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Original Article

DEVELOPMENT AND EVALUATION OF ANTIDIABETIC POLYHERBAL TABLET USING MEDICINAL PLANTS OF TRADITIONAL USE

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ABSTRACT

Objective: The aim of the present study is to develop and evaluate poly herbal tablet prepared for management of diabetes with enhanced disintegration time.

Methods: The polyherbal extract prepared using methanolic extract of selected traditionally used medicinal plants such as *Adenanthera pavonina, Kigelia africana, Parkia biglandulosa* and *Syzygium jambos*e (1:1:1:2) was evaluated in the alloxan monohydrate induced diabetic rat model. The polyherbal tablets were prepared by wet granulation method with excipients microcrystalline cellulose, dicalcium phosphate dehydrate and sodium starch glycolate. After preformulation studies tablets were evaluated by using weight variation, hardness, friability and disintegration time. The diabetic rats treated with polyherbal extract were compared with the diabetic control rats group.

Results: Positive results were obtained in the observed parameters, thus favoring the use of the plants. Pre-formulation study revealed that all the evaluated parameters were found to be within the acceptable limits. The weight variation of the formulated tablets was 1.43 % RSD. The disintegration time of the formulations was found to be 9.50 minutes. The tablets also underwent accelerated stability over the period of three months. No marked changes were observed in all the parameters evaluated during three months of accelerated stability study.

Conclusion: Laboratory-scale preparation of polyherbal tablet can lead to new powerful and stable oral dosage formulations for diabetes mellitus and lighten the synergistic area of action of herbs.

Keywords: Medicinal plants, *Adenanthera pavonina, Kigelia africana, Parkia biglandulosa*, *Syzygium jambose*, Polyherbal tablet

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INTRODUCTION

Plants have played a unique integral role in providing food, medicine, clothing, shelter, etc. Natural products have been extensively explored to discover new drugs [1]. In fact, plants have been used for medicinal purpose since 5000 y [2]. Approximately 70-90% of the population in developing countries continues to use ancient drugs based on plant extracts [3]. The inherent usefulness of traditionally used medicinal plants should be encouraged for worldwide reception and for the benefit of humanity. Scientific assessment and authentication of traditional medicine are being essential to open any other possibilities for the development of alternate medicine and therapeutic approaches [4]. The most influential and promising elements are the secondary metabolite present in the plants [5]. Secondary metabolites of plant origin are molecules or macromolecules biosynthesized in plants, including alkaloids, glycosides, tannins, lignans, etc. that have a variety of beneficial therapeutic uses for humans, such as their antiallergics, antitumor, antioxidants, anti-inflammatory, antidiabetic activity [6]. Plants are always are the presentative source of medicine as many more drugs which are used presently have been derived from them directly or indirectly [7]. There is a large collection of plants with antidiabetic potential only some of these have been scientifically proven and many more have yet to be explored and tested [8]. The prevalence of diabetes mellitus is increasing compared to recent years; therefore, various researches are being to discover a better medicine to cure this disease [9]. Herbal medicines are usedin treating diabetes mellitus has become important throughout the world. The world Health Organization has also suggested and authorized this drilling, particularly in countries where access to treating diabetes is not enough. There is widespread interest in using natural products with antidiabetic activity, by virtue of side effects related to the usage of insulin and oral hypoglycemic agents. The available literature shows that there are more than 400 species of plants that show hypoglycemic activity [10]. Current diabetes mellitus medications emphasisonmonitoring to control blood glucose levels of the blood to a normal level. During the treatment modern synthetic drugs causes side effects with some serious medical complication. Hence, acts as savior as an alternative medication treatment as traditionally used medicines have been used since long time [6].

This study has focused on four plants which are *Adenanthera pavonina, Kigelia africana*, *Parkia biglandulosa* and *Syzygium jambose* to developed new polyherbal formulation useful to treat diabetes mellitus. *Adenanthera pavonina* belongs to the Mimosaceae family, commonly known as the red-beaded tree. It is an important medicinal plant of the "Indian subcontinent". Various parts of Adenanthera pavonina being traditionally used plants, have been used in the treatment of gout, diabetes, diarrhea, asthma, inflammation, rheumatism, tumors and ulcers and as a tonic [11]. Earlier phytochemical research has shown that the leaves contain octacosanol, dulcitol, beta-sitosterol glycosides, flavones and Stigmasterol and the alcoholic extract of the leaves contains an alkaloid. It is reported to have a large number of flavonoids, mainly gallic acid, terpenoids, tannins, sterols (beta-sitosterol, beta-sitosterol-3β-D-glucoside), triterpinoids (nonacosane and entriacontane) and saponins (sapogenins) [12, 13]. *Kigelia Africana* (Bignoniaceae), known as the african sausage tree, is traditionally used as medicinal planteffective for a wide range of therapeutic activities, such as antidiabetic, anticancer, antimalarial, antibacterial, analgesic, antileprotic and antidiarrheal, anti-inflammatory, anti-urolithiasis, antioxidant, etc. [14], Whereas several compounds have been recognized from the plant such as lupeol, β-sitosterol, sitosteryl β-D-glucoside, canofilol, pomolic acid, hydroxypomolic acid, iridoids, naphthoquinones and coumarins with potential pharmacological activity [15, 16]. *Parkia biglandulosa* is a large, beautiful, evergreen tree known as the badminton ball tree because of its brown beaded flower heads that resemble a badminton ball [17]. Preliminary qualitative tests revealed the presence of plant metabolites such as carbohydrates, alkaloids, tannins, flavonoids, saponins, and glycosides. The secondary metabolites present in *Parkia biglandulosa* provide a basis for its traditional uses [18]. Various plants of parkia species are traditionally used to treat different ailments, such as diabetes, diarrhea, wounds, hypertension, cough, chronic hemorrhoids, conjunctivitis, and measles [19]. *Syzygium jambos* (Myrtaceae) has traditionally been used to treat asthma, chronic

bronchitis, diarrhea, epilepsy, and inflammation [20]. The phytochemical studies on the parts of the plant showed the presence of different bioactive constituents, such as glycosides, triterpenoids, phenolic compound and volatile oils [21]. The plant has also been reported to have important pharmacological activities such as antimicrobial, antinociceptive, antitumor, antidiabetic, anti-inflammatory, antifungal, antioxidant and hepatoprotective activities [22]. The present investigation was conducted to develop and evaluate polyherbal tablet containing methanolic extracts of *Adenanthera pavonina, Kigelia africana, Parkia biglandulosa* and *Syzygium jambos* by wet granulation method for effective treatment of diabetes mellitus.

MATERIALS AND METHODS

Collection and authentication

Leaves of *Adenanthera pavonina* and *Syzygium jambos* were collected from Mumbai region, Leaves of *Kigelia africana* and bark of *Parkia biglandulosa* were collected from Pune region. The plants were authenticated from the Botanical survey of India, Pune. Plant specimens of the collected plants were submitted to the Department of Herbarium. (Reference no. BSI/WRC/IDEN. CER./2017/579, BSI/WRC/100-1/Tech./2019/01, BSI/WRC/IDEN. CER/2019/H3).

Preparation of extracts

The collected plant material were powdered and subjected to Soxhlet extraction with three different solvents with increasing polarity, such as petroleum ether, chloroform and methanol, separately. However, methanolic extract was selected for further study, the dried extracts were stored in a container at 4 °C and protected from light. Polyherbal extract was prepared in the composition 1:1:1:2 using methanolic extract obtained from *Adenanthera pavonina, Kigelia africana, Parkia biglandulosa* and *Syzygium jambos*e plants.

Acute toxicity study

The OECD-425 guidelines were followed for acute toxicity study. On overnight fasting, 2000 mg/kg of the polyherbal extract orally administered to 5 swiss albino mice. Only normal saline administered to one group as a normal control. For the next 24 h rats were observed individually for symptoms of toxicity and mortality or any signs of acute toxicity.

Antidiabetic activity

200 mg dose, which was $1/10^{th}$ of the maximum dose of acute toxicity study, was selected for assessment of antidiabetic activity. An intraperitoneal injection of alloxan monohydrate (150 mg/kg) dissolved in normal saline used to induce diabetes in overnight fasted rats. Freshly prepared solution was used for administration. The rats with elevated levels of glucose in plasma 200 mg/dl after 72 h of injection of alloxan were confirmed used for the experiment. Five groups of rats were formed, contains six rats in each. Group I: Normal-control rats group received the vehicle (Tween 80, 3% v/v in normal saline water); Group II: Diabetic-control alloxan-treated rats group received the vehicle; Group III: Standard group administered Glibenclamide (5 mg/kg of body weight); Group IV: Rats (diabetic) were administered polyherbal extract (200 mg/kg of body weight) with the vehicle. The extract treatment dose was administered orally using a cannula and blood was drawn each time from the retro-orbital plexus. The blood glucose levels of the rats were estimated on days 0, 7, 14 and 21 using the glucometer. The results of statistical analysis were expressed in terms of mean±SEM. One-way ANOVA and Dunnett's tests were used. Statistically value of $P<0.05$ was considered statistically significant. Polyherbal extract administered group was compared, diabetic control group.

Formulation composition of polyherbal tablet

In the present study polyherbal tablet was formulated by methanolic extracts of *Adenanthera pavonina, Kigelia africana, Parkia biglandulosa* and *Syzygium jambos*e by wet granulation method. Table 1 shows the detail of the composition of the formulation. Polyherbal extract was accurately weighed and passed through sieve no. 20. Granulating paste was made by adding weighed microcrystalline cellulose with water. Wet coherent mass is produced by mixing excipients with this granulating paste. To form granules, wet coherent mass passed through sieve 22. The granules dried in an oven at 40-45°.

Table 1: Formulation composition of polyherbal tablet

S. No.	Ingredients	Weight (mg)
1	Polyherbal extract	200
2	Microcrystalline cellulose	100
3	Dicalcium phosphate	160
4	Sodium starch glycolate	20
5	Povidone k30	15
6	Magnesium Stearate	5

Evaluation of powder blend

Before compression, the lubricated powder blends characterized for different preliminary compression parameters like bulk density, tapped density, carr's index and angle of repose to determine the flow behavior [23].

Loose bulk density

It was determined using a granulated cylinder filled with a previously weighed powder blend with measuring volume. Bulk density is calculated by taking ratio of weight of powder blend with volume consumed by its packing.

Tapped density

It was determined by pouring a powder blend to graduated cylinder which is tapped on the hard surface. The tapping continued till no further change in volume of powder blend in cylinder was observed. Tapped density is calculated by taking ratio of weight of powder blend with volume of tapped packing.

Carr's index

It was determined using bulk and tapped density, Carr's index of powder blend was calculated using the equation, Carr's index = Tapped density–Bulk density/Tapped density × 100

Angle of repose

The accurately weighed powder blend was placed in the funnel. The height of the funnel has been adjusted so that the funnel tip touches apex of the heap or powder blend. The powder blend allowed to flow freely through the funnel to the surface. The dust cone diameter was measured and the angle of repose was calculated using the equation:

$$\text{Tan } \theta = h/r \text{ Where, } h = \text{Pile height, } r = \text{Pile radius}$$

Physical characterization of polyherbal tablets

Various physical characteristics such as thickness, weight variation, friability, hardness, and disintegration time of compressed tablet were evaluated using pharmacopoeia methods [24].

Color and appearance

Color and appearance of formulated tablets were visually inspected.

Weight variation test

Randomly 20 tablets were weighed for average weight calculation by individually weighed tablet. The deviation from the mean and tablet weight was calculated and expressed as percentage

Hardness

Hardness of the tablet was measured using a previously calibrated Monsanto hardness tester.

Friability test

Friability determines the combined effect of shock and abrasion. Friability was tested according to the pharmacopeia for the tablets with the Roche friabilitor (100 revolutions 25 rpm). For the friability of acceptance, it should no longer be greater than 1.0%. Friability was calculated from the equation,

% friability = [W0-Wt/W0] × 100 Where, W0 = initial weight, Wt = final tablet weight

Thickness

Tablet thickness was measured using vernier caliper

Disintegration time

It was determined by using disintegration test apparatus kept at 37±0.5 °C of the immersion liquid. The required time for complete disintegration of was noticed. Tablets disintegrate when above gauge no particles observed and which passed quickly through the 10 # mesh screen.

Stability study

The polyherbal formulation was subjected for accelerated stability studies as per to ICH guidelines [25]. The tablets stored at 40±2 °C and 75±5% RH for 3 mo duration. The tablets were evaluated for description, % friability and disintegration test compared with the initially studied evaluation parameter of tablets.

Ethical statement

The animal experimentation protocol has been approved with reference no. (IAEC/01/18-19/PN01), by Institutional Animal Ethics Committee (IAEC) prior to initiate the animal study.

RESULTS AND DISCUSSION

In acute toxicity study, polyherbal extract-treated rats showed no evident behavioral change observed up to 2000 mg/kg body weight dose, within 72 h observation period no mortality detected. Rats treated with Alloxan induced diabetes group showed a marked increase in glucose level observed in rats with contrast to the normal control group. The glibenclamide treated animals showed decrease in serum glucose level in contrast to diabetic control rats. After administration of polyherbal herbal extract to diabetic rats there is the decline in blood glucose level observed (fig. 1). The polyherbal extract treated group of rats showed a significant reduction in blood glucose level by 145.31±8.24 mg/dl on 21st day of the experiment compared to diabetic control rats group (table 2).

Table 2: Effect of polyherbal extracts on blood glucose level in wister rats

Groups	Blood glucose level (mg/dl)			
	0 d	7th day	14th Day	21st Day
Normal Control	95.33±3.630	98.33±5.16	96.5±4.288	97.21+2.380
Diabetic Control	281.17±15.814	282.33±15.54	292.67±11.935	295.01+10.25
Diabetic+Standard	279.17±9.96^{ns}	228.17±13.81**	186.83±19.321**	146.7±23.46**
Polyherbal extract	272.2±0.06^{ns}	224.14±9.54**	180.04±22.39**	145.31±8.24**

Values are expressed as Mean+SEM n=6, ^{ns}p>0.05, **p<0.01 respective Diabetic control (One way ANOVA followed by Dunnett's test)

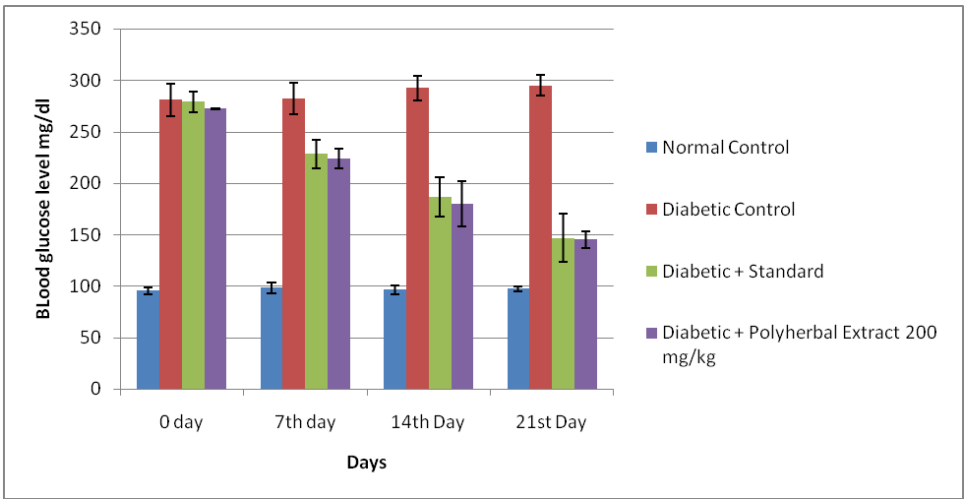

Fig. 1: Effect of polyherbal extract on blood glucose level (mg/dl) of rats

The study revealed that polyherbal herbal extract produces a potent antidiabetic activity. The activity exerted by polyherbal extract might be due to the cumulative effect of the phytochemicals present.

Based in preformulation studies, the flow properties of the powder blend prepared from combining polyherbal extract with excipients are good. The observed parameters for preformulation evaluation of powder blend are shown in the following table 3.

Table 3: Preformulation parameters for powder blend

S. No.	Parameters	Results
1.	Bulk Density(g/ml)	0.50+0.12
2.	Tapped Density(g/ml)	0.56+0.07
3.	Carr's Index (%)	16+0.04
4.	Angle of repose	23.95+0.01

The polyherbal tablets are brown in color with smooth surface. The results of the post-compression parameters such as weight variation, hardness, friability and disintegration are shown in table 4. In all the formulations the hardness test indicates a good mechanical resistance whereas friability indicates that the tablets had good mechanical strength.

Table 4: Physical evaluation of the polyherbal tablets

S. No.	Parameters	Results
1.	Color	Brownish
2.	Odor	Characteristic
3.	Texture	Smooth
4.	Weight variation (% RSD)	1.43
5.	Hardness (kg/cm^2)	3.41
6.	Thickness(mm)	5.00
7.	Friability (%)	0.01
8.	Disintegration (minutes)	9.50

The accelerated stability study of the polyherbal formulation was conducted at specified conditions of temperature as well as relative humidity. The three months data for various parameters are depicted in table 5. The developed herbal was found to be stable up to 3 mo.

Table 5: Accelerated stability studies of developed polyherbal formulation

Parameters	Initial	I st month		II nd month		III rd month	
		RT	40 °C	RT	40 °C	RT	40 °C
Nature	Compact solid	Compact solid	Compact solid	Compact solid	Compact solid	Compact solid	Compact solid
Color	Brown	Brown	Brown	Brown	Brown	Brown	Brown
Odour	Characteristics	Characteristics	Characteristics	Characteristics	Characteristics	Characteristics	Characteristics
Texture	Smooth	Smooth	Smooth	Smooth	Smooth	Smooth	Smooth
Thickness (mm)	5	5	5	5	5	5	5
Average weight (mg)	500	500	500	500	500	500	500
Friability (%)	0.01	0.01	0.03	0.05	0.10	0.07	0.11
Disintegration (min)	9.50	9.50	9.42	9.20	9.01	9.35	9.10
Hardness (kg/cm^2)	3.41	3.41	3.35	3.23	3.17	3.02	3.41

CONCLUSION

In Indian literatures the utilization of medicinal plants and polyherbal formulations for treatment of various ailments is described. The inclination of pharmaceutical investigations is moving away from single-component investigations to use of combinations of multicomponent. There is mounting proof to demonstrate that medicinal plants hold synergistic combination, which also includes side-effects counteracting combinations. Bearing in mind this information, the synergistic activity of Parkia biglandulosa, Adenanthera pavonina, Kigellia africana and Sygiumjambose in the form of the polyherbal formulation was studied. Further in future investigations are required to assess possible mechanism of action responsible for the antidiabetic activity.

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AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

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