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Formulation and Evaluation of Fast Disintegrating Tablets of Fluoxetine and Olanzapine

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ABSTRACT:

The aim of present study was to formulate fast disintegrating tablets of Fluoxetine and Olanzapine. FDT of FLX & OLZ helps in swallowing problem for the patients. Fluoxetine is an anti depressive and serotonin agent. Fluoxetine is readily absorbed from GI tract following oral administration. Half life of FLX is 1-3 days. Olanzapine is an anti psychotic agent. Olanzapine absorbed from the GI tract. Half life of Olanzapine is 33hours. Olanzapine is used in treatment of schizophrenia. FDTs improved clinical effects of bipolar disorder, leading to quick onset of action of Fluoxetine and Olanzapine. The study was design to optimize aqueous solubility and dissolution rate of Olanzapine by solid dispersion using PVPK30 water soluble carriers in different concentration (1:1, 1:2, 1:3, and 1:4). Characterization of prepared solid dispersion was carried out using methods such as FTIR and DSC. Fast disintegrating tablets were formulated by using PVPK30 as polymer, superdisintegrants like cross-carmellose sodium, sodium starch glycolate, and crosspovidone, MCC as binder, mannitol as diluent, magnesium stearate as lubricant and talc as glident. The prepared tablets were evaluated for number of parameters like weight variation, hardness, friability, in vitro dissolution study and stability study. The best release for FDT was shown by formulation F8 as compare to the marketed conventional tablets and less disintegration time of F8 formulation is 27 sec. Drug release of F8 formulation after 30minutes more than 85%. Drug and polymer interaction is not found shown in FTIR. F8 formulation was found to be stable.

KEYWORDS: Fluoxetine, Olanzapine, Fast disintegrating tablets

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INTRODUCTION:

Fast disintegrating tablets are solid dosage form which are dissolving or disintegrate instantly in the mouth without water needed.[1] Uncoated tablets are intended to be placed in the mouth where tablets are dispersing rapidly before being swallowed.[3] One important drawback of this dosage form is 'Dysphagia' or difficulty in swallowing for many patients like psychiatrics or geriatrics. Fast disintegrating tablets are put on the tongue, which disintegrate or dissolve rapidly within a few seconds. Drug which are dissolve or disperse in the saliva. Fast disintegrating tablets are also called as mouth dissolving tablets, orodispersible tablets, rapimelts, porous tablets, orally disintegrating tablets, melt in mouth etc. Oral route of administration is the convenient route for the patient because of easy ingestion, pain avoidance, and patient compliance.[2]

Advantages of fast disintegrating tablets [2, 3, 4]

- Convenient to administer for geriatric, pediatric and bed ridden patients who have difficulty in swallowing or Dysphagia.
- Fast onsets of action as tablets get disperse rapidly along with rapid dissolution and absorption in oral cavity.

- Water is not needed swallow the dosage form. Convenient for the patient travelling because not have immediate water.
- Good mouth feel for pediatric patients as sweeteners used to avoid the taste of bitterness of drug.
- Cost effective.
- Chemical stability is good.

Limitations of fast disintegrating tablets [4, 10]

- Fast disintegrating tablets usually having insufficient mechanical strength. Hence, careful handling is required.
- The tablets may leave unpleasant taste and grittiness in oral cavity if not formulated properly.
- Larger doses of drugs which are difficult to formulate into fast disintegrating tablets e.g. rifampin (600mg), ethambutol (1000mg) etc.

Approaches of FDTs which are include: Freeze drying, sublimation, molding, spray drying, mass extrusion. [6] Fluoxetine is an antidepressive agent used for the handling of unipolar mental depression. [8] Fluoxetine is well absorbed after oral administration.[7] Olanzapine is an atypical antipsychotic agent, for treatment of schizophrenia, acute mania with bipolar disorder, agitation and psychotic symptoms in dementia.[10] So, in these conditions the quick onset of action of drug is highly desirable. Fluoxetine and Olanzapine is suitable candidate for FDTs.

Materials and methods

Materials

Fluoxetine was gifted by Intas lab Pvt. Ltd. Ahmedabad, Olanzapine was gifted by Cadila Healthcare Ltd, cross carmellose sodium, crosspovidone and sodium starch glycolate gifted by S.D. fine chemicals Pvt. Ltd.Mumbai, PVPK30 purchase by ACS chemical, Ahmedabad, mannitol, magnesium stearate, MCC, talc purchased from Finar chemicals ltd. Ahmedabad.

Methods:

Phase solubility studies [11]

Phase solubility studies were carried out at room temperature according to the method reported by Higuchi and Connors. Adding fixed amount of drug and different Polymer in different ratio of taken with distilled water in stoppered conical flask and shaken for 24 hours at 37 ºC and 300 rpm on electromagnetic stirrer. The solutions were filtered through Whatman filter paper. The filtrates were suitably diluted and analyzed, UV/Vis spectrophotometer. The stability constant Ks (stability constant) for the complex were determined from the graph using following equation:

Ks = Slope/Intercept (1- slope)

(eq. no.1)

1:1 complex apparent stability constant (Ka) was determined as follows:

Ka = (slope - 1)/intercept.

Statistical analysis[11]

Comparision between dissolution profiles of different samples an independent mathematical approach model for calculating a similarity factor f_2 proposed by Moore and Flanner was used. The similarity factor f_2 is measure of similarity in the % dissolution between two dissolution curves by equation:

$F2=50\times\log\{[1+(1/n)\sum_{t=1}^{n}(R_t-T_t)^2]^{-0.5}\times100\}$ (**eq.no.2)**

Where,

n= number of withdrawal point

R_t = % dissolve of reference at time point

T_t= % dissolve of test at time point

A value of 100% for the similarity factor suggests that the reference and test profiles are similar, whereas smaller values imply an increase in dissimilarity between release profiles. FDA suggests this analysis for an immediate release of solid oral dosage forms.

Preparation of Olanzapine solid dispersion with PVPK30: Kneading method[11]

Solid dispersion of Olanzapine and PVP K30 weight ratios 1:4 respectively were prepared by the kneading method as follows. Appropriate amounts of Olanzapine and PVP K30 was wetted with water and kneaded thoroughly for 45 min in a glass mortar and then dried at 50^0C until dry. Dried powder was passed through 120# sieve and stored in desiccators until further evaluation.

Characterization of solid dispersion[11]

Fourier Transform Infrared Spectroscopy

FTIR spectra of powder samples were obtained by using a spectrophotometer by potassium bromide (KBr) pellet method. 2 mg of sample is added in 200 mg of KBr. The scanning range was 650-3800 cm^{-1} and the resolution was 2 cm^{-1}.

Differential scanning Calorimetry (DSC)

DSC scans of the powdered samples were recorded by

using Jade DSC Perkin Elmer, USA. All samples are weighed 8- 10 mg and heated at the scanning rate of 10 ^{o}C/min under dry nitrogen flow (20 ml / min) between 50 and 300 ^{o} C. Aluminum pans and lids were used for all samples. Pure water and indium were used to calibrate the DSC temperature scale and enthalpic response.

Preparation of Fast Disintegrating tablet:

Tablets containing Fluoxetine and Olanzapine solid dispersion were prepared by direct compression method. Tablets are compressed directly from powder blends of solid dispersion and suitable excipients. Olanzapine solid dispersion (KMPVPK30), directly compressible Mannitol, Superdisintegrant (Crosspovidone, Sodium starch glycolate, Cross carmellose sodium), Microcrystalline Cellulose PH 101, and Talc were mixed together for 20 min. Magnesium stearate, was then added and mixed for 5 min. The powder blend was compressed into the tablets on tablet punching - machine.

Table-1 Formulation of fast disintegrating tablets

Ingredients *	F1	F2	F3	F4	F5	F6	F7	F8	F9
Olanzapine equivalent to KMPVP	60	60	60	60	60	60	60	60	60
Fluoxetine	20	20	20	20	20	20	20	20	20
Cross povidone	5	10	15	--	--	--	--	--	--
Sodium starch glycolate	--	--	--	5	10	15	--	--	--
Cross carmellose sodium	--	--	--	--	--	--	5	10	15
Mannitol	30	30	30	30	30	30	30	30	30
Microcrystalline cellulose PH 101	82	77	72	82	77	72	82	77	72
Magnesium stearate	2	2	2	2	2	2	2	2	2
Talc	1	1	1	1	1	1	1	1	1
Total	200	200	200	200	200	200	200	200	200

*** All values are in mg**

Pre compression evaluation parameter of Blend

(A) Angle of repose (ɵ)[10]

The angle of repose of powder is determined by the funnel method. The accurately weighed powder is taken in a funnel. The powder was allowed to flow through the funnel freely on to the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation.

$$\tan ɵ = h/r \quad \textbf{(eq.no.3)}$$

$$ɵ = \tan^{-1} h/r \quad \textbf{(eq.no.4)}$$

Where,

ɵ = angle of repose

h = height of pile

r = radius of pile on horizontal

Table-2 Angle of repose

Angle of repose	Category
25-30	Excellent
30-35	Good
35-40	Fair
40-45	Poor
45-50	Very poor

(B) Bulk density[10]

Bulk density was determined by pouring the blend into a graduated cylinder. The bulk volume (Vb) and weight of the blend (M) was determined. The bulk density is expressed in gm/ml and is given by following equation

$$\text{Bulk density} = M/Vb \quad \textbf{(eq.no.5)}$$

Where,

M = mass of powder taken

Vb= Bulk volume of the powder.

(C) Tapped density:

It is the ratio of total mass of the powder to the tapped volume of the powder. Volume was measured by tapping the powder for 500 times and the tapped volume was noted if the difference between these two volumes is less than 2%. If it is more than 2%, tapping is continued for 100 times and tapped volume was noted. Tapping was continued until the difference between successive volumes is less than 2 %. It is expressed in g/ml and is given by following equation:

$$\text{Tapped density} = M/Vt \quad \textbf{(eq. no. 6)}$$

M = Mass of powder taken

VT = tapped volume of the powder

(D) Carr's Index

It is also one of the sample methods to evaluate flow property of a powder by comparing the bulk density

and tapped density. A useful empirical guide is given by the Carr's compressibility index. It indicates the ease with which a material can be induced to flow. It is expressed in percentage and is given by following equation:

Compressibility index =100 (Dt - Db) /Dt

(eq. no. 7)

Where,

Dt is the tapped density of the powder.

Db is the bulk density of the powder.

Table-3 Carr's Index

Carr's Index	Category
5-12	Excellent
12-16	Good
18-21	Fair
23-35	Poor
35-38	Very poor
More than 40	Extremely poor

(E) Hausner ratio

Hausner ratio is an indirect index of ease of powder flow. It is calculated by following formula.

Hausner's ratio = Dt / Db

(eq. no. 8)

Where,

Dt is the tapped density. Db is the bulk density.

Lower hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25).

Table-4 Hausner ratio

Limit	Category
1.2-1.3	Excellent
1.3-1.4	Good
1.4-1.5	Fair
1.5-1.6	Poor

(F) FTIR Studies

The powder blends (drug: superdisintegrants=1:1) were kept for one month after which they were physically evaluated and IR studies were carried out.

Post compression Evaluation of Fast disintegrating tablet

The formulated tablets were evaluated for different parameters like general characteristic, weight uniformity, hardness, wetting time, disintegration test and drug release profile.

(A) Weight variation test:

Twenty tablets were taken and their weight was determined individually and collectively on a digital weighting balance. The average weight of one tablet was determined from the collective weight. Then individual tablets were weighed and the individual weight was compared with an avg. weight. IP limit for weight variation in case of tablets weight up to 120 mg is ±10%, 120 mg to 300 mg is ±7.5% and more than 300 mg is ± 5%. The weights were determined to within ±7.5% by using weigh balance.

%wt. variation= [(avg.wt . – individual wt.)/avg.wt.]×100 **(eq. no. 9)**

(B) Hardness:

Hardness of tablet is evaluated by Monsanto hardness tester**.** The hardness is measured in kg/cm^2.s A tablet hardness of about 2-4 kg/cm^2 is considered adequate for mechanical stability.

(C) Friability:

Friability of the tablets was measured by using Roche friabilator. Friability is also mechanical strength of tablet. Friability was evaluated by Roche Friabilator with 100 revolution rotating or 25 per minute for 4 min by using 6 tablets. According to IP tablets should have limit < 1% for acceptance.

% Friability=

(Wt. of 20 tab before rotation-Wt. of 20 tab after rotation) ×100/ Wt. of 20 tablets before rotation

(D) Wetting time:

Five circular filter papers of 10 cm diameter were placed in a Petri dish with a 10cm diameter. 10 ml of water containing methyl red, 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 upper surface of the tablet was noted as a wetting time.

(E) In vitro disintegration time:

The disintegration test was performed using an USP disintegration apparatus, with distilled water at 37±0.5^{0}C. The time reported to obtain complete disintegration of six tablets were recorded and average was reported.

(F) In vitro dissolution of Fast Disintegrating Tablet:

Dissolution study was conducted for all the formulation (F1-F9) using USP type-II paddle apparatus. The release study was carried out in USP Type-II dissolution apparatus containing 900ml 0.1N HCL as dissolution medium. Temperature of the dissolution medium was maintained at 37±0.5ºC, aliquot of

dissolution medium was withdrawn were filtered through Whatman filter paper at fixed time interval and was replaced with fresh dissolution medium. The absorbance of filtered solution was checked by using UV-visible double beam spectrophotometer at 219& 249nm and concentration of the drug was determined from standard calibration curve. The withdrawn samples were analyzed by an UV spectrophotometer at219 & 249 nm using 0.1N HCL as a blank. Dissolution study was conducted for pure drug (FLX & OLZ), optimized formulation and marketed formulation (DEPTAN OZ) as mention in above procedure.

(G) Drug content Uniformity:

Take 10 tablet of each formulation and find content of individual tablet. The preparation complies if not more than one individual content is outside the limit of 85 to 115% of the average content and none is outside the limits of 75 to 125% of average content. The preparation fails to comply with the test if more than 3 individual contents are outside the limits of 85% to 115% of average content.

Accelerated Stability study

The stability studies of prepared tablets were conducted on optimized formulation tablets. The 20 tablets wrapped with aluminum foil were stored in the stability chamber maintained at 40±2^{0}C and 75±5% RH for four week. The sample was collected after four week. The sample analyzed for its disintegration time, hardness, friability and in vitro dissolution study.

Result and discussion:

Phase solubility studies.

Table-5Comparision of solubility for ratio of drug and different polymer

Polymer	Drug : Polymer	Increased solubility
Olanzapine pure	1:1	6 fold
Olanzapine : PVPk30	1:1	13 fold
Olanzapine : Poloxamer	1:1	6fold
Olanzapine : PEG 4000	1:1	10 fold

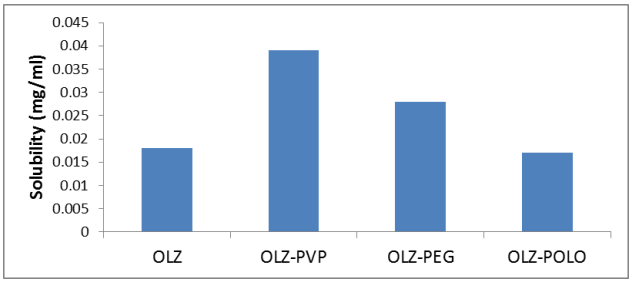


Figure: 1 solubility study of OLZ and different polymers in 1:1 ratio

Here Olanzapine pure and Olanzapine with Poloxamer not shown major different in solubility. PEG is increased solubility of Olanzapine is 10 fold but PVP K30 is higher improvement in solubility of Olanzapine

Table-6Phase solubility of drug in water with PVP

Phase solubility in Water with PVP	
Conc. Of Polymer PVP (%w/v)	**Solubility (mg/ml)**
0	0.019
10	0.042
20	0.062
30	0.077
40	0.092
50	0.061

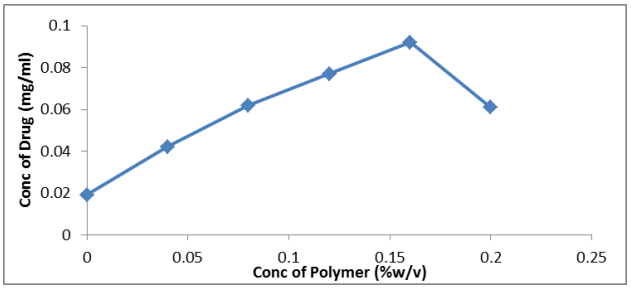


Figure: 2.Phase Solubility study of OLZ in water with PVP

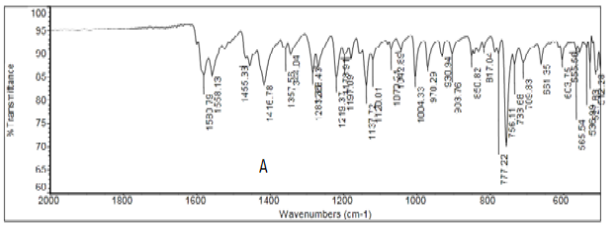
From above fig shown PVP K30 gives better solubility in different concentration. 40%w/w concentration gives 0.092 mg/ml then increasing concentration 50% w/w decrease solubility so 1:4 ratio of Drug: PVP is using in final formulation preparation.

Characterization of solid dispersion

Fourier Transform Infrared Spectroscopy (FTIR)

Fourier transform infrared spectroscopy (FTIR) has been used to assess the interaction between carrier and guest molecules in the solid state. Upon preparing SDs, the

peak band of the guest shifts in the absorption spectrum. The FTIR spectra of all samples are shown in Fig.



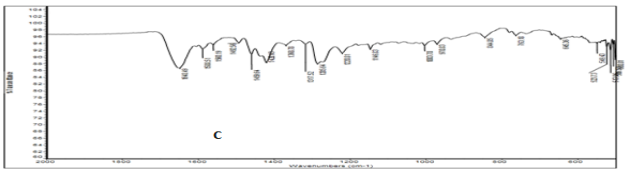


Fig 3. FTIR spectra of (A) Pure Olanzapine (B) PVPK30 only (C)KNPVP

Differential Scanning Calorimetry:

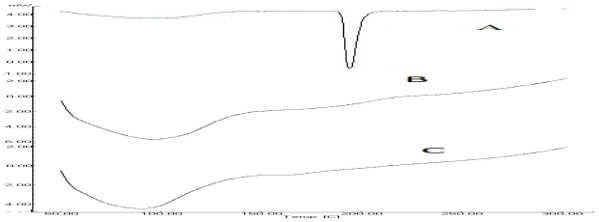


Fig. 4 (A) Pure OLZ (B) PVP (C) KNPVP

6.3 In vitro Dissolution of solid dispersion

Table-7In vitro dissolution of solid dispersion in distilled water

OLZ and its SDs	Cumulative % drug release					
Time(min)	**10**	**20**	**30**	**40**	**50**	**60**
Pure OLZ	8.60±0.28	9.55±0.12	10.51±0.38	13.28±0.44	16.52±0.81	19.33±0.67
PMPVP	9.50±0.55	14.08±1.18	18.23±1.10	21.95±0.68	26.14±1.23	28.55±0.59
SEPVP	19.46±0.42	27.26±0.81	35.55±1.04	42.08±0.56	47.29±1.01	61.58±0.72
KNPVP	22.63±1.21	28.63±1.01	36.94±0.66	43.93±0.78	50.50±1.22	84.26±1.18

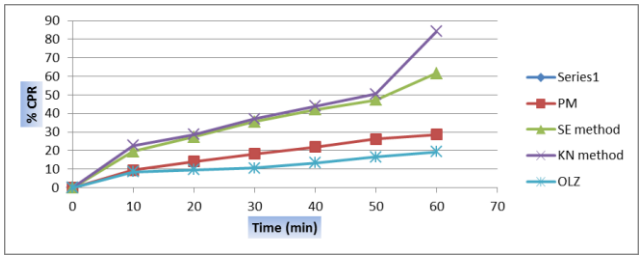


Figure 5.in vitro dissolution profiles of pure Olanzapine drug, and its SDS of PMPVP, SEPVP, KMPVP

Statistical analysis

MDT reflects the time for the drug to dissolve and is the first statistical moment for the cumulative dissolution process that provides an accurate drug release rate. It is accurate expression for drug release rate. A higher MDT value indicates greater drug retarding ability. MDT values of Olanzapine and its SDs with PVP were calculated using equation.

$$MDT_{in\ vitro} = \frac{\sum_{i=1}^{n} t_{mid}\,\Delta M}{\sum_{i=1}^{n} \Delta M}$$

i= dissolution sample number,

n= number of dissolution times,

t_{mid} = time at the midpoint between times t_i and t_{i-1},

ΔM= the amount of OLZ dissolved between times t_i and t_{i-1}.

Table-8 % Drug dissolved within 10 minutes (DP_{10min}) & mean dissolution time (MDT), similarity factors from pure Olanzapine, its SDs.

	OLZ	**PMPVP**	**KMPVP**	**SEPVP**
Dp10	8.59	9.50	28.63	19.45
MDT	14.87	19.16	14.26	17.30
F_2	---	37.49	70.66	42.83

From above dissolution data and based on statistical analysis of SDs prepared with different method in which KMPVP prepared by kneading method was considers for final formulation preparation.

Precompression Evaluation parameter

Table 9. Precompression Evaluation parameter

Formulation code	Angle of repose	Bulk density	Tapped density	Carr's index	Hauser ratio
F1	34.71±1.18	0.62±0.23	0.84±0.24	29.89± 1.20	1.41±0.04
F2	33.51±0.98	0.65±0.26	0.85±0.14	27.40± 1.12	1.34±0.03
F3	32.54±1.14	0.66±0.30	0.90±0.24	26.70± 1.02	1.33±0.01
F4	35.01±1.18	0.53±0.22	0.79±0.14	28.91± 0.98	1.51±1.23
F5	34.10±0.95	0.54±0.24	0.85±0.09	28.04± 0.84	1.47±1.04
F6	32.03±1.06	0.55±0.21	0.88±0.04	27.80± 1.25	1.34±1.18
F7	33.03±1.14	0.55±0.30	0.81±0.15	25.10± 1.26	1.43±0.64
F8	**32.08± 0.92**	**0.56± 0.30**	**0.84± 0.26**	**23.80± 0.99**	**1.36±0.73**
F9	31.04±0.85	0.60±0.32	0.86±0.22	29.80± 1.28	1.35±0.14

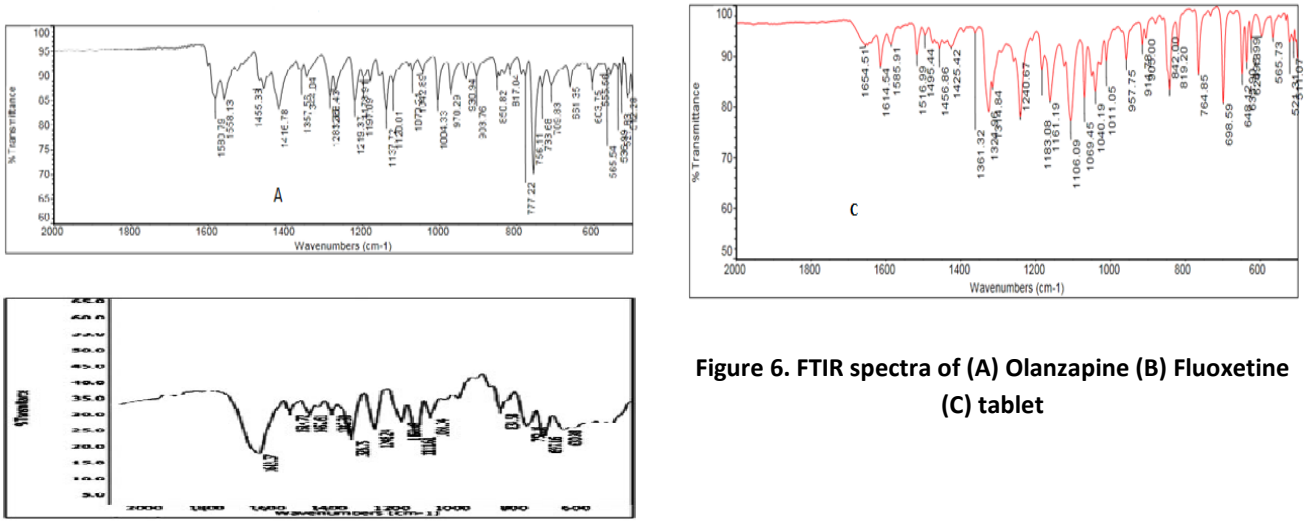


Figure 6. FTIR spectra of (A) Olanzapine (B) Fluoxetine (C) tablet

Post-compression Evaluation parameter

Table-10 Evaluation parameter of tablet

Batch code	Uniformity of weight (mg)	Drug content (%)		Friability (%)	Hardness (kg/cm^2)
		FLX	**OLZ**		
F1	198.4±1.21	88.20±1.05	93.43±1.06	0.87±0.33	3.0±0.76
F2	197.3±1.53	91.10±1.08	91.22±0.01	0.82±0.55	2.6±0.98
F3	192.5±1.23	90.90±1.02	87.32±0.03	0.81±0.56	2.8±0.54
F4	200±2.45	91.78±1.23	88.37±0.24	0.80±0.33	3.1±0.45
F5	200.2±2.55	92.34±0.92	83.92±0.83	0.78±0.67	2.8±0.23
F6	193.4±3.30	87.63±1.20	92.62±1.02	0.75±0.45	3.2±0.34
F7	193.5.4±2.30	85.42±1.53	91.85±1.09	0.88±0.54	3.1±0.54
F8	**200.1±3.40**	**94.89±1.02**	**95.89±1.43**	**0.79±0.78**	**2.9±0.34**
F9	199.7±3.43	92.20±1.30	93.57±1.87	0.84±0.89	2.7±0.23

Table-11 Wetting, disintegration and in - vitro dispersion time of tablet

Batch code	Wetting time	Disintegration time	In vitro dispersion time
	(sec)	(sec)	(sec)
F1	96±0.79	121±0.24	49±0.15
F2	88±0.41	127±1.13	42±0.73
F3	69±1.3	102±1.21	39±1.24
F4	100±1.04	142±1.03	68±0.03
F5	92±0.55	115±0.84	40±1.15
F6	56±0.23	97±1.18	34±0.98
F7	37±0.30	54±0.64	29±1.26
F8	**21±0.85**	**27±0.98**	**16±0.26**
F9	33±1.19	42±1.29	28±0.21

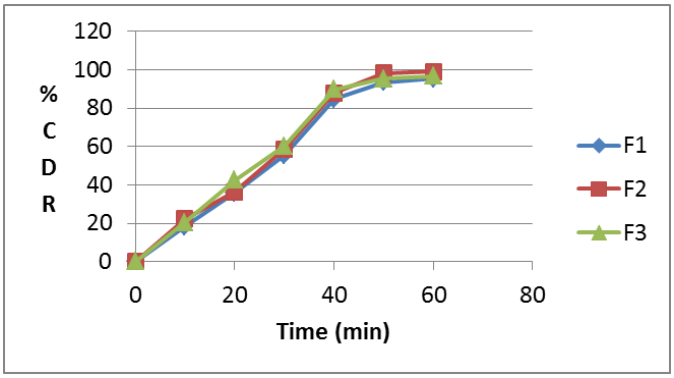


Figure7 Dissolution study of tablet (Fluoxetine) F1 to F3.

In- vitro dissolution data

Table-12 in – vitro dissolution data for FLX (0.1 N HCl)

Time	% Cumulative drug release								
(hr)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
10	18.30±1.2	22.40±1.4	20.50±0.3	21.10±0.7	28.35±1.5	27.56±2.2	21.32±0.9	29.90±1.4	26.50±2.1
20	35.70±1.3	36.30±0.6	42.50±1.7	30.80±0.8	47.50±1.2	41.2±2.1	35.72±0.4	60.90±0.1	43.50±1.9
30	55.45±1.3	58.72±0.6	60.32±1.9	54.98±1.7	62.51±1.4	65.60±0.5	61.02±1.3	85.60±1.8	67.80±0.3
40	84.70±0.1	87.90±0.6	89.60±0.9	80.10±0.8	91.80±0.4	93.70±1.6	90.15±1.2	95.90±0.6	90.70±0.1
50	93.40±2.3	98.30±3.1	95.20±2.4	83.40±2.3	99.30±0.8	99.50±0.4	96.92±0.5	99.89±0.9	99.70±0.7
60	95.30±1.5	99.10±0.7	96.70±0.9	91.30±0.7	99.40±1.4	99.60±0.7	99.50±1.2	100.9±1.3	100.8±1.2

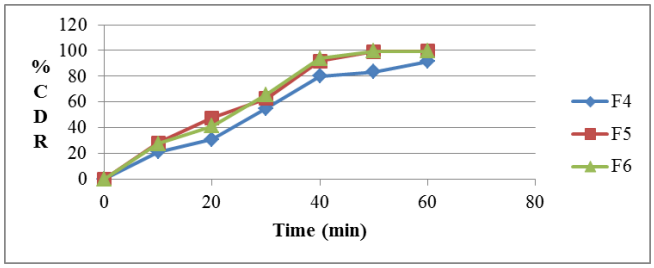


Figure8. Dissolution study of tablet (Fluoxetine) F4 to F6.

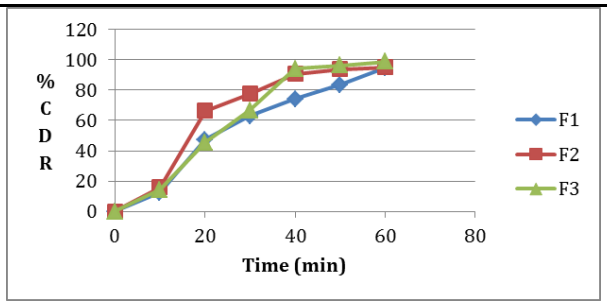


Figure 10. In vitro Dissolution study of tablet (Olanzapine) F1 to F3.

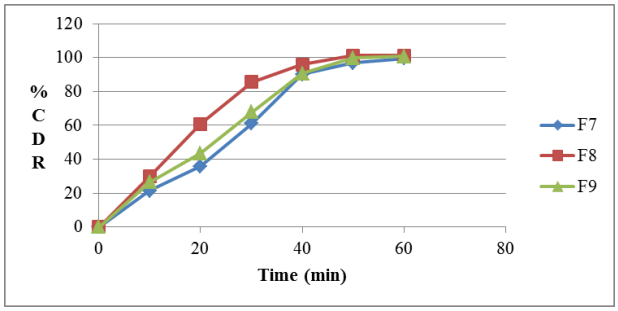


Figure 9. Dissolution study of tablet (Fluoxetine) F7 to F9

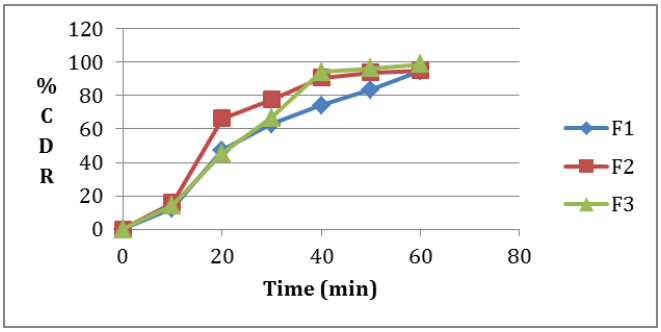


Figure11 Invitro Dissolution study of tablet (Olanzapine) F4 to F6.

Table-13 in – vitro dissolution data for OLZ (0.1 N HCl)

Time (hr)	% Cumulative drug release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
10	12.29±0.3	15.82±1.5	14.35±0.9	16.11±1.6	17.06±0.7	20.92±2.1	22.64±1.8	25.96±0.1	23.35±1.6
20	47.25±0.5	66.28±0.6	45.45±0.9	56.37±1.2	51.62±1.5	52.53±1.8	53.35±0.4	58.50±1.3	49.18±2.3
30	62.9±0.3	77.51±0.7	66.65±1.6	78.50±1.1	84.88±0.2	93.94±1.5	96.69±2.3	97.30±0.9	94.90±1.5
40	74.11±0.7	90.61±0.2	94.13±1.5	87.98±1.4	92.59±0.1	96.27±1.2	97.12±2.7	98.44±0.3	96.33±1.5
50	83.56±1.3	93.82±1.5	96.46±0.7	94.80±0.2	96.72±1.6	98.61±0.2	97.2.56±1.3	99.20±1.5	96.66±0.6
60	94.88±2.7	95.23±1.8	98.79±0.4	99.84±2.6	99.05±3.4	99.59±2.4	98.1±2.1	99.90±1.9	99.19±2.9

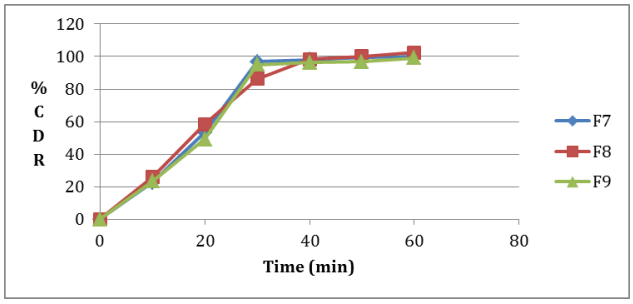


Fig. 12 Dissolution study of tablet (Olanzapine) F7 to F9.

Accelerated stability study of batch F8[11]

In order to determine the change in - vitro release profile on storage, stability study of b F8 batch was carried out at 40 ^{0}C in a humidity chamber having 75% RH. Sample were withdrawn after four-week interval and evaluated for change Hardness, disintegration time and friability.

Table 14 Result of stability study of F8

Parameter	Initial (F8)	After storage at 40°C for 1 month (F8)
Disintegration time(sec.)	27±0.98	29
Friability	0.79±0.78	0.83±0.78
Hardness(kg/cm2)	2.9±0.34	3.1±0.69

CONCLUSION:

From present work it was concluded that Solid dispersion of Kneading method by using Drug: PVPK30 ratio of 1:4 was better than other methods of solid dispersion.

Tablets prepared by direct compression method by using three superdisintegrating agents like crosscarmellose sodium, crosspovidone and sodium starch glycolate. In which cross carmellose sodium was better than cross povidone and sodium starch glycolate.

Prepared tablets were evaluated by following evaluation parameter hardness, friability, weight variation, content uniformity, disintegrating time, wetting time, in vitro dissolution and stability study.

The F8 formulation shows 85% drug release in 15min while using 10% concentration and disintegration time is 27 sec. in which increase of concentration of cross carmellose sodium no any improvement in dissolution and disintegration so it was optimized formulation. Formulation F8 was stable after 1 month shown in stability study.

REFERENCE:

1. Witold B, Renata Jachowicz, Przemyslaw Pelka, "Orally disintegrating tablets- A Review.'' *Saudi pharm. j,* **2015**, 23, 437-443.
2. Sharma D, Kumar D, Singh M, Singh G, Rathore M, "Fast disintegrating tablets – A Review.'' *J. drug deli.& therapeutic.* **2012**, 2 (3), 74-86.
3. Nitan B, Bhandari N, Sharma P, Singh K, "Fast dissolving tablets – A Review.'' *Int. j. res. j. pharm.* **2012**, 3 (9), 59-64.
4. Siddiqui N, Garg G, Sharma P, "Fast dissolving tablets – A Review.'' *Int. j. pharm. sci. rew. res.* **2010**, 4(2), 87-96.
5. http://en.wikipedia.org/wiki/Fluoxetine

6. http://en.wikipedia.org/wiki/Olanzapine
7. Mundhe V, Burande S, Kondapure A, Arsul V, Zarekar S, "Formulation and evaluation of mouth dissolving tablet of Olanzapine by co processing superdisintegrants." *Asia. J. pharm. tech. Innovation.* **2013**, 1(1), 1-20.
8. Lavakumar V, Divya I, Ravichandiran V, Sowmya C, Venkateshan N, Niranjan M, "Preparation and evaluation of Fluoxetine hydrochloride oral dispersible tablets." *Int. j. pharm. sci.* **2014**, 6(2), 216-222.
9. Indumathi D, Grace R, "Design and optimization of orodissolving tablet of antidepressant drug by superdisintegrants addition method." *Int. j. pharm. sci.res.* **2010**, 2(2), 1- 9.
10. Debjit B, Chiranjib B, Krishnakanth, Pankaj, Margret C, "Fast dissolving tablets – A Review.'' *J. chem. & pharm. res.***2009**, 1(1), 163-177.
11. Yadav P, Kumar V, Singh U, Bhat H, Mazumder B, "Physicochemical characterization and in vitro dissolution studies of solid dispersions of Ketoprofen with PVP K30 and D-mannitol." *Saudi pharm. j.* **2013**, 21, 77-84.