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Optimize, Formulate & Characterize Fast Dissolving Tablets of *Cyathea Gigantan* Leaf Extract

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Abstract:

In recent times natural products are becoming an integral part of human health care system, because there is a now popular concern over toxicity and side effects of modern drugs. There is also a realization that natural medicines are safer and allopathic drugs are often ineffective in several aliments. Medicinal plants existed even before human being made their appearance on the earth. Man's existence on this earth has been made possible only because of the vital role played by plant kingdom in sustaining his life. Since the down of civilization, in addition to food crops, man cultivated herbs for his medicinal needs. A fast-dissolving drug delivery system, in most cases, is a tablet that dissolves or disintegrates quickly in the oral cavity upon the contact with saliva, resulting in solution or suspension of the administered medicine. FDT dosage forms, also commonly known as fast melt, quick melt, orally disintegrating tablets, and or dispersible systems, have the unique property of disintegrating the tablet in the mouth in seconds.

Key Word: Fast-dissolving, Disintegrating Tablets,FDT,

Introduction;

Drugs may be administered to the human body by various anatomical routes. Despite tremendous advancements in diverse drug delivery approaches, oral route remains the most preferred route of drug administration. Owing to its low cost, ease of administration, greater flexibility in dosage form design, greater patient acceptance and compliance resulting from convenience of oral drug administration, more than 50% of the drug delivery systems available commercially are oral ones. Despite of numerous advantages, this route also suffers from some disadvantages like variable drug absorption due to food effect and rapid metabolism

due to high metabolic activity. Poorly water-soluble drugs present considerable difficulties in formulation. Majority of compounds undergo hepatic first-pass metabolism during digestive absorption, leading to low bioavailability of drugs as large amount of drug is metabolized before reaching the systemic circulation, thus requiring administration of larger doses. These drugs can be successfully formulated for oral administration, but care needs to be taken with formulation design to ensure consistent bioavailability. Therefore, the choice of formulation is of critical importance in establishing a successful product for oral administration of drugs[1,2]

Orodispersable tablets (ODTs), being best alternative of conventional tablets, defined as a solid dosage form containing medicinal substance that disintegrates within a matter of seconds when placed upon tongue[3]. Two different types of dispersible tablets distinguished as one that disintegrates/dissolves instantaneously in the mouth and to be swallowed without the need for drinking water[4] while the other tablet formulation can be readily be dispersed in water to form a dispersion[6] which is easy to ingest by the patient The ODTs formulations have interesting features like exceptional taste masking ability extremely low disintegration time, and pleasant mouth feel . bioavailability and as result of reduced dosage, improved clinical performance through a reduction of unwanted effects

Cyathea Gigantea

Cyathea Gigantea is a tree fern found extensively in moist open areas of Northeastern to Southern India, Thailand, Srilanka, Nepal and Western Java. The Cyatheaceae is the scaly tree fern family and includes the world's tallest tree ferns, which reach heights up to 20 m. Traditionally the fresh rhizome of *C. Gigantea* mixed with black pepper seeds powdered and taken orally with milk twice a day for one week in stomach against white discharges.[7]

C. Gigantea have several active constituents like triterpenes, sterols, saponins, flavonoids, hentriacontane, β-sitostenone, β-sitostanone, diploterol, sitosterol, hopan-29-ol and whole plant contains oleanolic acid[8].Oleanolic acid is a triterpenoid having antitumor, hepatoprotective and antiviral activity. Oleanolic acid is found to exhibit strong anti-HIV activity. Dietary phytosterols like β- sitosterol is having anticancer activity. Herbal drugs play a major role in the treatment of hepatic disorders. In the absence of reliable liver protective drugs in modern medicine, in India, a number of medicinal plants and their formulations are used to cure hepatic disorders in traditional systems of medicine. Several studies were conducted in the field of drug discovery and development but due to the side effects of modern medicine, natural remedies are considered to be effective and safe alternate treatments for hepatotoxicity[9,10].

RESULTS AND DISCUSSIO

Selection of the plant

On the basis of literature review and discussion with the traditional medical practitioners, leaves of *Cyathea Gigantea*, was selected for preparation of fast dissolving tablets and optimization, characterization of prepared fast dissolving tablets.

Preliminary Phytochemical Analysis

The phytoconstituents were identified by chemical tests, which showed the presence of various constituents in the methanol: water (70:30) extracts the phytochemical screening of extract of *C. Gigantea* showed the

presence of triterpenes, sterols, flavonoids, phenols and saponins and these antioxidant phytochemicals of *C. gigantea* might contribute to its hepatoprotective activity. The results shown that the presence of tanning, steroids, saponins and flavonoids. The results are shown in **Table 1.**

Table 01: Preliminary phytochemical studies of dried leaves of *Cyathea Gigantea*

S. No.	Constituents	Tests	Methanol :Water extracts
1.	CARBOHYDRATES	Molisch's test	-
		Fehling's test	-
2.	GLYCOSIDES	Legal's test	-
		Borntrager's test	-
		Baljet test	-
3.	FIXED OIL AND FATS	Spot test	-
		Saponification test	-
		Millon's test	-
4.	PROTEINS& AMINO ACIDS	Ninhydrin test	-
		Biuret test	-
5.	SAPONINS	Foam test	+
6.	PHENOLIC COMP. AND TANNINS	$FeCl_3$ test	+
		Lead acetate test	+
7.	PHYTOSTEROLS	Salkowski test	+
		Libermann-bucchard test	+
8.	ALKALOIDS	Dragendorff's test	-
		Mayer's test	-
		Wagner's test	-
		Hager's test	-
9.	FLAVONOIDS	Lead acetate test	+
		Con. H_2SO_4 test	+
		FeCl3 test	+

Development of Analytical Method for Estimation of *Cyathea Gigantean*

Scanning of Cyathea gigantea

The scanning of *Cyathea Gigantean* methanol: water (70:30) extract was performed to determine the wavelength at which absorb maximum of UV radiation when the solution of Cyathea gigantea was exposed to UV radiation. The Scanning of *Cyathea gigantea* extract was done by placing solutions of different dilutions (100, 10, 1 µg / mL) of stock solution (1 mg/mL) in Phosphate Buffer Saline pH-7.4 under UV Spectrophotometer.

The results of scanning of Cyathea gigantea at 100, 10, 1 µg / mL showed that the solution of the 100 µg / mL has maximum absorbance at wavelength of *276* nm. This wavelength is selected as λ_{max} for the determination of absorbance of different concentration of solutions.

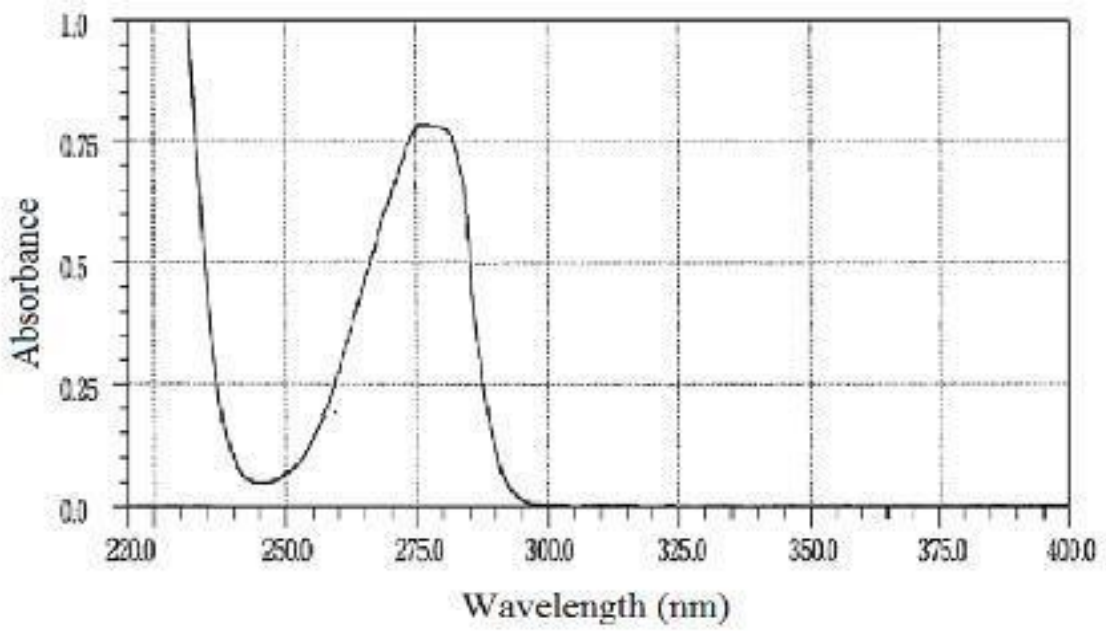

Figure 01: **Calibration Curve of *Cyathea Gigantea* by U.V Spectroscopy Method**

The calibration curve of *Cyathea Gigantea* in Phosphate Buffer Saline (PBS)

pH-7.4 was prepared to identify the linearity range of *Cyathea Gigantea*. The calibration curve was prepared by examining the absorbance of *Cyathea Gigantea* solutions of 10, 20, 40, 60, 80 and 100 µg / mL in Phosphate Bufer Saline pH-7.4 under UV Spectrophotometer at λ_{max} of *276* nm. The results of absorbance of *Cyathea Gigantea* solutions are shown in the Table 2

Table 02: Data for preparation of Calibration Curve of *Cyathea Gigantea* in Phosphate Buffer Saline (pH – 7.4) at λ_{max} *276* nm

Sr. No.	Concentration of Terbutaline Sulfate (µg / mL)	Absorbance ± SD (n=3)
1	10	0.077 ± 0.06
2	20	0.156 ± 0.07
3	40	0.317 ± 0.05
4	60	0.466 ± 0.09
5	80	0.632 ± 0.07
6	100	0.796 ± 0.08

All values are average of three determinations (n=3)

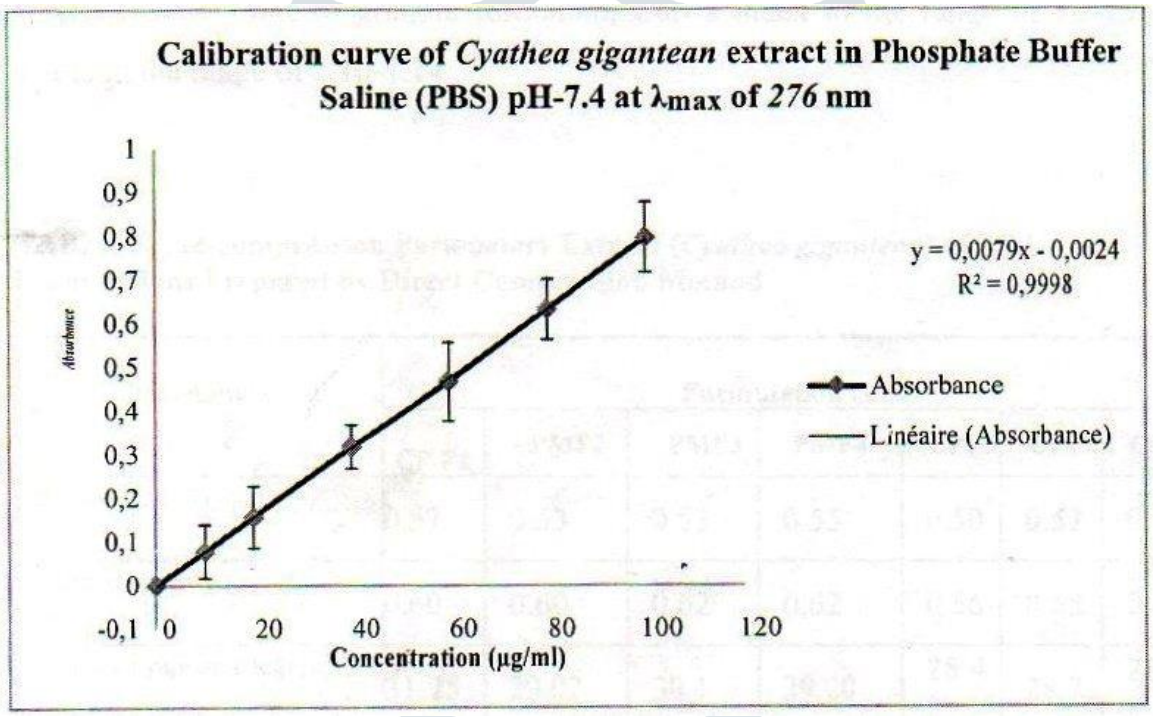

Figure 02: Calibration Curve of *Cyathea Gigantea* in Phosphate Buffer Saline (pH-7.4) at λ_{max} of *276* nm

The results of calibration curve of *Cyathea Gigantea* in Phosphate Buffer Saline (PH – 7.4) showed that curve is straight line with r^2 =0.9998.

Precompression Studies:

Co-processed superdisintegrants were prepared by solvent evaporation using crospovidone and croscarmellose sodium in different ratios (1:1, 1:2. & 1:3). The co-processed superdisintegrants were evaluated for their flow and compression properties in comparison with physical mixture of superdisintegrants. The angle of repose of co-processed superdisintegrants was found to be <25o which indicate excellent flow in comparison to physical mixture of superdisintegrants (>30o) due to granule formation, Carr's index in the range of 10-15% and Hausner's ratio in the range of 1.10-1.14.

TABLE 03. Pre-compression Parameters Extract (*Cyathea Gigantean*) of FDT Formulations Prepared by Direct Compression Method

Parameters	Formulation code						
	CP F1	PMF2	PMF3	PMF4	CPF5	CPF6	CPF7
Bulk density (g/cc)	0.57	0.53	0.53	0.55	0.50	0.52	0.51
Tapped density (g/cc)	0.60	0.60	0.62	0.62	0.56	0.58	0.58
Angle of repose (degree)	31.25	29.02	30.1	29.20	28.43	28.72	28.87
Carr's index (percent)	17	13	13	12	12	11.53	13
Hausner's Ratio	1.05	1.13	1.13	1.12	1.12	1.11	1.13

Evaluation of Formulated fast dissolving Tablet:

Fast dissolving tablets of herbal were prepared using co-processed superdisintegrants and physical mixture of superdisintegrants. Directly compressible mannitol (Pearlitol SD 200) was used as a diluent to enhance mouth feel. A total of six formulations and control formulation CP0 (without superdisintegrant) were designed. As the blends were free flowing (angle of repose $<30^0$ and Carr's index <15% Table 6), tablets obtained were of uniform weight (due to uniform die fill), with acceptable variation as per IP specification i.e., below 7.5%.

Drug content was found to be in the range of 99 to 101%, which is within acceptable limits. Hardness of the tablets was found to be in the range of 2.86-3.16 kg/cm^2.

Friability below 1% was an indication of good mechanical resistance of the tablets.

Wetting time, which are important criteria for understanding the capacity of disintegrants to swell in presence of little amount of water were found to be in the range of 60-135 sec.

Among all the designed formulations, formulation, CP1 was found to be promising and displayed an *in vitro* dispersion time of 25 sec, which facilitates their faster dispersion in the mouth

Overall, the formulation CPF5 containing 4% w/w of co-processed superdisintegrant (1:1 mixture of crospovidone and croscarmellose sodium) was found to be promising and has shown an *in vitro* dispersion time of 25 sec, wetting time of 60 sec when compared to the formulation PM1 containing 4% w/w of Physical mixture of superdisintegrant (1:1 mixture of crospovidone and croscarmellose sodium) which shows 35 sec and control formulation (CPF1) which shows 124 sec, dissolution time.

In-vitro Dissolution studies of Tablet using dissolution apparatus:

In vitro dissolution studies on the promising formulation CP1, control (CP0) and PM1 were carried out in pH 6.8 phosphate buffer, and the various dissolution parameter values viz., percent drug dissolved in 2 min to 60 mint was performed. Formulations CP1 and PM1 which contains superdisintegrants releases 96%, and 89.00% drug respectively at the end of 60 min. while formulation without superdisintegrants have release 71%. Study revealed that increase in the drug release was observed when superdisintegrants used in formulations. The rapid drug dissolution might be due to easy breakdown of particles and rapid absorption of drug into the dissolution medium

. Table 03: In-vitro Dissolution studies of optimized and control formulation

Time (Min)	Formulation code		
	PM F2	CP F5	CP-F1 (Control)
2	0.98	1	8
5	10	13	18
10	33	44	23
15	43	58	34
25	54	66	47
45	74	82	56
60	81	96	64

CPF1is control formulation, CPF5is promising fast dissolving tablet formulation, PMF1 is formulation containing physical mixture of superdisintegrants in 1:1 rati

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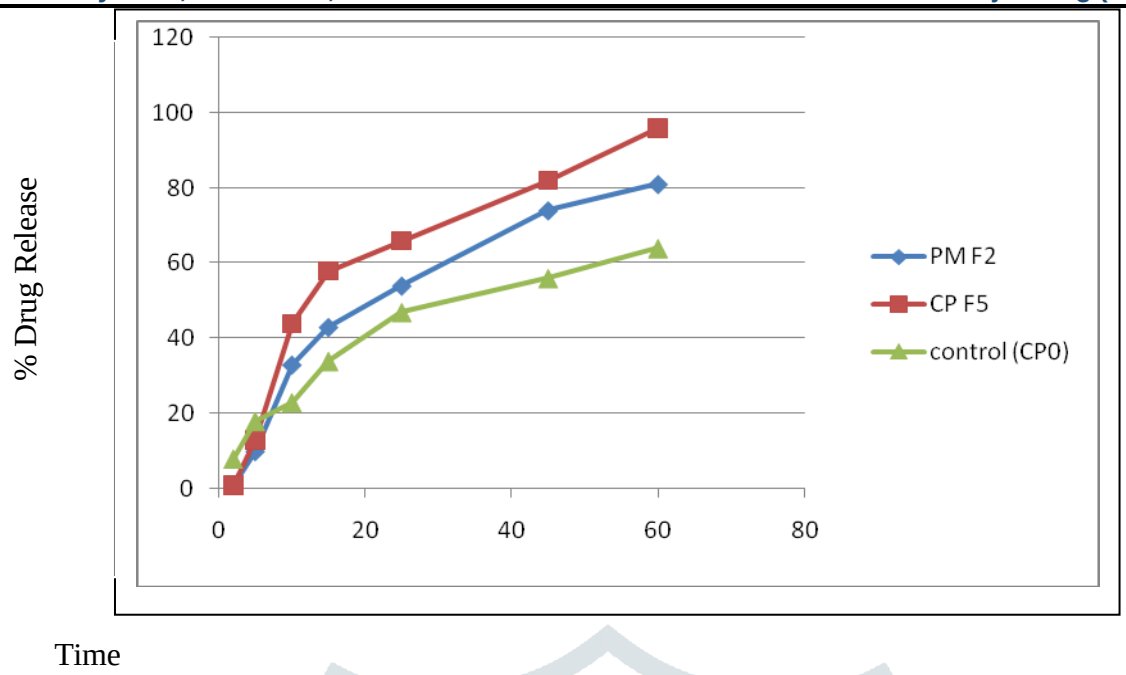

Figure 04: In-vitro Dissolution studies of optimized and control formulation

CONCLUSION

Summary In the present research work an attempt has been made to optimize, formulate and characterize fast dissolving tablet (s) of *Cyathea Gigantean* leave extract. Co-processed superdisitegrants consisting of crospovidone and croscarmellose sodium exhibited good flow and compression characteristics.

Cyathea gigantean leaves extract tablets containing co-processed superdisintegrants exhibited quick disintegration and improved drug dissolution. It was found that the total maximum amount of drug from the optimised batch was released in first 4 minutes of the dissolution study. The tablets disintegrated within 50 sec under experimental in vitro laboratory conditions. It can be concluded from the present work that co-processed superdisintegrants of crospovidone and croscarmellose are superior to physical mixture of crospovidone and croscarmellose used in herbal fast dissolving tablets.

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