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Formulation and Evaluation of Fast Disintegrating Tablets of Caffeine by Using Effervescent Formulation Approach

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ABSTRACT

In recent decades, a variety of pharmaceutical research has been conducted to develop new dosage forms. Among them, the fast disintegrating tablet (FDTs) is one of the most widely employed commercial products to facilitate ease of medication. Upon introduction into the mouth, these tablets dissolve or disperse in the mouth in the absence of additional water and the active pharmaceutical ingredients are readily released from the dosage form. The popularity and usefulness of these formulations resulted in development of several ODT technologies. These tablets are convenient for young children, elderly and patients with swallowing difficulties, and in situations where a potable liquid (water) is not available. The popularity and usefulness of these formulations resulted in development of several ODT technologies. Caffeine acts as a central nervous system stimulant produces increased wakefulness, faster and clearer flow of thought, increased focus, and better general body coordination. Soluble effervescent tablets get dissolved quickly when put in water to give a solution which can be easily consumed by patients with temporarily warding off drowsiness and restoring alertness. The present investigation describes the formulation methodology, evaluation parameters and future aspects of fast disintegrating tablets (FDTs).

Key Words: Fast disintegrating tablets (FDTs), Effervescence, Caffeine, Sodium Bicarbonate, Citric Acid, Sorbitol.

INTRODUCTION

Fast dissolving tablets are continuously gaining great success in the pharmaceutical market. The most popular solid dosage forms are tablets and capsules but the major drawback of these dosage forms for some patients is the difficulty to swallow it [1]. FDTs are not only preferable for people who have swallowing difficulties, but also are ideal for active people. Suitable drug candidates for such systems include neuroleptics, cardiovascular agents, analgesics, antiallergics and drugs for erectile dysfunction [2]. Such a tablet disintegrates instantaneously when placed on tongue, releases the drug that dissolves or disperses in the saliva. As the oral mucosa is highly vascularized, drugs that are absorbed through the oral mucosa can directly enter into the systemic circulation, bypassing the gastrointestinal tract (GIT) and therefore first-pass metabolism in the liver. This result to a rapid onset of action, and greater bioavailability of the drug than those observed from conventional tablet dosage form [3,4]. There are several salient features of fast dissolving drug delivery system. These are ease of administration to the patient who cannot swallow, such as the pediatric, geriatric & psychiatric patients, elderly, stroke victims, bedridden patients, patient affected by renal failures. There is no need of water to swallow the dosage form, which is highly convenient feature for patients who are traveling. It also undergoes rapid dissolution and absorption of the drug produces quick onset of action. These also provide good mouth feel property that helps to change the perception of

medication as bitter pill particularly in pediatric patient. Pregastric absorption can result in improved bioavailability and as a result of reduced dosage; improve clinical performance through a reduction of unwanted effects [5].

MATERIALS AND METHODS

Materials:
Caffeine was obtained as gift sample from Merck Lab Mumbai, India. Sorbitol, citric acid, Sodium bicarbonate, sodium saccharine, talc and magnesium stearate were purchased from CDH, New Delhi. All the ingredients used were of analytical grade.

Methodology:
Preparation of Fast Dissolving Tablets
Different formulations of caffeine were produced using different concentration of sodium bicarbonate and citric acid as effervescence producing agent by effervescent technique. All the ingredients (except purified talc) were accurately weighed and sifted through # 44 mesh separately. The drug and diluents were mixed in small proportion in geometric order. The ingredients after sifting through #44 mesh were thoroughly mixed .The tablets of weight 400 mg were prepared by directly compressed method on a 10- station rotary tablet machine (Single punching Machine) using 7 mm round flat punches. The tablets were prepared according to the formulae shown in Table 1 [6].

Characterization of Caffeine loaded FDTs
All the tablets were evaluated for following different parameters which includes:

Thickness and diameter
Thickness and diameter of tablets were determined using Vernier caliper. Randomly five tablets from each batch were selected and used, and an average value was calculated [7].

Friability
The friability of a sample of randomly selected ten tablets was measured by using the Roche Friabilator (Electro Lab). Ten tablets were weighed and rotated at 25 rpm for 4 minutes. Tablets were dusted and re-weighed. Tablets were reweighed after removal of fines (dedusted) and the percentage of weight loss was calculated and the limit of the percent friability was kept below 1%. [7].

Hardness
For each formulation, the hardness of five tablets was determined using the Monsanto Hardness tester (Cadmach). The limit for crushing strength of the tablets was kept in range of 3 -5 kg/cm^2 [8].

Weight variation
Twenty tablets were randomly selected from each formulation batch and individually weighed from electronic precision balance (CTG 302B-300). The average weight of the selected tablets was measured and comparing the individual tablet weights to the average. The percentage weight variation was calculated and then compared with specification as per I.P. shown in Table 2 [9].

Water absorption ratio
A piece of tissue paper folded twice was put in a small Petri dish (internal diameter = 6.5 cm) containing 5 ml of distilled water. The weight of the tablet before keeping in the petridish was noted (Wb). Completely wetted tablet from the petridish was taken and reweighed (Wa). The water absorption ratio R can be measured by the following formula.

$$R = (Wa - Wb)/Wa \times 100$$

Where, Wa is the weight of the tablets before the test and Wb is the weight of the tablet after water absorption [9].

***In vitro* Disintegration test**
The disintegration time was measured using disintegration test apparatus. One tablet was placed in each tube of the basket. The basket with the bottom surface made of a stainless steel screen (mesh no. 10) was immersed in water bath at 37 ± 2ºC. The time required for complete disintegration of the tablet in each tube was determined using a

stop watch. To be complied with the Pharmacopoeial standards, dispersible tablets must disintegrate within 3 min when examined by the disintegration test for tablets.

***In vitro* dispersion time**

In vitro dispersion time was measured by dropping a tablet in a beaker containing 50 ml of phosphate buffer solution pH 6.8 at 37±0.5°C. Three tablets from each formulation were randomly selected and in vitro dispersion time was recorded [10].

Drug content

For the drug content ten tablets were weighed, crushed and powdered. An amount of the powder equivalent to 100 mg of caffeine was taken and dissolved in 100 ml of pH 6.8 buffer, filtered, diluted suitably and analyzed for drug content at 271 nm using UV-Visible double beam spectrophotometer (UV 2201 SYSTRONICS) [10].

Dissolution study

In vitro dissolution of caffeine loaded fast dissolving tablets was studied in USP type-II dissolution test apparatus (LABINDIA, DS 8000) employing a paddle stirrer at 50 rpm using 900 ml of pH 6.8 phosphate buffer as dissolution medium at 37±0.5ºC. One tablet was used in each test. Aliquots of dissolution medium (5 ml) were withdrawn at specified intervals of time and analyzed for drug content by measuring the absorbance. The volume withdrawn at each time interval was replaced with fresh quantity of dissolution medium. Cumulative percent of caffeine released was calculated and plotted against time [11].

Wetting time

To perform this test, a piece of tissue paper folded twice was placed in a small petridish (internal diameter 6.5 cm) containing 6 ml of distilled water. A tablet was placed on the paper, and the time for complete wetting was noted. Three trials for each formulation batch and the standard deviation were also measured [12].

RESULTS AND DISCUSSION

Caffeine loaded fast dissolving tablets (FDTs) were formulated and optimized via effervescent technique. The prepared tablets were evaluated for all physical parameters which were found to be within the acceptable limits. Formulations were white in color with no odor and smooth circular surface. Weight variation of all formulations was found to be within the range of 399mg to 404mg. A tablet requires certain amount of hardness to withstand the mechanical shocks during handling, packaging and at the time of application. The hardness of the prepared tablet varied from 3.4 to 4.2 Kg/cm^2 which show good mechanical strength with sufficient hardness. The friability of all the formulation was found to be less than 1.0 % which was within the official acceptable limits. The results shows resistance to loss of weight indicates the tablet's ability to withstand abrasion in handling, packaging and shipment. The wetting time for all the formulations was found to be less than one minute for the optimized one which indicates quicker disintegration of the tablet. The disintegration time of the tablets varied from 58 to 40 seconds. The tablets with increasing effervescent agents may disintegrate faster. The drug content of all the formulations varied from 94.62 to 98.6%. The cumulative *in vitro* drug release was found to be 95.58% to 99.83% at the end of fifteen minutes. The formulation code F5 shows maximum release of 98.6% within 15min. Formulation F5 is considered as promising formulation and the drug release followed the controlled mechanism of Higuchi kinetics (r^2 =0.9845).

Table 1: Formulation of FDTs by Effervescent Method

Formulation ingredients (mg/tablet)	FORMULATION CODE				
	F1	F2	F3	F4	F5
Drug	100	100	100	100	100
Sorbitol	250	240	230	220	210
Sodium bicarbonate	30	40	50	60	70
Citric acid	10	10	10	10	10
Saccharine	5	5	5	5	5
Magnesium Stearate	5	5	5	5	5
Total	400	400	400	400	400

Table 2: Weight variation specification as per I.P.

Average Weight of Tablets	% deviation
80 mg or less	±10
More than 80 mg but less than 250 mg	±7.5
250 mg or more	±5

Table 3: Evaluation Parameters

Evaluation Parameter	Formulation code				
	F1	F2	F3	F4	F5
Thickness (mm)	2.9±0.09	3.0±0.12	3.2±0.15	2.9±0.13	3.1±0.18
Diameter(mm)	10.8±0.02	10.9±0.14	11.1±0.15	10.9±0.16	11.2±0.23
Shape	Circular	Circular	Circular	Circular	Circular
Hardness (kg/cm^2)	3.4±0.15	3.6±0.13	3.8±0.09	4.1±0.05	4.2±0.02
Friability (%)	0.52±0.10	0.60±0.10	0.71±0.09	0.50±0.07	0.66±0.06
Weight variation	404±1.51	403±1.18	402±1.45	401±1.59	399±0.58
Wetting Time (Seconds)	37±1.8	32±1.5	31±1.7	28±1.2	23±1.0
Water Absorption Ratio (%)	55.31±0.70	63.47±0.69	68.44±0.92	74.74±0.71	80.20±0.66
Disintegration Time (Seconds)	58±2.18	54±1.47	49±2.18	46±1.50	40±1.50
In vitro dispersion Time	75±2.3	120±3.0	66±2.8	55±2.5	52±2.58
Drug content (%)	94.62±0.51	96.68±0.25	97.71±0.28	98.26±0.35	98.6±0.28

(n=3)

Table 4: Data for *In vitro* cumulative percent drug release of caffeine loaded FDTs

Time (min)	Cumulative Percent (%) drug release				
	F1	F2	F3	F4	F5
0	0	0	0	0	0
3	30.45±0.04	34.11±0.071	38.33±0.041	41.1±0.026	43.16±0.032
6	36.12±0.023	39.32±.0043	43.5±0.049	47.1±0.014	53.35±0.052
9	54.35±0.081	58.4±0.071	69.33±0.062	73.5±0.056	81.53±0.045
12	78.44±0.065	82.24±0.074	84.45±0.039	86.44±0.041	88.4±0.86
15	87.6±0.072	91.55±0.036	93.13±0.048	94.1±0.054	98.6±0.035

(n=3)

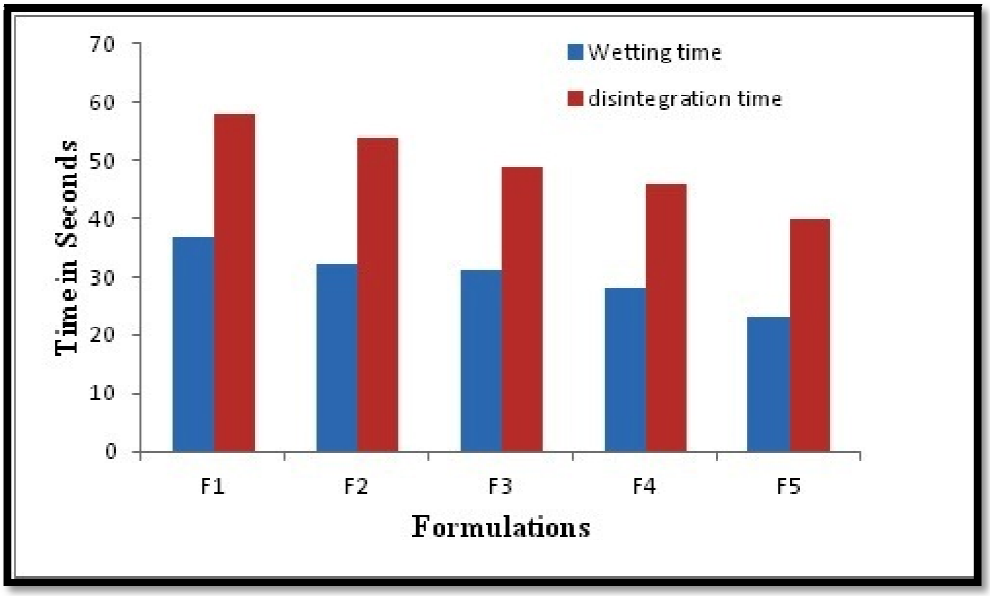

Figure 1: Comparison of wetting and disintegration time of Caffeine Loaded FDTs

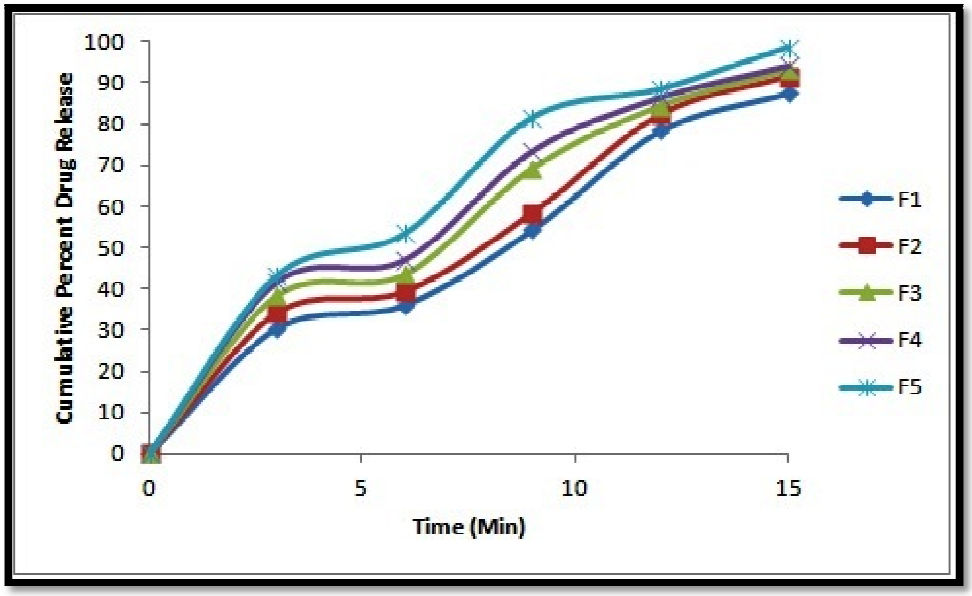

Figure 2: Graph representing *in vitro* cumulative percent drug release of caffeine loaded FDTs

CONCLUSION

The fast dissolving tablets have potential advantages over conventional dosage forms as it avoids the hepatic first pass metabolism so increases the systemic availability of drug i.e caffeine. Fast dissolving tablets of caffeine is successfully prepared by using effervescent technique. By using various technologies and the multiple applications of fast dissolving tablets will definitely fulfill the patient`s need as there is low dosing, rapid onset of action, increased bioavailability, low side effect which increase its popularity in the near prospect. Results suggests that the FDTs containing Sodium bicarbonate and Sorbitol in the ratio of 1:3 (F5) shows best results in terms of cumulative percent drug release, hardness and disintegration time. Results concluded that disintegration and wetting time get decreased by increasing the concentration of effervescent agents.

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