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Formulation and evaluation of polyherbal anti-diabetic tablet for oral drug delivery system

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***Abstract*---**The Present Investigation was aimed to develop a Polyherbal tablet formulation for effective treatment of diabetes mellitus. Polyherbal tablets containing various Herbal extracts were prepared using different super disintegrants in varying concentrations to achieve minimum disintegration time. Pre-compression Parameters for all blends were within acceptable range of pharmacopoeial specifications. Formulation F4 showed minimum disintegration time of 14.20 minutes. Hence, it was selected as an optimised formulation and subjected to stability study. Stability study results revealed that, formulation F4 was a stable formulation having better disintegration time and % friability and could be used for effective treatment of diabetes mellitus.

***Keywords*---**polyherbal tablet, anti-diabetic activity, effective treatment, diabetes mellitus.

Introduction

Diabetes is endocrine metabolic disorder, characterised by elevated blood sugar level. Hyperglycemia arises due to either absolute or relative insulin

deficiency or cellular resistance towards insulin [1]. Prevalence of diabetes is rising all over word by alarming rate. India stood at the first position with highest number of diabetic subjects [2, 3, 4]. The most upsetting trend of disease is onset age shifting 10 years earlier. Long term uncontrolled hyperglycaemia may rise diabetic complications at later age. Numbers of modern medicines are available for glycaemic control but major draw-back is long term side effects. Herbal medicines have great demand in developed as well developing countries. As per one estimate by WHO still 80% population of the developing countries still depends on herbal products for their prime healthcare.

Safer medication for many chronic diseases has re-emergence of formulation of potentherbal formulations for many health problems. Previous study was an attempt to evaluate the pharmacognostical standardization of Pterocarpus Marsupium, Heartwood of Vijaysar is antibiotic and hypoglycaemic, and is used to control blood sugar. Kino gum, obtained from incisions in bark, has astringent, anti-diarrhoeal, and anti- haemorrhagic properties. Leaves are used externally to treat boils, sores, and other skin diseases, while flowers are febrifuge.

Cyperus Rotundus (dried rhizome) Ethno-pharmacological relevance: Cyperus rotundus L. (Cyperaceae) is a medicinal herb traditionally used to treat various clinical conditions at home such asdiarrhea, diabetes, pyresis, inflammation, malaria, and stomach and bowel disorders. In present study we have attempted to prepare a Polyherbal solid form i.e tablets, of the above-mentioned extracts [5, 6, 7].

Materials and Methods

Materials

S.No.	Name of the Materials	Manufacturer/Supplier	Use in Formulation
1	Pterocarpus Marsupium	Mother Herbs Pvt. Ltd Patparganj, New Delhi	Active Ingredent
3	Micro Crystalline Cellulose	IIMT University Meerut	Diluent/Disintegrant
4	Na-Methyl Paraben	-	Preservative
5	Starch	-	Binder/Disintegrant

Equipment Required

S. No	Instruments	Suppliers
1	weight balance	Shimadzu corporation
2	Hardness tester	Monsanto, India
3	pH Meter	
4	Roche Friablator	Electro lab, India
5	FTIR Spectroscopy	Shimadzu corporation, Japan
6	DSC	-

7	Tray dryer	-
8	Uv- Spectrophotometer	Lab India
9	Disintegrator	Electro lab, India
10	Dissolution apparatus	Electro lab, India

Collection and Authentication

Whole plant of Pterocarpus Marsupium, heart wood of Pterocarpus Marsupium Linn. It consists of dried juice obtained by making vertical incisions to the stem bark of the plant Pterocarpus Marsupium Linn., belonging to family Leguminosae were collected from CCS University Meerut, in the month of February to March. All these plants were authentified by Dr. K.C Shah, Botanist-Visiting professor at CCS University, Meerut U.P. (Herbarium No. 042/041/044/048/049/050).

Extract Preparation

The plant materials of Pterocarpus Marsupium were cut into slices and shade dried ground to a coarse powder and passed through a 80 mesh sieve. The powdered plant materials were subjected to extraction using different extraction methods such as Soxhlet apparatus, maceration, percolation using different solvents, and subjected to phytochemical screening and further study.

Preformulation Study

Angle of Repose

The angle of repose was calculated using the fixed height approach to estimate the flow parameters of the physical mixtures in all formulations. A funnel with a 10mm inner diameter stem was suspended from the platform at a height of 2cm. About 10g of sample was progressively transferred came into contact with the funnel's steam. The radius of the powder cone was estimated by drawing a crude circle around the pile base. The following formula was used to compute the angle of repose from the average radius.

$$\theta = \tan^{-1}(h/r)$$

Where,

θ = Angle of repose
h = Height of the pile
r = Average radius of the powder cone

Loose Bulk Density

Bulk densities of all types of granules were assessed by gently pouring 25g of material into a 100 ml graduated cylinder through a glass funnel. The sample's volume was measured and recorded. By pouring a weighed quantity of mix into a graduated cylinder and measuring the volume and weight, the apparent bulk density was established.

LBD = Weight of the powder/volume of the packing

Tapped Bulk Density

By gently pouring 25g of material through a glass funnel into a 100ml graduated cylinder, the tapped densities of all types of granules were calculated. From a height of 2 inches, the cylinder was tapped until a steady volume was reached. The sample's volume after tapping was measured, and the tapped density was determined. A graduated cylinder containing a known mass of medicine Excipients blend was used to determine it. At 2-s intervals, the cylinder was permitted to fall from a height of 10cm onto a hard surface under its own weight. The tapping was kept going until there was no more change in volume.

TBD = Weight of the powder/vol of the tapped packing

Compressibility Index

The compressibility index of the blends was determined by Carr's compressibility index.

Compressibility index (%) = (TBD-LBD)×100/TBD

Hausner's Ratio

It is the measurement of frictional resistance of the drug. The ideal range should be 1.2–1.5. It is determined by using the following formula:

Hausner's ratio= TBD/LBD

Loss on Drying

A well-mixed granules (1g) was placed in a shallow weighing bottle with a dry glass stopper. The materials were uniformly dispersed and put into the drying chamber (Sartorius moisture balance). The bottle's cap was removed, and the contents were dried for a set amount of time to achieve a consistent weight.

Loss on drying (%) = ([Initial weight – Final

Preparation of Anti-diabetic Tablet

In the present study, dried powder of extract was formulated into tablet dosage form by direct compression method. Formulation has the following composition: Pterocarpus Marsupium, Starch, MCC, Na-Methyl Paraben, and Talc.

Evaluation of Tablets

All the formulated tablets were subjected to following evaluation parameters:

Color and Appearance

The compressed tablets were examined for their color and appearance.

Weight Variation Test

20 pills were randomly chosen and weighed to establish the average weight. Weighing each tablet separately was also done. In each example, the percentage variation from the average weight was computed. Only two of the sample size ton's tablets stray from the average weight by a bigger percentage, and none by more than double that amount.

Hardness and Friability Test

The hardness and friability were tested for the tablets using calibrated hardness tester (Monsanto) and Roche friabilator (4 min at 25 rpm) tests, respectively.

Disintegration Test for Tablets

A rust-proof wire gauge disc is placed at the lower end of a glass of plastic tube 80–100 mm long with an internal diameter of about 28 mm and an external diameter of 30–31mm. Six pills were inserted in the tube, and the tube was raised and lowered so that the entire up and down movement was repeated 28–32 times/min. When no particles remain above the gauge, which easily pass through mesh, the tablets are dissolved (10 mesh screen).

Thickness

The thicknesses of the tablets were evaluated by Vernier calipers.

In-Vitro Anti-Diabetic Activity: 6.9.1 α-amylase Inhibition Assay

α-amylase was dissolved in phosphate buffer saline (PBS, 0.02mol/L, pH 6.8) at a concentration of 0.1mg/ml. Various concentrations of sample solutions (0.25mL) were mixed with α-amylase solution (0.010ml) and incubated at 37 °C for 5 min. Then the reaction was initiated by adding 0.1ml 1.0% (w/v) starch substrate solution to the incubation medium. After incubation at 37 °C for 3 min, the reaction was stopped by adding 1mL DNS reagent (1% Dinitrosalicylic acid, 0.05% Na2SO3 and 1% NaOH solution) to the reaction mixture and boiling at 100 °C for 5 min. After cooling to room temperature, the absorbance (Abs) at 532nm was recorded by a spectrophotometer. The inhibition percentage was calculated by the following equation:

$$\text{Inhibition (\%)} = [(Abs1 - Abs2)/Abs1] \times 100$$

where,

Abs1=sample

Abs2 = control.

Stability Studies

Optimised formulation F4 was subjected to accelerated stability study at 40±2°C and 75±5 % RH for 1, 2 & 3-months. After each month interval, the samples were observed for any change in physical appearance. Tablets were analysed for % friability and disintegration testing. It was observed that surface was devoid of

any change in colour or appearance of any roughness. The results obtained are mentioned in table 7. Results revealed that, there were no significant changes in all parameters analysed.

Results and Discussion

Preformulation Study

Table.1 Flow properties and corresponding Angle of Repose

Flowability	Angle of Repose
Excellent	26-31
Good	32-38
Fair	39-44
Passable	45-50
Poor	51-56
Very Poor	57-68
Very, Very Poor	>68

Table.2 Powder Flow according to Compressibility Index and Hausner's Ratio

Compressibility Index	Type of Flow	Hausner's Ratio
< 1.00	Excellent	1.00-1.12
12-16	Good	1.13-1.20
17-22	Fair	1.21-1.28
23-26	Passable	1.29-1.34
27-31	Poor	1.35-1.46
32-35	Very Poor	1.47-1.56
>37	Very, Very Poor	>1.65

Table.3: Evaluation of Powder Blends

Formulation	Bulk Density (gm/ml)	Tapped Density (gm/ml)	Carr's Index (%)	Hausner's Ratio	Angle of Repose
F1	0.50	0.60	16.68	1.32	26.78
F2	0.54	0.58	11.67	1.20	28.80
F3	0.48	0.54	10.76	1.17	25.77
F4	0.44	0.62	12.00	1.18	22.90
F5	0.52	0.53	14.72	1.12	20.89
F6	0.46	0.48	12.52	1.11	23.56

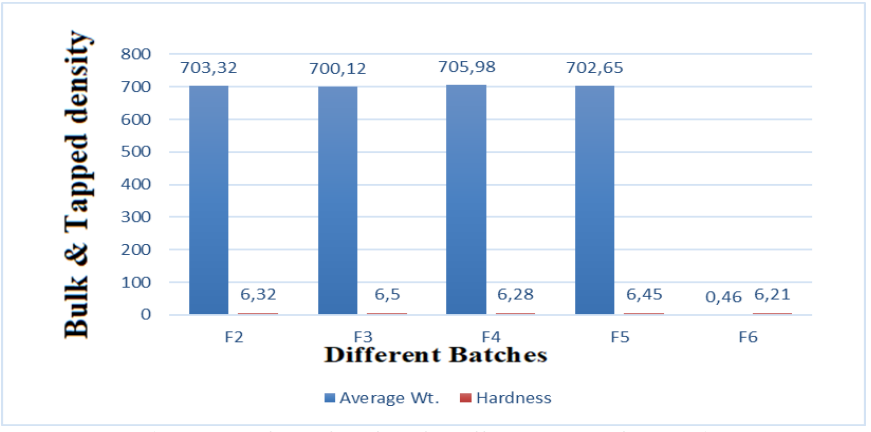

Fig.1 Powder Blends of Bulk & Tapped Density

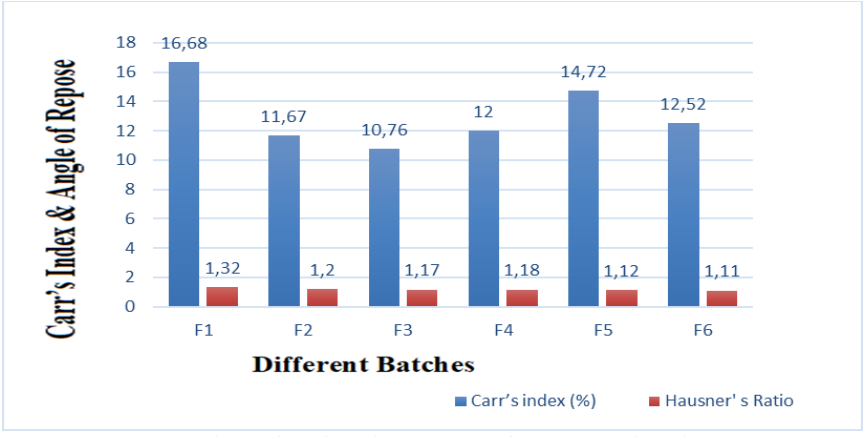

Fig.2 Powder Blends of Carr's Index & Angle of Repose

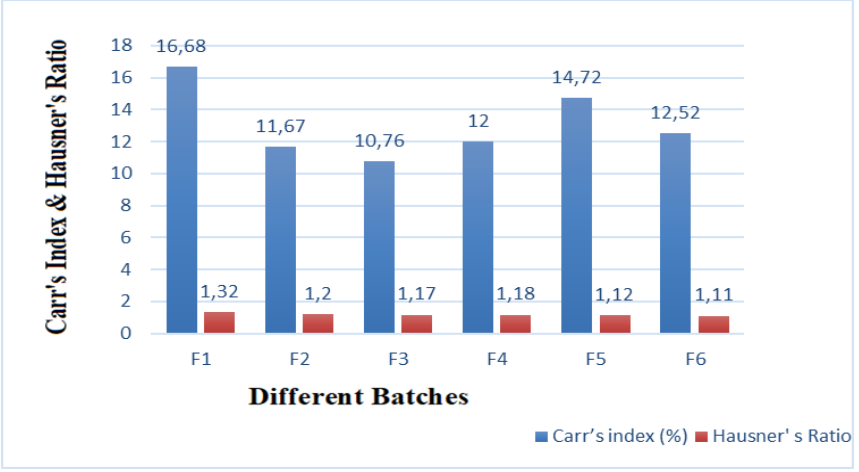

Fig.3 Powder Blends of Carr's Index & Hausner's Ratio

Tablet.4 Development of Anti-diabetic Tablet

Ingredients (Mg)	F1	F2	F3	F4	F5	F6
Pterocarpus Marsupium	50	50	50	50	50	50
Starch	10	10	10	15	10	10
Micro crystalline Celloulose	05	10	05	15	05	10
Na-Methyl Paraben	0.5	0.5	0.5	1.0	0.5	0.5
Talc	02	02	02	2.5	02	02

Table.5: Evaluation of Polyherbal Tablet

Formulation	Average weight (mg)	Hardness (Kg/cm2)	Thickness (mm) %	Friability	Disintegration Time (min)
F1	701.20	6.10	7.03	0.56	15.24
F2	703.32	6.32	7.05	0.45	16.20
F3	700.12	6.50	7.09	0.85	12.17
F4	705.98	6.28	7.04	0.58	14.20
F5	702.65	6.45	7.01	0.76	16.12
F6	701.34	6.21	7.08	0.46	10.19

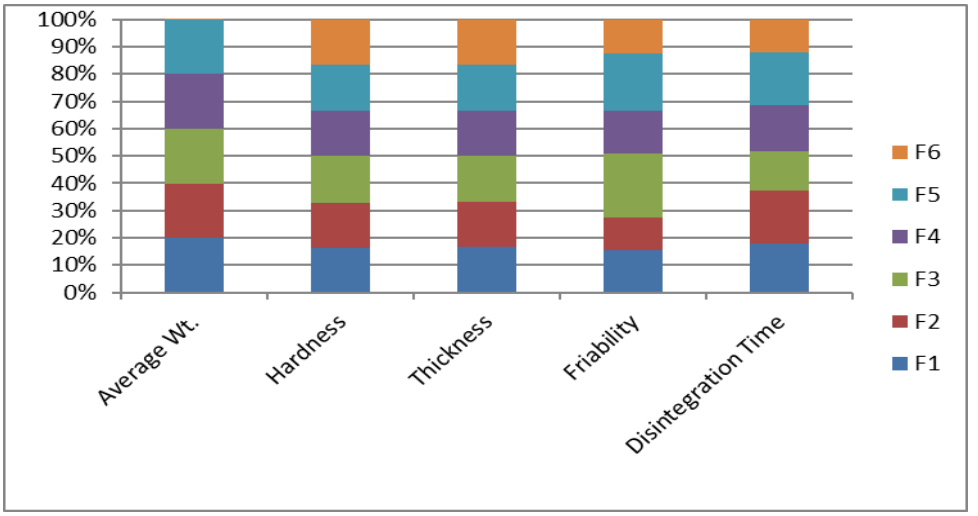

Fig.4 Evaluation of Polyherbal Tablet

In-vitro Anti-Diabetic Activity

α -Amylase Inhibition Assay

Standard Acarbose

Polyherbal Formulation

Table.6: In vitro Anti-diabetic Activity

Compounds	Concentration	Absorbance	S-C	S-C/S	% inhibition	IC50
	50µg	0.190	0.006	0.04663344	4.623212330	
Acarbose	100µg	0.210	0.021	0.12961754	11.89172541	
	250µg	0.230	0.044	0.17584067	18.524060 1	1500.75
	500µg	0.278	0.2	0.39211289	35.2012876	
	1000µg	0.329	0.146	0.42722718	45.71270381	
	500µg	0.264	0.3	0.33211262	35.19119761	
	Control	0.182				
	50µg	0.205	0.021	0.10243902	10.24390244	

Pterocarpus Marsupium	100µg	0.256	0.072	0.28125	28.125	
	250µg	0.344	0.16	0.46511628	46.51162791	272.20
	500µg	0.528	0.344	0.65151515	65.15151515	
	1000µg	0.816	0.632	0.7745098	77.45098039	
	Control	0.182				

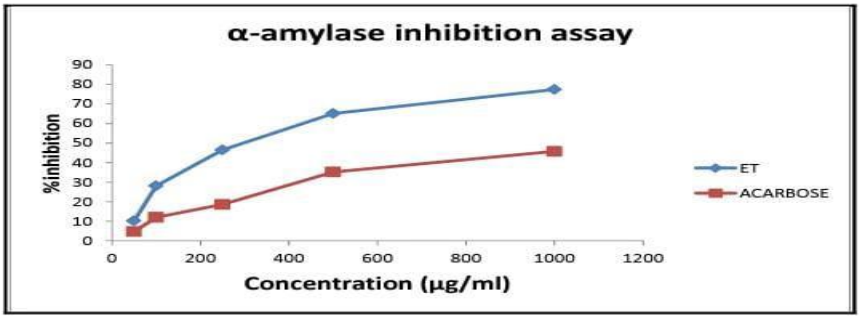

Fig.5 Graphical Representation of the α-Amylase Inhibition Assay

Stability Studies

From the results it was found that formulation F4 was the best formulation amongst the 6 formulations. Thus formulation F4 was selected for stability studies. Formulation F4 was analyzed for Colour, Appearance, Average Wt. (mg), % Friability and Disintegration Time (min) at the end of each month up to three months, results are shown in Table 3.10.

Table.7 Stability studies of selected formulation F4

Evaluation Parameters	Initial	1st Month	2nd Month	3rd Month
Colour	Green	Green	Green	Green
Appearance	Smooth	Smooth	Smooth	Smooth
Average weight (mg)	705.98	705.80	705.58	704.70
Thickness (mm)	7.04	7.00	6.08	6.00
% Friability	0.58	0.50	0.48	0.40
Disintegration Time (min)	14.20	14.15	14.10	14.00

Conclusion

The Present Investigation was aimed to develop a Polyherbal tablet formulation for effective treatment of diabetes mellitus. Polyherbal tablets containing various

Herbal extracts were prepared using different super disintegrants in varying concentrations to achieve minimum disintegration time. Pre-compression Parameters for all blends were within acceptable range of pharmacopoeial specifications. Formulation F4 showed minimum disintegration time of 14.20 minutes. Hence, it was selected as an optimised formulation and subjected to stability study. Stability study results revealed that, formulation F4 was a stable formulation having better disintegration time and %friability and could be used for effective treatment of diabetes mellitus.

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