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DEVELOPMENT AND EVALUATION OF FAST-DISSOLVING TABLETS OF AN ANTI-GOUT DRUG BY SUBLIMATION METHOD

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Keywords:

Fast-dissolving tablets, Allopurinol, Solid dispersion, Superdisintegrant, Subliming agent, Xanthine oxidase inhibitor

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ABSTRACT: The purpose of the current research was to formulate and evaluate patient-friendly allopurinol solid dispersion based fast-dissolving tablets using a sublimation technique in order to accomplish rapid drug dissolution. In the present study, an effort was made to fasten the release of allopurinol from oral tablet dosage form by the conversion of the drug into solid dispersion form followed by further incorporation of allopurinol solid dispersions with superdisintegrants and camphor/ammonium bicarbonate as the subliming agents. The prepared fast-dissolving tablets of allopurinol solid dispersion were analyzed for pre-compression and post-compression parameters. Based on the results obtained for *in-vitro* drug release studies, it was observed that the formulation F8 showed a fast release profile of about 99.51% in 30 min and a disintegration time 40 sec in comparison with other formulations. The initial dissolution rate was 34.25% / 10 min for the best formulation, F8. FT-IR studies disclosed that there were no interactions between drugs and excipients. The current investigation revealed the potential for the rapid dissolution of allopurinol solid dispersion fast-dissolving tablets prepared by the sublimation method.

INTRODUCTION: Drug administration through the oral route has wide acceptability up to 50 % to 60% of the total dosage forms. The popularity of solid dosage forms is due to their advantages, such as accuracy of dosage, ease of administration, self-medication possibility, pain avoidance, and patient compliance. The main limitation of solid dosage forms in the case of a few patients is the swallowing difficulty.

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Drinking water plays a significant role in the swallowing of oral dosage forms. Patients face inconvenience swallowing the tablet dosage forms when there is the unavailability of drinking water, in case of kinetosis (motion sickness) and sudden coughing episodes during the allergic condition, common cold and bronchitis [1].

Hence, tablets that can disintegrate or dissolve rapidly in the oral cavity have gained more attention. Such tablets may also be suitable for active patients. Fast-dissolving tablets are also called melt-in-mouth, mouth-dissolving, quick-dissolving, orodispersible, *etc.* [2]. Allopurinol is a xanthine oxidase inhibitor and the most commonly used medication for the treatment of

gout. Allopurinol is a bicyclic structure consisting of a pyrazole ring fused to a hydroxyl-substituted pyrimidine ring. It is used as a gout suppressant and radical scavenger. Allopurinol belongs to BCS Class II as the drug is slightly soluble in water [3].

The current research investigation is mainly focused on the formulation and evaluation of fast-dissolving tablets of an antigout drug, allopurinol. Several batches of the fast-dissolving tablets of allopurinol solid dispersion were prepared by sublimation using various subliming agents (camphor & ammonium bicarbonate) and superdisintegrants (sodium starch glycolate & crospovidone) in various compositions to achieve rapid release of allopurinol from tablet dosage forms.

MATERIALS AND METHODS: Allopurinol was received as a gift sample from Niksan Pharma Chem, India. Hydroxy propyl cellulose was procured from Jig Chem Universal, Mumbai. Sodium starch glycolate (SSG), crosspovidone and magnesium stearate were obtained from Loba Chemie, Tarapur.

Ammonium bicarbonate, talc, and mannitol were procured from Finar Chemicals Ltd., Oxford Laboratory, Mumbai, and Himedia Laboratory, Nashik. Camphor was procured from Qualikems Fine Chem, Vadodara. Aspartame and microcrystalline cellulose were purchased from Shree Sai Enterprise, Gujarat, India.

Preformulation Studies: Pre-formulation study is the initial step in the rationale development of the dosage forms and involves an evaluation of physico-chemical characteristics of a drug substance alone and in combination with additives used in formulation[4]. Such studies include the determination of colour, taste, odour, solubility determination, melting point & compatibility among the ingredients used in formulations.

Drug Carrier Excipients Compatibility Test:

Fourier Transform Infra-Red (FT-IR) Analysis [9]: An FT-IR spectrophotometer was utilized for the sample analysis. About 4 mg to 5 mg of the test sample was mixed with dry potassium bromide, and the sample was analyzed at the transmission mode in 4000-400 cm^{-1} wave number range [5].

Formulation Development:

UV Scan Spectrum of Allopurinol Solid Dispersion: UV absorption spectra of allopurinol and its solid dispersion were determined in phosphate buffer solution, pH 6.8, by scanning the sample solutions in 200 nm - 400 nm range at a path length of 1 cm. Allopurinol solid dispersion exhibited maximum absorption (λ_{max}) at the wavelength of 250 nm.

Calibration of Standard Curve of Allopurinol Solid Dispersion: Allopurinol solid dispersion equivalent to 100 mg of allopurinol was accurately weighed and dissolved in 100 ml of pH 6.8 phosphate buffer solution in a 100 ml volumetric flask. From the prepared stock solution, suitable dilutions were done to get concentrations of 4 µg/ml, 8 µg/ml, 12 µg/ml, 16 µg/ml, and 20 µg/ml, respectively. The absorbance of each solution was determined by a UV-visible spectrophotometer at the λ_{max} of 250 nm using pH 6.8 phosphate buffer solution as blank.

Formulation of Allopurinol Solid Dispersions: Allopurinol solid dispersion was prepared by solvent evaporation technique using hydroxy propyl cellulose as a continuous phase in the weight ratio of 1:0.5. Initially, the physical mixture of allopurinol and hydroxy propyl cellulose was dissolved in a round bottom flask consisting of 10 ml of ethanol. The solvent was allowed to evaporate in a vacuum oven at a temperature not exceeding 45 ^{o}C. The resultant solid dispersion of allopurinol was pulverized in a mortar with the help of a pestle, set aside in a vial, and further stored in desiccators until its further use.

Preparation of Fast-Dissolving Tablets of Allopurinol Solid Dispersions by Sublimation Method [6]: The fast-dissolving tablets of allopurinol solid dispersions were prepared using camphor/ammonium bicarbonate as the subliming agents. Sodium starch glycolate and crospovidone were utilized as superdisintegrants. Each of the superdisintegranting agents was employed in 3 different compositions. Microcrystalline cellulose was used as diluents, magnesium stearate as a lubricant, and talc as a flow promoter. Aspartame was used as a sweetening agent and mannitol for pleasant mouth feel. All the ingredients were passed through # 60 sieve followed by mixing in

geometric fashion. The resultant uniformly mixed blend was then subjected to compression into tablets using a Secor tablet compression machine (punches flat-faced, 12 mm diameter) in order to prepare 650 mg tablets. Finally, the prepared tablets were subjected to the process of sublimation by keeping in hot air oven at 40 ºC for 6 h. A total of ten formulations was developed and composition of the formulations was mentioned in **Table 1.**

TABLE 1: FORMULATION OF VARIOUS BATCHES OF ALLOPURINOL SOLID DISPERSION AND ALLOPURINOL FAST-DISSOLVING TABLETS

Ingredients	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)	F7 (mg)	F8 (mg)	F9 (mg)	F10 (mg)
Allopurinol SD equivalent to allopurinol 300 mg	450	450	450	450	450	450	450	450	450	--
Allopurinol pure drug	--	--	--	--	--	--	--	--	--	300
Camphor	10	20	--	--	10	20	--	--	10	--
Ammonium bicarbonate	--	--	10	20	--	--	10	20	10	20
Sodium starch glycolate	20	20	20	20	--	--	--	--	--	--
Crosspovidone	--	--	--	--	20	20	20	20	20	20
Aspartame	02	02	02	02	02	02	02	02	02	02
Mannitol	40	40	40	40	40	40	40	40	40	40
Magnesium stearate	04	04	04	04	04	04	04	04	04	04
Talc	04	04	04	04	04	04	04	04	04	04
Microcrystalline cellulose	120	110	120	110	120	110	120	110	110	260
Total (mg)	650	650	650	650	650	650	650	650	650	650

Evaluation of Fast-Dissolving Tablets of Allopurinol Solid Dispersions:

Evaluation of Pre-compression Characteristics:

Angle of Repose: The angle of repose was determined by the fixed funnel method in which a funnel was mounted upright to the stand at a 6 cm height. 5 g of the sample powder was poured into the funnel by closing the open end with the thumb, and then took off thumb.

The maximum height of the powder heap (h) formed was noted. The radius of heap (r) was determined, and finally, the value of angle of repose (θ) was calculated using the formula [7].

$$\theta = \tan^{-1}(h/r)$$

In which θ = angle of repose

Bulk Density: To determine bulk density of powder, the quantity of powder (passed through standard # 40 sieve) was poured into a measuring cylinder and the initial (height) volume of the powder, also known as bulk volume, was noted. Powder bulk density was further calculated using the below-mentioned formula [8].

$$D_b = M / V_b$$

In which D_b = bulk density expressed in g/cm^3, M = mass of powder, V_b = bulk volume of powder.

Tapped Density: The tapped density of powder was measured for a known mass of blend (M) in a measuring cylinder. It was then tapped for 100 tappings (fixed time). The minimum volume (V_t) occupied by the blend in the measuring cylinder was noted down [9]. The formula computed the tapped density (ρt);

$$D_t = M / V_t$$

D_t = tapped density expressed in g/cm^3, M = mass of powder, and V_t = tapped powder volume.

Carr's Index or % Compressibility [10, 11]: The value of Carr's index signifies the flow characteristics of powder and is calculated as,

$$CI = (D_t - D_b) / D_t \times 100$$

CI = Carr's index, D_t = tapped density of powder, D_b = bulk density of powder.

Hausner's Ratio: Hausner's ratio is an indirect indicator of ease of powder flow and is computed using formula [12].

$$\text{Hausner's Ratio} = D_t / D_b$$

In which D_t = tapped density of powder, D_b = bulk density of powder, Lower Hausner's ratio (<1.25) denotes better flow characteristics compared to higher ones (>1.25).

TABLE 2: RELATIONSHIP BETWEEN PERCENTAGE COMPRESSIBILITY & FLOWABILITY

Percentage compressibility	Flowability
5 – 10	Excellent
12 – 16	Good
18 – 21	Fair passable
23 – 25	Poor
33 – 38	Very poor
< 40	Very very poor

Evaluation of Post-compression Characteristics:

Physical Appearance: Physical appearance of core tablets comprises the measurement of various features such as tablet colour, shape, surface texture, smoothness, embossing, chipping, debossing, cracks, *etc*.

Tablet dimensions – thickness and diameter

The thickness of the prepared tablets was determined for 10 pre-weighed tablets from each formulation utilizing a Vernier calliper, expressed as average thickness in mm**.** Tablet thickness must be within ± 5% variation of a standard. The diameter of the developed FDTs was determined.

Weight Variation: For the weight variation test, 20 tablets were randomly chosen from each tablet formulation and individually weighed to check for the weight variation [13]. According to Indian Pharmacopoeia, the weight variation specification is mentioned in **Table 3.**

TABLE 3: WEIGHT VARIATION SPECIFICATION AS PER INDIAN PHARMACOPOEIA

Average tablet weight	% Deviation allowed
80 mg or less	±10
80 mg to 250 mg	±7.5
250 mg or more	±5

Tablet Hardness: Tablet hardness or crushing strength is the force applied across the diameter of the tablet to break it. The resistance of tablets towards abrasion, breakage or chipping, under transportation conditions, handling, and storage before use depend on its hardness. Tablet hardness was determined for each formulation by Strong Cobb hardness tester [14].

Friability: The Friability test was performed employing Roche friabilator to assess the effect of shocks and friction, which may cause tablet chipping, capping, or breakage problems. A prior weighed sample of tablets was taken in the plastic chamber of the friabilator that revolves at a speed of 25 rpm for 4 min, and the tablets were dropped at a distance of 6 inches with each revolution. Tablets after the friability test were de-dusted and re-weighed. The core tablets must not lose > 1% of their weight.

% Friability = Initial weight of tablets – Final weight of tablets / Initial weight of tablets x 100

Wetting time & Water Absorption Ratio [15, 16]: A piece of tissue paper folded twice was arranged in a small petri plate (6.5 cm internal diameter) consisting of 6 ml of pH 6.8 phosphate buffer solution. A pre-weighed tablet was placed on the paper, and the time taken for complete wetting was noted utilizing a stopwatch. The wetted tablet was further re-weighed. The following formula calculated the water absorption ratio (R),

$$R = W_a – W_b / W_b \times 100$$

W_a = weight of tablet after water absorption, W_b = weight of tablet before water absorption.

Drug Content: The prepared fast-dissolving allopurinol solid dispersion tablets were analyzed for their drug content. 03 tablets from each formulation were weighed and powdered finely. About 450 mg of allopurinol solid dispersion, equivalent to 300 mg of allopurinol was weighed accurately and dissolved completely in pH 6.8 phosphate buffer solution, followed by filtration. One ml of filtrate was diluted to 100 ml with a pH 6.8 phosphate buffer solution. A UV-visible spectrophotometer measured the absorbance of the resulting solution at a λ_{max} of 250 nm.

***In-vitro* Dispersion Time:** For the determination of *in-vitro* dispersion time, 3 tablets from each formulation were dropped separately in measuring cylinders of 10 ml capacity containing 6 ml of pH 6.8 phosphate buffer solution. Time taken for the complete dispersion of each tablet was noted.

***In-vitro* Disintegration Time:** *In-vitro* disintegration times for the prepared tablet formulations were assessed using USP disintegration test apparatus with pH 6.8 phosphate buffer solution (900 ml) as disintegration medium maintained at 37 °C ± 2 °C. The time taken for the complete disintegration of tablets with no palpable mass left out in the apparatus was determined.

***In-vitro* Dissolution Studies:** *In-vitro* dissolution study for the developed fast dissolving tablets of allopurinol solid dispersion was performed using type II (paddle type) USP dissolution testing apparatus" at a stirring speed of 50 rpm and a temperature of 37 °C ± 0.5 ° in pH 6.8 phosphate buffer solution. At each specified time interval, 5 ml of sample was withdrawn with replacement by fresh dissolution medium. Samples were analyzed by UV- visible spectrophotometer at 250 nm against the blank. The percentage drug release was calculated using an equation obtained from the calibration curve. The *in-vitro* drug release studies were conducted in triplicate, and the graph was plotted considering the mean values of drug release with respect to time.

RESULTS AND DISCUSSION:

Pre-formulation Studies of Allopurinol: Drug & excipients interaction studies were carried out by checking physical appearance and FT-IR analysis. The below-mentioned pre-formulation studies were done on allopurinol and excipients used in the formulation.

Analytical Report for API:

TABLE 4: ANALYTICAL REPORT FOR ALLOPURINOL

Pre-formulation test	Results
Description	An odourless, tasteless, white crystalline powder
Solubility	Sparingly soluble in water; soluble in ethanol (96%); slightly soluble in ether
Category	Proton pump inhibitor
Melting Point	274^{o}C

TABLE 5: ALLOPURINOL CHARACTERIZATION

Test	Result
Particle size (µm)	11.25
Bulk density (g/cm^3)	0.525
Tapped density (g/cm^3)	0.610
Carr's index	13.95
Hausner's ratio	1.16
Angle of repose (^{o})	29.65

Drug Excipients Compatibility Studies: The interaction studies were done to determine any drug interaction with the excipients used to prepare fast-dissolving tablets.

Interpretation of Allopurinol:

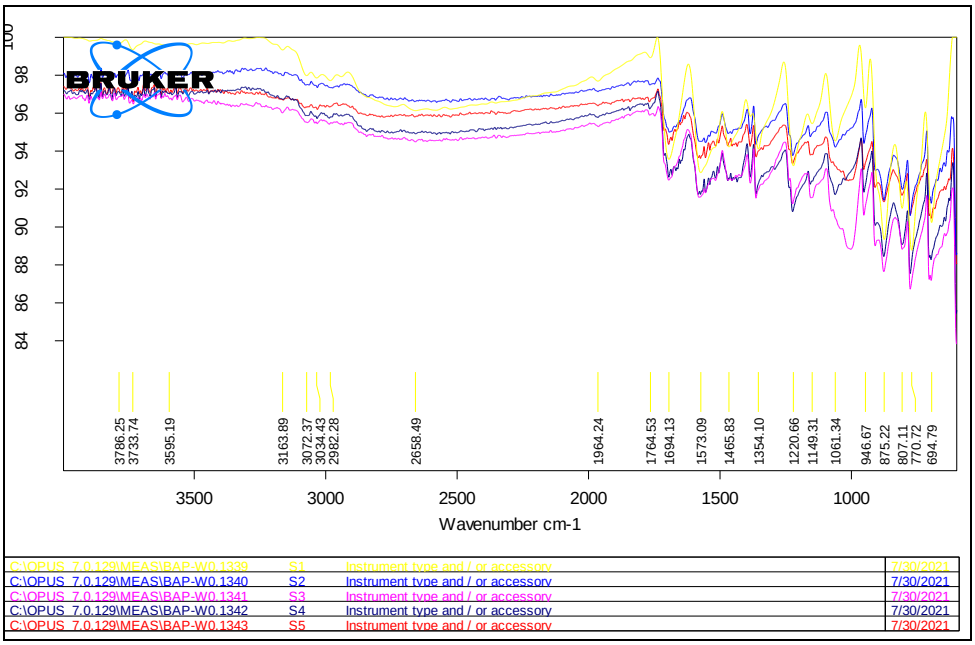

FIG. 1: FT-IR SPECTRA OVERLAY FOR S1 –S5. (S1: allopurinol pure drug; S2: physical mixture of allopurinol + crosspovidone + camphor; S3: allopurinol +sodium starch glycolate + camphor; S4: allopurinol + crosspovidone + ammonium bicarbonate; S5: allopurinol + sodium starch glycolate + ammonium bicarbonate)

Based on the FT-IR spectra, it was evident that there was no physical incompatibility of pure drug with the casuperdisintegrants, subliming agents, and other excipients used in the formulation of allopurinol solid dispersion fast-dissolving tablets.

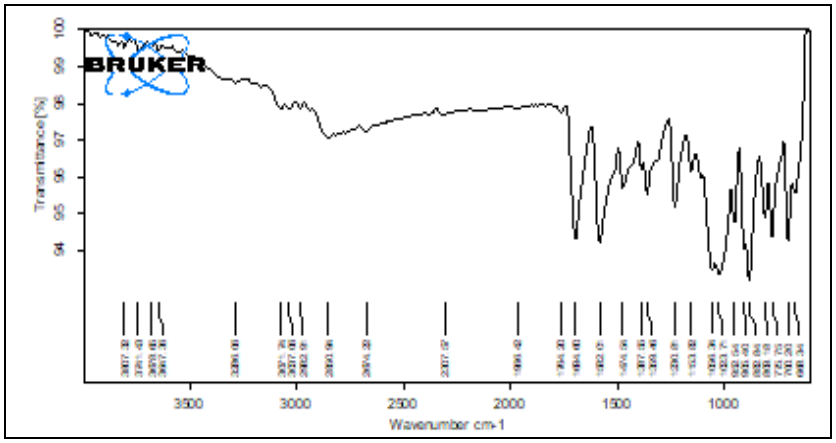

FIG. 2: FT-IR SPECTRA FOR PHYSICAL MIXTURE OF ALLOPURINOL + CARRIER (HPC) + SODIUM STARCH GLYCOLATE + AMMONIUM BICARBONATE

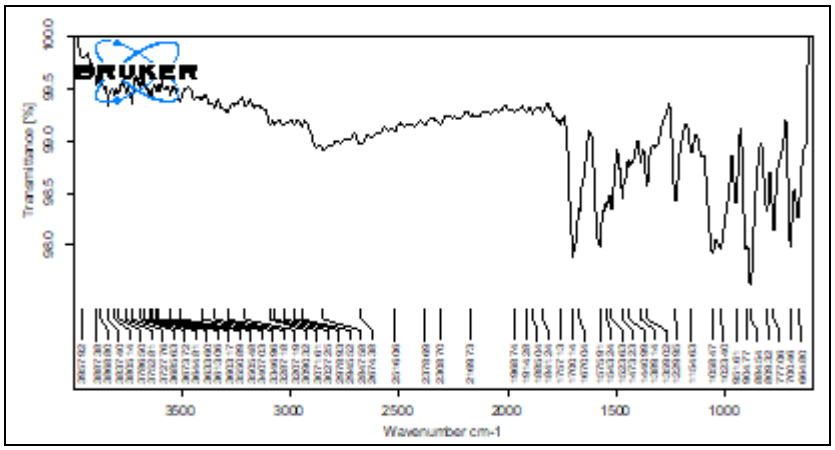

FIG. 3: FT-IR SPECTRA FOR PHYSICAL MIXTURE OF ALLOPURINOL + CARRIER (HPC) + CROSSPOVIDONE + AMMONIUM BICARBONATE

TABLE 6: FT-IR SPECTRA INTERPRETATION OF ALLOPURINOL PURE DRUG

Interpretation	Characteristic peak at wave number (cm^{-1})
CH in plane deformation	770.96, 805.24, 902.81, 1149.21 & 1219.05
Ring vibration	1576.21
CO stretching	1691.71 & 1764.71
CH stretching	3071.95
NH	3616.95

Inference: FT-IR studies were done to determine the possible incompatibilities between chosen drug allopurinol, physical mixtures (various combinations) of drug with carrier, superdisintegrants & subliming agents used in the formulation of fast-dissolving tablets.

FT-IR of allopurinol exhibited the following peaks at 770.96, 805.24, 902.81, 1149.21 & 1219.05 cm^{-1} (CH in-plane deformation); 1576.21 cm^{-1} (ring vibration); 1691.71 & 1764.71 cm^{-1} (CO stretching); 3071.95 cm^{-1} (CH stretching) and 3616.95 cm^{-1} (NH functional group). The physical mixture of the drug with ingredients used in the formulations clearly exhibited retention of the characteristic peaks of allopurinol, hence no incompatibility between allopurinol, carrier, super disintegrants & other excipients used in formulation was revealed.

Formulation Development:

Standard Curve of Allopurinol Solid Dispersion: The standard calibration curve of allopurinol solid dispersion was constructed in phosphate buffer solution, pH 6.8, as depicted in **Fig. 3**. Drug concentration in µg/ml & absorbance followed a linear relationship. The curve obeyed Beer-Lambert's law & the correlation coefficient value (R^2) in phosphate buffer solution, pH 6.8 is found to be 0.999.

TABLE 7: STANDARD CALIBRATION CURVE OF ALLOPURINOL SOLID DISPERSION

Concentration (µg/ml)	Absorbance at 250 nm (in phosphate buffer solution, pH 6.8)
0	0.000
04	0.205
08	0.424
12	0.635
16	0.848
20	1.019

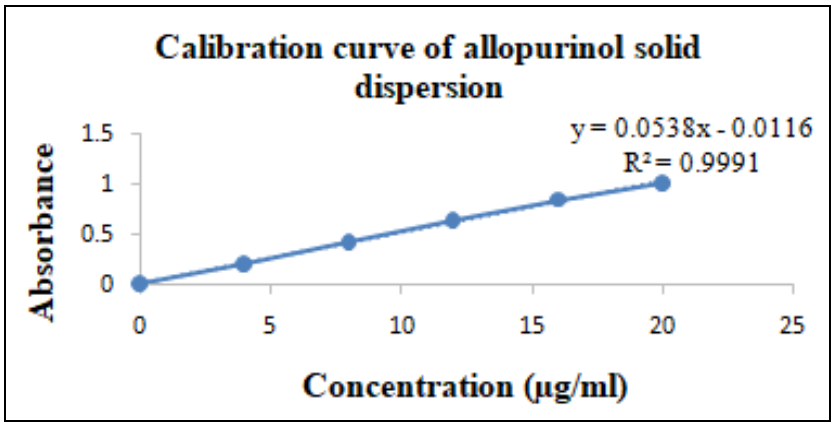

FIG. 4: STANDARD CALIBRATION CURVE OF ALLOPURINOL SOLID DISPERSION IN PHOSPHATE BUFFER SOLUTION, PH 6.8 AT λ_{max} OF 250 nm

Allopuinol solid dispersion was prepared by solvent evaporation method using hydroxy propyl cellulose in the ratio of 1:0.5. Fast dissolving tablets of allopurinol solid dispersion were prepared by sublimation technique using sodium starch glycolate & crospovidone as super-disintegrants as well as camphor & ammonium bicarbonate as subliming agents. A total of ten formulations were prepared (F1, F2, F3, F4, F5, F6, F7, F8, F9, and F10). The developed FDTs were subjected to pre-compression and post-compression analysis; the results were represented in **Tables 8** & **9**.

TABLE 8: PRE-COMPRESSION ANALYSIS OF ALLOPURINOL SOLID DISPERSION FAST-DISSOLVING TABLET FORMULATIONS

Formulation	Angle of repose (°)	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Carr's Index	Hausner's ratio
F1	30.58 ± 0.25	0.38 ± 0.02	0.46 ± 0.08	17.39 ± 0.12	1.21 ± 0.02
F2	28.72 ± 0.37	0.39 ± 0.04	0.47 ± 0.02	17.02 ± 0.20	1.20 ± 0.06
F3	27.45 ± 0.26	0.36 ± 0.07	0.43 ± 0.06	16.27 ± 0.15	1.19 ± 0.03
F4	26.58 ± 0.39	0.37 ± 0.06	0.44 ± 0.02	15.90 ± 0.10	1.18 ± 0.02
F5	29.84 ± 0.22	0.37 ± 0.04	0.45 ± 0.03	17.07 ± 0.15	1.16 ± 0.06
F6	27.98 ± 0.27	0.35 ± 0.06	0.42 ± 0.02	16.66 ± 0.22	1.20 ± 0.02
F7	25.60 ± 0.30	0.37 ± 0.04	0.44 ± 0.04	15.90 ± 0.08	1.19 ± 0.08
F8	24.07 ± 0.19	0.40 ± 0.05	0.45 ± 0.08	14.89 ± 0.04	1.13 ± 0.02
F9	26.15 ± 0.30	0.35 ± 0.06	0.42 ± 0.05	16.66 ± 0.40	1.20 ± 0.04
F10	27.32 ± 0.33	0.36 ± 0.04	0.43 ± 0.04	16.27 ± 0.22	1.19 ± 0.06

Note: Mean ± S.D. of three determinations

It was evident from the FTIR studies that there was no incompatibility between alloppurinol, carrier, superdisintegrants, subliming agents, and other excipients used in the formulation of tablets. The angle of repose (Ɵ) of all the developed formulations was found to be within the 24.07 ± 0.19 to 30.58 ± 0.25 range. The results obtained suggested that the powder blend demonstrated good flow characteristics. Bulk density was observed to be in the range of 0.35 ± 0.06 to 0.40 ± 0.05 g/cm^3. Tapped density values were in the range of 0.42 ± 0.02 to 0.47 ± 0.02 g/cm^3. Carr's index & Hausner's ratio of all the prepared formulations were present in 14.89 ± 0.04 to 17.39 ± 0.12 & 1.13 ± 0.02 to 0.35±0.05 range, respectively. Results indicated that the prepared powder blend of fast-dissolving tablets showed good flow characteristics.

TABLE 9: POST COMPRESSION ANALYSIS OF ALLOPURINOL SOLID DISPERSION FAST DISSOLVING TABLET FORMULATIONS

Formulation	Hardness (Kg/cm^2)	Friability (%)	Wetting time (sec)	Water absorption ratio	Drug content (%)	Disintegration time (sec)
F1	3.3 ± 0.20	0.54 ± 0.02	62 ± 1.52	145 ± 1.52	96.82 ± 1.15	114 ± 1.28
F2	3.1 ± 0.15	0.60 ± 0.04	65 ± 1.64	159 ± 1.63	97.86 ± 1.22	102 ± 1.10
F3	2.8 ± 0.08	0.75 ± 0.06	48 ± 1.25	165 ± 1.71	96.12 ± 1.34	105 ± 1.39
F4	2.7 ± 0.06	0.70 ± 0.04	45 ± 1.33	168 ± 1.48	95.34 ± 1.47	080 ± 1.50
F5	3.1 ± 0.20	0.55 ± 0.02	71 ± 1.46	175 ± 0.27	92.56 ± 1.29	089 ± 1.25
F6	2.9 ± 0.12	0.70 ± 0.08	49 ± 1.12	152 ± 1.55	88.98 ± 1.28	090 ± 1.36
F7	2.6 ± 0.05	0.54 ± 0.04	39 ± 1.29	204 ± 1.42	96.63 ± 1.59	045 ± 1.14
F8	2.6 ± 0.20	0 .50 ± 0.02	34 ± 1.31	208 ± 1.27	98.25 ± 1.56	040 ± 1.33
F9	2.7 ± 0.09	0.73 ± 0.04	40 ± 1.40	185 ± 1.35	97.34 ± 1.20	058 ± 1.41
F10	2.6 ± 0.10	0.65 ± 0.08	43 ± 1.57	196 ± 1.40	96.88 ± 1.38	052 ± 1.68

Note: Mean ± S.D. of three determinations.

The tablets were subjected to post-compression analysis, including physical appearance, tablet dimensions – thickness and diameter, weight variation, Friability, hardness, and drug content. The developed FDTs of all the ten formulations were observed to be in a slight off-white colour, round, flat in shape, and smooth in texture. The values of thickness and diameter for the ten formulations were observed to be 0.5 mm ± 0.2 and 1.2 mm ± 0.1, respectively. The results of weight variation test for all the formulations of FDTs were found to be within the acceptable limits. Hardness values for the prepared formulations were in 2.6 ± 0.05 kg/cm^2 to 3.3 ± 0.20 kg/cm^2 range. The % friability was observed in the range of 0.50% ± 0.02 to 0.75% ± 0.06 and the values of drug content in the range of 95.75% ± 0.01 to 99.38% ± 0.01. The results indicated that the developed FDT formulations passed the tests for % friability and drug content. Wetting time for all the developed formulations of FDTs was observed to be in 34 sec to 71-sec range, as shown in **Fig. 5**. Water absorption ratios of all ten formulations were found in the range of 145 ± 1.52 to 208 ± 1.27. Wetting time, *in-vitro* dispersion time, and water absorption ratio were found to be faster for the formulation F9 containing subliming agent camphor & superdisintegrant crosspovidone than other formulations. The drug content in the formulations was found to be in the range of 88.98% ± 1.28 to 98.25% ± 1.56. According to the pharmacopoeial standards, the dispersible tablet must disintegrate within 3 min. All formulated batches have shown less disintegration time i.e., 40 sec ± 1.33 to 114 sec ± 1.28, indicating the suitability of formulation for fast dissolving tablets **Fig. 6.**

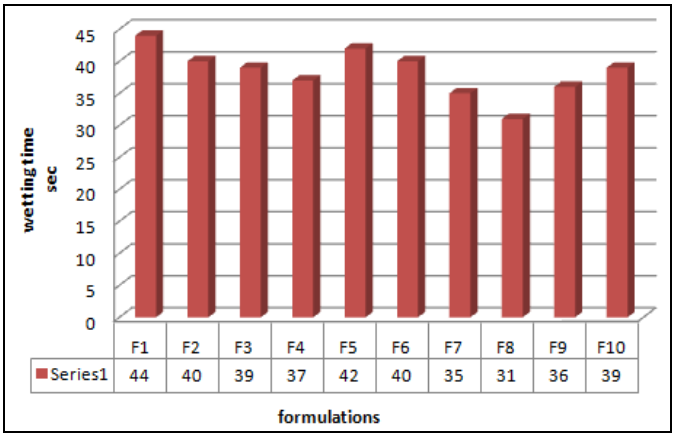

FIG. 5: RESULTS OF WETTING TIME STUDY

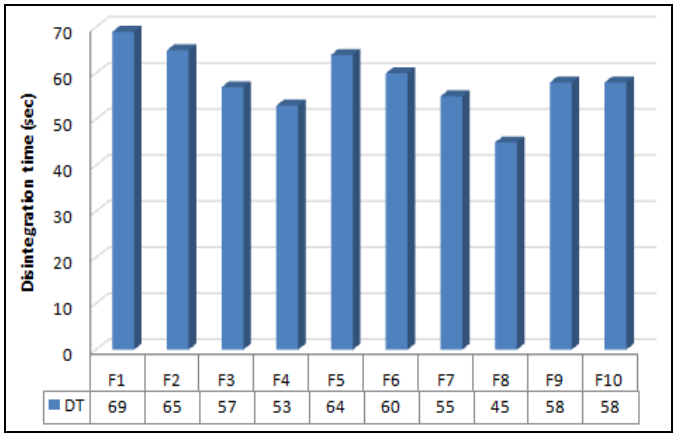

FIG. 6: RESULTS OF IN VITRO DISINTEGRATION TEST

***In-vitro* Drug Release Studies:** The *in-vitro* drug release study was performed for a duration of 60 min. The cumulative % drug release from F1 to F4 formulations was observed to be 75.09%, 81.20%, 83.57%, 87.36%, respectively **Table 10** & **Fig. 7** and for F5 to F8 formulations was found to be 89.70%, 90.96%, 99.32%, 99.51%, respectively. For the formulation F9 it was 83.61%, and a

combination of subliming agents – camphor and ammonium bicarbonate was utilized. For the formulation F10, 65.29% of % drug release was observed at the end of 60 min.

TABLE 10: *IN-VITRO* RELEASE STUDIES OF PREPARED FAST-DISSOLVING TABLET FORMULATIONS OF ALLOPURINOL SOLID DISPERSIONS & ALLOPURINOL

Time (min)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
0	0	0	0	0	0	0	0	0	0	0
10	16.50	20.72	22.83	25.30	26.81	28.16	30.40	34.25	21.46	10.97
20	27.65	32.13	35.30	37.09	37.54	40.62	46.93	57.68	33.70	24.32
30	48.34	47.80	50.64	53.55	55.20	68.35	63.48	99.51	49.24	40.65
40	59.29	60.68	65.28	68.20	70.36	75.92	99.32	--	62.80	49.10
50	66.20	74.39	80.62	84.69	85.54	88.41	--	--	75.29	55.46
60	75.09	81.20	83.57	87.36	89.70	90.96	--	--	83.61	65.29

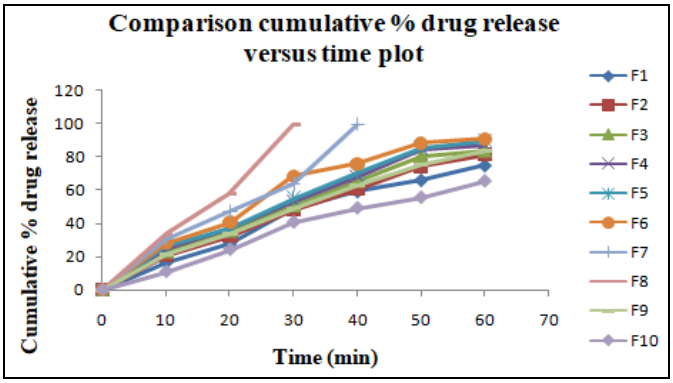

FIG. 7: DRUG RELEASE PROFILES OF ALLOPURINOL SOLID DISPERSION FDTs (F1 - F9) AND ALLOPURINOL FDTs (F10)

CONCLUSION: Solid dispersions of allopurinol were successfully prepared using hydroxy propyl cellulose by a solvent evaporation method. Fast-dissolving tablets of allopurinol solid dispersion were developed utilizing various super disintegrants-sodium starch glycolate, crosspovidone and subliming agents (camphor and ammonium bicarbonate) by sublimation technique. The physical properties of developed formulations were found to be well within the limits of the official standards. All prepared tablet formulations were found to be disintegrated within 114 sec, when examined for the *in-vitro* disintegration time. Among all the formulations, formulation F8 containing crosspovidone in higher amounts and ammonium bicarbonate has shown the fastest disintegration time of 40 sec and a higher percentage of drug release, 99.51% within 30 min. Overall, the results obtained demonstrated that fast-dissolving tablets of allopurinol solid dispersion can be prepared successfully using ammonium bicarbonate as a subliming agent (F8). The developed fast-dissolving tablets disintegrated within a few seconds without water requirement. Thus, the present study demonstrated the potential for rapid disintegration, followed by drug dissolution, which may lead to improved bioavailability, effective therapy and enhanced patient compliance.

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