



Formulation and Evaluation of Enteric Coated Tablets of Duloxetine Hydrochloride

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ABSTRACT

Duloxetine hydrochloride is an acid labile antidepressant drug which degrades in acidic environment. The study was aimed to formulate enteric coated tablets of Duloxetine hydrochloride using (Protectab enteric M1) to avoid degradation in the stomach and to improve the therapeutic efficiency. Five formulations (F-I to F-V) were prepared by direct compression method, without & with addition of calcium carbonate as an alkalizing agent. Prepared tablets were evaluated for various post compression parameters. Among the formulations, the drug release of F-I formulated without addition of calcium carbonate, F-II & F-III prepared with 5mg & 15mg of calcium carbonate were not within the I.P limit. So in F-IV and F-V, calcium carbonate concentration was increased to 25 mg & 30 mg which showed drug release of 95.78% and 100.67% at 45 min which was within the I.P limit. Hence F-IV & F-V formulations were selected for enteric coating and F-IV formulation was coated with 4% Protectab enteric M1 polymer(E-IV), and F-V was coated with 8% Protectab enteric M1 polymer(E-V). Formulation E-IV fails in the disintegration test and Formulation E-V passed the disintegration test of the enteric coated tablets. Hence E-V was selected as a best formulation which showed better drug release compared to marketed drug and stability study revealed, E-V formulation was stable even after stored at 25±2°C/60%±5%RH and 40±2°C/75%±5%RH for a period of 3 months. Hence the study concluded that formulation E-V satisfied all the criteria for enteric coated tablets.

Keywords: Calcium carbonate, Duloxetine Hydrochloride, Enteric coated tablets, Stability study.

INTRODUCTION

Duloxetine hydrochloride is one of the most commonly used antidepressant drug which is a selective serotonin and norepinephrine reuptake inhibitor (SSNRI) used to balance the hormones such as dopamine, serotonin and norepinephrine.¹ Duloxetine hydrochloride is an acid labile drug which degrades in acidic environment of the stomach thus leading to therapeutic inefficiency. The study was aimed to formulate enteric coated tablets of Duloxetine hydrochloride using methacrylic acid copolymer (Protectab enteric M1) to avoid degradation and to bypass the acidic pH of the stomach, to improve the therapeutic efficacy and to increase the Duloxetine release in the intestine compared to the marketed Duloxetine hydrochloride enteric coated tablet.² Five formulations (F-I to F-V) were prepared by direct compression method without & with addition of calcium carbonate as an alkalizing agent. Best formulation was taken and coated with enteric polymer and the drug release of the formulation was compared with marketed enteric coated tablet of Duloxetine hydrochloride.

MATERIALS AND METHODS

Materials

Duloxetine hydrochloride was obtained from MetroChem API Pvt. Ltd, Hyderabad, India. Mannitol anhydrous was

procured from Shandong Tianli Pharmaceutical Co. Ltd, China. Microcrystalline cellulose-PH 112 was procured from Accent Microcell Pvt. Ltd, Gujarat, India. Calcium carbonate was procured from Par Drugs and Chemicals Pvt. Ltd, Vadodara, India. Povidone-K30 from Boai NKY Pharmaceuticals Ltd, China, Croscarmellose sodium from Prachin Chemicals Pvt. Ltd, Ahmedabad, India, Instacoat moist shield and Insta coat glow from Ideal Cures Pvt. Ltd, Mumbai, India and Protectab Enteric MI polymer was procured from Bharat Coats, Chennai, India. All other chemicals and reagents used were of analytical grade.

Methods

Preformulation Studies

Preformulation can be defined as an investigation of physical and chemical properties of drug substance alone and when combined with excipients. It is the first step in the rational development of dosage forms.³

Organoleptic properties

The organoleptic property like color, odor and taste of the API was evaluated. A small quantity of Duloxetine HCl was taken in a butter paper and the colour was viewed in well-illuminated place. Very less quantity of Duloxetine HCl was used to assess the taste with the help of tongue as well as smelled to get odor.



Solubility test

Solubility of Duloxetine hydrochloride in water, DMSO, methanol and ethanol was determined by using sonicator at room temperature.⁴

FT-IR studies

Infrared spectra matching approach was used for the detection of any possible chemical reaction between the drug and the excipients. A physical mixture of drug and excipients in highest concentration was prepared and mixed with suitable quantity of potassium bromide.⁵ Samples were compressed to form a transparent pellet using a hydraulic press at 10 tons pressure and scanned between 4000- 500 cm⁻¹ in a shimadzu FT-IR (IR Affinity-1) spectrophotometer.

Precompression Parameters

The prepared powder blends were evaluated for angle of repose, bulk density, tapped density, compressibility index and Hausner's ratio. The angle of repose was determined by fixed funnel method to assess the flow property.⁶ Bulk density is the ratio between a given mass

of the powder or granules and its bulk volume. Tapped density is the ratio between a given mass of powder or granules and the constant or fixed volume of powder or granules after tapping. Bulk and tapped density were determined using digital bulk density apparatus.⁷ The compressibility index and the Hausner ratio are determined by measuring both the bulk volume and tapped volume of the powder.⁸

$$\text{Compressibility index (\%)} = \frac{\text{TD} - \text{BD}}{\text{TD}} \times 100$$

Where, TD = Tapped density, BD = Bulk density

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

Formulation of Duloxetine Hydrochloride Uncoated Tablets

Duloxetine Hydrochloride tablets were prepared by direct compression method as per the composition shown in Table 1. Five formulations (F-I to F-V) were prepared by direct compression method.

Table 1: Composition of Duloxetine Hydrochloride Uncoated Tablets

Ingredients	Quantity per Tablet (mg)				
	Formulation Code				
	F-I	F-II	F-III	F-IV	F-V
Duloxetine hydrochloride	20.00	20.00	20.00	20.00	20.00
Mannitol anhydrous	50.00	45.00	45.00	40.00	40.00
Microcrystalline cellulose - PH 112	45.00	45.00	35.00	30.00	25.00
Calcium carbonate	-	5.00	15.00	25.00	30.00
Povidone-K30	10.00	10.00	10.00	10.00	10.00
Croscarmellose sodium	16.00	16.00	16.00	16.00	16.00
Colloidal silicon dioxide	1.00	1.00	1.00	1.00	1.00
Magnesium stearate	3.00	3.00	3.00	3.00	3.00
Average weight of each uncoated tablet	145.00	145.00	145.00	145.00	145.00

Direct compression method

The active ingredient was passed through the sieve # 40. The other ingredients given in the formulation table were passed separately through the same sieve. All the materials (including the active ingredient) were taken in a poly bag and mixed for 10 minutes for uniform mixing. Magnesium stearate and talc were passed through the sieve # 60 and mixed together with the powder mixture in a polybag for 5 minutes to get a uniform blend. Finally, the powder mixture was compressed into tablets using rotary tablet compression machine of 7.14 mm round shape punches and dies.⁹

Post compression parameters

The prepared Duloxetine Hydrochloride uncoated tablets were evaluated for parameters such as hardness, thickness, weight variation, friability, drug content,

disintegration time and *in-vitro* drug release studies.

General appearance

The tablets should be free from cracks, depressions, pinholes etc. The color and polish of the tablets should be uniform on whole surface. The surface of the tablets should be smooth. The tablets were examined externally under a biconvex lens for surface cracks, depressions and pinholes.¹⁰

Thickness and hardness test

Thickness of the tablet was measured by using vernier caliper. Thickness values were expressed in millimeter. Hardness (diametric crushing strength) is the force required to break a tablet across the diameter. The hardness of tablets was determined using a Monsanto hardness tester. The tablet is placed across the diameter in between the spindle and anvil. The knob is adjusted to



hold the tablet in position. The pressure is increased slowly to break the tablet. The value was expressed in Kg/cm².¹⁰

Weight variation test

Twenty tablets were selected at random and average weight was determined. Then individual tablets were weighed and the individual weight was compared with the average weight. Not more than two of the tablets weight should deviate from the average weight by more than the percentage deviation and none should deviate from the average weight by more than twice that percentage deviation.¹⁰

Percentage deviation of the tablets were calculated by using the following formula

Percentage deviation =

$$\frac{(\text{Weight of tablet (mg)} - \text{Average weight of tablet (mg)})}{\text{Average weight of tablet (mg)}} \times 100$$

Friability

Friability is tested by using Roche friabilator. Friabilator is

Assay of Duloxetine hydrochloride by HPLC method¹²

Chromatographic conditions

Column	: Inertsil ODS (250x 4.6 mm) C8 column.
Mobile phase	: 55:37:8 V/V (Buffer: acetonitrile (ACN):methanol.
Buffer	: 0.3% w/v solution of potassium dihydrogen phosphate. Adjust to pH 5.7 with orthophosphoric acid.
Flow rate	: 2.0 ml/minute.
Injection volume	: 20 µl.
Wavelength	: 240 nm.
Column Temperature	: 30°C.

Preparation of standard solution

Accurately weighed 20 mg of Duloxetine hydrochloride was transferred to a 20ml volumetric flask, dissolved and diluted to the mark with methanol to obtain a standard solution of 1000 µg/ml. This solution (1 ml) was further diluted to 10 ml with mobile phase to obtain a working standard stock solution of 100µg/ml for the HPLC method.

Preparation of sample solution

Twenty tablets were weighed and finely powdered. A mass equivalent to 20 mg of Duloxetine hydrochloride was weighed and transferred in a 100 ml volumetric flask, mixed with methanol (60 ml) and sonicated for 20 min. The solution was filtered through whatman filter paper

made up of a plastic drum fixed with a machine which rotates at 25 rpm for 100 revolutions. Tablet falls from 6 inches height in each turn within the apparatus.¹¹ The percentage friability of the tablets were calculated by the formula.

$$\text{Percentage Friability} = \frac{W1 - W2}{W1} \times 100$$

Where,

W1 = Weight of tablets before testing, W2 = Weight of tablets after testing.

Disintegration test

The disintegration time of tablets from each formulations were determined using disintegration test apparatus. Disintegration test was carried out at 37°C±2°C in 900 ml of distilled water. One tablet was placed in each of the six tubes of the apparatus containing distilled water.² One disk was added to each tube. The time taken in seconds for complete disintegration of the tablets with no palpable mass remaining in the apparatus was measured.

and the residue was washed thoroughly with methanol. The filtrate and washings were combined in a 100 ml volumetric flask and diluted to the mark with methanol. An aliquot of this solution (0.2 ml) was further diluted to 10 ml with methanol to obtain a solution containing 4 µg/ml of Duloxetine hydrochloride and subjected to HPLC analysis.

Sample injection procedure

20 µl of filtered sample solution and standard solution were separately injected into HPLC system. The chromatogram was recorded and responses were measured for major peaks. The content of Duloxetine hydrochloride in the powder mixture was calculated by using the following equation.

$$\text{Content of Duloxetine HCl} = \frac{\text{Sample area}}{\text{Standard area}} \times \frac{\text{Standard weight}}{\text{Sample weight}} \times \frac{P}{100} \times \text{Avg.}$$

Where, P – Purity of Duloxetine hydrochloride, Avg. Wt – Average weight in mg.



In vitro drug release studies

Drug release studies were carried out by using USP Type II paddle dissolution test apparatus at 100 rpm for 45 min in 0.1 N HCl (900ml) maintained at $37^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$. 10 ml of sample were taken at 5,10,15,20,30 and 45 min intervals and 10 ml volume of fresh buffer was added to kept volume of dissolution medium constant and samples after suitable dilution were analyzed using UV spectrophotometer at 289 nm.¹³

Formulation of Duloxetine Hydrochloride Enteric Coated Tablets

Formulation F-IV and F-V were selected as the best formulations based on drug release. The best formulations F-IV was coated with 5.80 mg (E-IV) and and F-V was coated with 11.80 mg (E-V) of protectab enteric M1 polymer. Duloxetine Hydrochloride enteric coated tablets were prepared by direct compression method as per the composition shown in Table: 2.

Enteric coating of tablets⁹

Seal coating

Accurately weighed ethyl cellulose was milled using colloidal mill for 20 minutes to reduce particle size and dissolved in acetone to form uniform coating solution and applied into uncoated tablets.

Moisture prior coating

The solid material of insta coat moisture shield white was dissolved in isopropyl alcohol and then mixed with methylene dichloride and uniformly mixed by using colloidal mill for 30 minutes and then applied into uncoated tablets. This process of moisture prior coating is performed after seal coating process.

Enteric coating

Protectab enteric M1 bharath coat (methacrylic acid co polymer) powder was mixed with isopropyl alcohol. Iron oxide red was added to this solution and milled using colloidal mill to form uniform coating solution and then applied into uncoated tablets.

Polish coating

The tablets obtained are smooth and evenly colored but have a dull surface appearance. Polishing is carried out in canvas lined coating pans and the process consists of applying thin layer of waxy materials to impart shine to the finished tablets.

Evaluation of Duloxetine Hydrochloride Enteric Coated Tablets

The enteric coated tablets were evaluated for the parameters such as Thickness, Weight variation, Hardness, Disintegration time, Assay and *In vitro* dissolution studies.

Table 2: Composition of Duloxetine Hydrochloride Enteric Coated Tablets

Ingredients	Quantity per Tablet (mg)	
	Formulation Code	
	E-IV	E-V
Duloxetine hydrochloride	20.00	20.00
Mannitol anhydrous	40.00	40.00
Microcrystalline cellulose - PH 112	30.00	25.00
Calcium carbonate	25.00	30.00
Povidone-K30	10.00	10.00
Croscarmellose sodium	16.00	16.00
Colloidal silicon dioxide	1.00	1.00
Magnesium stearate	3.00	3.00
Seal Coating		
Insta coat moist shield white	3.00	3.00
Isopropyl alcohol	20.00	20.00
Methylene dichloride	10.00	10.00
Enteric Coating		
Protectab Enteric M1	5.80	11.80
Isopropyl alcohol	30.00	60.00
Methylene dichloride	30.00	60.00
Ironoxide red	0.20	0.20
Polish Coating		
Insta coat glow	1.00	1.00
Isopropyl alcohol	3.50	3.50
Methylene dichloride	3.50	3.50
Average weight of each enteric coated tablet	155.00	161.00

Disintegration test

The disintegration test was carried out according to I.P procedure on six tablets using disintegration test apparatus with disks in 0.1 N HCl (pH 1.2) maintained at $37^{\circ}\text{C} \pm 2^{\circ}\text{C}$ for 2 hours.² After 2 hours 0.1 N HCl was replaced with phosphate buffer 6.8 pH. A disk was added to each tube and operated for further 60 minutes. The disintegration time of each tablet was recorded.

In vitro drug release studies

Drug release studies were carried out by using USP Type II paddle dissolution test apparatus at 100 rpm for 2 hrs in 0.1 N HCl (900ml) maintained at $37^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$. 10 ml of sample was taken and analyzed by using UV spectrophotometer at 289 nm. Then the dissolution medium was replaced with 6.8 pH Phosphate buffer (900 ml) and tested for drug release for 45 minutes at $37^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$ temperature and 100 rpm speed. After 5, 10, 15 and 45 minutes, 10ml samples were taken out and 10 ml volume of fresh phosphate buffer pH 6.8 was added to kept volume of dissolution medium constant and sample

was analyzed after suitable dilution using UV spectrophotometer at 289 nm.¹³

Stability studies

Stability studies were carried out for the optimized formulation (E-V) at $25\pm 2^\circ\text{C}/60\%\pm 5\%\text{RH}$ and $40\pm 2^\circ\text{C}/75\%\pm 5\%\text{RH}$ for 3 months.¹⁴ The selected clear ALU-ALU packed formulations were stored at $25\pm 2^\circ\text{C}/60\%\pm 5\%\text{RH}$ and $40\pm 2^\circ\text{C}/75\%\pm 5\%\text{RH}$ for 3 months and their physical appearance, average weight, thickness, hardness, disintegration test, assay and *in vitro* drug release were evaluated at specified intervals of time (every month).

RESULTS AND DISCUSSION

Preformulation studies

The organoleptic properties like color, odor and taste of the API were evaluated. The color of Duloxetine hydrochloride was found to be white. Duloxetine hydrochloride does not show any characteristic odor and the taste was found to be bitter. Duloxetine hydrochloride showed similar color, taste and odor as per the I.P specifications. The solubility studies revealed that Duloxetine HCl was very much soluble in DMSO, soluble in methanol, ethanol and sparingly soluble in water. FT-IR spectroscopic studies indicated that the drug is compatible with all the excipients. The FT-IR spectrum of physical mixture showed all the characteristic peaks of Duloxetine hydrochloride, thus conforming that no interaction of drug occurred with the components of the formulation.

Precompression parameters

Angle of repose of Duloxetine hydrochloride powder blend was found in the range of $24^{\circ}.23'$ to $30^{\circ}.09'$ which indicates the flow of Duloxetine hydrochloride was excellent. The above results revealed that the all the formulations (F-I to F-V) possess excellent flow. Bulk density of Duloxetine hydrochloride was found between

0.305 ± 0.3 to $0.640 \pm 0.1 \text{ g/cm}^3$. Tapped density ranges between 0.351 ± 0.5 to $0.745 \pm 0.3 \text{ g/cm}^3$. Compressibility index values was found to be in the range of 13.11 ± 0.1 to $18.55 \pm 0.7 \%$ and the hausner's ratio lies between 1.15 ± 0.5 to 1.17 ± 0.3 . Compressibility index of formulation-I belongs to fair flow and compressibility index of other formulations indicates that the blend belongs to good flow property.

Post compression parameters

The general appearances of all formulations (F-I to F-V) were examined. The color of the tablets was found to be yellow, round shape. The surface was found to be smooth with no cracks, depressions and pinholes. The thickness of tablets was found in the range of 3.22 ± 0.055 to $3.40 \pm 0.017\text{mm}$. All the formulations showed uniform thickness. Hardness of Duloxetine hydrochloride tablets was found in the range of 6.60 ± 0.29 to $7.50 \pm 0.49 \text{ kg/cm}^2$. All the formulations possessed good mechanical strength. The accepted percentage deviation was ± 7.5 for 130 – 324 mg tablet weight as per I.P. The results of weight variation test showed that the weight of tablets ranges from 144.50 ± 1.20 to 146.03 ± 0.12 for all the formulations that is well within the I.P limit (± 7.5). Hence all the tablets passed the weight variation test. In the friability test, the maximum weight loss should not be more than 1%. The friability values of formulations (F-I to F-V) were found to be in the range of 0.10 ± 0.010 to $0.16 \pm 0.005\%$ respectively. Hence all the tablets passed the friability test. Disintegration test of Duloxetine hydrochloride uncoated tablets ranges from 5 min 45 sec to 9 min 30 sec. The acceptable disintegration time of uncoated tablet limit as per I.P is NMT 15 minutes. Hence all the tablets passed the disintegration test. The content of Duloxetine hydrochloride in all formulations were found in the range of 98.55% to 102.16% which was within the acceptable I.P limits. The results of post compression parameters of Duloxetine uncoated tablets were given in Table-3.

Table 3: Post Compression Parameters

Formulation code	Thickness (mm)	Hardness (kg /cm ²)	Weight variation (mg)	Friability (%)	Disintegration (min)
F-I	3.22 ± 0.055	7.20 ± 0.32	145.50 ± 1.55	0.14 ± 0.007	8 min 30 sec
F-II	3.35 ± 0.010	6.60 ± 0.29	144.50 ± 1.20	0.12 ± 0.004	8 min
F-III	3.40 ± 0.017	7.00 ± 0.27	145.25 ± 1.08	0.10 ± 0.010	5 min 45 sec
F-IV	3.36 ± 0.016	7.50 ± 0.49	145.00 ± 0.13	0.16 ± 0.005	7 min 30 sec
F-V	3.29 ± 0.020	7.20 ± 0.24	146.03 ± 0.12	0.12 ± 0.003	9 min 30 sec

*All the values are expressed as mean \pm standard deviation; n=3.

Duloxetine hydrochloride tablets (F-I to F-V) were prepared by direct compression method and subjected to *in vitro* drug release studies. Formulation F-I showed only 12.57% of drug release at the end of 45 min. So to increase the drug release it was planned to add calcium carbonate as an alkalinizing agent in formulation F-II and F-III. 5mg of calcium carbonate was added in formulation F-

II and 15mg in formulation F-III. But formulation F-II and F-III showed only 28.96% and 64.50% drug release at the end of 45 min which was not within the IP limit. So in formulation F-IV calcium carbonate content was further increased to 25mg and in formulation F-V 30mg calcium carbonate is added. Formulation F-IV and F-V showed maximum drug release at the end of 45 min (95.78% and



100.67%) which was within the IP limit. This may be due to the alkaline pH nature due to the addition of calcium carbonate in formulation F-IV and F-V which showed

more drug release than other formulations. The dissolution data and release profiles of Duloxetine uncoated tablets were given in Table-4 and Fig-1.

Table 4: *In vitro* Dissolution Studies of Duloxetine Hydrochloride Uncoated Tablets

Time (min.)	Percentage Drug Release (%)				
	Formulation Code				
	F-I	F-II	F-III	F-IV	F-V
5	6.70 ± 0.32	24.78 ± 0.32	34.97 ± 0.20	36.98 ± 0.32	37.78 ± 0.22
10	8.78 ± 0.22	24.98 ± 0.39	36.98 ± 0.38	41.87 ± 0.21	41.78 ± 0.23
15	9.74 ± 0.36	25.32 ± 0.32	37.87 ± 0.37	64.98 ± 0.32	67.65 ± 0.22
20	10.96 ± 0.27	26.96 ± 0.34	43.96 ± 0.31	76.88 ± 0.16	79.89 ± 0.16
30	11.57 ± 0.22	27.97 ± 0.22	50.78 ± 0.28	85.67 ± 0.37	88.78 ± 0.080
45	12.57 ± 0.28	28.96 ± 0.10	64.50 ± 0.13	95.78 ± 0.22	100.67 ± 0.11

*All the values are expressed as mean ± standard deviation; n=3.

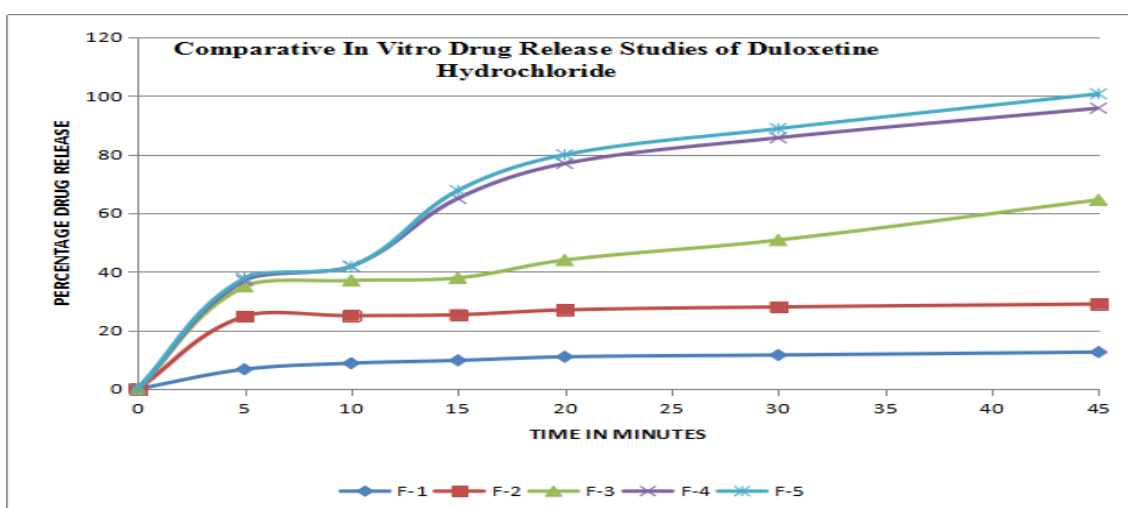


Figure 1: *In Vitro* Drug Release Profiles of Duloxetine Hydrochloride Uncoated Tablets

Formulation F-IV and F-V were selected as the best formulations based on drug release. The best formulations F-IV was coated with 5.80 mg (4% coating thickness) and F-V was coated with 11.80 mg (8% coating thickness) of protectab enteric M1 polymer and named as E-IV and E-V respectively. Formulation E-IV showed increased thickness after coating process. The weight of tablets also improved further upon addition of 4% coating solution. But formulation E-IV failed in disintegration test as it does not withstand in 0.1 N HCl for 2 hr. Formulation

E-V withstand in 0.1 N HCl for 2 hr and disintegrate in alkaline medium after 15 min and 30 seconds which is almost similar compared to the marketed Duloxetine HCl enteric coated tablets. Hence formulation E-V was considered as best formulation and the drug release behavior of formulation E-V was compared with the marketed Duloxetine HCl enteric coated tablets. The evaluation results of Duloxetine HCl enteric coated tablets are given in table: 5.

Table 5: Evaluation of Duloxetine Hydrochloride Enteric Coated Tablets

Formulation code	Thickness (mm)	Weight Variation (mg)	Disintegration Time (min)	
			0.1N HCl buffer	pH 6.8 Phosphate buffer
E-IV	3.48 ± 0.071	158.12±2.25	50 min	-
E-V	3.42± 0.026	160.50±1.90	-	15 min 30 sec
Marketed sample	2.90± 0.055	210.00±2.50	-	15 min 40 sec

*All the values are expressed as mean ± standard deviation; n=3.

The percentage drug release of marketed sample and formulation (E-V) was found to be 97.98±0.52% and 100.53±0.85 % at end of 2 hour and 45 minutes. The drug release from formulation E-V was found to be better than the marketed

product. This may be due to increase in addition of calcium carbonate as an alkalinizing agent in formulation E-V. The comparative dissolution profiles of marketed sample and formulation (E-V) were given in fig-2 .

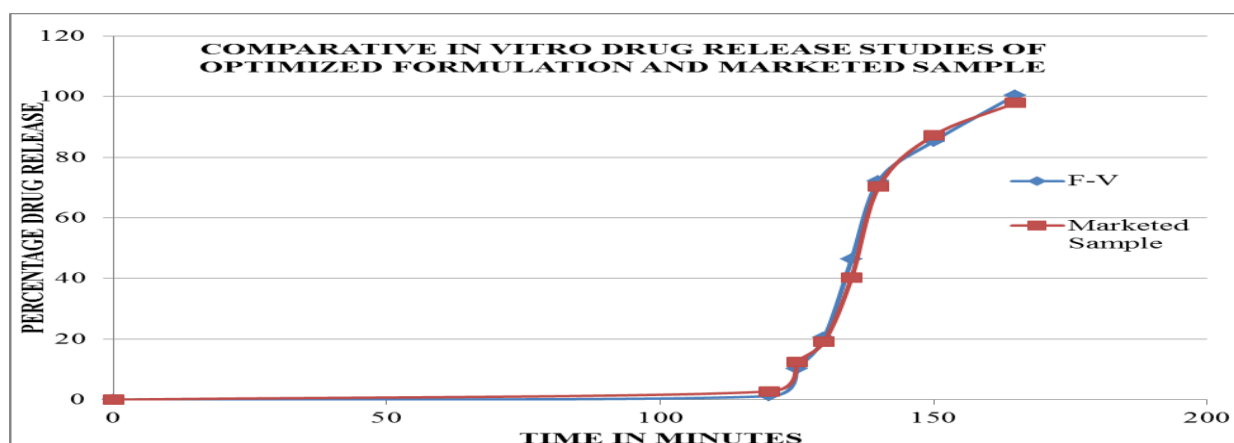


Figure 2: Comparative *In Vitro* Drug Release Profiles of Duloxetine HCl Marketed Sample and Formulation (E-V)

Stability studies

The best formulation (E-V) was selected for the stability study and stored at $25\pm 2^{\circ}\text{C}/60\%\pm 5\%$ RH and $40\pm 2^{\circ}\text{C}/75\%\pm 5\%$ RH for 3 months. The tablets were evaluated for various parameters like physical appearance, average weight, thickness, hardness, disintegration, *in vitro* drug release and drug content at every one month. The results of stability studies revealed that there was no significant changes found in physical appearance, average weight, thickness, hardness, disintegration, *in vitro* drug release and assay during the period of three months even after stored at $25\pm 2^{\circ}\text{C}/60\%\pm 5\%$ RH and $40\pm 2^{\circ}\text{C}/75\%\pm 5\%$ RH. The study revealed that the formulation E-V was stable at $25\pm 2^{\circ}\text{C}/60\%\pm 5\%$ RH and $40\pm 2^{\circ}\text{C}/75\%\pm 5\%$ RH even after stored for three months.

CONCLUSION

A total of five formulations (F-I to F-V) of Duloxetine hydrochloride uncoated tablets were developed by direct compression method. From all the above observation it was concluded that the formulation F-V containing 30mg calcium carbonate as an alkalinizing agent along with mannitol and microcrystalline cellulose as diluent was selected as the best formulation among the five formulations and 8% coating solution of Protectab enteric M1 polymer was applied as enteric coating(E-V). Formulation E-V showed better drug resistance in acidic medium and release the drug in alkaline medium as per I.P specification and showed rapid drug release in intestine than marketed Duloxetine hydrochloride enteric coated tablet. Hence the study concluded that formulation E-V satisfied all the criteria for enteric coated tablets.

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