Research Article

Formulation Development and Evaluation of Antidiabetic Polyherbal Tablet

Komal Patel [1*], Lal Hingorani[2], Vinit Jain[3]
[1] School of Pharmacy, RK University, Rajkot and Parul Institute of Pharmacy, Vadodara, Gujarat, India.
[2] Director, Pharmanza Herbal Pvt. Ltd., Dharmaj, Gujarat, India.
[3] Shree Dhanvantary Pharmacy College, Kim, Gujarat, India.
***Corresponding author's E-mail:** komalnishit@gmail.com

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ABSTRACT

The objective of the present study was to develop and evaluate anti-diabetic poly herbal tablet with improved disintegration time. The major challenge in polyherbal tablet is optimization of disintegrant composition. Twelve different blends were prepared by combining varying concentrations of super disintegrants to achieve short disintigration time. The tablets were prepared by wet granulation method using a binder solution containing starch. Preformulation study was carried out to evaluate powder flow characteristics. The results revealed that, the prepared blends possess good flow properties. The formulated polyherbal tablets were evaluated by postcompression parameters like, description, hardness, thickness, weight variation, friability and disintegration time. Formulation F9 containing Sodium starch glycolate (1.5%) and Crosspovidone (3.5%) showed minimum disintegration time of 10.10 minutes. All other parameters for formulation F9 were within acceptable pharmacopoeial limits. Formulation F9 was also subjected for accelerated stability study for three months and was evaluated for description, hardness, friability and disintegration time. Results of short term stability study were also found to be satisfactory and were comparable to initial formulation. Hence, the prepared polyherbal formulation F9 can be used as a stable, patient compliant and cost effective solid dosage form.

Keywords: Diabetes mellitus, Polyherbal, Sodium Starch Glycolate, Crosspovidone.

INTRODUCTION

Diabetes is endocrine metabolic disorder, characterised by elevated blood sugar level. Hyperglycaemia 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.[2] India stood at the first position with highest number of diabetic subjects.[3-4] The most upsetting trend of disease is onset age shifting 10 years earlier.[5] Long term uncontrolled hyperglycaemia may rise diabetic complications at later age.[6] Numbers of modern medicines are available for glycaemic control but major draw-back is long term side effects.[7]

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 potent herbal formulations for many health problems. Previous study was an attempt to evaluate the pharmacognostical standardisation of Momordica charantia, leaves of Gymnema sylvestre, stems of Tinospora cordifolia, bark of Cinnamomum zeylanicum, rhizome of Curcuma longa and roots of Withania somnifera.8 In present study we have attempted to prepare a Polyherbal solid form i.e tablets, of the above-mentioned extracts.

MATERIALS AND METHODS

Collection and Authentication

Whole plant of Momordica charantia, leaves of Gymnema sylvestre, stems of Tinospora cordifolia, bark of Cinnamomum zeylanicum, rhizome of Curcuma longa and roots of Withania somnifera were collected from Anand, Gujarat, in the month of March-May. All these plants were authentified by Dr. Darshika Shah, Botanist-Visiting professor at M S University, Vadodara, Gujarat. (Herbarium No. 044/045/046/047/048/049).

Extract Preparation

Hydroalcoholic extract of *Momordica charantia, Gymnema sylvestr, Withania somnifera, Cinnamomum zeylanicum*, aqueous extract of *Tinospora cordifolia* and Ethyl acetate extract of *Curcuma longa* were prepared and spray dried individually.

Each extract was individually weighed accurately according to following composition

Formulation Development of Polyherbal Tablet

Dispensing and Sifting

Accurately weighed quantities of all extracts were dispensed as per formulation table 2 in clean dispensing booth and sifted through 40# sieve.

Dry Mixing

The sifted material was taken in polybag and mixed properly for 10 minutes.

Binder Solution Preparation

Accurately weighed quantity of starch was dispensed and mixed with IPA in a glass beaker properly. The above mixture was properly stirred to get homogeneous binder solution.

Wet Granulation

Above dry mixed blend was granulated with the binder solution by adding drop wise with continuous mixing to get optimum granulation. The wet mass was passed through 18# sieve and then dried in tray dryer at 40°C to get optimum loss on drying.

Milling & Sifting

The dried blend was sifted through 22# sieve and weighed.

Lubrication

The blend was lubricated with magnesium stearate which was previously dispensed according to %yield and sifted through 60# sieve. The blend was properly mixed in polybag.

Compression

The lubricated blend was compressed on 8-station compression machine using 12.5 mm round standard concave punch for 600mg strength of tablets. The temperature of processing area was maintained at 25°C to 30°C and relative humidity was kept 30 to 32 %.

Different batches of formulation F1 to F12 were prepared by wet granulation technique as per the composition given in table 2.

Evaluation of Poly Herbal Formulation[9]

Evaluation of Powder Blends

Before compression, the lubricated blends were evaluated for different precompression parameters like bulk density, tapped density, angle of repose, Carr's index and Hausner's ratio to determine the flow behaviour.

Bulk Density

The powder sample under test equivalent to 10 gm was accurately weighed and filled in a 50-ml graduated cylinder. Powder was levelled and the unsettled volume, V0 was noted. The bulk density was calculated in g/cm3 by the formula,

$$\text{Bulk density } (\rho 0) = M/V0$$

Where, M = Mass of powder taken, V0= Apparent unsettled volume

Tapped Density

The powder sample under test equivalent to 10 g was filled in 50 ml graduated cylinder. The mechanical tapping of the cylinder was carried out using tapped density apparatus at a constant rate according to pharmacopoeia. Volume was considered as a tapped volume Vf.

The tapped density was calculated in g/cm3 by the formula,

$$\text{Tapped Density } (\rho t) = M/Vf$$

Where, M = Mass of powder taken, Vf = tapped volume

Angle of Repose

Angle of repose was determined by using funnel method. The accurately weighed blend was taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap or head of blend. The drug excipient blend was allowed to flow through the funnel freely on to the surface. The diameter of the powder cone was measured and angle of repose was calculated using the equation,

$$\tan \theta = h/r$$

Where, h = Height of pile, r = Radius of pile

Relationship between angle of repose and powder flow was determined as per pharmacopoeial standards, mentioned in table 3.

Compressibility Index (Carr's Index)

Based on the bulk density and tapped density, the % compressibility index of the granules was computed using the equation,

Compressibility (Carr's) index = Tapped density – Bulk density/ Tapped density × 100

Flow properties of blends were determined from the scale of flowability as shown in table 3.

Hausner's Ratio

It was determined using the formula,

Hausner's ratio = Tapped density/Bulk Density

Flow properties of blends were determined from the scale of flowability as shown in table 4.

Evaluation of Tablets[10]

Formulated tablets were evaluated for physical parameters like, description, hardness, thickness, weight variation, friability and disintegration testing.

Description

The compressed tablets were examined for their colour and general appearance.

Hardness

Test was performed using calibrated Monsanto hardness tester on ten tablets. Hardness reflects tablet crushing strength and measured in Kg/cm2.

Thickness

Thickness of prepared tablets was measured in millimetres using digital Vernier calipers.

Weight variation test

The average weight was determined by randomly selecting and weighing 20 tablets. Each tablet was also weighed individually. The deviation from the average weight in each case was calculated and expressed as percentage. Not more than two of the tablets from the sample size should deviate from the average weight by a greater percentage and none of the tablets should deviate by more than doubled that percentage.

Friability Test

Friability determines combined effect of shock and abrasion. Friability was tested as per pharmacopoeia for the tablets by using Roche friabilitor (100 revolutions at 25 rpm). For acceptance friability, should not be more than 1.0%. The friability was calculated by the equation,

$$\% \text{ Friability} = [W0 – Wt / W0] \times 100$$

Where, W0 = Initial weight of tablets, Wt = Final weight of tablets

Disintegration Test for Tablets

The disintegration test was performed using Electrolab disintegrating apparatus. One tablet was placed in each of the six tubes of the basket and the apparatus was maintained at 37 ± 0.50°C of the immersion liquid. The time required for complete disintegration of tablet was noted. The tablets are disintegrated when no particles remain above the gauge, which readily has passed through 10# mesh screen.

Stability Study

The optimized formulation F9 was selected for the stability studies. Drug composition or degradation occurs during stability, because of chemical alteration of the active ingredients or due to product instability, lowering the concentration of the drug in the dosage form. The accelerated stability studies were carried out according to ICH guidelines by storing the samples at 40 ± 2°C and 75 ± 5% RH for 3 months. The tablets were evaluated for description, %friability and disintegration testing and compared with tablets which were evaluated immediately after manufacturing.

RESULTS AND DISCUSSION

Description

Prepared tablets were of green colour and devoid of any rough surface throughout. Surface of all tablets was found smooth without imperfactions.

Evaluation of Powder Blends

Formulation F1 to F9 were prepared by wet granulation technique and all powder blends were subjected to preformulation study as mentioned in methodology. All blends were evaluated for bulk density, tapped density, angle of repose, compressibility index and Hausner's ratio to assess flow behaviour. All blends showed good flow properties to be compressed in form of tablet. The data in table 5 reveals the same.

Evaluation of Polyherbal Tablets

The prepared tablets were characterized for different parameters such as hardness, friability, thickness, weight variation and disintegration time, which are summarized in table 6. For all formulations hardness, thickness and average weight of tablets were found with in proper range as mentioned in table. Friability was found to be less than 1.0%. The disintegration time for tablet was in range 10.10 min to 15.30 min. Formulation F9 containing Sodium starch glycolate (1.5%) and Crosspovidone (3.5%) showed minimum disintegration time of 10.10 minutes. Blend flow properties of F9 batch were also found satisfactory. Hence, it was considered as an optimised formulation.

Stability Study

Optimised formulation F9 was subjected to accelerated stability study at 40 ± 2°C and 75 ± 5 % RH for 1, 2 and 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.

Table 1 Composition of Polyherbal Extract

Sr. No	Name of Material	Qty. (mg)
1	*Gymnema sylvestre* Extract	150
2	*Momordica charantia* Extract	150
3	*Tinosporia cordifolia* Extract	100
4	Cinnamonum Extract	100
5	*Curcuma longa* Extract	50
6	*Withania somnifera* Extract	50

Table 2: Formulation composition of Polyherbal Tablets

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Herbal Extract	600	600	600	600	600	600	600	600	600	600	600	600
Di basic calcium phosphate	37.95	34.43	30.9	37.95	34.43	30.9	16.81	13.28	9.76	13.28	9.75	6.23
Micro crystalline celloulose	20	20	20	20	20	20	20	20	20	20	20	20
Starch	20	20	20	20	20	20	20	20	20	20	20	20
Sodium Starch glycolate	7.05	10.57	14.1	-	-	-	10.57	10.57	10.57	-	-	-
Cross carmellose sodium	-	-	-	7.05	10.57	14.1	-	-	-	14.1	14.1	14.1
Crosspovidone	-	-	-	-	-	-	17.62	21.15	24.67	17.62	21.15	24.67
Talcum	10	10	10	10	10	10	10	10	10	10	10	10
Magnesium sterate	10	10	10	10	10	10	10	10	10	10	10	10
Total weight (mg)	705	705	705	705	705	705	705	705	705	705	705	705

Table 3: Flow properties and corresponding Angle of Repose

Flowability	Angle of Repose
Excellent	25-30
Good	31-35
Fair	36-40
Passable	41-45
Poor	46-55
Very poor	56-65
Very, very poor	>66

Table 4: Powder Flow According to Compressibility Index and Hausner's Ratio

Compressibility Index	Type of Flow	Hausner's Ratio
<10	Excellent	1.00-1.11
11-15	Good	1.12-1.18
16-20	Fair	1.19-1.25
21-25	Passable	1.26-1.34
26-30	Poor	1.35-1.45
31-35	Very poor	1.46-1.59
>35	Very, Very poor	>1.60

Table 5: Evaluation of Powder Blends

Formulation	Bulk Density (gm/ml)	Tapped Density (gm/ml)	Carr's Index (%)	Hausner's Ratio	Angle of Repose
F1	0.48	0.57	15.79	1.19	26.70
F2	0.47	0.55	14.55	1.17	27.60
F3	0.50	0.54	7.41	1.08	23.21
F4	0.45	0.51	11.76	1.13	24.15
F5	0.50	0.56	10.71	1.12	23.92
F6	0.46	0.53	13.20	1.15	25.15
F7	0.48	0.57	15.79	1.19	26.26
F8	0.53	0.62	14.52	1.17	25.12
F9	0.45	0.50	10.00	1.11	24.64
F10	0.48	0.57	15.79	1.19	26.92
F11	0.46	0.53	13.21	1.15	25.77
F12	0.48	0.56	14.29	1.17	26.25

Table 6: Evaluation of Polyherbal Tablet

Parameter	Average weight (mg)	Hardness (Kg/cm^2)	Thickness (mm)	% Friability	Disintegration Time (min)
F1	703.19	5.50	6.08	0.61	14.45
F2	702.82	5.51	6.10	0.64	14.30
F3	701.32	5.53	6.09	0.63	14.50
F4	704.21	5.33	6.08	0.89	15.30
F5	700.15	5.40	6.08	0.87	15.25
F6	703.59	5.37	6.09	0.88	15.15
F7	701.15	5.54	6.10	0.59	10.55
F8	705.80	5.57	6.08	0.62	10.50
F9	704.63	5.60	6.08	0.57	10.10
F10	703.20	5.30	6.08	0.87	15.10
F11	704.38	5.31	6.10	0.87	15.00
F12	702.48	5.33	6.09	0.88	15.20

Table 7: Stability Study of Polyherbal Tablet

Physical Parameter	Results After			
	Initial	1 month	2 month	3 month
Colour	Green	Green	Green	Green
Appearance	Smooth	Smooth	Smooth	Smooth
Average weight (mg)	704.5	704.5	704.4	704.4
Thickness (mm)	6.08	6.08	6.08	6.08
% Friability	0.543	0.557	0.552	0.540
Disintegration Time (min)	10.00	10.15	10.55	10.45

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. Precompression parameters for all blends were within acceptable range of pharmacopoeial specifications. Formulation F9 showed minimum disintegration time of 10.10 minutes. Hence, it was selected as an optimised formulation and subjected to stability study. Stability study results revealed that, formulation F9 was a stable formulation having better disintegration time and %friability and could be used for effective treatment of diabetes mellitus.

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