

FORMULATION AND EVALUATION OF MOUTHDISSOLVING TABLETS FROM EXTRACTED CAFFEINE

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ABSTRACT:

Caffeine is an xanthine derivative mild CNS activity largely found in Cofee Cafea Arabica , tea Thea sinsensis , which is the largest consumed drink after water in the world. Here the research work is an attempt to mask mouth dissolving caffeine tablet which is an anti psychotic drug and analgesic with antihypertensive and diuretic drug. The caffeine was extracted by the following method. First the leaves of coffee and fruit pulp, seeds were collected from medicinal/ herbal garden of Jeypore College of Pharmacy, which was confirmed by Swaminathan Research centre, Jeypore , as Cofea Arabica plant. It was percolated in hot water overnights and filtered . The collected sample was placed in separated funnel and added chloroform. After swirling it was stood for time till two phases separated and the chloroform was collected and evaporated till caffeine was found in crystal form. Micromeritics study of pure drug measured by tapped density, bulk density, angle of repose, carr's index , hausner's ratio which found to be 0.1742,0.2632,33.82%,1.52,33.52 respectively. Superdisintegrants such as sodium starch glycolate was used to optimized. Different binders were uded along with optimized superdisintegrant concentration. The tablets were prepared by direct compression technique. The tablets were evaluated for hardness, friability, weight variation, wetting time, disintegration time, and uniformity of content. Optimized formulation was evaluated by in vitro dissolution test.

Keywords : caffeine , partition coefficient , superdisintegrant, dissolution

MANUSCRIPT :

Caffeine is a central nervous system (CNS) stimulant of the methylxanthine class. It is the world's most widely consumed psychoactive drug. Unlike many other psychoactive substances, it is legal and unregulated in nearly all parts of the world. There are several known mechanisms of action to explain the effects of caffeine. The most prominent is that it reversibly blocks the action of adenosine on its receptor and consequently prevents the onset of drowsiness induced by adenosine. Caffeine also stimulates certain portions of the autonomic nervous system.[1] (DNA) and ribonucleic acid (RNA). Caffeine is a bitter, white crystalline purine, a methylxanthine alkaloid and is chemically related to the adenine and guanine bases of deoxyribonucleic acid The coffee tree, scientifically known as *Coffea arabica*, is native to Abyssinia and Ethiopia, but grows well in Java, Sumatra, and other islands of the Dutch East Indies; in India, Arabia, equatorial Africa, the islands of the Pacific, in Mexico, Central and South America and the West Indies. The plant belongs to the large sub-kingdom of plants known scientifically as the Angiosperms, or Angiospermæ, which means that the plant reproduces by seeds which are enclosed in a box like compartment, known as the ovary, at the base of the flower. The word Angiosperm is derived from two Greek words, sperm sperma, a seed and ageion, pronounced angeion, a box, the box referred to being the ovary.[3] Extraction of Caffeine from Tea/ coffee leaves Principle Extraction is a method used for the separation of organic compound from a mixture of compound. This technique selectively dissolves one or more compounds into an appropriate solvent. The solution of these dissolved compounds is referred to as the extract. In the case of Caffeine extraction from tea powder, the solubility of caffeine in water is 22mg/ml at 25°C, 180mg/ml at 80°C, and 670mg/ml at 100°C. Here the organic solvent Chloroform is used to extract caffeine from aqueous extract of tea powder because caffeine is more soluble in chloroform (140mg/ml) than it is in water (22mg/ml). The chloroform - caffeine mixture can then be separated on the basis of the different densities of chloroform and water because chloroform is much denser than water and insoluble in it. Residual water is separated from chloroform by drain out the chloroform through separating funnel, thus chloroform passed through the funnel while polar solvents such as water is still remains in the funnel. Water and chloroform is slightly soluble in each other. So, after separating the solvents, residual water will remain the organic layer. Mainly anhydrous sodium sulfite is used for the removal of water from organic layer. Anhydrous sodium sulfite is an insoluble inorganic solid which will absorb water, thus drying it. Superdisintegrants such as sodium starch glycolate was optimized. Different binders were optimized along with optimized superdisintegrant concentration. The tablets were prepared by direct compression technique. The tablets were evaluated for hardness, friability, weight variation, wetting time, disintegration time, and uniformity of content. Optimized formulation was evaluated by in vitro dissolution test. US Food and Drug Administration Center for Drug Evaluation and Research (CDER) defines, in the "Orange Book," an ODT as "a solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue." European Pharmacopoeia described ODTs as "uncoated tablets intended to be placed in the mouth where they disperse rapidly before being

swallowed” and as tablets which should disintegrate within 3 minutes [6]. Fast disintegrating tablets (FDTs) are also known as “fast dissolving,” “mouth dissolving,” “rapid dissolve,” “quick disintegrating,” “orally disintegrating,” “rapimelt,” “fast melts,” “orodispersible,” “melt in mouth,” “quick dissolving,” “porous tablets,” “EFVDAS,” or “effervescent drug absorption system”. The bioavailability of drugs may be increased due to absorption of drug in oral cavity and also due to pregastric absorption of saliva containing dispersed drugs that pass down into the stomach. Moreover, the amount of drug that is subjected to first-pass metabolism is reduced as compared to standard tablet [8]. The target populations for these new fast-dissolving/disintegrating dosage forms have generally been pediatric, geriatric, and bedridden or mentally disabled patients. Patients with diarrhea, persistent nausea, or vomiting, who are traveling, or who have little or no access to water are also good candidates for FDTs Sodium starch glycolate (Primogel, Explotab) and directly compressible Mannitol (D-Mannitol) were purchased from Qualikems Fine Chem Pvt. Ltd. Sodium stearyl fumarate was purchased from Himedia. Sodium saccharin was purchased from Loba Chemie, Mumbai, and talc from Nice Chemicals Private Limited, Hyderabad, India. All other chemicals and reagents that were of analytical grade were used.

The most important parameter that needs to be optimized in the development of fast disintegrating tablets is the disintegration time. Fast disintegrating tablets were prepared firstly using different excipients (binders and superdisintegrants) and then evaluated for various parameters like friability, hardness, and disintegration time to select the best combination for formulation of fast disintegrating tablets. The combination with lowest disintegration time, optimum hardness, and friability was selected for further study.

MATERIAL METHOD & RESULT

Micromeritics study of pure drug (CAFFEINE) measured by tapped density, bulk density, angle of repose, Carr's index, Hausner's ratio which found to be 0.1742, 0.2632, 33.82%, 1.52, 33.52 respectively. The calibration curve of CAFFEINE with 0.1N HCL and distilled waters with enhanced ratio calibrated a straight line with regression value of 0.999 at 242 nm. Solubility study with solvents distilled water and 0.1N HCL found as 15.78, 84.29mg/100mL respectively. Dissolution of pure drug was found to 20.18%DR after 30min..

Table 1: Formula for 1 tablet (200 mg) of different concentrations of sodium starch glycolate (data in mg).

Sr. no.	Ingredients	F1	F2	F3
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1	Caffeine	2	2	2
2	Sodium starch glycolate	2 (1%)	4 (2%)	8 (4%)
3	Polyvinylpyrrolidone K-30	4	4	4
4	Sodium stearyl fumarate	3	3	3
5	Talc	3	3	3
6	Sodium saccharin	5	5	5
7	Mannitol	181	179	175

Table 2: Formula for 1 tablet (200 mg) for the optimization of polyvinylpyrrolidone K-30 or microcrystalline cellulose with optimized concentration of sodium starch glycolate.

Contents	Caffeine (mg)	SSG (mg)	PVK- 30 (mg)	MCC (mg)	Sodium stearyl fumarate (mg)	Talc (mg)	Sodium saccharin (mg)	Mannitol (mg)
Formula no.								
F1	2	8	2	—	2	2	5	179
F2	2	8	4	—	2	2	5	177
F3	2	8	6	—	2	2	5	175

Table 3: Formula of caffeine FDT prepared by direct compression method (data in mg).

Sr. no.	Ingredients	Formula for 1 tablet (200 mg)	Formula for 110 tablets (200 mg)
1	Caffeine	2	220
2	Sodium starch glycolate	8	880
3	Microcrystalline cellulose	2	220
4	Sodium stearyl fumarate	5	550
5	Talc	3	330
6	Sodium saccharin	5	550
7	Mannitol	175	19250

2. Evaluation Parameters

2.1. Weight Variation

Twenty tablets were selected and weighed on digital weighting balance and average weight was determined. Then individual tablets were weighed, and the individual weight was compared with an average weight

2.2. Thickness

Thickness of tablets was determined using vernier caliper

2.3. Hardness

The crushing strength of the tablets was measured using a Monsanto hardness tester The hardness is measured in kg/cm^2 [13].

2.4. Friability

Ten tablets were weighed and placed in a Roche friabilator and the equipment was rotated at 25 rpm for 4 min. The tablets were taken out, de-dusted, and reweighed. The percentage friability of the tablets was measured as per the following formula

2.5. In Vitro Disintegration Test

The test was carried out on 6 tablets using digital tablet disintegration tester. Distilled water at $37^{\circ}\text{C} \pm 2^{\circ}\text{C}$ was used as a disintegration media, and the time taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured in seconds

2.6. Wetting Time

A Petri dish containing 6 mL of distilled water was taken. A tablet containing a small quantity of amaranth color was placed on it. Time required for the upper surface of the tablet to become complete red was noted [16].

2.7. Drug Content Uniformity

Ten tablets (200 mg) were powdered in mortar pestle, and the blend equivalent to 2 mg of caffeine was weighed and dissolved in 100 mL of 6.8 pH phosphate buffer solutions. The solution was sonicated, filtered through whatman filter paper, and suitably diluted with 6.8 pH phosphate buffer, and the drug content was analyzed by using double beam UV spectrophotometer at 242 nm, respectively. Each sample was analyzed in triplicate.

2.8. In Vitro Dissolution Study

The release of formulated FDTs was determined using USP eight-stage dissolution testing apparatus-2 (paddle method). The dissolution test was performed using 500 mL of phosphate buffer solution, pH 6.8 at $^{\circ}\text{C}$ and 50 rpm. A sample (5 mL) of the solution was withdrawn from the dissolution apparatus at specific time intervals, and the samples were replaced with fresh dissolution medium. The samples were filtered through Whatman filter paper. Absorbance of these solutions was measured at 242 nm using a double beam UV spectrophotometer. Cumulative percentage (%) of drug release was calculated using standard plot of caffeine [17]

2.9. Drug-Excipient Compatibility Studies

These studies were performed in order to confirm the drug-excipient interaction. These studies mainly include FTIR spectroscopy. FTIR spectra of pure drugs and formulated FDT containing drug were recorded on FTIR spectrophotometer. The scanning range was from 4000 to 600 cm^{-1} , and the resolution was 1 cm^{-1} . The scans were evaluated for presence of principal peaks of drug, shifting and masking of drug peaks, and appearance of new peaks due to excipient interaction. This spectral analysis was employed to check the compatibility of drugs with the excipients used.

2.10. Accelerated Stability Studies

Accelerated stability studies are conducted at temperature of $40 \pm 2^\circ\text{C}$ (oven) and at ambient humidity as well as at room temperature (Desiccator). The tablets were withdrawn on the 15th and 30th days and analyzed for hardness, friability, drug content uniformity, and in vitro disintegration time which are the most important parameters for fast disintegrating tablets.

3.1. Optimization of Superdisintegrant Sodium Starch Glycolate

Superdisintegrants are generally used by formulation scientists for developing FDTs or for improvement of solubility for drugs. The primary requirement for such dosage forms is quicker disintegration. The amount of superdisintegrants was optimized in the formulation of FDTs. were prepared using different concentrations of sodium starch glycolate to study its effect on disintegration time. The results for optimization of superdisintegrant concentration in FDTs by direct compression method are shown

Table 4: Evaluation parameters for the optimization of sodium starch glycolate.

Sr. no.	Evaluation parameters	F1 (1%)	F2 (2%)	F3 (4%)
1	Weight variation (IP)	Passed	Passed	Passed
2	Friability (%)	0.8	0.8	0.1
3	Hardness (Kg/cm^2) $\pm$ S.D	2.2 ± 0.57	1.6 ± 0.28	1.5 ± 0.28
4	Disintegration time (sec) $\pm$ S.D	80 ± 2.34	59 ± 6.67	34 ± 2.63

Average of three determinations.

Table 5: Evaluation parameters for the optimization of polyvinylpyrrolidone (PVP K-30) or microcrystalline cellulose as binder with optimized concentration of sodium starch glycolate.

Evaluation parameters	Weight variation (IP)	Friability (%)	Hardness (Kg/cm ²) ± S.D	Disintegration time (sec) ± S.D
Formula no.				
F1	Passed	0.1	2.2 ± 0.28	60 ± 1.78
F2	Passed	0.2	1.8 ± 0.28	45 ± 1.67
F3	Passed	0.5	2.0 ± 0.00	69 ± 2.89

FTIR OF CAFFEINE:

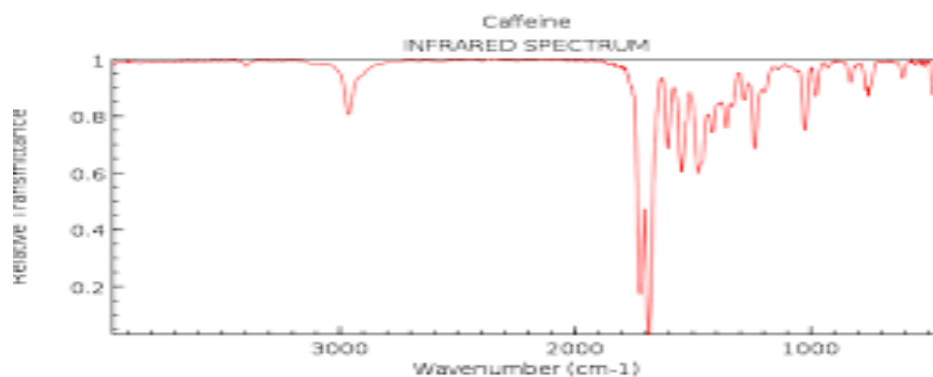


Table 6:

Stability data of caffeine FDT at room temperature and at ambient humidity.

Time interval	Data of three primary batches on								
	0 day			15th day			30th day		
Evaluation parameters	B-1	B-2	B-3	B-1	B-2	B-3	B-1	B-2	B-3
Hardness (Kg/cm ²) ± S.D	1.5 ± 0.29	1.8 ± 0.29	1.5 ± 0.29	1.5 ± 0.00	1.5 ± 0.00	1.7 ± 0.29	1.5 ± 0.00	1.5 ± 0.29	1.5 ± 0.29
Friability (%)	1	0.6	1	0.2	0.3	0.2	0.1	0.1	0.1
Drug content uniformity (mg) ± S.D	100.8 ± 3.36	95.6 ± 2.34	93.8 ± 1.24	99.5 ± 2.14	94.5 ± 2.67	94.8 ± 1.23	98.3 ± 2.74	95.4 ± 2.36	95.7 ± 1.71
Disintegration time (sec) ± S.D	39 ± 2.28	47 ± 1.80	42 ± 3.01	42 ± 3.97	50 ± 4.52	47 ± 1.66	46 ± 2.83	49 ± 2.52	48 ± 3.75

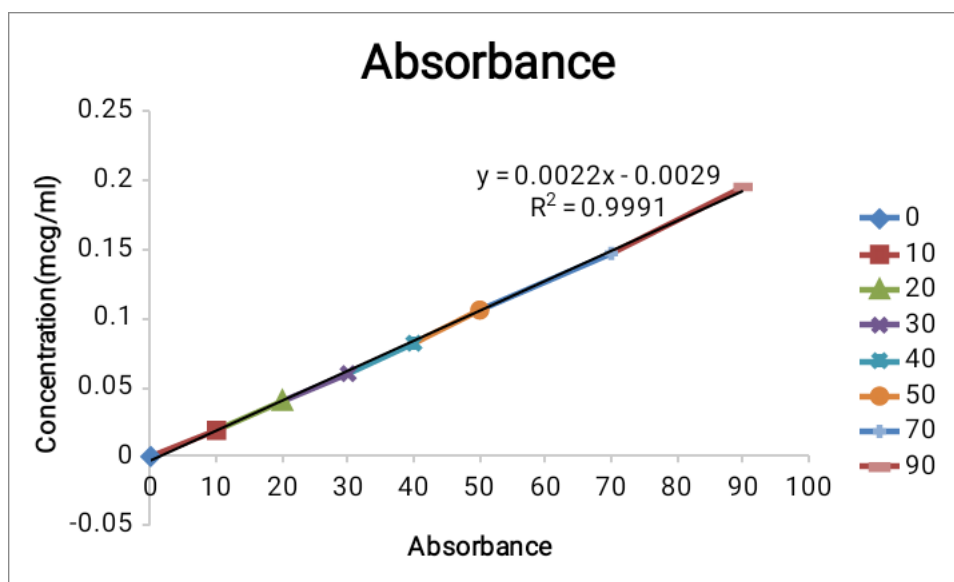
Calibration curve of Caffeine with distilled water

Table 12 Calibration curve of caffeine with distilled water

Concentration(mcg/ml)	Absorbance
0	0
10	0.019
20	0.04
30	0.06

40	0.082
50	0.106
70	0.147
90	0.195

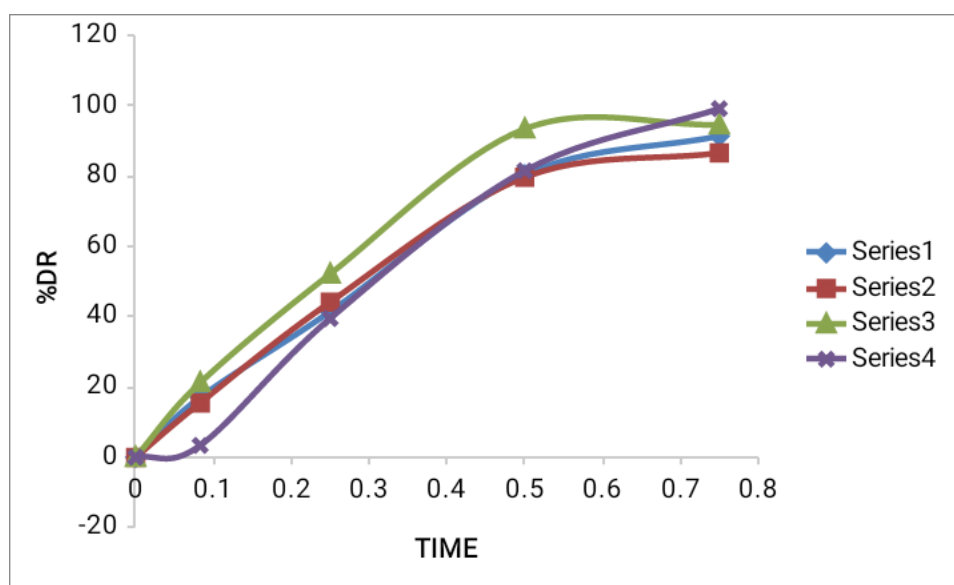
Calibration curve of caffeine with distilled water



COMPARATIVE ZERO ORDER RELEASE KINETICS OF DIFFERENT FORMULATION

TIME	% DR		
	F1	F2	F3
0	0	0	0
0.083(5 min)	17.04951	15.473	21.19888
0.25(15 min)	41.40595	44.12672	52.13779
0.5(30min)	80.37625	79.65732	93.38967
0.75(45min)	91.33664	86.53421	94.53555

COMPARATIVE ZERO ORDER RELEASE KINETICS OF DIFFERENT FORMULATION



Series1- pure drug

Series2- F1

Series3-F2

Series4- F3

CONCLUSION

Fast disintegrating tablet is a promising approach with a view of obtaining faster action of the drug and would be advantageous in comparison to currently available conventional dosage forms. The FDT dosage form had a good balance over disintegration time and mechanical strength. The prime objective of the study was to develop caffeine fast disintegrating tablet by using commonly available excipients and conventional technology. From the study, it was concluded that by employing commonly available pharmaceutical excipients such as superdisintegrants, hydrophilic and swellable excipients, and proper filler, a fast disintegrating tablet of caffeine can be developed which can be commercialized.

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