Effect of Diabecon (D-400), an Ayurvedic Herbomineral Formulation on Diabetic Retinopathy

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ABSTRACT
This study was conducted on a polyherbal formulation, Diabecon, in patients with diabetic retinopathy. Thirty patients with diabetic retinopathy were given Diabecon at a dose of 2 tablets, thrice daily for a period of 3 months. The patients were monitored according to eye testing for diabetic retinopathy subjects (ETDRS) and Airlie House Classification. The drug effectively helped in the resorption of retinal and vitreal haemorrhage as well as soft and hard exudates, and showed a promise in retardation of components producing venous dilatation, microaneurysm and promotion of neovascularisation. The results indicate that Diabecon is a safe drug to prevent complications such as retinopathy in diabetic patients.

INTRODUCTION
Diabetes mellitus (DM), a disorder of carbohydrate metabolism, is characterised primarily by hyperglycaemia and glycosuria with secondary anomalies of the metabolism of proteins and fats. Diabetic retinopathy, one of the common complications of diabetes, is a major cause of blindness in developed as well as developing countries. Probably the first written reference to diabetes is found in the Ebers Papyrus of ancient Egypt dating back to about 1550 BC. Diabetic retinopathy is a specific microvascular complication of both insulin dependant (type 1) and non-insulin-dependant (type 2) diabetes. The prevalence of retinopathy is strongly linked to the duration of diabetes. Nearly all type 1 diabetics and over 60% of type 2 diabetics will have developed some degree of retinopathy after 20 years of being diabetic.

Surveillance and treatment of diabetes-related complications should be a part of routine care among all diabetic patients. Intensive treatment designed to keep glucose levels close to normal has been shown to reduce the risk of developing long-term complications including retinopathy and slow down the progression of pre-existing retinopathy in insulin-dependent diabetes. The natural history and screening recommendations for diabetic retinopathy, nephropathy and neuropathy must be understood, since even advanced disease can be asymptomatic. Till date, no effective medical management has been developed and available treatment is confined to photocoagulation and vitreous surgery. Apart from the effective management of DM, drugs like aldose reductase inhibitors, antiplatelet agents, interferon, vasodilators and growth hormone inhibitors are in use with variable results. There is a great
need to find a drug that can be effective in the management of diabetic retinopathy. Diabecon is a combination of drugs containing Balsamodendron mukul, Gymnema sylvestre, Pterocarpus marsupium, Eugenia jambolana, Momordica charantia, Ocimum sanctum and Asparagus racemosus, etc. which are antidiabetic, safe, easily available and devoid of side effects.

MATERIALS AND METHODS
Thirty patients with non-insulin-dependent diabetes mellitus (NIDDM) and insulin-Dependent Diabetes Mellitus (IDDM) were included in the clinical study according to the classification and grading of retinopathy (Table 1). The study was conducted in the Department of Ophthalmology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India. The patients were examined and were subjected to modern diagnostic investigations like direct/indirect ophthalmoscopy, fluorescence angiography and fundus photography. The patients were graded according to the classification of diabetic retinopathy i.e. the Airlie House Classification and ETDRS.
Table 1: Features of Retinopathy Graded by Detailed Fundus Drawings

<table>
<thead>
<tr>
<th>type of lesion</th>
<th>0 Not present</th>
<th>1 Mild</th>
<th>2 Moderate</th>
<th>3 Advanced</th>
<th>4 Far advanced</th>
<th>5 End stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Angiopathy (A) Venous dilation, estimated by A/V ratio, and associated changes</td>
<td>A/V= &lt;1/1.5; normal retinal vessels</td>
<td>A/V=11.5 but &lt;1/2; uniform vessel caliber</td>
<td>A/V=1/2 but &lt;1/2.5; tortuosity and slight variation in caliber</td>
<td>A/V=125 but &lt;1/3; marked tortuosity and variations in caliber in less than 1/2 of the vascular tree</td>
<td>A/V=1/3 or even marked tortuosity and variations in caliber in 1/2 or more of the vascular tree.</td>
<td></td>
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<tr>
<td>Micro-aneurysms and haemorrhages (retinal edema and preretinal haemorrhage included), estimated by area of fundus involved</td>
<td>Not present</td>
<td>&lt;1/12 of fundus area and pin-point lesions</td>
<td>1/12 to &lt;2/12 often with larger intraretinal haemorrhage s</td>
<td>2/12 to &lt;3/12 intraretinal and occasionally preretinal haemorrhages</td>
<td>3/12 or over (if over, indicate how much); intraretinal and preretinal haemorrhages</td>
<td></td>
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<tr>
<td>Neo-vascularisation, estimated by area of fundus involved</td>
<td>Not present</td>
<td>Not present</td>
<td>&lt;1/12 of fundus area</td>
<td>1/12 to &lt;2/12</td>
<td>2/12 or over (if over 3/12, indicate how much)</td>
<td></td>
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<tr>
<td>2. Exudates (E), soft and hard, estimated by area of fundus involved</td>
<td>Not present</td>
<td>&lt;1/12 of fundus area</td>
<td>1/12 to &lt;2/12</td>
<td>2/12 to &lt;3/12</td>
<td>3/12 or over (if over 4/12 indicate how much)</td>
<td></td>
</tr>
<tr>
<td>3. Proliferative retinopathy (P), angiopathic (Pa) and nonvascular (Pn), estimated by area of fundus involved and extent of the arc formed around the macula</td>
<td>Not present</td>
<td>&lt;1/12 of fundus area of &lt;45° arc around</td>
<td>1/12 to &lt;2/12 or 45° to &lt;90° arc</td>
<td>2/12 to &lt;3/12 or 90° to &lt;180° arc</td>
<td>3/12 or over 180° arc or over (if over 4/12 or over 225°, indicate how much)</td>
<td></td>
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<tr>
<td>4. Vitreous haemorrhage (V), estimated by area of fundus obscured</td>
<td>Not present</td>
<td>&lt;2/12 of fundus area obscured</td>
<td>2/12 to &lt;4/12</td>
<td>4/12 to &lt;8/12</td>
<td>8/12 or over</td>
<td></td>
</tr>
</tbody>
</table>


All the patients were administered Diabecon, 2 tablets thrice daily for 12 weeks, in addition to conventional antidiabetic treatment. A regular follow-up was done at intervals of a month, for a period of 3 months. The mean grades of symptoms of each visit were recorded and compared with the baseline symptom scores.

**RESULTS**

The results were compiled and the effect of Diabecon on various symptoms was evaluated. The mean grade in micro-aneurysm before treatment was 2.228 ± 4.084. After 90 days, it was found to be 0.466 ± 0.650. There was a significant inhibition of micro-aneurysm (Figure 1). The mean grade in haemorrhages before treatment was 2.034 ± 0.815. After treatment it was found to be 0.866 ± 0.832.
The significant reductions in haemorrhages suggest that Diabecon helps in resolution of retinal and vitreal haemorrhages (Figure 2). A combined evaluation for both soft and hard exudates was conducted. The mean grade in exudates before treatment was $2.034 \pm 0.816$ whereas after treatment it was found to be $1.316 \pm 0.81$. The exudation was reduced significantly indicating the anti-inflammatory effect of Diabecon (Figure 3). The overall mean grade for retinitis proliferans before the start of treatment was $0.583 \pm 0.925$. After treatment the mean grade was $0.550 \pm 0.891$. Diabecon inhibited the proliferative changes in retina and controlled progressive retinal damage (Figure 4). Visual acuity of all the patients was recorded before the administering the drug and at the end of drug therapy. It was observed that 60% of patients showed improvement of vision by at least one line on Snellen's chart. On funduscopic examination, the improvement in neovascularisation and resolution of exudates was significant (Figure 5).
DISCUSSION
Diabetic retinopathy is a highly specific vascular complication of both type 1 and type 2 diabetes. The prevalence of retinopathy is strongly related to the duration of diabetes. After 20 years of diabetes, nearly all patients with type 1 diabetes and >60% of patients with type 2 diabetes have some degree of retinopathy. Diabetic retinopathy poses a serious threat to vision. In the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR), 3.6% of younger-onset patients (aged <30 years at diagnosis, an operational definition of type 1 diabetes) and 1.6% of older-onset patients (aged ≥30 years at diagnosis, an operational definition of type 2 diabetes) were legally blind. In the younger-onset group, 86% of blindness was attributable to diabetic retinopathy. In the older-onset group, where other eye diseases were common, one-third of the cases of legal blindness were due to diabetic retinopathy. Overall, diabetic retinopathy is estimated to be the most frequent cause of new cases of blindness among adults aged 20–74 years.

Screening strategies depend on the rates of appearance and progression of diabetic retinopathy and on risk factors that alter these rates. Vision-threatening retinopathy virtually never appears in type 1 patients in the first 3–5 years of diabetes or before puberty. Over the subsequent 2 decades, nearly all type 1 patients develop retinopathy. Upto 21% of patients with type 2 diabetes have recently been found to have retinopathy during initial diagnosis of diabetes and developed some degree of retinopathy over subsequent decades.

In general, the progression of retinopathy is orderly, advancing from mild non-proliferative abnormalities, characterised by increased vascular permeability, to moderate and severe non-proliferative diabetic retinopathy (NPDR), characterised by vascular closure, to proliferative diabetic retinopathy (PDR), characterised by the growth of new blood vessels on the retina.
and posterior surface of the vitreous. Pregnancy, puberty and cataract surgery can accelerate these changes.

Loss of vision due to diabetic retinopathy results from several mechanisms. Initially, central vision may be impaired by macular edema or capillary non-perfusion. Secondly, the new blood vessels of PDR and contraction of the accompanying fibrous tissue can distort the retina and lead to tractional retinal detachment, producing severe and often irreversible vision loss. Third, the new blood vessels may bleed, adding the further complication of preretinal or vitreous hemorrhage.

There are several epidemiological studies describing the onset and progression of diabetic retinopathy. The WESDR can serve as a representative model. The WESDR attempted to identify all diabetic patients treated by physicians in an 11-county area in Southern Wisconsin. Between 1979 and 1980, 1,210 patients with younger-onset diabetes and 1,780 patients with older-onset diabetes were enrolled the study. Patients had several clinical assessments, including seven-field stereo-fundus photographs and measurement of glycated haemoglobin. A 4-year follow-up examination repeated the fundus photographs. The WESDR found the relationship described above between onset of retinopathy and duration of diabetes. It also established that progression of retinopathy was a function of baseline retinopathy. The more severe the baseline retinopathy, the greater the frequency of progression to vision-threatening retinopathy. Conversely, among type 2 diabetic patients whose baseline photographs showed no retinopathy, there was less PDR or progression to severe macular oedema over 4 years. The WESDR epidemiological data were limited primarily to white Northern European extraction populations and may not be applicable to African-American, Hispanic-American, or Asian-American populations or to others with a high prevalence of diabetes and retinopathy.

There has been extensive research on potential risk factors for retinopathy. There is now a large and consistent set of observational studies documenting the association of poor glucose control and retinopathy.

In the Diabetes Control and Complications Trial (DCCT), a definitive relationship was demonstrated in type 1 diabetes between hyperglycaemia and diabetic micro-vascular complications, including retinopathy, nephropathy and neuropathy. A group of 1,441 patients with type 1 diabetes who had either no retinopathy at baseline (primary prevention cohort) or with minimal-to-moderate NPDR (secondary progression cohort) were treated either by conventional therapy or intensive diabetes management with three or more daily insulin injections or a continuous subcutaneous insulin infusion. In contrast, conventional therapy included one or two daily injections of insulin. The patients were followed for 4–9 years with a seven-field stereoscopic photography every 6 months. The DCCT showed that intensive insulin therapy reduced or prevented the development of retinopathy by 27% as compared with conventional therapy. In addition, intensive therapy reduced the progression of diabetic retinopathy by 34–76%. Early treatment with intensive therapy was most effective. However,
intensive therapy had a substantial beneficial effect over the entire range of retinopathy. This improvement was achieved with an average 10% reduction in HbA₁c from 8 to 7.2%.

The largest and longest study on patients with type 2 diabetes, the United Kingdom Prospective Diabetes Study (UKPDS), conclusively demonstrated that improved blood glucose control in these patients reduces the risk of developing retinopathy and nephropathy and possibly reduces neuropathy. The overall microvascular complications rate was decreased by 25% in patients receiving intensive therapy versus conventional therapy. Epidemiological analysis of the UKPDS data showed a continuous relationship between the risk of microvascular complications and glycaemia, such that for every percentage point decrease in HbA₁c (e.g., 9-8%), there was a 35% reduction in the risk of microvascular complications.

The results of the DCCT and UKPDS showed that while intensive therapy does not prevent retinopathy completely, it reduces the risk of the development and progression of diabetic retinopathy. This can be translated clinically to a preservation of eyesight and reduced need for laser treatment.

In this study, Diabecon used as an adjuvant with conventional treatment in NIDDM and IDDM patients had many benefits in patients with diabetic retinopathy. Diabecon resolved retinal and vitreal haemorrhages and its subsequent prevention. It also enhanced the absorption of hard and soft exudates by its anti-inflammatory properties. It produced retardation of microaneurysm and proliferative changes in the retina. The visual acuity in all patients improved, thereby slowing progressive visual loss. During the course of therapy and after the withdrawal of drug no adverse effects were reported.

CONCLUSION
Diabecon was an effective adjuvant for retinopathy in diabetic patients along with other conventional diabetic drugs, where resolution of retinopathy was also enhanced.

REFERENCES
