ORIGINAL ARTICLE

Development, evaluation, and biological characterization of antidiabetic oral polyherbal tablets

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Abstract

Introduction: Design and development of oral polyherbal tablet formulation is still a challenge in modern pharmaceutics. The oral polyherbal tablet formulation presents many technical problems to the pharmacists. The main objective of the present study was to develop, evaluate, and biological characterized antidiabetic tablets. **Material and Methods:** Here, we used potentially active *Alstonia scholaris*, *Pterocarpus marsupium,* and *Embelia ribes* which are the medicinal plants or herbs used for the antidiabetic activity. In this work, polyherbal tablets were prepared using hydroalcoholic extracts of *A. scholaris* (leaves and material), *P. marsupium* (bark), and *E. ribes* (seeds) by the compression method for the treatment of diabetes. Polyherbal tablets were prepared and evaluated by weight variation, hardness, friability, and disintegration time. **Result:** The optimized formulation was investigated the antidiabetic activity in streptozotocin-induced diabetic rats fasting blood glucose level was measured on 0, 7, and 15 days. We find that evaluation parameters of polyherbal formulation were within acceptable pharmacopoeial limits. **Conclusion:** No marked changes were noticed in all the evaluated parameter during study. The laboratory scale preparation of polyherbal tablet formulation may be used as stable, solid dosage form and this work done may help in progress of field of antidiabetic activity of polyherbal tablet formulation.

Key words: Polyherbal formulation, polyherbal tablets, antidiabetic, *Alstonia scholaris*, *Pterocarpus marsupium*, *Embelia ribes* and streptozotocin

INTRODUCTION

Plants occupy a unique position in this planet since they are the foundation to life on the earth. They are the primary producers in all food chains. Plants directly supply 90% of human calorific intake and 80% of proteins intake. Plants are being used as a potential source of medicine for time immemorial. India is the source of wealth of a large number of medicinal herbs and they are opting for the traditional medicine methods. Hence, it is imperative that this great natural resource is augmented and utilized in accordance with the development of technology and the needs of human beings.

The current millennium sets the goal of side effect free treatment by the way of nutraceuticals. The global interest on traditional medicine has gained importance as a number of plants have been cited in curing diseases successfully. Medicinal plants are an integral part of the ethnobotanical aspects of the people of Asia for centuries. The modern medicine has evolved from folk medicine and traditional system only after thorough chemical and pharmaceutical screening. Advanced microbial and chemical methods can synthesize medicinal and aromatic compounds, but the cost in many cases is expensive.

However, synthetic medicine can cause side effects and as a result, people are more favorable to use natural compounds obtained from plants. It is estimated that 20,000 plant species are used for medicinal purposes. In 1985 recorded that 74% of 119 plant derived drugs were discovered as a result of chemical studies to isolate the active substances responsible for their traditional use.

The Asiatic flora includes tropical, subtropical, and temperate species, which provide systems for herbal based drugs and

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these systems play a major role in overall health care. It has reported that more than 80% of people in Asia are still depending on traditional and folk remedies for day-to-day medical needs. More than 70% of India's 1.1 billion populations still use the traditional herbal medicine.

Scientists have reported the use of phytochemical analysis of plants, used in folklore for the treatment of cancer, yielding a number of compounds with antitumor activity. Plants from many families have shown to accumulate alkaloids, which possess anti-HIV activity. Hussein reported several plant-derived drugs and aromatic compounds.

These include antimalarial agent from *Artemisia annua*, forskolin from roots of *Coleus*, which is used for preventing the clotting of blood in reducing intraocular pressure in cases of glaucoma. Forskolin also acts as an aid to nerve regeneration following trauma.[1-10]

Traditional Medicines in India

In India, about 7300 plant species are used in traditional health-care systems such as Ayurveda, Siddha, Unani, and folk healing practices. The booming of traditional medicine industry results in an increasing demand on medicinal plant products. About 90% of the medicinal plants come from natural habitats. The declining availability of such plants and the fading of local traditional knowledge make the sustainable management of natural habitats a crucial environmental issue in South India, concerning biodiversity conservation and welfare of local communities.

Research Approach to Herbal Products

The path of reverse pharmacology, arising from observational therapeutics is complementary to other approaches for natural drug development [Figure 1].

The diversity of medical uses of plant is at times daunting for a new entrant to the field. However, for a multidisciplinary research and a development network, the options of research approach provide deep motivation for the identification of new pharmacophores. Besides expanding the herbal therapeutic and preventive armamentarium, new pharmacophores may help to evolve new targets of drug action as well as a possibility for combinatorial chemistry on the novel pharmacophores.

For example, curcumin has been a target molecule for a significant endeavor for a large number of combinatorial compounds. The Council of Scientific and Industrial Research in India has initiated sizeable and meaningful efforts for the development of herbal-based formulations for diabetes, arthritis, and hepatitis by a national network program. Interesting and novel activities have been detected with the selected plants and some of the active ingredients of therapeutically demonstrable effects, for example, glycemic control and inhibition of glycosylated hemoglobin level coupled with a reduction in *in vitro* formation of Amadori products. The diverse approaches to herbal drugs have led to interesting hits and novel activities, which need further in-depth drug development efforts, both as herbal and new single molecule drugs.

Tablet is defined as a compressed solid dosage form containing medicaments with or without excipients. According to the Indian Pharmacopoeia Pharmaceutical tablets are solid, flat, or biconvex dishes, unit dosage form prepared by compressing a drugs or a mixture of drugs, with or without diluents. They vary in shape and differ greatly in size and weight, depending on the amount of medicinal substances and the intended mode of administration. It is the most popular dosage form and 70% of the total medicines are dispensed in the form of tablet. All medicaments are available in the tablet form except where it is difficult to formulate or administer.[11-21]

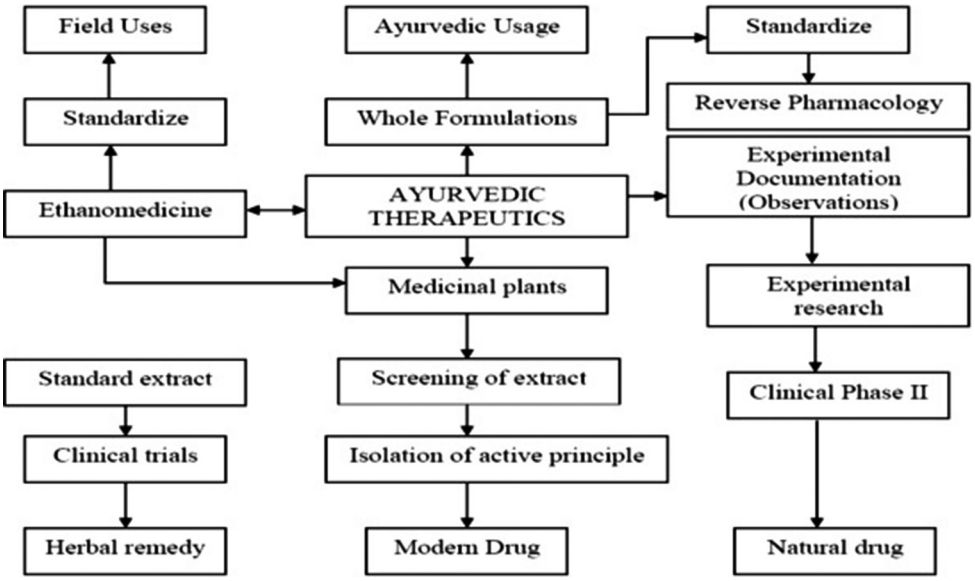

Figure 1: Research approach to herbal products (R and D path for natural products)

The polyherbal formulation contains at least two herbs with various phytoconstituents having comparative or disparate therapeutic potential has been collectively producing desirable effects during the management of human illness.

The present study was aimed to develop polyherbal tablet formulation containing hydroalcoholic extracts of *Alstonia scholaris* (leaves and material), *Pterocarpus marsupium* (bark), and *Embelia ribes* (seeds) by the compression method for the treatment of diabetes.

MATERIALS AND METHODS

A. scholaris (leaves and material), *P. marsupium* (bark), and *E. ribes* (seeds) were collected from authorized local herbal supplier Firoz Brothers Attar, Kamri Marg, Ujjain (M.P.) (GSTIN: 23ACIPB0667J1ZU) dated February 24, 2018.

Preparation of Extracts

Powder of leaves and material of *A. scholaris,* heartwood of *P. marsupium*, and seeds of *E. ribes* were coarsely powdered passed through 20# sieve. Now, this powder extracted and prepared separately about 200 g with hydroalcoholic mixture of 70% ethanol and 30% water in a Soxhlet apparatus for 12–24 h, respectively. The solvent was removed under reduced pressure, with respect to dried plant material. The powdered plant material first extracted with petroleum ether to remove fatty materials and then extracted from ethanol solvent. The dried extract was stored in desiccator till further use.

Formulation of Polyherbal Tablet

The hydroalcoholic extract of *A. scholaris* (leaves and material), *P. marsupium* (bark), and *E. ribes* (seeds) are the compression method for the treatment of diabetes. The dried powder extract and other ingredients were mixed uniformly and then mixture was blended and granulated. The granules were then compressed into tablets. The composition of formulation is described in Table 1.

Evaluation of Polyherbal Tablets

Formulated tablets were evaluated for the following parameters:

Weight variation

Weight variation was carried out to ensure that each of polyherbal tablets contains the proper amount of drug [Table 2]. The test was carried out by weighing the 20 tablets individually using analytical balance, then calculating the average weight, and comparing the individual tablet weights to the average. The percentage of weight variation is calculated using the following formula:

$$\% \text{ Deviation} = \frac{\text{Average weight} - \text{Individual weight}}{\text{Average weight}} \times 100$$

Hardness test

The hardness of the polyherbal tablet is defined as the force applied across the diameter of the tablet to break the tablet. The resistance of the tablet to chipping, abrasion, or breakage under the condition of storage, transportation, and handling before usage depends on its hardness. The tablet was placed between two anvils; the force applied to the anvils, and the crushing strength that just causes the tablet to break was recorded.

Friability

It is the phenomenon whereby polyherbal tablet surfaces are damaged and/or show evidence of lamination or breakage when subjected to mechanical shock or attrition. Roche friabilator is the equipment which is used for the determination of friability. It is expressed in percentage. Note down the initial weight of the tablets individually (W initial). Tablets are placed in aplastic chamber which revolves at 25 rpm and they are subjected to fall from a height of 6 inches in the friabilator for about 100 revolutions. Then measure the weight of the tablet (W final) and observe any weight difference before and after the friabilator processing.

Limits: Loss in weight <0.5% to 1% of the initial weight of the tablet should be considered as acceptable limits.

Percentage of friability is calculated as follows:

$$F = \frac{Wi - Wf}{Wi} \times 100$$

Table 1: Compositions of polyherbal tablets

Ingredients (mg)	F1	F2	F3	F4	F5	F6
A. scholaris	110	110	110	110	110	110
P. marsupium	110	110	110	110	110	110
E. ribes	110	110	110	110	110	110
Talc	250	240	230	220	210	200
MCC	60	65	70	80	85	90
Magnesium stearate	10	15	20	20	25	30
Net weight (mg)	650	650	650	650	650	650

A. scholaris: Alstonia scholaris, P. marsupium: Pterocarpus marsupium, E. ribes: Embelia ribes

Table 2: Weight variation specification as per the United States Pharmacopeia

The average weight of polyherbal tablets (mg)	Maximum percentage difference allowed
130 or less	±10.0
130–324	±7.5
More than 324	±5.0

Where,
F = Friability
Wi = Initial weight
Wf = Final weight

Disintegration time

Take three polyherbal tablets in the disintegrator apparatus, then adjust the apparatus in such a manner that the complete up and down movement of both the tube in the beaker containing distilled water was repeated for 30 time/min when the particles remained above the screen which was readily passed through it was recorded as the disintegration time of the samples.

Evaluation of Antidiabetic Activity

Procurement and selection of animals

Wistar albino rats of either sex weighing between 100 and 150 g of either sex were obtained from Animal House, PBRI, Bhopal (M.P.). The animals were stabilized for 1 week; they were maintained in standard condition at room temperature; normal light dark cycle. They had been given standard pellet diet and water *ad libitum* throughout the course of the study. The animals were handled gently to avoid giving them too much stress, which could result in an increased adrenal output.

Induction of diabetes mellitus

Rats were made diabetic by a single injection of streptozotocin (STZ) (60 mg/kg, i.p.) prepared in citrate buffer (0.1 M, pH 4.5) after overnight fasting. Blood was drawn from the tail vein 24 h after the injection and the glucose level was estimated by glucose oxidase method using Accu-Chek Glucometer before and 72 h after STZ injection. Animals showed blood glucose level more than 250 mg/dl were selected for further antidiabetic activity.

Treatment groups: Polyherbal formulations

After 72 h of STZ injection, animal with BGL ≥250 mg/dl was divided into different groups (with five animals each) for antidiabetic study of formulations.

1. Group I (NC): Normal control; normal rats orally treated with vehicle distilled water
2. Group II (DC): Diabetic control; diabetic rats orally treated with vehicle distilled water
3. Group III (PC): Positive control standard (treated with glipizide 5 mg/kg b.wt after the 3rd day of STZ injection)
4. Group IV (F5): Treated orally with formulation F5 with dose of 650 mg/kg b.wt after the 3rd day of STZ injection.

The fasting glucose levels were determined on days 0, 7, and 14 days of formulation administration. During the experimental period, the rats were weighed every day and the mean change in body weight was determined.

RESULTS

Evaluation of Polyherbal Tablets

The prepared tablets were described for various parameters, for example – hardness, friability, weight variation, and disintegration time which are described in Table 3.

1. Weight variation: All the formulations passed the weight variation test and it was acceptable [Table 3]
2. Hardness: The hardness of the tablets was observed to be in the range of 3.9 and 4.4 kg/cm^2 [Table 3]
3. Friability: The value of friability of prepared tablets was found to lie in between 0.51% and 0.57% [Table 3]. Friability was observed to be under 1.0% demonstrating a decent mechanical resistance
4. Disintegration time: The result of the disintegration time of the tablet is shown in Table 3. The disintegration time for tablet was observed to be between 15.43 min and 16.20 min.

Evaluation of Antidiabetic Activity

Antidiabetic activity of F5

Induction of diabetes in test rats was confirmed by the presence of a high fasting plasma glucose level. The impact of F5 on serum glucose levels of normal and STZ-induced rats is appeared in Table 4.

After the administration polyherbal tablet (F5) to diabetic animals, a critical decrease in blood glucose level was observed. The finding exhibited that F5 produces potent antidiabetic activity.[22-24]

DISCUSSION AND CONCLUSION

In developing countries, traditional and herbal medicine including the folk medicinal practice scatters to nearly 70% of the population because of accessibility, affordability, as well as the time tested dependability. They mainly use or dependent on herbal medicine because of the side effects of the most of the modern drugs. Hence, the herbal medicine was selected for the present research.

Traditional plant-based medicines still exert great deal of importance to people living in developing countries and also serve as source to discovery of new drug candidates for a variety of diseases that threaten human health.

Herbs play a significant role in the treatment of diabetes as compared to allopathic medicines because of less side effects, ease, and simple accessibility. This present project is based on to formulate polyherbal tablets of hydroalcoholic extract of *A. scholaris* (leaves and material), *P. marsupium* (bark), and *E. ribes* (seeds) by the compression method for

Table 3: Evaluation of polyherbal tablets

Parameters	Standard value	Observed value					
		F1	F2	F3	F4	F5	F6
Weight variation	5%	Passes	Passes	Passes	Passes	Passes	Passes
Hardness (in Kg/cm^2)	2.5 to 5	3.9	4.3	4.4	4.1	4.1	4.4
Friability (in %)	0.5 to 1.0	0.56	0.53	0.51	0.54	0.56	0.57
Disintegration time (in min)	15	15.43	15.70	15.98	16.10	15.40	16.20

Table 4: Effect of polyherbal tablets on fasting plasma glucose level in rats

Group	Treatment	Dose	Blood glucose level (mg/dl) in STZ		
			Day 0	Day 7	Day 14
I	Normal control	Vehicle 2 ml/kg	90.00±7.00	101.00±7.50	110.00±8.40
II	Diabetic control	STZ 60 mg/kg	275.30±10.50	290.00±11.20	298.00±10.11
III	Positive control (Diabetic+Glipizide)	5 mg/kg	242.00±5.00	147.00±3.50	115.05±2.50
IV	Formulation-F5	650 mg/kg	259.00±6.25	149.00±1.57	120.00±2.10

STZ: Streptozotocin

the treatment of diabetes. The dried powder extract and other ingredients were mixed uniformly and then mixture was blended and granulated. The granules were then compressed into tablets. These have been used by many researchers and local practitioners for the treatment of diabetes and other disorders.

The hardness of formulation was estimated in kg/cm^2 with the assistance of Monsanto tester. Among all the formulations prepared, F5 has been observed to most worthy one as far as weight variation and disintegration time.

This formulation indicated obvious hardness characteristics (4.1 kg/cm^2), which encouraged its fast disintegration (15.40 min).

The friability (0.56 %) of formulation demonstrated that the tablets were mechanically stable. On the basis of various specifications, formulation batch F5 was selected as the optimized batch, further antidiabetic examine was done on F5. The present examination demonstrates that polyherbal tablet was found to diminish the glucose level in STZ-induced diabetic animals. STZ has been appeared to acute free radical production and causes tissue damage.

It is reported that the extract of *A. scholaris* (leaves and material), *P. marsupium* (bark), and *E. ribes* (seeds) containing flavonoids on chief chemical constituents. The flavonoids compounds could have induced the observed impacts. However, it is reported that flavonoids constitute active biological principles of most medicinal plants with diabetic properties.

Thus, the active principle may be responsible for the observed antidiabetic effect of the polyherbal tablet. Polyherbal tablets containing extracts of *A. scholaris* (leaves and material), *P. marsupium* (bark), and *E. ribes* (seeds) formulated for the treatment of diabetes mellitus. After view of result, it is concluded that formulation and evaluation are great.

Formulation F5 indicated least disintegration time of 15.40 min. Subsequently, it was chosen as enhanced formulation and subjected to antidiabetic activity. The administration of polyherbal tablet (F5) exhibited significant antidiabetic effects by controlling the blood glucose level.

The polyherbal tablet is rich in flavonoid and this suggests that the antidiabetic activity of polyherbal formulations is due to the presence of phenolic content. Hence, the developed polyherbal formulation might prove to be a safe alternative for the existing antidiabetic synthetic drug.

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