International Journal of Pharmacy and Biological Sciences
ISSN: 2321-3272 (Print), ISSN: 2230-7605 (Online)
IJPBS | Volume 6 | Issue 2 | APR-JUN | 2016 | 122-129
Original Research Article – Pharmaceutical Sciences

ZALTOPROFEN FAST DISINTEGRATING TABLETS: FORMULATION AND *IN-VITRO* EVALUATION STUDIES

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ABSTRACT

The main objective of the work was to carry out preparation of Zaltoprofen fast disintegrating tablets by selecting different nature and concentrations of super disintegrating agents in order to ensure rapid onset of at the administrated site i,e. mouth. In the current research work Zaltoprofen fast disintegrating tablets were formulated from F1-F9 by preferring three suitable disintegrating agents such as cross povidone, copvidone and plantago ovata with 2, 3 and 4 percentage concentrations by direct compression method and evaluated for all pre, post Compression parameters including In-vitro dissolution studies. Based on the obtained results Zaltoprofen (F6) formulation containing plantago ovata with 3 percentage shown myrid significance in all determined pre compressional parameters like bulk density, tapped density, angle of repose, carr's index and hausners ratio as well as post compressional parameters like hardness, friability, weight variation, wetting time, disintegration time, drug content including dissolution studies. All formulations of dissolution studies, the optimized formulation F6 has shown fastest, better release pattern and was found to be 98.9±1.98 within 30 minutes to ensure desirable pharmacological action in the mouth.

KEY WORDS

Zaltoprofen, Fast Disintegrating Tablets, Angle of repose, in vitro evaluation.

INTRODUCTION

Oral route is the most prominent route of drug delivery for both solids and liquids. In this concern, solid dosage forms are most popular because of dose accuracy, ease of manufacture, ease of administration, inexpensive, self medication and patient compliance. The most common type of solid oral dosage forms are tablets and capsules. The main drawback of solid dosage form is dysphasia which means swallowing of solids is difficult or painful. So these are uncommon for pediatrics, geriatrics, patients with mental problems and non cooperative patients. Due to this reason, development of mouth dissolving tablets is fascinated to increase the patient compliance without need of water. Mouth dissolving tablets are also called as rapid dissolving tablets, orodispersible tablets, fast dissolving tablets, fast disintegrating tablets, quick dissolving tablets. In USP, all above terms are expressed as orodispersible tablets.[1-2]

According to United States Pharmacopoeia, the orodispersible tablets may be defined as solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly within a matter of seconds when placed upon the tongue. This means that the tablets dissolve or disintegrate in the oral cavity without use of water. In this regard, the tablets need to improve disintegration time, dispersion time, drug release studies, bioavailability and patient compliance and also need to mask the bitter taste of the drug and to maintain the drug stable at

accelerated condition i.e. 40°C/75% RH up to 6 months period as per ICH guidelines.

The development of mouth dissolving tablets is mainly composed of super disintegrates, taste masking agents and flavoring agents to improve the patient compliance. Whenever swallowing of tablets are difficult, the mouth dissolving tablets place a prominent role for the patients.[3] In these regard Zaltoprofen chemically it was (2RS)-2-(10-oxo-10,11-dihydrodibenzo [b,f]thiepin-2-yl) propanoic acid, is nonsteroidal anti-inflammatory drug (NSAIDs) with powerful analgesic and anti inflammatory action. It has a unique action in inhibiting bradykinin (BK) induced nociceptive responses more potently than other NSAIDs[4]. It was obtained as white, crystals or crystalline powder is freely soluble in acetone, soluble in methanol and ethanol and practically insoluble in water and frequently which is used in the treatment of RA. In these RA patients it was necessary to get the rapid absorption from the site of administration. Based on these requirements, the present work planned to fabricate Zaltoprofen mouth dissloving tablets and their evaluation studies.

MATERIALS

Zaltoprofen (IPCA Pvt Ltd, Mumbai), Spray dried lactose, (DR.Reddy's Laboratories Hyderabad,) Crospovidone, Copovidone, Plantgo ovata, Colloidal silicon di oxide (Aurobindo Pharmaceuticals Hyderabad), Microcrystalline cellulose (PH-101), Neotame (SD Fine Chemicals Pvt Ltd, Mumbai), Magnesium stearate and Sodium lauryl sulphate (Qualikems Fine Chem Pvt Ltd, Vadodara). All the above following materials were either AR/LR grade were used in the above work and which were supplied from the manufacturer.

METHODOLOGY

Preparation of standard calibration curve for Zaltoprofen

Dissolve required quantity of Zaltoprofen (100mg) in same volume (100ml) of pH 6.8 buffer solution. From which, serial dilutions were made to obtain the concentration 2, 4, 6, 8, 10 & 12 mcg/ml of Zaltoprofen solutions. The absorbance was measured at 243 nm using UV-visible spectrophotometer[5].

Determination of drug-excipient compatibility studies:

One of the requirements for the selection of suitable excipients (or) carrier for pharmaceutical formulations is its compatibility. Hence, FTIR studies were carried out for pure Zaltoprofen as well as powder mixture of excipients by potassium bromide pellet method to confirm the absence of any possible chemical interaction between the drug and other polymers from 4000 to 400cm $^{-1}$.

Determination of precompressional parameters:

The angle of repose (θ) of the granules was determined by using funnel method. Bulk density (BD) and tapped density (TD) were calculated by formula: BD = Bulk mass/Bulk volume; TD = Bulk mass/Tapped volume. Compressibility index and Hausner's ratio of the granules was determined by using the formula: CI (%) = [(TD-BD/BD)] ×100 and HR = TD/BD, respectively[6]. The experiments were performed in triplicate and average values with SD were noted. The results were shown in Table: 02

Formulation of Zaltoprofen Fast disintegrating tablets

Direct compression method

Direct compression is very simple and cost effective method to formulate the oro dispersible tablets. This method is suitable for both low and high dose formulations due to the availability of free flowing excipients in the market. The selection of super disintegrates and taste masking agents play a major role for fast disintegrating technology[7].

The above selected Zaltoprofen was passed through mesh no 100 and mixed with sufficient quantity of super disintegrating agents such as crospovidone, copovidone and plantgo ovata etc. After that blend the required quantity of other excipients like spray dried lactose, microcrystalline cellulose as diluents, sodium lauryl sulphate as solubilizing agent , neotame as sweeting agent, colloidal silicon di oxide and magnesium stearate as glidant and lubricant, lemon juice as flavoring agent etc. by geometrical dilution. The powder mixture was compressed in an electrically driven Tablet punching machine (Rimek, Mumbai) using 8 mm punch to obtain tablets. The weight of the tablets was maintained at 300±7.5 mg. The composition of the tablets was given below Table: 01

Table: 01 Formulation of Zaltoprofen Fast disintegrating tablets from F1-F19

Ingrediants	F1	F2	F3	F4	F5	F6	F7	F8	F9
Zaltoprofen	80	80	80	80	80	80	80	80	80
Crospovidine	6	-	-	9	-	-	12	-	-
Copovidone	-	6	-	-	9	-	-	12	-
Plantago ovata	-	-	6	-	-	9	-	-	12
Spray dried lactose	140.2	140.2	140.2	132.4	132.4	132.4	124.6	124.6	124.6
MCC	60	60	60	60	60	60	60	60	60
Magnesium stearate	6	6	6	9	9	9	12	12	12
Sod.lauryl sulphate	3	3	3	3	3	3	3	3	3
Neotame	1.5	1.5	1.5	3	3	3	4.5	4.5	4.5
Coll. Silicon di oxide	3	3	3	3	3	3	3	3	3
Lemon flavour	0.3	0.3	0.3	0.6	0.6	0.6	0.9	0.9	0.9
Total weight (in mg)	300	300	300	300	300	300	300	300	300

Evaluation of postcompressional parameters:

The thickness of the tablet was measured by Digital vernier calipers. 20 tablets were selected at a random and average weight was calculated. Then individual tablets were weighed and the weight was compared with an average weight. Tablets were evaluated for hardness using Monsanto hardness tester and friability using Roche friabilator. For estimation of drug content, tablets were randomly selected and powdered finely. The powder equivalent to one tablet was added to 100ml of methanol in a conical flask and was placed on a rotary shaker. The solution was filtered through a 0.22µ filter then absorbance was measured using systronics UV–Vis spectrophotometer, against p^H 6.8 buffer solution as blank at a wave length of 243 nm[8].

For estimation wetting time, tablet was carefully placed on the surface of tissue paper in the petridish at room temperature. The time required for water to reach the upper surface of the tablets and completely wet them was noted as the wetting time.

The Water absorption ratio, R, was determined according to the following equation: $R = 100 (Wa - W_b) / W_b$; W_b and W_a are the weight before and after water absorption respectively. Disintegration of tablets was determined using a USP disintegration testing apparatus type II (Paddle) (Electrolab ED-2L, India). In which tablets were placed into an apparatus and disintegration time was recorded.

***In-vitro* dissolution study**

The drug release was determined using USP - II rotating paddle type apparatus (Electrolab TDT-08L, India) at 75 rpm using 900ml of p^H 6.8 buffer solution as dissolution medium and temperature maintained was 37 ± 0.5 ºC. Aliquot of 5 ml of dissolution medium was withdrawn at specified time intervals and the absorbance of solution was measured by UV- spectro photometric method at 243 nm and concentration of the drug was determined from standard calibration curve[9].

Stability study

Stability study was done for the optimized formulation for a period of three months at 40±2C°, 75±5% RH to provide evidence on how the quality of a drug substance varies with time under the influence of a variety of environmental factors such as temperature, humidity, light and enables recommended storage conditions.

RESULTS AND DISCUSSION

Zaltoprofen standard graph was plotted by taking absorbance on y-axis & concentration on x-axis. From the obtained data, it has produced a straight linear curve and the r^2 value was found to be 0.998 and obey's beer's law. The graph was shown in Figure 1.

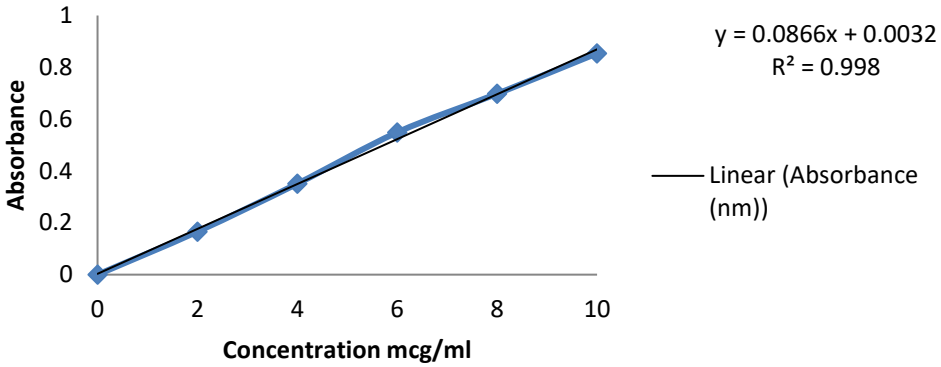

Figure: 01 Zaltoprofen standard graph

The compatibility studies were performed using FTIR spectrophotometer. The characteristic absorption peaks of Zaltoprofen pure drug and mixture of other excipients were obtained at different wave numbers. The characteristic peaks were observed aromatic-C-H stretching 2939.95 cm^{-1}, arile stretching-C-H 2360.44 cm^{-1}, C=O Stretching 1281.47 cm^{-1}, O-H stretching 1078.98 cm^{-1} and C-S-C stretching 1419.35 cm^{-1} obtained in pure Zaltoprofen and with exicipients were used. The above results were indicating that there was no incompatibility between the drug and excipients used. (Shown in Figure 2)

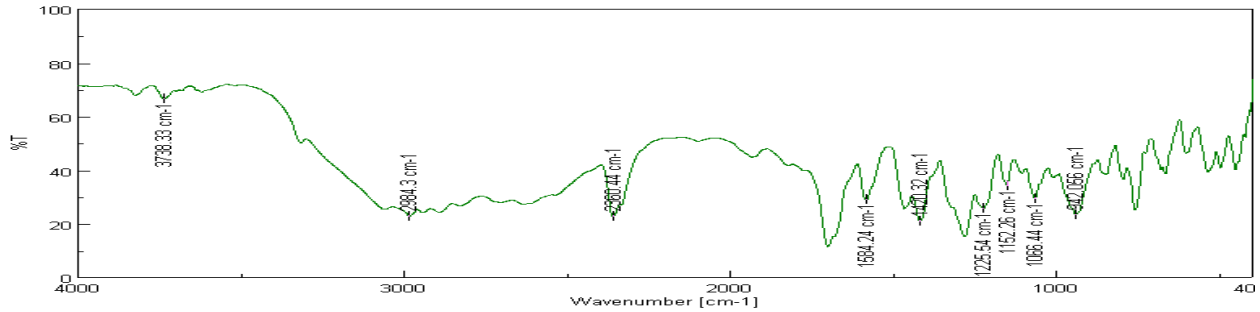

Figure: 02 FTIR-Spectrum of pure Zaltoprofen

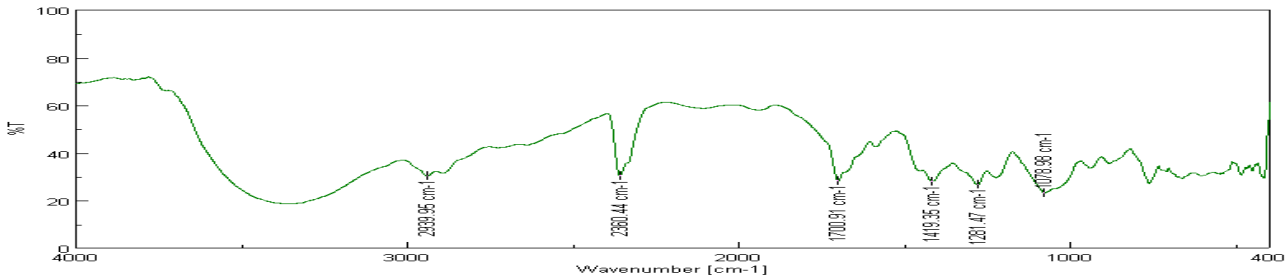

Figure: 03 FT-IR Spectra of Zaltoprofen with all Excipients

Evaluation of powder blend

The Zaltoprofen power blend was evaluated for various physical properties (Table 2). The bulk densities for the powder blend of Zaltoprofen formulations (F1-F9) ranged between 0.448± 0.007 g/ml to 0.706± 0.020 g/ml; and tapped density ranged between 0.565± 0.011 g/ml and 0.809± 0.016 gm/ml when determined by the tap densitometer. These values of bulk density indicate good packing characteristics. The Carr's index (CI) for all the formulations were ranged from 11.42± 1.446 to 20.59± 1.446, indicating desirable flow properties. The value of Hausner's ration was ranged from 1.130± 0.017 to 1.259± 0.023. The flow properties of powder blends were further analyzed by determining the angle of repose for all formulations values ranged between 20.20± 0.603 and 29.17± 0.242.

Table: 02 Evaluation of Zaltoprofen powder blend

Formulation	Bulk density (gm/ml)	Tapped density(gm/ml)	Angle of repose(θ)	Carr's Index	Hausner ratio
F1	0.448± 0.007	0.565± 0.011	29.17± 0.242	20.59± 1.446	1.259± 0.023
F2	0.524± 0.018	0.628± 0.03	28.71± 0.306	18.55± 1.425	1.228± 0.022
F3	0.565± 0.010	0.696± 0.014	27.39± 0.321	18.82± 1.565	1.232± 0.024
F4	0.654± 0.030	0.787± 0.028	23.83± 0.534	16.86± 0.916	1.20± 0.017
F5	0.572± 0.009	0.692± 0.013	25.57± 0.403	17.32± 1.415	1.207± 0.021
F6	0.674± 0.012	0.795± 0.017	23.55± 0.261	15.23± 0.352	1.167± 0.023
F7	0.691± 0.021	0.780± 0.013	21.63± 0.488	11.42± 1.446	1.130± 0.017
F8	0.706± 0.020	0.809± 0.016	22.09± 0.886	12.70± 1.36	1.147± 0.021
F9	0.670± 0.011	0.776± 0.015	20.20± 0.603	13.65± 1.567	1.169± 0.028

Evaluation of Zaltoprofen fast dissolving tablets

All the formulations (F1-F9) were produced under similar conditions to avoid processing variables. The weight variation, hardness, friability, thickness and content uniformity of all formulations were found to be within acceptable limits as per official specifications. Weight of the optimized Zaltoprofen FDTs formulation (F6) was 300.667±1.319 mg, hardness was 4.233±0.315 kg/cm^2 and thickness was 3.41±0.161 mm. The percentage friability of all the formulations was ranged from 0.520±0.044 to 0.597±0.067 which were less than 1% of their weight. The values of the hardness test and percent friability indicated good handling properties of the prepared Zaltoprofen FDTs. The drug content (assay) uniformity in the Zaltoprofen tablets was ranged from 98.01±0.730 to 99.04±0.606. Further Disintegration, wetting time and water absorption ratio of FDTs Zaltoprofen optimized formulation (F6) was found to be 45±0.4sec, 48±0.4 sec and 52±0.4sec respectively. (Shown in Table: 03)

Table: 03 Evaluation of Zaltoprofen Fast dissolving tablets

Formulation	Thickness (mm)	Hardness Kg/cm^2	Fraibility (%)	Wt.variation (mg)	Assay (%)	Disintegration time(sec)	Wetting time(sec)
F1	3.73±0.114	4.723±0.304	0.543±0.064	300.200±1.199	98.01±0.730	210±0.9	214±0.1
F2	3.57±0.171	4.622±0.301	0.583±0.063	300.333±1.405	98.82±0.657	181±0.4	189±0.6
F3	3.49±0.194	4.572±0.287	0.547±0.058	298.100±3.332	97.83±0.708	120±0.4	125±0.4
F4	3.87±0.121	4.822±0.308	0.583±0.062	301.900±1.212	98.16±0.577	95±0.4	97±0.2
F5	3.47±0.151	4.314±0.301	0.597±0.067	300.200±2.621	97.46±0.545	75±0.4	79±0.9
F6	3.41±0.161	4.233±0.315	0.523±0.062	300.667±1.319	99.04±0.606	45±0.4	48±0.4
F7	3.48±0.176	4.523±0.307	0.520±0.0474	301.100±0.466	98.07±1.067	122±0.4	127±0.5
F8	3.59±0.127	4.677±0.398	0.523±0.058	300.667±1.143	98.31±1.162	147±0.4	152±0.6
F9	3.93±0.188	4.876±0.198	0.520±0.044	299.101±2.242	98.17±0.606	240±0.2	250±0.4

***In-vitro* dissolution studies:**

The *In vitro* dissolution behavior of Zaltoprofen fast disintegrating tablets of all formulation from (F1 to F9) carried out in pH 6.8 phosphate buffer. In these studies, formulations F1, F2 and F3 were fabricated with 2% concentrations of super disintegrating agents, there after F3 has shown 82.40±2.78 percentage drug releases which was greater than (F1) 76.52±4.12 and (F2) 79.8±1.98 .

In case of formulations F4, F5 and F6 were manufactured with 3% concentrations of fast disintegrating agent and results were noted as F6 has released significant percentage release which was 98.9±1.89 within 30 minutes and it was greater than

(F4) 89.7±1.52, (F5) 91.7±1.47 and rest of other formulations.

As well as comparatively Formulations of F7, F8 and F9 has designed with 4% concentrations of disintegrating agents and progressed least release profile. It was found to be 80.1±2.13, 79.8±2.64 and 72.5 ±1.97 respectively due to increased concentration of super disintegrating agent which diminished the release profile.

Finally from the obtained results, it was concluded that 3% concentration of plantago ovate as fast disintegrating agent showed good in disintegration time, wetting time and dissolution rate of ZPF FTDs, The faster dissolution rate of F6 batch was optimized compared to all other formulations.

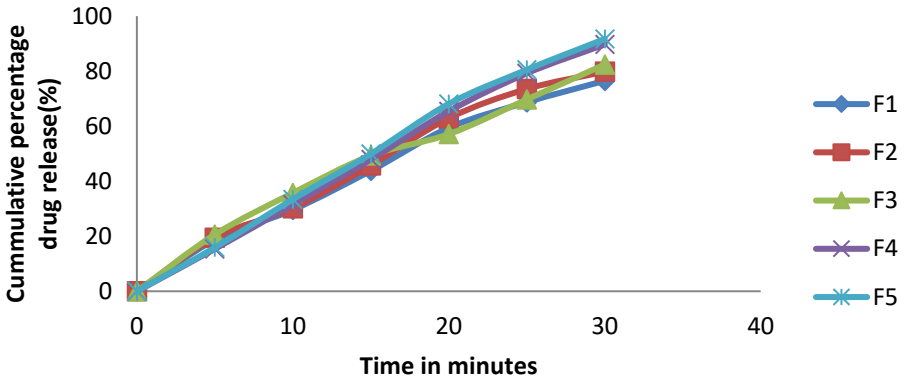

Figure: 04 *In-vitro* dissolution profile of Zaltoprofen Fast dissolving tablets from F1-F5

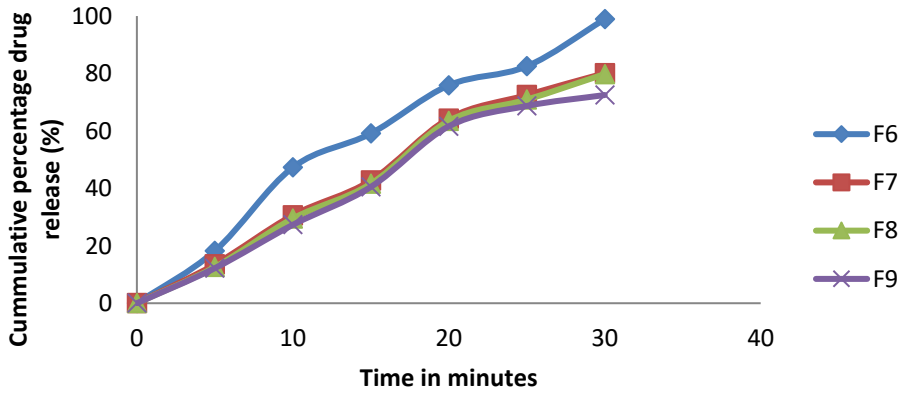

Figure: 05 *In-vitro* dissolution profile of Zaltoprofen Fast dissolving tablets from F6-F9

The accelerated stability studies (Table: 4) were carried out on the optimized formulation, ie., F6. The formulation was stored at 40±2C°, 75±5% RH for 3 months to assess their long term stability. After stability study, tablets were subjected to various post copmpressional parameters and *in vitro* drug release study. The results indicated that, there were no changes observed in tablets characteristics after stability study and it was shown in Table: 04

Table: 04 Stability studies of optimized formulation (Zaltoprofen–F6) at 40±2 °C & 75±5%RH

Time period	Thickness (mm)	Hardness Kg/cm^2	Fraibility (%)	Wt.variation (mg)	Assay (%)	Disintegration time(sec)	Wetting time(sec)
Initial	3.41±0.161	4.233±0.315	0.523±0.062	300.667±1.319	99.04±0.606	45±0.4	48±0.4
Ist month	3.40±0.159	4.123±0.314	0.519±0.058	300.658±1.317	99.03±0.604	42±0.3	42±0.6
II nd month	3.39±0.147	4.120±0.309	0.517±0.054	300.649±1.314	99.02±0.601	40±0.2	39±0.7
III rd month	3.38±0.142	4.198±0.305	0.515±0.050	300.640±1.310	99.01±0.597	39±0.2	37±0.5

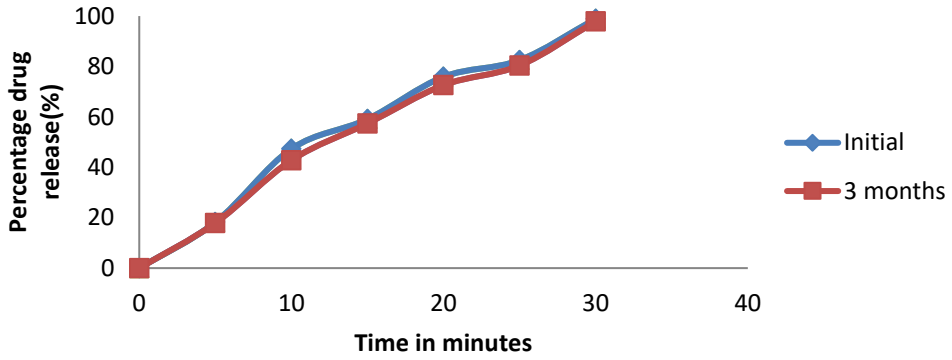

Figure: 06 *In-vitro* dissolution studies of optimized formulation (Zaltoprofen-F6) at 40±2 °C & 75±5%RH at Initial and after 3 months

SUMMARY AND 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 revealed that there was no drug-excipients interaction between ZPF and excipients. It was observed that the formulation F6 containing 3 % (w/w) of plantago ovata was found to be promising showing disintegration time of 45±0.4 seconds, wetting time of 48±0.4 second and highest dissolution rate (98.9±1.89) in 30 min. when compared to other formulations of ZPF. It was concluded that super disintegrants such as plantago ovata showed better disintegrating time, wetting time and dissolution property than the cross povidone and copovidone in the formulation of fast disintegrating tablets.

REFERENCES

1. Vemula VR, Legishetty V and Lingala S. Solubility enhancement techniques. International Journal of Pharmaceutical Sciences Review and Research. 2010, 5: 41-51.
2. Varshney HM and Chatterjee A. Formulation, Evaluation and In-vitro Release Characteristics of Zaltoprofen Suppositories. Asian Journal of Pharmaceutical and Clinical Research. 2012, 4: 235-238.
3. Bansal M, Bansal S and Garg G. Formulation And Evaluation Of Immediate Release Tablets Of Zaltoprofen, Scholar Academic Journal of Pharmacy. 2013, 2: 398-705.
4. Papdiwal A, Pande V and Sagar k. Design and characterization of zaltoprofen nano suspension by precipitation method. Scholar Research library. 2014, 6: 161-168.
5. Katageri AR and Sheikh MA. Cyclodextrin A gift to pharmaceutical world review. International Research Journal of Pharmacy. 2012, 3: 52-56.
6. Khan Y and Durakshan M. Cyclodextrin: an overview. International Journal of Bio Assay. 2013, 55-57.

7. Harikrishna E, Gupta RM and Jyothi S. Spherical crtstallization of zaltoprofen for enhancement of micromeritic properties and dissolution rate. International Journal of Pharmaceutical Science and Research. 2012, 3: 2024-2030.
8. Akiladevi D, Shanmugapandiyan P, Jebasingh D and Basak S. Preparation and evaluation of paracetamol by solid dispersion technique. International Journal of Pharmacy and Pharmaceutical Science. 2011, 3: 188-191.
9. Singh SK, Kumar S, Chander P and Kumar P. Application of some novel techniques for solubility enhancement of mefenamic acid, a poorly water soluble drug. International Journal of Pharmaceutical Science and Drug Research. 2009, 1: 164-17.

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