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FABRICATION AND EVALUATION OF *COSTUS PICTUS* HERBAL TABLET

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ABSTRACT

In spite of all the advances in therapeutics, diabetes still remains as a major cause of morbidity and mortality in the world. Herbal formulations are becoming popular nowadays particularly in the treatment of diabetes. Curative properties in the Medicinal plants are due to the presence of various complex chemical substance of different composition, which are found as secondary plant metabolites in one or more parts of the plants. Formulation and evaluation of anti-diabetic activity of herbal tablets were prepared from the leaves extract of the plant *Costus pictus*. Herbal tablet was formulated using a dry plant extract of *Costus pictus*, with varied concentration of binder polyvinyl pyrolidone K30 and with various excipients as, aerosil, micro crystalline cellulose and magnesium stearate. The tablets were prepared by direct compression method. The results of physicochemical parameters and pre-compression studies revealed that all the values were within the acceptable limit. The evaluation of formulated tablets as weight variation, friability, hardness, disintegration time and *in-vitro* drug release were performed. All the evaluation of the formulated tablets were found to be within the pharmacopoeial limits. The optimized formulation F4 were subjected for anti-diabetic effect in wistar albino rabbits for 14 days and effect on blood glucose levels were studied. The stability studies were conducted for 45 days and found to be stable.

KEYWORDS: *Costus pictus*, pyrolidone, variation, friability, hardness, disintegration.

INTRODUCTION

Herbal Medicine is the oldest form of healthcare known to mankind. Herbal medicinal products are defined as any medicinal product, exclusively containing one or more active substances. A large number of medicinal plants are used in the treatment of diabetes. A number of traditional herbal medical practices have been adopted for the diagnosis, prevention and treatment of various diseases. Many such practices were experimentally proved depicting the scientific insight behind their traditional adoption. This attempts to prove scientific insight behind the traditional adaption. Less toxicity, better therapeutic effect, Good patient compliance and Cost effectiveness are the Reasons for choosing drug from natural origin. Diabetes mellitus (DM) is a group of metabolic disorders characterized by hyperglycaemia hypertriglyceridaemia and hypercholesterolaemia, resulting from defects in insulin secretion or action or both.[1]

Diabetes mellitus (DM) is a known metabolic disorder of varied etiology characterized by chronic hyperglycemia due to relative deficiency of insulin or its resistance. Diabetes is associated with disturbances of carbohydrate, fat and protein metabolism.[2] The presence of DM confers increased risk of many devastating complications such as cardiovascular diseases (CVD), peripheral vascular disease (PVD), coronary artery disease (CAD), stroke, neuropathy, renal failure, retinopathy amputations and blindness.[3] Since oral hypoglycemic agents cause side effects, there is a growing interest in herbal remedies for the treatment of diabetes mellitus. Many plant preparations are used in folk medicine to manage diabetes mellitus. New oral hypoglycemic compounds from medicinal plants may provide a useful source for development of pharmaceutical entities or as a dietary adjunct to existing therapies.[4,5] Herbal drugs are considered to be less toxic and free from side-effects compared to synthetic drugs. Around the world and especially in developing countries about 80% of the people are using herbal remedies. The products are considered as less toxic, safe, better cultural acceptability, efficacy, potency and less adverse effects.

The medicinal plant *Costus pictus* (C.pictus) is a very popular plant belonging to the family of zingiberaceae which is also been used as an ornamental climbing plant having anti-diabetic property.[6]

Most conventional oral drug products, such as tablets and capsules, are formulated to release the active drug immediately after oral administration, to obtain rapid and complete systemic drug absorption, accompanying pharmacodynamic effects.

MATERIALS AND METHODS

Materials

Costus pictus plant extract was received as a gift sample from Green Chem laboratories, Bangalore. Polyvinyl pyrolidone K30, magnesium stearate, microcrystalline cellulose and aerosil were procured from S.D fine chemicals. All other chemicals used were of pharmaceutical grade.

Methods

Phytochemical Analysis

The phytochemical tests were carried out to find the presence of phytoconstituents using the standard procedures. Chemical test for carbohydrates, proteins, alkaloids, steroids/ terpinoids, flavonoids, tannins, glycosides, saponins, fixed oils and fats were carried out.[7]

Physicochemical Properties

The organoleptic characters[8] of the samples were evaluated based on the method described by Siddiqui *et al*. organoleptic evaluation refers to evaluation of the formulation by colour, odour, taste and texture.

The drug was subjected to various physicochemical parameters like determination of pH, solubility, melting point, water-soluble ash, acid-insoluble ash, total ash, viscosity, density, moisture content, swelling factor and particle size determination.[9-12]

Preformulation Studies [14, 15]

Preformulation studies were performed to assess the physicochemical properties and release characteristics of the formulated formulations.

Angle of Repose

Flow properties of the physical mixtures of all the formulations were determined by calculating angle of repose by 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 heap of blend. The drug excipients blend was allowed to flow through the funnel freely on to the surface 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.

Bulk Density

Apparent bulk density was determined by pouring a weighed quantity of blend into graduated cylinder and the volume occupied by the samples were determined.

Bulk density = Mass of the powder (g) / Bulk volume of powder (cc)

Tapped Density

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.

Tapped density = Mass of the powder (g) / Tapped volume of powder (cc)

Compressibility

It is also one of the simple methods to evaluate the flow property of the powder by comparing the bulk density and tapped density which is given by Carr's compressibility index.

Compressibility index (%) = (Tapped density - Bulk density) x 100 / Tapped density

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.

$$\text{Hausner ratio (IH)} = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

Formulation of Tablets

Herbal tablets were prepared by using direct compression technique with varied concentration (1% - 5%) of polyvinyl pyrolidone K30 (PVP) as a binder.[13] The composition of various formulations is given in Table 1. All the ingredients were passed through sieve no. 100 and mixed with 1% aerosil, microcrystalline cellulose and 1% magnesium stearate. The micromeritic properties were determined for all the mixtures. The powder mixture possesses good flow properties and good packing ability. Thus, the mixtures were directly compressible. Tablets were compressed each of 300mg on a 16 stage stationary rotary punching machine fitted with 8-mm flat-shaped punches. No manufacturing defects were observed in tablets like capping, lamination and chipping.

Evaluation of Herbal Tablet[16-19]

All the formulated Tablets were subjected to the following evaluation parameters.

Colour and Appearance

The compressed tablets were examined for their colour and appearance.

Thickness

Control of physical dimension of the tablet such as thickness is essential for consumer acceptance and tablet uniformity. The thickness and diameter of the formulated tablet (F1–F4) were measured by taking 3 tablets from each batch using Vernier calipers and expressed in mm.

Hardness

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The Monsanto hardness tester was used to determine the tablet hardness. Hardness was expressed in Kg/cm^2.Three tablets were randomly picked from each formulation and hardness of the tablets was determined.

Friability

Tablet strength was tested by using Roche Friabilator. 20 tablets were weighed and placed in the friabilator and operated at for 100 revolutions (4min), taken out and were redusted. The percentage weight loss was calculated by weighing the tablets again. The % friability was then calculated by.

$$F = \frac{(W_{initial}) - (W_{final})}{(W_{intial})} \times 100$$

Weight Variation

Ten tablets were selected randomly from each batch and weighed individually. The average weight was noted and standard deviation was calculated. The tablet passes the test if not more than two tablets fall outside the percentage limit and none of the tablet differs by more than double the percentage limit.

Uniformity of Drug Content

The drug content was performed to check the dose uniformity in the formulation. Randomly ten tablets were weighed and powdered. A quantity equivalent to 100mg of *Costus pictus* was

taken in a 100ml volumetric flask, dissolved, and made up to the volume with phosphate buffer P^H 6.8. After suitable dilutions the drug content was determined by UV spectrophotometer.

***In- vitro* Dissolution Studies**

The release rate of *Costus pictus* herbal tablets were conducted using dissolution testing apparatus II (Paddle method). The dissolution test was carried out using 900 ml of phosphate buffer P^H 6.8, at 37 ± 0.5^0C and 50 rpm. 10ml of the sample was withdrawn from the dissolution apparatus at regular intervals up to 24 hours and withdrawn sample was replaced with fresh dissolution medium. The samples were filtered through 0.45 µ membrane filter and the absorbance was measured at specific wavelength using UV spectrophotometer. The extent of drug release was estimated by plotting a graph against time versus percentage cumulative drug release.[20]

Anti-diabetic activity

Approval of Animal for the Study

The study was conducted after obtaining the approval from Committee members for the Purpose of Control and supervision on Animals (CPCSEA) and Institutional Animal Ethics Committee (IAEC), Proposal number NCP/IAEC/NO.24/2012-13.

Selection of Animals and Induction of Diabetes

Wister albino rabbits were purchased and all animals were allowed to the new environment for 7 days at suitable environmental condition and provided them standard food. Animals above 1.5-2.5 kg were selected for experiment. The rabbits were fed on a standard pellet diet (Hindustan Lever Ltd., Bangalore, India) and water *ad libitum* and maintained at 28–30^0C. After laboratory acclimation for 7 days, the rabbits were starved for 48 h and divided into groups. The initial blood glucose levels were checked and injected with alloxan 150mg/kg dose by intra venal route through marginal ear vein in normal saline. The blood glucose levels were checked after 72 hrs of alloxan injection. The animals were considered diabetic when the blood glucose level was raised beyond the 200mg/dl and this condition was observed at the end of 72 hrs after alloxan injection. Alloxan induces DNA fragmentation in pancreatic islets and cell damage has been attributed to the production of toxic free radicals.[21]

Grouping of Animals

The experimental rabbits were divided into four groups of six animals in each group. Group I, animals served as normal healthy controls, which received 0.5% w/v carboxy methylcellulose sodium (CMC) , Group II as untreated diabetic control, Group III, diabetic rabbits given herbal tablets of *Costus pictus* with a dose of (120 mg/kg p.o.) which was selected on the basis of earlier reported toxicity studies on herbal tablets of *Costus pictus*.[22], Group IV reference drug (diabetic –induced) group being treated with Glipizide (5mg/kg). The drugs were administered orally via a standard orogastric cannula; anti-hyperglycemic activity in diabetic rabbits was assessed by fall in fasting blood glucose level. Blood samples were collected directly from a pinna venule using a syringe carrying a #26 needle on day 1, 7 and 14days after the last dose of treatment. The blood sugar was determined using a glucometer (Simple one touch Johnson & Johnson Co., USA).[23]

Stability Studies of optimized Herbal tablet formulation

The optimized formulation of the drug was subjected to accelerated stability studies at specified conditions of temperature and relative humidity of 25^0C/60% RH, 30^0C/60% RH, and 40^0C/75% RH, for 3 months.[24, 25]

RESULTS AND DISCUSSION

The present study was planned to evaluate the anti-diabetic property of *Costus pictus* herbal tablets. Physicochemical properties of *Costus pictus* extract were studied and all the properties were found to be within the limits as shown in Table -3 The mucilage gave positive results for Proteins, Alkaloids, Flavonoids, Terpenoids, Saponins and Tannins. The particle size was found to be 45-50µm. The acid – insoluble ash was 0.92% ± 0.008, the pH of the mucilage was 6.2and the density was found to be of 0.995gm/ cc. (Table -4)

Pre-compression Study of Powder Blend

Herbal tablets of *Costus pictus* were developed by using different concentration of polyvinyl pyrolidone which are known to be beneficial in improving the release characteristics. The pre- compression parameters obtained for all formulations are tabulated in table 5. The value of angle of repose was found to be in the range of **$28^0$23' to $32^0$67'**. This indicates good flow property of powder blend. The bulk density was found in the range from **0.418 to 0.427 gm/cc**. The tapped density was found in the range from **0.475 to 0.485 gm/cc**. Hausner ratio value ranges between **1.13 to 1.15** as the results are in the range of < 1.18 indicates good

flow. Carr's index value ranges between **12.0 to 13.07%** indicates that the powder blend have the required flow property for direct compression.

Evaluation Parameters of the Formulated Herbal Tablet

The compressed tablets were found to be round shaped, smooth and brown in colour. The herbal tablets were prepared by direct compression method using the binder polyvinyl pyrolidone to provide sufficient drug release retardation to the tablets .The results are shown in the table 6. The prepared herbal tablets were evaluated for thickness, hardness, friability, average weight variation, drug content and disintegration time all the studies were performed in triplicates and the results were expressed as standard deviation. The hardness for the tablets of each batch was between **4.7 to 5.2 kg / cm^2**, which ensures good handling characteristics of all the batches. The % friability was less than **1%** in all the formulations ensuring that the tablets were mechanically stable. The weight variation for different formulations was found to be **0.87 to 1.59%**, indicates consistency in each batch. The drug content was found to be **97.04 to 99.12%**, with low standard deviation indicates batch to batch consistency. The disintegration time was found to be in the range of **11.4 to 12.4 min** for all batches.

In-vitro dissolution studies were performed for all the formulations using USP dissolution apparatus II at 50 rpm using 900 ml of phosphate buffer P^H 6.8 as dissolution medium. The samples withdrawn were analysed by using UV spectrophotometer. The drug release from the formulations F1, F2, F3 and F4 were found to be 96.64, 97.64%, 98.44 and 99.12% respectively at the end of 240 min. As per the results formulation F4 is the optimized formulation.

The glucose level was significantly high in alloxan treated group when compared to that of control and drug treated group. On repeated administration of the extract and standard drug for 14 days, a significant decrease in glucose level was observed in diabetic rabbits. Table 8 shows the blood glucose levels in rabbits of different groups. The stability studies were carried out to the optimized formulation and found no characteristic changes.

Table 1: Composition of Herbal Tablets of *Costus pictus*

Ingredients (mg/tablet)	Formulation code			
	F1	F2	F3	F4
Costus pictus	120	120	120	120
Polyvinyl pyrolidone K30	1.2	2.4	3.6	4.8
Magnesium stearate	10	10	10	10
Aerosil	10	10	10	10
Micro crystalline cellulose	158.8	157.6	156.4	155.2
Total weight (mg)	300	300	300	300

Table 2: Standards of Pre-compression Parameters

Flow character	Carr's index	Hausner ratio	Angle of repose [ɵ]
Excellent	≤ 10	1.00-1.11	25-30
Good	11-15	1.12-1.18	31-35
Fair(aid not needed)	16-20	1.19-1.25	36-40
Passable (may hang up	21-25	1.26-1.34	41-45
Poor (must agitate/vibrate)	26-31	1.35-1.45	46-55
Very poor	32-37	1.46-1.59	56-65
Very, very poor	>38	>1.60	>66

Table 3: Phytochemical Analysis of *Costus pictus*

S.NO	PHYTOCONSTITUENTS	AQUEOUS METHANOLIC EXTRACT
1.	Carbohydrates	-
2.	Proteins	+
3.	Alkaloids	+
4.	Steroids	-
5.	Flavonoids	+
6.	Glycosides	-
7.	Terpenoids	+
8.	Tannins	+
9.	Saponins	+
10.	Fixed oils	-

(+) and (-) Indicates presence and absence of phytoconstituents in Costus pictus extract

Table 4: Physicochemical Properties of *Costus pictus*

S.No	Properties	Observation
		Costus pictus
1	Organoleptic evaluation • Colour • Odour • Taste • Appearance	 Brown pleasant Sour Smooth
2	P^H	6.2
3	Solubility	Slightly soluble in water and greatly soluble

		in 50% methanol.
4	Melting point	138-140^{0}C
5	Total ash	1.37%±0.006
6	Acid-insoluble ash	0.92%±0.008
7	Water-soluble ash	0.35%±0.004
8	Viscosity	1.81cp±0.005
9	Density	0.995gm/cc
10	Particle size	45-50µm
11	Yield (%)	28.5% w/v

Table 5: Pre-compression Study of Powder Blend

S.No	Formulation code	Angle of repose	Bulk density (gm/cc)	Tapped density (gm/cc)	Compressibility index (%)	Hausner ratio
1	F1	28^{0}23’	0.425	0.485	12.37	1.14
2	F2	31^{0}52’	0.419	0.482	13.07	1.15
3	F3	32^{0}67’	0.427	0.477	10.48	1.11
4	F4	29^{0}42’	0.418	0.475	12.0	1.13

Table 6: Evaluation Parameters of Herbal Tablet

Formulation code	Thickness (mm)	Weight variation (%)	Hardness (kg/cm^2)	Friability (%)	Drug content (%)	Disintegration time (min)
F1	3.54	1.29±0.01	4.7±0.3	0.84±0.03	97.04±0.2	12.2±0.3
F2	3.56	1.51±0.02	5.1±0.1	0.80±0.01	98.09±0.4	11.4±0.1
F3	3.53	0.87±0.03	5.2±0.2	0.83±0.02	98.62±0.5	12.3±0.2
F4	3.51	1.39±0.05	4.9±0.3	0.79±0.03	99.12±0.3	12.4±0.1

Table 7: Drug Release Studies

Time (min)	Percentage drug release			
	F1	F2	F3	F4
30	10.07±0.12	10.87±0.05	10.98±0.03	11.71±0.05
60	22.34±0.04	23.56±0.02	24.12±0.06	24.96±0.03
90	34.23±0.02	36.28±0.07	36. 23±0.04	38.02±0.06
120	49.87±0.04	51.26±0.12	50.58±0.08	52.98±0.08
150	63.19±0.01	66.47±0.05	66.98±0.09	69.05±0.04
180	76.31±0.05	78.28±0.09	78.56±0.11	81.25±0.09
210	87.81±0.03	88.25±0.08	88.79±0.06	90.12±0.11
240	96.64±0.07	97.64±0.11	98.44±0.05	99.12±0.12

Table 8: Anti-Hyperglycaemic Activity of *Costus pictus* in Experimental Rabbits

S.No	GROUPS	0th Day	7th Day	14th Day
1	Control (Normal saline 1ml/kg)	138.9±3.52**	129.7±2.41**	128.9±5.91**
2	Diabetic Control (Alloxan 150mg/kg)	267.2±3.55	277.8±2.14	282.3±2.63
3	Alloxan+ *Costus pictus* F4 formulation 120 mg	279.8±3.36	163.8±3.51**	122.4±3.82**
4	Alloxan +Glipizide (5mg/Kg)	278.2±2.32	151.4±3.51**	143.3±5.34**

*Data represents mean ± SEM. (n=5); *p<0.05; **p<0.01*

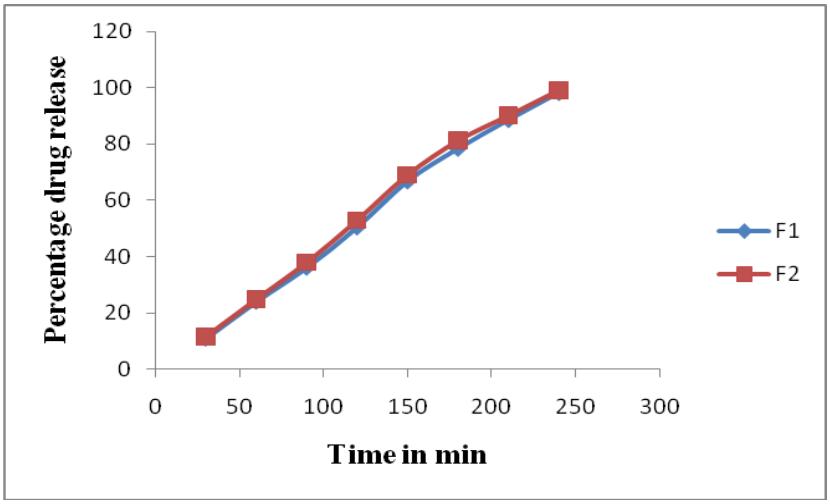

Fig. 1: Invitro Drug Release of F1 and F2 Formulations

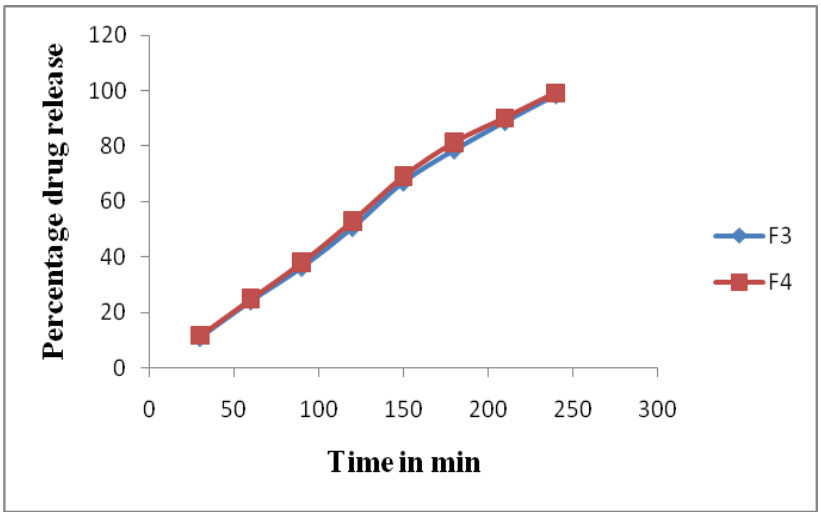

Fig. 2: Invitro Drug Release of F3 and F4 Formulations

CONCLUSION

On the basis of this study, it could be concluded that the optimized formulation F4 exhibited anti-diabetic activity for its significant improvement in the symptoms and signs were

observed during the animal studies. For studying the sustained effect of anti-diabetic activity long term studies can be performed by using herbal polymers compared with synthetic polymers.

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