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Clinical efficacy of Diabecon in treatment of type 2 diabetes mellitus, in newly diagnosed diabetic patients and in those on drug treatment (Glibenclamide and Metformin) in Erbil Governarate-Kurdistan Region/ Iraq.

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Abstract:

Various herbs have been found beneficial in the management of type 2 diabetes and are gaining considerable recognition in the management of type 2diabetes worldwide. The present study was planned to evaluate the clinical efficacy of Diabecon (Herbal formulation) as a mono therapy and also as an adjunct with other oral hypoglycemic agents, in the management of type 2 DM. A total of 80 patients of either sex, between 30-68 years of age, in whom the diagnosis of type 2 diabetes was confirmed, and who were willing to give informed consent were included in the study.All enrolled patients were categorized into 4 groups. Group A included 20 newly diagnosed patients who were not consuming any oral hypoglycemic agent (OHA), while group B included 20 patients who were already consuming glibenclamide but were not controlled, while group C included 20 patients who were already consuming metformin but were not controlled and lastly group D included 20 patients who were already consuming glibenclamide and metformin combination but were not controlled. Patients from all the groups were advised to consume Diabecon at a dose of 2 tablets, three times daily (30 minutes) before meal for a period of 3 months, either as monotherapy for group A or as adjunct in the other three groups.

For all the patients, fasting blood glucose (FBG) and postprandial blood glucose (PPG) were assessed at the time of enrollment and thereafter every month, for 3 months, While Glycoselated haemoglubin (HbA1c), Total cholesterol (TC), Triglyceride (TG), High density lipoprotein-Cholesterol (HDL-c), Low density lipoprotein-Cholesterol (LDL-c), Basal serum insulin, C-peptide and body weight (BW) were assessed at the time of enrollment and after 3 months.

Diabecon significantly reduced FBG, PPG and HbA1c in all groups, which indicating an improved glucose homeostasis under the influence of this herbal formulation. There was a mild improvement in serum basal insulin and C-peptide level after using Diabecon either as monotherapy or as adjunct to glibenclamide, metformin or glibenclamide and metformin combination in those with type 2 diabetic patients who were not controlled by such oral hypoglycemic agent. Diabecon caused improvement of lipid profile including TC, TG and LDL-c to a variable extent in all groups except for group B. Its main effect is on the reduction of TC which could be beneficial since hypercholesterolemia is strongly associated with cardiovascular disease. A significant reduction in body weight was noticed at the end of the study among all groups except in group B who showed an increase in body weight but it was not significant. This weight reduction is a desired effect in type 2 diabetic patients and may play a role in improving insulin resistance. Most of the patients reported a sense of well-being and no side effect were recorded either by patient or observer except rare cases of gastric upset.

Therefore, it may be concluded that Diabecon is clinically effective herbal formulation in the management of type 2 diabetes either as a monotherapy in newly diagnosed patients or as an adjunct therapy in patients on conventional OHAs.

Key word: diabcone, Glibenelmide, metformin.

الخلاصة:

لقد تم إيجاد أعشاب مختلفة مفيدة في علاج النوع الثاني لمرض السكّري ولقد حازت هذه الأعشاب على إعتراف كبير في علاج هذا الداء حول العالم. ولقد تم تنظيم الدراسة الحالية لتقييم الكفاءة السريرية وسلامة علاج الـ(Diabecon خلطة عشبية) كعلاج أحادي وأيضا كمساعد لعوامل نقص سكر الدم الفموية الأخرى (OHAs) في علاج النوع الثاني من مرض السكري. ولقد تضمنت الدراسة على ما مجموعه 80 مريضا ومن كلا الجنسين، والذين تتراوح أعمارهم بين 30- 68 سنة، والذين تم تأكيد تشخيص النوع الثاني لمرض السكّري لديهم ومن الذين كانوا يرغبون لإعطاء الموافقة المطّلعة .

تم تصنيف جميع المرضى المسجّلين إلى 4 مجموعات. تضمّنت المجموعة (أ) 20 حالة مشخّصة حديثا والتي كانت لا تتناول أي عامل نقص سكر الدم الفموي، بينما تضمّنت المجموعة (ب) 20 مريضا والذين كانوا يتناولون علاج الـغليبينكلاميد ولكن لم يتم السيطرة على نسبة السكر في الدم، بينما تضمّنت المجموعة (ج) 20 مريضا الذين كانوا يتناولون علاج الـميتفورمين ولكن لم يتم السيطرة نسبة السكر في الدم وأخيرا تضمّنت المجموعة (د) 20 مريضا والذين كانوا يتناولون تركيبة من الـغليبينكلاميد و الـميتفورمين ولكن لم يتم السيطرة على نسبة السكر في الدم. ولقد تم نصح المرضى من كلّ المجموعات لتناول علاج الـ Diabecon على شكل جرعة من قرصين ثلاث مرات يوميا قبل وجبة الطعام ولمدة 3 أشهر، أمّا كعلاج أحادي للمجموعة (أ) أو كمساعد في المجموعات الأخرى الـثلاثة

تم فحص مستوى جلوكوز الدم في جميع المرضى قبل الإفطار الـ (FBG) ونسبة جلوكوز الدم بعد الأكل الـ (PPBG) في وقت التسجيل في البحث وفيما بعد كلّ شهر، ولمدة ثلاثة شهور، بينما يتم تقييم نسبة الجلوكوز في الهيموغلوبين الـ (HbA1c) و نسبة الكولوستيرول الكلية(TC) ، و نسبة الدهون الثلاثية المعقدة ال(TG) ، و نسبة الكولوستيرول البروتين الدهني عالي الكثافة (HDL-C) ، و نسبة الكولوستيرول البروتين الدهني واطيء الكثافة ال(LDL-C) ،ونسبة أنسيولين المصل الأساسي، ونسبة سي بيبتايد الـ (C-peptide) ووزن الجسم (BW) في وقت التسجيل وبعد 3 شهور.

خفّض علاج الـ Diabecon مستوى جلوكوز الدم قبل الإفطار الـ ,(FBG) مستوى جلوكوز الدم بعد الأكل الـ(PPBG) و نسبة الجلوكوز في الهيموغلوبين الـ (HbA1c) بشكل ملحوظ (إختلاف معنوي) عند جميع المجموعات بعد تناوله، مما يشير إلى وجود تحسن في توازن نسبة جلوكوز الدم بسبب تأثير هذه الخلطة العشبية. وكان هناك تحسن معتدل في مستوى أنسيولين المصل الأساسي و ونسبة سي بيبتايد بعد إستخدام الـ Diabecon أمّا كعلاج أحادي أو كمساعد لـغليبينكلاميد أو لـميتفورمين أو لـغليبينكلاميد و الـميتفورمين معاً عند أولئك المرضى المصابون بداء السكري من النوع 2 والذين لم يتم السيطرة على نسبة جلوكوز الدم من خلال العوامل نقص سكر الدم الفموية الأخرى (OHAs)

تسبّب علاج الـ Diabecon بتحسين التحليل الدهني والمتضمن نسبة الكولوستيرول الكلية(TC) ، ونسبة الدهون الثلاثية المعقدة ال(TG) ، ونسبة الكولوستيرول البروتين الدهني واطيء الكثافة ال (LDL-C) بنسب متغيّرة في جميع المجموعات ماعدا المجموعة (ب). إن تأثيره الرئيسي يكمن في تخفيض الكولوستيرول الكلية (الـ TC و الذي يمكن أن يكون مفيدة لكون زيادة الكولستيرول في الدّم تكون مرتبطة بقوة بأمراض الأوعية القلبية. ولقد لوحظ إنخفاض مهم في وزن الجسم عند نهاية الدراسة بين كلّ المجموعات ماعدا المجموعة (ب) والتي أظهرت زيادة في وزن الجسم لكنّها لم تكن مهمة.

يكون إنخفاض الوزن رغبة مطلوبة عند مرضى السكري من النوع الثاني والذي قد يلعب دور في تحسين مقاومة الأنسيولين. ولقد تحسن حال أغلب المرضى ولم يتم تسجيل أي آثار جانبية من قبل المرضى أو المراقب ماعدا بعض الحالات النادرة من الإضطرابات المعوية.

لذا، يستنتج من هذا بأن علاج الـ Diabecon هو عبارة عن وصفة عشبية فعّالة سريريا في علاج مرض السكري من النوع الثاني، كعلاج أحادي في المرضى المشخّصين حديثا وكعلاج مساعد في المرضى الذين يتعاطون عوامل نقص سكر الدم الفموية (OHAs) التقليدية.

Introduction:

Diabetes mellitus encompasses a group of heterogeneous disorders characterized by a defect in insulin secretion and increased cellular resistance to the action of insulin, resulting in hyperglycemia and other metabolic disturbances[1]. Hyperglycaemia occurs because of uncontrolled hepatic glucose output and reduced uptake of glucose by skeletal muscle with reduced glycogen synthesis [2]. This high blood sugar produces the classical symptoms of polyuria, polydipsia and polyphagia [3]. The main types of diabetes are:Type 1 diabetes Mellitus: accounts for 10% of cases globally. It results from a cell mediated autoimmune attack against pancreatic ß-cells [4]. Type 1 diabetic

patients are usually young (children or adolescents) and not obese when they first develop symptoms [2]. The classical symptom is weight loss in addition to the symptoms mentioned above [3].Type 2 diabetes Mellitus: accounts for 90% of diabetes cases globally [5]. Type 2 diabetes is characterized by disorder of insulin secretion and/or insulin resistance [6,7]. Traditionally, Type 2 diabetes is common in individuals over the age 40 years; it is often associated with obesity, decreased physical activity and heredity [8]. Treatment is initially dietary, although oral hypoglycaemic drugs usually become necessary, and about one-third of patients ultimately require insulin [2].

Diabecon is a herbomineral formulation containing *Gymnema sylvestre, Momordica charantia, Eugenia jambolana, Pterocarpus marsupium and Yasad bhasma* as its main ingredients, has been found to be effective in lowering blood glucose levels in experimental trials [9]. It has also been reported to reduce blood sugar [10,11.12,13] and triglyceride levels in several multicentric clinical trials [14]. The aim of the present study is to evaluate the clinical efficacy of Diabecon as monotherapy in newly diagnosed type 2 diabetic patients, and its combination with glibenclamide, metformin and also with both, in those diabetic patients who were not controlled with them, In regard of improving fasting blood glucose, postprandial blood glucose and glycosylated hemoglobin in Hawler province ,and also to show the effect of diabecon on serum basel insulin and c peptide , lipid profile and body weight.

Materials and Methods:

This study was carried out over seven months started from 12th December 2009 till the 13th July 2010, which was carried out in Layla Qassem diabetic center in Erbil city (Kurdistan region). The study included 98 type 2 diabetic patients (56 male and 42 female) with an age range from 30-68 year (mean 48±0.9). They were divided into four groups according that either they were newly diagnosed or not, and on which drug already they were.

The ninety eight patients (56 male and 42 female) with an age range from 30 to 68 years old (48 ± 0.9 and after losing some patients and some others were not responded just only eighty patients were remained and were divided into four groups according to that either they were newly diagnosed or not, and on which drug already they were.

Group A patients included twenty patients who were newly diagnosed as diabetic patients and put on two tablets of Diabecon three times daily as an oral anti diabetic drug. Group B patients included twenty patients who were already on glibenclamide (5ml once daily) and added two tablets of Diabecon three times daily as an adjuvant. Group C included twenty patients who were already on metformin (500 mg twice daily) and added two tablets of Diabecon three times daily as an adjuvant. Group D patients included twenty who were already on glibenclamide and metformin (same doses as before), then two tablets of Diabecon three times daily as adjuvants were added. All groups were followed up during treatment period after 4th, 8th and 12th weeks from starting Diabecon treatment.

Inclusion Criteria:

Only type 2 diabetic patients included in this study.

Exclusion criteria:

Patients with those having severe hypertension, a history of angina, myo-cardial infarction, chronic heart failure, chronic liver disease, cerebrovascular accident, renal failure, pregnancy, patients with severe diabetic complications , patients with endocrine causes like Cushing's syndrome were excluded from this trial. Also patients who were alcoholic or on other

medications that might affect the study were excluded.

Blood samples:

On the first day before starting treatment, venous blood from a fasting patient for at least eight hours was collected. The serum was utilized for determination of serum basal insulin, C-peptide, Total Cholesterol, Triglyceride, High density lipoprotein Cholesterol and low density lipoprotein cholesterol. Commercial kits were used for the measurements.

Estimation of HbA1c was based on latex immunoagglutination inhibition methodology (Crain,1987) [22].

The same procedure was carried out for patients after 12 weeks. While for fasting blood glucose and postprandial blood glucose blood is withdrawn by puncturing the finger on monthly basis and using glucose meter. Postprandial blood sugar is measured by same way and exactly after two hours from administering a standard test meal to the patient which was about 495 Kcal.

Statistics:

All the parameters results in all of the groups were represented as the mean ± the standard error (SE).Paired sample t-test was applied to compare between the values before treatment and their corresponding values after 1, 2, and 3 months of treatment and P values of < 0.05 were considered statistically significant.

Results:

Group A: patients treated with diabecon for three months.

Table-1: Comparison of Diapason effects on fasting blood glucose, postprandial blood glucose and glycosylated hemoglobin before and 1, 2, 3 months after treatment. (n=20).

Month treatment	FBG (mg/dl) (Mean ±SE)	PPG (mg/dl) (Mean ± SE)	HbA1c (%) (Mean ± SE)
Pretreatment	183.6 ± 12.2	220.2 ± 14.8	10.1 ± 0.4
After 1 month	161.8± 13.1***	187.6± 14.9**	
After 2 months	161.9± 11.7***	189.2 ± 15.8*	
After 3 Months	162.4± 10.1***	193.7 ± 15.6*	9.0 ± 0.5*

*P<0.05 as compared to pretreatment values

**P<0.01 as compared to pretreatment values

***P<0.001 as compared to pretreatment values.

Table-2: Comparison of Diabecon effects on Total Cholesterol, Triglyceride, High density lipoprotein Cholesterol and low density lipoprotein cholesterol before and three months after treatment. (n=20).

Month treatment	TC (mg/dl) (Mean ± SE)	TG (mg/dl) (Mean ± SE)	HDL-c (mg/dl) (Mean ± SE)	LDL-c (mg/dl) (Mean ± SE)

Pretreatment	229.6 ± 8.0	243.5 ± 20.5	44.7 ± 1.7	113.0 ± 8.2
After 3 months	193.4±8.2***	211.5 ± 17.9	37.5 ± 1.1**	105.8 ± 5.8

**P<0.01 as compared to pretreatment values.

***P<0.001 as compared to pretreatment values.

Group B: patients treated with diabecon for three months who were already on glibenclamide .

Table-3: Comparison of Diabecon effects on fasting blood glucose, postprandial blood glucose and glycosylated hemoglobin before and 1, 2, 3 months after treatment. (n=20).

Month treatment	FBG (mg/dl) (Mean ± SE)	PPG (mg/dl) (Mean ± SE)	HbA1c(Mean ± SE)
Pretreatment	173.7 ± 12.3	224.5 ± 11.5	9.7 ± 0.5
After 1 month	150.6 ± 9.2**	200.8 ± 12.7*	
After 2 months	149.1 ± 9.4**	191.8± 13.5**	
After 3 Months	153.5 ± 9.4**	185.4± 13.3**	8.7 ± 0.4*

**P<0.01 as compared to pretreatment values.

***P<0.001 as compared to pretreatment values.

Table-4: Comparison of Diabecon effects on Total Cholesterol, Triglyceride, High density lipoprotein Cholesterol and low density lipoprotein cholesterol before and three months after treatment. (n=20).

Month treatment	TC (mg/dl) (Mean ±SE)	TG (mg/dl) (Mean ±SE)	HDL-c (mg/dl) (Mean ± SE)	LDL-c (mg/dl) (Mean ± SE)
Pretreatment	217.9 ± 11.7	270.9 ± 24.3	46.0 ± 1.4	107.0 ± 7.6
After3 months	219.4 ± 10.0	260.2 ± 14.9	43.2 ± 1.5	116.6 ± 6.7

Group C: patients treated with diabecon for three months who were already on metformin

Table-5: Comparison of Diabecon effects on fasting blood glucose, postprandial blood glucose and glycosylated hemoglobin before and 1, 2, 3 months after treatment. (n=20).

Month treatment	FBG (mg/dl) (Mean ± SE)	PPG (mg/dl) (Mean ± SE)	HbA1c (%) (Mean ± SE)
Pretreatment	144.1 ± 9.5	179.1 ± 13.8	8.4 ± 0.4
After 1 month	130.6 ± 6.6*	166.6 ± 10.9*	
After 2 months	130.4 ± 7.1*	158.7 ± 9.8**	
After 3 Months	127.5 ± 5.7*	149.5 ± 7.1**	7.5 ± 0.2**

*P<0.05 as compared to pretreatment values

**P<0.01 as compared to pretreatment value

Table-6: Comparison of Diabecon effects on Total Cholesterol, Triglyceride, High density lipoprotein Cholesterol and low density lipoprotein cholesterol before and three months after treatment. (n=20).

Month treatment	TC (mg/dl) (Mean ± SE)	TG (mg/dl) (Mean ± SE)	HDL-c (mg/dl) (Mean ± SE)	LDL-c (mg/dl) (Mean ± SE)

Pretreatment	208.5 ± 8.7	232.8 ± 16.0	47.4 ± 1.7	102.2 ± 5.2
After 3 months	191.0 ± 8.4	228.3 ± 13.1	42.1 ± 1.2*	94.6 ± 6.2

*P<0.05 as compared to pretreatment values.

Group D: patients treated with diabecon for three months who were already on both glibenclamide and metformin.

Table-7: Comparison of Diabecon effects on fasting blood glucose, postprandial blood glucose and glycosylated hemoglobin before and 1, 2, 3 months after treatment. (n=20).

Month treatment	FBG (mg/dl) (Mean ± SE)	PPG (mg/dl) (Mean ± SE)	HbA1c (%) (Mean ± SE)
Pretreatment	144.7 ± 8.0	174.6 ± 12.9	8.1 ± 0.3
After 1 month	139.6 ± 8.3	159.0 ± 9.5*	
After 2 months	137.6 ± 7.7*	151.8± 10.9**	
After 3 Months	138.6 ± 6.8*	149.2 ± 9.0**	7.2± 0.2***

*P<0.05 as compared to pretreatment values
**P<0.01 as compared to pretreatment values
***P<0.001 as compared to pretreatment values

Table-8: Comparison of Diabecon effects on Total Cholesterol, Triglyceride, High density lipoprotein Cholesterol and low density lipoprotein cholesterol before and three months after treatment. (n=20).

Month treatment	TC (mg/dl) (Mean ± SE)	TG (mg/dl) (Mean ± SE)	HDL-c (mg/dl) (Mean ± SE)	LDL-c (mg/dl) (Mean ± SE)
Pretreatment	**216.8 ± 9.8**	**269.3 ± 15.8**	**44.1 ± 2.0**	**112.7 ± 5.3**
After 3 months	**197.8 ± 9.1***	**242.1 ± 17.3**	**39.6 ± 2.2****	**101.1±4.8****

*P<0.05 as compared to pretreatment values
**P<0.01 as compared to pretreatment values

Discussion:

Many herbs have been shown to have hypoglycemic action in animals and humans [15]. However, none (alone) is accepted as a dependable antidiabetic drug. Careful formulation of herbal remedies is very essential. Diabecon, is one of such formulation [16], which is a polyherbal formulation with established blood sugar lowering effects [10,11.17], has a combination of herbs with antidiabetic and hypolipidemic actions [18]. They include *Eugenia jambolana, Momordica charantia, Pterocarpus marsupium, Tinospora cordifolia, Ficus glomerulata, Gymnema sylvestre, Ocimum sanctum and Shilajeet* in this formulation which are well-recognized, easily available indigenous preparations and possessing significant blood sugar lowering properties [14,19], in type 2 diabetic patients[20].

Diabecon has also been found to reduce serum cholesterol and triglyceride levels in many experimental trials [21] and in several multicentric clinical trials [14]. These properties of Diabecon encourage us to investigate the efficacy of Diabecon among diabetic patients in Hawler province.

By this study we observed Diabecon caused significant reduction in the FBG and PPG of the newly diagnosed type 2 diabetic

patients and also of those type 2 diabetic patients who were already on glibenclamide, metformin or glibenclamide and metformin combination but were not controlled by these oral hypoglycemic agent. Therefore, it can be concluded that Diabecon is clinically effective in the management of type 2 diabetic patients, as a monotherapy in newly diagnosed patients and as an adjunct with glibenclamide, metformin or glibenclamide and metformin combination in those patients who are on these drugs but were not controlled, in Hawler province.

As well as Diabecon significantly reduced glycosylated haemoglobin level in all the groups, and this is an indication of its overall glycaemic control due to the effect of Diabecon. There was a mild improvement in serum basal insulin and C-peptide level after using Diabecon either as monotherapy or as adjuvant to glibenclamide, metformin or glibenclamide and metformin combination in those type 2 diabetic who were not controlled by such oral hypoglycemic agent.

Generally Diabecon has a good effect on lipid profile especially on serum total cholesterol and this could be beneficial either by preventing or delaying cardio-vascular complication due to dyslipidemia.

Diabecon also causes weight reduction in type 2 diabetic patients and this weight reduction is important since it could help in improving of insulin sensitivity and as a result leads to improving blood glucose level.

Conclusion:

By this study we can conclusively state that Diabecon has definite beneficial effects on fasting blood glucose and postprandial blood glucose levels when used as monotherapy in newly diagnosed type 2 diabetic patients or as adjuvant to glibenclamide, metformin or glibenclamide and metformin combination in those type 2 diabetic who were not controlled by such oral hypoglycemic agent, in Erbil city, There were no clinically significant adverse reactions, either reported by patients, or observed by the investigators and the overall compliance to the treatment was good. Therefore, it may be concluded that Diab econ is clinically effective in the management of type2 diabetic patients, as a mono therapy in newly diagnosed patients and as an adjunct in patients on conventional oral hypoglycemic agents.

References:

1- Umpierrez Guillermo, E. and Kitabchi Abbas, E. Management of type 2 diabetes evolving Strategies for Treatment. Obstetrics and Gynecology Clinics. June; 2001. Vol. 28 (2).Pp:1-16.

2- Rang, H.P.; Dale, M.M.; Ritter, J.M.; and Flower, R. J. Rang and Dale's Pharmacology. 6th ed. CHURCHILL LIVINGSTONE: ELSEVIER. 2007.

3- Cooke, D.W.and Plotnick, L.Type 1 diabetes mellitus in pediatrics. Pediatr Rev; 2008. Vol. 29. Pp: 374-84.

4- American Diabetes Association. Clinical Practice Recommendations. Diagnosis and classification of diabetes mellitus. Diabetes Care; 2004.Vol. 27. Pp: 5-10.

5- Masur, K.; Therenod, F. and Zanker, K. Diabetic and cancer. Epidemiological evidence and molecular links. Front diabetes; 2008. Vol. 19.Pp: 1-18.

6- DeFranzo, R A.; Bonadonna, R.C., and Ferrannini, E. Pathogenesis of NIDDM .In Albert KGMN, Zimmet P, Defronzo RA editors. International Text book of Diabetes Mellitus. 2nd ed. Chichester: wiley, 1997. Pp: 635-712.

7- Reaven, G. M. The role of insulin resistance in human disease. Diabetes. 1998. Vol. 37. Pp: 1595-1607.

8- Eriksson, T.; Saloranta, C.and Widen E. Non-esterified fatty acids, do not contribute to insulin resistance in

persons at increased risk of developing type 2 diabetes mellitus. Diabetologia. 1991. Vol. 34. Pp: 192-197.

9- Anturlikar, S. D.; Gopumadhavan, S.; Chauhan, B.L.and Mitra, S.K. Effect of Diabecon (D-400), a herbal formulation on blood sugar of normal and alloxan-induced diabetic rats. Indian J Physiol Pharmacol; 1995. Vol. 39 (2). Pp: 95-100.

10- Dubey, G.P.; Agrawal, A.and Singh, A. Evaluation of Diabecon (D-400), an indigenous herbal preparation in diabetes mellitus. Ind. J. Int. Med. 1993. Vol. 3 (6). Pp: 183-6.

11- Yajnik, V.H.; Acharya, H.K.; Vithlan, M.P.and Yajnik, N.V. Efficacy and Safety of Diabecon (D-400), A Herbal Formulation, in Diabetic Patients. The Indian Practitioner; 1993. Vol. 12 (46). Pp: 917-922.

12- Maji, D.and Singh, A.K. Clinical trial of Diabecon (D-400), a herbomineral preparation in diabetes mellitus. Jour. Diab.Assoc.India. 1995. Vol. 1. Pp: 1-4.

13- Mitra, S.K.; Hemavati, T.S.and Mohan, A.R. Rajesh. Anti-diabetic effect of Diabecon (D-400), an Ayurvedic Herbal Preparation in non-insulin dependent Diabetes Mellitus Patients. The Antiseptic. 1995. Vol. 92 (9). Pp: 342-345.

14- Maji, D. and Singh, A. K. Effect of Diabecon (D-400), an Ayurvedic Herbal Formulation on Plasma Insulin and C-Peptide Levels in NIDDM Patients. The Indian Practitioner; 1996. Vol. 1 (49). Pp: 69-73.

15- Singh, A.K.and Shaw, B.P. Evaluation of D-400–A Herbomineral Preparation on Patients with Diabetes Mellitus. The Antiseptic. 1995. Vol. 7 (92). Pp: 263-265.

16- Seshaiah, V. and Sundaram, A. Moses A, Balaji, V. Ramkumar, Mitra SK. Diabecon (D-400) in the Treatment of Diabetes Mellitus. The Indian Practitioner. 1997. Vol .7 (50). Pp: 589-593.

17- Mohan, A. R. ; Chauhan, B. L.; Mitra, S.K. and Kulkarni, R. D. Safety, efficacy and tolerability of Diabecon (D-400), an Ayurvedic hypoglycaemic formulation, in healthy male medical students. Current Medical Practice. 1993. Vol. 37 (12). Pp: 245-255.

18- Kumar Prasanna, K.M.; Dharmalingam Mala,and Kulkarni Kala Suhas. Evaluation of Clinical Efficacy of Diabecon with Reference to Insulin-Levels in Diabetic Patients. Medicine Update. 2002. Vol.7. Pp: 67-70.

19- Yajnik, V.H.; Acharya, H.K.and Yajnik, N.V. Efficacy of D-400 in NIDDM Patients having Microalbuminuria. The Indian Practitioner; 1995. Vol. 9 (48). Pp: 851.

20- Ganguly, D.; Banerjee, T.; Singh, A. K, and Mitra, S.K . Effect of D- 400, an ayurvedic herbomineral formulation in non-insulin dependent diabetes mellitus cases. The Antiseptic. 1995. Vol. 92 (12). Pp: 460–462.

21- Mitra, S. K.; Gopumadhavan, S.; Muralidhar, T. S.; Anturlikar, S.D. and Sujatha, M.B. Effect of D-400, a herbomineral preparation, on lipid profile, glycated haemoglobin and glucose tolerance in streptozotocin induced diabetic rats. Indian J. Exp. Biol; 1995c. Vol. 33. Pp: 798-800.

22- Craine, J. E. Latex agglutination immunoassays, Americam laboratory; 1987. Vol. 5 (3). Pp: 34.