Indian Journal of Pharmaceutical Education and Research | Association of Pharmaceutical Teachers of India

Evaluation of *Caralluma attenuata* Starch as an Alternative Tablet Excipient to Potato and Mai e Starch: Assessment by Preformulation and Formulation Studies

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ABSTRACT

Submitted: 31/5/2010 Revised: 24/1/2011 Accepted: 9/4/2011

Starch isolated from *Caralluma attenuata* plant was studied as an alternative pharmaceutical excipient to maize and potato starch. The *C. attenuata* starch has been evaluated by series of tests as mentioned in Indian Pharmacopoeia before being used for evaluation. It was tested along with maize and potato starch as an alternative excipient by performing battery of preformulation and formulation tests. The results obtained for *C. attenuata* starch were comparable with maize and potato starch and the *C. attenuata* starch can be used as a pharmaceutical excipient in tablets preparation.

Keywords: *Caralluma attenuata*, starch, binder, excipient, maize starch, potato starch.

INTRODUCTION

Very often a drug is rarely administered in its original form. Most of the times a convenient dosage form is made using a formulation, which contains a number of excipients. Excipients are non drug components of a formulation / pharmaceutical ingredients and are added to ensure acceptability, physicochemical stability during the shelf life, uniformity of composition, dosage and optimum bioavailability and functionability of the drug product. Despite their inertness and utility in the dosage form, excipients can influence absorption of drugs. Excipients used in the pharmaceutical industry includes diluents or fillers, binders or adhesives, disintegrants, lubricants, glidants or flow promoters, colors, flavors, sweeteners etc. All the excipients used in pharmaceutical industry should be acceptable to regulatory agencies, chemically stable and free from viable micro-organisms including pathogens [1].

Starch is a polysaccharide, widely used as binder, diluent, glidant and disintegrating agent in oral solid dosage formulations and also as dusting powder and lubricant. Commercially starch is obtained from maize (*Zea mays*), potato (*Solanum tuberosum*), rice (*Oryza sativa*), tapico (*Manihot utilissima*) and wheat (*Triticum aestivum*) [2, 3]. Many scientists working on various sources of starch and even on modified forms, so as to present a form that will be more useful in pharmaceutical manufacturing. Hence, the search for new starches is a continuous ongoing process worldwide.

In this manuscript, we report the isolation of starch from a new plant source (*Caralluma attenuata*) and its use as an alternative binder and disintegrant to maize and potato starch following an evaluation in preformulation and formulation studies.

Caralluma attenuata Wight. (Asclepiadaceae) is a thick, succulent, perennial fleshy herb and used as vegetable. The tip of the plant tastes bitter; the bitter taste followed by sweet taste resembles that of liquorice. The fleshy herb grows up to a altitude of 2000 ft high [4, 5]. The juice of this plant mixed with black pepper is recommended to take orally for treatment of migraine [6] and is eaten raw as cure for diabetes [7].

MATERIALS AND METHODS

Paracetamol was purchased from Hychem Labs, Hyderabad, India. Maize and potato starch were purchased from S.D. Fine Chemicals, Mumbai, India. Talc was purchased from Accord Labs, Hyderabad. Magnesium stearate was purchased from Ottokemi, Mumbai. Aspirin was purchased from Oxford Laboratory, Mumbai.

Collection of plant material and isolation of starch

The fresh whole plants of *Caralluma attenuata* Wight. (7 kg) were colleted in the month of November 2008, from Osmania University campus, Hyderabad, Andhra Pradesh and from Raghavapur village, Medak district, Andhra Pradesh.

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Following thorough washing with water the roots were separated. Then it was chopped and crushed in a blender to a pasty mass, using sufficient amount of water. The pasty mass was diluted with water, filtered using fourfold muslin cloth to remove pulpy mass. The filtrate was collected and kept aside for about 30 min; the supernatant liquid was decanted to give crude starch and washed several times with purified water to yield pure starch by centrifugation at 3000 rpm. The purified starch was dried in a hot air oven at 70 °C. The yield was ~2.07% (w/w). The electron photograph of purified *C. attenuata* starch is illustrated in Fig. 1.

Evaluation of *C. attenuata* starch as per monograph

The *C. attenuata* starch was evaluated for various parameters viz., description, solubility, identification, ash values (total ash, acid insoluble, water insoluble and sulphated ash), test for fluorescence, test for oxidizing substances, test for acidity, test for iron, loss on drying as described in Indian Phramacopoeia for starch [8] and amylose content was determined as described by Martinez and Prodolliet [9].

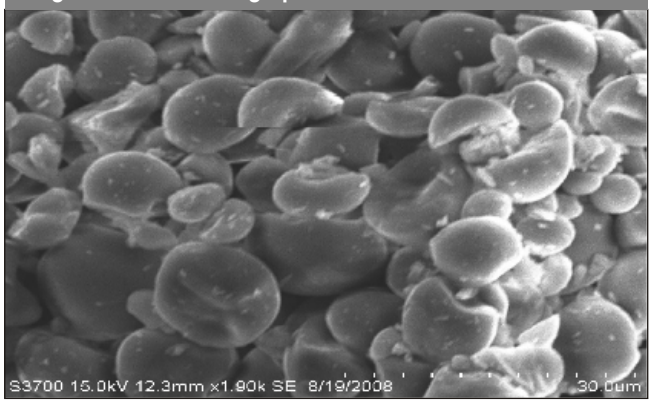
Evaluation of *C. attenuata* starch by preformulation studies

Purified starch obtained from *C. attenuata* was subjected to preformulation studies like particle size, size distribution, flow properties, determination of moisture content and compatability with drug before using it for formulation studies [8, 10].

Sieve analysis was done in order to determine the particle size distribution. 5 g of *C. attenuata* starch was weighed and placed on the sieve shaker (Jayanth, Industries, Hyderabad) arranged in size range of 80-1785 µm. The sieve shaker is shaken in a definite manner for a period of 10 min. Weight retained on each sieve is determined and size distribution series were plotted from the data obtained.

Micrometry was done to determine the particle size of *C. attenuata* starch [2, 11]. The number of particles lying within a certain range is plotted against the size range/mean particle size known as frequency distribution curve.

Fig. 1 Electron micrograph of *Caralluma attenuata* starch



The flow properties of *C. attenuata* starch were assessed by the Angle of repose, Compressibility index (CI) and Hausners ratio (HR) methods. The angle of repose was determined by the funnel method as described in literature[1] according to the relationship: Tan Ø = 2h/d, where h is the height of the heap and d is the diameter of the heap. To determine the density of the samples, the powder was gently poured in to 10 cm^3 graduated cylinder to a total volume of 10 cm^3. The bulk density was calculated as the ratio between weight (g) and volume (cm^3). To determine the ultimate tapped density the cylinder was tapped over 1.0 inch vertical drop, at 1 s interval, until no measurable change in volume was noticed. The CI and HR were determined from the bulk density and tapped density according to the relationships: $CI = [(\rho_{t-} \rho_b) \rho_{t\,x}\, 100]$ and $HR = \rho_t/\rho_b$, where ρ_t and ρ_b are the tapped density and bulk density, respectively. Determination of bulk density was done on bulk density apparatus (Pathal Electrical Works, Mumbai). The obtained flow property (Angle of repose, CI and HR) values were compared with the standard values [12].

Compatibility of paracetamol and aspirin with *C. attenuata* starch was studied by IR spectra (Shimadzu FT-IR 8400S).

Formulation studies

The effect of *C. attenuata* starch as a binder, disintegrant, binder & disintegrant was determined by dry and wet granulation techniques. Five types of paracetamol (wet granulation technique) and aspirin (dry granulation technique) tablets were prepared by using *C. attenuata,* maize, potato starches in varying compositions in different formulations as binder, disintegrant, binder & disintegrant. Each batch consists of 50 tablets. The strength of paracetamol and aspirin in finished tablets was 500 and 350 mg, respectively. The composition of various formulations of paracetamol and aspirin tablets was given in Table 1 and 2 respectively.

The tablets were compressed using a 10 stationed Rimek Minipress using D-11 caplet punches for paracetamol and aspirin tablets were prepared by D-12 round punches. The weight of each paracetamol tablet is 635 mg and aspirin is 445 mg including all excipients. The effect of *C. attenuata* starch as excipient in preparation of tablets was compared with tablets prepared from maize and potato starch. Further the tablets were evaluated for weight variation, friability, hardness, and disintegration and dissolution tests as mentioned in the Indian Pharmacopoeia [8, 13]. The disintegration tests were performed at 37 °C ± 2^0C in distilled water, using Campbell Electronics disintegrator. Similarly the dissolution tests were performed using V-Scientific dissolution (rotating paddle) apparatus. Assays were made in triplicate

Table 1: Composition of paracetamol tablets

Ingredients	Ingredients quantity in grams				
	F1	F2	F3	F4	F5
Paracetamol	0.5	0.5	0.5	0.5	0.5
C. attenuata starch (binder)	-	0.06	-	0.06	-
C. attenuata starch (disintegrant)	-	0.06	-	-	0.06
Maize starch (binder)	0.06	-	-	-	0.06
Maize starch (disintegrant)	0.06	-	-	0.06	-
Potato starch (binder)	-	-	0.06	-	-
Potato starch (disintegrant)	-	-	0.06	-	-
Magnesium stearate	0.005	0.005	0.005	0.005	0.005
Talc	0.01	0.01	0.01	0.01	0.01

Table 2: Composition of aspirin tablets

Ingredients	Ingredients quantity in grams				
	F1	F2	F3	F4	F5
Aspirin	0.350	0.350	0.350	0.350	0.350
C. attenuata starch (binder)	-	0.042	-	0.042	
C. attenuata starch (disintegrant)	-	0.042	-	-	0.042
Maize starch (binder)	0.042	-	-	-	0.042
Maize starch (disintegrant)	0.042	-	-	0.042	-
Potato starch (binder)	-	-	0.042	-	-
Potato starch (disintegrant)	-	-	0.042	-	-
Magnesium stearate	0.0035	0.0035	0.0035	0.0035	0.0035
Talc	0.007	0.007	0.007	0.007	0.007

The optimised formulations were subjected to accelerated stability studies as per WHO and ICH guidelines under zone II, which are temperate and subtropical climatic zone were carried out [14, 15].

RESULTS AND DISCUSSION

Evaluation of *C. attenuata* starch as per monograph

C. attenuata starch is a colourless powder with no taste and odour. The granules are ovoid or pear shaped and 63-29-14 μ in size. The amylose content was 13.5%, which is less than amylose content of potato and maize starch and in other analysed parameters the results were comparable to potato and maize starch (Table 3).

Evaluation of *C. attenuata* starch by preformulation studies

Sieve analysis: The size of particle is expressed by the sieve number, which describes diameter of spheres that passes through the sieve aperture as asymmetric particle. The percent distribution of particles was tabulated in Table 4.

Micrometry: Table 5 shows the comparative particle size distribution of *C. attenuata* starch with maize and potato starch. The comparative results shows that the 70% *C. attenuata* starch cumulative size distribution is ranging from 10-30 μm, which is similar to maize starch, where as potato starch major size distribution range is 40-70 μm.

Flow properties: The Angle of repose, CI and HR give qualitative assessment of the internal cohesive and frictional effects under low levels of external loading, as might be applied in powder mixing, or in the tablet die or capsule shell filling operations. The results were tabulated in Table 6. The results are similar to those obtained from maize starch and greater than potato starch.

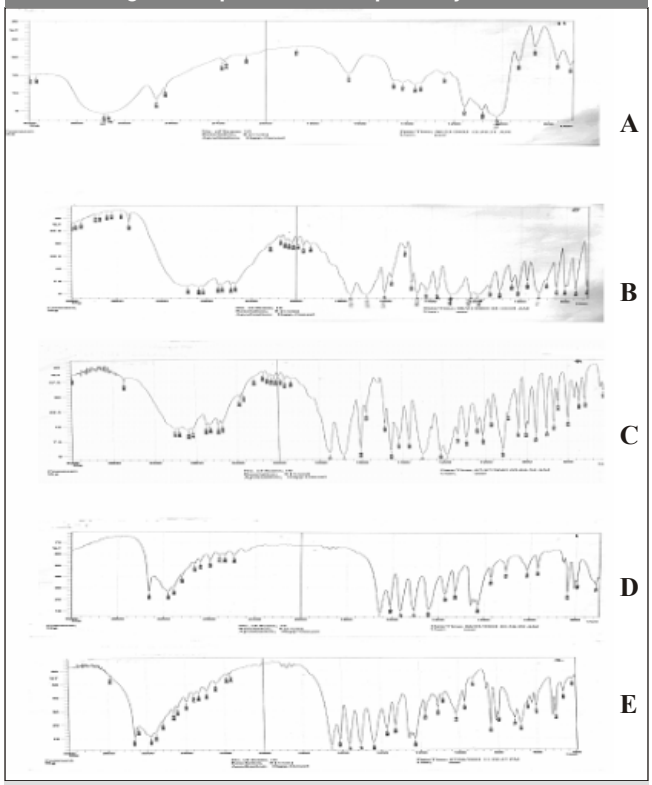
Compatibility of paracetamol and aspirin with *C. attenuata*, maize and potato starch was evaluated by IR spectra and found that both paracetamol and aspirin are compatible along with *C. attenuata*, maize and potato starch (Fig 2).

Formulation studies

C. attenuata starch possesses suitable rheological properties and compressibility, permitting its use in compression technology. There by, the design of paracetamol and aspirin tablets using *C. attenuata*, maize and potato starch in varying compositions as a binder, disintegrant, binder and disintegrant was performed.

Both paracetamol and aspirin tablets were evaluated for

Fig. 2: IR Spectras of compatibility studies



A: Caralluma starch, B: Aspirin, C: Aspirin with Caralluma starch, D: Paracetamol, E: Paracetamol with Caralluma starch

weight variation, friability, hardness and disintegration test as per the Indian Pharmacopoeia and results were compile in Table 7 and 8. From these two tables it is evident that the prepared paracetamol and aspirin tablets weight variation content compiles the weight variation tolerance for uncoated tablets. Similarly, the percentage friability of all the formulations was within the limits of 0.5% and the hardness was within the scope of 3-4 kg/cm^2 limits.

Paracetamol tablets prepared by wet granulation using *C. attenuata* starch as binder and disintegrant posses higher disintegration time, however, the disintegration time is with in the specified time of 30 min. Paracetamol tablets prepared from *C. attenuata* starch as a disintegrants, is comparable with disintegration time of paracetamol tablets prepared from maize as binder and disintegrant. On the other hand the aspirin tablets prepared by dry granulation using various formulations had disintegration time in the range of 10-20 sec. The results of aspirin tablets prepared from *C. attenuata* starch either as binder, disintegrant and binder and disintegrant compiles with the results of aspirin tablets prepared from maize and potato starch.

Dissolution: Following dissolution experiments, the cumulative and the comparative in *vitro* drug release of paracetamol and aspirin in different formulations were

Table 3: Evaluation of mai e, *C. attenuata* and potato starches

Parameters	Maize starch	*C.attenuata* starch	Potato starch
Source	*Zea mays*	*Caralluma attenuata*	*Solanum tuberosum*
Description	Very fine, colorless powder	Fine, white or slightly greenish powder	Coarse, colorless granular powder
Odour	Odorless	Odorless	Odorless
Taste	Tasteless	Tasteless	Tasteless
Solubility	Insoluble in water and 95% ethanol	Insoluble in water and 95% ethanol	Insoluble in water and 95% ethanol
Size	29.7-18-14 µm	63-29-14 µm	102.6-23.6-14 µm
Shape	Polyhedral or sub spherical	Simple granules, ovoid or pear shaped	Simple granules, ovoid or pear shaped
Test for iron	Passes the limits	Passes the limits	Passes the limits
Loss on drying	2.5%	3.9%	4.7%
Test for mucilage	(+) ve	(+) ve	(+) ve
Total ash	0.2%	0.3%	0.4%
Acid insoluble ash	0.06%	0.08%	0.06%
Water insoluble ash	0.07%	0.09%	0.08%
Sulphated Ash	0.2%	0.4%	0.5%
Test for fluorescence	(-) ve	(-) ve	(-) ve
Test for oxidizing substances	(+) ve	(+) ve	(+) ve
Amylose content	25%	13.5%	19%

Values are mean of triplicates.

Table 4 : Si e distribution of *C. attenuata* starch by sieve analysis

Sieve number	Particle size range (µm)	Amount of spheres retained (mg)	%Weight fraction retained	Cumulative % retained
8/16	1785-890	0.02	0.48	0.48
16/30	890-420	0.06	1.20	1.68
30/60	420-199.5	0.110	1.0060	2.68
60/100	199.5-126.5	0.208	4.17	6.83
100/150	126.5-96	0.287	5.74	12.59
150/170	96-81	3.858	77.16	89.75
Left over on 170	Above 81	4.547	89.75	89.75

Values are mean of triplicate, 9.06% loss of material during sieving.

Table 5: Particle si e distribution of starches by micrometry

Mean size range	Size range (µm)	Maize starch			Potato starch			*C. attenuata* starch		
		Avg. of 5 samples	%	% cumu-lative	Avg. of 5 samples	%	% cumul-ative	Avg. of 5 samples	%	% cumula-tive
5	0-10	-	-		-	-	-	-	-	- -
15	10-20	66.2	66.2	66.2	7.4	7.4	7.4	30.2	30.2	30.2
25	20-30	33.6	33.6	99.8	25.6	25.6	33	41.4	41.4	71.6
35	30-40	-	-	-	-	-	-	-	-	-
45	40-50	0.2	0.2	100	23.2	23.2	56.2	16.8	16.8	88.4
55	50-60	-	-	-	18	18	74.2	6.8	6.8	95.2
65	60-70	-	-	-	18.6	18.6	92.8	4.8	4.8	100
75	70-80	-	-	-	-	-	-	-	-	-
85	80-90	-	-	-	4.4	4.4	97.2	-	-	-
95	90-100	-	-	-	2.6	2.6	99.8	-	-	-
105	100-110	-	-	-	-	-	-	-	-	-
115	110-120	-	-	-	0.2	0.2	100	-	-	-

Table 6: Rheological properties and compressibility of mai e, *C. attenuata* and potato starches

Parameters	Maize starch	*C. attenuata* starch	Potato starch
Bulk density	0.40	0.41	0.74
Tapped density	0.57	0.66	0.86
Angle of repose	34	38.2	25.6
Hausner ratio	1.41	1.57	1.16
Carr's index (%)	29.1	36.8	13.9
Moisture content (%)	2.5	4.1	5.0

Table 7: Pharmaceutic properties of paracetamol tablets

Starch type	Hardness (kg/cm^2)	Friability (%)	Weight variation	Disintegration (sec±SEM)
Maize starch as binder & disintegrant	4-5	0.1	Complies	3.00 ± 0.3
Potato starch as binder & disintegrant	4-5	0.1	Complies	1.00 ± 0.08
C. attenuata starch as binder	4-5	0.2	Complies	25.70 ± 0.08
C. attenuata starch as disintegrant	4-5	0.1	Complies	3.95 ± 0.03
C. attenuata starch as binder & disintegrant	4-5	0.3	Complies	18.50 ± 0.04

Table 8: Pharmaceutic properties of aspirin tablets

Starch type	Hardness (kg/cm^2)	Friability (%)	Weight variation	Disintegration (sec±SEM)
Maize starch as binder & disintegrant	2.5-3.5	0.38	Complies	16.00 ± 0.21
Potato starch as binder & disintegrant	2.5-3.5	0.32	Complies	11.3 ± 0.07
C. attenuata starch as binder	2.5-3.5	0.39	Complies	17.0 ± 0.19
C. attenuata starch as disintegrant	2.5-3.5	0.38	Complies	18.0 ± 0.19
C. attenuata starch as binder & disintegrant	2.5-3.5	0.31	Complies	14.6 ± 0.27

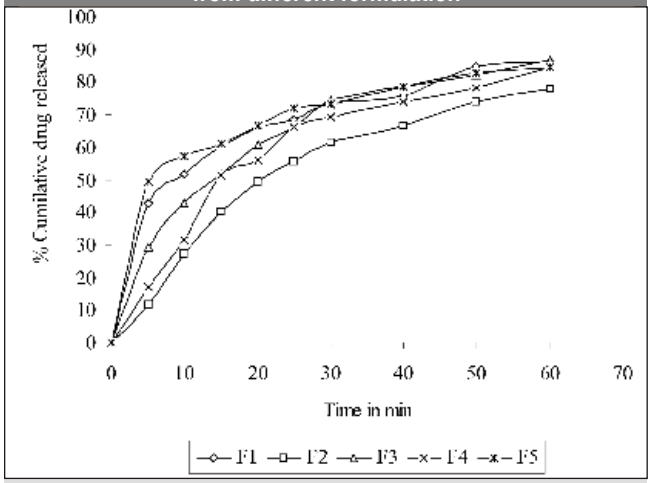
illustrated in Table 9 and 10. The graphical representations of drug release in comparative to other formulations were depicted in Fig. 3 and 4. The results presented are the mean of triplicate readings. The results of dissolution studies indicate that 80% of paracetamol and aspirin were released from tablets within 60 min. The over all dissolution time indicated that the tablets prepared from *C. attenuata* starch as binder, disintegrant, binder & disintegrant was significantly comparable with drug releasing time of paracetamol and aspirin tablets prepared from maize and potato starch.

Stability studies evaluations under zone II, i.e. 40±2^{0}C; 75±5% RH were carried out for six months, there is no changes in physical appearance of optimised tablets as well as the content uniformity and dissolution profile of tablets were with in the limits of monograph.

CONCLUSIONS

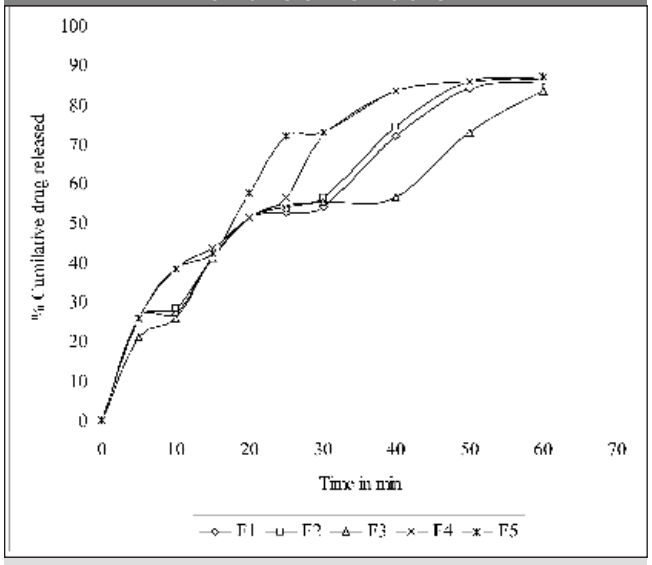
C. attenuata starch was evaluated as an alternative natural starch along with maize and potato starch following its isolation from *C. attenuata* plant. The battery of tests done on *C. attenuata* starch met the specification mentioned in Indian Pharmacopoeia. Following this, the preformulation studies results suggest that *C. attenuata* starch has similar properties like maize and potato starch. Besides it has shown compatibility with paracetamol and aspirin. Finally the dissolution results did not preclude us to state that *C. attenuata* can be used as an alternative pharmaceutical excipient (especially as a binder and disintegrant) to maize and potato starch for tablets preparation.

Fig. 3: Comparative *in vitro* release of paracetamol from different formulation



F1-F5 contains 500 mg of paracetamol per tablet; F1 - Maize starch as binder & disintegrant; F2 - *C. attenuata* starch as binder and disintegrant; F3 - Potato starch as binder & disintegrant; F4 - *C. attenuata* starch as binder, maize starch as disintegrant and F5 - *C. attenuata* starch as disintegrant, maize starch as binder

Fig. 4: Comparative *in vitro* release of aspirin from different formulation



F1-F5 contains 350 mg of aspirin per tablet; F1 - Maize starch as binder & disintegrant; F2 - *C. attenuata* starch as binder and disintegrant; F3 - Potato starch as binder & disintegrant; F4 - *C. attenuata* starch as binder, maize starch as disintegrant and F5 - *C. attenuata* starch as disintegrant, maize starch as binder

REFERENCES

1. Lieberman HA, Lachmann L, Schwortz JB, editors. Pharmaceutical Dosage Forms: Tablets. 1st ed. Vol. 2. Marcel Dekker: New York; 1989; p. 151-70.
2. Wallis TE. Text book of Pharmacognosy. 5th ed. New Delhi: CBS Publications and Distributor; 1985; p. 7-19.
3. Wade A, Weller PJ, editors. Hand book of Pharmaceutical Excipients. 2nd ed. Washington: American Pharmaceutical Association; 1994; p. 483-8.
4. Gamble JS. Flora of the Presidency of Madras. Vol. 2, Calcutta: Botanical Survey of India; 1957; p.860-1.
5. Chopra RN, Nayar SL, Chopra IC. Glossary of Indian medicinal plants. New Delhi: CSIR Publications; 1956; p. 51.
6. Srinivasacharulu Y. Yogarathnakaram. Vol. 2, Nellore: Swatantra Press; 1931; p. 678.
7. Venkatesh S, Reddy GD, Reddy BM, Ramesh M, Appa Rao AVN. Antihyperglycemic activity of *Caralluma attenuata*. Fitoterapia, 2003; 74: 274-9.
8. Anonymous. Indian Pharmacopoeia. Vol. 2, New Delhi: The Controller of Publications, Govt of India; 1996; p. A43-A109.
9. Martinez, Prodolliet. Determination of amylose in cereal and non-cereal starches by a colorimetric assay: collaborative study. Starch 1996; 48: 81-5.
10. Lachman L, Lieberman HA, Kanig JL. The Theory and Practice of Industrial Pharmacy. 3rd ed. Bombay: Varghese Publication House; 1987; p.176-94.
11. Kokate CK. Practical Pharmacognosy, 4th ed. Delhi: Vallabh Prakshan; 2004; p. 113-4.
12. Schmidt PC, Rubensdorfer P. Evaluation of Ludipress as a 'Multipurpose Excipient' for direct compression. Part I: Powder characteristics and Tableting properties. Drug Dev Ind Pharm 1994; 20: 2899-925.
13. Jennifer D, Johannes K, editors. Pharmaceutical Dissolution Testing. London: Taylor & Francis, 2005; p.315-40.
14. Carstensen JT, Rhodes CT, editors. Drug Stability Principles and Practices. 3rd ed. Vol 107, New York: Marcel Dekker, 2000; p.612-3.
15. Mazzo DJ, editor. International stability testing. Illinois: Interpharm Press, 1999; p.255-7.