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Antidiabetic Activity of Newly Formulated Oral Polyherbal Tablets in Alloxan Induced Diabetic Rats

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Abstract

Anacardium occidentale, *Aegle marmelos* and *Achyranthes aspera* are the medicinal plant and used for the treatment of diabetes mellitus. There is major challenge in bioavailability of herbal products when administered in raw form, and it can be overcome in the form of polyherbal tablets. In the present study polyherbal tablets were prepared using hydroalcoholic extracts of *Anacardium occidentale* (bark), *Aegle marmelos* (leaves) and *Achyranthes aspera* (aerial parts) by dry granulation method for the management of diabetes. Tablets were prepared and evaluated by using weight variation, hardness, and friability and disintegration time. The optimized formulation was investigated the antidiabetic activity in Alloxan-induced diabetic albino rats. Fasting blood glucose level and changes in body weight were measured on days 0, 8 and 15. At the end of 15 day, serum lipid profile and protein were assessed. The finding of weight variation, hardness, friability and disintegration time of polyherbal tablets were within acceptable pharmacopoeial limits. Among six formulations prepared (F1 to F6), F1 showed appreciable results, and subjected for antidiabetic activity. After the administration of F1, blood glucose levels were monitored at specific intervals and it was found that they were significant lowered with improvement in body weight and lipid profile. From the results, it has been concluded that the prepared polyherbal tablets has the potential to act as an antidiabetic drug.

Keywords: Polyherbal tablets; Antidiabetic; *Anacardium occidentale*; *Aegle marmelos*; *Achyranthes aspera*; Alloxan

Introduction

Medicinal Plants have been known for a considerable length of time and are exceptionally regarded everywhere throughout the world as a rich source of therapeutic agents for the avoidance of various ailments. Therapeutic plants are used from several years as a result of safety, adequacy, social worthiness and lesser side effects when contrasted with synthetic drugs. Today around half of total populace is thoroughly relies on the plant derived products as a primary health care with no side effects [1]. Over the most recent couple of years, there has been an exponential development in the field of natural prescription in diabetes mellitus. These medications are picking up fame on account of their characteristic inception and less side effects. Recent scientific investigations have affirmed the viability of a considerable lot of these herbs in the management of diabetes mellitus. Also, the use of lower doses of more than one herb may allow much better safety [2].

The utilization of herbal medicines for the treatment of diabetes mellitus has picked up significance all through the world. The World Health Organization has likewise suggested and empowered this training, particularly in nations where access to the traditional treatment of diabetes isn't sufficient. There is an expanded interest for utilizing natural products with antidiabetic activity, by virtue of the side effects related with the utilization of insulin and oral hypoglycemic agents. The available literature demonstrates that there are in excess of 400 plant species showing hypoglycemic activity [3].

Tablets are characterized as unit dose, temper clear strong arrangements containing at least one active ingredient [4]. The blend of different herbs (polyherbal) in a specific proportion will give desirable therapeutic impact in tablet because the potent phytochemical constituents of individual plants are insufficient to accomplish the advantageous impact [5]. The polyherbal formulation contains at least two herbs with various phytoconstituents having comparative or disparate therapeutic potential have been collectively producing desirable effects during the management of human illnesses [6]. The ubiquity of the polyherbal formulation is remarkable due to their wide therapeutic range i.e., compelling at a low dose and safe at high dose, however delivers less side effects while misused [7].

The present investigation was aimed to develop Polyherbal tablet containing hydroalcoholic extracts of *Anacardium occidentale* (bark), *Aegle marmelos* (leaves) and *Achyranthes aspera* (aerial parts) by dry granulation method for effective treatment of diabetes mellitus.

Materials and Methods

The bark of *Anacardium occidentale*, leaves of A. marmelos and whole aerial part of A. aspera were collected from rural area of Bhopal (M.P).

Preparation of extract

The petroleum ether and ethanol (70%) of *A.occidentale*, *A. marmelos* and *A. aspera* were prepared, separately by using soxhlet apparatus.

Formulation of polyherbal tablet

The hydroalcoholic extract of *A.occidentale, A.marmelos* and *A. aspera* was formulated into tablets by dry granulation method. The

dried powder extract and other ingredients were mixed uniformly and then the mixture was blended and granulated. The granules were compressed into tablets in an 8 station machine. The compositions of formulation are depicted in (Table 1).

Ingredient (mg)	F1	F2	F3	F4	F5	F6
Anacardium occidentale extract	100	100	100	100	100	100
Aegle marmelos extract	100	100	100	100	100	100
Achyranthes aspera extract	100	100	100	100	100	100
Talc	250	225	215	205	200	190
MCC	50	65	75	80	85	90
Magnesium Stearate	10	20	20	25	25	30

Table 1: Compositions of polyherbal tablets.

Evaluation of polyherbal tablets

Formulated tablets were evaluated for following parameters.

Weight variation

Twenty (20) tablets were selected randomly from formulation and their average weight was determined. Individual weights of each tablet were additionally determined utilizing the equivalent and contrasted with the normal weight.

$\% W=\{(W_o - W)/W_o\} \times 100$

Where,

% W=Weight variation in percentage

W_o=Average weight of tablet

W=Individual weight of tablet

Friability

Friability of the tablet was determined by utilizing Roche friabilator. In this device 20 numbers of tablets subjected and revolved. The combined impact of the abrasion and shock by using a plastic chamber that revolves at 25 rpm dropping at a distance of 6 inches.

$\% F= \{(W0 - W)/W_0\} \times 100$

Where,

% F=Friability in percent

W_o=Initial weight of tablet

W=Weight of tablet after test

Hardness

Hardness is the property of a material that enables it to resist plastic deformation usually by penetration, resistance to bending, scratching, cutting or abrasion. The force is measured in kilograms and when used in production, a hardness of 4 Kg/cm^2 is considered minimum for a satisfactory tablet. The hardness of tablets was measured using the Monsanto hardness tester.

Disintegration test (DT)

One tablet was placed in each of six tubes of DT apparatus. Disintegration test was performed at 37 ± 2°C. Disintegration time defined as time required disintegrating and passing all fragments through the sieve (#10) [8-10].

Evaluation of Antidiabetic Activity

Induction of experimental diabetes in rats

Subsequent to fasting, diabetes was initiated by a solitary intraperitoneal injection of 120 mg/kg body weight of 'Alloxan monohydrate' in distilled water. The animals were permitted to drink 5% glucose solution overnight to overcome the drug-induced hypoglycaemia. These animals were tested for diabetes following 15 days and animals with blood glucose (fasting) were chosen for experimentation.

Experimental Protocol

Animals were partitioned into four gatherings of 6 rats each.

Group I: Normal-control and got the vehicle (0.5 ml distilled water/day/rat)

Group II: Diabetic-control and got the vehicle (0.5 ml distilled water/day/rat)

Group III: Standard group administered Glibenclamide (600 µg/kg p.o.) for 15 days.

Group IV: Rats (diabetic) were administered polyherbal formulation for 15 days.

The fasting glucose levels were determined on days 0, 8th and 15th of formulation administration. During the experimental period, the rats were weighed every day and the mean change in body weight was determined [11,12].

Assessment of biochemical parameters

Total cholesterol, triglycerides and protein were determined on day 15 by the glucose oxidase method, using an auto-analyzer [13-15].

Statistical analysis

All analysis was performed utilizing graph pad prism for Windows. All statistical analysis is expressed as mean ± Standard Error of the Mean (SEM). Data were analyzed by one way ANOVA, where applicable $p<0.05$ was considered statistically significant, compared with vehicle followed by Dunnett's test.

Results

Evaluation of polyherbal tablets

The prepared tablets were described for various parameters, for example, hardness, friability, weight variety and disintegration time, which are condensed in (Table 2).

Weight variation

All the formulations passed the weight variation test, and it was acceptable (Table 2).

Hardness

The hardness of the tablets was observed to be in the range of 4 and 4.5 kg/cm^2 (Table 2).

Friability

The value of friability of prepared tablets was found to lie in between 0.51% to 0.55% (Table 2). Friability was observed to be under 1.0%, demonstrating a decent mechanical resistance.

Disintegration time

The results of the disintegration time of the tablet are shown in (Table 2). The disintegration time for tablet was observed to be between 15.24 to 16.32 min.

Formulation	Hardness (kg/cm^2)	Weight Variation	% Friability	Disintegration Time (min)
F1	4	Passes	0.54	15.24
F2	4.5	Passes	0.53	15.63
F3	4.3	Passes	0.55	15.86
F4	4	Passes	0.51	15.92
F5	4.5	Passes	0.52	16.05
F6	4.2	Passes	0.53	16.32

Table 2: Evaluation of Polyherbal Tablet.

Evaluation of Antidiabetic Activity

Antidiabetic activity of F1

Induction of diabetes in test rats was confirmed by the presence of a high fasting plasma glucose level. The impact of F1 on serum glucose levels of normal and Alloxan-induced rats are appeared in (Table 3).

Group	Treatment	Blood glucose (mg/dl)		
		Day 0	Day 8	Day 15
I	Normal	85.00 ± 6.00	95.00 ± 6.50	104.00 ± 6.02
II	Diabetic Control	270.15 ± 11.15	280.00 ± 12.10$^{\#}$	295.00 ± 10.12$^{\#}$
III	Diabetic+Glibenclamide	240.00 ± 6.00	140.00 ± 3.40***	110.04 ± 2.00***
IV	Formulation-I	243.00 ± 6.50	145.00 ± 1.60**	116.00 ± 2.16**

Table 3: Effect of polyherbal tablets on fasting plasma glucose level in rats.

The animals treated with Alloxn in particular diabetic control group, a noteworthy increment in serum glucose level was seen on 0, eighth and fifteenth day contrasted and normal control bunch rats. The animals treated with glibenclamide showed huge lessening in serum glucose level contrasted with diabetic control rats. After the administration polyherbal tablets (F1) to diabetic animals, a critical decrease in blood glucose level was observed. The findings exhibited that F1 produces potent antidiabetic activity.

Biochemical parameters of F1

Table 4 displayed results of lipid profiles in control and experimental rats. The animals of diabetic control demonstrated critical increment in serum triglycerides and total cholesterol, while decline in protein when contrasted with normal animals. The F1 treated animals indicated noteworthy decline in complete cholesterol and triglycerides; and huge increment in protein. Every one of these impacts was seen on day 15. The outcome of lipid profile demonstrated that F1 produces significant anti-hyperlipidaemic activity.

Amid the examination, the body weights of rats before and after treatment were estimated (Table 5). The outcomes displayed that diminished in body weight of rats after induction of diabetes, and increased in body weight of rats after treatment with F1.

Group	Treatment	TC (mg/dL)	TG (mg/dL)	Total protein (g/dl)
I	Normal	61.50 ± 3.01	75.00 ± 3.50	8.00 ± 1.0
II	Diabetic Control	170.00 ± 19.05	110.0 ± 5.00	4.50 ± 0.5
III	Diabetic+Glibenclamide (600 µg/kg)	85.00 ± 1.70**	78.00 ± 6.00**	7.90 ± 0.5**
IV	Formulation-I	100.00 ± 2.50**	80.00 ± 5.50**	7.80 ± 0.5**
Values are expressed as mean ± S.E.M (n=6). Values are statistically significant at #P<0.001 vs. normal group; *P<0.05 vs. diabetic control group.				

Table 4: Determination of biochemical parameters after administration of polyherbal tablets.

Group	Treatment	Initial weight (g)	Final weight (g)
I	Normal	151.00 ± 6.00	180.00 ± 5.00
II	Diabetic Control	180.00 ± 7.00	160.00 ± 6.00
III	Diabetic+Glibenclamide	165.00 ± 5.80	180.00 ± 6.00*
IV	Formulation-I	170.00 ± 5.10	195.00 ± 7.80*

Table 5: Antidiabetic effect of Formulation-I treatment on body weight.

Discussion

Herbs plays significant job in the treatment than the allopathic medicines because of less side effects, ease and simple accessibility. The examination work done on that premise and the chose plants for the formulation was truly demonstrated for the remedial utilization of antidiabetic purpose. The polyherbal antidiabetic tablets were assessed for different parameters, for example, weight variation, hardness, friability and disintegration time, which were observed to be worthy according to the Pharmacopoeial specifications.

The hardness of formulation was estimated in kg/cm^2 with the assistance of Monsanto tester. Amongst all the formulations prepared, F1 has been observed to be the most worthy one as far as weight variation and disintegration time. This formulation indicated obvious hardness characteristics (4.0), which encouraged its fast disintegration (15.24 min). The friability (0.54) of formulation demonstrated that the tablets were mechanically stable. The whole formulated tablet breezed through the weight variation test. The disintegration time of formulation was not more than 16.32 min. On the basis of various specifications, formulation batch 1 was selected as the optimized batch. Further antidiabetic examine was done on F1.

The fundamental mechanism underlying hyperglycemia includes over-production (excessive hepatic glycogenolysis and gluconeogenesis) and diminished usage of glucose by the tissues. The consequences of the present examination demonstrate that polyherbal tablets were found to diminish the glucose level in alloxan induced diabetic animals. Alloxan has been appeared to actuate free radical production and cause tissue damage. The pancreas is particularly vulnerable to the activity of alloxan-induced free-radical harm. Induction of diabetes with alloxan is related with a characteristic loss of body weight, which is because of increased muscle wasting and because of loss of tissue proteins. The distinctions in the body weights saw amid the time of treatment of the rats treated with polyherbal tablets were increased when contrasted with the diabetic control, which might be because of its defensive impact in controlling muscle wasting, i.e., reversal of gluconeogenesis and may also be due to proper glycemic control. In alloxanized animals, there was an expansion in the estimation of total cholesterol and triglycerides, with the exception of protein esteems, while the polyherbal tablets treated group demonstrated an expanded estimation of protein esteems, and diminished total cholesterol and triglycerides in a huge way. This decreased the total cholesterol and triglycerides; it might be assumed that the polyherbal tablets is responsible for the improvement of the transcription of lipoprotein lipase similar to that of insulin, since in the untreated or under treated diabetes animals, the level of triglycerides and cholesterol increments because of expanded production of very low density lipoprotein and unavailability of protein lipase which hydrolyses the triglycerides to very low density lipoprotein because of insulin insufficiency [12, 16-18].

It is reported that the extract of *A.occidentale*, *A. marmelos* and *A. aspera* containing flavonoids as chief chemical constituents. The flavonoid compounds could have induced the observed impacts. However, it is reported that flavonoids constitute active biological principles of most medicinal plants with hypoglycemic and antidiabetic properties. Thus, this active principle may be responsible for the observed antidiabetic effect of the polyherbal tablets.

Conclusion

Polyherbal tablets containing extracts of *A. occidentale, A.marmelos* and *A. aspera* were formulated for the treatment of diabetes mellitus. In view of results it is concluded that the formulation and evaluations are great. Formulation F1 indicated least disintegration time of 15.24 min. Subsequently, it was chosen as an enhanced formulation and subjected to antidiabetic activity. The administration of polyherbal tablet (F1) exhibited significant antidiabetic effect by controlling the blood glucose level. The polyherbal tablet is rich in flavonoid, and this suggests that the antidiabetic activity of polyherbal formulation is due to presence of phenolic content. Further in future examinations are required to assess the stability study of optimized formulation.

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