IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Research Article
January 2020 Vol.:17, Issue:2

Studying the Effect of Different Super Disintegrants on the *In-Vitro* Release of Fluoxetine Hydrochloride Fast Dissolving Tablets

IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Maha A. Marzouk, Dina A. Osman, Omnia S. Mohammed*

Pharmaceutics Department, Faculty of Pharmacy, Al-Azhar University, Nasr City, Cairo, Egypt.

Submission: 24 December 2019
Accepted: 29 December 2019
Published: 30 January 2020

HUMAN JOURNALS
www.ijppr.humanjournals.com

Keywords: Fluoxetine HCl, Fast dissolving tablets, *In-vitro* dissolution, Crospovidone

ABSTRACT

The objective of this work is to design and evaluate Fluoxetine HCl (FLX) fast dissolving tablets (FDTs) using different super disintegrants such as crospovidone (CP), croscarmellose (Ac-di-sol), indion and sodium starch glycolate (SSG), at different concentrations of 2%, 3%, 4% by direct compression method and studying their effect on the *in-vitro* release of FLX HCl. The powder blend of FDTs was evaluated for the pre-compression parameters and the values were within prescribed limits, Also the prepared tablets were evaluated for post-compression parameters e.g. wetting time, water absorption ratio, disintegration time, content uniformity and *in-vitro* dissolution which also were found to be satisfactory and within the limits. Upon comparison the effect of different super disintegrants on the *in-vitro* release of FLX from the prepared tablets, it was as the following descending order: crosspovidone> crosscarmellose> sodium starch glycolate> indion, Also it was found that as the concentration of super disintegrant increase; the time of *in-vitro* release decrease, hence crospovidone of concentration 4% had the least *in-vitro* release time.

INTRODUCTION

The tablet is still the most convenient dosage form existing today due to ease of self-administration, compact in nature, easy to manufacture, also it can be given in an accurate dose[1]. One main drawback of solid dosage forms is the difficulty in swallowing (dysphagia) or chewing for some patients mainly in pediatric and geriatric patients. The problem of swallowing is a common experience in geriatric patients due to choking fear, hand tremors, dysphasia and in young patients due to undeveloped muscular and nervous systems and in schizophrenic patients which leads to poor patient compliance[2]. Difficulties in swallowing of tablets and capsules are also occurring when water is not available, in diarrhea, common cold associated with coughing, allergic condition, and bronchial infection[3].

The fast-dissolving solid dosage form turns into a soft paste or liquid form which makes swallowing easier, and thus it lacks the risk of choking[4]. According to EP, the FDT should disperse or disintegrate in less than 3 minutes. The basic perspective in the development of ODT is the use of super disintegrants i.e. croscarmellose, sodium starch glycolate (primogel, exploited), polyvinylpyrrolidone (polyplasdone), etc., which provide rapid dispersion of the tablet before putting in the mouth so that the drug is rapidly released in the saliva[5]. In addition to those definitions, FDA recommends that orally dissolving tablets should be considered as solid oral preparations that disintegrate fast in mouth, with an *in-vitro* disintegration time of approximately less than or equal to 30 seconds, when the disintegration test conducted to the United States Pharmacopeia (USP) disintegration test method[6].

FLX has become the first-line drug in the pharmacotherapy of patients with depression. This is because it has tolerability and safety advantages over the tricyclic agents[7]. FLX is a selective serotonin reuptake inhibitor (SSRI) for oral administration. Since its approval and introduction for the treatment of depression at the beginning of 1988, FLX has become the most prescribed antidepressant drug around the world. It is the only antidepressant medication that has the Food and Drug Administration (FDA) approval for the treatment of depression in children and adolescents (FDA, 2003). The concept of formulating fast dissolving tablets containing FLX offers a suitable and practical approach in serving the desired objective of rapid disintegration and dissolution characteristics with increased bioavailability.

Advantages of fast dissolving tablets[8,9]:

1. Accurate dosing: Being unit solid dosage form, provide the luxury of accurate dosing, ease of portability and manufacturing, good physical and chemical stability and an ideal alternative for pediatric and geriatric patients.

2. Enhanced bioavailability: Bioavailability of drugs is enhanced due to absorption from mouth, pharynx, and esophagus.

3. Rapid action: Fast onset of therapeutic action as the tablet gets disintegrated rapidly along with quick dissolution and absorption in the oral cavity.

4. Patient compliance: No need of water to swallow the dosage form. Hence, it is convenient for patients who are traveling and do not have immediate access to water.

5. Ease of administration: Convenient to administer especially for geriatric, pediatric, mentally disabled and bedridden patients who have difficulty in swallowing.

6. Obstruction free: No risk of suffocation in airways due to physical obstruction when swallowed, thus providing improved safety and compliance.

7. Enhanced palatability: Good mouthfeel, especially for pediatric patients as taste masking technique is used to avoid the drug bitterness.

8. Simple packaging: No specific packaging is required. It can be packaged in push-through blisters.

9. Business avenue: Provide new business opportunities in the form of product differentiation, line extension, uniqueness and life cycle management.

10. Cost effective: Conventional processing and packaging equipment allow the manufacturing of tablets at a low cost.

11. Stability: for an extended period of your time, since the drug remains in solid dose type until it's consumed. So, it combines the advantage of solid dose type in terms of stability and liquid dose type in terms of bioavailability.

An ideal ODT should meet the following criteria[10],

1-Water is not needed to swallow, however, it should dissolve or disintegrate within the mouth within a few seconds.

2- Be compatible with taste masking.

3- Be moveable while not fragility concerning.

4- Have a pleasing mouthfeel.

5- Leave minimum or no residue within the mouth upon oral administration.

6- Exhibit low sensitivity to conditions as temperature and wetness.

7- Allow the manufacture of the pill mistreatment standard process and packaging equipment at low value.

MATERIALS AND METHODS:

MATERIALS:

FLX, crospovidone, croscarmellose, sodium starch glycolate, indion, and microcrystalline cellulose were gift samples kindly supplied by Epico Co., (Egypt).

Establishing of calibration curve of FLX HCl:

A stoke solution containing 100 µg/ml of drug in PBS of pH 6.8 was prepared. Aliquots of 0.2, 0.4, 0.6, 0.8, 1, 1.2, 1.4 and 1.6 milliliters were separately diluted to 10 ml with PBS of pH (6.8) using a suitable measuring flask to produce concentrations of 2, 4, 6, 8, 10, 12, 14 and 16 µg/ml respectively. The absorbance of the prepared solutions was measured spectrophotometrically at a predetermined wavelength λ_{max} of (225 nm) versus PBS of pH (6.8) as a blank[11].

Formulation of FDTs By direct compression (F1-F12):

Ingredients were passed through mesh screen no. 60 and weighed in geometrical order. The drug (Table No. 1) and other excipients (except magnesium stearate), was mixed in ascending order of their weight. The powder mixture was blended for 20 min to have a

uniform distribution of the drug in the formulation. Then, magnesium stearate was added and mixed for not more than 1 min (to ensure good lubrication). All the materials were directly compressible so this uniformly mixed blend was compressed into tablets using a single tablet punching machine.

Table No. 1: Composition of FLX FDTs (1-30).

F	Drug (mg)	Superdisintegrants (%)				Excipients (mg)				
		CP	Ac-di-sol	SSG	Indion	Avicel 101	Sacchrine .Na	Mg. st	talc	Mannitol Up to
F1	10	2	-	-	-	60	1	2	1	200
F2		3	-	-	-					
F3		4	-	-	-					
F4		-	2	-	-					
F5		-	3	-	-					
F6		-	4	-	-					
F7		-	-	2	-					
F8		-	-	3	-					
F9		-	-	4	-					
F10		-	-	-	2					
F11		-	-	-	3					
F12		-	-	-	4					

Drug-excipients compatibility

1-Differential Scanning Calorimetry (DSC):

The DSC thermograms were recorded for the physical mixture of drug with different super disintegrants, to detect drug-polymers compatibility. Accurately weighed samples were placed on an aluminum plate, sealed with aluminum lids and heated at a constant rate of 5ºC /min, over a temperature range of 0 to 250ºC.

2-Fourier Transform Infrared Spectroscopy (FTIR) :

FTIR spectra for the physical mixture of drugs with different super disintegrants were recorded to detect drug-polymers interaction, using a Fourier transform infrared spectrophotometer. The IR spectrum of the samples was prepared using KBr (spectroscopic grade) disks using hydraulic pellet press at a pressure of seven to ten tons. The scanning range was 400-4000 cm^2.

Evaluation of Blend:

The prepared blend is evaluated using the following tests.

a- Angle of repose:

The angle of repose was determined by using the funnel method. The accurately weighed blend was taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap of the blend. The drug excipient blend was allowed to flow through the funnel freely on to the surface. The diameter of the powder cone was measured and the angle of repose was calculated using the following equation[12].

$$\tan \theta = h/r \qquad \theta = \tan^{-1} h/r$$

Where, θ = Angle of repose. r = Radius of the cone. h = height of the cone.

b- Bulk density:

Bulk density was determined by pouring a weighed quantity of tablet blend into a graduated cylinder and measuring its height. Bulk density is the ratio of the mass of tablet blends to bulk volume. It was calculated in gm/cm^3 by the formula,

Bulk Density (BD) = Weight of granules (m) /untapped volume of granules (v)[13].

c- Tapped density:

An accurately weighed amount of tablet blend is poured in a graduated cylinder and its height is measured. Then the cylinder was allowed to 100 taps under its weight onto a hard surface. The tapping was continued until no further change in height was noted it was calculated in gm/cm^3 by the formula[14].

Tapped Density (TD) = Weight of granules (m) / tapped volume of granules (v).

Here; m = weight of powder or granules (gm).

v = Tapped Volume (cm^3).

d- Carr's index:

Carr's compressibility index was determined by the given formula[14],

$$I=Dt-Db/Dt\times100$$

Where, Dt denotes the tapped density, and Db is the bulk density of the powder.

e- Hausner's ratio:

Hausner's ratio was determined by the given formula[15]:

$$\text{Hausner's ratio} = Dt/Db$$

Where, Dt shows the tapped density, Db is the bulk density.

Lower Hausner's ratio (<1.25) indicates better flow properties than higher ones (>1.25).

Evaluation of the prepared FLX FDTs:

The prepared tablets from each formulation were subjected to the following quality control tests.

a Drug content:

Five tablets from each formulation were randomly selected, accurately weighed. Each tablet was pulverized to a very fine powder and a known amount of drug that is equivalent to 10 mg of FLX was transferred into a 100-ml volumetric flask. Phosphate buffer solution of pH 6.8 was used to dissolve the drug and the solution was made up to the mark. Then 1 ml was withdrawn into a 10-ml volumetric flask and diluted with buffer solution. The solution concentration was measured spectrophotometrically at 225 nm and the concentrations of drug in µg/ ml was determined by using the regression equation[16].

b Weight variation test:

From whole formulae, five tablets were taken randomly and then compared with the average weight for the weight variations[17].

USP 30-NF25 limits for weight variation in case of tablets weighing up to 130mg or less is ± 10%, 130 mg to 324 mg is ± 7.5% and more than 324 mg is ± 5%.

c Thickness:

The thickness and diameter of the tablets were determined using a micrometer screw gauge. Five tablets from each type of formulation were used and average values were calculated. It is expressed in mm[18].

d Hardness:

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablet of each formulation was determined using Hardness tester[19].

e Friability :

To achieve % friability within limits (0.1-0.9%) for an FDT is a challenge for a formulator since all methods of manufacturing of FDT are responsible for increasing the % friability values. Friability of each batch was measured in "Electro lab friabilator". Ten pre-weighed tablets were rotated at 25 rpm for 4 min or a total of 100 revolutions, the tablets were then reweighed and the percentage of weight loss was calculated by the following equation[20].

Percentage friability = (Initial weight - Final weight) / Initial weight x 100

f Wetting time:

A piece of tissue double folded paper was placed in a Petri dish containing 6ml of water. The tablet was placed on the paper, and the time for complete wetting of the tablet was measured in seconds. The method was slightly modified by maintaining water at 37ºC[21].

g Water Absorption Ratio (R):

The weight of the tablet before keeping in the petri dish was noted (Wb) using a digital balance. The wetted tablet from the petri dish was taken and reweighed (Wa`). The water absorption ratio, R, was determined according to the following equation[22]:

$$R = 100 (Wa – Wb)/ Wb$$

Where, Wa= Weight of the tablet after absorption, Wb= Weight of the tablet before absorption.

h *In-vitro* Disintegration test:

The test was carried out on 6 tablets using the apparatus specified in I.P.-1996 distilled water at 37°C ± 2°C was used as a disintegration media and the time in the second taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured in seconds[23].

i *In-vitro* release study:

The *in-vitro* release study was carried out in the USP dissolution test apparatus type 2 known (Paddle dissolution apparatus), using phosphate buffer of pH 6.8 as dissolution medium (900ml) and the temperature maintained at 37 ± 0.5ºC. The speed of the paddle was set at 50 RPM, then 5 ml dissolution medium was withdrawn and the same amount (5ml) of fresh medium was replenished to the dissolution medium. The calculations of the concentration were calculated by referring to the standard curve at λ_{max} 225 nm. The release of the drug was performed in replicates of three[24].

RESULTS AND DISCUSSION:

Calibration curve of FLX HCl :

The calibration curve of FLX HCl was linear (R^2 = 0.999) over the concentration range of 2-16 µg/ ml. the solution of FLX HCl obeys Beeŕ s lambert law within the tested concentrations of the drug at the predetermined λ_{max} 225 nm. The absorbance of each sample was plotted against the corresponding concentration as shown in figure no.1.

Table No. 2: Relation between the concentration of FLX HCl in pH 6.8 and absorption at λ_{max} 225 nm.

FLX conc (µg/ml)	Absorbance ± S.D.
0	0.0
2	0.09 ± 0.002
4	0.15 ± 0.004
6	0.23 ± 0.012
8	0.3 ± 0.006
10	0.37 ± 0.003
12	0.444 ± 0.015
14	0.518 ± 0.008
16	0.594 ± 0.001

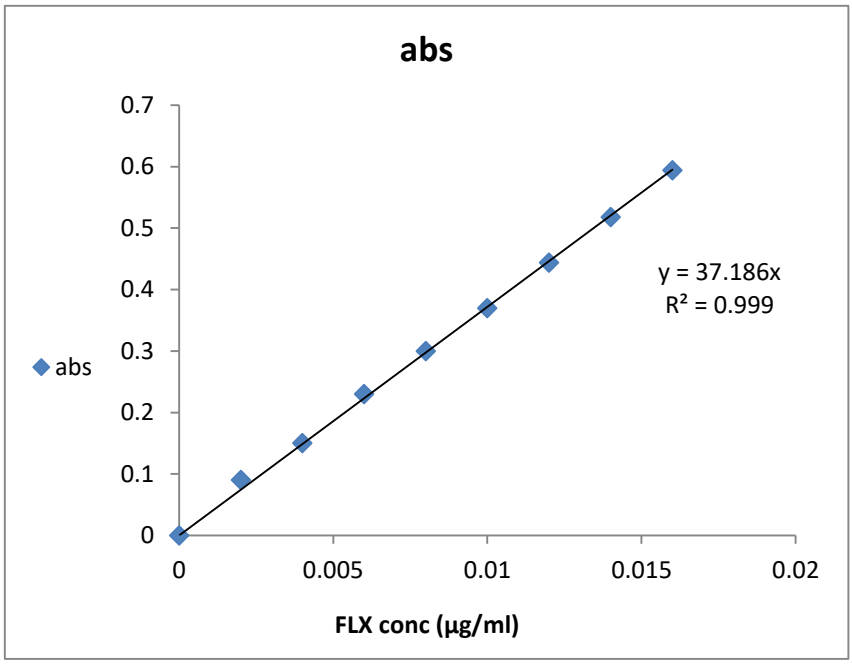


Figure No. 1: Standard Calibration curve of FLX in PBS of pH 6.8 at λ_{max} 225 nm.

DSC and FTIR studies

DSC thermogram of FLX was shown in Figure no. 2, a single sharp endothermic peak at a temperature range between 154 and 160°C, with a T peak of 157.5°C[25]. The endothermic event corresponding to FLX's melting point (157–162°C) as per USP. The characteristic FTIR absorption peak of FLX HCl was shown in Figure no. 3, for C-F stretching was around 1107 cm^{-1}, C=C stretching was located at 1564 Cm^{-1}, N-H stretching was seen at 3010 cm^{-1}, C-H stretching for phenyl group was seen at 1947 cm^{-1}, C-H bending appeared at 1445 cm-1 and 1188 cm^{-1}, C-N vibration was present in pure FLX HCl powder sample[26].

The DSC thermograms of FLX with different super disintegrants showed no change in the endotherm of the pure drug of FLX, indicating the compatibility. The IR spectra of all the tested samples showed the prominent characterizing peaks of pure FLX which confirmed that no chemical modification of the drug had been taken place and no chemical interaction between drug and polymers[27].

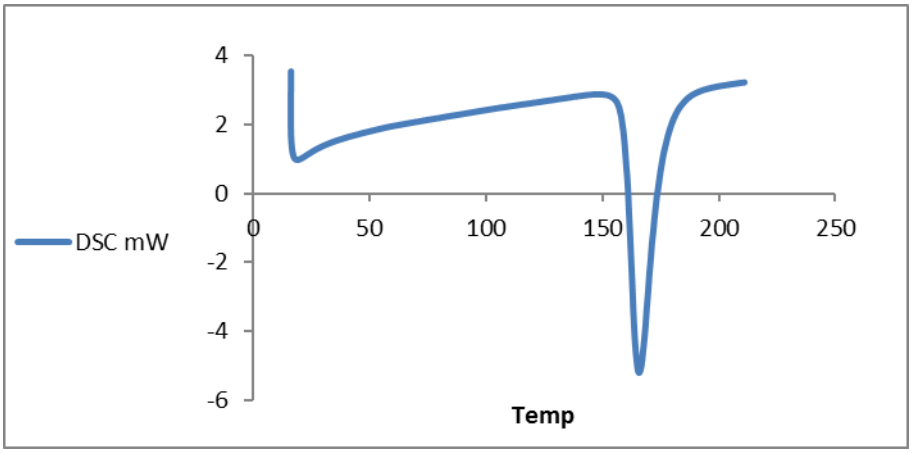


Figure No. 2: DSC thermogram of FLX HCl.

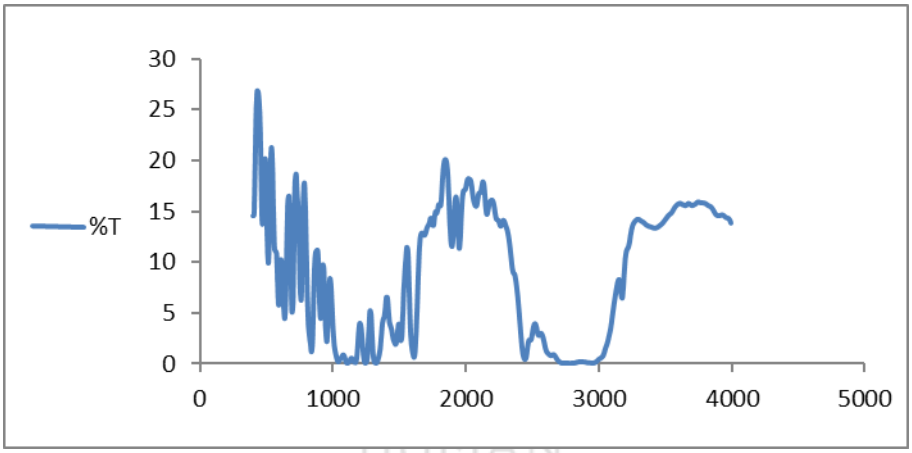
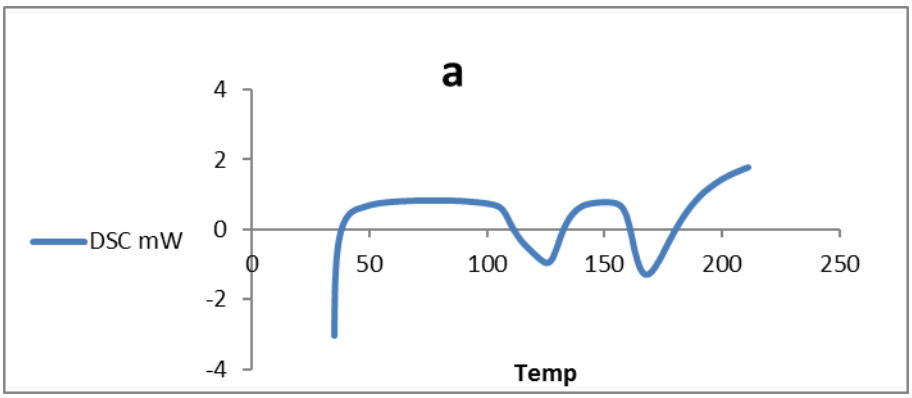


Figure No. 3: FTIR spectra of FLX HCl.



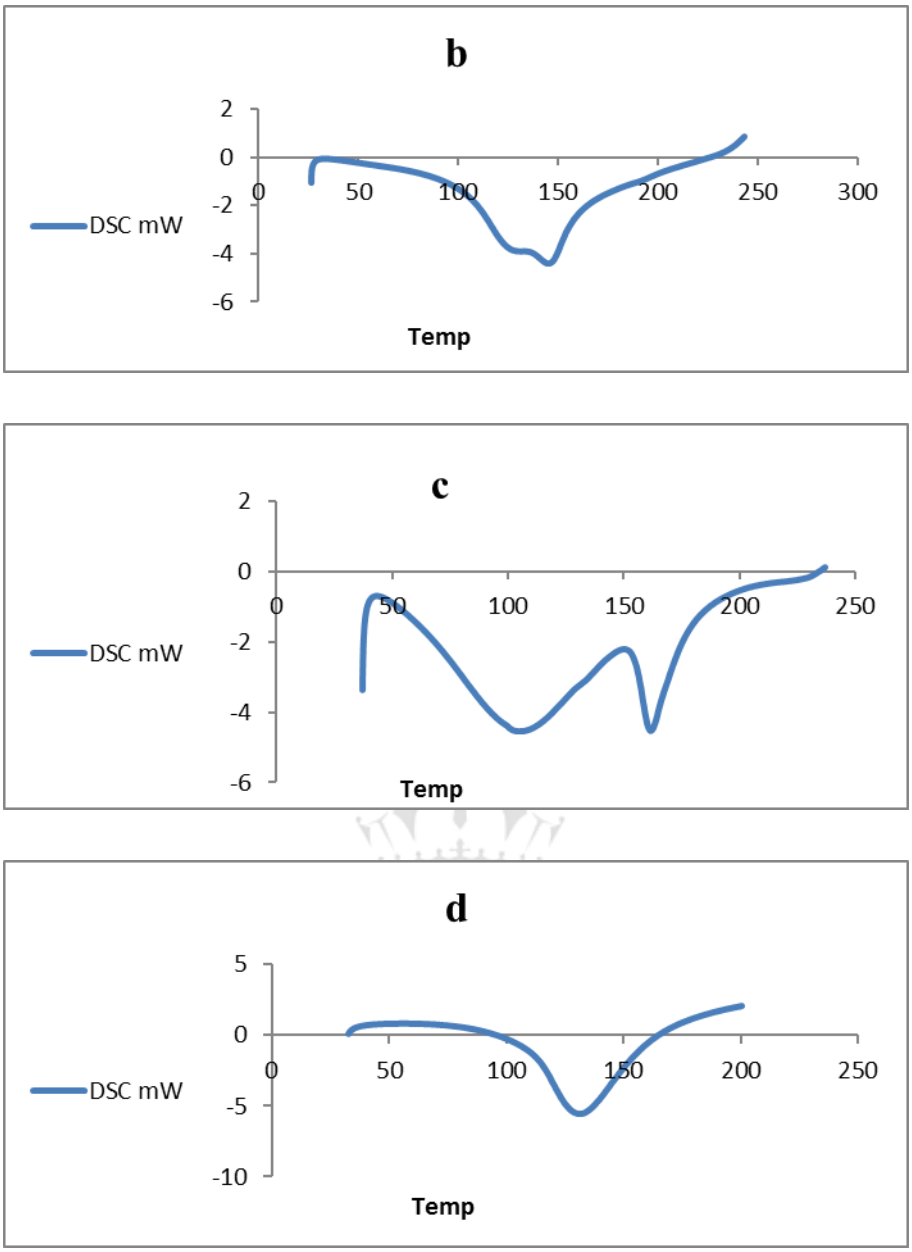


Figure No. 4: DSC thermogram of FLX HCl physical mixture with,

a- CP. b- Ac-di-sol. c- SSG. d- indion.

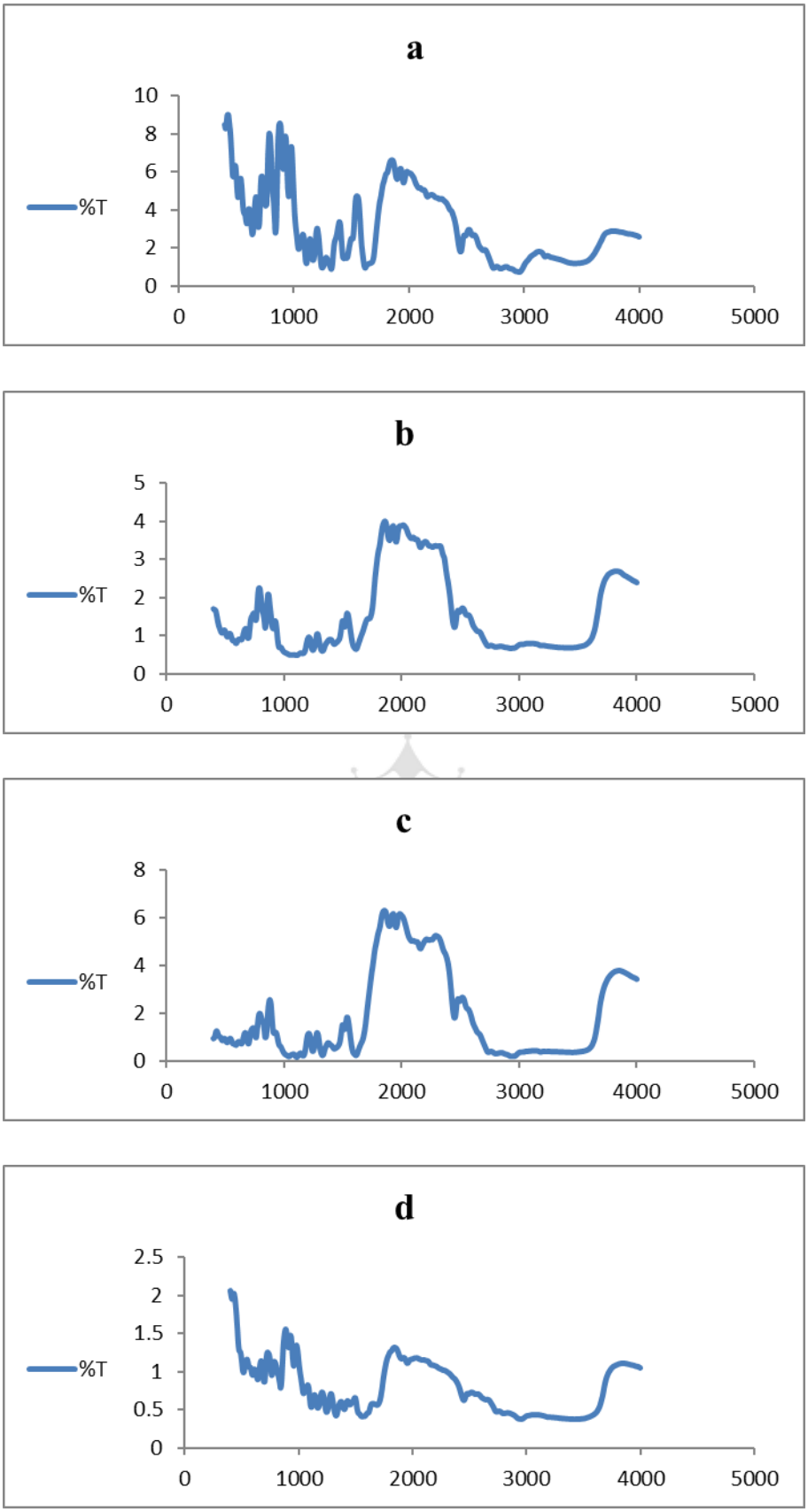


Figure No. 5: FTIR spectra of FLX physical mixture with, a- CP. b- Ac-di-sol. c- SSG. d- indion.

Pre-compression evaluation

a-Angle of repose:

The angle of repose for the formulated blend was carried out and the results were shown in table no. 3. It concludes all the formulations blend was found to be in the range 26.85° to 29.36° which falls within the official USP limits.

b-Powder density:

All formulae exhibited values of Hausner's ratio between 1.079 to 1.184 which indicates excellent to good flowability. All formulae exhibited values of CI between 7.40 to 15.587 which indicate excellent to good flowability.

Table No. 3: Characterization of the prepared powder blends of FLX FDTs.

Formulae	Bulk density gm/ml)	Tapped density gm/ml)	Carr's index (%)	Angle of repose (θ)	Hausner's ratio
F1	0.502	0.549	8.561	27.13	1.093
F2	0.497	0.544	8.639	28.04	1.094
F3	0.417	0.494	15.587	28.47	1.184
F4	0.492	0.554	11.191	29.08	1.126
F5	0.435	0.484	10.124	27.32	1.113
F6	0.476	0.524	9.161	27.22	1.101
F7	0.478	0.523	8.604	28.22	1.094
F8	0.454	0.499	9.018	26.85	1.099
F9	0.488	0.527	7.40	28.19	1.079
F10	0.485	0.533	9.005	27.21	1.098
F11	0.451	0.495	8.889	29.36	1.097
F12	0.480	0.529	9.263	27.01	1.102

Evaluation of the prepared FLX FDTs.

a- Content uniformity :

Table no.4 shows the content uniformity of all formulae. It was found that all formulae comply with the pharmacopoeial requirement regarding the content uniformity which is (90-

100%) **(USP, 2011)**. FDTs drug content ranged from 95.5- 100.1 % indicating a uniform distribution of a drug in the tablets.

b- Thickness :

The thickness of the prepared tablets is tabulated in table no. 4. Mean thickness values ranged from 2.85- 2.98 mm.

c- Hardness :

Table no.4 shows the different hardness values of tablets manufactured by different methods. The average values of hardness ranged from 3.65- 4.52 kg/cm^2.

d- Friability :

Tablet friability is an indicator of tablets' physical strength. The mean percent of tablet friability ranged from 0.304- 0.657 % that was less than 1% in all formulations as shown in table no. 4. Also, tablets show no breaks, cracking or capping during the test ensuring that these tablets are mechanically stable.

e- Uniformity of weight :

Weight variation test is performed to ensure uniformity in the weight of tablets in a batch. Table no. 4, shows the uniformity of the weight of different formulae. The mean weight of all formulations ranged from 198.32- 201.67 mg.

Table No. 4: Post compression parameters of FLX FDTs

F	Drug content (%)	Thickness (mm)	Hardness (Kg/cm^2)	Friability (%)	Average weight (mg)
F1	99.2±0.08	2.98±0.01	3.76±0.1	0.493±0.04	201.67±0.7
F2	95.9±0.12	2.927±0.03	3.75±0.13	0.506±0.01	199.33±0.5
F3	95.5±0.03	2.936±0.01	3.65±0.21	0.497±0.05	198.32±0.4
F4	96.4±0.20	2.91±0.012	4.52±0.3	0.54±0.02	199.23±0.8
F5	99.7±0.19	2.93±0.036	3.71±0.16	0.657±0.04	198.66±0.3
F6	98.9±0.04	2.933±0.04	3.83±0.1	0.304±0.05	199.33±0.4
F7	100.1±0.01	2.963±0.01	3.76±0.22	0.406±0.03	200±0.65
F8	99.1±0.21	2.853±0.02	3.76±0.15	0.570±0.01	200.66±0.1
F9	97.3±0.05	2.95±0.07	3.89±0.13	0.561±0.04	200±0.62
F10	99.5±0.22	2.95±0.015	4.35±0.22	0.491±0.03	200±1.07
F11	98.1±0.23	2.95±0.034	3.66±0.3	0.537±0.01	199.66±0.9
F12	98.8±0.06	2.94±0.01	4.36±0.11	0.508±0.02	199±0.26

*****All the values are expressed as mean± SD.

f- wetting time and water absorption ratio :

The wetting time corresponds to the time taken for the tablet to disintegrate when kept motionless on the tongue[28]. Wetting is closely related to the inner structure of tablets. Table no.5 shows the average wetting times and water absorption ratios of different formulations. The tablets prepared had wetting time values ranged from 9.64-13.53 seconds. It was evident from the water absorption ratio studies that all the formulations were absorbed the nearly equal amount of water and ranged from 66.33- 69.75%.

g- *In-vitro* disintegration time :

Table no.5 shows the results of the disintegration time of different formulations which is ranged from 9.31-14.71 seconds. The results of the in-vitro disintegration time of all the tablets were found to be within the prescribed limits and satisfied the criteria of fast dissolving tablets.

Table No. 5: Post compression parameters of FLX FDTs (F1 - F12).

Formulation code	Water absorption ratio (%)	Wetting time(Sec)	Disintegration time (Sec)
F1	66.33	10.33±1.15	11.23±2.44
F2	68.24	10±2.00	9.96±1.81
F3	68.56	9.64±3.02	9.47±2.07
F4	67.34	11.19±1.59	11.67±2.15
F5	69.18	10.34±2.23	10.56±2.56
F6	69.01	10±1.42	9.31±1.0
F7	67.89	12.33±2.11	12.33±2.52
F8	69.54	11.75±1.64	11.45±1.86
F9	69.75	11±3.01	10.09±0.05
F10	66.57	11.31±1.17	13.44±0.10
F11	69.39	13.53±1.25	13.25±2.27
F12	66.79	13.41±1.89	14.71±1.79

h- *In-vitro* dissolution study :

Figures 6&7 show the *in-vitro* dissolution performance of different formulae in comparison with commercial oral tablets of Fluoxetine (Prozac). It the super disintegrant, CP (4%) seems to be the best. This is due to its highly porous structure and water wicking mechanism into the porous network of tablets and hence increases in the concentration of CP accounts for rapid drug release. CP containing tablets rapidly exhibits high capillary activity and pronounced hydration with a little tendency to gel formation. Also, the rapid increase in the dissolution of FLX tablets containing Ac-di-sol may be due to rapid swelling and rapid disintegration into primary particles[29].

The release is in the following descending order of super disintegrants: CP > Ac-di-sol > SSG > indion. Also, it was clear from the obtained results that, the concentration of disintegrating agents directly proportional to the dissolution rate, e.g. dissolution time decrease by increasing disintegrants concentration. Hence, concentration of super disintegrant (4%) is better than 3% and 2%, but it was observed that indion is more effective in concentration 2%, this is due to concentration of super disintegrant crossing the critical

concentration of super disintegrant, so more amount of phosphate buffer required to swell and to disintegrate the tablet[30].

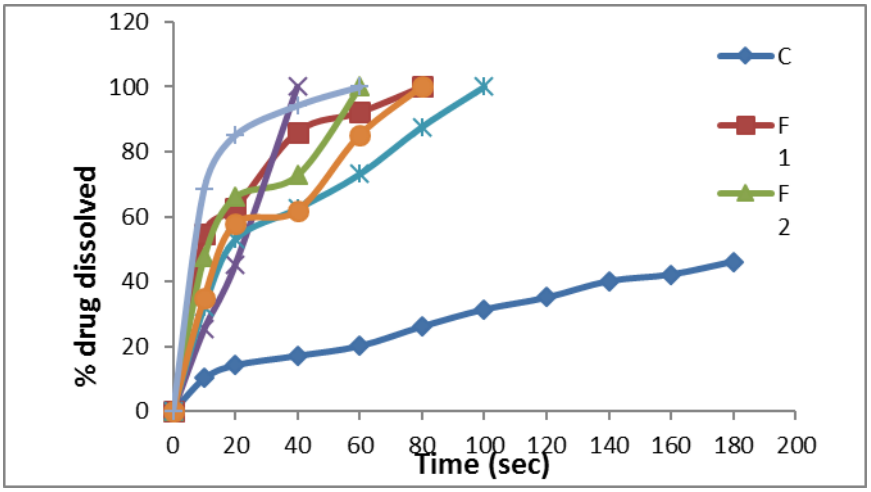


Figure No. 6: Percentage FLX dissolved from FDTs in presence of CP and Ac-di-sol.

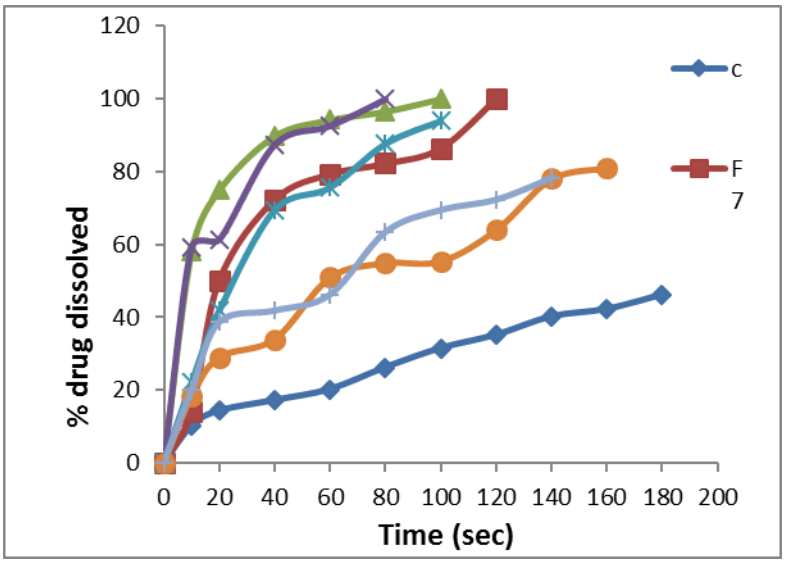


Figure No. 7: Percentage FLX dissolved from FDTs in presence of SSG and indion.

CONCLUSION

In the present study, the disintegrating properties of the Crosspovidone, croscarmellose sodium, Sodium starch glycolate, and indion on the *in-vitro* release of Fluoxetine HCl had been studied. First, fast-dissolving tablets were formulated. DSC FTIR studies showed no interaction between the drug and the disintegrants. Then, pre-compression and post-compression parameters for the drug were evaluated and were found satisfactory & within the limits. All the superdisintegrants showed a rapid disintegration, which is required for

faster drug dissolution and improved bioavailability. Overall, the results suggest that the convenience of the formulation of fast dissolving tablets of Fluoxetine containing Crosspovidone (4%) as super disintegrant.

REFERENCES

1. Habib W, Hontz J. Fast dissolving drug delivery system critical review in therapeutics, Drug carrier system. pmed. 2000, 1:61-72.
2. Noorjahan A, Amrita B, Kavita S. In vivo evaluation of taste masking for developed chewable and orodispersible tablets in humans and rats. Pharm Dev Technol. 2014, .19(3): 290-5.
3. Bogner RH, Wilkosz MF. Fast Dissolving Tablets: New dosage convenience for patents U.S. Pharm. 2002, 27:34-43.
4. Ahmed SZ, Bader MA, Mahmoud M, Tamer MS. Taste-masked orodispersible tablets of cyclosporine self nanoemulsion lyophilized with dry silica. Pharm Dev Technol. 2014, 9(8):1-8.
5. Bhowmik D, Chiranjib B, Krishnakanth, Pankaj and Chandira RM. Fast Dissolving Tablet: An Overview. J. Chem. Pharm. Res. 2009, 1(1):163-177.
6. Abay FB, UgurluT. Orally Disintegrating Tablets: A Short Review. J. Pharm. Drug Dev. 2015, 3(3):1-7.
7. Bharathi A, Mounika B, Tejaswi K, Naik DS. effect of super disintegrants on the formulation and evaluation of orodispersable tablets of fluoxetine hydrochloride. W. J. P. P. S. 2018, 7(2): 1071-1086.
8. Deepak S, Dinesh K, Mankaran S, Gurmeet S, Singh RM. Taste masking technologies: a novel approach for the improvement of organoleptic property of pharmaceutical active substance. I. R. J. P. 2012, 3(4):108-116.
9. Darade SC, Patil PB, Kalkotwar RS. Formulation and evaluation of orodispersible tablet containing piroxicam by sublimation method. Ind. J. Pharm & Pharmacology. 2017, 4(2):77-82.
10. Patel B, Ranawat MS, Chauhan CS. Jaimin Modi Design, Development and Characterization of Immediate Release Tablet of Pioglitazone. J. P. S. B. R. 2013,3(2): 91-99.
11. Mukhopadhyay A, Pradhan K, Samanta R. Development and validation of an UV- spectrophotometric method for the estimation of fluoxetine in pure and tablet dosage forms. IJPSR. 2014, 5(8):3418-3424.
12. Kumar NP, Nayyar P, Kumar SP. Fast dissolving tablets - A review. Middle-East J. Sci. Res. 2015, 23(1):142-8.
13. Bele MH. Pharmaceutics formulation and processing of conventional dosage form. First Edition. Carrer Publication; 2012. p. 48-55, 128-131.
14. Jaya S, Amala V. Formulation and *in vitro* evaluation of oral disintegrating tablets of amlodipine besylate. Int J Appl Pharm 2019;11:49-54.
15. Leon Lachman, Herbert A. Liberman. The Theory and Practice of Industrial Pharmacy: Special Indian Edition. 2009; pp: 325-328, 513
16. Kumar SS, Ravendra V, Vikash C, Prakash SS. Orally disintegrating tablets: A dosage form that extends the market exclusivity and patent protection. World J Pharm Pharm Sci. 2014;3(7):526-46.
17. Govedarica B, Injac R, Dreu R, Srcic S. Formulation and evaluation of immediate-release tablets with different types of paracetamol powders prepared by direct compression. Afr. J. Pharm & Pharmacol. 2011, 5(1): 31-4.
18. Rao S, Rodhay G, Padmalatha K. Design and evaluation of mouth dissolving tablets of telmisartan by using different super disintegrants. Indo American Journal of Pharmaceutical Research. 2017:7(09).
19. Likhith HM, Senthilkumar K, Prashanta Tavari, DR Nagesh. A Review on Fast Dissolving Tablets by Using Co-Processed Superdisintegrants. Ijppr.Human, 2019; 16 (3): 148-164.
20. Khan S, Kataria P, Nakhat P, Yeole P, Taste masking of ondansetron hydrochloride by polymer carrier system and formulation of rapid-disintegrating tablets. AAPS Pharm.Sci.Tech.; 8(2), 2007, 46.
21. Deepika J, Mishra A. A review - Formulation and development of orodispersible tablet. Int J Pharm Erudition. 2014, 4(1):21-38.
22. Puneet M, Kumar SP, Rishabha M. A review on recent advances of oral mouth dissolving tablet. J Drug Discov Ther. 2014, 2(18):17-22.

23. Prateek S, Ramdayal G, Kumar SU, Ashwani C, Ashwini G, Mansi S. Fast dissolving tablets: A new venture in drug delivery. Am J PharmTech Res. 2012, 2(4):252-79.
24. Dey P, Maiti S. Orodispersible tablets: A new trend in drug delivery. J Nat Sci Biol Med. 2010,1(1):2-5.
25. Silva MA, Kelmann RG, Foppa T, Cruz AP, Bertol CD, Sartori T, Granada A, Carmignan F, Murakami FS. Thermoanalytical study of fluoxetine hydrochloride. J. therm. anal. cal. 2007, 87(2):463–467.
26. Ampati S, Hanumakonda A, Maheshwaram V. Formulation and evaluation of nasal in situ gel of fluoxetine hydrochloride. I. A. J. P. S. 2016, 3(6): 573-581.
27. Sireesha P, Kiranjyothi K. formulation and evaluation of antidepressant orodispersible tablets. Int. J. Curr. Pharm. 2016, Res. 8(2): 52-60.
28. Indhumathi D, Rathnam, G. Design and optimization of orodissolving tablet of antidepressant drug by superdisintegrants addition method. Int. J. Pharm. Sci. Rev & Res. 2010, 2(2):1-8.
29. Divya L, RavichandiranV, Lavakumar V, Sowmya C, Venkateshan N, Babu MN. Preparation and evaluation of fluoxetine hydrochloride oral dispersible tablets. Int. J. Pharm. Pharm. Sci. 2014, 6(2):216-222.
30. Shankarrao KA, Mahadeo GD, Balavantrao. Formulation and *In-vitro* Evaluation of Orally Disintegrating Tablets of Olanzapine-2-Hydroxypropyl-β-Cyclodextrin Inclusion Complex. Iran. J. Pharm. Res. 2010, 9(4):335–347.