Academic Sciences International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 6 suppl 2, 2014

Research Article

PREPARATION AND EVALUATION OF FLUOXEITINE HYDROCHLORIDE ORAL DISPERSIBLE TABLETS

L. DIVYA, V.RAVICHANDIRAN, V. LAVAKUMAR*, C. SOWMYA, N.VENKATESHAN, M.NIRANJAN BABU

Department of Pharmaceutics, Seven Hills College of Pharmacy, Tirupathi, AP, School of Pharmaceutical Sciences, VISTAS, Chennai, TN, Sevenhills College of Pharmacy, Tirupathi, AP, Department of Pharmaceutics, OMER EL MUKHTAR University, Al-Beida, Libiya, Department of Pharmaceutical Chemistry, SBCP, Sivakasi, TN, India, Principal, Sevenhills College of Pharmacy, Tirupathi, AP, India. Email:shcpresearch@gmail.com

Received: 05 Oct 2013, Revised and Accepted: 03 Jan 2014

ABSTRACT

The oral route of administration still continue to be the most preferred route due to its manifold advantages including ease of ingestion, pain avoidance, versatility and most importantly patient compliance. Recent advances in novel drug delivery systems aim to enhance safety and efficacy of drug molecule by formulation and to achieve better patient compliance. One such approach is 'mouth dissolving tablets'. Their growing importance was underlined recently when European Pharmacopoeia adopted the term "Orodispersible Tablets" as a tablet that to be placed in the mouth where it disperses rapidly before swallowing. It is one of the fastest growing segments in the pharmaceutical market. The model drug used in the present study is an antidepressant drug used for the handling of unipolar mental depression The present study was aimed to investigate on the best superdisintegrants which is more reliable for the preparation of oral dispersible tablets of Fluoxeitine hydrochloride and it was concluded that the combination of the superdisintegratants (CCS: CP) shows the drug release profile in less time and hence it was concluded that the combination of superdisintegrants was best when compared individually.

Keywords: mouth dissolving tablets, superdisintegratants, patient compliance, antidepressant.

INTRODUCTION

Oral route of drug administration have wide acceptance up to 50-60% of total dosage forms. Solid dosage forms are popular because of ease of administration, accurate dosage, self medication, pain avoidance and the most importantly the patient compliance. The most popular solid dosage forms are tablets and capsules; one important drawback of these dosage forms for some patients however is the difficulty to swallow. [1]

Drinking water plays an important role in the swallowing of the solid oral dosage forms. Often times people experience inconvenience in swallowing conventional dosage forms such as tablets, capsules when water is not available in the cases of motion sickness (kinetosis) and sudden episodes of coughing during allergic conditions and bronchitis.[2] For these reasons, tablets which can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention. Rapidly dissolving or disintegrating tablets are not only indicated for people who have swallowing difficulties, but also ideal for active people.[3]

'Fast Dissolve', 'Quick Dissolve', 'Rapid Melt', 'Quick Disintegrating', 'Mouth Dissolving', 'Orally Disintegrating', 'Oro Dispersible', 'Melt-In-Mouth', etc. are terms that represent the same drug delivery system. Recently orally disintegrating (OD) tablet technology has been approved by United States pharmacopoeia (USP), center for drug evaluation and research (CDER) .USFDA defined OD tablet as "a solid dosage form containing medical substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue". Recently European pharmacopoeia also adopted the term "oro-dispersible tablets" as a tablet that is to be placed in the mouth where it disperses rapidly before swallowing.

The dosage forms dissolve or integrate in the patient's mouth within 15 seconds to 3 minutes without the need of water or chewing.[4] despite various terminologies used; oro-dispersible tablets are here to offer unique form of drug delivery with many advantages over the conventional oral solid dosage forms. [5]

Salient features of Oro-dispersible Drug Delivery System:

1. Ease of administration for patients who are mentally ill, disabled and uncooperative.
2. Requires no water.
3. Quick disintegration and dissolution of the dosage form.
4. Overcomes unacceptable taste of the drugs.
5. Can be designed to leave minimal or to residue in the mouth after administration and also to provide a pleasant mouth feel.[6]
6. Provides good stability, accurate dosing, easy manufacturing, and small packaging size and easy to handle by patients.
7. Bioavailability of drugs that are absorbed from mouth, pharynx, and esophagus is increased.
8. Pregastric absorption of drugs avoids hepatic metabolism, which reduces the dose and increase the bioavailability.

Disintegrants and Superdisintegrants

Disintegrants are the substances or a mixture of substances added to a tablet to facilitate its breakup or disintegration after administration, which play major role in the formulation of ODT. Starches, clays, cellulose and cross linked polymers are most commonly used disintegrants. Super disintegrants are similar to the above but with more intense action and more porous in nature.

Basically, the disintegrants major function is to oppose the efficacy of the tablet binder and the physical forces that act under compression to form the tablet. The mechanism by which tablet is broken down into smaller particles and then produces a homogeneous suspension or solution is based on

1. By capillary action
2. High swell ability of disintegrants
3. Capillary action and high swell ability
4. Chemical reaction (release of gases).

Depression is a common psychiatric disorder affecting about 120 million people worldwide, and statistics clearly identify it as a major public health problem.[7] Medication is the most common treatment for depression.

The drug used in the present study was a model antidepressant. These antidepressants are the drugs which elevate mood in depressive illness.

Fluoxetine hydrochloride, chemically, (±)-N-methyl-3-Phenyl-3-[(α, α,α-trifluoro-p-tolyl)] propylamine hydrochloride is an antidepressant drug used for the handling of unipolar mental depression.[8] Fluoxetine is well absorbed after oral administration. Peak plasma concentration is reached in six to eight hours. Systemic bioavailability is greater than 85% and does not appear to be affected by food.

MATERIALS AND METHODS

Fluoxeitine hydrochloride,Starch was purchased from final chemicals Ltd, ahmedabad.,Mannitol was purchased from oxford laboratory, Mumbai., Magnesium stearate was purchased from Himedia laboratories pvt Ltd, Mumbai., Talc was purchased from Accord labs, Hyderabad.

Methods

Preformulation testing is the first step in the rational development of dosage forms of a drug. It can be defined as an investigation of physical and chemical properties of drug substance, alone and when in combined with excipients.

FTIR

I.R spectroscopy can be used to investigate and predict any physiochemical interaction between different components in a formulation and therefore it can be applied to the selection of suitable chemical compatible excipients while selecting the ingredients.

Formulation of oro-dispersible fluoxeitine hydrochloride tablets

Preparation of fluoxeitine hydrochloride oro-dispersible tablets by wet granulation method

Fluoxetine raw material and all excipients mentioned in the following table were passed through sieve no.60 before granulation and lubrication. The required quantity of Fluoxetine and other excipients (except lubricants and glidants) were weighed and mixed uniformly. Then the mixture was made to a damp mass using alcoholic PVP 10 % as binding agent. Then the prepared mass was passed through sieve no. 16. The prepared granules were dried in an oven at a temperature of 50°C for one hour. The granules obtained were lubricated and punched into tablets with an average weight of 200 mg, using Cadmach tabletting machine.

Preparation of fluoxeitine hydrochloride oro-dispersible tablets by direct compression method

The tablets were formulated employing direct compression method using 8mm flat-faced punches. It is the process by which tablets are compressed directly from mixtures of the drug and excipients without preliminary treatment such as granulation.

Preparation of fluoxeitine hydrochloride oro dispersible tablets by sublimation method

Fluoxetine raw material and all excipients mentioned in the following table were passed through sieve no.60 before granulation and lubrication. The required quantity of Fluoxetine and

other excipients including camphor of about 30 mg as sublimating agent (except lubricants and

glidants) were weighed and mixed uniformly. Then the mixture was made to a damp mass using alcoholic PVP 10 % as binding agent. The granules were evaluated and punched into tablets with an average weight of 200 mg, using Cadmach tabletting machine.

The prepared tablets were allowed to sublimate by placing in the tablets in tray dryer for 20 min at 80 º C. removal of volatile material by sublimation generated a porous structure due to this the tablet dissolve with in 10-20 seconds and exhibit sufficient mechanical strength for practical use. The quantity for one tablet was tabulated in table 1.

Table 1: Preparation of fluoxeitine oral dispersible tablets (quantity for one tablet)

s.no	Form.code	Fluoxeitine (mg)	Mannitol (mg)	Starch (mg)	Ccs (mg)	Cr.p (mg)	Camphor (mg)	Talc (mg)	Mg.st (mg)
1	DF1	200	155	15	-	-	-	20	2
2	DF2	200	155	-	15	-	-	20	2
3	DF3	200	155	-	-	15	-	20	2
4	DF4	200	155	-	7.5	7.5	-	20	2
5	SF1	200	155	15	-	-	30	20	2
6	SF2	200	155	-	15	-	30	20	2
7	SF3	200	155	-	-	15	30	20	2
8	SF4	200	155	-	7.5	7.5	30	20	2
9	WF1	200	155	15	-	-	-	20	2
10	WF2	200	155	-	15	-	-	20	2
11	WF3	200	155	-	-	15	-	20	2
12	WF4	200	155	-	7.5	7.5	-	20	2

Evaluation

Pre-compression evaluation for granules

Various pre-compression parameters like bulk density, tapped density, hausner's ratio, compressibility index (%) and angle of repose were determined for granules and results were listed in following tables.

Angle of repose

Angle of repose of the granules was measured by fixed funnel method. The accurately weighed granules were taken in the funnel. The granules were allowed to flow through the funnel freely on to the surface.

The diameter of the granules cone was measured and angle of repose was calculated using the following equation.

$\tan \theta = h / r$,

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

Where, θ is the angle of repose, h is the height in cm; r is the radius in cm

Determination of bulk density, Tapped density

Both loose bulk density and tapped density are determined. A quantity of 2 gms of granules from each formula, previously shaken to break any agglomerates formed, are introduced in to 10 ml measuring cylinder and the intial weight is noted.

The bulk density is expressed in terms of g/mL and calculated by formula,

$D_B = W / V_B$

Where, W is the weight of the powder

V_B is the bulk volume of the powder

Tapped density

A quantity of 2 gms of granules from each formula, previously shaken to break any agglomerates formed, are introduced in to 10 ml measuring cylinder and the intial weight is noted. The tapped Volume is measured by tapping the powder for 100 times and the tapped volume is noted.

It is expressed in terms of g/mL and is calculated by formula,

D_T = W / V; Where, W is the weight of powder, V_T is the tapped volume of the powder

Density related properties

The compressibility index of the granules and powder was calculated from the difference between tapped and bulk densities divided by the tapped densities and the ratio expressed as a percentage.

% Compressibility index = D_T- D_B/DT x 100

The hausner ratio was calculated by dividing the tapped density by the bulk density of the granule.

Hausner's ratio = D_T/D_B

Where, D_T is the tapped density, D_B is the bulk density

Post-compression Evaluation of fluoxeitine hydrochloride oro-dispersible tablets

The post-compression parameters were tested and their results were listed in following tables.

Shape and color of tablets

Uncoated tablets were examined under a lens for the shape of the tablet and color was observed by keeping the tablets in light [9].

Uniformity of thickness

Three tablets were picked from each formulation randomly and thickness was measured individually. It is expressed in mm and standard deviation was also calculated.

Hardness

Hardness or Tablet crushing strength (T_{cs}) is the force required to break the tablet or ability of a tablet to withstand mechanical shocks while handling. It was measured by using Monsanto hardness tester.[10] it was expressed in terms of kg/cm^2.

Weight variation

The weight of the tablet being made was routinely determined to ensure that a tablet contains the proper amount of drug. Twenty tablets selected randomly were weighed individually, calculating the average weight and comparing the individual weights to the average.

Friability test

Friability of tablet was determined by using Electrolab, EF-friabilator. It is expressed in percentage (%).

The tablets are subjected into a plastic chamber revolving at 25 rpm for 4 minutes or run upto 100 revolutions by dropping a tablet at height of 6 inches in each revolution. Preweighed tablets were placed in friabilator and subjected for 100 revolutions.[10] Tablets were dusted using a muslin cloth and again reweighed and friability (%F) can be calculated.

% friability of tablets less than 1 % are considered acceptable.

Estimation of drug content

10 tablets were weighed and triturated

The tablet triturate equivalent to 10 mg of the drug was weighed accurately, dissolved in pH 1.2 buffer and diluted to 100 ml with the same [11]. Further dilutions were done suitably to get a concentration of 10 mcg / ml with simulated gastric fluid pH 1.2. Absorbance was read at 226 nm against the reagent blank, and the concentrations of Fluoxeitine hydrochloride in mcg / ml was determined by using the regression equation.

$$\text{Drug content} = \frac{\text{test absorbance}}{\text{std absorbance}} \times \frac{\text{std. dilution}}{\text{test dilution}} \times \text{avg. wt}$$

Wetting Time

A piece of tissue paper folded twice was placed in a small petri plate (internal diameter = 6.5 cm) containing 10ml of water.

A tablet was placed on the paper, and the time for complete wetting of the tablet was measured in seconds[12]. The method was slightly modified by maintaining water at 37° C.

Water absorption ratio

Piece of tissue paper folded twice was placed in a small Petridish containing 6 ml of water.

A tablet of known weight was put on the paper and the time required for complete wetting of tablet was measured [12]. The wetted tablet was then weighed, water absorption ratio R was determined using the following equation and the result is shown in table-7 & 8.

R = 100 x Wa / Wb – Wa

Where Wb is weight of tablet before water absorption and

Wa is weight of tablet after water absorption.

Dispersion Time

The tablets was dropped in the beaker containing 10 ml of the simulated saliva of ph 6.7 and the time was noted where the tablets are completely dispersed [13].

In vitro drug dissolution studies

Apparatus: USP II (paddle)

RPM: 50

Temperature: 37°± 0.5°C

Dissolution medium: 900ml of pH 6.6 phosphate buffer

Absorbance measured: 266 nm

Procedure

Dissolution rate of the tablets prepared was studied using dissolution test apparatus USP II employing a paddle stirrer at 50 rpm & at 37°± 1°C. Phosphate buffer of pH 6.6 (900ml) was used as a dissolution fluid. Samples of 5 ml each were withdrawn at 2, 4, 6, 8, 10, 12 and 15 minutes.

The samples were suitably diluted with the dissolution fluid and assayed for Fluoxeitine hydrochloride at 266nm and using the corresponding dissolution fluid as blank.

Each sample withdrawn was replaced with an equal amount of drug free dissolution fluid.[14]

RESULTS AND DISCUSSION

Compatibility studies

An I.R study was carried out to check the compatibility between the selected excipients and fluoxeitine hydrochloride. spectra obtained for I.R studies at wavelength from 4000 cm^{-1} 400 cm^{-1} are showing in fig 1-3.

Precompression parameters of granules

Result of pre-compression parameter for tablets prepared by direct compression, wet granulation and sublimation methods:

Pre-compression parameters

The results of pre-compression parameters like bulk density, tapped density, angle of repose, carr's index and hausners ratio were tabulated in table 2-4

IR Images

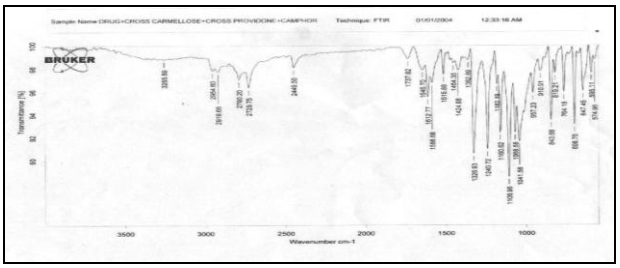

Fig. 1: IR Spectrum of Drug (Fluoxeitine hydrochloride)

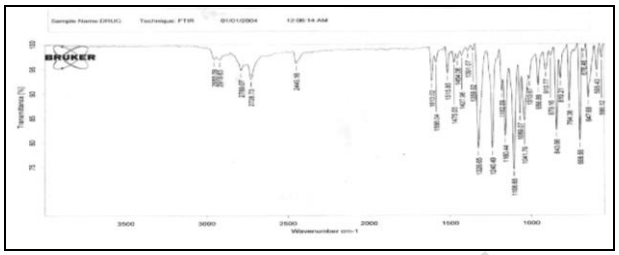

Fig. 2: IR Spectrum of Drug+ superdisintegrant (CCS)

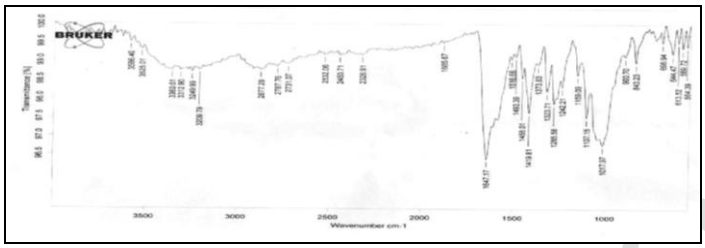

Fig. 3: IR Spectrum of Drug + superdisintegrant (cross povidone)

Table 2: Pre compression parameters of direct compression method

Formulation code	Bulk density (gm/cm³) ±SD, n=3	Tapped density(gm/cm³) ±SD, n=3	Angle of repose (degree) ±SD, n=3	Carr's index (%)±SD, n=3	Hausner's ratio ±SD, n=3
DF 1	0.740 ± 0.001	0.768 ± 0.001	28.18 ± 0.07	14.771 ± 0.02	1.21 ± 0.01
DF 2	0.754 ± 0.001	0.783 ± 0.001	26.73 ± 0.05	17.827 ± 0.01	1.21 ± 0.02
DF 3	0.742 ± 0.001	0.783 ± 0.001	27.84 ± 0.02	16.780 ± 0.01	1.18 ± 0.03
DF 4	0.751 ± 0.001	0.767 ± 0.001	27.32 ± 0.02	17.829 ± 0.01	1.20 ± 0.01

Table 3: Pre compression parameters of Sublimation method

Formulation code	Bulk density (gm/cm³) ±SD, n=3	Tapped density(gm/cm³) ±SD, n=3	Angle of repose (degree) ±SD, n=3	Carr's index (%)±SD, n=3	Hausner's ratio ±SD, n=3
SF 1	0.820 ± 0.001	0.832 ± 0.003	26.93 ± 0.01	16.019 ± 0.001	1.18 ± 0.01
SF 2	0.832 ± 0.002	0.848 ± 0.001	27.34 ± 0.01	14.397 ± 0.531	1.20 ± 0.03
SF 3	0.819 ± 0.002	0.833 ± 0.0001	27.22 ± 0.01	16.019 ± 0.003	1.19 ± 0.02
SF 4	0.850 ± 0.003	0.863 ± 0.001	27.16 ± 0.01	16.019 ± 0.001	1.16 ± 0.05

Table 4: Pre compression parameters of wet granulation method

Formulation code	Bulk density (gm/cm³) ±SD, n=3	Tapped density(gm/cm³) ±SD, n=3	Angle of repose (degree) ±SD, n=3	Carr's index (%)±SD, n=3	Hausner's ratio ±SD, n=3
WF 1	0.781 ± 0.01	0.783 ± 0.01	25.56 ± 0.09	13.92 ± 0.02	1.145 ± 0.015
WF 2	0.793 ± 0.06	0.826 ± 0.03	26.76 ± 0.11	13.31 ± 0.04	1.170 ± 0.036
WF 3	0.781 ± 0.01	0.816 ± 0.01	26.36 ± 0.05	13.69 ± 0.10	1.137 ± 0.010
WF4	0.778 ± 0.01	0.812 ± 0.009	25.93 ± 0.01	12.15 ± 0.10	1.139 ± 0.025

Values are means of SD± n=3

Bulk density, tapped density, hausners ratio, compressibility index, angle of repose of granules and powders of all formulations were performed and compared. And the flow properties of all the granules and powder were found to fall within the official USP limits.

Post compression evaluation of compressed tablets Results of Post-Compression Tablets Prepared By Direct Compression, Sublimation and wet granulation methods

Post-compression parameters

The results of post-compression parameters like bulk hardness, thickness, friability and weight variation were tabulated in table 5-7.

All the post compression parameters of tablet like hardness, friability, drug content, weight variation, disintegration tie were performed and compared between different superdisintegrants used in the tablet formulation.

Table 5: Post compressional parameters for direct compression method

Formulation code	Hardness (Kg/ cm²) ±SD	Friability (%)	Thickness (mm) ± SD	Weight variation (mg) ± SD
DF 1	2.60 ± 0.10	0.59 ± 0.01	4.62 ± 0.02	201.0 ± 1.00
DF 2	2.26 ± 0.05	0.60 ± 0.01	4.76 ± 0.01	202.3 ± 0.57
DF 3	2.03 ± 0.15	0.58 ± 0.01	4.68 ± 0.02	197.7 ± 0.57
DF 4	2.73 ± 0.20	0.65 ± 0.01	4.79 ± 0.01	200.0 ± 0.00

Table 6: Post compressional parameters for sublimation method

Formulation code	Hardness (Kg/ cm²) ±SD	Friability (%)	Thickness (mm) ± SD	Weight variation (mg) ± SD
SF 1	2.10 ± 0.10	0.52 ± 0.01	4.68 ± 0.005	201.0 ± 1.00
SF 2	2.13 ± 0.05	0.56 ± 0.01	4.83 ± 0.010	198.3 ± 0.57
SF 3	2.40 ± 0.10	0.55 ± 0.01	4.75 ± 0.010	203.0 ± 1.00
SF 4	2.53 ± 0.05	0.59 ± 0.01	4.86 ± 0.010	200.0 ± 1.00

Table 7: Post compressional parameters for wet granulation method

Formulation code	Hardness (Kg/ cm²) ±SD	Friability (%)	Thickness (mm) ± SD	Weight variation (mg) ± SD
WF 1	2.83 ± 0.05	0.493 ± 0.02	4.56 ± 0.020	199.0 ± 1.000
WF 2	3.10 ± 0.10	0.536 ± 0.01	4.71 ± 0.010	198.0 ± 1.000
WF 3	3.50 ± 0.10	0.500 ± 0.01	4.66 ± 0.005	200.3 ± 0.577
WF 4	3.56 ± 0.05	0.530 ± 0.02	4.71 ± 0.010	201.7 ± 1.520

Values are means of SD± n=3.

It was found to be all the tablet hardness was found to be with in the range of 2 to 4 Kg/ cm².

In vitro dispersion time

The in vitro dispersion time is measured by the time taken to undergo uniform dispersion. Rapid dispersion within the several minutes was observed in all the formulations.

The in –vitro dispersion data is tabulated in the table 8, 9 and 10. The in-vitro dispersion time of Fluoxeitine hydrochloride prepared by direct compression, granulation and sublimation method were found to be in the range of 16 to 38.33 sec fulfilling the official requirements

Dissolution study

***In vitro* dissolution studies**

Dissolution rate was studied by using USP type- II apparatus (USP XXIII Dissolution test apparatus at 50 rpm) using 900 ml of phosphate buffer pH (6.6) as dissolution medium. Temperature of the dissolution medium was maintained at 37 ± 0.5° C, aliquot of dissolution medium was withdrawn at every 2 minutes interval and filtered. The absorbance of the filtered solution was measured by UV spectrophotometric method at 226 nm and the concentration of the drug was determined from standard calibration curve. The dissolution of Fluoxetine hydrochloride from the tablets is shown in the figure shows the drug release profiles.

Table 8: Post compressional parameters for direct compression method

Formulation code	Invitro dispersion time* (sec) ±SD	Wetting time (sec) ±SD	Water absorption ratio* ± SD	Drug content (%) ± SD
DF 1	27.0 ± 1.00	48.33 ± 1.15	84.00 ± 1.00	99.30 ± 0.22
DF 2	24.67 ± 0.57	43.00 ± 1.00	71.67 ± 2.68	99.61 ± 0.06
DF 3	22.00 ± 1.00	39.00 ± 1.00	67.33 ± 1.52	99.23 ± 0.29
DF 4	18.33 ± 1.15	37.67 ± 1.15	59.13 ± 0.11	99.62 ± 0.01

Table 9: Post compressional parameters for sublimation method

Formulation code	Invitro dispersion time* (sec) ±SD	Wetting time* (sec) ±SD	Water absorption ratio* ± SD	Drug content* (%) ± SD
SF 1	21.67 ± 1.15	49.00 ± 1.00	77.00 ± 1.00	99.30 ± 0.05
SF 2	18.00 ± 1.00	41.67 ± 0.57	67.33 ± 1.00	100.10 ± 0.06
SF 3	17.00 ± 1.00	39.00 ± 1.00	63.00 ± 1.00	99.65 ± 0.01
SF 4	16.00 ± 1.00	38.00 ± 1.00	55.00 ± 1.00	100.7 ± 0.06

Table 10: Post compressional parameters for wet granulation method

Formulation code	Invitro dispersion time* (sec) ±SD	Wetting time (sec) ±SD	Water absorption ratio ± SD	Drug content (%) ± SD
WF 1	38.33 ± 0.57	53.00 ± 1.00	86.00 ± 1.00	100.80 ± 0.03
WF 2	35.67 ± 1.52	43.67 ± 0.57	76.33 ± 0.57	99.54 ± 0.09
WF 3	35.33 ± 2.08	42.00 ± 1.00	72.67 ± 1.15	98.62 ± 0.05
WF 4	30.33 ± 0.57	40.00 ± 1.00	67.00 ± 1.00	99.57 ± 0.01

The rapid increase in dissolution of Fluoxeitine hydrochloride tablets containing cross carmellose sodium may be due to rapid swelling and disintegrates rapidly into primary particles. Crosspovidone containing tablets rapidly exhibits high capillary activity and pronounced hydration with a little tendency to gel formation. The formulation containing crosscarmellose sodium and crosspovidone in the ratio of 1:1 shows higher percentage cumulative drug release i.e., 98.98 ± 0.009 % at the end of 12 minutes. As the method of preparation of tablets changed to sublimation, the dissolution of the drug from the tablets prepared by camphor sublimation method, the cumulative drug release profiles show good for sublimation method when compared to direct compression and wet granulation methods.

Table 11: *Invitro* drug release data of fluoxeitine hydrochloride oral dispersible tablet formulations prepared by direct compression method

Time (mints)	Cumulative % drug release			
	DF 1	DF 2	DF 3	DF 4
0	0.00 ±0.00	0.00 ±0.00	0.00 ±0.00	0.00 ±0.00
2	30.16 ± 0.020	35.08 ± 0.015	40.72 ± 0.010	42.14 ± 0.015
4	39.03 ± 0.011	44.12 ± 0.010	48.03 ± 0.020	48.54 ± 0.015
6	51.15 ± 0.025	50.01 ± 0.015	63.15 ± 0.030	63.92 ± 0.020
8	69.18 ± 0.03	67.90 ± 0.010	72.12 ± 0.025	77.23 ± 0.035
10	82.09 ± 0.015	79.63 ± 0.015	78.44 ± 0.020	81.65 ± 0.010
12	90.14 ± 0.032	85.48 ± 0.041	89.71 ± 0.020	92.96 ± 0.041
15	91.44 ± 0.015	92.75 ± 0.020	95.75 ± 0.01	94.45 ± 0.010
20	96.92 ± 0.015	-	-	-

(DF – Formulation prepared by direct compression method)

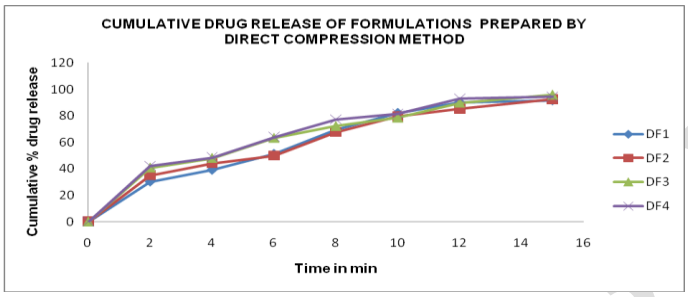

Fig. 4: Cumulative drug release of formulations prepared by direct compression method.

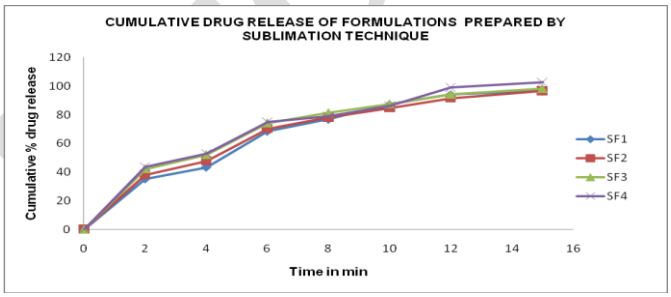

Fig. 5: Cumulative drug release of formulations prepared by sublimation technique.

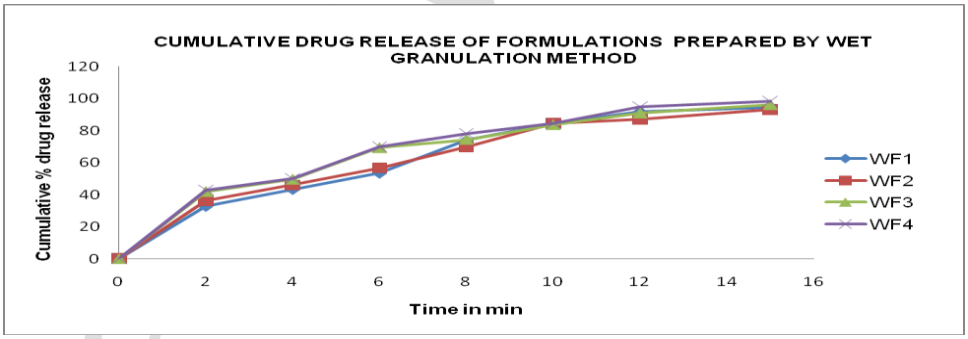

Fig. 6: Cumulative drug release of formulations prepared by direct compression method.

Table 12: *Invitro* drug release data of fluoxeitine hydrochloride oral dispersible tablet formulations prepared by sublimation technique

Time (mints)	Cumulative % drug release			
	SF 1	SF 2	SF 3	SF 4
0	0.00 ±0.00	0.00 ±0.00	0.00 ±0.00	0.00 ±0.00
2	35.13 ± 0.020	38.23 0.015	42.23 ± 0.015	43.66 ± 0.020
4	43.35 ± 0.010	47.90 ± 0.020	52.12 ± 0.015	52.97 ± 0.005
6	68.45 ± 0.011	70.18 ± 0.020	74.23 ± 0.015	75.08 ± 0.015
8	76.83 ± 0.015	78.14 ± 0.025	81.34 ± 0.020	78.97 ± 0.023
10	87.14 ±0.015	84.66 ± 0.032	87.43 ± 0.010	86.14 ± 0.026
12	94.13 ± 0.015	91.63 ± 0.015	94.16 ± 0.015	98.98 ± 0.009
15	96.46 ± 0.030	96.68 ± 0.144	98.25 ± 0.015	102.67 ± 0.002

(SF –formulation prepared by sublimation method)

Table 13: *Invitro* drug release data of fluoxeitine hydrochloride oral dispersible tablet formulations prepared by wet granulation method

Time (mints)	Cumulative % drug release			
	WF 1	**WF 2**	**WF 3**	**WF 4**
0	0.00 ±0.00	0.00 ±0.00	0.00 ±0.00	0.00 ±0.00
2	32.64 ± 0.010	36.43 ± 0.020	41.91 ± 0.015	42.83 ± 0.015
4	43.25 ± 0.009	46.07 ± 0.020	49.54 ± 0.020	49.88 ± 0.020
6	53.44 ± 0.020	56.70 ± 0.020	69.24 ± 0.009	69.90 ± 0.153
8	74.05 ± 0.009	70.03 ± 0.020	74.34 ± 0.009	78.16 ± 0.025
10	84.36 ± 0.025	84.50 ± 0.026	83.65 ± 0.010	84.39 ± 0.010
12	91.94 ± 0.015	87.09 ± 0.040	90.82 ± 0.01	94.75 ± 0.030
15	94.33 ± 0.011	93.32 ± 0.0251	96.13 ± 0.015	98.29 ± 0.010

(WF- formulation prepared by wet granulation method)

CONCLUSION

Based on the observations, it can be concluded that the formulated oro-dispersible tablets of Fluoxeitine hydrochloride may have wide acceptance compared to the conventional dosage forms.

From the data obtained, it is observed that formulations with crospovidone as disintegrant exhibit quicker dispersion time and wetting time than compared to croscarmellose sodium but the percentage cumulative drug release was shown more in case of croscarmellose sodium than crospovidone so it indicated that amongst them the formulation containing in combination of these two superdisintegrants were suitable to formulate oral disintegrating tablets by sublimation method as it allows the formation of pores on the tablet surface upon sublimation which allows faster dispersion and more percentage cumulative drug release with less time when compared to other methods like direct compression and wet granulation. The order of superdisintegrants was as follows.

Crospovidone croscarmellose sodium > crospovidone > croscarmellose sodium > starch.

And hence formulations containing the combination of the was concluded to be the best form for formulating the oral dispersible tablets.

REFERENCES

1. Indurwade NH, Rajyaguru TH, Nakhat PD.Novel Approach – Fast Dissolving Tablets. Indian Drugs 2002; 39(8): 405-9.
2. Watanae Y, Koizumi K, Zama Y, Kiriyama M, Matsumoto M.New Compressed Tablet Rapidly Disintegrating in Saliva in the Mouth using Crystalline Cellulose and a Disintegrant. Bio Pharmaceutical Bulletein 1995; 8: 1308-10.
3. Bi Y, Yonezawa Y, Sunanda H.Rapidly Disintegrating Tablets prepared by the wet compression method- mechanism and optimization. Journal of pharmaceutical sciences 1999; 88(10):1004-1010.
4. Rakesh KR.Orally Disintegrating Tablets- Novel Approach to Drug Delivery. The Pharma Review 2004; 2(12):34-6.
5. Pfister WR, Ghosh TK.Orally Disintegrating Tablets: Products, Technologies, and Development Issues. Pharm Tech 2005; 25(9): 44-50.
6. Bandari S, Mittapalli R, Gannu R, Yamsani M.Orodispersible Tablets: An Overview. Asian Journal of Pharmaceutical Sciences 2008:1-11.
7. Robin H, Bogner: Fast Dissolving tablets. www.US.Pharmacist, Jobson Publication, 2007.
8. Gerard J. Tortora and Bryan Derrickson : Principles of Anatomy and Physiology, John Wiley & Sons, edition 13th vol 1, 2000: 482.
9. Adel M Aly, Semreen M, Mazen K.Superdisintegrants for solid dispersion to produce rapidly disintegrating Tenoxicam tablets via camphor sublimation. Journal of Pharmaceutical Sciences 2005:68-78.
10. Mehta RM. Pharmaceutics-I, Vallabh Prakashan, 2nd edition. 1997.
11. Gilbert S. Banker, Neil R. Anderson. Tablets In: Lachman L, Lieberman HA., editor. The Theory and Practice of Industrial Pharmacy. Special Indian edition, CBS publishers 2009; 293-373.
12. Sarasija S, Pandit V, Joshi HP.Preparation and evaluation of mouth dissolving tablets of Salutamol sulphate. Indian Journal of Pharmaceutical Sciences 2007; 69(3): 467-469.
13. Yunxia B, Hisakazu S, Yorinobu Y, Kazumi D, Akinobu O.Preparation and evaluation of a compressed tablets rapidly disintegrating in oral cavity. Chemistry and Pharmacy Bulletein 1996; 44(11): 2121-2127.
14. Venkatesh DP and Geetha Rao CG.Formulation of taste masked oraldispersible tablets of Ambroxol hydrochloride. Asian Journal of Pharmaceutics 2008; 2(4): 261-264.