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Effect of an Herbal Fromulation (Indrayanadi Yog) on Blood Glucose Level

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Abstract

Now a days Diabetes Mellitus is a matter of global concern as its worldwide incidences increasing day by day along with various complications. As the gravity of complications leads the patients towards a hatred life, that's why now a days its treatment is a challenging one for all physicians. Although it is a non-communicable disease it is considered to be one of the five leading causes of death universally. Recently there is a global focus on searching an appropriate cost effective, non-toxic, plant based antihyperglycaemic agents. The present study was planned to verify the effect of fruit juice of Citrulluscolocynthis and powder of Trachyspermum ammiseeds in compound form on different biochemical parameters like F.B.S., P.P.B.S., HbA1c of Diabetic patients in order to evaluate its ani-hyperglycaemic activity.

Keywords: Antihyperglycaemic, HbA1c, Citrulluscolocynthis, Trachyspermum ammi.

Introduction

Diabetes mellitus is a metabolic disorder ¹characterised by hyperglycaemia, glycosuria, Hyperlipemia, Negative Nitrogen balance in some times Ketone urea. Our body utilize energy from food to keep working just like a vehicle needs fuel for running. Diabetes affects the body's ability to use energy. For this purpose body produce a hormone called insulin that "unlocks" the cell of the body and let's sugar move from the blood into the cells, where it can be used for energy. In Diabetes either body does not make enough insulin or it does not respond to the action of the insulin. WHO projects death due to diabetes will be double between 2005 and 2030. The prevalence of diabetes for all age-groups worldwide was estimated as 2.8% in 2000 and will be 4.4% in 2030. The total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030^{2,3}. Diabetes has emerged as a major healthcare problem in India. According to Diabetes Atlas published by the International Diabetes Federation (IDF), there were an estimated 40 million persons with diabetes in India in 2007 and this number is predicted to rise to almost 70 million people by 2025. It is estimated by International Diabetic Federation that by 2025 every fifth diabetic subject in world will be an Indian^{4,5}.

In Ayurveda the traditional Indian medicine about 2000 plant species are considered to have medicinal value⁶. It's estimated that around 70,000 plant species from inches to towering trees, have been used for medicinal purpose. Since the antiquity Diabetes has been treated with plant medicines. Now a days more than 400 plants species having hypoglycaemic property and many of them still remain to be scientifically evaluated^{7,8}. Keeping this in view, presentstudy was undertaken to work on a formulation composed by two drugs, i.e. INDRAYANA (*Citrulluscolocynthis*) and YAVANI (*Trachyspermum ammi*) in order to evaluate its anti-hyperglycaemic effect as it is used as a Folklore medicine in Jaiselmer area of Rajathan for Diabetes.

Also in Ayurvedic classics Indrayana⁹⁻¹¹ and Yavani^{12,13} both are referred as anti-diabetic drug. (i.e. Pramehaghna)

Plant Profile

Trachyspermum ammi (L.) popularly known as bishop's weed, vavani belonging to the family Apiaceae, is an annual, aromatic and herbaceous plant. It is profusely branched with aheight of 60-90 cm small, erect with soft fine hair. It has many branched leafy stems, feather-like leaves 2-3 pinnately divided, segments linear with flowers terminal and compound¹⁴. Yavani is indigenous to India and Egypt¹⁵. Fruit, consists of two mericaprs, greyish brown, ovoid, compressed, about 2 mm longand 1 mm wide with pale coloured protuberances, 5 ridges and 6 vittae in each mericarp, usually separate, 5 primary ridges pale in colour, odour, characteristic, thymolic, taste, pungent¹⁶. Thymol and Carvacrol are the major active principles of T.ammi with numerous pharmacological activities such as Antimicrobial, antibiotic, diuretic, antiseptic, pesticidal, anticholinergic, inhibitory activity against hepatitis C virus (HCV) protease, antifungal, nematicidal. Gastro protective, Insecticidal, Mosquito repellent activity, Anti-hyperlipidaemic, Abortifacient activity, Hypotensive activity¹⁷. T. ammi used as stomachic, appetiser, anthelmintic, carminative, laxative, cure ascites, splenomegaly, piles, vomiting, abdominalpain, diuretic, galactogoggue etc¹⁸.

Citrulluscolocynthis(*L*.) Schrad is a scabrid perennial twining herb or climber, usually prostrate or spreading on the ground with slender stem and bifid tendrils belongs to family Cucurbitaceae. Leaves 4-10 X 1-5-9 cm, deeply 3-7 lobed, lobes acute or sub-acute, pinnatified, petioles deeply hirsute. Fruits globose, 5-7 cm diameter, variegated green and pale white, yellow when ripe and pulp bitter and spongy with numerous seeds. The plant distributed in warm, arid habits in sandy soil throughout India up to 1500m, abundantly in Rajasthan

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including Barmer, Jaiselmer, Jodhpur, Ajmer. Apart from India it is distributed in Western Asia, Africa and Mediterranean region. Colocynthin (the bitter principle), Quercitin, colocynthetin, Citrulluin, Citrulluene and Cucurbitacin are the major chemical constituent of C.colocynthis and possess pharmacological like activity Antimicrobial, Anti hyperglycemic, Anti-inflammatory, Anti-cancer, Larvicidal, Local anesthetic, Hepatoprotective, Hypolipidemic, Antioxidant, Laxative. Anti-histaminic, Cardiac depressant, Anticoagulant, Anti acetylcholine, Antiimplantation¹⁹. The fruit is bitter and used as purgative, antipyretic, carminative, leucoderma, ulcer, asthma, bronchitis, jaundice, enlargement of spleen, dyspepsia, constipation, inflammation, joint pain, elephantiasis, uterine pain etc²⁰.

Aims and Objectives of the study: i. To access the hypoglycaemic effect of the formulation. ii. To verify the Folklore claim. iii. To provide a cost effective remedy of Diabetes. iv. To develop an easy home-made remedy.

Material and Methods

Collection of Drugs: Fruits of Indrayana (*Citrulluscolocynthis*) was collected with the help of Local people in the month November from Jag village, Dudutehsil, 30 km. away from Jaipur and authenticated by the scientific screening committee of N.I.A. Pharmacy. The drug Yavani (*Trachyspermum ammi*) was procured from pharmacy of N.I.A.

Processing of Drug: Yavani (*T.ammi*) was triturated 3 times with the fresh juice of the fruit pulp of Indrayana and allow drying. Then it was subjected to powder and filled in the capsule.

Dosage form: Capsule. **Dose:** 3 caps thrice daily orally. (Approx. 3 gm. /day). **Vehicle:** Luke warm water. **Trial design:** single arm study (without control group)

Selection of Patients: Inclusion criteria: Newly detected diabetic cases with history of 0-5 years, Case with fasting blood sugar range <300 mg/dl, Age group 30-70 years, Non-Insulin dependent Diabetes mellitus, Body mass index (BMI) in the range 25-40.

Exclusion criteria: Chronic Diabetic cases, Cases with F.B.S >300 mg/dl, Juvenile Diabetic cases, Age >70 years, Insulin dependent D.M., Cases with complication like Retinopathy,

Nephropathy etc., Cases with other complicated diseases along with D.M., Pregnancy and lactation.

43 patients randomly selected from the O.P.D and I.P.D of N.I.A, Jaipur. All of them informed about different angles of the trial and allow them to decide their willing ness to involve in the trial. 37out of 43 patients gave their consent and I.C. was recorded as per appendix-V of schedule-Y of Drug and Cosmetic act 1940, amended version 2005. There after all the subjects gone through both clinical and Laboratory investigations along with detailed case history. Before the trial related activity the protocol was presented in front of Ethics committee of National Institute of Ayurveda, Jaipur and after minor modifications, it was approved for further research.

Investigations: Blood sugar both fasting and Post Prandial, Urine Sugar, Total Leucocyte count, Blood Urea, Serum Creatinine, SGOT, SGPT, HbA1c (only before and after trial). All investigations were carried out in a regular interval of 15 days along with before and after treatment.

Total Duration of Treatment: 60 days

Assessment Criteria: After completion of treatment, the results were assessed by using following criteria: FBS and PPBS level, HbA1c value. Apart from these 3 criteria other investigations are carried out only for safety of the patients. These values were recorded both before and after treatment. In order to assess clinical improvements different subjective parameters were also taken into consideration i.e., excessive urination (polyuria), turbidity of urine, tiredness, excessive sleeping, excessive sweating, excessive thirst (polydipsia) and excessive hunger (polyphagia).

Results and Discussion

After the treatment, it is observed that there is 27.76% reduction in Fasting Blood Sugar level. Statistical analysis is carried out (paired student t-test) and 'P' Values is drawn which is highly significant (table-1)

On statistical evaluation, it is observed that there is 36.62% reduction in Post Prandial Blood Sugar level which is highly significant (table-2).

On statistical evaluation, it is observed that there is 11.52% reduction in Glycosylated hemoglobin level. Statistical analysis is carried out (paired student t-test) and 'P' Values is drawn which is highly significant (table 3).

Table–1 Effect of the Formulation on Fasting Blood Suc

Effect of the Formulation on Fasting Blood Sugar									
N	Mean		Dif	% of	SD	SD SE	т	р	Domonk
	BT	AT	D 11.	Change	SD	SE	I	Г	Kennal K
30	198.70	143.53	55.17	27.76	30.90	5.64	9.78	< 0.001	H.S.

Table-2

Effect of the Formulation on Post Prandial Blood Sugar									
Ν	Mean		D:f	% of	% of SD	SE	Т	Р	Remark
	BT	AT	DII.	Change					
30	272.70	172.83	99.87	36.62	26.05	4.76	20.99	< 0.001	H.S.

Table-3

Effect of the Formulation on HbA1c (Glycosylated hemoglobin)									
Ν	Mean		D:f	% of	SD	SE	т	р	Domonia
	BT	AT	DII.	Change	50	SE	I	Г	Kelliark
30	7.49	6.62	0.86	11.52	0.35	0.06	13.58	< 0.001	H.S.



Figure-1 Effect of the formulation on Fasting Blood Sugar



Figure-2 Effect of the Formulation on Post Prandial Blood Sugar



Effect of the Formulation on HbA1c (Glycosylated hemoglobin) Table-4 Primary Phytochemical Screening of both plants

Sl.	Name of the organic	T.ammi	C.colocynthis
1.	Alkaloid	-	+
2.	Carbohydrate	+	+
3.	Fat and Oil	+	-
4.	Glycoside	+	+
5.	Phenol	-	+
6.	Protein	+	+
7.	Reducing sugar	+	+
8.	Saponin	+	+
9.	Starch	-	+
10.	Tannin	+	+
11.	Anthraquinones	-	+
12.	Flavonoids	+	+

Apart from above data the Screening also reveals that *C.colocynthis* contains electrolytes such as Calcium,Iron, Potassium, Sulphur, Magnesium, Sodium, and Copperwhereas *T.ammi* contains manganese and zinc in addition to *C.colocynthis*.

Diabetes is defined as a state in which homeostasis of carbohydrate and lipid metabolism is improperly regulated by insulin. This results primarily in elevated fasting and postprandial blood glucose levels. If this imbalanced homeostasis does not return to normalcy and continues for a protracted period of time, it leads to hyperglycaemia that in due course turns into a syndrome called diabetes mellitus. The curative properties of medicinal plants are mainly due to the presence of various complex chemical substances of different composition which occur as secondary metabolites.²¹ They are grouped as alkaloids, glycosides, flavonoids, saponins, tannins, carbohydrate and essential oils. Plant based natural constituents can be derived from any part of the plant like bark, leaves, flowers, roots, fruits, seeds, etc.²² Previous study suggested that Saponin, Flavonoids, Phenols and Tannin have antihyperglycaemic activity^{23,24}.

Recent study suggested in detail the structure activity relationship among saponins isolated from various sources and their hypoglycaemic activity. The 3-O-glucuronic acid moiety of oleanolic acid possesses strong hypoglycaemic activity.²⁵ Regarding mechanism of action, it is proposed that these compounds act as hypoglycaemic by delaying the transfer of glucose from the stomach to the small intestine, the main site glucose absorption and by inhibiting the glucose transport at the site of intestinal brush border membranes. Drugs that reduce Post prandial hyperglycaemia (PPHG) by suppressing the absorption of carbohydrate are effective in NIDDM prevention and treatment. Polyphenols, apart from their much-cited antioxidant activities, also have been reported to inhibit α amylase and sucrose, and have been shown to be the principle substance for suppressing PPHG. Furthermore, these polyphenols also inhibit glucose transport across the intestine by inhibiting sodium glucose co-transporter-1(S-GLUT-1).As both

the drugs containing Saponin, Flavonoids, Phenols and tanins and hence probably be responsible for the Anti-hyperglycaemic activity.

Pharmacological researches have proved that the effects of anthraquinones are reliant on the occurrence of burning up of acid and hence they are consumed as glycosides. In this case, the function of the bowel vegetation has also been involved. This is true because, when aglycone is soaked into the internal system and enters the blood vessels, it has an influence on the protein synthesis of the body perhaps leading to the formation of enzymes. However, all these are still a probability considering the fact that when a person swallows a dose of anthraquinones it takes at least 8-14 hours to start action and this is also the same time period for the protein or enzyme synthesis have its affect. However, the end outcome is the prostaglandins of the PGE series that enhances the tetchiness of the soft muscles of the bowl wall. The most likely reasons for the irritation of the bowl wall could be the spur in the local cyclic AMP manufacture and the hang-up of Na+ /K+-ATPase. As the drug C.colocynthis contains anthraquinone, probably cause the antihyperglycaemic activity in the observed results. Both the drugs contain micronutrient like zinc, ferrous, magnesium, chromium etc. are helpful to the patient suffering from Diabetes, specially chromium and zinc improves the glucose intolerance.Some study reveals the insulinotropic action of Citrullus colocynthis²⁶. It contains wide number of active constituent that may interact with several body metabolism and directly or indirectly influence the glucose or insulin metabolism.

In type-II diabetes mellitus elevation of glucose and free fatty acid leads to generation of reactive oxygen species and oxidative stress²⁷. These metabolism abnormalities not only induce the late diabetic complications but also lead to insulin resistance, β -cell dysfunction and impaired insulin secretion²⁸. Citrulluscolocynthis with antioxidant property /free radical scavenging activity and lipoperoxidation is active against oxidative stress and may induce a positive effect on diabetic metabolic abnormalities²⁹. The favourable effect of a substance with antioxidant properties on oxidative metabolic derangement of hyperglycaemia has been reported in severalstudies³⁰. The beneficial multiple activities like manipulating carbohydrate metabolism by various mechanisms, preventing and restoring integrity and function of β -cells, insulin-releasing activity, improving glucose uptake and utilization and the antioxidant properties present in medicinal plants offer exciting opportunity to develop them into novel therapeutics. The trial drug apparentlyhave achieved such a multimodal therapeutic effects to induce the observed clinical and biochemical benefits.

Conclusion

The trial drug shows significant result on objective parameter like reduction in Fasting Blood Sugar level, reduction in Post Prandial Blood Sugar level, reduction in HbA1c(GHB) level along with clinical improvements on excessive urination, turbidity of urine, excessive thirst, burning sensation in hand and leg, excessive sweating, excessive sleeping, excessive International Research Journal of Biological Sciences _ Vol. 2(4), 67-71, April (2013)

hunger, tiredness. So finally it is concluded that the drug signifies its anti-hyperglycaemic activity and fulfil the objective of a cost effective home remedy for diabetes. The *multifactorial pathogenicity* of diabetes demands *multi-modal* therapeutic approach. Thus, future therapeutic strategies require the combination of various types of multiple agents.

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