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Fast Dissolving Tablets of Ibuprofen

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ABSTRACT: The present study was to enhance the solubility and dissolution rate of poorly water soluble drug, Ibuprofen by solid dispersion methods. In the present work, solid dispersion of Ibuprofen was prepared with a carriers like polyethylene glycol 6000 (PEG6000), Urea and β-cyclodextrin by using solvent evaporation and Inclusion Complex methods in the 1 : 1, 1 : 2 and 1 : 3 ratios of drug and carrier respectively. Fast onset of action is major concern in the relief of various types of pains. As the patient with severe paining conditions such as rheumatoid arthritis and osteoarthritis and also inflammations. So to overcome these problems concept of a patient-friendly tablet example fast-dissolving tablet (FDT) has emerged. FDTs are solid single unit dosage forms that are placed in the mouth allowed to disperse/dissolve in the saliva without the need of water and to provide a quick onset ofaction.

KEYWORDS: Ibuprofen,PEG6000,Urea,β-cyclodextrin, Fast dissolving tablets.

I. INTRODUCTION:

Oral mucosal drug delivery system is widely applicable as novel site for administration of drug for immediate and controlled release action by preventing first pass metabolism and enzymatic degradation due to GI microbial flora. It is subdivided into buccal and sublingual in which buccal cavity is widely applicable for drug administration through mucosa in case of sublingual route mostly useful for fastest onset of action as in the case of angina pectoris.

The buccal mucosa lines the inner cheek and buccal formulations are placed in the mouth between the upper gingival (gums) and cheek to treat local and systemic conditions. The buccal route provides one of the potential routes for typically large, hydrophilic and unstable proteins, oligo nucleotides and polysaccharides, as well as conventional small drug molecules. The oral cavity has been used as a site for local and systemic drug delivery.

Dysphagia or difficulty in swallowing is common among all age groups. Dysphagia is common in about 35% of the general population, as well as additional 30-40% of elderly institutionalized patients and 18-22% of all persons in long term care facilities. This disorder is also associated with a number of pathological conditions including stroke, Parkinson's disease, neurological disorders, AIDS etc.

Parkinsonism, motion sickness, unconsciousness, elderly patients, children, mentally disabled persons,unavailability of water. Common complaints about the difficulty in swallowing tablets in the order of frequency of complaints are size, surface, form and taste of tablets.

The tablets is the most widely used dosage form existing today because of its convenience in terms of self administration, compactness and ease in manufacture. However, geriatric, pediatric and mentally ill patients experiences difficulty in swallowing conventional tablets, which leads to poor patient compliance. To overcome these problems, scientists have developed innovative drug delivery system known as mouth dissolving / disintegrating tablets (MDTs) rapimelts are also called as orodispersible tablets, quick disintegrating tablets, mouth dissolving tablets, fast disintegrating tablets, fast dissolving tablets, rapid dissolving tablets, porous tablets, and orally disintegrating tablets. However, of all the above terms, United States Pharmacopoeia (USP) approved these dosage forms as rapimelts. Recently, European Pharmacopoeia has used the terms orodispersible tablet for tablets that disperses readily and within 3 minutes in mouth before swallowing. Fast dissolving tablets are those when put on tongue

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disintegrate instantaneously releasing the drug which dissolve or disperses in thesaliva.

Some drugs are absorbed from the mouth, pharynx and oesophagus as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greaterthan those observed from conventional tablets dosage form. Their growing importance was underlined recently when European pharmacopoeia adopted the term "orodispersibles tablet" as a tablet that to be placed in the mouth where it disperses rapidly before swallowing. The bioavailability of some drugs maybe 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.

Ibuprofen was the first member of Propionic acid derivatives to be introduced in 1969 as a better alternative to Aspirin. Gastric discomfort, nausea and vomiting, though less than aspirin or Indomethacin, are still the most common side effects. Ibuprofen is the most commonly used and most frequently prescribed NSAID. It is a non-selective inhibitor of cyclo-oxygenase-1 (COX-1) and Cyclooxygenase-2 (COX-2). Although, its anti inflammatory properties may be Weaker than those of some other NSAIDs, it has a prominent analgesic and antipyretic role. Its effects are due to the inhibitory actions on cyclo-oxygenases, which are involved in the synthesis of prostaglandins. Prostaglandins have an important role in the production of pain, inflammation and fever.

II. MATERIALS AND METHOD

Ibuprofen, β-Cyclodextrin, Urea, Micro CrystallineCellulose, Cros Povidone, Cros CarmelloseSodium, Talc, Magnesiumstearate, Sucrose, Lactose all materials and chemical are purchased from pharmafabricon Madurai.

METHODS

Solid dispersion of ibuprofen

Ibuprofen is a Non-Steroidal Anti-inflammatory Drug. One of the major problems with this drug is its practically insoluble in water. In the present work undertaken was to enhance the solubility and dissolution rate of Ibuprofen by solid dispersion technique using water soluble carriers like PEG, Urea and β-cyclodextrin. The prepared solid dispersions were evaluated for drug content, In vitro dissolution rate studies, solubility studies and interactions between drug and carriers.

METHOD OF PREPARATION I:

Preparation of Inclusion Complex using β - Cyclodextrin:

One gram of β - Cyclodextrin is dissolved in 100ml of boiling water. Add one gram of Ibuprofen in boiled water (while hot). It is cooled and then solution is formed within 30 minutes. The solution is filtered; the Ibuprofen and β - Cyclodextrin inclusion complex was obtained as residue. It is dried to mass and then passed through the sieve no:40.

METHOD OF PREPARATION II:

Solvent Evaporation method using Urea as carrier:

Ibuprofen and Urea as per the ratio of 1:1, 1:2 and 1:3 weredissolved in a minimum amount of methanol and Chloroform. [Solvents such as chloroform and methanol are used in the ratio (1:1)].The solvent was removed by evaporation on magnetic stirrer at the temperature 40°C for 1hr. The resulting residue was dried for 2 hour and stored overnight in desiccators. After drying, the residue was ground in a mortar and sieved through a mesh # 60. The resultant solid dispersions were stored in desiccators until further investigation.

Parameters	Ibuprofen : Urea (Solvent Evaporation)			Ibuprofen : β-Cyclodextrin (Inclusion Complex)		
	1 :1	1 :2	1 :3	1 :1	1 :2	1 :3
Percentage Yield	60%	58%	94.35%	44.50%	36.60%	29.50%
Percentage Drug Content	95.12%	95.93%	97.50%	72.36%	78.46%	88%
Percentage Drug Release	76.09%	82.73%	94.52%	71.51%	76.68%	84.40%

International Journal of Pharmaceutical Research and Applications
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From the above table, by considering the parameters such as Percentage Yield, Percentage Drug content and Percentage Drug release, it is concluded that the solid dispersion by solvent evaporation of Ibuprofen and Urea is the suitable method for Formulation of Fast Dissolving Tablets ofIbuprofen and the best ratio of Ibuprofen and Urea was found to be **1:3** The ratio (1:3) will be taken forthe furtherFormulation of Fast Dissolving Tablets of Ibuprofen.

Preparation of fast dissolving tablet by direct compression method:

In general direct compression method involves the direct compaction of tabletting mixture without the step of granulation, provided the tabletting mixture should have enough flow properties and should form a robust tablet. For suppose, if the tabletting mixture is not having good flow properties, we can either use direct compression vehicles (DCV) for improving the flow and compatibility of tabletting mixture or by subjecting the mixture for granulation process (wet or dry granulation).

Evaluation of fast dissolving tablets:

Preparation of calibration curve:

A known weight (100mg) of drug (Ibuprofen) is dissolved and diluted to 100ml using Phosphate buffer solution (pH7.4) to form a primary stock solution (1000µg/ml). The stock solution is further diluted using Phosphate buffer solution (pH7.4) to 10µg/ml concentration. The resultant solution is scanned in the range of (222nm) by ultra visible spectrophotometer to get absorption maximum (λ max). From the above prepared stock solution, different concentration (1 to 10µg/ml) solutions are prepared using Phosphate buffer solution (pH7.4). The absorbances of these solutions are measured at λ max (222nm) by UV-spectrophotometer. A standard curve is plotted using concentration on X-axis and the absorbance obtained onY-axis.

Post compressional evaluation of fast dissolving tablets:

1) Generalappearance:

Five tablets from different batches are randomly selected and organoleptic properties such as colour, odour, taste, shape are evaluated.

2) Thickness and diameter:

Thickness of tablet is determined using vernier caliper. Five tablets from each batch are used and an average value is calculated.

3) Hardness

The tablet hardness, which is the force required to break a tablet in a diametric compression force. The hardness tester used in the study is Monsanto hardness tester, which applies force to the tablet diametrically with the help of an inbuilt spring and expressed in kg/cm^2.

4) Weightvariation

Weight variation test is done with 20 tablets. It is the individual variation of tablet weight from the average weight of 20 tablets.

Average weight of tablet (mg)	%Deviation
80mg or less	± 10
More than 80 mg but less than 250	± 7.5
250 mg or more	± 5

5) Friability Test

The friability of tablets is measured using Roche friabilator. Tablets are rotated at 25 rpm for 4 minutes or upto 100 revolutions. The tablets are then reweighed after removal of fines and the percentage of weight loss iscalculated.

$$\%friability = \frac{(Initial\ weight - final\ weight)}{Initial\ weight} \times 100$$

6) Drugcontent

The tablet is randomly selected from each batch, weighed individually and powdered. The powder equivalent to 10mg of Ibuprofen are weighed and dissolved in 100 ml of Phosphate buffer solution (pH 7.4) to obtain the stock solution. From the stock solution suitable dilution are prepared and analyzed using UV-spectrophotometer at 222nm.

7) Disintegration test

International Journal of Pharmaceutical Research and Applications
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Disintegration is defined as "state in which no residue of the tablet or capsule remains on the screen of the apparatus". The in vitro disintegration time is determined using disintegration test apparatus. A tablet is placed in each of six tubes in the apparatus and a disc is added to each tube. Suspend the basket rack in the beaker containing 900 ml of distilled water at 37^0 C and move the basket containing tablets up and down through a distance of 5-6 cm at a frequency of 28-32 cycles per minute. The time in seconds taken for complete disintegration of the tablet with no discernible mass remaining in the apparatus aremeasured.
Uncoated tablets: 5- 30 minutes Coated tablets: 1-2 hours
Fast Dissolving tablets: less than 3 minutes (European Pharmacopoeia)

8) In-vitro dissolutiontest

The release rate of Ibuprofen from fast dissolving tablets is determined using USP dissolution test apparatus II (paddle type). The dissolution test is performed using 900ml of Phosphate buffer (pH 7.4) at 37 ± 0.5^0c and rotation speed of 50 rpm. A sample of 5ml solution is withdrawn from the dissolution apparatus every 5 minutes for 30 minutes with fresh dissolution medium. Absorbances of these solutions are measured at 222 nm using UV spectrophotometer. Cumulative percentage drug release is calculated using an equation obtained from a standardcurve.

III. RESULTS AND DISCUSSION:

TABLE: I CALIBRATION OF IBUPROFEN

S. No	Concentration(µg/ml)	Absorbance
1.	5	0.230
2.	10	0.492
3.	15	0.735
4.	20	0.978
5.	25	1.231

Regression value=0.99991

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Volume 6, Issue 4 July-Aug 2021, pp: 785-794 www.ijprajournal.com ISSN: 2249-7781

TABLE II: FORMULATION OF FAST DISSOLVING TABLET OF IBUPROFEN

INGREDIENTS	F1	F2	F3	F4	F5	F6
Solid Dispersion Equivalent To Ibuprofen	400mg	400mg	400mg	400mg	400mg	400mg
Microcrystalline Cellulose	90mg	90mg	90mg	90mg	90mg	90mg
Cros Povidone	18mg	24mg	30mg	-	-	-
Cros Carmellose Sodium	-	-	-	18mg	24mg	30mg
Talc	12mg	12mg	12mg	12mg	12mg	12mg
Magnesium Stearate	12mg	12mg	12mg	12mg	12mg	12mg
Sucrose	6mg	6mg	6mg	6mg	6mg	6mg
Lactose	62mg	56mg	50mg	62mg	56mg	50mg

F1 (3%), F2 (4%), F3 (5%) – Cros Povidone
F4 (3%), F5 (4%), F6 (5%) – Cros Carmellose sodium

TABLE III PREFORMULATION STUDY OF FAST DISSOLVING TABLETS OF IBUPROFEN

PARAMETERS	F1	F2	F3	F4	F5	F6
Bulk density(g/cm^3)	0.434	0.441	0.405	0.491	0.576	0.428
Tapped density(g/cm^3)	0.537	0.545	0.517	0.628	0.714	0.517
%Compressibility or Carr's index	19.18%	19.08%	17.2%	21.44%	19.32%	17.2%

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 785-794 www.ijprajournal.com ISSN: 2249-7781

Hausner's ratio	1.23	1.23	1.2	1.4	1.2	1.2
Angle of Repose(^{0})	30.71	32.07	32.08	29.02	29.95	25.25

F1(3%), F2(4%), F3(5%) – Cros Povidone
F4(3%) , F5(4%), F6(5%) – Cros Carmellose sodium

TABLE: IV
EVALUATION OF FAST DISSSOLVING TABLETS OF IBUPROFEN

PARAMETERS	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
Thickness	4.08mm	4.08mm	4.08mm	4.2mm	4.04mm	4.18mm
Diameter	12.1mm	12.06mm	12.1mm	12.06mm	12.04mm	12.14mm
Hardness	3.44kg/cm^2	3.7 kg/cm^2	3.9 kg/cm^2	3.8 kg/cm^2	4 kg/cm^2	3.9 kg/cm^2
Disintegration time	123sec	73sec	46sec	65sec	50sec	32sec
Dissolution	78.35%	85.71%	92.28%	87.95%	93.09%	96.67%
Percentage Drug content	95.93%	94.51%	95.35%	97.35%	96.74%	96.95%

F1(3%), F2(4%), F3(5%) – Cros Povidone
F4(3%) , F5(4%), F6(5%) – Cros Carmellose sodium

TABLE: V
PERCENTAGE DRUG RELEASE FROM DIFFERENT FORMLATIONS

Time(min)	**PERCENTAGE DRUGRELEASE**					
	F1	**F2**	**F3**	**F4**	**F5**	**F6**
0	0	0	0	0	0	0
5	51.95%	50.14%	55.39%	52.31%	78.71%	68.94%
10	55.59%	56.30%	60.88%	57.41%	79.16%	73.87%
15	63.80%	59.63%	79.46%	63.07%	85.17%	83.55%
20	69.56%	68.59%	80.18%	69.75%	88.26%	91.33%
25	74.84%	75.85%	85.57%	74.85%	91.74%	93.22%

International Journal of Pharmaceutical Research and Applications
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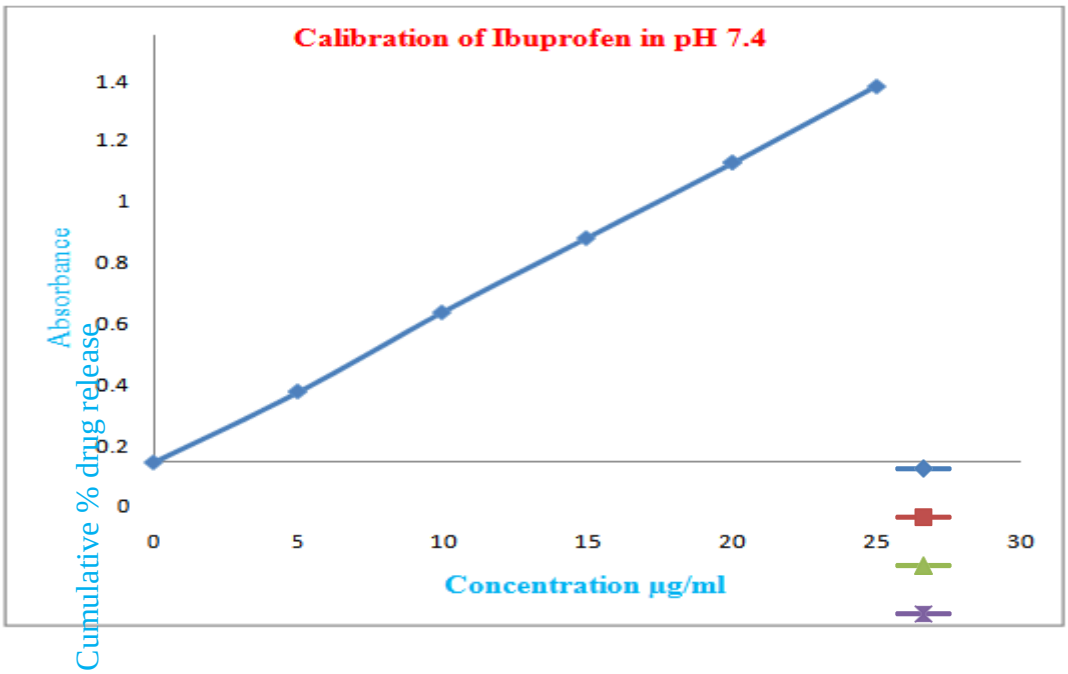
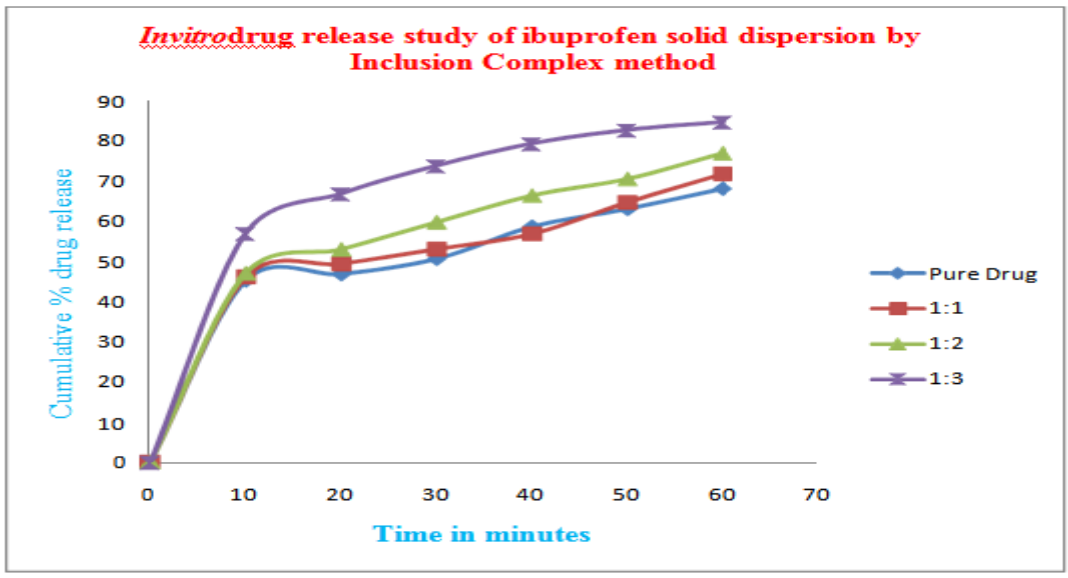
30	78.35%	85.71%	92.28%	87.95%	93.09%	96.67%

F1(3%), F2(4%), F3(5%) – Cros Povidone
F4(3%) , F5(4%), F6(5%) – Cros Carmellose sodium

GRAPH : I



GRAPH : II



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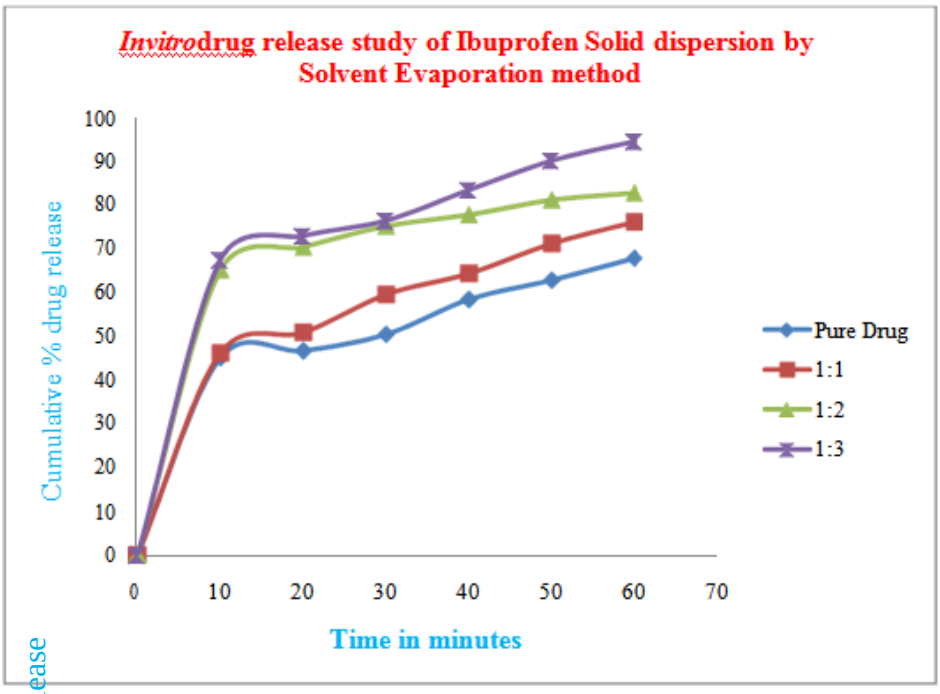
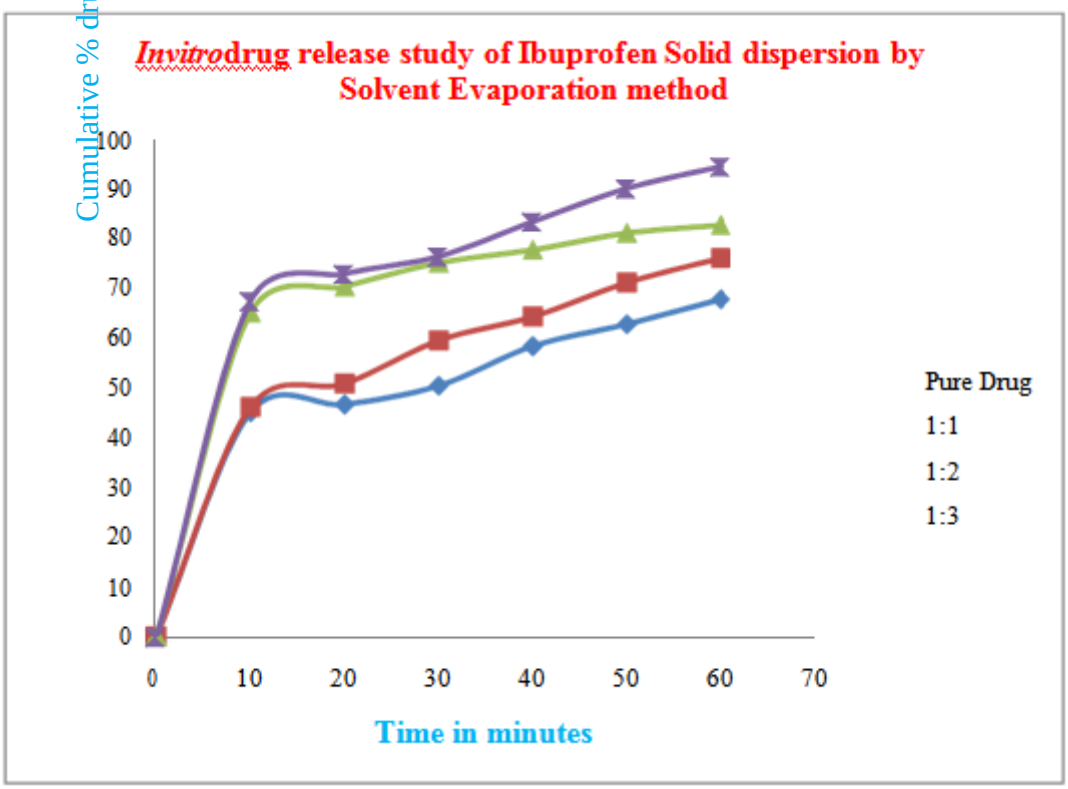


GRAPH : III



GRAPH : IV

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IV. CONCLUSION:

In the present study, the fast dissolving tablets of Ibuprofen, a Non-steroidal Anti-Inflammatory Drug (NSAID) was formulated with an objective to improve patient compliance and achieve rapid onset of action. In all the Six formulations [F_1 to F_6], the super disintegrants [Cros Carmellose sodium and Cros Povidone] were used at differentConcentrations.

Among all Formulations, the formulation F_6 containing 5% of Cros Carmellose sodium has shown the better results with Disintegration time of 32 seconds and 96.95% of Drug release in the Invitro Dissolution study at the end of 30 minutes. When compared to marketed formulation which has Disintegration time of 53 seconds and drug release of 67.82% within 30minutes.

Hence, F_6 may be considered for further development.

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