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Clinical Evaluation of Antidiabetic Polyherbal Ayurvedic Formulation- *Madhujeevan Churna* using *Stevia rebaudiana*

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Abstract

The present study aims at evaluating the clinical efficacy of antidiabetic polyherbal Ayurvedic formulation Madhujeevan Churna containing Stevia rebaudiana on 45 NIDDM patients. Madhujeevan Churna was formulated using known Ayurvedic antidiabetic herbs- Curcuma longa, Aegle marmelos, Gymnema sylvestre, Azadirachta indica, Emblica officinalis, Salacia reticulata, Syzygium janbolanum, Momordica charantia and Stevia rebaudiana. Mild to moderate diabetics, whose glucose lowering effect is unsatisfactory, despite the use of conventional oral hypoglycemic were selected. The blood glucose levels were estimated by reported methods initially and then after 15 days on OPD basis upto 90 days. Clinical examination, including patient's compliance and acceptability of the formulation was also evaluated. Madhujeevan Churna has shown marked glucose lowering effect. Stevia rebaudiana has enhanced the antidiabetic activity of other drugs, and masked their bitter taste. The result reveals that Madhujeevan Churna can be a safe, acceptable and effective alternative or adjuvant to the conventional oral hypoglycemic.

Key words: *Formulation development, Madhujeevan Churna, Antidiabetic, Polyherbal Ayurvedic formulation, Stevia rebaudiana, Clinical evaluation*

INTRODUCTION

As per Ayurveda, food in human body is transformed first into 'Rasa' and then successive process involve its conversion into blood, muscle, fat, bone marrow, and reproductive elements. Thus, food is basic to all metabolic transformations and life activities. Lack of nutrients and improper transformation of foods, leads to a variety of disease conditions. In the present situation, medical scientists are conducting researches in ayurvedic remedies for degenerative, psychosomatic disorders and life style related diseases. Diabetes is also one of life style related disease. Diabetes mellitus result when your body doesn't adequately regulate the sugar levels in your body. There are two types of diabetes. Type 1 (insulin dependent diabetes mellitus (IDDM) usually occurs before age 30. Type 2 (Non Insulin Dependent Diabetes Mellitus (NIDDM)) usually occurs over 40 years of age and accounts for about 90 percent of cases. More than a million new cases are diagnosed in India and rest of the world each year. There is an estimated 143 million people worldwide suffering from diabetes[1] up to 50 percent of the people who have diabetes does not know it in early stages. For many years they remain undiagnosed. It may affect people of all ages, races and income levels.

The treatment available for the insulin dependent diabetes mellitus (IDDM) patients requires daily injection of insulin to prevent catabolic cascade culmination in diabetic ketoacidosis, coma, and death. Non insulin dependent diabetes mellitus (NIDDM) reprints about variety of diabetic states in which the β – cells are usually sufficient to oppose the ketogenic actions of glucagon but not to prevent hypoglycaemia.

The use of oral hypoglycaemic drugs may be effective in controlling blood glucose level, but may not prevent all the complications of diabetes.[2] Therapy of NIDDM involves modifications of life style and diet, an exercise and use of oral hypoglycaemic agents. Tolbutamide, chlorpropamide, phenformin, metformin etc. have shown their effectiveness in management of type II diabetes[3,4]. From this brief overview of diabetes classification and modern therapy, it can be seen that current methods of treatment for all types of diabetes mellitus fail to achieve the ideals of hypoglyclemia and the prevention of diabetic complications. Promising fields of research such as pancreatic transplants offer little hope to the majority of the world's diabetics, for whom such procedures will be too expensive and difficult to obtain. Most developing countries cannot

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even afford adequate conventional therapy. Further, problems with conventional therapy in developing countries include supply, storage and injection, dietary control and complications from malnutrition, a lack of trained healthcare workers and the lack of education for the patients. In such situations, the incidence of diabetes related mortality is far greater than in well served urban areas.

Therefore, there is a clear need for alternate sources of both oral and parenteral antidiabetic drugs and alternate strategies for diabetes therapy. Various plants screened for blood glucose lowering activities show that traditional antidiabetic plants gave positive results. It is clear from these observation that the study of traditional remedies for diabetes mellitus may yield and excellent return in potential sources of antidiabetic drugs.

A great medicinal flora, ***Gymnema sylvestre*** has shown miraculous role in the control of diabetes mellitus in both IDDM and NIDDM. The pharmocodynamic and clinical studies suggest that the hypoglycemic activity of *Gymnema* may be mediated through stimulation of insulin release (and possibly by pancreatic regeneration or repair), stimulation of enzymes responsible for glucose uptake and utilization and (or inhibition of intestinal absorption of glucose[5,6,7,8]. A clinical trial recently conducted in the US provides further support for the use of *Gymnema* in the management of diabetes[9].

Aegle marmelos The aqueous extracts of the stem and root bark are used[10] to treat malaria, fever, jaundice, and skin diseases such as ulcers, urticaria, and eczema. In pharmacological trials, both the fruit and root showed antiamoebic and hypoglycaemic activities.

Curcuma longa Curcuma longa contains[11] an essential oil (5%), an alkaloid, starch grains, yellow matter curcumins and other curcuminoids, turmeric oil (5-8%), turmerol, a coporioc acid (0.1%) as a free acid, and veleric acid (0.1%). *C. longa* showed[12] antidiabetic activity. ***Azadirachta indica*** A recent study[13] showed that Neem leaf extract is effective hypoglycemic agent and can act only in presence of suitable stimuli like glucose load. They suggested that Neem leaf extract basically act through potentiation of insulin secretion in response to glucose load and thus, is helpfully NIDDM ***Salacia reticulata*** Anthocyanidines, catechins, phenolic acids, quinines, triterpene quinine and related triterpenoids (celastroloids), mangiferin, gutt- percha, and dulcitol, salacinol and kotalanol[14].

Syzygium jambolinum Delphinidin- 3 gentiobioside, malvidin- 3 laminaribioside, petunidin- 3 gentiobioside, glucose, fructose, gallic acid, malic acid, Eugenia triterpenoids A and B, oleanolic acid (fruits), jamboline, myricyl alcohol, quercetin. Fruits- juice used[15] as carminative, diuretic, stomachic beneficial in chronic diarrhea and spleen enlargement.

Momordica charantia In the clinical evaluation, carries out at Wagharkar Hospital and Research institute, it was found that karela in combination with other herbal hypoglycemic drugs showed marked reduction in blood glucose level and no side effect were observed[16].

Emblica officinalis[17] *Emblica officinalis* extract also have been shown to possess powerful antidiabetic, lipid-lowering, antisclerotic, hepatoprotective and anticancer activities. ***Stevia rebaudiana*** *S. rebaudiana* contains sterioside and rubaudioside as diterpene glycosides [18]. These are 300 times [19] sweeter than sugar. It also contains sequiterpene lactones[20] that are responsible for bitter after taste. S. rebaudiana acts as anti-diabetic[21], anti-hypertensive [22], anti-lipidemic [23], anti-yeast, antibacterial[24], anticaricinogeni[25] and antifungal. It is considered as GRAS by USFDA[26].

All these medicinal plants have been claimed to be useful in controlling diabetes mellitus. These plants have been reported as antidiabetic and antioxidant activities in normal glucose, loaded and Alloxan induced diabetic rats and rabbits.

MATERIALS AND METHODS

Materials

The crude drugs were procured from Satara Ayurvedic Arkashala, Satara, as authentic sources. Also, these crude drugs were authenticated by Prof. B.D. Mohite, Botany department, SGM College, Karad, (M.S.) India. (Authentication voucher number- SGM-KARAD(M.S.,INDIA)/BOTANYDEPT./B.D.PATIL/05).

Methods

The dried rhizome of *Curcuma longa*, the dried leaves of *Aegle marmelos*, *Gymnema sylvestre*, *Azadirachta indica* and *Stevia rebaudiana,* the dried fruit of *Emblica officinalis* and *Momordica charantia* and the dried bark of *Salacia reticulate* and *Syzygium janbolanum,* were powdered and passed through sieve no. 22 to form a moderately coarse powder. The following formula was developed using suitable quantity of *S. rebaudiana* as natural sweetener and nutraceuticals. Each 100 gm of *Madhujeevan Churna* contains-

G. sylvestre	15gm
C. longa	15gm
S. zambolanum	15gm
S. reticulata	10gm

Emblica officinalis	10gm
A. marmelos	10gm
M. charantia	10gm
A. indica	15gm
S. rebaudiana	10.0%

Human safety trial

Clinical trial of antidiabetic potential of *Madhujeevan Churna* without *Stevia* (*MC*) and *Madhujeevan Churna* with *Stevia* (*MCS*) was studied with the permission of Ethical committee on human safety trail.

The study was conducted at Dr. Shyam Ayurvedic Clinic, 35 b/7 Mangalwar Peth, Karad- 415110 (M.S.) India, between 12/2/2008 to 12/5/2008 on OPD basis. 45 patients of NIDDM comprising males and females were included in clinical trial after written consent.

Inclusion Criteria – A total number of 45 patients of either sex between 35 to 65 years of age in whom the diagnosis of NIDDM was confirmed and who are willing to give written consent were included in the study. The WHO diagnostic criteria (1980) were considered for the diagnosis of NIDDM for newly diagnosed patients.

Exclusion Criteria – Insulin dependent diabetes mellitus patients (IDDM), NIDDM patients with acute complications of diabetes were excluded from the clinical study. Pregnant and lactating women, patients with concomitant severe illness requiring other medicating, patients with severe hypertension and the patients having history of severe unstable angina, myocardial infarction, CVAS, renal failures, and those patients who were not willing to give written consent were also excluded from the study.

Study design- 50 patients were required for the study but 30 NIDDM patients were selected by keeping *in vivo* the exclusion criteria. Patients whose, diabetes is uncontrolled despite of oral hypoglycemic use that is who are already receiving antidiabetic therapy but are still diabetic were selected for the study, after taking the written informed consent.

The study was conducted in patients of either sex. The patients who are diagnose diabetic as per WHO criteria age was between 18- 70 years and who were willing to giving written informed consent, and interested to take herbal medicine were included in inclusion criteria. Exclusion criteria was applied to those patients who requires insulin therapy or anticipating to required insulin therapy during the period and who have a serious disorder of heart, liver, kidney bone marrow and who have a history of alcoholism, drug abuse, psychosis, antagonistic personalities, poor compliance with study protocol. Patients were advised by physician to take 10gm *Madhujeevan Churna* twice a day after meal. Patients were receiving/ administered this daily dose with maintenance of other conditions given by physician. During therapy with *Madhujeevan Churna*, diet, exercise and medications were advised to be maintaining as per usual routine of the patients. Clinical assessment was done at the time of enrollment in the study and then every after 15 days for the period of 3 months. Each assessment was comprisement of history and clinical examination. Principle, sign, symptoms and detailed of adverse event during the previous 15 days were recorded. Laboratory investigations such as fasting and post prandial venous blood glucose concentrations was assets at the time of commencement of the study and after every 15 days to monitor the progress up to 3 months. Similarly glycosylated haemoglobin level was assets before end of the study. The % haemoglobin was determined by measuring absorbance of 415 nm for the glycolated Haemoglobin fractions and the total Hb fractions calculating the ratio of absorbance and comparing the ratio to that of calibrator carried by separation procedure.

Methods

Blood and urine glucose level were estimated by glucose oxidase method and glycosylated haemoglobin method. The blood of patients was collected in oven dried test tube and few mg of sodium fluoride was added as an anticoagulants, (sodium fluorides prevents gluconeogenesis). The blood with anticoagulant in all the test tube was subjected for centrifugation to collect the plasma. This plasma was immediately transferred with the help of dropper to another set of test tube. This was used for measurement of glucose level. Phosphate buffer, peroxidase fasting reagent and glucose oxidase reagent were prepared and used for the analysis of samples. These tests were performed in the pathological laboratory.

The age of the patients ranged from 35 to 65 mean ± standard deviation. The diabetic diet and necessary exercise were explained to the patients. The venous blood samples were collected initially and after every fifteen days. Every time both the fasting and post prandial samples were collected. The patients wishing to continue their previous conventional drugs were allowed to do so. After every fifteen days the blood sugars and urine sugar estimation as well as the compliance and acceptability was assessed on the basis of symptoms experienced by the patient.

Each patient was advised to consume 5 gm of *Madhujeevan Churna* two times a day before half an hour of principle meals on empty stomach with water. This dose was irrespective of their age, chronicity and body weight. Besides blood and urine sugar estimation, the improvement in the NIDDM symptoms were assessed using a predefined symptoms score seal for polyuria, weakness, burning sensation of palm and nocturnal enuresis, from 0 to III. (O=absent, I=mild, II=Moderate, III=sever).

Glucometer – Strips method

Lower and higher range regent pad reaction of glucostix reagent strips are based on the reaction of the enzyme glucose oxidase which is specific for glucose. Glucose oxidase catalyses the oxidation of glucose[27] in blood by oxygen in the atmosphere, producing gluconoic acid and hydrogen peroxide. In the presence of peroxidase, the ortho toludine in the reduced form is oxidized by the hydrogen peroxide producing a shade of green colour on the lower range pad with intensity proportional to the glucose concentration. On the higher range pad, in the presence of peroxidase, the amino antipyrine and the dichloro hydroxybenzene sulfonate in reduced form are oxidized by the hydrogen peroxide producing a shade of orange colour with and intensity proportional to the glucose concentration [28].

Estimation of Glycosylated Hemoglobin (GH_b)

a. Haemolysate Preparation

0.5 ml of lysing reagent dispensed into tubes labeled. CALIBRATOR, CONTROL, SAMPLE, 1, 2 etc. Then 0.1 ml of well mixed blood sample placed into the appropriate labeled tube. It is mixed until complete, lysis is evident. This is allowed to stand for 5 minute.

b. Glycohemoglobin Separation

Cap is removed from Glycohemoglobin ion exchange resin tubes and labeled as CALIBRATOR, CONTROL, SAMPLE, 1, 2 etc. Then 0.1 ml of hemolysate from the step A placed in to the appropriately labeled resin tube. Filter separator is positioned in the tube so that the rubber sleeve is approximately 2 cm above from the liquid level. Then the tubes are fixed on the rocker or rotator and mixed continuously for 5 min. then the tubes were removed from the rotator. Filter separator was pushed on to the tube until the resin was firmly packed. Supernant liquid poured into another tube or directly into a cuvette for absorbance measurement. The instrument was adjusted to zero absorbance at 415 nm using de ionized water as the blank. Then the absorbance values for calibrator, control sample 1,2 etc. were recorded. These reading are for glyco – hemoglobin.

c. Total Hemoglobin fractions

0.5 ml deionised water dispensed into the tubes labeled calibrator, control, sample 1,2 etc. 0.02 ml of hemolysate from step A placed into the appropriately labeled tube and mixed well. By using deionised water the instrument was adjusted to zero absorbance to 415 nm. The absorbance values for calibrator control and samples were recorded.

RESULTS AND DISCUSSION

The polyherbal Ayurvedic compound *Madhujeevan Churna* has shown marked glucose lowering effect as shown in Table No. 1. There was considerable change in the fasting blood sugar levels and post prandial blood sugar levels. Also there was a considerable change in the urine sugar percentage in fasting as well as the post prandial urine samples. The clinical symptoms polyuria, weakness, burning sensation of palms and soles, nocturnal enuresis were also minimized significantly, within the three months period. *Stevia rebaudiana* has enhanced the antidiabetic activity of others drugs, and masked their bitter taste. There was no clinically significant adverse reaction, either reported by the patients or observed by the investigators. The overall compliance to the treatment was excellent. All the patients reported a sense of well being. The result reveals the *Madhujeevan Churna* a polyherbal Ayurvedic power can be a safe acceptable and effective alternative or adjuvant to the conventional oral hypoglycemic agents.

Patients No. (2 and 17) have withdrawn themselves from the study because of their blood sugar level were under control. Patients No. (20 and 32) has withdrawn from study because of high glucose level. In Patient No. (33, 34, 39 and 42) there is slight elevation of blood glucose level in the forth 15 days due to taking extra sweet. Similarly in patient no. (31, 35, 36, 37 and 38), there is slight elevation of blood glucose level in the 3rd 15 days. During the study, the patients (No. 43, 44, 45, 46 and 47) served as control subjects (only, receiving the study drug). The opinion from all patients with there blood glucose level readings from pathology lab were collected and assets. It was observed that patient no. 1 to 3, 7, 8, 11, 12, 15, 19, 22, 25 and 29 showed a significant decreasing elevated blood glucose level as compare to other patients when given these formulations alone. While 4, 5, 6, 9, 10, 13, 14, 16, 18, 23, 24, 26, 27, 28 and 48 showed remarkable antidiabetic activity as compare to other patients with this formulation but having adjunct therapy with their previous half dose of allopathic agents. A wonderful thing in case of patient's no. 21 and 22 proves a significant antidiabetic effect without insulin.

Table No 1. Effect of *Madhujeevan Churna* containing natural sweetener on blood glucose level of NIDDM patients.

Pt no.	Age in year	Sex	Initial reading	15 days	15 days	15 days	15 days	15 days	15 days
1	71	Male	202.4 (FS)	201	198	175	171	168	155
			258.1 (PP)	255	244	231	202	198	164
2	78	Male	198 (FS)	195	172	164	154	135	131
			223 (PP)	220	214	218	205	196	171
3	46	Male	152 (FS)		134	101	144.4	114.8	118.5
			193.5 (PP)	192.9	192.5	148	192.5	137	196.2
4	76	Male	121(FS)	118	98	102	101	108	105
			140 (PS)	137.5	133.5	129.5	128	125	124
5	49	Male	299.6 (FS)	213	190	132	119	179	105
			373.6 (PS)	284	273	205	162	265	203
6	67	Female	212.1 (FS)	209	240	210	196.2	170	190
			248.3 (PS)	284	232	212	209	208	205
7	58	Male	244.6 (FS)	241	205	198	199	201	192
			306.1 (PS)	287.8	217.4	203.7	170.7	155.5	155.5
8	61	Male	104 (FS)	133.3	90.47	85.71	104.76	102	101.5
			128.5 (PS)	180.7	130.57	133.3	142.85	101.4	125.9
9	65	Female	148.9 (FS)	141	131	132	128	122	109
			204.5 (PS)	212.8	203.8	174	155	156.8	248.7
10	58	Male	148.3 (FS)	142	129	128	109	105	108
			224.9 (PS)	275	216.6	184.9	223	177.7	159.2
11	63	Female	116 (FS)	115	118	105	105.5	102	102.2
			176.1 (PS)	104.3	142.8	137.3	134.5	178.3	175.1
12	50	Female	180.2 (FS)	178	171	164	168	158	133.3
			244.1 (PS)	225	254	196	177.7	207	233.3
13	61	Male	192 (FS)	181	175	168	169	165	151
			296 (PS)	333	382.9	270	266	270	125.9
14	78	Male	144.3 (FS)	140.2	138	139	127	124	119
			280.7 (PS)	358.3	300	287	237	258	283.3
15	60	Female	202(FS)	198	204	192	167	151	152
			226.4 (PS)	186	230	122	175.1	121	119
16	65	Female	140 (FS)	160	105	118.5	115	114	116
			200 (PS)	233.5	188.7	155.5	154	152	153
17	45	Male	276.5 (FS)	290.8	215	211	210	208	200
			300.1 (PS)	380	396	259.8	250	248	238
18	52	Male	204.1 (FS)	172.3	204.1	201.2	198	190	188
			266.2 (PS)	243.7	328.1	256	204	198	175
19	62	Male	179.2 (FS)	179.5	171.6	162.9	158.4	149	140
			226.2 (PS)	221.2	248.3	148	137	130	125
20	50	Male	106.3 (FS)	105	117.2	112.9	104.3	101	98
			148.6 (PS)	152.8	128.7	121.2	120.5	118	103
21	65	Male	154.3 (FS)	152	101	159	141	135	130
			192.8 (PS)	195	105	144	127	120	118
22	57	Male	214 (FS)	298	261	254	232.1	202.3	200
			266 (PS)	398	282.6	225.4	225.2	178.1	168
23	60	Male	228 (FS)	216.1	213.3	180.2	171.4	169.2	158
			344.8 (PS)	341.6	400	280	240.3	266.6	252
24	49	Male	192.1 (FS)	181	177	173	166	152	146
			256.7 (PS)	337.5	151.4	107.4	88.8	90	95
25	62	Male	164.3(FS)	161.2	162.4	159.2	155.4	150	148
			188.3 (PS)	256.7	164.8	218.5	188.8	190	185

contd..

Pt no.	Age in year	Sex	Initial reading	15 days	15 days	15 days	15 days	15 days	15 days
26	42	Male	186.2(FS)	149.1	148.2	144.2	136.1	135	130
			236.6 (PS)	254.1	258.3	185.1	177.1	166	157
27	66	Male	152.1 (FS)	14.2	138	125.9	121	118	116
			178.6 (PS)	208.3	162.5	148.1	144	138	130
28	75	Male	118(FS)	118	115	113	109	106	102
			176.6 (PS)	304.1	176.1	172.1	171	151	146
29	66	Female	209(FS)	210	199	195	191.3	172.4	168
			216 (PS)	148	118.2	119.2	121.2	121.1	118
30	63	Male	204(FS)	198	196	188	187.3	185	175
			208 (PS)	124	138.6	94.7	136	134	133
31	58	Male	103.3 (FS)	101	98	99	96	98	97
			156.2 (PS)	152.5	109.1	108.4	105.2	102	101
32	70	Female	121.1 (FS)	119	118	117	116.1	112	101
			156.5 (PS)	138.3	131	128	124	122	118
33	55	Female	104.8 (FS)	102	101	98	99.1	97.2	95
			132.4 (PS)	131	130	125.5	125.2	128	126
34	54	Female	98.6 (FS)	98.4	92.5	98.2	97.1	97.1	95
			128.6 (PS)	132	124	121.5	121	118	109
35	69	Male	204.3 (FS)	203	198	194	193.1	189	182
			252.6 (PS)	242	239	235.2	235.1	213	203
36	49	Male	204.2 (FS)	203	197	177	178	175	169
			246.2 (PS)	242.5	241	236.5	238.2	228	215
37	46	Male	98.4 (FS)	98.3	98.4	97.5	97.6	97.2	96
			132.8 (PS)	131.5	129.4	128.2	128.4	122.2	121
38	50	Male	160 (FS)	159	154	156	158	157	148
			292.1 (PS)	258.5	245.8	235.2	235.1	224	216
39	40	Male	132(FS)	129	128	129	129	118	105
			144.7 (PS)	142.2	142.3	141.9	141.5	136	132
40	62	Male	198(FS)	181	185	174	163	161	143
			201.2 (PS)	198.3	191.2	178.4	171.7	172.1	169
41	44	Male	152.7(FS)	149	152.5	148	147	147.1	135
			172.1 (PS)	168.2	165.2	161.3	158.4	158.2	149
42	80	Male	136(FS)	135	129	122	122.5	118.3	108
			160.7 (PS)	158.8	149.2	147.1	145.5	148.1	141
43	63	Male	276.9 (FS)	261	258	248	232	235	231
			302(PS)	272	248	245.5	245	248	225
44	52	Female	245(FS)	241	235.2	222.1	218	218.5	205
			284 (PS)	281	198	195	178	103.3	102
45	55	Female	247 (FS)	241	238	239	226.1	202.5	201
			298.6 (PS)	292	245	202	198	175.5	168

FS: Fasting sugar
PS: Prandial sugar

But these two patients who have been receives insulin treatment previously shows a better impact of this formulation with insulin. Actually the physician could not stop insulin treatment for these two patients.

The fundamental cause of NIDDM is unknown. The course and complication of the disease are greatly variable. Control of blood sugar on a twenty four hours basis the desired goal in the management of diabetes mellitus, so as to prevent or delay its secondary complications. Diet, physical exercise and inclusion of dietary fiber have been used with limited success. In view of the reduction in blood glucose and glycosylated hemoglobin, it may be postulated that the treatment with *Madhujeevan Churna* may lead to regeneration / repair of pancreatic damage in type II diabetes mellitus. Due to number of side effects of allopathic therapy, a lot of people are turning towards ayurveda for the treatment of various diseases and syndromes. Diabetes mellitus is a

metabolic disorder and patient suffering from diabetes mellitus has to take medication life long. Ayurveda, the traditional Indian System of medication pays dividends in the long run when the medication has to be continued for a very long period of time. The main aim of therapy is up root the diseases than to cure the symptoms only, as in most of the treatments in Allopathy.

Antidiabetic activity of polyherbal formulation (*Madhujeevan Churna*) was studied on 30 NIDDM patients. During the study period the patients have responded well to the study drug. Form the overall study it reveals that Blood sugar level of diabetic patients goes on decreasing every after 15 days when treated with test samples. After 3 months, Blood sugar of maximum patients reacted to normal level some patients shows a significant and remarkable effect but adjuvant therapy of Allopathy. It such patients are treated with prolonged therapy of antidiabetic polyherbal formulation then there will be no longer time to find safe and effective herbal remedy for such disease as an alternative therapy. From the study of their blood glucose level, it is clear that polyherbal formulation (Madhujeevan *Churna*) having marked antidiabetic activity. The polyherbal formulation Madhujeevan *Churna* has shown marked improvement in controlling the blood sugar level. There was a significant reduction in dosage requirement of oral hypoglycemic drugs observed in patients who were treated with adjuvant therapy. Patients (no. 21 and 23) have withdrawn themselves from the study who already treating with insulin.

Ayurveda is one of the major healthcare systems developed since human civilization in the Indian subcontinent which is based upon the experiences with nature and natural resources. Scientific evidences to prove the rationale of using this formulation in health care are essential to develop and prevent cultural heritage[29]. Ayurveda is based on empirical knowledge of Indian medicinal professional for a long time. However there is a long gap regarding all information due to lack of documentation. Therefore, scientist felt it urgent to make the information evidence based. Pharmaco- vigilance study is the best way established the evidence based medicine. Pharmaco- vigilance study indicates the clinical trial of any known drug for its known activity, which is yet to be established under modern scientific techniques[30].

Present study, therefore, aimed to investigate developed *Madhujeevan Churna* clinically, which are being used for a long time for its effect of blood sugar level. This developed *Madhujeevan Churna* with dried powder of leaves of *S. rebaudiana* highlights the better impact of antidiabetic potentials on NIDDM patients. It means that *Stevia* is most essential adjuent in herbal preparations especially those are used to treat diabetes.

CONCLUSION

On the basis of this clinical study it can be concluded that *Madhujeevan Churna* may elicit its hypoglycemic action by enhancing insulin release from pancreatic B islets and also accelerate glucose uptake and peripheral glucose utilizing process. This lends evidence to the use of *Madhujeevan Churna* as a potent antidiabetic. Diabetic mellitus is metabolic disorder and patients suffering from diabetes mellitus have to take medication life long time[10]. Due to number of side effect of allopathic therapy, patients are oriented towards herbal medicines for the treatment of various diseases. *Madhujeevan Churna* can be used as alternative adjuvant medicine to treat diabetes very well. Use of *Stevia* rebaudiana as a natural sweetener and nutraceutical in sweet polyherbal formulations is a new vista to provide a safe effective, palatable, suitable, elegant, acceptable preparation.

It was concluded that the developed formulation was pleasant and acceptable for all patients as it contents *S. rebaudiana* as natural sweetener in appropriate quantity and from pathological findings, it remarks that *Madhujeevan Churna* has significant improvement in controlling the blood sugar level in patients. Depending upon diabetic condition this product can be used as totally alternative or may be as adjuvant with other therapy. One of the most important achievements of this product is that the product has better impact on patients health. All the side effects which are related with allopathic are diminished with this adjuvant therapy. Patients feel a freshness and wellbeing without any harmful effects.

Future plan

Detailed phytochemical investigation, standardization and stability studies of these products according to ICH guidelines will be carried out to obtain acceptable and palatable preparation to consumers. As *Stevia* acts as antidiabetic, antihyperlipidemic, antihypertensive, nutraceutical its role in antidiabetic polyherbal formulation will be significant as compare to other preparations.

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