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Development & evaluation of herbal fast dissolving tablet of *Capparis divaricata* Lam

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Abstract

Fast dissolving tabletscan be disintegrated, dissolved or suspended by saliva in the mouth. Herbal medicines are effective in all types of diseases. Standardization assures a consistently stronger product with guaranteed constituents. The aim of this study was to formulate fast dissolving tablets of *Capparis Divaricata* Lam leaves extract to achieve faster disintegration in the oral cavity without water. Fast dissolving tablets of *Capparis Divaricata* Lam leaves extract were prepared by using different super disintegrants like crosspovidone, crosscarmellose sodium and sodium starch glycolate by direct compression method. FDTs were evaluated for physicochemical properties and *in-vitro* dissolution.

The drug release from FDTs increased with increasing concentration of superdisintegrants at certain extent and was found to be highest with formulations containing crosspovidone. The tablets were subjected to weight variation, drug content uniformity, hardness, friability, *in-vitro* disintegration time &*in- vitro* drug release studies.

Keywords: *Capparis divaricata* lam extract, Sodium starch glycolate, Microcrystalline cellulose, crosspovidonde..

1. Introduction

United States Food and Drug Administration (US-FDA) defined fast dissolving tablet (FDT) as "a solid dosage form containing medicinal substance or active ingredient which disintegrate rapidly usually within matter of seconds when placed upon the tongue." Fast dissolving tablets are also known as mouth dissolving tablet, it dissolve or disintegrate in the oral cavity without the need of water. Most fast dissolving tablets must include substances to mask the bitter taste of the active ingredient. This masked active ingredient is then swallowed by the patient's saliva along with the soluble and insoluble excipients. It has been concluded that faster dissolution, faster the absorption (only the unionized form of drug) onset of action the time for disintegration of fast dissolving tablets is generally considered to be less than one minute. Recent advance in novel drug delivery system aims to enhance the safety and efficacy of the drug molecule by formulating a dosage form being for the administration. So designing fast dissolving tablets is one of approach to enhance onset of action.[1] Fast or mouth dissolving tablets have been formulated for pediatric, geriatric, patients and for active patients who are busy and traveling and may not have access to water. In many elderly persons will have difficulties in taking conventional oral dosage forms (solutions, suspensions, tablets and capsules) because of hand tremors. Fast dissolving tablet can be prepared by different methods as direct compression, freeze-drying, spray drying, sublimation and wet granulation method.[2] Herbal medicines are effective in all types of disease. Standardisation assures a consistently stronger product with guaranteed constituents. Herbal formulations in general can be standardized schematically as to formulate the medicament using raw materials collected from different localities and a comparative chemical efficacy of different batches of formulation is to be observed. A preparation with better clinical efficacy has to be selected.[3]

The aim of this study is to formulate fast dissolving tablet with sufficient mechanical integrity and to achieve faster disintegration in oral cavity without water. For achieving this goal the microcrystalline cellulose is used as diluents, lactose is used as binder; magnesium stearate is used as lubricant. For enhance faster dissolution rate along with faster disintegration using superdisintegrants like cross povidone, cross carmellose sodium and sodium starch glycolate are used indifferent propotion in formulation of tablets.

Capparis divaricata Lam. commonly known as caper bush, belonging to the genus *Capparis* of family Capparidaceae, found throughout the India especially in the Deccan Peninsula from Maharashtra southwards to Tamil Nadu [4]. *Capparis* species exhibit different pharmacological activities. The fruits, roots, and seeds of *Capparis* have been used traditionally as antirheumatic, tonic, expectorant, antispasmodic and analgesic agents in Turkey and other countries [5].

In general, Capparidaceae family members contain glucosinolates, alkaloids, and flavonoids and have phytochemical differences in plant parts. *Capparis Divaricata* Lam contains flavonoids, Glycosides, Tannins, Alkaloids, Saponins in different plant extract after phytochemical screening.[6,7]

2. Materials and Methods

The fresh leaves of *Capparis divaricata* Lam. (Capparidaceae) were collected at the flowering stage in August from Sangli District, Maharashtra State, India. The plant was authenticated taxonomically from the Botanical survey of India Pune. Collection No. RVP01(2012). The leaves of the plant *Capparis divaricata* Lam were then dried in shade at room temperature for about 30 to 45 days, after which these parts were chopped and ground. Talc, Micro-crystalline cellulose, cross povidone, cross carmellose sodium, sodium starch glycolate, lactose and magnesium stearate are procured by Research lab fine chem. Industries Mumbai.

2.1 Method for Preparation of herbal Tablets

Herbal tablets of *Capparis divaricata Lam* were prepared by direct compression technique using various concentrations of Microcrystaline cellulose (MCC), Cross povidone, Cross carmillose cellulose, Sodium starch glycolate (SSG), Lactose, Magnesium stearate and Talc. All ingredients were blended in glass mortar uniformly. After the sufficient mixing of drug as well as other components finally compressed on a rotary tableting machine using 05-mm punches.

2.2 Formulation of herbal tablet by Direct Compression Method

Formulation design study is important for selection of appropriate excipients for preparation tablets. The different concentration of Microcrystaline cellulose (MCC), Sodium starch glycolate (SSG), Cross carmillose sodium, cross povidone for trial preparation of tablets. The trial batches of tablets were prepared by direct compression method using other commonly used excipients.

2.3 Preformulation Studies:

2.3.1 Methods of extraction of *Capparis divaricata* Lam.

Shade dried Leaves of the *Capparis divaricata* Lam. were used for the extraction. The extraction of above leaves of plant material was done by method by using ethanol as a solvent.

2.3.2 Preparation of Ethanolic Extract of the *Capparis divaricata* Lam.

Capparis divaricata Lam leaves Extract (CDLE): For the preparation of extract about 110 g of air dried, powdered leaves were charged in to Soxhlet's apparatus and successively extracted with 90% ethanol at room temperature. Extraction was continued until the solvent became colourless. The extract was evaporated to dryness using water-bath. The yield was obtained as 11.05 % w/w.

2.3.3 Preparation of Coarse/fine powder from the Concentrated Extract of the *Capparis divaricataLam.*

Collected concentrated extract of the *Capparis divaricata* Lam. were kept in a separate desicator for 5 day's using $Cacl_3$ as a moisture absorbing agent. After 5 days the dried powder was reduced to powder in the mechanical grinder and passed through a sieve no. 40 to obtain powder of desired size.

2.4 FT-IR Studies

In the preparation of *Capparis divaricata* Lam extract tablet formulations, drug and polymer may interact as they are in close contact with each other, which could lead to the instability of drug. Preformulation studies regarding the drug-polymer interaction are therefore very critical in selecting appropriate polymers. FT-IR spectroscopy was employed to ascertain the compatibility between *Capparis divaricata* Lam extract and selected polymers. The pure extract, drug-polymers combinations and formulations were subjected to FT-IR studies. Potassium bromide, pure drug, and the polymers were

heated to 105^0C for one hour to remove the moisture content if present in a hot air oven. Then in presence of IR lamp, potassium bromide was mixed with drug and /or polymer in 1:1 ratio. Grinding in smooth mortar can effect mixing. The mixtures were then placed in the sample holder of the instrument and the spectra were taken. The spectra were run from 4000 cm-1 to1000 cm-1 wave number. FT-IR spectrum of *Capparis divaricata* Lam extract was compared with FT-IR spectrum of *Capparis divaricata* Lam extract with polymer. The pure drug and the drug with excipients were scanned separately. Disappearance of *Capparis divaricata* Lam extract peaks or shifting of peak in any of the spectra was studied.

2.4.1 Preparation of standard stock solution [8]

10mg apigenin was dissolved in 100 ml of methanol solvent to produce 100ppm solution.

2.4.2 Determination of analytical wavelength

The resulting solution containing 100µg/ml was scanned between 200 to 400 nm. The lambda max was found to be 335nm and was used as an analytical wavelength.

2.4.3 Calibration curve for Apigenin (2–10µg/ml)

Appropriate volume of aliquots from standard apigenin above stock solution were transferred to different volumetric flasks of 10 mL capacity. The volume was adjusted to the mark with methanol to obtain concentrations of 2, 4, 6, 8 and 10 µg/mL. Absorbance spectra of each solution against methanol as blank were measured at 335 nm and the graphs of absorbance against concentration were plotted and shown in Figure.1

2.5 Evaluation of tablets

2.5.1 Pre-compression evaluation of powder: [9-13]

2.5.1.1 Angle of Repose

The angle of repose of powder blend was determined by the funnel method. The accurately weight powder blend were taken in the funnel. The values were found to be in the range of 10.30 to 16.69 All formulations showed the angle of repose within 30^0.The height of the funnel was adjusted in such a way the tip of the funnel just touched the apex of the powder blend. The powder 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.

2.5.1.2 Loosed Bulk density (LBD) & Tapped Bulk density (TBD)

The bulk density of a powder depends primarily on particle size distribution, particle shape, and the tendency of the particles to adhere to one another. Both loose bulk density (LBD) and tapped bulk density (TBD) were determined. The accurately weighed amount of sample taken in a 25 ml measuring cylinder measured/recorded the volume of packing and tapped 100 times on a plane hard wooden surface and tapped volume of packing recorded. The loose bulk density and tapped bulk density for all the formulations varied from 0.322gm/cm^3 to 0.7gm/cm^3 and 0.2gm/cm^3 to 1.02gm/cm^3 respectively.

2.5.1.3 Hausner's ratio (HR)

Hausner ratio of the powder was determined from the loose bulk density and tapped bulk density. Hausner ratio of all the formulation lies within the acceptable range. The Hausner's ratio of all the formulations is in the range of 1.08 to 1.67

2.5.1.4 Compressibility/Carr's index

The Compressibility Index of the powder blend was determined by Carr's compressibility index. It is a simple test to evaluate the LBD and TBD of a powder and the rate at which it packed down. The percent compressibility for all the nine formulations lies within the range of 7.6to 86%. All formulations are showing good compressibility.

2.5.2 Post-Compression Evaluation of herbal tablets [14-16]

2.5.2.1 Size and shape of tablets

The size and shape of the tablet can be dimensionally described, monitored and controlled.

2.5.2.2 General appearance

While considering the general appearance, the color, odor and texture of the tablet were observed.

2.5.2.3 Weight variation test

Randomly selected 20 tablets of each formulation were individually weighed. The average value was calculated and compared to individual tablet weights. It was found to be from 3.33±1mg to 6.88±0.00mg. The weight of all the tablets was found to be uniform.

2.5.2.4 Hardness test

Tablet requires a certain amount of strength or hardness and resistance friability to withstand mechanical shocks of handling in all processes. The hardness of the tablets was determined using Pfizer hardness tester. It is expressed in kg/cm^2. Hardness was maintained to be within 1.4±0.23kg/cm^2 to 2.2±0.42kg/cm^2. Three tablets were randomly picked and hardness of the tablets was determined.

2.5.2.5 Thickness

The thickness of the tablets was determined by using Vernier calipers. Five tablets were used, and average value was calculated. Thickness was found in the range from 2±0.01mm to 2±0.03mm respectively.

2.5.2.6 Percentage friability test

The friability of tablets was determined by Roche friabilator. Percentage of weight loss of 10 tablets randomly selected from each batch tumbled in friability apparatus. After 4 minutes of rotating at 25 rpm up to 100 revolutions, the dust of tablets was removed and the percentage of

weight loss was calculated. Friability was in between 0.14±0.00% to 1.00±0.00%. Results revealed that the tablets possess good mechanical strength.

2.5.2.7 Disintegration test

The process of breakdown of a tablet into smaller particles is called as disintegration. The disintegration time of tablets was determined using the digital microprocessor based disintegration test apparatus (Basket rack assembly, Lab India). One tablet was introduced into each tube and added a disc. The assembly was suspended in a 1000 mL beaker filled in with 0.1M hydrochloric acid. The volume of hydrochloric acid was such that the wires mesh at its highest point (at least 25 mm) below the surface of the water, and at its lower point (at least 25 mm) above the bottom of the beaker. The apparatus was operated and maintained at 37±2^{0}C. The time in seconds taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured and recorded.

2.5.2.8 *In-vitro* Dissolution test

In-vitro dissolution study was carried out with respect to *Capparis divaricata* Lam *extract powder* of the compounds present in herbal actives. This study was carried out using (USP I) basket type tablet dissolution test apparatus (Electro lab 8 vessels). A 900 mL of dissolution medium consists of 0.1M hydrochloric acid introduced into the vessel of the apparatus and warmed to 37±2^{0}C with a stirring speed of 100 rpm for 2 hrs. Aliquots of 5 mL were withdrawn from a zone midway between the surface of the dissolution medium and top of the rotating blade at predetermined time interval and an equal amount of fresh dissolution media maintained at the same temperature was replaced. The samples were analyzed by measuring the absorbance at 335 nm by UV-visible spectrophotometer (Shimadzu UV-1800). The cumulative percent drug release was calculated using an equation obtained from standard curve.

The operative assumption inherent in this procedure was that if the *Capparis divaricata* Lam leaves extract powder are demonstrated to have dissolved within time frame and under specified conditions the tablets do not suffer from formulation related problems.It has been observed that the cumulative percentage of drug release of all the formulations was more than 90% at the end of 2 hours.

2.5.2.9 *In-vitro* drug release studies details: -

Apparatus used : USP Type-I (Electro lab 8 vessels).
Dissolution medium : 0.1M hydrochloric acid
Dissolution medium volume: 900 ml
Temperature : 37±2°C
Speed of paddle : 100 rpm
Sampling intervals : 5 min.
Sample withdraw : 5 ml
Absorbance measured : 335nm.

3. Result and discussion

Pre-compression parameters are found within I.P. limits. Post compression parameters are evaluated and the results are as follows hardness tablet was in between 1.1 to 2.2.Friability was found in between 0.1 to 1.00%.Drug content was found within the acceptable limits. Disintegration time is shorter with increase in concentration of superdisintegrant.

3.1 *In vitro* release study

Different super disintegrant are used in different concentration. In vitro Release of F_9 batch was found to be 87.88% which was better as compared to other batches. When sodium starch glycolate was used in higheset concentration, an increase in drug release was observed. The rapid drug dissolution might be due to easy break down of particles and rapid absorption of drug in dissolution medium.

Table 1: Formulation table of herbal tablets of *Capparis divaricata* Lam

Sr. No.	Ingredients (mg/ tab)	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9
1	*Capparis divaricata Lam*	50	50	50	50	50	50	50	50	50
2	Talc	10	10	10	10	10	10	10	10	10
3	Microcrystaline cellulose (MCC)	80	78	76	80	78	76	80	78	76
4	Cross Providone(C.P.)	10	12	14	-	-	-	-	-	-
5	Cross Carmillose Sodium (C.C.S.)	-	-	-	10	12	14	-	-	-
6	Sodium starch glycolate (SSG)	-	-	-	-	-	-	10	12	14
7	Lactose	40	40	40	40	40	40	40	40	40
8	Magnesium Stearate	10	10	10	10	10	10	10	10	10
7	Total	200	200	200	200	200	200	200	200	200

Table 2: Standard calibration curve of standard Apigenin Sample (2 –10µg/ml) at 335 nm in methanol

Sr. No.	Concentration	Absorbance
1	0	0
2	2	0.111
3	4	0.195
4	6	0.301
5	8	0.396
6	10	0.498

Table 3: Pre-Formulation Evaluation of Powder Blend (Pre-compression)

Parameters	Powder blend for								
	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9
Angle of repose	11.30	14.036	10.30	15.2	16.69	16.63	14.93	16.38	15.52
Loose bulk density (g/cm^3)	0.48	0.44	0.53	0.322	0.33	0.44	0.7	0.51	0.42
Tapped bulk density (g/cm^3)	0.52	0.53	0.58	0.45	0.5	0.54	1.02	0.62	0.51
Hausners ratio	1.08	1.13	1.09	1.41	1.51	1.22	1.45	1.21	1.21
Compressibility index (%)	7.6	12	8.60	28.7	34	18.51	32	11	8

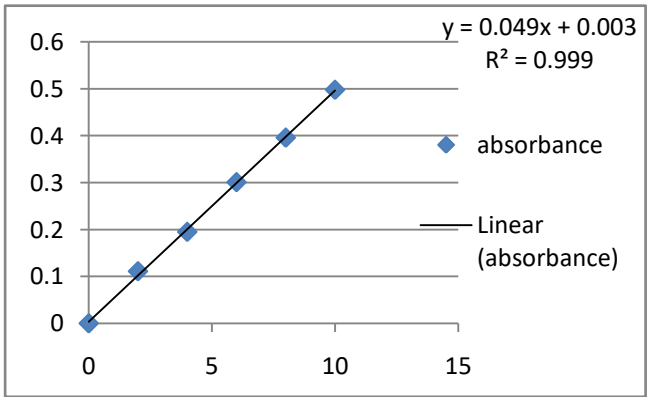
Table 4: Standardization of formulated herbal tablets (Post-Compression Evaluation)

Parameters	Formulation's								
	F_1	F_2	F_3	F_4	F_5	F_6	F7	F8	F9
Color	Greenish black	Greenish black	Greenish black	Greenish black	Greenish black	Greenish black	Greenish black	Greenish black	Greenish black
Odor	Charact-eristic	Charact-eristic	Charact-eristic	Charact-eristic	Charact-eristic	Charact-eristic	Charact-eristic	Charact-eristic	Charact-eristic
Texture	Smooth	Smooth	Smooth	Smooth	Smooth	Smooth	Smooth	Smooth	Smooth
Thickness (mm)	2±0.02	2±0.02	2±0.03	2±0.02	2±0.02	2±0.01	2±0.01	2±0.03	2±0.02
Diameter (mm)	7±0.08	7±0.06	7±0.05	7 ±0.01	7±0.09	7±0.12	7±0.12	7±0.05	7±0.08

Table 5: Drug Release Profile for *capparis divaricata* Lam of herbal tablet

Time in Min.	F_1 %CDR	F_2 %CDR	F_3 %CDR	F_4 %CDR	F_5 %CDR	F_6 %CDR	F_7 %CDR	F_8 %CDR	F_9 %CDR
0	0	0	0	0	0	0	0	0	0
5	24.48	24.34	25.14	28.98	28.19	27.18	38.28	41.29	39.97
10	35.12	38.19	34.18	40.9	39.5	35.40	46.45	46.45	46.58
15	48.18	50.12	48.43	50.12	51.41	52.40	60.02	61.41	63.43
20	65.20	68.41	59.98	68.14	69.22	70.40	72.14	72.91	74.18
25	70.45	75.12	70.12	73.14	74.18	72.5	77.12	78.14	84.30
30	78.19	79.13	75.14	78.18	80.12	78.6	81.13	85.14	87.98

Fig. 1: Calibration curve of Standard Apigenin sample



3.2 Drug- excipients Compatibility Studies

Fig. 2: FT-IR of *Capparis Divaricata* Lam leaves powder extract

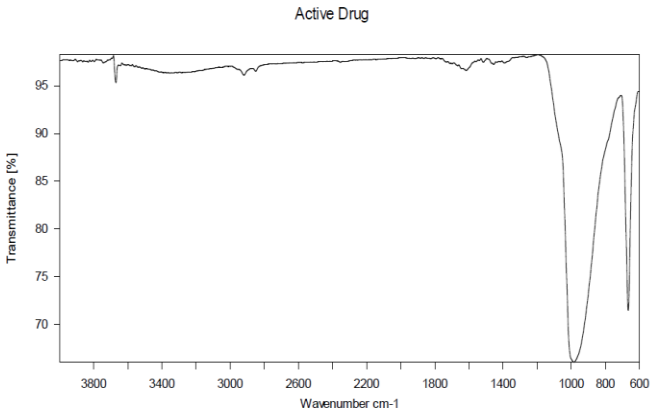


Fig. 3: FTIR of *Capparis Divaricata* Lam Leaves Extract +MCC+SSG+Talc+Magnesium stearate

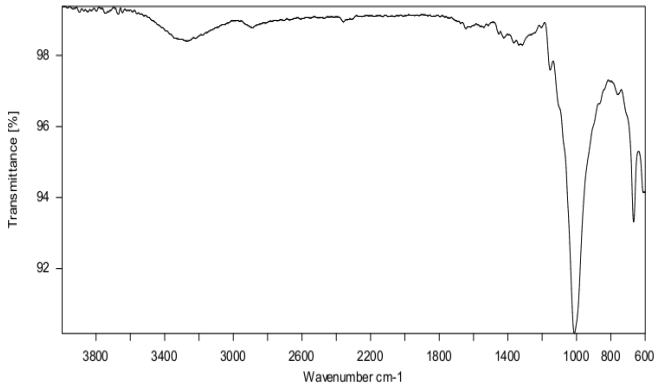


Fig. 4: *In-vitro* Drug Release profile of batch F1, F2 & F3

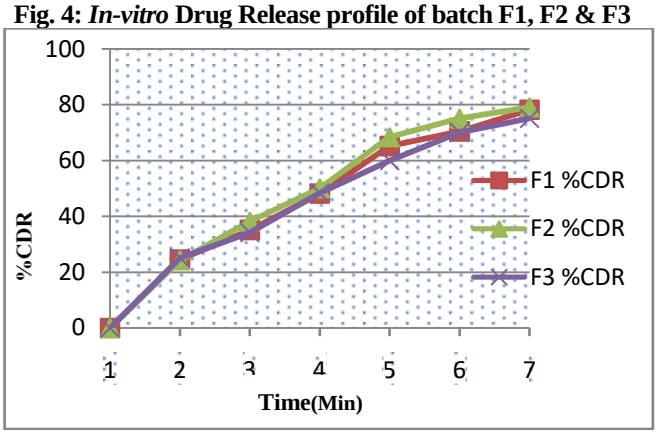


Fig. 5: *In-vitro* Drug Release profile of batch F4, F5 & F6

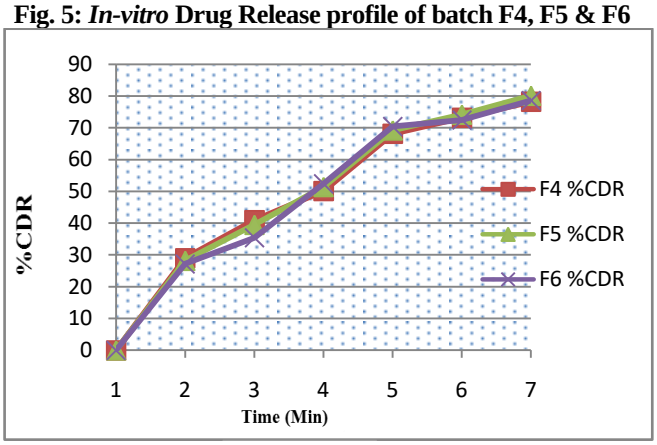
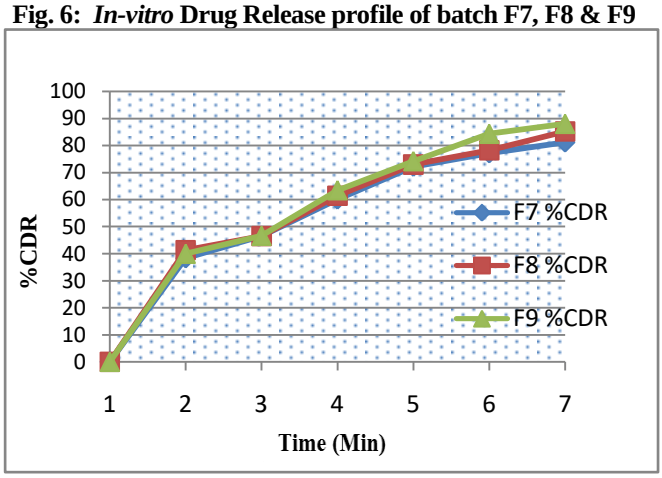


Fig. 6: *In-vitro* Drug Release profile of batch F7, F8 & F9



5. Conclusion: The prepared herbal fast dissolving tablets shows good disintegration property and dissolution rate. The comparative study of several superdisintegrants gives a conclusion that sodium starch glycolate at 7.4% concentration are suitable for the preparation of herbal fast dissolving tablets which will satisfy all the criteria and official limits.

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