated patients, the mean PPBS levels evaluated at the start and end of treatment showed 244.50 ± 33.23 mg/dl and 242.00 ± 53.74 mg/dl, respectively and was not found to be significant (Table 4).

**Analysis of Glycated Hemoglobin:** Of the 104 patients evaluated for glycated hemoglobin, the values reduced from 11.38 ± 2.23% at the start to 7.54 ± 0.55% at the end of the study, in 84 cases who received Diabecon, with statistically significant value of p < 0.028. In 20 patients who received placebo, there was no improvement in glycated hemoglobin (Table 5).

**Analysis of Fasting Insulin:** Fasting insulin levels were analyzed in 20 patients who had received Diabecon and the results showed that there was a significant increase in the plasma insulin levels from 15.69 ± 6.47 µmol/ml to 22.45 ± 10.44 µmol/ml after the treatment (p < 0.047). No significant improvement was observed in placebo-treated patients (Table 5).

**Analysis of Fasting C-peptide Levels:** Fasting C-peptide levels were analyzed in 20 patients receiving Diabecon. The results revealed an improvement in the C-peptide levels although not statistically significant probably due to the small sample size. In the placebo group, no improvement was observed (Table 5).

**Effect of Diabecon on Various Parameters Related to Diabetic Complications**

**Analysis of Microalbuminuria:** Microalbuminuria was analyzed in 41 patients on Diabecon. The results showed a significant reduction from 41.32 ± 8.00 mg/l before treatment to 30.10 ± 10.91 mg/l after treatment (p < 0.05, Table 5).

**Analysis of Lipid Profile:** Of the 15 clinical trials included, lipid profile was evaluated in five trials. In 90 patients
treated with Diabecon alone, the mean level of total cholesterol significantly decreased from 201.90 ± 15.40 mg/dl before treatment to 175.20 ± 11.30 mg/dl after treatment (p < 0.007). In six patients (three each of type 1 and type 2 DM) treated with Diabecon and OHAs/insulin, the mean total cholesterol levels significantly decreased from 182.83 ± 5.27 mg/dl to 166.50 ± 5.13 mg/dl (p < 0.01). HDL-c and LDL-c also decreased in the Diabecon-alone group with statistically significance of p < 0.05 and p < 0.004, respectively. In patients treated with Diabecon and OHAs/insulin, there was reduction, though not significant. Triglycerides showed a decreasing trend in patients treated with Diabecon alone but was not significant (Table 6).

**Adverse Effects:** The adverse reactions reported from the 15 clinical trials showed that out of 332 patients treated with Diabecon, one patient each reported skin rashes and gastritis with 0.60% (2/332) incidence (Table 8). None of the patients had hypoglycemic effects.

**Discussion**

Meta-analysis not only consists of combination of data but also includes epidemiological exploration and evaluation of results (‘epidemiology of results’). Thus, new hypotheses that were not proposed in single studies can be tested in meta-analyses. The number of patients included in clinical trials is often inadequate, as in some cases the required sample size may be difficult to achieve. Meta-analysis may, nevertheless, lead to identification of the most promising or urgent research question and may permit a more accurate calculation of the sample sizes needed in future studies.

Goals of a meta-analysis are to enable the overall significance of an effect to be evaluated, based on the multiple studies available, to estimate an overall effect size by combining the individual estimates in multiple studies.

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**Table 3. Comparative Analysis of FBS (Mean ± SD)**

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of patients</th>
<th>FBS (mg/dl)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Initial</td>
<td>12-24 weeks</td>
</tr>
<tr>
<td>Placebo</td>
<td>34</td>
<td>143.80 ± 46.95</td>
<td>140.30 ± 56.21</td>
</tr>
<tr>
<td>Diabecon alone</td>
<td>273</td>
<td>176.10 ± 33.51</td>
<td>119.70 ± 26.24</td>
</tr>
<tr>
<td>Diabecon + OHA/insulin</td>
<td>69</td>
<td>188.00 ± 59.09</td>
<td>139.80 ± 54.88</td>
</tr>
</tbody>
</table>

Statistical analysis: Paired ‘t’ test; NS = Not significant.

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**Table 4. Comparative Analysis of PPBS (Mean ± SD)**

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of patients</th>
<th>PPBS (mg/dl)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Initial</td>
<td>12-24 weeks</td>
</tr>
<tr>
<td>Placebo</td>
<td>34</td>
<td>244.50 ± 33.23</td>
<td>242.00 ± 53.74</td>
</tr>
<tr>
<td>Diabecon alone</td>
<td>287</td>
<td>263.40 ± 32.58</td>
<td>163.10 ± 34.74</td>
</tr>
<tr>
<td>Diabecon + OHA/Insulin</td>
<td>69</td>
<td>258.80 ± 49.11</td>
<td>198.70 ± 57.57</td>
</tr>
</tbody>
</table>

Statistical analysis: Paired ‘t’ test; NS=Not significant.

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**Table 5. Analysis of Glycated Hemoglobin, Fasting Insulin, C-peptide Levels and Microalbuminuria (Mean ± SD)**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>No. of patients</th>
<th>Treatment</th>
<th>Initial</th>
<th>24 weeks</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycated hemoglobin (%)</td>
<td>84</td>
<td>Diabecon</td>
<td>11.38 ± 2.23</td>
<td>7.54 ± 0.55</td>
<td>0.028</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>Placebo</td>
<td>9.00 ± 1.10</td>
<td>9.20 ± 1.30</td>
<td>NS</td>
</tr>
<tr>
<td>Fasting insulin (µmol/ml)</td>
<td>20</td>
<td>Diabecon</td>
<td>15.69 ± 6.47</td>
<td>22.45 ± 10.44</td>
<td>0.047</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>Placebo</td>
<td>6.30 ± 2.60</td>
<td>5.00 ± 2.90</td>
<td>NS</td>
</tr>
<tr>
<td>Fasting C-peptide levels (pmol/ml)</td>
<td>20</td>
<td>Diabecon</td>
<td>0.62 ± 0.20</td>
<td>0.84 ± 0.22</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>Placebo</td>
<td>0.51 ± 0.19</td>
<td>0.46 ± 0.17</td>
<td>NS</td>
</tr>
<tr>
<td>Microalbuminuria (mg/l)</td>
<td>41</td>
<td>Diabecon</td>
<td>41.32 ± 8.00</td>
<td>30.10 ± 10.91</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Statistical analysis: Paired ‘t’ test; NS = Not significant.

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Diabecon in Diabetic Retinopathy* (Mean ± SD)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Scores</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Initial</td>
<td>Final</td>
</tr>
<tr>
<td>Microaneurysm</td>
<td>2.23 ± 4.08</td>
<td>0.47 ± 0.65</td>
</tr>
<tr>
<td>Hemorrhages</td>
<td>2.03 ± 0.82</td>
<td>0.87 ± 0.83</td>
</tr>
<tr>
<td>Exudates</td>
<td>2.03 ± 0.82</td>
<td>1.32 ± 0.81</td>
</tr>
<tr>
<td>Retinitis proliferans</td>
<td>0.58 ± 0.93</td>
<td>0.55 ± 0.89</td>
</tr>
</tbody>
</table>

* = n = 30 both type 1 and type 2; Dose: Diabecon tablets, 2 t.i.d. for 12 weeks.

Table 8. Adverse Drug Reactions (ADR)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Total no. of patients</th>
<th>ADR</th>
<th>Incidence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabecon</td>
<td>332</td>
<td>2</td>
<td>0.60</td>
</tr>
</tbody>
</table>

Table 6. Lipid Profile Comparative Analysis of Diabecon Alone and Diabecon + OHA/Insulin (Mean ± SD)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Diabecon alone</th>
<th>Significance</th>
<th>Diabecon + Insulin*</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Initial</td>
<td>24 weeks</td>
<td>Initial</td>
<td>24 weeks</td>
</tr>
<tr>
<td>Cholesterol (mg/dl)</td>
<td>201.90 ± 15.40</td>
<td>175.20 ± 11.30</td>
<td>p &lt; 0.007</td>
<td>182.83 ± 5.27</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>185.00 ± 5.41</td>
<td>161.90 ± 15.15</td>
<td>NS</td>
<td>-</td>
</tr>
<tr>
<td>HDL-c (mg/dl)</td>
<td>55.46 ± 10.93</td>
<td>62.82 ± 14.13</td>
<td>p &lt; 0.05</td>
<td>51.60 ± 5.21</td>
</tr>
<tr>
<td>LDL-c (mg/dl)</td>
<td>128.90 ± 28.07</td>
<td>112.90 ± 24.54</td>
<td>p &lt; 0.004</td>
<td>168.04 ± 20.76</td>
</tr>
</tbody>
</table>

Total no. of trials: 5 open trials; Statistical analysis: Paired t-test. * = 4 type 1 and 86 type 2; 1 = All type 2 diabetes mellitus; NS = Not significant.

In the present meta-analysis, clinical trials and their details were tabulated and analyzed statistically. The outcome of this analysis showed marked improvement with Diabecon tablets in patients with DM.

Diabecon is a polyherbal formulation containing the extracts of Balsamodendron mukul, Gymnema sylvestre, Pterocarpus marsupium, Glycyrrhiza glabra, Casearia eucleula, Eugenia jambolana, Asparagus racemosus, Boerhavia diffusa, Sphaeranthus indicus, Tinospora cordifolia, Swertia chirata, Tribulus terrestris, Phyllanthus amarus, Gmelina arborea, Gossypium herbaceum, Berberis aristata, Aloe vera, Shilajit and powders of Momordica charantia, Piper nigrum, Ocimum sanctum, Abutilon indicum, Curcuma longa, Rumex maritimus, and Shilajeet as main constituents. Beneficial effects of Diabecon in NIDDM may be due to the synergistic action of its ingredients, which are well-documented.

The active ingredients of Gymnema sylvestre, which has been studied extensively for its beneficial action in DM are the gymnemic acids. Gymnema sylvestre has been shown to correct metabolic derangements in diabetic liver, kidney and muscle and reverse the hepatic pathological changes during the hyperglycemic phase by controlling hyperglycemia.

Results of different studies have shown that extracts of Gymnema sylvestre exert a stimulatory effect on insulin release by increasing the cellular permeability.

Gymnema sylvestre suppresses the elevated blood glucose level by inhibiting intestinal glucose absorption. Some studies have also shown its usefulness in regeneration or revitalization of residual β-cells in NIDDM and IDDM patients, enhancing endogenous insulin, which is supported by the raised insulin levels in serum after Gymnema sylvestre supplementation. Gymnema sylvestre is not only responsible for blood glucose homeostasis but also increases the activity of enzymes; thus affording a better utilization of glucose by insulin-dependent pathways (it controls the levels of phosphorylase, gluconeogenic enzymes and sorbitol dehydrogenase). It was also observed that Gymnema sylvestre increases uptake and incorporation of glucose into glycogen and proteins (hepatic, renal and muscular). The active ingredient of Pterocarpus marsupium is epicatechin and several studies have documented its antihyperglycemic activity. In one study, which assessed the effect of Pterocarpus marsupium, a decrease in blood sugar levels by 38% and 60% on the 15th and 30th day was observed; there was also a decrease in the hepatic and renal weights. Similarly, the renal glycogen content increased 10-folds, while the glycogen content in the hepatic and skeletal muscle decreased by 75% and 68%, respectively. Pterocarpus marsupium also re-normalized the activities of hexokinase, glucokinase and phosphofructokinase. Pterocarpus marsupium also exhibits α-glucosidase inhibitory activity comparable to that of metformin. Epicatechin increases the cAMP content of the islets, which is associated with increased insulin release, conversion of proinsulin to insulin and cathespin B activity. Eugenia jambolana is known to decrease hepatic glucose production, and prevent hyperglycemia (antihyperglycemic activity). It also has α-glucosidase inhibitory activity, and restores altered key metabolic enzymes involved in carbohydrate metabolism. The prevention of hyperglycemia is by enhanced peripheral utilization of glucose. Its neuroprotective actions protect from diabetic...
neuropathies. Diabecon effectively reduces risk of diabetic retinopathy. An effective adjuvant to conventional OHAs, Diabecon resolves, prevents and retards retinal and vitreal microaneurysm, and proliferative retinal changes. Eugenia jambolana has aldose reductase inhibitory activities; thus Diabecon prevents acceleration of cataract formation in diabetics. Diabecon effectively reduces risk factors of coronary artery disease by modulating lipid profile due to anticholesterolemic properties, reduces levels of free fatty acids and re-normalizes lipid abnormalities associated with NIDDM. Eugenia jambolana has also been reported for its potent antihypercholesterolemic activity.

A significant decrease in blood glucose and significant increase in plasma insulin levels were observed in both the normal and diabetic rats with daily oral administration of Boerhaavia diffusa. There was also a significant reduction of glycosylated hemoglobin and an increase in the total hemoglobin level. The herb is also shown to influence activities of the hepatic enzymes such as hexokinase, glucose-6-phosphate and fructose-1,6-bisphosphate. A significant increase in the hexokinase activity and a decrease in the activities of glucose-6-phosphate and fructose-1,6-bisphosphate were observed in Boerhaavia diffusa-fed diabetic rats. It also improved the oral glucose tolerance test and the effect was more prominent when compared with glibenclamide.

In both IDDM and NIDDM, morbidity and mortality from cardiovascular disease is greatly increased, possibly due to the increased serum lipid. Furthermore there is considerable evidence that control of serum lipids results in the reduction of the incidence of coronary heart disease. It is therefore important to understand the effects of the treatments used in diabetes on serum lipids and lipoproteins. In this combination of Diabecon, Commiphora mukul plays a complementary role by re-normalizing the serum lipids and cholesterol possibly due to its androgen receptor and glucocorticoid receptor antagonistic activities that potentially aids the person suffering from diabetes.

Different studies have reported that isolates and extracts of Momordica charantia contains hypoglycemic principles such as foetidin, momordin or charantin, which are an insulin-like peptide (polypeptide p-insulin). According to some investigators, this glucoside (polypeptide p-insulin) is useful for the management of both IDDM and NIDDM. Furthermore, the possibility exists that the plant extract mimics or improves insulin action at the cellular level, or that it even possesses an extra-pancreatic action. Furthermore, the possibility exists that the plant extract mimics or improves insulin action at the cellular level, or that it even possesses an extra-pancreatic action. Further, the possibility exists that the plant extract mimics or improves insulin action at the cellular level, or that it even possesses an extra-pancreatic action. Extract of Momordica charantia enhances insulin secretion from the islets of Langerhans, enhances peripheral glucose utilization, prevents glycogenolysis in liver tissue and increases serum protein levels. Significant inhibition of gluconeogenesis by Tribulus terrestris, along with reduction in plasma triglyceride levels have been documented. The antihyperglycemic activity of the extracts of Aloe vera has been extensively documented and the hypoglycemic effect of Aloe vera might be mediated via stimulation of synthesis and/or release of insulin from the β-cells of Langerhans. Piperine, the active alkaloid of Piper nigrum has been evaluated for its glucose regulatory efficacy and daily oral administration of the herb for 15 days lowered blood glucose concentrations and hepatic glucose-6-phosphatase enzyme activity.

Curcuminoids from Curcuma longa have an ameliorating influence on diabetic nephropathy, possibly by their ability to lower blood cholesterol levels. Analysis of documented data on enzymuria, albuminuria, activity on renal ATPases and fatty acid composition of renal membranes indicate that curcuminoids significantly arrest the progression of diabetic nephropathy.

Oxidative stress has a critical role to play in the initiation of hyperglycemia; it is also responsible for tissue damage and vascular endothelial dysfunction, which may lead to diabetic complications. Many of the herbs used in Diabecon act as powerful antioxidants. The antioxidant activities of Glycyrrhiza glabra, Eugenia jambolana, Curcuma longa, Casearia esculenta, Asparagus racemosus, Tinospora cordifolia, Berberis aristata, Phyllanthus amarus, Suertia chirata, Aloe vera and Curcuma longa have contributory role in the antihyperglycemic activity of Diabecon.

**Conclusion**

The outcome of this meta-analysis, which included 15 clinical studies, carried out between 1993 and 2004, in 435 patients with DM indicated significant clinical efficacy and safety of Diabecon tablets. The cumulative data analysis revealed significant improvement in laboratory parameters (FBS, PPBS, glycated hemoglobin, lipid profile, fasting insulin levels and microalbuminuria), which determine DM. Adverse events were negligible (<1%) in Diabecon-treated patients and did not necessitate withdrawal of the drug. The overall drug compliance was very good. Therefore, it may be concluded that Diabecon, a multi-ingredient formula, is effective and safe in patients with DM due to its antihyperglycemic effect and euglycemic phenomenon. Significant improvements in lipid profile, which included total cholesterol, HDL-c, LDL-c levels and in diabetic retinopathy and microalbuminuria were also observed in patients treated with Diabecon. Adverse effects were observed in only two out of 332 patients treated with...
Diabecon. These adverse effects were mild in nature and did not necessitate withdrawal of the drug. The findings of the 15 clinical trials with Diabecon clearly indicated the beneficial effects of drug in DM and related complications with additional information on long-term safety.

References