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DEVELOPMENT AND EVALUATION OF POLYHERBAL ANTIDIABETIC TABLET

Nikita U. Dhake*, Mona Y. Agrawal, Dr. Yogesh P. Agrawal, Rajashri R. Dhonnar and Akash S. Nimbone

Government College of Pharmacy, Kathora naka, Amravati, 444602.

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***Corresponding Author**
Nikita U. Dhake
Government College of Pharmacy, Kathora naka, Amravati, 444602.

ABSTRACT

The main objective of the project is to formulate and evaluate polyherbal antidiabetic tablet. Polyherbal antidiabetic formulation consist of four herbs viz., Syzygium cumini (leaves), Aloe barbadensis (whole leaf), Tinospora cordifolia (stem) and Triphala churna. The granules were prepared by wet granulation technique. The granules prepared out from the extract of above four herbs were investigated for preliminary studies like bulk density, tapped density, hausners ratio, compressibility index and angle of repose. Three different batches of tablet were prepared (F1, F2 and F3) using direct compression method. The present study deals with the evaluation of formulated tablet (Hardness, Thickness, Disintegration time, Friability, Loss on drying and weight variation). Stability studies were carried out to determine the stability The antidiabetic potential of formulation was determined by inhibition of carbohydrate digestive enzyme i.e. α– amylase enzyme and α-glucosidase enzyme.

KEYWORDS: The granules were prepared by wet granulation technique.

INTRODUCTION

Diabetes is a group of metabolic disorders characterized by elevated blood glucose levels due to impaired insulin secretion, insulin action, or both. Abnormalities in carbohydrate, lipid and protein metabolism are due to the importance of insulin as an anabolic hormone. People with type 2 diabetes are asymptomatic in the early stages of the disease, but hyperglycemia, especially in children, can lead to polyuria, polydipsia, polyphagia, weight loss, and blurred vision due to absolute insulin deficiency. may occur. Uncontrolled diabetes can lead to stupor

and coma, and if left untreated can lead to death from ketoacidosis and, rarely, nonketotic hyperosmolar syndrome.[1] Most plants contain carotenoids, flavonoids, terpenoids, alkaloids and glycosides, which often have antidiabetic effects. The hypoglycemic effect produced by plant treatments is due to the plant's ability to improve pancreatic tissue function, often achieved by increasing insulin secretion or decreasing intestinal glucose absorption. An increasing number of people are now living with diabetes, raising concern among the medical community and the general public. The main purpose of this article is to introduce a number of medicinal plants that are effective in treating diabetes and other mechanisms of plant compounds used to lower blood sugar levels and increase insulin secretion.[2]

MATERIALS AND METHODS

Collection and Authentication

The leaves of jamun tree, whole leaf of aloe vera and stem of giloy plant collected from local area of Amravati (Maharashtra) in December 2022. The above herbs were authenticated by Dr.

P.A. Gawande, Head of Botany Department, Sant Gadge Baba Amravati University. Vouncher specimens and sanpic material was deposited in Pharmacognosy and phytochemistry Laboratory, Government College of Pharmacy, Amravati.

Preparation of extract

S.cumini and Aloe vera leaves and giloy stem were washed with water and shade dried. S.cumini and Aloe vera leaves were ground with a mechanical grinder. 500 g of the pulverized leaves were then Soxhlet extracted. 26.3 g of S.E. A cumini leaf extract and 24.6 g of aloe vera leaf extract were obtained. The extract was dried in a water bath. In addition, giloy/guduchi stems were washed with water, cut into 2-2.5 inch pieces and hammered. I added 4 times its weight of water and cooked it over low heat. Water evaporated to only a quarter of its original volume. The water was then filtered through a new cotton cloth. The filtered water was again exposed to mild heat. When the water evaporates completely, it leaves a whitish residue that can be dried. The dried residue was known as guduchi kvath and this kvath was used in the formulation of tablets.

Preliminary Phytochemical Analysis

The extracts of S. cumini, Aloe barbadensis, T.cordifolia and triphala were subjected to preliminary phytochemical analysis for the detection of primary and secondary metabolites.

Development of Formulation[3,4]

Wet granulation technology was chosen because it is convenient for small-scale preparations. The standardized extracts and other ingredients contained in each formulation were weighed, ground and sieved through Sieve #. 80 Individually All ingredients except talc and magnesium stearate were mixed together, ground with a mortar and pestle, and sieved again through sieve no.80. This material was mixed with the slowly added gum acacia solution. After mixing, the powder mass was sieved with sieve number 10. Granules are obtained via sieve no.18 and dried at room temperature. After drying, the granules were sieved again with no. 2 sieve. Remove granules larger than 18 and store in a desiccator. The powder blend was compressed into 550 mg tablets on a single punch manual rotary tablet press using an 11 x 8 mm punch set with appropriate compression pressure. The granules were mixed with talc and magnesium stearate before punching, the mold cavity was adjusted to the required weight and the granules were punched into tablets.

Preformulation studies[5]

The following pre-compression parameters were tested for granules.

- **Angle of Repose:** Determined using the funnel method. Accurately weighed granules were placed in the hopper and the height of the hopper was adjusted so that the tip of the hopper just touched the top of the pile. The granules flowed freely over the surface through the hopper. The diameter of the powder cone was measured and the angle of repose was calculated using the formula: $\tan \theta = h/r$

  Where, θ = angle of repose, h = height of powder cone formed, r = radius of powder cone formed

- **Loose Bulk Density (LBD):** It is determined by pouring a weighed quantity of granules into a graduated cylinder and measuring the volume and weight of the powder.

  LBD = weight of the powder / volume of the packing

- **Tapped Bulk Density (TBD):** It is determined by placing a graduated cylinder, containing a known mass of granules. The cylinder was allowed to fall under its own weight onto a hard surface from the height of 10cm at two seconds intervals. The tapping was continued until no further change in volume was noted.

  TBD = weight of the powder / volume of the tapped packing

- **Hausner`s ratio:** It is measurement of frictional resistance to the drug. The ideal range should be 1.2 – 1.5. It is determined using the following formula:

  Hausner`s ratio: TBD / LBD

- **Compressibility Index:** The compressibility index of the blend was determined using Carr`s compressibility index.

  Compressibility index (%) = (TBD – LBD) X 100 / TBD
- **Loss on drying**: One gram of granules was transferred into a dried, glass stoppered shallow weighing bottle. The contents were distributed evenly and placed in the drying chamber. The stopper was removed from the bottle and the contents were dried for a specified time to achieve a constant weight.

Loss on drying (%) = (Initial weight – Final weight) / (Initial weight) X 100

Evaluation of Tablet[6]

A. Hardness

Tablet hardness is the force required to break a tablet in a diameter compression test. Hardness is affected by colorant loading, binder concentration, and compression, which are related to the fill/kraft ratio. Hardness is the property of a material that allows it to withstand plastic deformation, usually caused by indentation. However, the term hardness can also refer to resistance to bending, scratching, abrasion, or cutting. For each formulation, tablet hardness was measured using a Monsanto hardness tester and the mean and hardness were calculated.

B. Thickness

The thickness of tablets is measured with a micrometer or vernier caliper. With a vernier caliper, the tablet is placed between the two jaws of the vernier caliper and the thickness of the tablet is determined by reading the scale. The unit is cm.

C. Weight Variation Test

Procedure: To conduct this test, 20 tablets were taken from the batch, each tablet was weighed, and the average tablet weight was determined.

IP Specification: A tablet passes the test if no more than 2 individual weights differ from the average weight by more than the percentage shown in the table, and no more than twice that percentage.

D. Friability

Friability is a test that measures weight loss when tablets are subjected to a standardize agitation process. For each formulation, tablet friability was measured using a Roche

Fribilator (Remi Equipments). Percent weight loss of 20 randomly selected tablets from each batch shaken in the crusher. After 4 minutes at a rotation speed of 25 rpm, the tablets were dedusted and the percent weight loss was calculated.

Friability = 100 (1-w/wk)

E. Disintegration Time

The disintegration test was performed according to IP specifications. Six tablets were used for testing and water was used as the disintegration medium. The temperature of the medium was maintained at 370° C. and the beaker was filled with a volume of 800 ml, taking care that the tablets were always below the water level at the highest and lowest positions of the basket rack assembly. A disc was placed over each tablet to prevent the tablets from floating in the medium. The device was run until all tablets had disintegrated.

F. In Vitro Dissolution Studies

Regulatory requirements make dissolution testing of multi-herbal medicines difficult due to the widely varying composition. The ingredients of polyherbal medicines are often mixtures of multiple herbal ingredients. Developing a solution is much more complex than developing individual components that are defined.

Accelerated Stability Studies[6]

Environmental conditions affects the stability conditions of the drug dosage form during its storage. Temperature, Light, Air, Humidity, and Package Components are some of the environmental conditions. All formulations were exposed to accelerated temperature conditions for 3 months to enhance stability. H. Room temperature (25 ± 2°C)/60% RH, 5°C/ambient temperature, and 40°C/75% RH. Various parameters such as tablet color, odor, texture, average weight, hardness, friability and disintegration time were studied under accelerated temperature conditions.

In-vitro antidiabetic study[7,8]

- **α-Amylase Inhibition assay**

α-Amylase (0.5 mg/ml) was mixed with samples at various concentrations (100–500 µg doses inhibit α-amylase enzyme µg/ml), to which was added 1% starch solution and 100 µl of 0.2 mm phosphate buffer was added (pH -6.9). The reaction was carried out at 37°C. for 5 minutes and stopped by adding 2 ml of 3,5-dinitrosalicylic acid reagent. The reaction mixture was heated at 100° C. for 15 minutes and diluted with 10 mL of distilled water in an ice bath.

α-amylase activity was determined by measuring the color intensity at 540 nm with a spectrophotometer.

Acarbose is used as a standard. Acarbose inhibits α-amylase Enzyme.

% of Inhibition is given by formula: A_C - A_S / A_C x 100

Where, A_C is absorbance of control and A_S is absorbance of sample.

- **α-Glucosidase Inhibition assay:** Inhibitory effects were determined by incubating 1 ml of starch solution (2% w/v maltose) with 0.2 M Tris buffer (pH 8) and various sample concentrations (100-500 mg/ml). The reaction mixture was incubated at 37°C for 10 minutes. Reactions were initiated by adding 1 ml of α-glucosidase enzyme (1 U/ml) and incubating at 35° C. for 40 minutes. The reaction was then stopped by adding 2 ml of 6N HCl. Color intensity was measured with a spectrophotometer at 540 nm.

Acarbose is used as a standard. Acarbose inhibits α-glucosidases Enzyme.

% of Inhibition is given by formula: A_C - A_S / A_C x 100

Where, A_C is absorbance of control and A_S is absorbance of sample.

RESULTS

Table no. 1: Preliminary phytochemical analysis.

Sr.no.	Phytoconstituents	Extracts			
		Ethanolic S.cumini	Methanolic A.barbadensis	Aqueous Tinospora cordifolia	Aqueous Triphala churna
1.	Carbohydrate	--	++	--	++
2.	Proteins	--	--	--	--
3.	Amino acid	--	--	--	--
4.	Glycosides	--	++	++	--
5.	Tanins	++	++	++	++
6.	Flavonoids	++	++	--	++
7.	Alkaloids	++	++	++	++
8.	Sterols	--	++	++	++
9.	Saponins	--	++	--	--

Table no.2: Composition of Polyherbal tablet for trial.

Ingredients	F1 (mg)	F2 (mg)	F3 (mg)
Ethanolic extract of Syzgium cumini	50	25	75
Methanolic extract of Aloe barbadensis	50	75	25
Aqueous extract of T. Cordifolia	50	25	50
Triphala churna	50	50	75
Starch	20	20	20
Talc	5	5	5
Magnesium stearate	5	5	5

Acacia gum	5	5	5
Lactose	315	340	290

Fig.no.1: Polyherbal antidiabetic tablets.

Table no.3: Preformulation studies of herbal dried extract.

Parameters	**F1**	**F2**	**F3**
Angle of repose	26.14±0.106	28.56±0.126	25.39±0.145
Loose bulk density (g/cm^3)	0.374±0.002	0.394±0.0018	0.341±0.002
Tapped bulk density (g/cm^3)	0.527±0.002	0.514±0.0017	0.52±0.0005
Hausner`s ratio	1.406±0.017	1.314±0.01	1.492±0.005
Compressibility index (%)	28.67±0.038	22.55±0.067	32.86±0.038
Loss on drying (%)	0.944±0.020	0.962±0.010	0.972±0.007

Table no.4: Evaluation Parameters of Polyherbal tablet for various batches.

Sr.no.	**Parameters**	**F1**	**F2**	**F3**
1.	Colour	Brownish	Brownish	Brownish
2.	Odor	Charactetistic	Characteristic	Characteristic
3.	Texture	Smooth	Smooth	Smooth
4.	Hardness	7.23±0.028	7.094±0.028	6.792±0.064
5.	Thickness (mm^2)	3.4±0.244	3.5±0.248	3.6±0.323
6.	Weight variation (%w/w)	1.13±0.043	1.23±0.017	2.06±0.018
7.	Friability (%w/w)	0.424±0.028	0.358±0.011	0.454±0.013
8.	Disintegration (min.)	13.8±0.860	12.4±0.509	10.4±0.509

Table no.5: Stability testing parameters of tablet.

Paramet ers	**Observations**									
	Initials	**30 days**			**60 days**			**90 days**		
		RT/ 60% RH	**5^{0}C/ Ambient**	**40^{0}C/ 75% RH**	**RT/ 60% RH**	**5^{0}C/ Ambient**	**40^{0}C/ 75% RH**	**RT/ 60% RH**	**5^{0}C/ Ambient**	**40^{0}C/ 75% RH**
Colour	Brownish	NC	NC	NC	NC	NC	NC	NC	NC	NC
Odor	Character istic	NC	NC	NC	NC	NC	NC	NC	NC	NC
Texture	Smooth	NC	NC	NC	NC	NC	NC	NC	NC	NC
Average	1.47	1.47	1.47	1.47	1.47	1.45	1.45	1.43	1.41	1.41

weight										
Hardness (Kg/cm^2)	7.03	7.03	7.03	7.03	7.01	7.01	7.00	7.00	7.00	6.99
Friability (%)	0.412	0.412	0.412	0.412	0.412	0.412	0.410	0.410	0.410	0.407
Disintegr ation time (minute)	12.2	12.2	12.2	12.2	12.2	12.2	12.19	12.19	12.18	12.17

Table no.6: In- vitro diabetic assay studies.

Sr.no.	Initials	IC50 values (µg) for	
		α-amylase enzyme	α-glucosidase enzyme
1.	Sample	352.64±5.79	263.33±7.18
2.	Acarbose	81.45±6.21	56.23±7.24

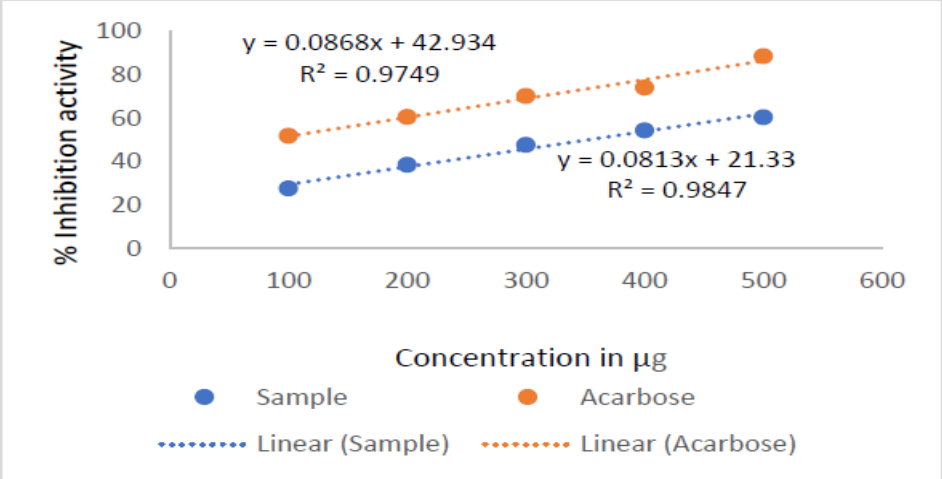

Fig no.2: Alpha amylase inhibition activity.

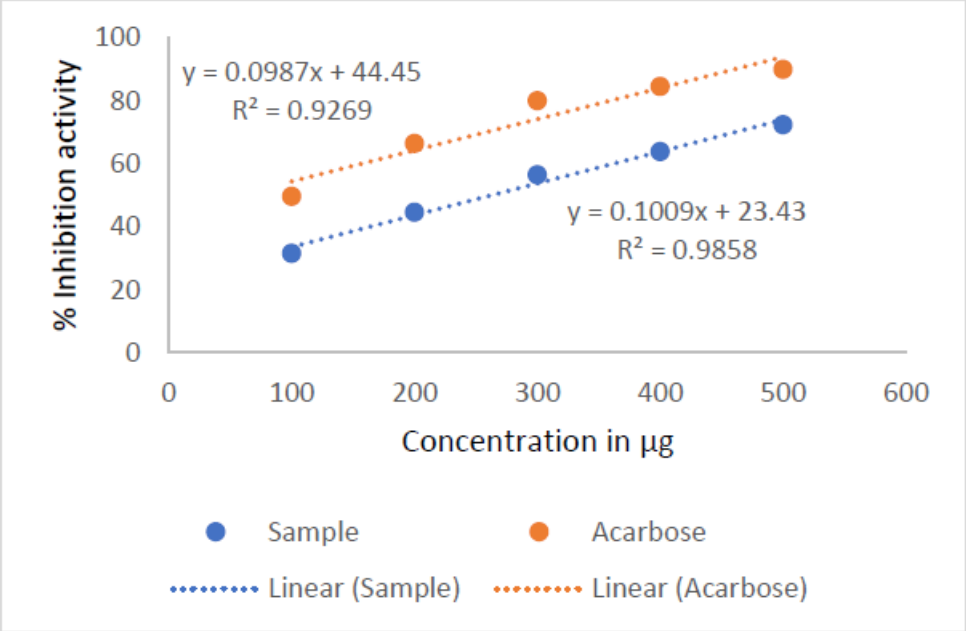

Fig.no.3: Alpha glucosidase inhibition assay.

DISCUSSION

Three trail batches of polyherbal tablet were formulated. Preformulation studies like determination of bulk density, tapped density, angle of repose, hausner ratio, compressibility index of tablet granules was done. After the performance of preformulation studies, polyherbal tablet was prepared from the above granules. A whole tablet of 550mg was prepared. Three different formulas were used for making 550mg of tablet and were named as F1, F2 and F3. Later the evaluation of prepared polyherbal tablet was done. Hardness, weight variation, thickness, loss on drying and disintegration test of tablet was determined. Hardness was found to be 7.03 Kg/cm^2, friability was 0.412%, thickness was 3.4mm^2, weight variation was 1.47mg and disintegration time was found to be 12.2 min. The stability study revealed that the formulation remain stable at different room temperature for long period of time i.e. 90days. Very slight change was observed in evaluation parameter values at the end of 60^{th} day or 90^{th} day. The change was very minute. Hence, we can say that the formulation passes the stability study. In-vitro antidiabetic assay of polyherbal antidiabetic tablet was done. Alpha – amylase inhibition assay and alpha- glucosidase inhibition assay was performed. The standard drug used was Acarbose which is a commonly used marketed antidiabetic formulation. Prepared polyherbal tablet was able to significantly inhibit the both enzymes The IC_{50} values of tablet for both enzymes were 352.64±5.79 and 263.33±7.18 and that of Acarbose were 81.45±6.21 and 56.23±7.24. This shows that less concentration of acarbose is required to inhibit 50% of enzyme in body. However, the prepared polyherbal tablet also shows significant inhibition at minimum concentration. Hence, we conclude that our formulation has good antidiabetic property.

CONCLUSION

The data presented in this study; it was demonstrated that the developed polyherbal antidiabetic tablet formulation possess significant, therapeutically efficacious, suitable vehicle for drug delivery in low cost but definitely with high potential. Developed new polyherbal tablet formulation is suitable for Diabetes Mellitus treatment.

REFERENCES

1. Akram T Kharroubi and Hisham M Darwish. Diabetes mellitus: The epidemic of the century, World Journal of Diabetes, 2015; 6: 850-867.
2. Wesam Kooti, Maryam Farokhipour etal. The role of medicinal plants in diabetes: a systemic review, Electronic Physician, 2016; 8: 1832-1842.

3. Harikesh Maurya, Tirath Kumar. Formulation, Standardization and evaluation of polyherbal dispersible tablet, International Journal of Applied Pharmaceutics, 2019; 11.
4. Margret Chandira, B. Jayakar. Formulation and Evaluation of herbal tablet containing Ipmoea digitata linn. Extract, International Journal of Pharmaceutical sciences review and research, august 2010; 3.
5. Sanjay Kumar Kushwaha, Mohan Lal Korl. Development and evaluation of Polyherbal tablet from some Hepatoprotective herbs, Scholars Academic Journal of Pharmacy, 2014; 3(3): 321-326.
6. T. Sampath Kumar et al. Formulation and Evaluation of in-vitro antidiabetic Polyherbal tablets from some traditional used herbs. The journal of Phytopharmacology, 2021; 10: 173-179.
7. Zainab Riaz et al. In Vitro investigation and evaluation of Novel drug based on Polyherbal extract against type 2 diabetes, Hindawi Journal of Diabetes research, 2020.
8. Ramana Murty Kadali SLDV et al. In-vitro evaluation of antidiabetic activity of aqueous and ethanolic leaves extracts of Chloroxylon swietenia, 2017.