



Polyherbal Capsule: Formulation and Evaluation for Antidiabetic activity

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Abstract: The well-known plant components for their anti-diabetic properties are one natural product with such potential is the pomegranate (*Punicagranatum*), with hypoglycemic activity noted from its flowers. Oil of *Illiciumverum* is extracted from the pericarps of its fruit that possesses different biological activities, such as antifungal, antioxidant, and antibacterial properties. *Nyctanthesarbor-tristis* (Family-Oleaceae), commonly known as night-flowering Jasmine has high medicinal values in Ayurveda. The popular medicinal use of this plant is anti-diabetic. The current study's objective was to create a polyherbal dosage form and assess its effectiveness and stability. The various methanolic extracts of all plants medicines were combined in the various ratios to create the polyherbal extract. Both *in vitro* antioxidant and *in vitro* antidiabetic activity of the extract were evaluated. The medication was then put into capsules with a 0 size and evaluated for every aspect of a capsule. The stability of the most recent medicine was examined under diverse circumstances.

Introduction:

Diabetes is a serious public health concern across the world. Hyperglycemia is a symptom of diabetes mellitus, which is triggered by an insulin shortage or it's less binding on receptors or both. It is one of the most serious health issues that have now turned into a world-wide spread. Diabetes' global incidence has risen quickly during the last four decades [1]. diabetes is increasing rapidly in India but a systematic understanding of its distribution and time trends is not available for every state of India. We present a comprehensive analysis of the time trends and heterogeneity in the distribution of diabetes burden across all states of India between 1990 and 2023. However, the World Health Organization has programmed to inhibit the rise in diabetes incidence and premature mortality from by 1/3rd by year 2030 but the results are not promising. It has been estimated recently that the cases of diabetes from 20-79 age will upsurge from 41 million in 2015 to 51 million in 2030 (1 in 10 adults) [2]. In allopathic system of medicines, insulin and oral anti-diabetic medications used now a day to treat diabetic complications are efficient in lowering blood

glucose levels along with a variety of adverse effects. Several herbal medicines and minerals are mentioned in the literature for the effective control of diabetes mellitus. The herbal medicines are considered safe as they have fewer side-effects than allopathic system of medicines [3, 4]. Evaluating the hypoglycemic ability of medicinal plants has therefore become essential. In the current study, *in vitro* antidiabetic activity is being investigated, a polyherbal extract made from an equal mixture of A polyherbal antidiabetic formulation were made through extracts of *P. granatum* [5], *I. verum* [6] and *Nyctanthesarbor-tristis* [7] have anti-diabetic activity, but there is no study conducted on the combination of these selected plant extract. So we attempt to make polyherbal anti-diabetic formulation from *Punicagranatum* (fruit), *Illicium verum* (flower) and *Nyctanthes arbor-tristis* (flower) and evaluated their antioxidant and anti-diabetic properties [8].

Materials and Methods

Pomegranate (*Punica granatum* L.) appears to be native to some parts of Asia (Iran, Malesia, and India), America



(USA, Peru), Africa (Equatorial region), and Europe (Turkey). The fruits are consumed mostly fresh or in the form of derived productions like juice, paste, jam, and wine. *Illicium verum* (Illiciaceae) is an aromatic evergreen tree bearing purple-red flowers and anise-scented star-shaped fruit. It grows almost exclusively in southern China and Vietnam. Its fruit (star anise) is an important traditional Chinese medicine as well as a commonly used spice. The characteristically shaped fruit is used to treat vomiting, stomach aches, insomnia, skin inflammation and rheumatic pain. *Nyctanthes arbor-tristis* L. (Oleaceae), are shrubs or small trees with soft white hairs, young branches sharply quadrangular. Leaves are opposite, ovate, apex acute or acuminate,

rough with short stiff hairs, margin is entire or with few large distinct teeth, base is rounded or slightly cuneate, with the main nerves conspicuous beneath.

Preparation of extracts:

All plant drugs were individually dried, powdered and extracted with methanol for 12 h. The extracts concentrated below 60° were stored at cool area. The dried extracts were mixed in ratio 1:1:1:1 in order to get a polyherbal extract [9].

Formulation of Polyherbal granules: The granules from polyherbal extract were prepared through wet granulation method. In this method the four herbal extracts were taken in same ratio and mixed with the excipients in the ratios mentioned below in Table 1.

Table 1: Various composition of polyherbal formulation

F. Code	PH1	PH2	PH3
Ingredients			
Punica granatum	100	50	150
Illicium verum	100	100	100
Nyctanthes arbor-tristis	100	150	50
Lactose	50	50	50
Micro crystalline cellulose	5	5	5
Magnesium carbonate	5	5	5
Starch paste	10 % Aqueous solution paste		

Pre-formulation study: Preformulation involves the application of biopharmaceutical principles to the physicochemical parameters of drug substance are characterized with the goal of designing optimum drug

delivery system. It includes assessment of different parameters like bulk and tap density, Hausner's ratio, Carr's index, angle of repose in order to determine the flow properties polyherbal granules (Table 2) [10].

Table 2: Flow Property Measurements Polyherbal formulation

S No.	Parameter	PH1	PH2	PH3
1	Bulk density	0.807 g/ml	0.713 g/ml	0.782 g/ml
2	Tapped Density	0.772 g/ml	0.682 g/ml	0.712 g/ml
3	Carrs index	5.11 %	4.01 %	4.72 %
4	Hausners ratio	1.15 ± 0.02	1.13 ± 0.04	1.14 ± 0.01
5	Angle of repose	21.15°	18.05°	20.11°

Capsule evaluation parameters: The parameters like organoleptic characters, average weight, weight variation, disintegration time, moisture content and dissolution rate were determined in order to evaluate the capsules of polyherbal granules (Table 3).

Average weight of capsules: Average weight of 20 capsules was calculated using a digital weighing balance.

Weight variation: Randomly 20 capsules were selected, weighed individually and their average weight was compared with weight of individual capsule [11].



Drug Content: Six capsules' contents were poured into a mortar, the dose-equivalent quantity (20 mg) was measured, and the drug content of the capsules was ascertained using the method described in IP [12].

Disintegration time: In this method six random capsules were placed in all the six tubes of the Basket rack and dipped into the beaker containing 900 ml medium. The Simulated Gastric fluid (SGF) was upheld at $37\pm 2^\circ$. The

basket was moved 5-6 cm in height, at the rate of 28-32 cycles per minute through a motor driven shaft. The time was noted in which the capsules pass through a 10 mesh screen and have disintegrated [13].

Moisture content: It was determined by taking 5 g of sample and drying it in the hot air oven at $100-110^\circ$ until the persistent weight is obtained. Any change in the weight of dried sample was calculated [14].

Table 3: Physicochemical parameters of polyherbal capsule formulation

S. No.	Parameter	PH1	PH2	PH3
1	Total ash	3.23	3.23	2.83
2	Acid insoluble ash	0.56	0.44	0.51
3	Sulphated ash	1.68	1.08	1.18
4	Water soluble extractive	12.67	11.02	11.45
5	Ethanol soluble extractive	15.68	13.98	14.01
6	pH	7.05	7.15	7.21
7	Moisture content	1.35 %	2.01 %	1.01 %
8	Average weight	515	531	498
9	Weight variation	490-510 mg	490-510 mg	490-510 mg
10	Disintegration time	2 min 25 sec	2 min 89 sec	3 min 21 sec
11	Loss on drying	2.64 %	2.21 %	2.82 %

In vitro antidiabetic activity:

α -Amylase inhibition activity: To estimate the in vitro antidiabetic activity, the procedure was utilized. The absorbance was estimated at 540 nm using UV-Visible spectrophotometer. A sample blank reaction was produced in the same way using the plant extract without enzyme. Acarbose as positive control was used.

Percentage inhibition was calculated using following equation [15]

$$\text{Inhibition (\%)} = \frac{(AC-AB)-(AS-ASB)}{(AC-ACB)} \times 100$$

Where A is absorbance; C is control; CB is Control Blank; S is absorbance of sample and SB is sample blank (Table 4, Figure 1).

Table 4: in vitro alpha amylase inhibitory activity of Polyherbal formulation

Concentration	25 $\mu\text{g/ml}$	50 $\mu\text{g/ml}$	100 $\mu\text{g/ml}$	150 $\mu\text{g/ml}$	200 $\mu\text{g/ml}$
Acarbose	48.04 \pm 1.65	61.11 \pm 2.08	72.98 \pm 2.03	79.15 \pm 1.85	92.10 \pm 1.74
PH1	43.18 \pm 1.68	55.74 \pm 1.59	64.21 \pm 1.42	73.05 \pm 1.52	90.21 \pm 1.62
PH2	40.11 \pm 1.11	51.04 \pm 1.02	60.01 \pm 1.16	70.02 \pm 1.02	88.15 \pm 1.05
PH3	36.05 \pm 1.11	43.11 \pm 1.11	55.01 \pm 1.01	63.02 \pm 1.02	80.11 \pm 1.01

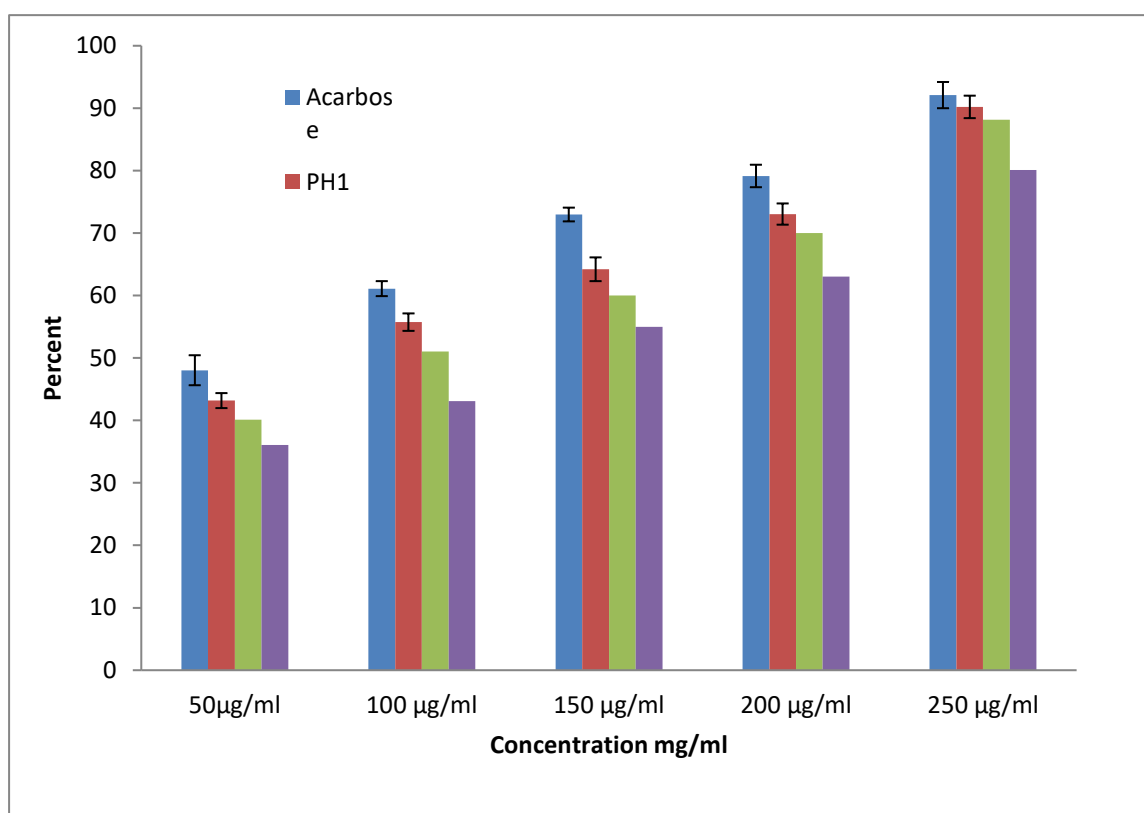


Figure 1: in vitro alpha amylase inhibitory activity of Polyherbal formulation

α -glucosidase assay: In order to estimate the in vitro antidiabetic activity by α -glucosidase assay the method was used. It was estimated as a percentage inhibition.

$$\text{Inhibition (\%)} = \frac{\text{AN} - \text{AT}}{\text{AN}} \times 100$$

Where AN is absorbance of negative control; AT is Absorbance of test sample (Table 5, Figure 2) [16].

Table 5: in vitro alpha glucosidase inhibitory activity of polyherbal formulation

Concentration	25 µg/ml	50 µg/ml	100 µg/ml	150 µg/ml	200 µg/ml
Acarbose	45.41 ± 1.45	58.42 ± 2.64	68.31 ± 3.12	75.21 ± 2.23	84.24 ± 3.01
PH1	41.12 ± 1.94	53.13 ± 1.64	61.25 ± 1.35	69.23 ± 1.29	79.12 ± 1.87
PH2	36.08 ± 1.14	45.12 ± 1.21	54.01 ± 1.12	62.13 ± 1.11	72.11 ± 1.01
PH3	39.11 ± 1.04	49.01 ± 1.13	58.21 ± 1.05	64.03 ± 1.05	75.07 ± 1.11

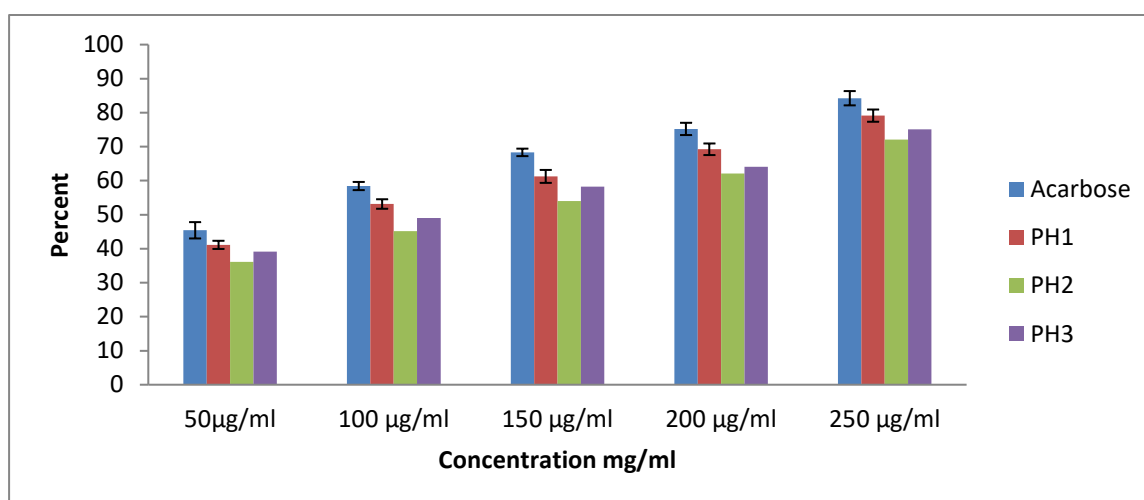


Figure 2: in vitro Alpha Glucosidase inhibitory activity of Polyherbal formulation

Results and Discussion:

The organoleptic properties of developed formulation were brown colored, bitter in taste, and had a characteristic odor. Moisture is one of the major factors responsible for the deterioration of the drugs and formulations. Low moisture content is always desirable for higher stability of drugs. Moisture contents of the prepared formulations PH1, were below 10% in the range of 1.05w/w Bulk density, Tapped Density, Carr's index, and Hausner Ratio Study of bulk density and tapped density are important as density of a powder defines its packaging for individual drugs and formulations. In the α -amylase assay, the PH1 formulation have significant inhibitory activity ($p < 0.05$) of the α -amylase enzyme except at 50 $\mu\text{g/mL}$. At all concentrations tested, there were significant differences ($p < 0.05$) in the α -glucosidase assay and α -amylase. However at higher concentrations, ethanol extract exhibited highest inhibition. The IC50 values for the inhibition of α -amylase and α -glucosidase indicate that PH1 showed appreciable α -amylase and α -glucosidase inhibitory effects. This study indicates that PH1 could be useful in management of diabetes. It is predicted that diabetic complications occur as a result of the oxidative stress due to the formation of free radicals with the glucose oxidation and the subsequent oxidative degradation of glycosylated proteins. Therefore the use of antioxidants along with anti-diabetic drugs are frequently recommended to avoid such complications. The formulation PH1 showed antioxidant activity along with in vitro anti-diabetic activity.

Conclusion: In light of phyto-pharmacological research,

polyherbal capsule was found to be reasonably stable under accelerated conditions. The effectiveness of polyherbal combinations of selected plants against diabetes was examined through *in vitro* method. A polyherbal mixture of plants shown potent anti-diabetic properties in an *in vitro* research. More research using more focused methods is required to identify the components responsible for the activity and the process by which it happens. Plants and plant products can exert promising antidiabetic efficacy based on recent studies. Plant sources of antidiabetic agents are very much popular from the ancient era as they are relatively safer and much cheaper alternatives than synthetic drugs.

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