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Formulation and Evaluation of a poly herbal antidiabetic tablet containing *Oryza sativa* var. Joha Rice, *Dillenia indica* L and *Syzygium cumini* L extracts

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Abstract | **Original Research Article**

Background: The present study is aimed to formulate and evaluate an antidiabetic herbal tablet containing *Oryza sativa L*. var Joha Rice, *Dillenia indica* and *Syzygium cumini* Lam. of Assam. ***Material & Methods:*** The plants materials were obtained from local area and authenticated by botanist and extracted using solvent ethanol using soxlet apparatus. The poly herbal tablet is prepared using extract of (*Oryza sativa* (seed) L., *Dillenia indica* (fruit) and *Syzygium cumini* (Lam.) (seed) various excipients viz., carbopol, ethylcellulose, MCC, dibasic calcium phosphate and PEG-4000 by granulation method and evaluated by using Weight variation, Hardness, Friability, Thickness and Disintegration Time. ***Results:*** Preformulation studies of prepared six formulation powder were studied and showed Angle of repose in the ranges from 22.32 to 34.65, bulk density in the range from 0.43 to 0.56 g/cm^3, tapped density in the range from 0.54 to 0.65 g/cm^3, Carr's Index in the range 13.84 to 23.21%, hausner ratio in the range of 1.16 to 1.30 and. Loss on drying (LOD) in the range of 0.84 to 1.04%. Tablet formulations were evaluated and found weight variation within limit with average theoretical weight 400mg, hardness of in the ranges from 4.44 to 4.71 Kg/cm^{2,} % Friability was within range of 0.68 to 0.76, disintegration time in the range of 12 min 32 sec to 23 min 20 sec, thickness was found 4.5 ±0.01 to 4.5 ±0.02 and found formulation remain stable in stability testing. ***Conclusion:*** The poly herbal tablet is prepared using extract of (*Oryza sativa* (seed) L., *Dillenia indica* (fruit) and *Syzygium cumini* (Lam.) (seed) and formulation passed pharmaceutical dose form evaluation tests.

Keywords: *Oryza sativa L*. var Joha Rice, *Dillenia indica*, *Syzygium cumini*, Preformulation studies, Antidiabetic tablet.

INTRODUCTION

Diabetes mellitus is one of the leading metabolic diseases affecting almost 50% of elderly population and a cause of death. As per WHO reports, 422 million peoples suffering from diabetics globally in 2014 and in 2012 diabetes was the direct cause of 1.5 million deaths and high blood glucose was the cause of another 2.2 million deaths[1]. According to the International Diabetes Foundation[2], India has more number of diabetes patients than any other country in the world, Diabetes currently affects more than 62 million Indians, which is more than 7.1% of the adult population[3], and nearly 1 million Indians die due to diabetes every year[2]. According to the Indian Heart Association, India is projected to be home to 109 million individuals with diabetes by 2035[4].

A study by the Agency for Healthcare Research and Quality (AHRQ) in 2010 found that, diabetes with complications was one of the twenty most expensive conditions seen in U.S. inpatient hospitalizations in 2011, with an aggregate cost of nearly $5.4 billion for 561,000 stays. It was among the top five most expensive conditions for uninsured patients, at an aggregate cost of $440 million for 62,000 hospitalizations [5].

Various studies were conducted in India for economic burden of diabetics treatment which include direct diabetics treatment and its related complications. A study from Chennai reporting on costs from 2008 and 2009 found that total costs for patients without complications were INR 4,493 (USD 92.15) compared to INR 14,691.75 (USD 301.32) for patients with complications[6].

Studies in India estimate that, for a low income Indian family spend with a diabetic patient spend more than 20% of family income in the treatment of diabetics on average monthly between 3000 to 8000 INR. Diabetes for five years would have spent around Rs 1,50,000 on diabetes treatment only. After 10 years one would have spent Rs 4,00,000 and after 20 years one would have spent Rs 15,00,000. The increase in cost with time is due to the increase in complications. The costs of diabetes affect everyone, everywhere, and are a major financial problem [7].

India is a poor country in which 92% populations having income less than 10000 INR per month and even nearly 75 percent of them survive on a monthly income of less than Rs 5,000[8]. In this scenario, it is very difficult to do the treatment of diabetics for poor Indians. Due to high cost of modern medicines it is difficult to bear the cost for common poor people.

That is why present study is aimed to formulate a cost effective antidiabetic herbal tablet using commonly available indigenous herbal antidiabetic plants (*Oryza sativa L*. belongs to the family Poaccae , *Dillenia indica* belongs to the family Dilleniaceae and *Syzygium cumini* var. or *Ugenia caryophyllifolia* (Lam.) belongs to the family Myrtaceae) of Assam.

MATERIAL AND METHODS

Collection of Plant Material

The plant materials, Viz., *Oryza sativa* L Var. Joha Rice, *Dillenia indica* L fruit and *Syzygium cumini* (L.) fruit seeds were collected from Local Village of Nagaon District of Assam in the months of December and January 2016.

Authentication of Plant Materials

The plant materials, Viz., *Oryza sativa* L Var. Joha Rice, *Dillenia indica* L fruit and *Syzygium cumini* (L.) Seed were authenticated by Taxonomist Dr. Farishta Yasmin, HOD and Associate Professor, Department of Botany, Nowgong College, Nagaon, Assam with Ref. No. NC/BOT/2016/50 dated on 15.02.2017

Extraction of Plant Materials

Oryza sativa L Var. Joha Rice (Seed), *Dillenia indica* L fruit and *Syzygium cumini* (L.) Seed were coarsely powered with dry grinder and passed through sieve and extracted with ethanol in soxlet apparatus

Preparation of Herbal Tablet

All the individual herbal extracts weighed as per the quantity required on the digital balance and excipients were added and compressed into tablets in Single Rotary Tablet Press. After that tablets were tested for the physical properties like Weight variation, friability, tablets thickness, tablets hardness, and disintegration time.

Table-1: Composition of Various formulations with herbal extract

Ingredients	Quantity per tablet (mg)					
	F1	F2	F3	F4	F5	F6
Oryza sativa L Var. Joha Rice Seed extract	100	100	100	100	100	100
Dillenia indica L. fruit Extract	100	100	100	100	100	100
Syzygium cumini (L.) seed extract	100	100	100	100	100	100
Carbopol	20	30	40	-	-	-
Ethyl Cellulose	-	-	-	20	30	40
Microcrystalline Cellulose	40	40	40	40	40	40
Dibasic Calcium Phosphate	30	20	10	30	20	10
PEG 4000	10	10	10	10	10	10
Methyl Paraben	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%
Weight per tablet	400	400	400	400	400	400

PRE-FORMULATION STUDIES

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 following equation:

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

Where,

h = height of powder cone formed

r = radius of the powder cone formed

Relationship between angle of repose (θ) and powder flow-

Angle of Repose (θ)	Type of flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very Poor

Loose Bulk Density (LBD)

Apparent bulk density was determined by pouring a weighed quantity of blend into graduated cylinder and measuring the volume and weight.

$$LBD = \frac{\text{Weight of the powder}}{\text{volume of the packing}}$$

Tapped Bulk Density (TBD)

It was determined by placing a graduated cylinder, containing a known mass of drug excipient blend. The cylinder was allowed to fall under its own weight on to a hard surface from the height of 10 cm at two second intervals. The tapping was continued until no further change in volume was noted.

$$TBD = \frac{\text{Weight of the powder}}{\text{vol of the tapped packing}}$$

Compressibility Index (Carr's index)

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

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

Hausner 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 ratio= TBD / LBD.

Loss on Drying

A well-mixed granules (1g) 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 HERBAL TABLETS

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 a percentage. Not more than two of the tablets from the sample size deviate from the average weight by a greater percentage and none of the tablets deviate by more than double that percentage.

Hardness and Friability Test

The hardness and friability were tested for the tablets by using calibrated hardness tester (Monsanto) and Roche friabilitor (4 minute at 25 rpm) tests respectively.

Disintegration Test for Tablets

A glass of plastic tube 80-100 mm long with an internal diameter of about 28 mm and external diameter 30-31 mm fitted at the lower end with a disc of rust proof wire gauge. Six tablets were placed in the tube, raise and lower the tube in such a manner that the complete up and down movement is repeated 28 to 32 per minute. The tablets are disintegrated when no particles remains above the gauge, which readily pass through mesh (10 mesh screen).

Thickness and Diameter

The thicknesses and Diameter of the tablets were evaluated by using Vernier calipers.

Stability Testing

Prepared tablet formulations are tightly packed in plastic container for three months. Signs of degradation of tablets viz., Appearance (Cracking, chipping, mottling), Friability, Hardness and colour were observed and reported.

RESULTS AND DISCUSSIONS

PREFORMULATION STUDIES

Angle of Repose

Angle of repose for formulation powder were determined by using funnel method and results are given in Table-2.

Bulk Density, Carr's Index and Hausner Ratio

Apparent Loose bulk density (LBD) and Tapped Bulk Density (TBD) were determined and compressibility index (Carr's Index) and Hausner Ratio were calculated as per formula of formulated powder and results are given in Table-3.

Loss on Drying

The % loss on drying is calculated and the results are given the below table-4.

Table-2: Angle of repose for formulations

Formulation	Angle of Repose (θ)
F1	28.32
F2	34.65
F3	22.32
F4	30.50
F5	26.55
F6	31.44

Table-3: Bulk Density, Carr's Index and Hausner's ratio of Formulations

Formulation	Loose Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's Index (%)	Hausner's ratio
F1	0.43	0.56	23.21	1.30
F2	0.44	0.57	22.80	1.29
F3	0.52	0.63	17.46	1.21
F4	0.56	0.65	13.84	1.16
F5	0.51	0.60	15.00	1.17
F6	0.46	0.54	14.81	1.17

Carr's Index: 5-15 (Flow-Excellent), 12-16 (Flow-Good), 18-21 (Flow-Fair to passable), 23-35 (Flow-Poor), 33-38 (Flow- Very Poor), >40 (Flow- Very Very Poor)

Table-4: Loss on drying (%)of Formulations

Formulation	Loss on drying (%)
F1	0.89
F2	0.98
F3	1.02
F4	1.03
F5	1.04
F6	0.87

EVALUATION OF TABLETS FORMULATIONS

Physical Characteristics

The formulated tablets were studied for colour, odour and PH. The results are given in Table-5.

Weight Variation

The average weight was determined by randomly selecting and weighing 20 tablets and results are given in Table-6.

Hardness and Friability

The hardness and Friability of formulated tablets were determined and results are given in Table-7.

Disintegration Time

The disintegration time of formulated tablets were calculated and results are given in Table-8.

Thickness and Diameter

The thicknesses and Diameter of the tablets were evaluated by using Vernier calipers and results are given Table-9.

Stability Testing

The results of Stability testing of formulated tablets are given in Table-10.

Table-5: Physical Evaluation of Formulated Tablets

Formulation	Colour	Odour	P^H
F1	Dark Brown	Characteristics	6.54
F2	Dark Brown	Characteristics	6.57
F3	Dark Brown	Characteristics	6.34
F4	Dark Brown	Characteristics	6.45
F5	Dark Brown	Characteristics	6.38
F6	Dark Brown	Characteristics	6.55

Table-6: Weight variations of formulated Tablets

Formulation	**Weight variation (mg)** Mean ± SEM
F1	400±2.12
F2	400±2.42
F3	400±1.50
F4	400±1.78
F5	400±1.32
F6	400±2.52

Table-7: Hardness and Friability of formulated Tablets

Formulation	Hardness (kg/cm^2) Mean ± SEM	% Friability
F1	4.65±0.02	0.71±0.01
F2	4.57±0.03	0.73±0.01
F3	4.55±0.04	0.72±0.02
F4	4.71±0.01	0.70±0.01
F5	4.44±0.02	0.68±0.01
F6	4.54±0.02	0.76±0.02

Table-8: Disintegration time of formulated tablets

Formulation	Disintegration time
F1	19 min 54 sec
F2	18 min 45 sec
F3	13 min 14 sec
F4	23 min 20 sec
F5	12 min 32 sec
F6	15 min 30 sec

Readings are in average of 3 Tablets in each formulation

Table-9: Thickness and Diameter of formulated tablets

Formulation	Thickness (mm)	Diameter (mm)
F1	4.5 ±0.01	11.1 ±0.02
F2	4.5 ±0.02	11.1 ±0.02
F3	4.5 ±0.02	11.1 ±0.04
F4	4.5 ±0.01	11.1 ±0.02
F5	4.5 ±0.02	11.1 ±0.03
F6	4.5 ±0.02	11.1 ±0.04

Readings are in Mean and SEM of 6 Tablets in each formulation

Table-10: Stability testing of formulated tablets

	Storage condition	Colour	Odour	Weight variation (%)	Hardness (kg/cm2)	Friability (%)	Disintegration
F1	Initial	Dark Brown	Characteristics	400±2.12	4.65±0.02	0.71±0.01	19 min 54 sec
	After 90 days at $25^0C±2^0C$/ 60%±5% RH	Dark Brown	Characteristics	400±2.32	3.65±0.02	1.32±0.05	16 min 54 sec
F2	Initial	Dark Brown	Characteristics	400±2.42	4.57±0.03	0.73±0.01	18 min 45 sec
	After 90 days at $25^0C±2^0C$/ 60%±5% RH	Dark Brown	Characteristics	400±2.32	3.45±0.02	1.32±0.05	16 min 54 sec
F3	Initial	Dark Brown	Characteristics	400±1.50	4.55±0.04	0.72±0.02	13 min 14 sec
	After 90 days at $25^0C±2^0C$/ 60%±5% RH	Dark Brown	Characteristics	401±0.55	3.12±0.04	1.02±0.02	08 min 14 sec
F4	Initial	Dark Brown	Characteristics	400±1.78	4.71±0.01	0.70±0.01	23 min 20 sec
	After 90 days at $25^0C±2^0C$/ 60%±5% RH	Dark Brown	Characteristics	400±1.24	3.34±0.02	1.24±0.02	13 min 20 sec
F5	Initial	Dark Brown	Characteristics	400±1.32	4.44±0.02	0.68±0.01	12 min 32 sec
	After 90 days at $25^0C±2^0C$/ 60%±5% RH	Dark Brown	Characteristics	400±1.33	4.02±0.02	1.33±0.02	8 min 12 sec
F6	Initial	Dark Brown	Characteristics	400±2.52	4.54±0.02	0.76±0.02	15 min 30 sec
	After 90 days at $25^0C±2^0C$/ 60%±5% RH	Dark Brown	Characteristics	401±1.50	3.54±0.02	1.23±0.02	12 min 30 sec

The successful formulation of a stable and effective solid dosage form depends on the careful selection of the excipients that are added in the formulation. The drug and excipients must be compatible with one another to produce a product that is stable, efficacious and easy and safe to administer. The physical compatibility evaluation was performed in visual basis. The study implies that the drug, polymer and other excipients were physically compatible with each other as there were no changes of physically.

The overall objective of preformulation studies is to generate useful information in developing stable and bioavailable dosage forms that can be mass produced. The angle of repose of various granules prepared with different polymer was measured by funnel method. Angle of repose was found in the ranges from 22.32 to 34.65. So, with these range of angle of repose shows that granules have a good flow property. The bulk density of various granules prepared with different polymer was measured by graduated cylinder. The bulk density was found in the range from 0.43 to 0.56 g/cm^3. The tapped density of various granules prepared with different polymer was measured by measuring cylinder. The tapped density was found in the range from 0.54 to 0.65 g/cm^3. A flow property plays an important role in in tablet formulation because improper flow may cause more weight variation. Values of Carr's Index below 15% usually give rise to good flow properties but readings above 25% indicate poor flow properties. The compressibility index of various granules prepared with different polymer using bulk density and tapped density data was calculated. It was found in the range 13.84 to 23.21% and hence they exhibit good flow property. Hausner ratio is an indirect index of ease of powder flow. Lower hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25). The hausner ratio of various granules prepared with different polymer was calculated by using bulk density and tapped density data. It was found in the range of 1.16 to 1.30 which indicates better flow property. Loss on drying (LOD) was found in the range of 0.84 to 1.04%.

The evaluations of tablet formulations were done as per standard methods. Physical Evaluation (colour, odour and pH), Weight variations, hardness, Friability, disintegration time, Thickness and Diameter and stability testing were performed. The theoretical average weight of various formulated tablets was 400 mg and weight variation of various formulation are studied. The percentage deviation of the weight was within 10% as per monograph. The hardness of tablet was found in the ranges from 4.44 to 4.71 Kg/cm2. So, it was the sufficient hardness for tablet coating, transporting and packing. The % Friability was within range of 0.68 to 0.76. The values are within limit of the official monograph i.e., not more than 1%. The disintegration time of the various tablet formulation were studied and found in the range of 12 min 32 sec to 23 min 20 sec. The thickness of the various tablet formulation was found 4.5 ±0.01 to 4.5 ±0.02. The stability studies were performed after keeping the tablets at 25^{0}C±2^{0}C/ 60%±5% RH and observed after 90 days. The tablet formulations were found to be stable at 90 days.

CONCLUSIONS

Preformulation studies of herbal tablet containing *Oryza sativa L*. var Joha Rice, *Dillenia indica* and *Syzygium cumini* Lam. of Assam powers and prepared six herbal formulation were studied and showed a satisfactory result in evaluation. From this study, it can confirm that the prepared Herbal tablet formulations are cost effective having less side effect and easily available drugs. So that, our poor Indian people can afford this type of medicine rather than costly modern medicine.

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