



Formulation and evaluation of polyherbal syrup for antidiabetic syrup

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Abstract

Diabetes a dreadful disease is found in all parts of the world and is becoming a serious threat to mankind health. The results of the present study reveals a strong antidiabetic activity of the aqueous extract of *Embilica Officinalis*, *Trigonella foenum-graecum*, *Azardicta Indica*, *Ocimum Sanctum* *Syzygium Cumini* for polyherbal syrup in the present antidiabetic study of aqueous extraction of poly-herbal syrup were tested in In-vitro model method in present study. Poly-herbal syrup prepared successfully using decoction method and for the characterization study of poly-herbal syrup color, Odour, Taste, pH, Viscosity were checked and compared with standard. In-vitro studies for anti diabetic activity using Glucose bound test and Glucose diffusion test were performed. In the present work, hypoglycemic activity of the aqueous extracts of *Embilica Officinalis*, *Trigonella Foenum Graecum*, *Azadirect Indica*, *Ocimum Sanctum*, *Syzygium Cumini* are used to formulate a poly-herbal anti-diabetic syrup which showed a significant reduction of glucose concentration in *in-vitro* studies. Many plants exhibit antidiabetic activity and anti-inflammatory property.

Keywords: herbal plants, polyherbal syrup, formulation & evaluation studies, anti-diabetic activity

Introduction

Traditional Medicines derived from medicinal plants are used by about 60% of the world's population. Diabetes is an important human ailment afflicting many from various walks of life in different countries. A list of medicinal plants with proven antidiabetic and related beneficial effects and of herbal drugs used in treatment of diabetes is compiled. These include, *Allium sativum*, *Eugenia jambolana*, *Momordica charantia*, *Ocimum sanctum*, *Phyllanthusamarus*,^[1] *Pterocarpus marsupium*, *Tinospora cordifolia*, *Trigonella foenum graecum* and *Withania somnifera*. One of the etiologic factors implicated in the development of diabetes and its complications is the damage induced by free radicals and hence an antidiabetic compound with antioxidant properties would be more beneficial. In the last few years there has been an exponential growth in the field of herbal medicine and these drugs are gaining popularity both in developing and developed countries because of their natural origin and less side effects. Many traditional medicines in use are derived from medicinal plants, minerals and organic matter. A number of medicinal plants, traditionally used for over 1000 years named rasayana are present in herbal preparations of Indian traditional health care systems. In Indian systems of medicine most practitioners formulate and dispense their own recipes. The World Health Organization (WHO) has listed 21,000 plants, which are used for medicinal purposes around the world. Among these 2500 species are in India, out of which 150 species are used commercially on a fairly large scale. India is the largest producer of medicinal herbs and is called as botanical garden of the world^[1].

Diabetes and Significance

Diabetes is a chronic disorder of carbohydrate, fat and protein metabolism characterized by increased fasting and post prandial blood sugar levels. The global prevalence of diabetes is estimated to increase, from 4% in 1995 to 5.4% by the year 2025. WHO has predicted that the major burden will occur in developing countries. Studies conducted in India in the last decade have highlighted that not only is the prevalence of diabetes high but also that it is increasing rapidly in the urban population. It is estimated that there are approximately 33 million adults with diabetes in India. This number is likely to increase to 57.2 million by the year 2025.

Diabetes mellitus is a complex metabolic disorder resulting from either insulin insufficiency or insulin dysfunction. Type I diabetes (insulin dependent) is caused due to insulin insufficiency because of lack of functional beta cells. Patients suffering from this are therefore totally dependent on exogenous source of insulin while patients suffering from Type II diabetes (insulin independent) are unable to respond to insulin and can be treated with dietary changes, exercise and medication. Type II diabetes is the more common form of diabetes constituting 90% of the diabetic population^[2]. For the development of diabetic complications, the abnormalities produced in lipids and proteins are the major etiologic factors. In diabetic patients, extra-cellular and long lived proteins, such as elastin, laminin, and collagen are the major targets of free radicals. These proteins are modified to form glycoprotein due to hyperglycemia. The modification of these proteins present in tissues such as lens, vascular wall and basement membranes are associated with the development of

complications of diabetes such as cataracts, microangiopathy, atherosclerosis and nephropathy. During diabetes, lipoproteins are oxidized by free radicals. There are also multiple abnormalities of lipoprotein metabolism in very low density lipoprotein (VLDL), low density lipoprotein (LDL), and high density lipoprotein (HDL) in diabetes. Lipid peroxidation is enhanced due to increased oxidative stress in diabetic condition. Apart from this, advanced glycation end products (AGEs) are formed by non-enzymatic glycosylation of proteins. AGEs tend to accumulate on long-lived molecules in tissues and generate abnormalities in cell and tissue functions. In addition, AGEs also contribute to increased vascular permeability in both micro and macrovascular structures by binding to specific macrophage receptors. This results in formation of free radicals and endothelial dysfunction. AGEs are also formed on nucleic acids and histones and may cause mutations and altered gene expression [3].

Medicinal plants are being looked up once again for the treatment of diabetes. Many conventional drugs have been derived from prototypic molecules in medicinal plants. Metformin exemplifies an efficacious oral glucose-lowering agent. Its development was based on the use of *Galega officinalis* to treat diabetes. *Galega officinalis* is rich in guanidine, the hypoglycemic component. Because guanidine is too toxic for clinical use, the alkyl biguanides synthalin A and synthalin B were introduced as oral anti-diabetic agents in Europe in the 1920s but were discontinued after insulin became more widely available. However, experience with guanidine and biguanides prompted the development of metformin. To date, over 400 traditional plant treatments for diabetes have been reported, although only a small number of these have received scientific and medical evaluation to assess their efficacy. The hypoglycemic effect of some herbal extracts has been confirmed in human and animal models of type 2 diabetes. The World Health Organization Expert Committee on diabetes has recommended that traditional

medicinal herbs be further investigated.

Major hindrance in amalgamation of herbal medicine in modern medical practices is lack of scientific and clinical data proving their efficacy and safety. There is a need for conducting clinical research in herbal drugs, developing simple bioassays for biological standardization, pharmacological and toxicological evaluation, and developing various animal models for toxicity and safety evaluation. It is also important to establish the active component/s from these plant extracts [4].

Symptoms & Causes of Diabetes [5]

Symptoms of diabetes include:

- Increased thirst and urination
- Increased hunger
- Fatigue
- Blurred vision
- Numbness or tingling in the feet or hands
- Sores that do not heal
- Unexplained weight loss

Symptoms of type 1 diabetes can start quickly, in a matter of weeks. Symptoms of type 2 diabetes often develop slowly over the course of several years and can be so mild that you might not even notice them. Many people with type 2 diabetes have no symptoms. Some people do not find out they have the disease until they have diabetes-related health problems, such as blurred vision or heart trouble.

Indian medicinal plants with anti-diabetic and related Benefits

There are many herbal remedies suggested for diabetes and diabetic complications. Medicinal plants form the main ingredients of these formulations. A list of medicinal plants with antidiabetic and related beneficial effects is given in the below

Table 1: Indian Medicinal Plants with Anti-Diabetic and Related Benefits

S. No	Plant Name	Ayurvedic/common name/herbal formulation	Antidiabetic and other beneficial effects in traditional medicine
1.	<i>Annona squamosa</i>	Sugar apple	Hypoglycemic and antihyperglycemic activities of ethanolic leaf-extract, Increased plasma insulin level
2.	<i>Artemisia pallens</i>	Davana	Hypoglycemic, increases peripheral glucose utilization or inhibits glucose reabsorption
3.	<i>Areca catechu</i>	Supari	Hypoglycemic
4.	<i>Beta vulgaris</i>	Chukkander	Increases glucose tolerance in OGTT
5.	<i>Boerhavia diffusa</i>	punarnava	Increase in hexokinase activity, decrease in glucose-6-phosphatase and fructose bis-phosphatase activity, increase plasma insulin level, antioxidant
6.	<i>Bombax ceiba</i>	Semul	Hypoglycemic
7.	<i>Butea monosperma</i>	palasa	Antihyperglycemic
8.	<i>Camellia sinensis</i>	Tea	Anti-hyperglycemic activity, antioxidant
9.	<i>Capparis decidua</i>	Karir or Pinju	Hypoglycemic, antioxidant, hypolipidaemic
10.	<i>Caesalpinia bonducella</i>	Sagarghota, Favernut	Hypoglycemic, insulin secretagogue, hypolipidemic
11.	<i>Coccinia indica</i>	Bimb or Kanturi	Hypoglycemic
12.	<i>Emblica officinalis</i>	Amla, Dhatriphala, a constituent of herbal formulation, "Triphala"	Decreases lipid peroxidation, antioxidant, hypoglycemic
13.	<i>Eugenia uniflora</i>	Pitanga	Hypoglycemic, inhibits lipase activity
14.	<i>Enicostema littorale</i>	krimihrita	Increase hexokinase activity, Decrease glucose 6-phosphatase and fructose 1,6 bisphosphatase activity. Dose dependent hypoglycemic activity
15.	<i>Ficus bengalensis</i>	Bur	Hypoglycemic, antioxidant
16.	<i>Syzygium alternifolium</i>	Shahajire	Hypoglycemic and antihyperglycemic

17	<i>Terminalia bellerica</i>	Behada, a constituent of "Triphala"	Antibacterial, hypoglycemic
18	<i>Terminalia chebula</i>	Hirda	Antibacterial, hypoglycemic
19	<i>Murraya koenigii</i>	Curry patta	Hypoglycemic, increases glycogenesis and decreases gluconeogenesis and glycogenolysis
20	<i>Musa sapientum</i>	Banana	Antihyperglycemic, antioxidant

Aim & Objective

To formulate and evaluate polyherbal syrup formulation using aqueous plant extracts of Neem Leaves, jamun leaves, Tulsi leaves, Amla seeds, fenugreek seeds for anti-diabetic activity.

extract of each plant powder. Then formulate the poly herbal Anti-Diabetic syrup. To perform evaluation parameters in comparison to standard anti-diabetic syrup & perform the *In-Vitro* studies for anti diabetic activity.

Plan of Work

To collect required plant parts, & dry it. Prepare aqueous

Plant Profile

Table 2: Plant Profile of Polyherbal Syrup

S. No	Plants	Biological Sources	Chemical Constituents	Uses
1	Neem	<i>Azadirachta Indica</i>	Nimbin, nimbolide. Quercetin Azadirachtin.	Poultice, applied to boils, In worm, jaundice and in skin disease, Insect-repellent, Antiviral and antifungal, Rheumatism, Anti-Diabetic.
2	Tulsi	<i>Ocimum Santum</i>	Eugenol, nerol, eugenol methyl ether, α -selinene, and β -pinene, Camphor and, Cineole, linalool.	Expectorant, bronchitis, Stomachic, Carminative, Stimulant, Flavouring agent, Antifertility agent, Diaphoretic property, Spasmolytic, Anti-bacterial. [20]
3	Fenugreek	<i>Trigonella Foenum Graecum</i>	Gallic acid, Protocatechuic acid, Protodiscin, Quinic acid, Trigonellin, Trigoneosides,	Anti-hyperglycemic, Pancreas stimulant, Anti-diabetic, Anti-inflammatory, Analgesic, Neuroprotective, Antioxidant, Anti-carcinogen
4	Amla	<i>Embillica Officinalis</i>	phyllantine, phyllembein, phyllantidine, glutamic acid, proline, aspartic acid, alanine,	Immunomodulatory, Anti-diabetic and Anti-hyperglycemic, Antilipemic, Antioxidant, Hematogenic (helps in formation of red blood cells), Anti-anemic, Anti-inflammatory, Anti-hypertensive Anticancer.
5	Neredapandu	<i>Syzygium Cumini</i>	anthocyanins, glucoside, ellagic acid, isoquercetin, kaemferol, myrecetin.	Astringent, Antiemetic, Antihemorrhagic, Antihyperglycemic, Mild astringent, Digestive stimulant, Liver stimulant, Anti-inflammatory.

Excipient Profile

Table 3: Excipient Profile of Polyherbal Syrup

S. No	Composition	Uses	Chemical Structure
1	Glycerol	<ul style="list-style-type: none"> Humectant Solvent Lubricant Laxative 	<p>Glycerol (Glycerin)</p> <chem>OCC(O)CO</chem>
2	Hydroxy Ethyl Cellulose	<ul style="list-style-type: none"> Gelling agent Viscosifying agent Dissolving agent. 	$\left(\text{RO} \begin{array}{c} \text{OR} \\ \text{O} \end{array} \right)_n$ <p>R = H or CH₂CH₂OH</p>
3	Pippermint Oil	<ul style="list-style-type: none"> Topical Analgesic Flavouring agent Anti pruritic Nasal decongestant 	<chem>CC1=C(C)C(O)C=C1</chem>
4	Sodium Benzoate	<ul style="list-style-type: none"> Preservative Hyperammonemia treatment 	<chem>[Na+].[O-]C(=O)c1ccccc1</chem> <p>sodium benzoate</p>

Formulation of Herbal Syrup ^[3]**Table 4:** Formulation Ingredients

S. No.	Ingredients	Typical quantities
1.	Plant Extract	100ml
2.	Hydroxy Ethyl Cellulose	2g
3.	Glycerol	150ml
4.	Propylene Glycol	30ml
5.	Peppermint Oil	0.2ml
6.	Sodium benzoate	1g
7.	Purified Water	Up to 1000ml

Manufacturing Process**Stage 1) Preparation of active solution**

- Dispersed 2.0 g Hydroxyethyl cellulose in 300 ml purified water and allowed to swell at room temperature for 30 minutes. Added Sodium benzoate.
- Heated the solution to 80 degree Centigrade under stirring for 1 hour.
- Allowed the solution to cool to room temperature and added 100ml of plant
- Extract under stirring.

Step 2) Preparation of flavor solution:

- 0.15 ml Peppermint Oil in additional 5 g propylene glycol was prepared separately.

Stage 3) Preparation of vehicle solution:

- Add 150 grams glycerol to mixing vessel under stirring, rinsed the container with 50 ml purified water and added it to mixing vessel under stirring.

Stage 4) Preparation of final syrup:

- Added herbal extract to mixing vessel under stirring. Rinsed the containers with 10 ml purified water and added the rinsing to the mixing vessel under stirring. Give such 5 consecutive rinsing.
- Cooled the solution to 35-40 C.
- Added solution of peppermint Oil to mixing vessel under stirring, rinsed each container separately with 10 ml purified water each and added to the mixing vessel. And finally make up to 1000ml with purified water.

Evaluation Parameters ^[4]

- Color Examination:** Five ml final syrup was taken into watch glasses and placed against white back ground in white tube light. It was observed for its color by naked eye.
- Odour Examination:** Two ml of final syrup was smelled individually. The time interval among two smelling was kept 2 minutes to nullify the effect of previous smelling.
- Taste Examination:** A pinch of final syrup was taken and examined for its taste on taste buds of the tongue.
- Determination of pH:** Placed an accurately measured amount 10 ml of the final syrup in a 100 ml volumetric flask and made up the volume up to 100 ml with distilled water. The solution was sonicated for about 10 minutes. P^H was measured with the help of digital pH meter.
- Viscosity:** Viscosity is determined by using a Ostwald Viscometer.

In-vitro evaluation for anti-diabetic syrup ^[5]**(i) Glucose Bound Test**

Plant Extract was added to 25ml of glucose solution of increasing concentration (5, 10, 20, 50,100 m mol/L). The mixture was stirred well incubated in a shaker water bath at 37 degree centigrade for 6 hour. Centrifuge at 4800 rpm for 20 min and the glucose content in the supernatant was determined using UV Spectrophotometer.

(ii) Glucose Diffusion

It was performed according to the method. A total of 25 ml of glucose solution (20m mol / L) and the samples of plant extract (1%) were dialyzed in dialysis bags against 200ml of distilled water at 37 degree centigrade in a shaker water bath. The glucose content in the dialysate was determined at 30, 60,120 & 180 minutes using UV Spectrophotometer. A control test was carried out without sample.

Results & Discussion**Comparison of Evaluation Parameters of test & Standard Syrup****Table 5:** Evaluation Parameters Observation

S. No	Evaluation parameter	Standard Syrup	Test Syrup
1.	Color	Dark Yellow Green	Light Yellow Green
2.	Odor	Slightly Bitter	Aromatic
3.	Taste	Intensely Bitter	Slightly Bitter
4.	pH	6.52	5.43
5.	Viscosity	0.98 P	2.64 P

In-vitro anti-diabetic evaluation parameters**Effect of Glucose Bound Test****Table 6:** In-Vitro Glucose Bound test Result

S. No.	Concentration of Glucose (µg/mL)	Absorbance of UV	
		Standard	Test
1.	5	0.171	0.163
2.	10	0.165	0.152
3.	20	0.142	0.137
4.	50	0.127	0.129
5.	100	0.157	0.124

Effect of Glucose Diffusion**Table 7:** In-vitro Glucose Diffusion Results

S. No	Concentration of Glucose (µg/ml)	Absorbance of UV	
		Standard	Test
1.	5	0.165	0.152
2.	10	0.142	0.139
3.	20	0.127	0.118
4.	50	0.112	0.102
5.	100	0.98	0.78

Conclusion

Herbal medicines is still the main stay of about 75-80% for world population mainly in development Countries for primary health care because of better cultural acceptability, better compatibility with human body and lesser side effect.

Since from this study we conclude that the *Azadirachta Indica*, *Ocimum Sanctum*, *Embilica Officinalis*, *Trigonella Foenum Graceum*, *Syzigium Cumini* possess anti-diabetic activity as claimed in the literature survey. The present worker concluded that the formulation containing multiple aqueous herbal extracts for diabetic patients were successfully prepared. The formulations prepared are unique in it containing natural anti-oxidants for the oxidizable part of extracts. The drugs using in the formulation i.e. *Embilica officinalis*, *Eugenia jambolana*, *trigonella foenum-graecum*, *Azadirachta indica* and *Ocimum Sanctum* exhibit anti-diabetic activity in in-vitro studies. There is increasing demand by patients to use the natural products with antidiabetic activity. In recent times there has been renewed interest in the plant remedied. Thus the investigated work in this title formulation and evaluation of poly-herbal syrup for anti-diabetic activity will be benefited for entire mankind.

References

1. Manisha Modak *et al.* Indian Herbs and Herbal Drugs Used for the Treatment of Diabetes. *J. Clin. Biochem. Nutr.* PMID: PMC2275761. 2007; 40:163-173.
2. Ramachandran A, Snehalatha C, Viswanathan V. Burden of type 2 diabetes and its complications- the Indian scenario. *Curr. Sci.* 2002; 83:1471-1476.
3. Brownlee M. Advanced protein glycosylation in diabetes in diabetes and ageing. *Ann. Rev. Med.* 1996; 46:223-234.
4. Dey L, Anoja SA, Yuan CS. Alternative therapies for type 2 diabetes. *Alternative Med. Rev.* 2002; 7:45-58. [PubMed]
5. <https://www.niddk.nih.gov/healthinformation/diabetes/overview/symptoms-causes>
6. http://shodhganga.inflibnet.ac.in/bitstream/10603/28821/1/3/13_chapter%206
7. Swain Pramod Kumar¹, Nayak Durga Prasan Design. Development & Evaluation of a Poly herbal Syrup from some herbs used as Energy booster. *International Journal of Ayurvedic Medicine.* 2013; 4(4):374-378. ISSN: 0976-5921
8. Sindhu S, Nair, Vaibhavi Kavrekar¹, Anshu Mishra. Evaluation of *In Vitro* Anti diabetic Activity of Selected Plant Extracts *International Journal of Pharmaceutical Science Invention* ISSN (Online): 2319-6718. *ISSN (Print): 2319 – 670X www.ijpsi.org.* 2013; 2(4)12-19.