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FORMULATION AND EVALUATION OF FAST-DISSOLVING CAFFEINE TABLETS FOR CNS DEPRESSION MANAGEMENT: A COMPARATIVE STUDY OF POLYMERS

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Abstract-

Objective: The study aims to formulate and evaluate fast-dissolving caffeine tablets (FDTs) using different polymers to enhance dissolution and bioavailability for effective CNS depression management.

Methods: Fast-dissolving tablets were prepared using various polymers, including Cross carmelose Sodium, Sodium starch glycolate and Kyron T-314 by direct compression method. The formulations were evaluated based on pre-compression and post-compression parameters, such as hardness, friability, disintegration time, and in vitro drug release. A comparative analysis was conducted to identify the most effective polymer for optimizing the tablet's performance.

Results: The results indicated that polymer selection significantly influenced the disintegration time and drug release profile. Among the tested formulations, Kyron T-314 exhibited the fastest disintegration and highest dissolution rate, making it the most suitable candidate for fast-dissolving caffeine tablets.

Conclusion: The study confirms that fast-dissolving caffeine tablets formulated with an optimized polymer can provide rapid onset of action, improving patient compliance and therapeutic efficacy in CNS depression management. Further in vivo studies and stability assessments are recommended to validate these findings.

Keywords-Caffeine, central nervous system depression, adenosine receptor antagonist, alertness, medicinal uses, neuroprotection.

I. INTRODUCTION

Caffeine, a widely consumed central nervous system (CNS) stimulant, plays a crucial role in managing CNS depression by enhancing alertness, reducing fatigue, and improving cognitive function. It acts primarily by antagonizing adenosine receptors, thereby increasing neurotransmitter release and neuronal excitability. Caffeine is commonly used to counteract drowsiness, fatigue, and sedation caused by various CNS depressants. However, conventional caffeine tablets often suffer from delayed onset of action due to slow disintegration and dissolution in the gastrointestinal tract. This delay can reduce their effectiveness, especially in situations where rapid therapeutic action is required. To overcome this limitation, fast-dissolving tablets (FDTs) offer a promising solution by ensuring quicker drug release and absorption. Fast-dissolving tablets (FDTs) are solid oral dosage forms designed to disintegrate rapidly in the oral cavity without the need for water. These tablets enhance patient compliance, particularly for individuals with dysphagia, pediatric and geriatric patients, or those with restricted access to water. The development of FDTs has gained significant attention in the pharmaceutical industry due to their ability to improve bioavailability and ensure faster onset of action. In the case of caffeine, an FDT formulation can be highly beneficial for individuals needing immediate relief from CNS depression symptoms.

The choice of polymer in FDT formulation plays a critical role in determining the tablet's disintegration time, drug release profile, and overall effectiveness. Various natural and synthetic polymers are used to enhance the properties of FDTs, including superdisintegrants such as sodium starch glycolate, croscarmellose sodium, and crospovidone. These polymers aid in rapid disintegration by promoting water uptake and tablet swelling, leading to faster drug release. The selection of an appropriate polymer is essential to achieving the desired balance between mechanical strength and rapid dissolution.

In this study, a comparative evaluation of different polymers was conducted to determine their impact on the formulation and performance of fast-dissolving caffeine tablets. The formulations were prepared using the direct compression method, a widely preferred technique for FDTs due to its simplicity, cost-effectiveness, and ability to maintain drug stability. Various pre-compression and post-compression parameters were assessed, including powder flow properties, tablet hardness, friability, disintegration time, and in vitro drug release. The objective was to identify the

most suitable polymer that ensures rapid disintegration while maintaining the integrity and effectiveness of the tablet.

The significance of this study lies in its potential to enhance caffeine's therapeutic efficacy in CNS depression management. A well-optimized FDT formulation can provide immediate effects, improving cognitive alertness and reducing the lag time associated with conventional tablets. Furthermore, such a formulation could enhance patient adherence and convenience, particularly in emergency situations where rapid drug action is necessary.

II. MATERIAL AND METHOD

Material

Ingredients(mg)	**CT1**	**CT2**	**CT3**	**CT4**	**CT5**	**CT6**	**CT7**	**CT8**	**CT9**
Caffeine	100	100	100	100	100	100	100	100	100
Cross carmellose Sodium	4	6	8	-	-	-	-	-	-
Kyron T-314	-	-	-	4	6	8	-	-	-
Sodium starch glycolate	-	-	-	-	-	-	4	6	8
Aspartame	4	4	4	4	4	4	4	4	4
Flavour	4	4	4	4	4	4	4	4	4
Talc	4	4	4	4	4	4	4	4	4
Magnesium Stearate	4	4	4	4	4	4	4	4	4
Mannitol	30	30	30	30	30	30	30	30	30
Lactose	30	30	30	30	30	30	30	30	30
MCC	20	18	16	20	18	16	20	18	16
TOTAL	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**

Method:

Formulation of Fast-Dissolving Caffeine Tablets

Fast-dissolving tablets (FDTs) of caffeine were prepared using the direct compression method, a widely preferred technique due to its simplicity and effectiveness.

Pre-Compression Evaluation of Powder Blend

Before tablet compression, the powder blend was evaluated for various flow properties to ensure uniformity and ease of tablet formation. The parameters assessed included:

- **Bulk Density & Tapped Density:** Measured using a graduated cylinder to assess powder packing properties.
- **Compressibility Index (Carr's Index):** Calculated to determine the flowability of the powder.
- **Hausner's Ratio:** Used to assess powder cohesiveness and flow characteristics.
- **Angle of Repose:** Determined by the fixed funnel method to evaluate powder flow behavior.

3. Post-Compression Evaluation of Tablets

After compression, the caffeine FDTs were evaluated for various physicochemical properties to ensure formulation quality and performance.

a. Hardness Test

- Measured using a hardness tester (Monsanto or Pfizer hardness tester) to determine mechanical strength.

b. Friability Test

- Conducted using a friabilator (Roche friabilator) at 25 rpm for 4 minutes to assess tablet resistance to abrasion.

c. Weight Variation Test

- A random selection of **20 tablets** was weighed individually and compared with the average weight to ensure uniformity.

d. Disintegration Time

- Evaluated using a USP disintegration test apparatus with **distilled water at 37 ± 2°C** to measure the time required for tablet breakdown.

e. In Vitro Drug Release Study

- Performed using a **USP Type II (paddle) dissolution apparatus** in **900 mL of simulated gastric fluid (pH 1.2)** at **50 rpm and 37 ± 0.5°C**.
- Samples were collected at specific time intervals (e.g., 1, 2, 5, 10, 15 minutes), filtered, and analyzed using a UV-Visible spectrophotometer at **λmax of caffeine (~273 nm)**.
- The percentage drug release was calculated and compared across different formulations.

III. RESULTS

The DSC thermogram of Caffeine is shown in Figure 1. The DSC thermogram of Caffeine showed sharp peak at 236^0C. The identity of a compound was confirmed by comparison with that of an authentic sample and verification of the presence of functional groups in an unknown molecule was done by IR spectra**.** The IR spectra obtained was elucidated for important chromophore groups. The IR spectra showed peaks at 1645, 1597, 1500 and 1427 cm^{-1}. The various peaks are depicted in Figure 2.

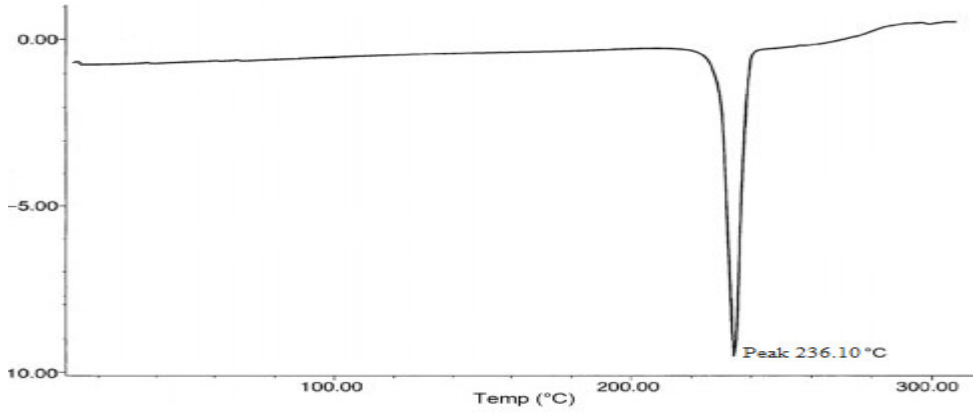

Figure 1: DSC Thermogram of Caffeine

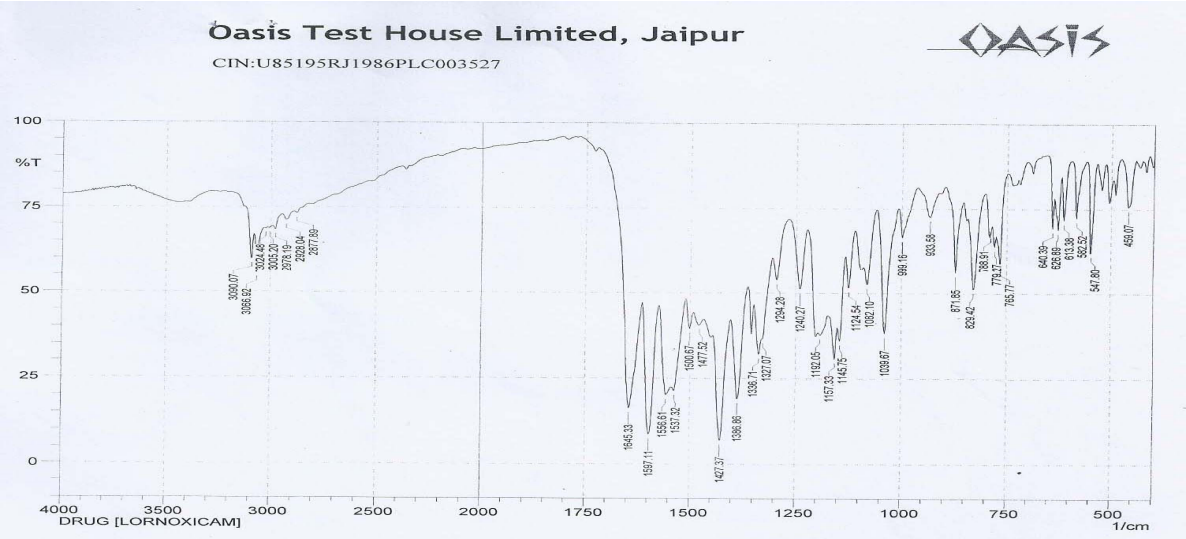

Figure 2: IR Spectra of Caffeine

Calibration Curve Data of Caffeine

Concentration	Absorbance (273 nm)
0.0	0
2.0	0.181
4.0	0.335
6.0	0.483
8.0	0.643
10.0	0.79
12.0	0.934

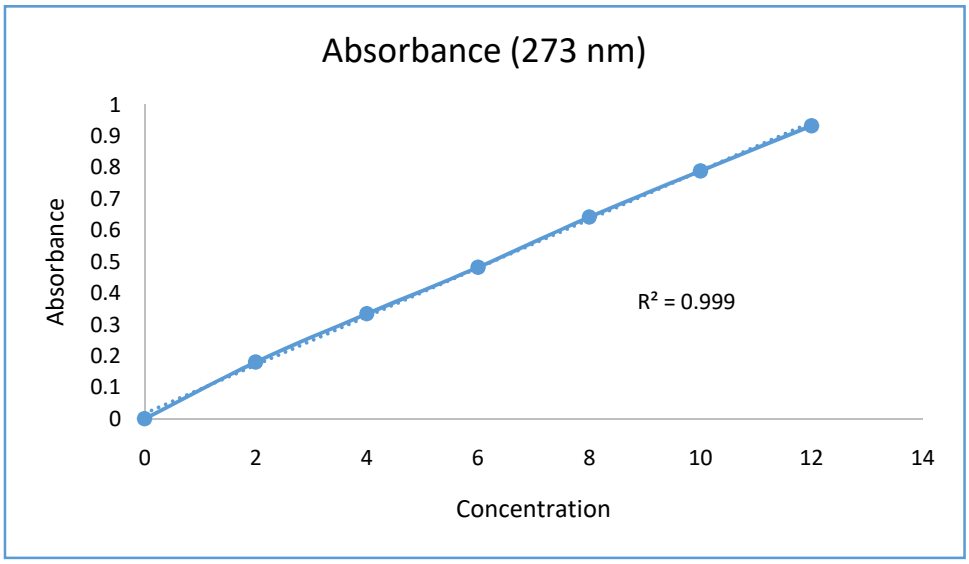

Figure 3: Calibration Curve of Caffeine

Characterization of blend of Caffeine tablet

Parameters / Formulation	Bulk Density (mg/ml)	Tapped Density (mg/ml)	Hausners Ratio	Compressibilty Index (%)	Angle of Repose 0
CT_1	0.461±0.011	0.511±0.015	1.108±0.090	09.78±0.15	24.11±1.38
CT_2	0.463±0.031	0.523±0.011	1.129±0.089	11.47±0.03	25.22±1.35
CT_3	0.455±0.017	0.516±0.013	1.134±0.019	11.82±0.18	24.25±1.40
CT_4	0.471±0.014	0.539±0.011	1.144±0.015	12.61±0.05	24.47±0.55
CT_5	0.482±0.011	0.551.±0.012	1.143±0.021	12.52±0.03	28.01±1.25
CT_6	0.481±0.021	0.561±0.016	1.166±0.025	14.26±0.19	24.29±1.17
CT_7	0.468±0.19	0.525±0.015	1.121±0.019	10.85±0.15	25.39±0.15
CT_8	0.465±0.018	0.535±0.013	1.150±0.0.29	13.08±0.05	26.25±0.29
CT_9	0.485±0.011	0.574±0.012	1.183±0.025	15.50±0.16	24.42±1.10

Characterization of Caffeine fast dissolving tablet

Parameters / Formulation	Weight (mg)	Hardness (Kg/cm^2)	Friability (%)	Disintegration Time (Sec)	Swelling Time (Sec)
CT_1	195.30±0.02	4.15±0.15	0.51±0.24	58±1.24	15±1
CT_2	190.50±0.04	3.11±0.01	0.55±0.21	42±1.14	14±2

CT_3	193.50±0.12	3.31±0.09	0.56±0.17	55±1.26	16±1
CT_4	196.22±0.13	3.55±0.12	0.51±0.15	53±1.25	21±1
CT_5	197.70±0.15	3.51±0.01	0.62±0.12	40±1.22	13±2
CT_6	198.10±0.21	3.29±0.10	0.71±0.32	49±1.31	17±2
CT_7	197.92±0.18	3.35±0.05	0.63±0.13	65±1.01	13±2
CT_8	198.50±0.14	3.50±0.09	0.62±0.20	42±1.19	22±2
CT_9	197.30±0.20	3.40±0.18	0.68±0.11	41±1.18	13±1

Drug Content in the Fast Dissolving Tablet of Caffeine

Parameters / **Formulation**	**Drug Content (mg per Tablet)**	**% Drug Content**
CT_1	93.65±0.02	93.65
CT_2	94.25±0.04	94.25
CT_3	93.75±0.12	93.75
CT_4	96.11±0.13	96.11
CT_5	97.35±0.15	97.35
CT_6	96.55±0.21	96.55
CT_7	94.96±0.18	94.96
CT_8	96.25±0.14	96.25
CT_9	95.15±0.20	95.15

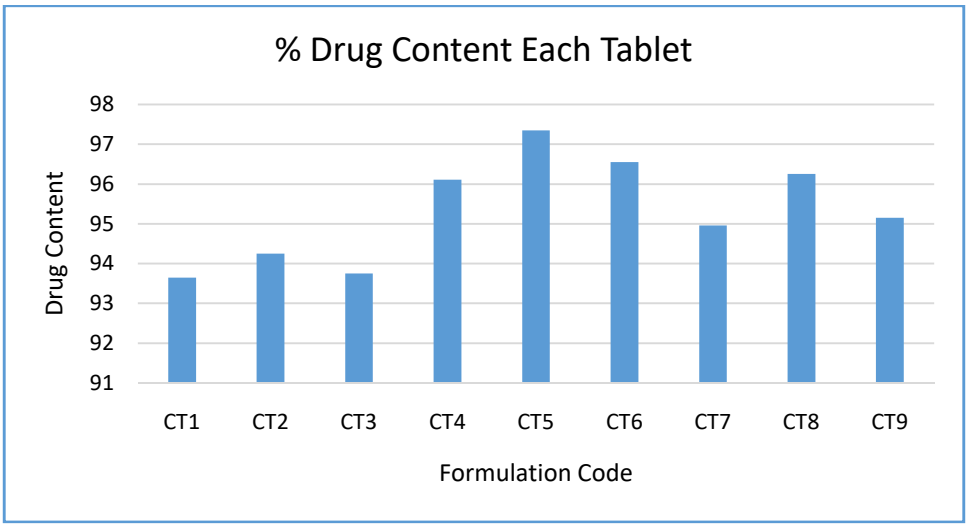

Figure 4: Drug Content in the Fast Dissolving Tablet of Caffeine

IV. CONCLUSION

Pre-compression parameters

Bulk Density and Tapped Density of the Blend were found as 0.455±0.017 to 0.485±0.011 and 0.511±0.015 to 0.574±0.012 respectively. Carr's index of the prepared blend fall in the range of 09.78±0.15 to 15.50±0.16 % and this is also supported by Hausner's factor values which were in the range of 1.108±0.090 to 1.183±0.025. Hence the prepared blends posses good flow property and can be used for manufacturing of the tablet. The values of angle of repose were found in the range of 24.11±1.38 to 28.01±1.25..

Post-compression Parameter

All the tablets were prepared under similar experimental conditions. All the formulation exhibited white colour, odourless, flat shaped with almost smooth surfaces. The average weight of the fast dissolving tablet was 190.50 to 198.50 mg. Hardness of prepared tablet was between 3.11±0.01 to 4.15±0.15 kg/cm^2 The percent friability of formulations was found to be 0.51±0.15 to 0.71±0.32 (less than 1.0%) and thus hardness and friability of all formulation are found within acceptable limits. The disintegration time is very important and it is desired to be less than 1 minute. The quick disintegration may assist quick swallowing and drug absorption in buccal cavity, thus greater bioavailability of the drug. Disintegration time of prepared fast dissolving tablet was found in the range of 40 to 65 seconds. Swelling time is the indicator for the ease of disintegration of the tablet in the buccal cavity. It was observed that swelling time of tablet was in the range of 13 to 22 seconds. It was found that the nature of superdisintegrants present affected the swelling of the tablets. Assay of the prepared formulation was performed to determine drug content uniformity and it was found between 93.65 to 97.35 % per. At the end of 5 minutes the cumulative percentage drug release from various fast dissolving tablets of Caffeine was found to be 97.35, 96.55, 96.25, 96.11, 95.15, 94.96, 94.25, 93.75 and 93.65% from CT_5, CT_6, CT_8, CT_4, CT_9, CT_7, CT_2, CT_3 and CT_1respectively. Kyron T-314, Co-procced superdisintegrant provides maximum release of the drug. The release of drug followed first order kinetics and mechanism of drug release was found to be diffusion controlled.

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