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Research Article

DEVELOPMENT AND EVALUATION OF MOUTH DISSOLVING ANTIINFLAMMATORY TABLET CONTAINING FENOPROFEN

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ABSTRACT

Fenoprofen belongs to Biopharmaceutical Classification System (BCS) class II drugs which are poorly soluble in water. The objective of present research work was to prepare fast dissolving tablets of fenoprofen using varying concentrations of three different sublimating agents to improve the dissolution rate. Seven formulations were prepared containing different concentrations of camphor, ammonium bicarbonate and thymol as sublimating agent along with primogel as a superdisintegrant. Tablets were manufactured by direct compression method. The prepared tablets were evaluated for pre-compression and post-compression parameters result, for all formulations result was within official limits. DSC studies revealed that there were no interactions between the drug and the excipients used. From *in vitro* drug release studies the dissolution studies, cumulative percentage of drug release versus time was evaluated. It also reflects that the formulations F4 and F15 containing 45 mg and 67.5 mg of thymol respectively showed fast drug release of 100.00% and 99.56 % respectively in 30 minutes as compared with formulations containing other sublimating agents. Among all the formulations, F6 and F7 tablets showed complete drug release within 30 minutes and rapid dissolution.

Keywords: Fenoprofen, Dissolution, Fast dissolving tablets, Drug release, Sublimating agent, Superdisintegrant.

1. INTRODUCTION

Conventional dosage forms are pioneer of drug administration systems. The most widely used and accepted is the oral route of drug administrations. The oral dosage forms are widely used for ease of self-administration and low cost as compared to other dosage forms [1]. It is however associated with some drawbacks such as dysphasia (difficulty in swallowing), low bioavailability and delayed onset of action. In order to overcome these issues, researchers have long explored the "oral cavity" to harness its drawback to enhance the drug's permeability as well as bioavailability. The "oral cavity" has a good permeability because of mucosal lining being relatively less keratinized in the buccal mucosa [2]. Drug absorbed via "oral cavity" directly enters into systemic circulation by a jugular vein ensuring, a rapid onset of action, avoidance of first pass metabolism, and drug degradation in gastric region and enzymatic hydrolysis in intestine [3]. Keeping in mind the advantages of the "oral cavity", an Oral Dispersible Tablet, commonly known as the Fast Dissolving Tablets are a widely accepted formulations. According to European pharmacopoeia "ODT (Oral Dispersible Tablet) should disperse or disintegrate in less than 3 minute when placed on tongue". Fast dissolving drug delivery system (FDDDS) is a newer concept which combines the advantages of both liquid and solid formulations and at the same time, offer advantages over the traditional dosage forms. Many patients, especially elderly find it difficult in swallowing tablets, capsules, fluids and thus do not comply with prescription, which results in high incidence of noncompliance oriented research has resulted in bringing out many safer and new drug delivery system. Rapidly disintegrating/dissolving tablet is one of such example, for the reason of rapid disintegration or even with saliva. Considering quality of life, most of these efforts have been focused on ease of medication. Among the various dosage forms developed to improve the ease of administration, the mouth dissolving tablet (MDT) is the most widely preferred commercial products [4]. The oral cavity is an attractive site for the administration of drugs because of ease of administration. Various dosage forms like Tablets, Capsules, and Liquid preparations are administered by oral route. During the last decade, mouth dissolving tablet (MDT) technologies that make tablets disintegrate in the mouth without chewing and additional water intake have drawn a great deal of attention. The MDT is

also known as fast melting, fast dispersing, rapid dissolve, rapid melt, and or quick disintegrating tablet. All MDTs approved by the Food and Drug Administration (FDA) are classified as orally disintegrating tablets. Recently, the European Pharmacopeia adopted the term orodispersible tablet for a tablet that disperses or disintegrates in less than 3 minutes in the mouth before swallowing. Such a tablet disintegrates into smaller granules or melts in the mouth from a hard solid to a gel-like structure, allowing easy swallowing by patients. The disintegration time for good MDTs varies from several seconds to about a minute [5]. Orally disintegrating tablets provide an advantage particularly for pediatric and geriatric Fast dissolving tablets are novel drug delivery system that dissolves, disintegrate or disperse the API in saliva within few seconds with or without intake of water. The faster the dissolution of drug into the solution, quicker is the absorption and onset of clinical effect [6-9]. The bioavailability of some drugs may increase due to absorption of drugs in oral cavity or also due to pregastric absorption of drug from saliva that pass down into the stomach. Natural and synthetic superdisintegrants like mucilage, cross linked carboxymethyl cellulose (croscarmellose) and sodium starch glycolate (primogel), poly vinyl pyrollidone etc provide immediate disintegration of tablets and facilitate the designof delivery system with desirable characteristics. These types of formulations are widely recommended for the drugs used in emergency. e.g., Cardiac agents, Asthma, Brain stroke, Antihyper-lipidemic etc [10-14].

2. MATERIAL AND METHODS

2.1. Material

Fenoprofen, β-Cyclodextrin, Tartaric Acid, Skimmed milk, Sodium starch glycolate, Crosspovidone, Sacharine sod., Starch avicel granules, Talc, Magnesium stearate were purchased from Sigma Aldrich India.

2.2. Pre-formulation study

2.2.1. Melting Point

Melting point of Fenoprofen was determined using Melting point apparatus (Tempo MP 98) all experiment were performed in triplicate.

2.2.2. Solubility analysis

The sample was qualitatively tested for its solubility in various solvents. It was determined by shaking 2 mg of drug sample in 5 ml of solvent (i.e. Dimethylsulfoxide, Water, Methanol, n-Hexane, Methylene chloride Phosphate buffer pH 6.8, Phosphate buffer pH 7.4 and 0.1N HCl etc) in small test tube and observed to disappear the sample completely.

2.2.3. Partition coefficient

The partition coefficient of drug was examined in n-Octanol: Phosphate buffer pH 6.8, n-Octanol: water system. It was determined by taking 5mg of drug in three separating funnel containing, 5ml of n-Octanol and 5ml respective buffer (i.e. PBS pH 6.8, PBS pH 7.4, and water). The separating funnel was shaken for 2 hour in a wrist action shaker for equilibrium. Two phases were separated and the amount of drug in aqueous phase was analyzed spectrophotometrically at 270 nm after appropriate dilution with respective buffer. The partition coefficient of drug was calculated using the following formula:

Partition coefficient, Log P= Amount of drug in organic phase/Amount of drug in aqueous phase

2.3. Medium used in the preparation of calibaration curve of fenoprofen

2.3.1. Phosphate buffer pH 6.8

Disodium hydrogen orthophosphate (28.8gm), and potassium dihydrogen orthophosphate (11.45gm), were mixed in 100ml of distilled water and volume was madeup to1000ml with distilled water.

2.3.2. Phosphate buffer pH 7.4

Disodium hydrogen orthophosphate (28.8gm), and potassium dihydrogen orthophosphate(19gm), and sodium chloride (8gm) were mixed in about 100ml of distilled water and the volume was made up with distilled water up to 1000ml, the pH of solution was adjusted to 7.4 immediately before use with 0.1N HCL or 0.1N NaOH as required.

2.3.3. Simulated gastric fluid (pH2.0)

A 50ml KCl solution (0.2M) was placed in 200 ml volumetric flask, and 85.0 ml HCl (0.2N) was then added and volume was made up with water. The solution was kept for 24 hrs, filtered and pH was adjusted to 2 with 0.1N HCl using pH meter.

2.4. Preparation of Standard Curve of Fenoprofen in PBS pH 6.8

Accurately weighed 50 mg of Fenoprofen was taken in 50 ml volumetric flask and dissolved in 2-3ml methanol and volume was made up with PBS (pH 6.8) to the mark. This resulted 1000µg/ml stock solution. From the above stock solution, 10ml was taken in another 100ml

volumetric and volume was made up with PBS (pH 6.8) to mark and the concentration of solution become 100µg/ml. After that from the above solution the aliquots of 1-10ml of stock solution were taken into a series of 10ml volumetric flask and volume was made up to the mark with PBS (pH 6.8) and it was analyzed at λmax 270 nm using UV spectrophotometer.

2.5. Preparation and characterization of ternary complex

2.5.1. Preparation of ternary complexes

Fenoprofen, β-cyclodextrin and Tarteric acid ternary complexes were prepared at 1:2:2,1:3:3,1:4:4 molar ratios, respectively, as described in respective sections.

2.5.2. Physical mixture (PM)

For physical mixtures, Fenoprofen, β -cyclodextrin and tartaric acid were weighed accurately, mixed thoroughly by trituration in a mortar and sieved through a 0.25-mm sieve. All physical mixtures were stored in a dessicator until further evaluation.

2.5.3. Kneaded complex (KC)

The kneaded complex of Fenoprofen, β-cyclodextrin and tartaric acid was prepared by wetting the physical mixture in a mortar with a minimum volume of ethanol/water mixture (15/85, V/V) and kneaded thoroughly with a pestle to obtain a paste, which was then dried under vacuum at room temperature, sieved through a 0.25-mm sieve and stored in a dessicator until further evaluation.

2.5.4. Spray dried complex (SDC)

A mixture of Fenoprofen, β -cyclodextrin and tartaric acid was dissolved in ethanol/water (15/85, V/V). The resultant clear solution was kept for stirring on a magnetic stirrer for 48 hours at room temperature so as to attain complexation equilibrium. Spray drying was carried out using a laboratory scale spray dryer under the following set of conditions: inlet temperature 112°C, outlet temperature 55°C, atomization air pressure 100 kPa, aspiration pressure -2.5 kPa, flow rate 12mL min^{-1}. The powder sample was sieved through a 0.25-mm sieve and stored in a dessicator until further evaluation.

2.6. Inclusion efficiences

The kneaded complex (25mg) were placed in 25 ml volumetric flask, methanol (10ml) was added, mixed throughly and sonicated for 30 min. The volume was made upto the mark with methanol. The solution was suitably diluted with the same solvent and assayed spectrophotometrically for drug content at 270 nm.

2.7. Dissolution studies

Dissolution studies were performed in phosphate buffer(PH 6.8, 900 ml) at 37±0.2°C using USPXXIII apparatus (Electrolab india) with the paddle rotating at 50 rpm each containig 6.25 mg drug were subjected to dissolution time intervals samples were withdrawn, filtered (whatman filter paper no. 41) and spectro-photometrically assayed for drug content at 270 nm.

2.8. Differential Scanning Calorimetry (DSC) Study

The Differential Scanning Calorimetric study was carried out using Mettler Toledo Differential Scanning Calorimeter. Samples were placed in an aluminum crucible and the DSC thermograms were recorded at heating rate of 100 C/ min in the range 30 to 300°C.

2.9. Preparation of mouth dissolving tablet containing fenoprofen, β-cyclodextrin, tarteric acid ternary complex

In this study the mouth dissolving tablets of fenoprofen (6.25mg) was prepared by direct compression method. Superdisintegrants (sodium starch glycolate, cross-povidone, cross carmellose) was used in different concentration (2%, 4%, 6%, 8% and 10%) in each formulation. Five formulations of fenoprofen were prepared. Saccharine sodium was used as main sweetner. All the ingredients were passed through # 60 mesh separately. The drug, superdisintegrant and diluents were mixed in small proportion each time and blending it to form uniform mixture and set aside. The other ingredients were weighed and mixed in geometrical order. Now the mixture was mixed thoroughly with lubricant. The tablets weighing 300 mg were formulated by direct compression technique using multi station tablet punching machine.

2.10. Precompression evaluation of powder mixture

2.10.1. Angle of repose(θ)

There is an empirical relationship between angle of repose and the ability of the powder to flow. It was determined using fixed funnel method. The funnel height was adjusted in such a manner that the tip of the funnel just touched the apex of the heap of the mixture of powders. The mixtures of powders were allowed to flow freely through the funnel onto the surface. The diameter

of the cone of powder was measured and angle of repose was calculated using the following equation.

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

Where h= height of the tip of powder from the base and r =radius of the cone

2.10.2. Bulk Density

Apparent bulk density was determined by pouring pre-sieved drug excipients blend into a graduated cylinder and measuring the volume and weight "as it is". It is expressed in g/cm^3.

2.10.3. Tapped Density

It was determined by placing a graduated cylinder, containing a known mass of drug excipient blend, on mechanical tapping apparatus. The tapped volume was measured by tapping the powder to constant volume. It is expressed in g/ml.

2.10.4. Cars Index (I)

It is expressed in percentage and is expressed by I = (Dt - Db)/ Dt .Where, Dt is the tapped density of the powder Db is the bulk density of the powder.

2.10.5. Hausners Ratio

It is expressed in percentage and is expressed by H = Dt/ Db. Where, Dt is the tapped density of the powder, Db is the bulk density of the powder.

All excipients were weighed accurately and the physical mixture formed after geometrical mixing was evaluated for various parameters. Table 1 shows results of precompression evaluation. Angle of repose was found in the range of 25 to 36° indicating that having passable to good flow property. The Carr's compressibility index value was less than 18 for all formulations physical mixture indicating having the good flow properties. For all the formulations the Hausner ratio was less than one indicating the physical mixture had better flow properties.

2.11. Evaluation of mouth dissolving tablets

2.11.1. Tablet Hardness

Hardness of the tablets was determined by using a Monsanto hardness tester. Three tablets from each batch was selected randomly and tested. The percentage deviation was calculated.

2.11.2. Uniformity of Weight

The weight variation test was done by taking twenty tablets weighed individually and collectively and the average weight was determined. The percentage deviation was calculated and checked for weight variation.

2.11.3. Friability Test

Friability was determined by taking 22 dedusted tablets. Roche friabilator was used for the purpose. Preweighed sample of 22 tablets were placed in the friabilator, which was then operated for 100 revolutions. After 100 revolutions the tablets were dusted and reweighed. The percentage deviation was calculated and checked for friability testing. Percentage friability was calculated for each batch by using this formula

Percentage friability = (initial weight-final weight/initial weight) × 100

2.11.4. In-vitro Disintegration Test

The test was carried out on 6 tablets using phosphate buffer pH 6.8 (saliva pH) at 37±2°C as disintegration media and the time in second taken for complete disintegration of the tablet with no palable mass remaining in the apparatus was measured in seconds. The test was performed in triplicate and mean ± SD calculated.

2.11.5. In-vitro Dissolution Study

The release rate of carvedilol from Mouth dissolving tablets was determined using United State Pharmacopoeia (USP) XXIV dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml of phosphate buffer solution of pH 6.8 at 37±0.5°C and 50 rpm. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus at regular intervals of 1 min for 15 min. Same quantity of fresh dissolution medium was added after each sampling. The samples were filtered through a 0.45µ membrane filter. Absorbance of these solutions was measured at 270 nm using a Shimadzu UV/Vis single beam spectrophotometer.

2.11.6. Wetting time

A circular tissue paper of 10 cm diameter was placed in three petridish with a 10cm diameter, one in each after folding. 10 ml of simulated saliva pH (phosphate buffer pH 6.8) was poured into the tissue paper placed in the petridish. A tablet was placed carefully on the surface of the tissue paper. The time required for the solution to reach upper surface of the tablet was noted as the wetting time. The percentage deviation was calculated and results were tabulated.

2.11.7. Water absorption ratio

A circular tissue paper of 10cm diameter was placed in three petridish with a 10cm diameter, one in each after folding. 10 ml of simulated saliva pH (phosphate buffer pH 6.8) was poured into the tissue paper placed in the petridish. Three tablets were weighed individually and placed one in each petridish. Fully wetted tablets were weighed individually. The water absorption ratio was calculated for every batch. The percentage deviation was calculated and results were tabulated. The water absorption ratio R was determined according to the following formula.

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

Where Wb is the weight of the tablet before keeping in the petridish and Wa is weight of Fully wetted tablet.

2.11.8. In Vitro Dispersion Test

This test is performed to ensure disintegration of tablets in the salivary fluid, if it is to be used as a fast dissolving tablet. *In vitro* dispersion time was measured by dropping a tablet in a measuring cylinder containing 6 ml of simulated salivary fluid of pH 6.8. Five tablets from each formulation were randomly selected and time required to disperse completely was noted.

2.11.9. Evaluation of taste by panel

The taste evaluation was done by panel testing. For panel testing 20 healthy human volunteers were selected. Then the selected panel of 20 healthy human volunteers was requested to taste all the formulations by keeping in the mouth till they disintegrated and rank.

2.11.10. Evaluation of prepared fenoprofen mouth dissolving tablets

By direct compression method the formulations were prepared using the super-disintegrant sodium starch glycolate (SSG). The hardness of the tablet formulations made by the direct compression method was found to be in the range of 3.06 to 3.70 Kg/cm^2, indicating good, mechanical strength with an ability to withstand physical and mechanical stress conditions during handling. In all the formulations, friability value was found to be less than 1%. The weight of all the tablets was found to be uniform with low values of standard deviation and within the prescribed IP 2010 limits. The percent drug content of all the tablets was found to be in the range of 98.72 to 101.23 of the expected fenoprofen content, which was within the acceptable limits. In vitro dispersion time, wetting time and water absorption ratio for all the fenoprofen formulations prepared by direct compression method were determined and the results are shown in table.

2.12. Formulation with skimmed milk

Table 1: Formula for mouth dissolving tablet with different concentration of Sodium starch glycolate

Ingredients (mg)	Formulation code				
	F1	F2	F3	F4	F5
Complex A	89	89	89	89	89
Sodium starch glycolate	6	12	18	24	30
Crosspovidone	-	-	-	-	-
Sacharine sod.	16	16	16	16	16
Starch avicel granules	182	176	170	164	158
Talc	4	4	4	4	4
Magnesium stearate	3	3	3	3	3
Total	300	300	300	300	300

Table 2: Formula for mouth dissolving tablet with different concentration of Crosspovidone

Ingredients (mg)	Formulation code				
	F6	F7	F8	F9	F10
Complex A	89	89	89	89	89
Sodium starch glycolate	-	-	-	-	-
Crosspovidone	6	12	18	24	30
Sacharine sod.	16	16	16	16	16
Starch avicel granules	182	176	170	164	158
Talc	4	4	4	4	4
Magnesium stearate	3	3	3	3	3
Total	300	300	300	300	300

Table 3: Formula for mouth dissolving tablet with different concentration of Croscarmellose sodium

Ingredients (mg)	Formulation code				
	F11	F12	F13	F14	F15
Complex A	89	89	89	89	89
Croscarmellose sodium	6	12	18	24	30
Sacharine sod.	16	16	16	16	16
Starch avicel granules	182	176	170	164	158
Talc	4	4	4	4	4
Magnesium stearate	3	3	3	3	3
Total	300	300	300	300	300

3. RESULTS AND DISCUSSION

3.1. Identification of drug

3.1.1. Physical Appearance

The drug Fenoprofen was white, oderless powder (table 4).

Table 4: Physical Appearance

Drug	Physical appearance	
	Reported	Observed
Fenoprofen	White colour, odourless powder	White colour, odourless powder

3.1.2. Melting Point

Melting point of Fenoprofen was determined using Melting point apparatus (Tempo) and found to be 168°C-171°C.

3.1.3. Solubility analysis

The sample was qualitatively tested for its solubility in various solvents. It was determined by shaking 2 mg of drug sample in 5 ml of solvent (i.e. Dimethylsulfoxide, Water, Methanol, n-Hexane, Methylene chloride Phosphate buffer pH 6.8, Phosphate buffer pH 7.4 and 0.1N HCl etc) in small test tube and observed the disappearance of the sample completely (table 5).

Table 5: Solubility profile

S. No.	Solvent	Solubility	Result
1	Dimethylsulfoxide, n-Octanol	Freely soluble	++++
2	Methanol, Methylene chloride	Soluble	+++
3	Ethanol (95%), Isopropanol	Sparingly soluble	++
4	Phosphate buffer PH 6.8	Slightly soluble	+
5	Phosphate buffer PH 7.4	Slightly soluble	+
6	0.1N HCl, Ethyl ether	Slightly soluble	+
7	n-Hexane, Water	Slightly soluble	+

++++1-10 Parts, +++10-30 Parts, ++30-100 Parts, +100-1000 Parts, - - -greater than 1000

3.1.4. Partition coefficient

The partition coefficient is given in table 6.

Table 6: Partition coefficient

Medium	Log P
n-Octanol:PBS pH 6.8	3.6
n-Octanol:PBS pH 7.4	3.3
n-Octanol:0.1 N HCl	3.47

3.2. Determination of λmax

The λmax was found to be 270 nm. After 3 days of storage at room temperature, the solution was again scanned and it was found to be unchanged.

3.3. Preparation of Standard Curve of Fenoprofen

The calibaration curve of fenoprofen in pbs pH 6.8 and in methanol (λ_{max}=270 nm) is depicted in fig. 1 and 2.

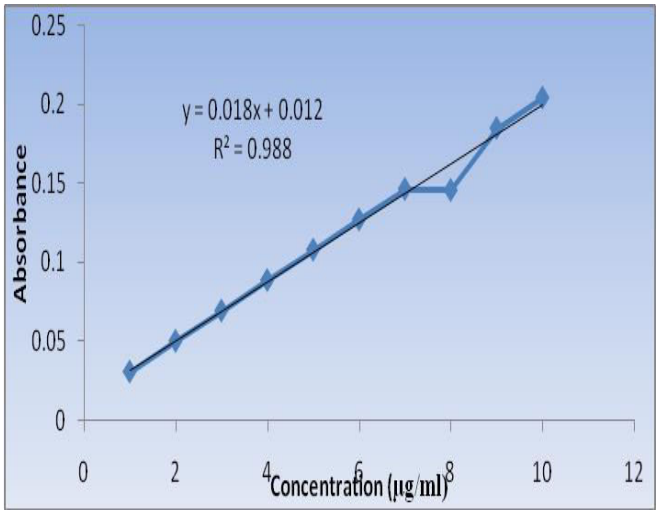

Fig. 1: Calibaration curve of fenoprofen in pbs pH 6.8 (λ_{max}=270 nm)

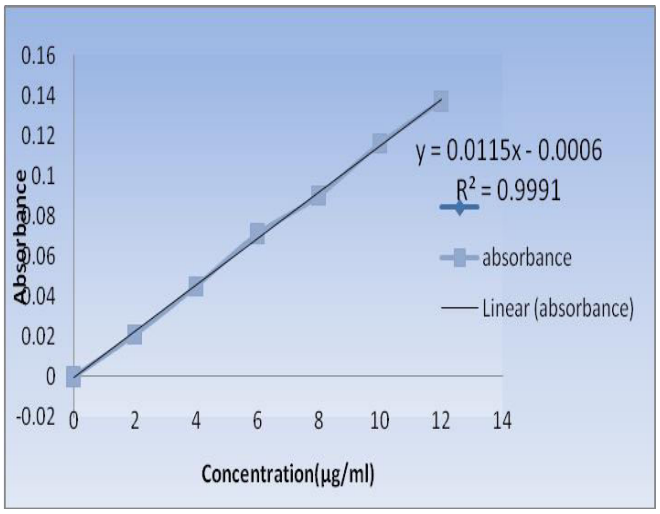

Fig. 2: Calibaration curve of fenoprofen in methanolsolution(λ_{max}=270 nm)

3.4. Inclusion efficiences

The kneaded complex (25mg) were placed in 25 ml volumetric flask, methanol (10ml) was added, mixed throughly and sonicated for 30 min. The volume was made upto the mark with methanol. The solution was suitably diluted with the same solvent and assayed spectrophotometrically for drug content at 270 nm.

3.5. Dissolution studies

Dissolution studies were performed in phosphate buffer(PH 6.8, 900 ml) at 37±0.2°C using USPXXIII apparatus (Electrolab india) with the paddle rotating at 50 rpm each containig 6.25 mg drug were subjected to dissolution time intervals samples were withdrawn, filtered (whatman filter paper no. 41) and spectrophotometrically assayed for drug content at 270 nm (table 8).

3.6. Differential Scanning Calorimetry (DSC) Study

The Differential Scanning Calorimetric study was carried out using Mettler Toledo Differential Scanning Calorimeter. Samples were placed in an aluminum crucible and the DSC thermograms were recorded at heating rate of 100°C/ min in the range 30 to 300°C.

Table 7: Inclusion efficiency of the drug and its preparation

S. No.	Type	Inclusion efficiences(%)				
1	Kneaded complex	1:2:2	1:2:3	1:3:3	1:3:4	1:3:4
		86.6±.3	91.4±.2	94.4±.3	97.5±.2	99.5±.3
2	Skimmed milk powder	1:1	1:1.5	1:2	1:2.5	1:3
3	Inclusion efficiency	89.2±0.3	93.1±0.4	95.4±0.2	98.3±0.4	99.7±0.2

Table 8:Dissolution profile of drug, physical mixture and complex n=3

S. No.	Time (min)	Cummulative % Drug release			
		Drug	Physical mixture	Complex A	Complex B
1	15	32.8±0.73	42.3±0.73	56.32±0.13	64.81±0.12
2	30	34.3±1.13	46±0.69	64.15±0.31	72.32±0.41
3	45	38.2±0.83	48±0.35	68.23±0.35	76.18±0.24
4	60	41.3±0.32	47±0.31	75.86±0.53	79.53±0.28
5	75	44.3±0.82	49±0.23	79.21±0.37	84.26±0.16
6	90	46.1±0.32	56.3±0.45	81.26	87.19±0.61
7	120	48.2±0.32	61±0.12	84.19±0.78	91.21±0.53

Fenoprofen fast dissolving tablets were prepared in seven formulations (F1 was control having nosublimating agent) by compressing powder blend using direct compression technique. The data obtained from post-compression parameters such as thickness, hardness, friability, weight variation, amount of drug content, wetting time, water absorption ratio and disintegration time are shown in table 12. Tablet hardness values lied between 3.72±0.10 to4.52±0.38 kg/cm^2 (acceptance range = 5-8 kg/cm^2) for all the formulations indicating good mechanical strength with an ability to withstand physical and mechanical stress conditions while handling. In all the formulations the friability values were less than 1% and met the Pharmacopoeial limits. The loss of percentage of weight of all the formulations in friability was 0.41±0.02 to0.68±0.01which was well below the allowed official limits. Wetting time of tablets prepared from

sublimation technique ranged from 27.31±0.58 to 96.01±1.00 seconds. Dispersion time values were found in the range from 41.23±2.08 to 111.01±2.00 seconds. Results of disintegration test lied between 111.01±2.00 to 88.04±2.00 seconds (acceptable disintegration time standards are 5 minutes).

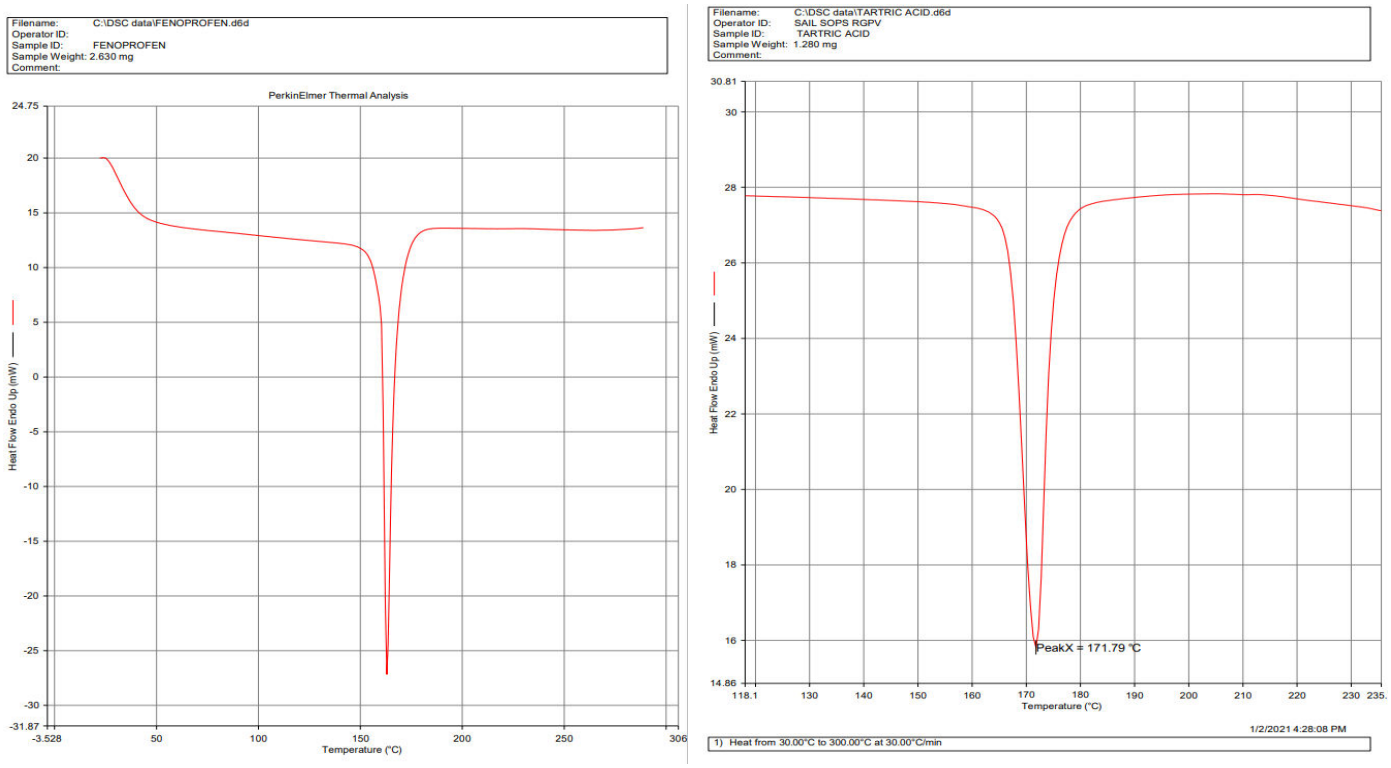

Fig. 3: DSC of pure Fenoprofen&tarteric acid

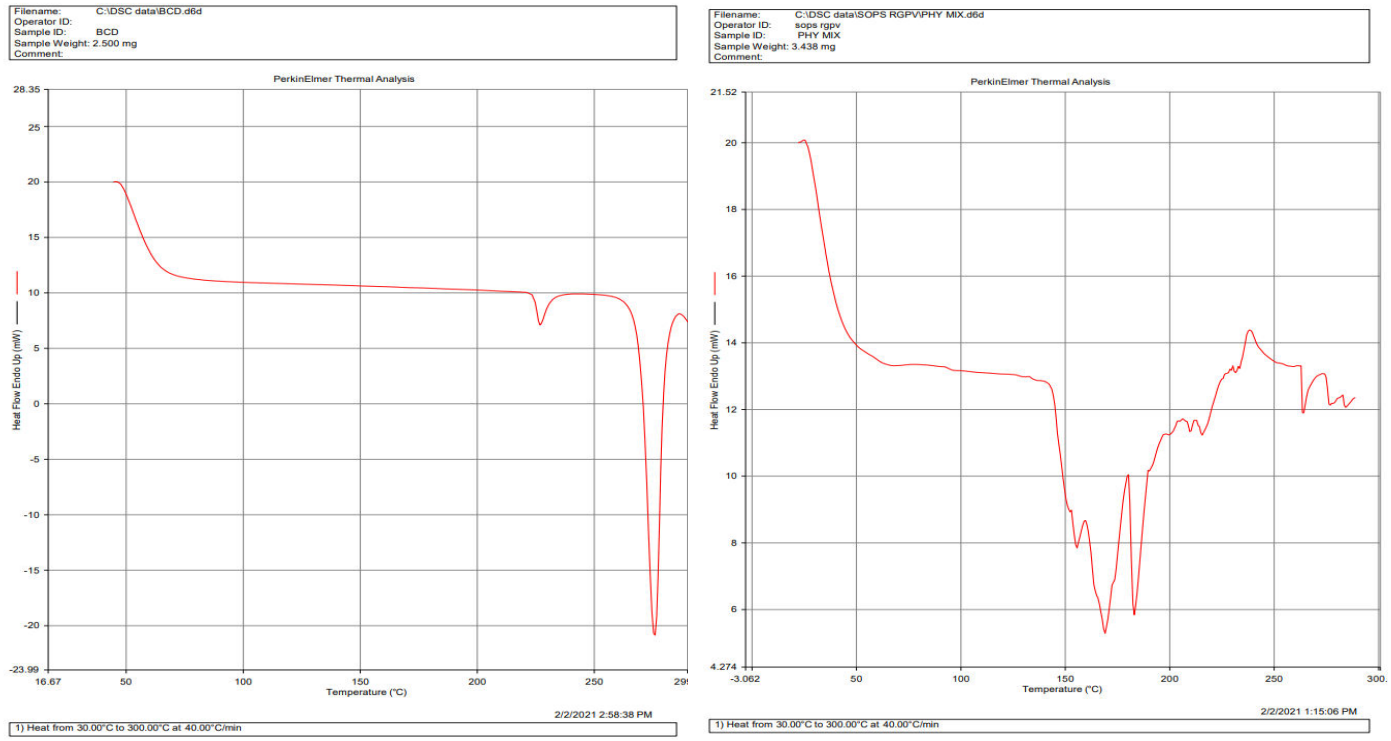

Fig. 4: DSC β-cyclodextrin&drug-β-cyclodextrin tarteric acid Physical mixture

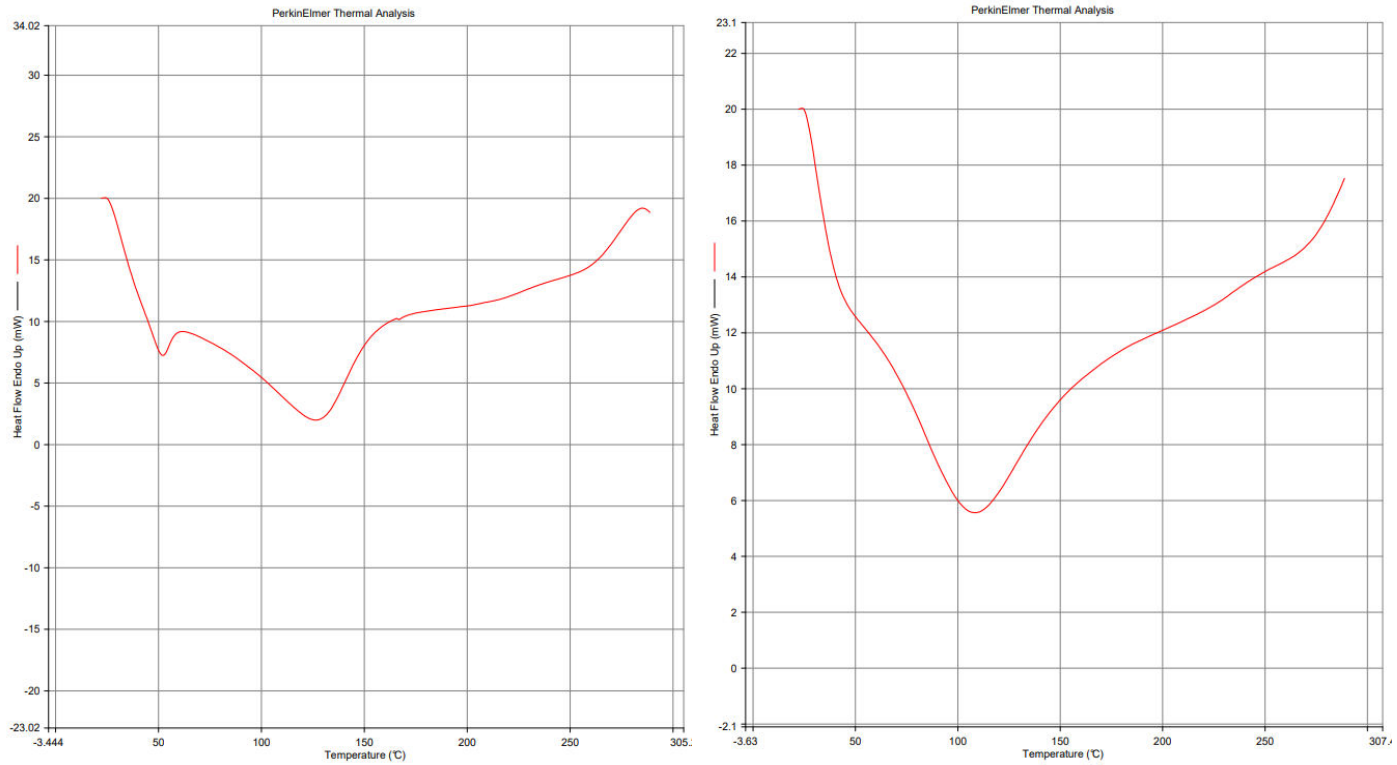

Fig. 5: DSC of Fenoprofen complex&complex A

Table 9: Pre-compression Evaluation with different concentration of sodium starch glycolate

Formulation code	Angle of repose (θ)	Bulk density (gm/cc)	Tapped density (gm/cc)	Compressibility index (%)	Hausner ratio
F1	29.74±0.15	0.5547 ± 0.0031	0.7818±0.0009	18.65±0.36	1.22±0.01
F2	26.22±0.64	0.5506±0.0014	0.6405±0.0089	14.01±1.42	1.16±0.02
F3	25.99±0.13	0.5367±0.0045	0.6317±0.0099	15.02±1.26	1.17±0.02
F4	30.64±0.53	0.5389±0.0026	0.6317±0.0074	14.68±1.11	1.17±0.02
F5	36.96±0.36	0.5352±0.0057	0.6461±0.0037	17.16±0.76	1.21±0.01

Table 10: Pre-compression Evaluation with different concentration of crosspovidone

Formulation code	Angle of repose (θ)	Bulk density (gm/cc)	Tapped density (gm/cc)	Compressibility index (%)	Hausner ratio
F6	21.40±1.62	0.5504±0.0087	0.6810±0.0009	19.18±1.34	1.24±0.02
F7	24.82±0.61	0.5274±0.0056	0.6223±0.0081	15.24±0.42	1.18±0.01
F8	27.33±0.51	0.5667±0.0041	0.6793±0.0006	16.57±0.61	1.20±0.01
F9	29.73±0.44	0.5826±0.0051	0.6527±0.0189	10.69±2.16	1.12±0.03
F10	31.94±0.89	0.5210±0.0017	0.6413±0.0004	18.76±0.23	1.23± 0.00

Table 11: Pre-compression Evaluation with different concentration of crosscarmellose

Formulation code	Angle of repose (θ)	Bulk density (gm/cc)	Tapped density (gm/cc)	Compressibility index (%)	Hausner ratio
F11	24.12±0.86	0.5507±0.0008	0.6739±0.0005	18.27±0.05	1.2236±0.0085
F12	29.06±0.58	0.5146±0.0023	0.6220±0.0012	17.26±0.50	1.2086±0.0074
F13	26.67±0.40	0.5330±0.0041	0.6587±0.0042	19.07±0.84	1.2357±0.0129
F14	24.38±0.67	0.5271±0.0019	0.6267±0.0029	15.88±0.16	1.1889±0.0022
F15	25.99±0.88	0.5617±0.0041	0.6724±0.0035	16.47±0.41	1.1972±0.0059

Table 12: Evaluation of tablet

F (Code)	Hardness (kg/cm^2)	Uniformity of weight (mg) (±SD), n= 20	Friability (%)	Wetting time (sec)	Water absorption ratio (%)	Disintegration time(sec)	Dispersion time (sec)	Drug content (%)
F1	3.72±0.10	294.41±5.82	0.41±0.02	96.01±1.00	32.30±1.01	88.04±2.00	111.01±2.00	98.73
F2	3.41±0.10	301.93±6.27	0.51±0.01	67.32±1.52	51.72±1.60	58.23±1.52	87.12±1.52	99.81
F3	3.31±0.10	301.42±5.57	0.71±0.02	47.34±1.15	75.76±1.28	45.13±1.53	74.02±2.64	99.81
F4	3.10±0.11	295.43±7.28	0.83±0.07	45.23±1.52	80.46±1.78	39.14±1.15	65.64±1.52	99.92
F5	3.02±0.11	294.34±5.06	0.85±0.03	36.43±2.08	84.74±2.97	35.47±2.51	53.32±2.08	99.63
F6	4.02±0.11	296.24±6.28	0.25±0.03	98.32±4.16	29.31±1.53	93.23±3.05	116.65±2.52	99.12
F7	3.91±0.20	301.51±6.05	0.52±0.02	69.34±1.53	48.18±1.26	61.12±2.00	91.01±2.00	98.85
F8	3.75±0.15	296.91±5.87	0.73±0.03	48.66±2.52	73.61±2.50	48.31±2.52	76.32±2.08	99.96
F9	3.86±0.31	297.92±5.29	0.46±0.08	47.34±1.52	78.01±1.00	41.08±2.00	73.66±1.52	99.94
F10	3.72±0.15	298.24±4.25	0.85± 0.02	39.68±2.51	81.92±1.79	38.07±2.51	64.02±3.61	98.66
F11	2.95±0.21	302.22±6.77	0.96±0.05	61.34±1.15	75.84±2.08	55.57±2.08	84.68±1.52	99.64
F12	3.44±0.40	301.01±6.91	0.86±0.04	50.02±2.00	96.52±2.64	47.43±2.51	71.10±2.64	97.87
F13	3.95±0.51	298.72±7.05	0.38± 0.03	39.68 ± 2.08	121.18 ± 2.49	35.10 ± 2.64	62.63 ± 0.58	98.87
F14	4.52±0.38	295.01±5.56	0.37± 0.03	38.32 ± 2.51	135.52 ± 2.07	27.57 ± 1.53	54.08 ± 1.00	96.96
F15	3.55±0.21	295.22±6.19	0.68± 0.01	27.31 ± 0.58	154.62 ± 4.47	111.01 ± 2.00	41.23 ± 2.08	99.19

Table 13: Release profle of formulations

Time (min)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15
	% release	% Release	% release	% release	% Release	% release	% release	% release	% release	% Release	% release	% release	% release	% release	% release
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1	27.331	41.886	45.731	52.160	61.327	23.221	41.231	42.951	46.682	56.291	38.9739	47.80	52.5043	54.5087	66.2913
2	32.326	47.628	48.512	53.603	63.744	31.886	44.892	46.127	52.342	61.690	47.6252	52.7556	57.6891	60.3121	68.6752
3	43.124	54.125	56.432	62.325	72.027	37.362	51.564	56.568	61.76	68.562	52.71	61.5013	62.7808	69.2382	74.3991
4	47.254	57.981	63.125	71.533	77.105	46.446	53.831	59.338	68.564	75.862	57.0969	75.4143	68.6657	76.1504	83.0317
5	54.325	72.718	74.812	77.786	83.014	51.573	66.896	68.566	72.440	83.853	56.8491	78.2295	78.8735	83.4382	88.5404
6	56.331	73.971	76.512	82.670	89.816	53.123	71.829	73.683	79.890	87.170	62.9947	82.1578	84.0177	89.7078	94.5447
7	62.104	77.326	79.136	87.729	94.079	58.738	75.192	76.364	85.875	91.716	63.36	86.5013	88.7436	95.7187	99.5643
8	64.461	78.415	80.712	92.799	96.812	62.623	77.831	78.625	88.773	95.631	70.46	87.6713	91.8992	98.8817	99.4926
9	67.124	81.412	82.557	95.264	99.577	68.879	79.807	81.568	92.280	97.705	72.01	94.5404	94.6557	99.9731	99.3916
10	72.121	86.124	87.268	97.516	99.292	73.436	82.657	85.690	95.749	98.692	76.3773	98.1804	98.9652	99.9756	99.3953
12	83.881	89.421	92.499	100.45	99.292	83.412	87.851	90.518	97.403	99.27	91.26	98.3804	98.9992	99.9794	99.3821
15	86.321	98.232	99.449	98.605	99.293	85.812	97.754	97.677	99.755	99.352	96.8947	99.4523	98.9991	99.9794	99.3726

The results of wetting time and disintegration time of all the tablets were found to be within the prescribed limits and satisfied the criteria of fast dissolving tablets. All the formulations possessed acceptable hardness, friability, wetting time and disintegration time which is an absolute requirement for any fast dissolving tablet. From the dissolution studies, cumulative percentage of drug release versus time was evaluated as presented in Fig. 5. Fig. represents the percentage release of all the formulations against time. It also reflects that the formulations F4 and F15 containing 45 mg and 67.5 mg of thymol respectively showed fast drug release of 100.00% and 99.56% respectively in 30 minutes as compared with formulations containing other sublimating agents. Among all the formulations, F6 and F7 tablets showed complete drug release within 30 minutes and rapid dissolution. The possible reasons and mechanisms for increased dissolution rates are formation of porous structure on the surface of tablet due to sublimation and the presence of super-disintegrants which enhance the water permeation (wicking action) into the tablet, which leads to a prompt wetting action, short disintegration time and finally causes the fast dissolution rate. It was observed that as

the concentration of sublimating agents was increased the drug release also increased, because as the concentration of sublimating agent increases, there will be more number of pores formed in the tablet, because of which water can enter and get absorbed in more quantity, which will lead to rapid disintegration. Drug release rates obtained for the formulations were subjected for kinetic treatment to know the order of drug release rates. Values of the drug release were attempted to fit into various mathematical models to observe the mechanism as showed in Table 13. The correlation coefficient values were obtained for all the five models.

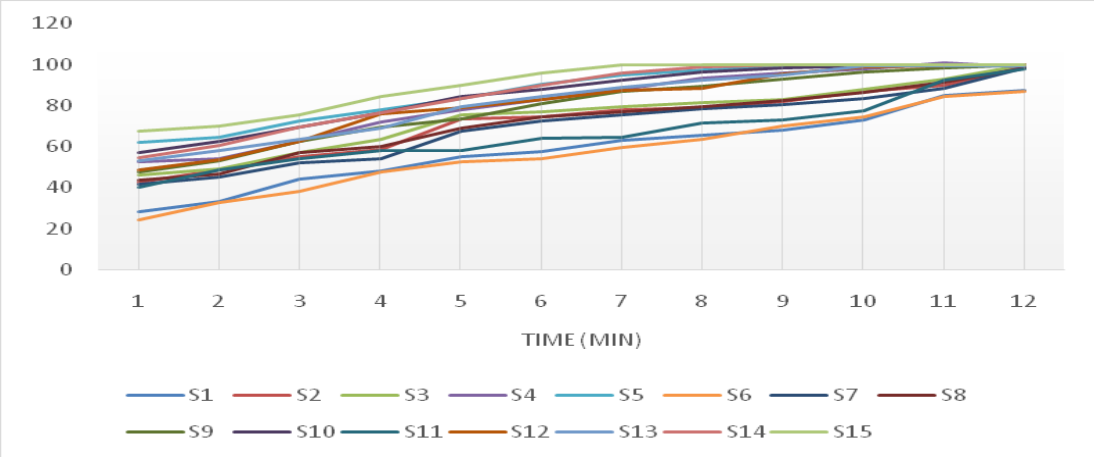

Fig. 5: Release profle of formulations

4. CONCLUSION

Among all the mouth dissolvinig antiinflammatory tablet containing fenoprofen formulations, F6 and F7 tablets showed complete drug release within 30 minutes and rapid dissolution Mouth Dissolving tablets are considered to be contemporary dosage forms. These dosage forms and their route of administration results in better efficacy, rapid onset of action, enhanced bioavailability, and improved patient compliance.

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Conflict of interest

None declared

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