Innovare Academic Sciences

International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 7, Issue 2, 2015

Original Article

FORMULATION AND OPTIMIZATION OF ORODISPERSIBLE TABLETS OF IBUPROFEN

RANJIT PRASAD SWAIN[1]*, P. SATISH[1], B. B. SUBUDHI[2], SATYAJIT PANDA[1]

[1]Department of Pharmaceutical Technology, Maharajah`s College of Pharmacy, Vizianagaram-535002, A. P, [2]School of Pharmaceutical Sciences, S'O'A University, Bhubaneswar, Odisha.
Email: ranjit.prasad797@gmail.com

Received: 01 Dec 2014 Revised and Accepted: 20 Jan 2015

ABSTRACT

Objective: The present study aimed to formulate, develop and optimize orodispersible tablets of ibuprofen.

Methods: Orodispersible tablets were prepared by direct compression technique using crospovidone, sodium starch glycolate, croscaramelose sodium, sodium carboxy methylcellulose as superdisintegrants at concentrations of 5, 7.5 and 10% w/w and mannitol used as diluent. The prepared powder mixtures are subjected to pre compression parameters including FTIR spectroscopy, DSC and micromeritics. The formulations were evaluated for tablet weight variation, hardness, friability, wetting time, absorption ratio, drug content, *in vitro* dispersion time, *in vitro* disintegration time and *in vitro* drug release studies.

Results: The results of micromeritics studies revealed that all formulations were of acceptable to good flowability. Crospovidone at 10% w/w concentration (F_3) showed the least *in vitro* disintegration time 38 seconds with acceptable hardness 3.93 kg/cm^3, friability 0.652% and good dissolution profile (D_5 min = 95.89%) in comparison with control (D_5 min = 18.29%). The optimized formulation showed $t_{90\%}$ drug release at 2.6 minutes. The FTIR and DSC studies were done for the optimized formula and showed no interaction between the drug and excipients.

Conclusion: It is concluded that crospovidone gives the best results at 10% w/w (F_3) for formulation of orodispersible tablets of ibuprofen with better pharmaceutical properties.

Keywords: Orodispersible, Ibuprofen, Superdisintegrant, Crosspovidone, Direct compression

INTRODUCTION

In recent years, in accordance with lifestyle changes, a demand has arisen for the development of dosage forms that can be readily handled and chosen by many patients [1]. Recent developments in technology have presented viable dosage alternatives for pediatrics, geriatrics, bedridden, nauseous or non-compliant patients, who face difficulty in swallowing or chewing solid dosage forms and are unwilling to take solid preparations due to a fear of choking. Hence, orodispersible tablets (ODTs) are a perfect fit for them [2]. ODTs are solid single-unit dosage forms that are placed in the mouth, allowed to disperse/dissolve in the saliva and then swallowed without the need for water [3].

We often experience inconvenience in swallowing conventional tablets when water is not available [4]. It is interesting that European Pharmacopoeia describes an ODT as a tablet that disperses readily and within 3 minutes before swallowing while according to the FDA. ODTs should have an *in vitro* disintegration time (DT) of 30 seconds or less [5]. 'Orodispersible tablet" appears in the European Pharmacopoeia defined as ''uncovered tablet for buccal cavity, where it disperses before ingestion". United States Food and Drug Administration (USFDA) defined ODT as "A solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue." The disintegration time for ODTs generally ranges from several seconds to about minutes [6]. ODTs have better patient acceptance, compliance, offer improved biopharmaceutical properties, efficacy, and increased bioavailability compared with conventional oral dosage. Lyophilizing, molding and compression methods require particular machines and are times consuming techniques. The hardness of the products was not enough to stand the process of packaging and transportation. Therefore, direct compression is the simplest, most convenient and easiest way to produce rapidly disintegrating tablets with sufficient structural integrity [7]. Super disintegrants should not only produce stronger tablets but also, disintegrate the tablet in the oral cavity in less than 30 seconds [8]. Lyophilized tablets show a very porous structure, drinking water which causes quick penetration of saliva into the poresal. Moulded tablets reveal rapid settling of the particles and moreover provide a pleasant disintegration and weak mechanical strength as well, yet mouth feeling [9]. To date, many technologies have been developed for preparing ODTs and the products of these technologies have been commercialized. Zydis® is a well-known technology that involves freeze-drying of suspensions or solutions containing active ingredients and water soluble polymer into pockets of blister packaging sheets. While tablets prepared using the Zydis® technology dissolve rapidly on the tongue, they tend to be very brittle and require careful handling [10]. The ODT system has advantages of solid dosage forms, such as good stability, accurate dosing, small packaging size, easy handling, easy administration and minimal risk of suffocation [11].

Therefore, it is beneficial for children, elderly, and schizophrenic patients who have difficulty in swallowing conventional solid dosage forms. It has been extending to more general patients requiring daily medication regimens [12]. Recently, many companies have researched and developed various types of orodispersible dosage forms. Cardinal Health was the first company to develop and market an orodispersible, freeze-dried porous wafer known as CIMA marketed an effervescent tablet known as Orasolv. Eisai and Ethypharm developed the EMP tablet and Flashtab respectively [13-14]. ODTs are more widely available as over the counter products for the management of many conditions such as allergies, cold and flu symptoms. To overcome the problems associated with conventional dosage forms, ODTs have been developed [15]. Clinically, non-steroidal anti-inflammatory drugs (NSAIDS) are the most frequently prescribed by physicians for pain and inflammatory disorders. Ibuprofen (BCS class II) 2-[4-(2-methylpropyl) phenyl propionic acid (fig. 1) a non-steroidal anti-inflammatory [16] drug which inhibits prostaglandin biosynthesis by blocking the enzyme cyclooxygenase, which converts arachidonic acid to prostaglandin. It is widely used in the treatment of mild to moderate pain and fever. Ibuprofen has less bioavailibilty compared to other conventional dosage forms, choosen as a model drug for this study [17]. Orodispersible tablet of ibuprofen with good bioavilibility was not avilable in the market, so our approach is to prepare orodispersible tablet of ibuprofen with different synthetic super disintegrants, which can give better bioavilibility, stability with sufficient mechanical strength.

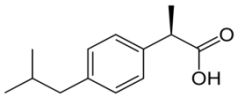

Fig. 1: Structure of ibuprofen

The aim of the study was to develop formulations of ibuprofen dispersible tablets. All the formulations should offer an acceptable disintegration time less than 3 minutes and at the same time and finally to increase dissolution rate, possess sufficient mechanical strength so that they will withstand the course of manufacturer and subsequent packaging. On the basis of these considerations, in the present study it was proposed to formulate an oral delivery system, in the form of an ODT of ibuprofen using four super disintegrating agents i. e., crospovidone, croscaramellose sodium, sodium carboxy methyl cellulose, sodium starch glycolate. The developed formulations aimed also to improve its palatability by a close association with a raspberry (flavoring agent) & the presence of sweet taste additive as aspartame.

MATERIALS AND METHODS

Materials

All materials used in this present research were commercial samples. Ibuprofen (Yarrow chem. Products, Mumbai), Mannitol (Yarrow chem. Products, Mumbai), Crospovidone (Yarrow chem. Products, Mumbai), Croscaramellose sodium (Yarrow chem. Products, Mumbai, India), Sodium carboxy methyl cellulose (Moly chem. Pvt. Ltd., Mumbai), Sodium starch glycolate (Yarrow chem. Products, Mumbai), Aspartame (Yarrow chem. Products, Mumbai), Rasp Berry (Virgina Dare, Broklyn, NY 11232), Magnesium Stearate (Yarrow chem. Products, Mumbai), Talc (Arrow chem. Products, Mumbai). All other chemicals were of analytical reagent grades.

Methods

Preparation of tablets

ODTs of ibuprofen were prepared by direct compression method using superdisintegrants according to the formulae given in table 1. ibuprofen 300 mg tablets containing 200 mg of drug were prepared. In all formulations mannitol used as a diluents. The specified quantity of ibuprofen and other excipients were accurately weighed and passed through 40# mesh screen prior to mixing. All the materials were transferred to mortar in a geometrical order and co-grounded for 15 minutes. Later by adding magnesium stearate and talc in required quantities the resulting powder mixture was compressed into tablets by using Rimek tabletting machine MINI PRESS 1(Karnavathi engineering Pvt. Ltd., Gujarat, India) using 10 mm flat surface punches. The compression force was adjusted to give tablet hardness in the pharmacopoeia range of ODTs (2-4 kg/cm^3).

Pre-compression evaluation

Fourier transform infrared spectroscopy (FTIR) study

IR study of pure drug ibuprofen and physical mixtures were performed to find out any possible drug-excipient interaction by KBr pellet method using (IR prestige 21 Shimadzu Corporation, Japan) spectrophotometer.

Differential scanning calorimeter (DSC) study

DSC thermogram of pure drug ibuprofen, crospovidone and different physical mixtures were (approximately 5 mg) scanned by using automatic thermal analyzer (Perkin Elmer, Pyris Diamond, Singapore).

Micromeretics study

Angle of repose (θ°)

The angle of repose of powder blends were determined by the funnel method. Accurately weighed powder blends were taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of the heap of the powder blends (2 cm). The powder blends were allowed to flow through the funnel freely onto its surface. The diameter of the powder cone was measured and angle of repose was calculated. [Cooper and Gunn, 1986]. Three determinations were performed.

$$\tan \theta = h/r \quad \ldots\ldots\ldots\ldots 1$$

$$\theta = \tan^{-1} h/r \quad \ldots\ldots\ldots\ldots 2$$

Where h is the height of pile; r is the radius of the base of the pile; θ is the angle of repose.

Table 1: Composition of different batches of orodispersible tablets of ibuprofen

Ingredients (mg/tablet)	Formulation Code												
	Control	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9	F_{10}	F_{11}	F_{12}
Ibuprofen	200	200	200	200	200	200	200	200	200	200	200	200	200
Mannitol	88	73	65.5	58	73	65.5	58	73	65.5	58	73	65.5	58
Crospovidone		15	22.5	30									
Crosscaramelose sodium					15	22.5	30						
Sodium carboxy methyl cellulose								15	22.5	30			
Sodium starch glycolate											15	22.5	30
Aspartame	4	4	4	4	4	4	4	4	4	4	4	4	4
Rasp Berry	2	2	2	2	2	2	2	2	2	2	2	2	2
Magnesium stearate	4	4	4	4	4	4	4	4	4	4	4	4	4
Talc	2	2	2	2	2	2	2	2	2	2	2	2	2
Total weight	300	300	300	300	300	300	300	300	300	300	300	300	300

Tablets are prepared in batch of 50.

Bulk density and tapped density

An accurately weighed quantity of the tablet (W), was carefully poured into the graduated cylinder and the volume (V_0) was measured. Then the graduated cylinder was closed with lid, set into the density determination apparatus (bulk density) apparatus. The density apparatus was set for 100 taps and after that, the volume (v_f) was measured and continued operation till the two consecutive readings were equal. The bulk density was calculated using the formulae.

$$\text{Bulk density } (\rho) = \frac{\text{Mass of a powder (w)}}{\text{Bulk volume(Vh)}} \ldots\ldots\ldots 3$$

$$\text{Tapped density } (\rho) = \frac{\text{Mass of a powder (w)}}{\text{Tapped volume(Vf)}} \ldots\ldots\ldots 4$$

Determinations were carried out in 3 replicates. The mean value of three determinations is considered.

Compressibility index and Hausner ratio

Carr's compressibility index or Carr's index (CI) determined the compressibility index of the powder blends. Hausner ratio (HR) was also determined for each powder blend. Three determinations were done for each formula.

$$\text{Consolidation index} = \frac{\text{Tapped density} - \text{Fluff density}}{\text{Tapped density}} \times 100 \ldots\ldots\ldots 5$$

$$\text{Hausner ratio} = \frac{\text{Tapped density}}{\text{Bulk density}} \ldots\ldots\ldots 6$$

Post-compression evaluation

Weight variation

Tablet designed to contain a specific amount of drug in a specific amount of tablet formula. The weight of the tablet was made is routinely measured to help ensure that a tablet contains the proper amount of drug. Randomly select ten tablets from each formulated batch and individually weighed. The average weight of the selected tablets was calculated by using an electronic balance (INFRA instruments Pvt., Ltd). table 2 represents the weight variation specifications as per the U. S. P. The tablets meets the USP test if no more than 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit.

Table 2: Weight variations specifications as per USP

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

Hardness

The hardness of the tablet indicates of its tensile strength and is measured in terms of load/pressure require to crush it when placed on its edge. The hardness has influence on disintegration and dissolution times and is such as a factor that may affect bioavailabilities. Monsanto hardness tester is used for measured the hardness of the formulated tablets. It is expressed in kg/cm^3.

Friability

Friability refers to loss in weight of tablets in the containers due to removal of fine particles from their surfaces. Friability generally reflects poor cohesion of tablet ingredients. Standard devices have been fabricated to measure friability such instruments, marketed as friability test apparatus' or 'friabilator'. The friability (F) of sample of 10 tablets measured using Roche friabillator (25 rpm for 4 minutes). Tablets were re-weighed after removal of fines (de-dusted) and the percentage of weight loss were calculated. It is expressed in (%). Friability below 1% is acceptable.

$$\%F = [(W_1 - W_2)/W_1] \times 1007$$

Wetting time and water absorption ratio

The wetting time of tablets can be measure using a simple procedure. A filter paper of 10 cm diameter was placed in a Petri dish with a 10 cm diameter. One milliliter of water containing amaranth, a water-soluble dye, was added to petri dish. A tablet was carefully placed on the surface of the filter paper. The time required for water to reach the upper surface of the tablet was noted as wetting time. Water absorption ratio is determined by difference between weight of the tablet before absorption and weight of the tablet after absorption.

$$R = \{(W_a - W_b) - W_b\} \times 100\ 8$$

Drug content

Drug content was measured by taking randomly 2 tablets per batch. An amount equivalent to 10 mg ibuprofen was dissolved in methanol, suitably diluted with 7.2-pH phosphate buffer and filtered. The absorbance of the solutions were measured spectro photometrically against the blank 7.2 pH phosphate buffer at 222 nm using U. V spectrophotometer (Cary 60) Agilent technologies, Malaysia.

Stability study

Storing tablets at 40 °C± 2 °C and 75± 5% relative humidity conducted stability study for six months. The drug content and dissolution behaviors from ODTs were tested in three-month intervals.

Each tablet was individually wrapped in an aluminum foil and packed in PVC bottle and put at above specified conditions in a heating humidity chamber (40 ° C± 2 °C and 75± 5% relative humidity) for six months. After three months intervals tablet sample was analysed for drug content and dissolution. The results are shown in Table 4.

***In-vitro* dispersion time**

Two tablets were placed in a 100 ml beaker containing phosphate buffer solution pH 7.2 at 37 °C. Time required to complete dispersion of tablet was observed.

***In-vitro* disintegration time**

The process of breakdown of a tablet into smaller particles is known as disintegration. It is used by using disintegration apparatus. Place one tablet in each 6 tubes of the basket. Add a disc to each tube and run the apparatus using 7.2 pH phosphate buffer maintained at 37 °C as the immersion liquid. The assembly should raise and lowered between 30 cycles per minute in the 7.2 pH phosphate buffer. The time in seconds taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured and recorded. It must be disintegrated within 3 minutes.

***In-vitro* dissolution studies**

In-vitro dissolution studies of the tablets was carried out in USP XXIII dissolution apparatus type II (Electro Lab, Mumbai, India) employing a paddle stirrer at 50 rpm using 900 ml of pH 7.2 phosphate buffer at 37 ± 0.5 °C as a dissolution medium. One tablet was used in each test. Aliquots of 5 ml each were withdrawn at specified time intervals (1, 3, 5, 10, 15, 30, 45 and 60 minutes.) and replaced with equal volume of fresh medium. The withdrawn aliquots were analyzed for drug content spectrophotometrically at λ_{max} 222 nm. Drug concentration was calculated and expressed as cumulative percent of the drug released. Results are of three determinants.

RESULTS AND DISCUSSION

Ibuprofen orodispersible tablets were prepared by direct compression method being the most simplest and economic technique. Mannitol was used as diluent to impart multidimensional benefits such as good aqueous solubility and good wetting properties that facilitating tablet breakdown as well as negative heats of solution. Crospovidone, croscaramellose sodium, carboxy methylcellulose, sodium starch glycolate used as super disintegrants leading to rapid breakdown and fast drug dissolution. The slight bitter taste was masked by sweetening agent aspartame. To improve patient compliance (palatability) of the drug raspberry was added in the formulation as flavoring agent.

Pre-compreesion evaluation

Fourier transform infrared spectroscopy

The FTIR anlysis of the pure drug ibuprofen and physical mixtur of optimised formulation (F_3) shown in the fig. 2, fig. 3. The spectrum of ibuprofen showed an intense, well defined infrared band at around 1718.58 cm^{-1} (carbonyl stretching of iso propionic acid group) and other spectrum at around 2954.95 cm^{-1} and 1066 cm^{-1}corresponding to the functional groups CH and NH blending respectively. The physical mixture of drug and excipients showed an intense band at 2954.95 cm^{-1}, 1720.50 cm^{-1} and 1076.38 cm^{-1}indicates no change in the functional groups. From the above interpretation, it is found that there is no major shifting in the frequencies of above said functional groups. Hence, above result conclude that no drug and excipients interaction were found.

Differential scanning calorimeter (DSC) study

Thermograms of ibuprofen pure drug and physical mixture of optimised formulation (F_3) are given in fig. 4, fig. 5. Pure drug ibuprofen shows melting endothermic peak at 80.78 °C, while physical mixture of drug and excpient showed the melting peak at 80.72 °C which indicates that all the ingredients, are compatible with each other.

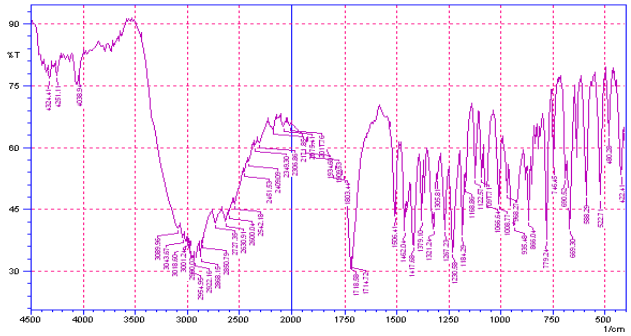

Fig. 2: FTIR of pure drug ibuprofen

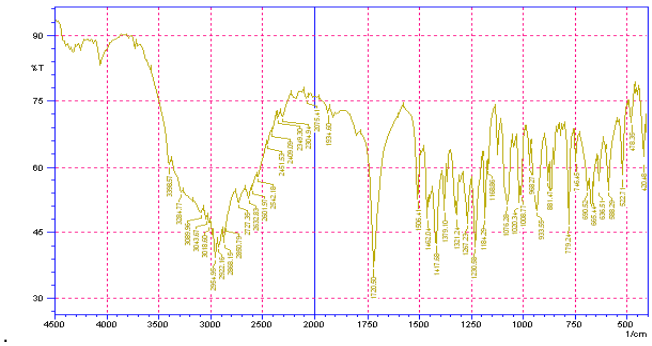

Fig. 3: FTIR of physical mixture of ibuprofen and excipients

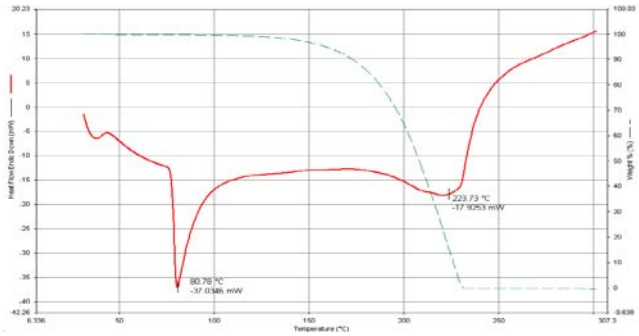

Fig. 4: DSC thermogram of pure drug ibuprofen

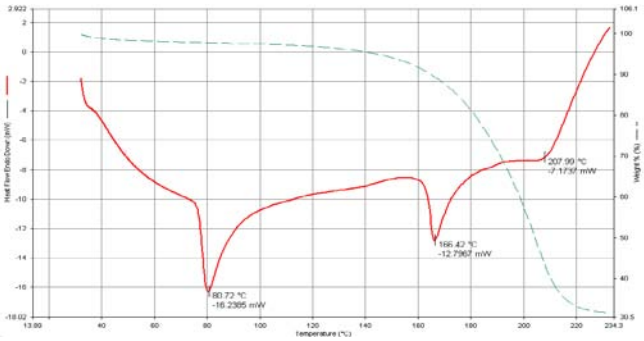

Fig. 5: DSC thermogram of physical mixture of ibuprofen and excipients

Micromeretics study

Angle of repose (θ) is a characteristic of the internal friction or cohesive of the particles. Its value will be high if the powder is cohesive and low if the powder is non-cohesive. All formulations showed good to acceptable flow properties as indicated by the values of angle of repose (24.3-27.1°). Prepared formulations of ibuprofen showed improved flow properties when compared to control formula (38°). More over Carr's compressibility index also ranges below 18 indicating improved flow properties compared to control (22.08). Hausner ratio for all formulations is also in the range of 1.17 conforming improved flow properties (Table 3).

Table 3: Physical properties of powder blends

Formulation code	Angle of repose	Bulk desity (gm/cm³)	Tapped density (gm/cm³)	% Compressibility	Hausner's ratio
Control	38±1.02	0.68±0.15	0.83±0.19	22.058	1.220
F_1	25.1±0.12	0.51±0.06	0.60±0.02	15	1.176
F_2	24.9±0.19	0.56±0.09	0.65±0.04	13.846	1.160
F_3	24.3±0.16	0.52±0.16	0.63±0.09	17.460	1.211
F_4	25.8±0.12	0.51±0.14	0.61±0.13	16.393	1.196
F_5	26.4±0.09	0.53±0.07	0.63±0.16	15.873	1.188
F_6	25.5±0.16	0.57±0.12	0.66±0.09	13.636	1.157
F_7	27.1±0.09	0.55±0.07	0.64±0.14	14.062	1.163
F_8	26.6±0.13	0.54±0.13	0.63±0.03	14.285	1.166
F_9	25.2±0.07	0.53±0.14	0.62±0.07	14.516	1.169
F_{10}	25.9±0.02	0.56±0.09	0.65±0.02	13.846	1.160
F_{11}	26.7±0.09	0.57±0.04	0.66±0.14	13.636	1.157
F_{12}	26.2±0.04	0.52±0.11	0.61±0.18	14.754	1.173

Results are mean of three determinations.

Post compression evaluation

Weight variation

Weight variation for all the formulations reported in table 4. The weight variation of different formulatd batches in the range of 299.3 to 301 mg. All the tablets from each formulation passed weight variation test, as the % weight variation was within the pharmacopeia limits of ±5% of the total.

Hardness test

Hardness of all formulation batches was found to be in the range of 3.66 to 3.93 kg/cm³. It indicates good mechanical strength with a capability to resist physical and perfunctory stress conditions during handling (Table 4).

Friability

Friability of all formulated batches was found to be in between 0.65 to 0.99%, indicates good mechanical resistance of tablets. The friability of optimized formulation was found to be 0.652% and it was reported in table 4.

Wetting time and water absorption ratio

Wetting time and water absorption ratio values were represented in table 4. Wetting time of all formulation batches were found to in the range of 9 to 140 seconds, which predicts a wide range of wetting time due to super disintregrants. In all the formulations F_3 formulation, which contains 10%, crospovidone showed the least wetting time (9 seconds) due to wicking action. The water absorption of formulation F_3 was with highest value of 1.87 indicating a high amount of water uptake due to superdisintegrant.

Drug content

Assay of ODTs was done with the help of U. V (Agilent Cary 60) and the drug content was estimated. Drug content of all formulation batches found to be in the range of 96.54% to 102%.

***In-vitro* dispersion time**

In-vitro dispersion time of all formulation batches found to be in the range of 42 seconds to 176 seconds. The control showed 43 minutes for dispersion in the phosphate buffer 7.2 pH. In all the formulations, F_3 formulation, which contains 10% crospovidone, showed the least dispersion time of 42 seconds (Table 4).

***In-vitro* disintegration time**

The rate of disintegration of formulations increased with variation in concentration of various superdisintegrants. Batch F_3 containing a higher amount of crospovidone disintegrates rapidly than other batches in 38 seconds (Table 4). The rapid disintegration assists swallowing and also plays a role in drug absorption in buccal cavity, thus promoting bioavailability. The control without super disintegrant showed 80 minutes of disintegration time. All the formulations showed satisfactory disintegration time.

Table 4: Physical properties of ibuprofen orodispersible tablets

Formulation Code	Weight variation (mg)	Hardness (Kg/cm³)	Friability (%)	Wetting time (Sec)	Absorption ratio	Drug Content	*In-vitro* dispersion time (Sec)	*In-vitro* disintegration time (Sec)
Control	299.7±0.23	3.73±0.24	0.986	210±0.63	2.83	98.57±0.14	43 min	80 min
F_1	299.3±0.15	3.66±0.12	0.756	11±0.52	1.033	99.70±0.02	75±0.82	40.16
F_2	299.5±0.16	3.76±0.11	0.904	10±0.94	1.410	101.84±0.01	55±0.23	40.5
F_3	299.3±0.09	3.93±0.07	0.652	9±0.69	1.878	98.06±0.19	42±0.45	38
F_4	301±0.14	3.76±0.07	0.813	22±0.69	1.645	96.94±0.04	83±0.24	55.33
F_5	299.7±0.14	3.60±0.18	0.877	19±0.90	1.654	98.51±0.34	63±0.15	52.5
F_6	299.6±0.04	3.830.24	0.712	14±0.83	1.758	97.58±0.27	52±0.14	42.75
F_7	299.5±0.12	3.83±0.12	0.997	19±0.76	1.733	101.28±0.36	140±0.4	55.33
F_8	298±0.18	3.70±0.15	0.925	18±0.97	1.745	98.5±0.14	113±0.29	50.33
F_9	299.7±0.08	3.66±0.24	0.685	140±0.24	1.775	98.69±0.35	97±0.46	46.50
F_{10}	300.8±0.012	3.83±0.21	0.875	42±0.14	0.743	96.54±0.16	176±0.14	47
F_{11}	299±0.20	3.83±0.17	0.744	41±0.46	1.379	99.14±0.23	149±0.26	46.83
F_{12}	300±0.14	3.76±0.04	0.926	39±0.16	1.878	101.08±0.16	127±0.48	45.50

Results are mean of three determinations.

***In-vitro* dissolution studies**

This orodispersible tablets are designed to disaggregate in the oral cavity and usually release and allow the active agent to dissolve fastly in the saliva improving the bioavailability of the drug.

In the present investigation, 12 batches of formulations were prepared with four different types of superdisintegrants. Three different batches of each superdisintegrant (5%, 7.5% and 10% w/w) were formulated. All the batches were compared with a control batch consisting without superdisintegrant.

In vitro drug release profile of the formulated batches was represented in fig. 6. Remarkable differences in the dissolution profile of different batches were observed. All formulae showed acceptable dissolution rate, where more than 85% of the label dose was dissolved within 30 minutes. These results indicate that superdisintegrant process used to prepare the orodispersible tablets enhanced the rate and extent of dissolution of ibuprofen. Control batch was able to give only about 51% of drug release within 1 hour. From the *in vitro* dissolution data, it was found that as the concentration of superdisintegrants increased the drug release also inceased.

In case of crospovidone, as the concentration was increased from 5% to 7.5% to 10% there was a significant increase in the $D_{5\ min}$ and $D_{15\ min}$ values respectively as shown in table 5. At the same time, there was also a reduction in the $t_{50\%}$ and $t_{90\%}$ values (Table 5). Similar results were also obtained with other superdisintegrants as represented in the table 5. Among the diferent batches of formulations F_3 batch consisting of 10% crospovidone showed the highest dissolution rate where around 90% of the label dose was dissolved within 2.6 minutes; this may be due to faster swelling with an increase in the concentration of the superdisintegrant, thus fascilitating the disintegrant to bring about faster disintegration and also improving dissolution. By keeping the superdisintegrant concentration constant (i. e. 10%), When compared with other superdisintegrants like sodium starch glycolate (F_{12}), sodium carboxy methyl cellulose (F_9) and croscaramellose sodium (F_6), the order of *in vitro* drug release was obtained in the following manner.

$$F_3 > F_6 > F_9 > F_{12}$$

The probable reason for delayed disintegration time and dissolution rate for F_6, F_9, F_{12} batches might be the slow water uptake and gelling tendency of those super disintegrants.

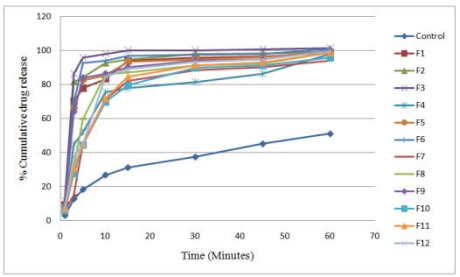

Fig. 6: Dissolution study of different batches of formulation

Table 5: Dissolution parameters of ibuprofen orodispersible tablets

Formulation code	$D_{5\ min}$	$D_{15\ min}$	$t_{50\%\ (Min)}$	$t_{90\%\ (Min)}$
Control	18.29	31.23	59.12	
F_1	78.07	94.158	2.5	13.98
F_2	84.265	94.89	2.48	8.18
F_3	95.89	99.98	1.9	2.6
F_4	52.02	78.07	4.9	35.07
F_5	82.8	93.45	2.57	12.59
F_6	92.664	96.849	2.2	4.92
F_7	44.563	79.708	6.29	42.08
F_8	44.963	84.512	4.12	27.5
F_9	44.991	89.376	2.49	13.75
F_{10}	45.499	82.469	5.29	48.22
F_{11}	59.746	87.358	5.15	25.79
F_{12}	84.046	90.472	5.02	18.29

$D_{5\ min}$ = dissolution rate after 5 minutes, $D_{15\ min}$ = dissolution rate after 15 minutes.

In terms of overall parameters the optimised formula (F_3) was subjected to accelerated stability studies at 40°C ± 2 °C and 75± 5% RH for six months with three months intervals represented in table 6.

There is no significant change in drug content at 3 months and 6 months (Table 6). The results for dissolution of optimised formulation show no appreciable change upto 6 months of accelerated stability studies in fig. (7).

Table 6: Drug content study of optimised formulation (F_3) at 40 °C ± 2 °C and 75± 5% relative humidity

Optimised formulation	Evaluation	0 month	3 months	6 months
F_3	Drug content	98.06±0.19	97.32±0.12	96.88±0.09

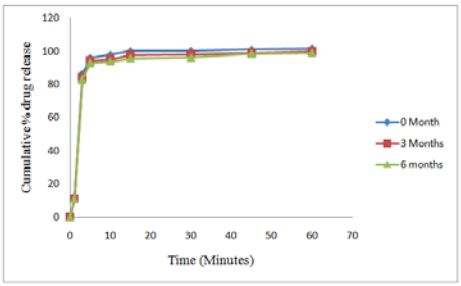

Fig. 7: Stability study of optimised formulation (F_3)

CONCLUSION

Solid dosage forms that can be dissolved or suspended with water in the mouth for easy swallowing are highly desirable for the paediatric and geriatric population, as well as other patients who prefer the convenience of readily administerd dosage form. ODTs of ibuprofen could be consider as useful oral delivery systems to increase the drug bioavailabilty.

From the study, it is concluded that crospovidone enhanced the rate of orodispersion and improved drug release rate. The optimum selected formula (F_3) has good stability. Thereby, the enhanced drug release leading to increased bioavailability of ibuprofen. Thus, a satisfactory orodispersible tablet of ibuprofren for large-scale production is feasible.

ACKNOWLEDGEMENT

The authors are greatly thankful to Mr. Subhakant Dhal and Mr. G. Maheswara Sastry for their unlimited helped during the manuscript preparation. We would like to thank all the staff of pharamaceutical technology department in the Maharajah's college of pharmacy for their efforts to fascilatate the use of the necessary instruments and materials during the entire course of this work.

CONFLICT OF INTERESTS

Declared None

REFERENCES

1. Yoshio K, Masazumi K, Shuichi A, Hiroaki N. Effect of preparation method on properties of orally disintegrating tablets made by phase transition. Int J of Pharm 2008;355:87-92.
2. Sudarshan S, Dhaval S. Development and characterization of mouth dissolving tablet of Zolmitriptan. Asian Pac J Trop Dis 2012;S457-S64.
3. Abdelbary G, Eouani C, Prinderre P, Joachim J, Reynier J, Piccerelle P. Determination of the *in vitro* disintegration profile of rapidly disintegrating tablets and correlation with oral disintegration. Int J Pharm 2005;292:29-41.
4. Kei-ichi K, Yoshiteru W, Kumiko M, Naoki U, Mitsuo M. New method of preparing high porosity rapidly saliva soluble compressed tablets using mannitol with camphor, a subliming material. Int J Pharm 1997;152:127-31.
5. Ritesh M, Zebunnissa R. Application of face centred central composite design to optimise compression force and tablet diameter for the formulation of mechanically strong and fast disintegrating orodispersible tablets. Int J Pharm 2012;430:18-25.
6. Abdelbary A, Elshafeey A, Zidan G. Comparitive effects of different cellulosic based directly compressed orodispersible tablets on oral bioavailability of famotidine. Carbohydr Polym 2009;77:799-806.
7. Parshu R, Tiwary A, Vikas R. Superior disintegrating properties of calcium cross-linked *Cassia Fistula* gum derivatives for fast dissolving tablets. Carbohydr Polym 2012;87:1098-104.
8. Simone S, Peter C. Fast dispersible ibuprofen tablets. Eur J Pharm Sci 2002;15:295-305.
9. Syusuke S, Yasunori I, Susumu K, Shigeru I. Preparation and evaluation of swelling induced-oally disintegrating tablets by microwave irradiation. Int J Pharm 2011;416:252-9.
10. Erno A, Bart M, Kenneth C. Fast disintegrating and conventional tablet formulations of risperidone in healthy volunteers. Clin Ther 2003;25(6):1687-99.
11. Seong H, Kinam P. Development of susutained release fast disintegrating tablets using various polymers coated ion exchange resin complexes. Int J Pharm 2008;353:195-204.
12. Takao M, Yoshinori M, Takeshi Y, Katsuhide T. Formulation design of a novel fast disintegrating tablet. Int J Pharm 2005;305:83-90.
13. Ahmed A, Adel A, Heba M. Enhanced dissolution of meloxicam from orodispersible tablets prepared by different methods. Bull Faculty Pharm Cairo University 2012;50:89-97.
14. Adamo F, Valentina B, Gian C, Celestino R, Carlos A. Fast dispersible/slow releasing ibuprofen tablets. Eur J Pharm Biopharm 2008;69:335-441.
15. Chanf R, Guo X, Burnside B, Couch R. A review of fast dissolving tablets. Pharm Tech 2000;52-8.
16. Covadong A, Ignacio N, Juan J, Gordon J, Potthast H, García-Arieta A. Investigation on the possibility of biowaviers for Ibuprofen. J Pharm Sci 2011;6(100):2343–9.
17. Dimal A, Dixit J, Usman K, Kashyap B. Estimation of ibuprofen and famotidine in tablets by second order derivaive of spectrophotometry method. Arabian J chem 2012;7:1-4.