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Research Article

Formulation and Evaluation of Zaltoprofen Fast Disintegrating Tablet

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Abstract

Zaltoprofen is a non-steroidal anti-inflammatory drug (NSAIDs) and has powerful inhibitory effects on acute and chronic inflammation with less adverse reactions on the gastrointestinal tract than other NSAIDs. The main objective of this study was to formulate and evaluate fast disintegrating tablets of zaltoprofen (ZPF) prepared by direct compression method using super-disintegrants with a view to enhance patient compliance. Two different super-disintegrants, such as crospovidone and sodium starch glycolate were used in different ratio (2-8% w/w). FTIR study reveals that there is no drug-excipients interaction between ZPF and excipients. The DSC/PXRD study revealed that the crystallinity of zaltoprofen was significantly reduced to amorphous. The dissolution study was carried out in pH6.8 phosphate buffer solution. It was observed that the tablets with 8% of crospovidone showed satisfactory results with disintegration time of 24sec, wetting time of 10sec and highest dissolution rate (100.89%) in 15min. It can be concluded that superdisintegrant, crospovidone showed better disintegrating time, wetting time and dissolution property than the sodium starch glycolate in the formulation of fast disintegrating tablets.

Keywords: Fast disintegrating tablets, zaltoprofen, crospovidone, sodium starch glycolate

Introduction

Fast-disintegrating tablet (FDT) technology is one of the recent innovative technologies in pharmaceutical formulations and the FDT formulation has become a fast-growing segment in oral drug delivery systems.[1] Fast dissolving/ disintegrating tablets 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. The FDT is also known as fast melting, fast dispersing, rapid dissolve, rapid melt and/or quick disintegrating tablet. FDTs can be administered easily without water, although taking water makes oral administration even easier.[2-3] All FDTs approved by the Food and Drug Administration (FDA) are classified as orally disintegrating tablets. In recent times, 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 FDTs varies from several seconds to about a minute.[4]

Advantages of oral fast-disintegrating tablets such as; the administration to patients who are unable to swallow such as the elderly, stroke victims, healthcare facility, bedridden patients and patients who refuse to swallow, such as paediatric, geriatric and psychiatric patients[5-6] more rapid drug absorption and thus bioavailability, as evident in one bioequivalence study (Selegiline) through pre-gastric absorption from the mouth, pharynx and oesophagus[5] most convenience and better patient compliance[6] product segregation, line extension and life-cycle supervision, exclusivity of product advertising and patient-life expansion.[7] Zaltoprofen, chemically it is 2-(10,11-dihydro-10-oxodibenzo (b, f) thiepin-2-yl) propionic acid, is a derivative of 2-arylpropionic acids (2-APA), an important group of non-steroidal anti-inflammatory drugs (NSAIDs) and has powerful inhibitory effects on acute and chronic inflammation with less adverse reactions on the gastrointestinal tract than other NSAIDs.[8] ZPF exerts anti-inflammatory actions and analgesic effects by inhibiting prostaglandin synthesis and through a peripheral mechanism by inhibition of bradykinin B2 receptor-mediated bradykinin responses in primary afferent neurons.[9-11] Zaltoprofen is an important group of NSAIDS in the treatment of rheumatoid arthritis and osteoarthritis as well as to relieve inflammation and pain after surgery, injury and tooth extraction.[12]

Materials and Methods

Materials

Zaltoprofen was obtained as gift sample from IPCA Pharmaceutical Ltd., Mumbai, India. Crospovidone (CP), sodium starch glycolate (SSG) and mannitol were obtained from Loba Chemie Pvt. Ltd., Mumbai, Maharashtra, India. Mannose, talc and

magnesium stearate were purchased from S.D Fine-Chem Ltd., Mumbai, Maharashtra, India. All other chemicals were of analytical grade.

Preparation of zaltoprofen fast disintegrating tablets

The fast disintegrating tablets of ZPF were prepared by using direct compression method. Two super-disintegrating agents such as crospovidone and sodium starch glycolate were used in varying concentration as shown in (Table 1). Accurately weighed 80 mg quantity of ZPF, super-disintegrating agent, mannose and mannitol were mixed and passed through the US Standard Sieve Sizes (# 45). Finally, magnesium stearate and talc were added as lubricating agent. The powder blend was subjected to compression into tablet using 8 station multi-punch tablet machine (Mini Press II Multi Tooling, Karnavati Engineering, Mehsana, Gujarat, India).

Table 1. Composition of zaltoprofen fast disintegrating tablets

Formulation Ingredients	F0	F1	F2	F3	F4	F5	F6
ZPF	80	80	80	80	80	80	80
Crospovidone	0	2.5	5	10	0	0	0
Sodium Starch Glycolate	0	0	0	0	2.5	5	10
Mannitol	39	36.5	34	29	36.5	34	29
Magnesium Stearate	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2
Mannose	2	2	2	2	2	2	2
Total (mg)	125	125	125	125	125	125	125

Evaluation of zaltoprofen fast disintegrating tablets

Evaluation of pre-compression parameters of powder

Prior to compression, powder were evaluated for their flow and compressibility parameters. Flow properties of powder were determined by angle of repose method. Compressibility index of powder were determined by Carr's index and Hauser ratio.[13-14]

Angle of repose

Angle of repose ( ) was determined using funnel method. The blend was poured through a funnel that can be raised vertically until a maximum cone height (*h*) was obtained. The radius of the heap (*r*) was measured and angle of repose was calculated.

$$\tan^{1}\frac{h}{r}$$

Compressibility index

The simplest way of measurement of free flow property of powder is compressibility, an indication of the ease with which a material can be induced to flow is given by % compressibility that is calculated as follows:

$$C \quad (\quad) / \quad 100$$

where, indicates tapped density and indicates bulk density

Hausner's ratio

Hausner's ratio is an index of ease of powder flow; it is calculated by following formula.

$$H \quad \frac{}{}$$

where, H refers to Hausner's ratio, ρ_t is tapped density, and ρ_b is bulk density.

Evaluation of post-compression parameters of tablets

Tablet thickness

Dimension of the tablets was measured by using a calibrated dial calliper. Five tablets of each formulation were picked out randomly and its thickness was measured individually.[15-16]

Weight variation test

The procedure described in Indian Pharmacopoeia[17] was employed to determine weight variation of tablets. Ten tablets were randomly selected from each batch and weighed on an electronic balance and mean weight was taken. Each tablet was then weighed individually and standard deviation in weight was calculated for each batch.[18]

Tablet hardness

Five tablets were randomly selected from each batch and hardness of tablets was determined by using Monsanto Hardness Tester. The mean values and standard deviation for each batch were calculated.[16] The hardness of optimised batch F3 was carried out on CT3 Texture Analyzer by using TexturePro Software (Brookfield Engineering Laboratories, Inc. Middleboro, Massachusetts, USA).

Tablet friability

Friability indicates the ability of a tablet to withstand mechanical shocks while handling. Friability of tablets were determined using Roche Friabilator and were expressed in percentage (%). Ten tablets were initially weighed ($W_{initial}$) and placed into the friabilator. The friabilator was operated at 25 rpm for 4 min or run up to 100 revolutions and then the tablets were weighed again (W_{final}). The loss in tablet weight due to abrasion or fracture was the measure of tablet friability. Percent friability (*f*) was calculated by using the following formula[16] and percentage friability of less than 1% was considered acceptable

$$f \quad (W_{\text{initial}} \quad W_{\text{final}}) \; W_{\text{initial}} \quad 100$$

Disintegration test

The disintegration time was determined by using USP Tablet disintegration test apparatus using 900 ml of distilled water without disk. Time taken by tablets (sec) for complete disintegration of the tablets until no mass remaining in apparatus was measured.[15-16]

Wetting time

The wetting time and capillarity of oral dispersible tablets were measured by a conventional method. Tablets were placed in a petridish containing 10 ml water at room temperature and the times for complete wetting of tablets were recorded.[16]

HPLC analysis

Distribution uniformity of the drug inside the different tablets was assessed by HPLC. The amounts of released ZPF were determined by Agilent 1200 HPLC. The data was collected and processed using EZ Chrome software. The chromatographic separation was achieved with LC-GC BDS C18 column 250 mm $\times$ 4.6 mm column. The mobile phase consisted mixture of methanol: water (85:15, v/v). The determination wavelength was monitored with UV detector at 242nm. The mobile phase was delivered through the column at flow rate 1.0 ml/min. The linearity was indicated by correlation coefficient (r^2) value of 0.998. The ZPF calibration curves, at concentrations varies from 2 to 12μg/ml, were used to evaluate all the samples with 20µl injection volume. Ten tablets were powdered and weigh accurately 10 mg equivalent of zaltoprofen from tablet powder and transferred into a 100 ml volumetric flask. Suitable concentration analysed using HPLC.

Characterization of zaltoprofen FDTs

Differential scanning calorimetry (DSC)

DSC was performed on pure zaltoprofen and final optimized batch tablet using a differential scanning calorimeter (DSC-60, Shimadzu, Japan). Samples (2-4mg) were sealed in aluminium pans. Next, DSC thermograms were recorded from 50 to 300°C at a heating rate of 20°C/min in air atmosphere.

X-ray powder diffraction (XRD)

The XRD of pure zaltoprofen and final optimized batch tablet were evaluated by Bruker AXS D8 Advance X-ray powder diffractometer (Bruker Biosciences Corporation Billerica, MA, USA) to assess the polymorphic state. Each diffractogram was recorded from 3 to 150^0 (2θ) at a scanning speed of 3^0/min and using Si(Li) PSD detector. Cu Kα radiation was used as the X-ray source at a wavelength 1.5406A^0; this was operated at a voltage of 40 kV and a current of 35mA.

FTIR spectroscopy

Fourier-transformed infrared (FTIR) spectra of pure zaltoprofen and final optimized batch tablet were obtained using an FTIR spectrometer (IR AFFINITY-1 CE, Shimadzu, Japan) equipped with a pyroelectric detector. Data were acquired using IR solution software. The spectra were measured over the range 4000-400 cm^{-1} with an instrument resolution of 4 cm^{-1}. Each individual spectrum was an average of 45 scan.

In vitro drug release study

The in vitro drug release study of zaltoprofen from the tablets were carried out using USP dissolution test apparatus type-II Paddle Method (Dissolution test TDT-08L plus, Electrolab, USP) in 900 ml of dissolution medium (phosphate buffer pH6.8) at 37 ± 0.5^0C temperature and rotated at 50 rpm. In this test, single tablet from each formulation was used for the studies. At specified time intervals, 5 ml samples were collected and immediately replaced with an equal volume of fresh medium. Samples were suitably diluted and analyzed by using UV-VIS Spectrophotometer (PharmaSpec UV-1700, Shimadzu Corporation, Kyoto, Japan) at λ_{max} 242 nm. All the tests were carried out in triplicate.[18]

Results and Discussion

Evaluation of pre - and post - compression parameter

Fast disintegrating tablets of zaltoprofen were prepared by direct compression method employing crospovidone and sodium starch glycolate as super-disintegrants in different ratio. A total of six formulations and a control formulation F0 (without super-disintegrants) were designed. The flow properties of the powder mixture are significant for the uniformity of mass of the tablets; the flow of the powder mixture were analyzed before compression to tablets. The values of pre-compression parameters evaluated were within prescribed limits and indicated a good free flowing property. Low Hausner`s ratio ($\leq$1.32), compressibility index ($\leq$ 16.24) and angle of repose ($\leq$9.36) values indicated a fairly good flowability of powder mixture. Table 2-3 depicts post-compression parameters of zaltoprofen FDTs. As the tablet powder blend was free flowing, tablets produced were of uniform weight with acceptable weight variation in the range from 126 mg

to 132 mg due to uniform die fill. Hardness (2.0-2.58 kg/cm^2) (Fig. 1) of F3 batch and friability loss (0.31-0.65 %) indicated that tablets had a fine mechanical resistance. Drug content was found to be high (≥98.70 %) in all the tablet formulations. Uniform distribution of the active agent was assessed by HPLC chromatograms (Fig. 2), the content of zaltoprofen was found inside the 98.02% of the theoretical value.

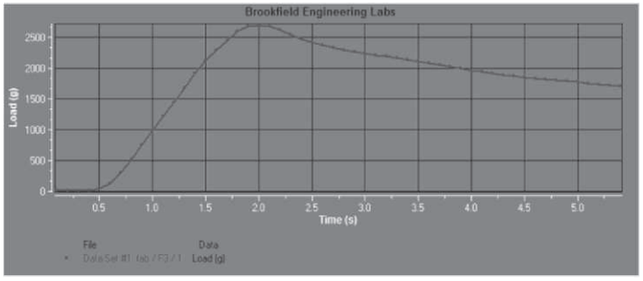

Fig. 1: Hardness testing of F3 by CT3 texture analyzer

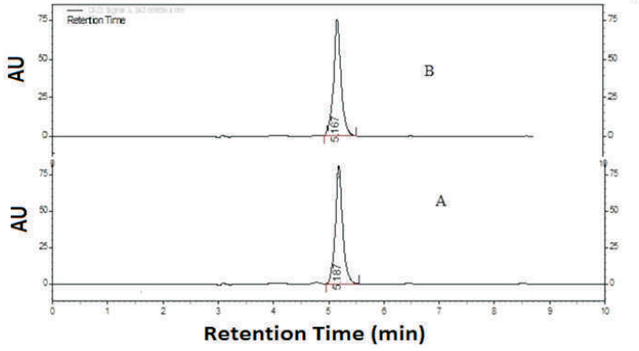

Fig. 2: HPLC Chromatograms of zaltoprofen (A) Standard 10 μg/ml; (B) F3 batch formulation

The most important parameter that needs to be optimized in the development of fast disintegrating tablets is the disintegration time of tablets. In this present study, it was observed that the disintegration time of the tablets had a significant effect with the increasing amount of super-disintegrants. However, disintegration time increased with the increase in the quantity of SSG in the tablets. This indicates that increase in the level of SSG had a positive effect on the disintegration of the tablets. At higher levels, SSG lead to the formation of a viscous gel layer[19] that acted as a thick barrier for further penetration of the disintegration medium and hindered the disintegration of tablet contents. Therefore, tablet disintegration is retarded to some extent with tablets containing SSG, while the faster disintegration of crospovidone tablets may be ascribed to its rapid capillary activity and pronounced hydration with little tendency to gel formation. Thus, these results suggest that the disintegration times can be decreased by using wicking type of disintegrants (crospovidone). Wetting time is an important criteria for understanding the capacity of disintegrants to swell in pressure of little amount of water were found to be in the range of 10-60 sec. Wetting time of the tablets significant decreased as the amount of crospovidone (2- 8%) increased. It is interesting to note that wetting time increased with the increase in the quantity of SSG (2-8%) in the tablets (Fig. 3). Thus, wetting time of tablets with crospovidone was found to be less than sodium starch glycolate. The post compression parameters such as hardness, friability, thickness, wetting time, weight variation, disintegration timeand drug content are shown in (Table 3).

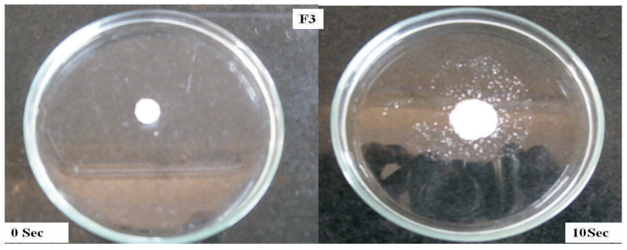

Fig. 3: Photographs of the wetting time of F3 formulation

Table 2. Pre-Compression parameters of zaltoprofen FDTs

Formulation code	Angle of repose (θ) ± SD, n=3	Compressibility (%) ± SD, n=3	Hausner's ratio (%) ± SD, n=3
F0	19.36±1.24	16.24±1.43	1.32±0.4
F1	14.57±1.12	14.41±1.29	1.27±0.5
F2	13.28±1.36	13.34±1.14	1.24±0.7
F3	12.35±1.31	10.19±1.92	1.28±0.5
F4	15.14±1.43	13.64±1.47	1.31±0.8
F5	14.35±1.83	12.40±1.32	1.29±0.6
F6	11.81±1.10	9.23±1.74	1.25±0.3

Table 3. Post-compression parameters of zaltoprofen FDTs

	Evaluation parameters						
Code	**Hardness (kg/cm^2) ±SD**	**Friability (% w/w) ± SD**	**Thickness (mm) ± SD**	**Wetting time (Sec) ± SD**	**Weight variation ± SD**	**Disintegration time (Sec) ± SD**	**Drug content (%) ± SD**
F0	2.58±0.8	0.65±0.8	1.78±0.2	60±0.7	132±0.8	65±0.6	98.7±0.6
F1	2.45±0.3	0.54±0.7	1.76±0.1	22±0.6	128±0.6	42±0.8	99.2±0.7
F2	2.43±0.4	0.43±0.6	1.74±0.3	16±0.4	129±0.5	30±0.7	99.9±0.3
F3	2.00±0.2	0.35±0.4	1.70±0.1	10±0.3	126±0.2	24±0.4	100.1±0.4
F4	2.44±0.6	0.52±0.5	1.77±0.5	15±0.4	130±0.6	34±0.6	99.8±0.6
F5	2.46±0.3	0.44±0.6	1.75±0.3	21±0.2	128±0.9	39±0.5	100.0±0.3
F6	2.41±0.2	0.31±0.3	1.71±0.2	26±0.1	127±0.4	46±0.2	101.0±0.1

SD refers to standard deviation, n=3

FTIR study

In order to further study whether zaltoprofen undergoes a polymorphic change during preparation of FDTs and to test for possible intermolecular interactions between ZPF and excipients, FTIR was used. The FTIR spectra of pure ZPF and optimized batch tablet (F2, F3, F5, and F6) are depicted in (Fig.4). Pure ZPF presents characteristic infrared spectra in the region of 3400-2400cm^{-1} explains carboxylic acid (COOH) functional groups, while 1280cm^{-1} suggests C-O group. It also exhibits characteristic infrared spectra in the C=O stretching region of functional carbonyl group band at 1700 cm^{-1}, showing its crystalline nature. All these principal IR peaks of ZPF were present in all formulations (F2, F3, F5 and F6). This clearly indicates that there is no interaction between ZPF and excipients.

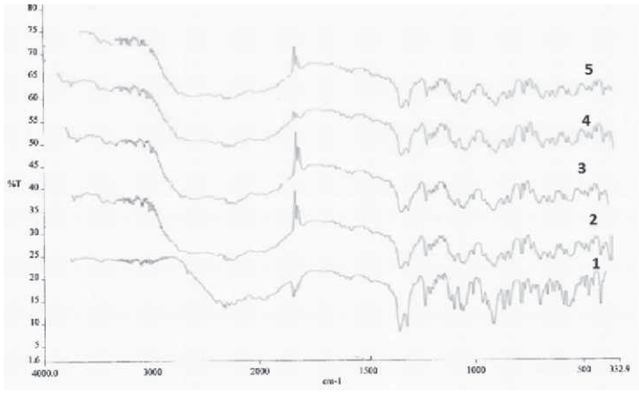

Fig. 4: IR spectra of (1) zaltoprofen; (2) F2; (3) F3; (4) F5; (5) F6

DSC study

DSC is a very useful tool in investigation of thermal properties of drug and its formulation. DSC studies were carried out on pure ZPF, CP and SSG and optimized batch tablet (F3 and F6). Pure ZPF displayed endothermic peak at 136.3°C corresponding to its melting point. Fig. 5A-C depicted thermograms of pure ZPF, CP and F3. CP showed endothermic peak at 68.9^{0}C due to its low melting point. The endothermic peak of F3 showed a very weak broad peak shifted to lower melting point at 103.4°C, with greatly reduced peak intensity. The differences in the thermal behaviour of ZPF in form of FDT batch F3, suggesting that the crystallinity of ZPF is decreased. Fig. 5D-E demonstrates thermograms of SSG and F6. The endotherm of SSG displayed broad peak appeared at 87.0°C corresponding to its melting point. The thermogram of F6 showed broad, reduced peak intensity shifted to lower melting point at 103.8°C. This variation in thermal peak along with reduced peak intensity, suggests the absence of crystallinity of ZPF. It has been known that transforming the physical state of the drug to the amorphous or partially amorphous state leads to a high-energy state and high disorder, resulting in enhanced solubility and faster dissolution.[20]

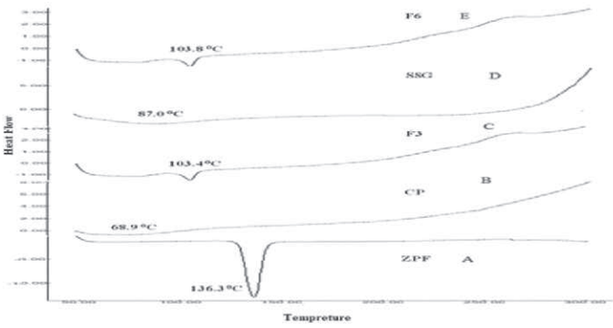

Fig. 5: DSC thermograms of (A) zaltoprofen; (B) crospovidone; (C) F3; (D) sodium starch glycolate; and (E) F6

XRD study

In order to clarify the physicochemical characteristics of pure ZPF and optimized batch tablet (F3), X-ray diffraction measurements were conducted as shown in (Fig. 6). The XRD of pure ZPF exhibited sharp, highly intense and less diffused peaks indicating the crystalline nature of drug. It showed sharp diffraction peaks at 2θ values of 10.33°, 15.36°, 19.22°, 22.98°, 24.97°, 27.67° and 31.83°. The XRD of batch F3 showed undefined, broad, diffuse peaks of low intensities, suggesting the absence of crystalline form of ZPF.

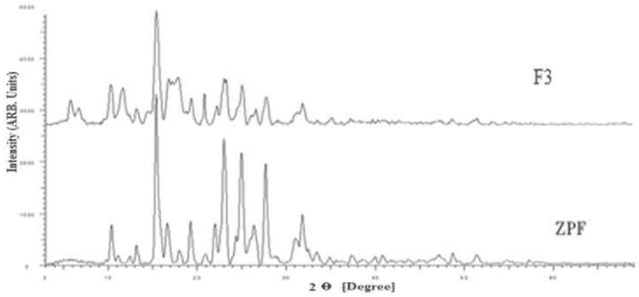

Fig. 6: XRD of pure zaltoprofen and F3 formulation

***In vitro* dissolution study**

The *in vitro* dissolution profile in Fig. 7 showed the dissolution behaviour of pure ZPF and all formulation batch tablet (F0 to F6) in pH 6.8. Pure ZPF showed maximum drug release up to 90.12% in 1h. The controlled formulation F0 showed improvement in dissolution rate upto 98.78% in 1h. Batch F1, F2 and F3 displays markedly increase in dissolution rate to an extent up to 101.94%, 101.73% and 100.89% in 45 min, 30 min and 15 min, respectively. It was observed that as the concentration of CP increased there was decrease in the disintegration time, wetting time and increase in dissolution rate of ZPF, *i.e.* directly proportional to the concentration of CP. Therefore, formulation F3 having disintegrants crospovidone in the concentration of 8% was selected as the optimized formulation. Batches F4-F6 showed a significant increase in dissolution rate to a level up to 99.20%, 99.83% and 100.31% in 45 min, 30 min and 15 min, respectively. It was observed that increase in concentration of SSG showed increase in disintegration time, wetting time and decrease in dissolution rate of ZPF, i.e. inversely proportional to the concentration of SSG. Almost 99% drug was released from the all the formulations. The faster dissolution rate of F3 batch compared to F0 and pure drug was observed and could be attributed to the improvement of wettability of ZPF particles due to the presence of superdisintegrants (CP). Many factors contributed to faster release rate such as decrease in particle size, decrease in agglomeration of particles, increase wettability and decrease in crystallinity of the drug.

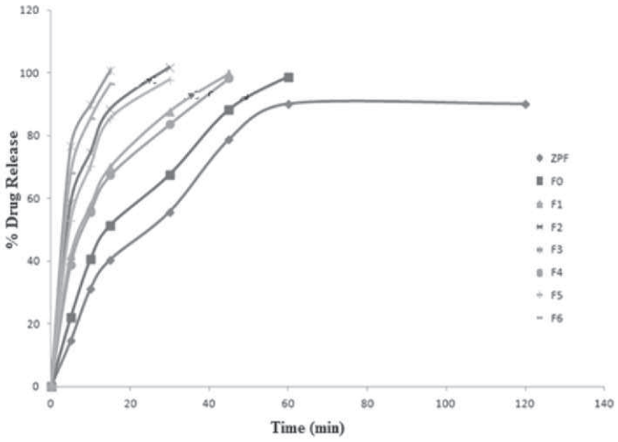

Fig. 7: In *vitro* dissolution profile of pure zaltoprofen and all batches of FDTs

Conclusion

The present investigation of this study was undertaken with an aim to formulate and characterize fast disintegrating tablets of zaltoprofen using direct compression method with the addition of super-disintegrating agents. FTIR study reveals that there is no drug-excipients interaction between ZPF and excipients. The DSC/PXRD study revealed that the crystallinity of zaltoprofen was significantly reduced to amorphous. It is observed that the formulation F3 containing 8% (w/w) of crospovidone was found to be promising showing disintegration time of 24 sec, wetting time of 10 second and highest dissolution rate (100.89%) in 15 min when compared to control formulation (F0) and pure ZPF. It was concluded that superdisintegrant, crospovidone showed better disintegrating time, wetting time and dissolution property than the sodium starch glycolate in the formulation of fast disintegrating tablets.

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References

1. Jeong SH, Yourong F, Frosta KP. Technology for making fast-disintegrating tablets. Oral Delivery 2007: 28-29.
2. Habibh W, Khankarik R, Hontz J. Fast-dissolve drug delivery system. Crit Rev Ther Drug Carrier Syst 2000; 17: 61-72.
3. Douroumis D. Practical approaches of taste masking technologies in oral solid forms. Expert Opin Drug Deliv 2007; 4: 417–426.
4. Yourong F, Yang S, Jeong SH, Kimura S, Park K. Orally fast disintegrating tablets: developments, technologies, taste-masking and clinical studies. Crit Rev Ther Drug Carrier Syst 2004; 21: 433-475.
5. Wilson CG, Washington N, Peach J, Murray GR, Kennerley J. The

scintiagraphy. Int J Pharm 1987; 40: 119-123.

6. Virely P, Yarwood R. Zydis- A novel fast dissolving dosage form. Manuf Chem 1990; 36-37.
7. Fix JA. Advances in quick-dissolving tablets technology employing Wowtab. In: Institute for Int. Resources, Conference on Drug Delivery Systems October, Washington DC, USA, 1998.
8. Tsurumi K, Kyuki K, Niwa M, Kokuba S, Fujimura H. Pharmacological investigations of the new anti-inflammatory agent 2-(10,11-dihydro-10-oxodibenzo thiepin-2-yl) propionic acid. 1st communication: inhibitory effects of rat paw edema. Arzneimittel forschung 1986; 36:1796-800.
9. Tang HB, Inoue A, Oshita K. Zaltoprofen inhibits bradykinin-induced responses by blocking the activation of second messenger signaling cascades in rat dorsal root ganglion cells. Neuropharmacology 2005; 48:1035-42.
10. Matsumoto M, Inoue M, Ueda H. NSAID zaltoprofen possesses novel anti-nociceptive mechanism through blockage of B2-type bradykinin receptor in nerve endings. Neurosci Lett 2006; 397: 249-53.
11. Hirate K, Uchida A, Ogawa Y, Arai T, Yoda K. Zaltoprofen, a non-steroidal anti-inflammatory drug, inhibits bradykinin-induced pain responses without blocking bradykinin receptors. Neurosci Res 2006; 54: 288-94.
12. Shigeru F, Nobuyoshi A, Emiko K, Akio H, Yoshihiro K, Nobuhiko K, Atsuhiro I, Anne Matthews, Michael Hall, Tadashi K. Involvement of CYP2C9 and UGT2B7 in the metabolism of zaltoprofen, a nonsteroidal anti-inflammatory drug, and its lack of clinically significant CYP inhibition potential. J Clin Pharmacol 2002; 54: 295-303.
13. Carter SJ. Copper and Gun's: Tutorial Pharmacy, 6th ed., CBS Publishers and Distributors, Delhi 1998; 225.
14. Aulton ME. Pharmaceutics: The science of dosage form design, 1st ed., Churchill Livingstone, London 1998; 247.
15. Basak SC, Selvin CDS, Sabapathy R. Formulation and in-vitro evaluation of amoxicillin dispersible tablets. The Indian Pharmacist 2006; 5: 71-73.
16. Lachman L, Lieberman HA. Pharmaeutical dosage forms of tablets. Vol II, Marcel Dekker 1981; 241-243.
17. Indian Pharmacopoeia. Ministry of Health and Family Welfare. Government of India, Vol II, Delhi 1996; 350.
18. Chowdhary KPR, Rao NR. Formulation and evaluation of dispersible tablets with pregelatinised starch. Indian Drugs 1998; 35: 368-370.
19. Bolhuis GK, Zuurman K, Wierik GH. Improvement of dissolution of poorly soluble drugs by solid deposition on a superdisintegrant: II, The choice of superdisintegrants and effect of granulation. Eur J Pharm Sci 1997; 5:63-69.
20. Dong-Han W, Min-Soo K, Lee S, Park JS, Hwang SJ. Improved physicochemical characteristics of felodipine solid dispersion particles by supercritical anti-solvent precipitation process. Int J Pharm 2005; 301:199-208.