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# Formulation and Evaluation of Extended Release Tablets of Darifenacin Hydro bromide

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***ABSTRACT***

***D****arifenacin Hydrobromide is a Potent and selective antimuscarinic (M3) agent used in Symptomatic treatment of urge incontinence and/or increased urinary frequency as may occur in adult patients with overactive bladder syndrome. The objective of present study was to develop an effective Extended Release(ER) tablets of Darifenacin Hydrobromide to release the drug over an extended period of time that provide therapeutically effective plasma concentration for the treatment of urinary incontinence in humans with extended duration of action and less number of doses. Darifenacin Hydrobromide ER tablets were prepared by direct compression method using hydrophilic polymers like HPMC (K4M, K15M, K100M, Metalose 60 SR 50) and Xanthan Gum. The ER tablets were evaluated for physicochemical, pre compression, post compression parameters and compared with the marketed product (ENABLEX). The % drug released from the extended release tablets (from F1 to F12) was found to be vary from 9.34% to 104.45% in 24 hours. The optimized formulation F12 showed 97.84% of drug release in 24 hours whereas the marketed extended release tablets (ENABLEX) showed 96.45% in 24 hours. There was no significant difference between the optimized formulation and marketed tablet (ENABLEX) in terms of invitro drug release profile. The extended release tablets prepared were found to be within the official limits with respect to hardness, weight variation, drug content, thickness etc. The optimized formulation (F12) follows first order kinetics and found to be stable for 3 months of period time.*

**Keywords:** *Extended release; matrix tablets; direct compression; Darifenacin Hydrobromide; Innovator (Enablex).*

## INTRODUCTION

**O**ral drug delivery is the most widely acceptable route of administration among all the routes of administration that has been explored for the systematic delivery of drug through different pharmaceutical dosage forms. More than 50% of drug delivery systems available in the market are oral solid drug delivery systems particularly tablets and capsules. They offer convenience and ease of administration, greater flexibility in dosage form design and ease of production and low cost [1].

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The extended release system is a modified drug release system that provides release of drug over an extended period of time. The ER systems may offer many advantages over immediate release dosage forms particularly in case of chronic disease conditions. The extended released dosage forms provide maintenance of plasma drug concentration within an optimal therapeutic range for prolonged duration of treatment, maximization of efficiency-dose relationship and minimization of the need for frequent dose intake. They improve control of condition i.e., reduced fluctuation in drug level [2].

Darifenacin Hydrobromide is a potent and selective antimuscarinic (M3) agent used in Symptomatic treatment of urge incontinence and/or increased urinary frequency and urgency as may occur in adult patients with overactive bladder syndrome. The recommended starting dose is 7.5 mg daily. Darifenacin Hydrobromide has low absorption rate. The mean oral bioavailability is approximately 15% and 19% after 7.5 mg and 15 mg daily doses at steady state. It has a half-life of 13-19 hours and is extensively metabolized in the liver, mainly via by CYP3A4 and CYP2D6. The problems associated with the drug Darifenacin Hydrobromide are high acid

solubility, low drug absorption and fast clearance, undesirable fluctuations in plasma concentration and short duration of action, thus necessitating frequent oral administration for adequate treatment [3].

Hence to overcome these problems the Darifenacin Hydrobromide is formulated in the form of extended release tablets that provide therapeutically effective plasma concentration for the treatment of urinary incontinence in humans with extended duration of action and less number of doses. This may also be helpful in improving the patient compliance.

## MATERIALS AND METHODS

### 1. Materials:

Darifenacin Hydrobromide (DH) was provided by Shasun Chemicals and Drugs Ltd, Hyd. HPMC K4M, HPMC K15, HPMC K100, Metalose 60 SH 50 and Opadry yellow were purchased from Colorcon, Hyd. Dibasic Calcium phosphate, Xanthan gum, Magnesium Stearate were purchased from Signet Chemicals Ltd, Hyd. India and all other materials used in this study were of analytical and pharmaceutical grade.

### 2. Methods:

**Drug Excipient Compatibilities studies:**

The compatibility of drug and formulation components is important prerequisite before formulation. It is therefore necessary to confirm that the drug does not react with the polymers and excipients under experimental conditions and affect the shelf life of product or any other unwanted effects on the formulation. As a part of the product development; the compatibility of various excipients with DH was evaluated4.

**Preparation of Darifenacin Hydrobromide tablets:** [5]

Darifenacin hydrobromide tablets were prepared by using Direct Compression method by using 8 mm round shaped concave punches. Before going to direct compression, all the ingredients were subjected to the following steps.

**Weighing:** The required quantities of Darifenacin Hydrobromide, Dibasic Calcium Phosphate (A-Tab), Hypromellose, Xanthan gum, Metalose 60 SH 50 and except Magnesium stearate were weighed.

**Sifting:** Sifted the drug, Dibasic Calcium Phosphate (A-Tab), Hypromellose, Xanthan gum, Metalose 60 SH 50 through #30 mesh and mixed the blend in a poly bag for uniform mixing of API.

**Lubrication:** Required amount of Magnesium stearate was weighed, passed through #80 mesh and mixed to above blend.

**Compression:** The Blend was compressed to tablets by using 8.0 mm round shaped, standard concave punches using 17 station compression machine.

Composition of extended release tablets of Darifenacin hydrobromide shown in Table 1.

**Table No. 1: Composition of extended release tablets of Darifenacin Hydrobromide**

| FC | Drug (mg) | Excipients (mg) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | DCP | HPMC K4M | HPMC K15M | HPMC K100M | Metalose 60 SH 50 | Xanthan gum | Mg. Stearate | Opadry yellow | FW (mg) |
| **F1** | 17.846 | 119.154 | 60 | - | - | - | - | 3 | 5 | 205 |
| **F2** | 17.846 | 119.154 | - | 60 | - | - | - | 3 | 5 | 205 |
| **F3** | 17.846 | 119.154 | - | - | 60 | - | - | 3 | 5 | 205 |
| **F4** | 17.846 | 159.154 | - | - | 20 | - | - | 3 | 5 | 205 |
| **F5** | 17.846 | 119.154 | - | - | - | 60 | - | 3 | 5 | 205 |
| **F6** | 17.846 | 129.154 | - | - | - | - | 60 | 3 | 5 | 205 |
| **F7** | 17.846 | 149.154 | - | - | - | - | 30 | 3 | 5 | 205 |
| **F8** | 17.846 | 139.154 | - | - | - | - | 40 | 3 | 5 | 205 |
| **F9** | 17.846 | 119.154 | 30 | 30 | - | - | - | 3 | 5 | 205 |
| **F10** | 17.846 | 119.154 | 20 | 40 | - | - | - | 3 | 5 | 205 |
| **F11** | 17.846 | 119.154 | - | 30 | 30 | - | - | 3 | 5 | 205 |
| **F12** | 17.846 | 119.154 | - | 20 | 40 | - | | 3 | 5 | 205 |

***FC- Formulation Code, DCP- Dibasic Calcium Phosphate, HPMC- Hydroxy Propyl Methyl Cellulose, FW- Final Weight***

**Pre compression evaluation parameters:**

**Organoleptic Evaluation:**The physical properties (Color and Odor) of API were studied visually and reported in Table 2.

**Loss on drying:** 1.5g of sample of DH was accurately weighed and the powder was kept in a moisture balance apparatus for 5 min at 65ºC and the moisture content was calculated.

**Water Content[6]:**Water Content of DH was determined by using karlfischer titration method.

**Solubility studies:** Darifenacin hydrobromide is classified as BCS II drug i.e. high permeability and low.

Solubility study was performed at room temperature or ambient temperature in phosphate buffer 1-12 pH. 250 ml of buffer or medium was taken in 250 ml volumetric flask, to this Darifenacin hydrobromide equivalent to 18 mg was added. This solution is then ultra-sonicated for 15 minutes with handshaking until the material was completely dissolved. Then the solution was filtered through 0.45µm nylon filter to get clear solution. Filtered solution was diluted to get a concentration approximately equal to that of standard preparation. Content of DH was estimated by HPLC method [7].

**Bulk density:** Bulk density was determined by pouring gently 25 gm of sample (DH) into 100 ml graduated cylinder. The volume occupied by the sample was recorded [8].

**Tapped density:** Tapped density was determined by using Electro lab density tester, which consists of a graduated cylinder mounted on a mechanical tapping device. An accurately weighed sample of powder was carefully added to the cylinder. Typically, the initial volume was noted, and the sample is then tapped (500, 750 or 1250 tapping) until no further reduction in volume is noted. Volume was noted and tapped density is calculated [9].

**Compressibility Index and Hausner ratio:** Both the compressibility index and the Hausner ratio were determined by using bulk density and the tapped density of a powder.

Indicates the flow properties of the powder and is measured by the ratio of tapped density to the bulk density.

**Angle of Repose:** The angle of repose has been used to characterize the flow properties of powders. Angle of repose is a characteristic related to inter particulate friction or resistance to movement between particles. This is the maximum angle possible between surface of pile of powder or granules and the horizontal plane [10].

$$\text{Tan } \theta = h / r; \quad = \text{Tan}^{-1} h / r$$

Where$\theta$ = angle of repose, h = height, r = radius.

A funnel was fixed at a height approximately of 2-4 cm over the platform. The loose powder was slowly passed along the wall of funnel, till the cone of the powder is formed and determines the angle of repose by measuring the height of the cone of powder and radius of the heap of powder.

**Particle size determination:** Particle size determination by using Sieve analysis method. Sieve no# 80, # 100, # 140, # 200, #230 and collector were taken and individual weight of each sieve was noted. These sieves were arranged in ascending order of their weight and connected to the Sieve Shaker. Weighed quantity of Darifenacin hydrobromide (100gm) was placed in ⍰ 80 mesh and then Sieve shaker was set to run for 5 min at amplitude of 40 (Intermittent shaking). Remove the set up from the sieve shaker after 5 min and weighed each mesh individually and calculate % drug retained in each size of mesh [11].

**Assay:** Assay is an indicative of the amount of the drug present in the dosage form. Here it gives the insight information about the substances of the process and about effect of changes. Decrease in assay % was insignificant and within limits for the formulations.

Assay was performed by using HPLC. It requires mobile phase, solvent, stock solution and test solution. Chromatographic conditions shown in Table 2

**Mobile phase:** Prepared a mixture of 500ml Water, 400 mL of methanol, and 100 mL of tetrahydrofuran, (50:40:10) and mixed well. Then filtered through 0.45µm nylon membrane filter and degassed. Mobile phase was used as solvent.

**Standard Stock solution preparation (2mg/mL):** Accurately weighed 20mg of Darifenacin Hydrobromide was taken into a 100ml volumetric flask and10ml of Acetonitrile was added and sonicated for 5 minutes, then diluted to volume with diluent and mixed well.

**Preparation of diluted standard solution:** Pipetted 5ml of above standard stock solution (2mg/ml) into a 100ml volumetric flask and diluted to volume with diluent and filtered through 0.45⍰m nylon membrane filter.

**Test preparation:** 5 tablets were taken and powdered then placed in 200mL of volumetric flask containing 20 mL Acetonitrile, andsonicated for about 15 minutes. The solution was made up to the volume with diluent and mixed well, then filtered through 0.45 µm nylon membrane filter.

**Procedure of injection sequence:** Injected 25 µl portion of the dissolution medium as blank, standard preparation, test preparation into the chromatogram, recorded the chromatogram and measured the response as the analyte peak respectively.

Calculations:

The concentration of drug present in the test formulation was calculated by using following formula;

$$\text{Assay (mg/tab):} \quad \frac{At^* Ws^* Td^* P^* Avg.wt}{As^* SD^* Wt^* 100}$$

$$\text{Assay (\%)} = \frac{\text{Assay (mg/tab)} * 100}{L}$$

Where,

At = peak area of DH for test preparation.

As = peak area of DH for standard preparation.

Ws = weight of DH working standard taken in mg.

P = potency of DH working standard calculated as API.

L = labeled amount of DH working standard calculated as API.

Wt. = weight of DarifenacinHydrobromide tablet taken.

Sd = Sample dilution. Td= Test dilution.

**Table No. 2: Chromatographic conditions**

| | |
|---|---|
| **Instrument** | **:** Agilent 1200 HPLC with pump, Injector, UV Detector and recorder |
| **Column** | : Kromasil 100- C8 (250 X 4.6 mm ID), 5µm |
| **Wave Length** | **:** 215 nm |
| **Flow rate** | **:** 1.0 mL / min |
| **Injection Volume** | **:** 10µl |
| **Column Temperature** | **:** 30ºC |
| **Run time** | **:** 25 min |
| **Solvent** | **:** Water and Acetonitrile in the ratio of 70:30 (v/v) |
| **Retention time** | **:** 6.0 minutes |

**Post compression evaluation parameters:**

**Weight variation test:**

Individual weights of 20 tablets were taken from each batch and the average weight was calculated and % weight variation was calculated by using the following formula.

$$\% \text{ Weight variation} = \frac{(\text{Weight of tablet} - \text{Average weight})}{\text{Average weight of tablets}} \times 100$$

**Hardness:**

Hardness of the tablets was determined by using the hardness tester (Monsanto tester). Average results were calculated for 3 tablets from each batch and reported and it is expressed in kp.

**Thickness:**

Thickness of the tablets was determined by using Digital Verniercalipers. 10 individual tablets from each formulation batch were taken and average were calculated. The mean and standard deviations were computed and reported and it is expressed in mm.

**Stability Studies for Optimized Formulation:**

Stability studies were conducted according to the ICH guidelines. The optimized formulation of Darifenacin Hydrobromide Extended release tablets were kept at different temperatures i.e. 30±2ºC, 400C±2ºC at 75% RH for about 3 months in stability chamber. The parameters like physical characterization and % content uniformity were evaluated and Samples were analyzed for assay, and dissolution at the end of 1 month, 2 months and 3 months.

## RESULTS AND DISCUSSIONS

**Drug-Excipient Compatibility Study:**

Drug and Excipients compatibility study was performed by using Bruker FT-IR spectrophotometer. From the spectra, it would be concluded that, there was no interaction between drug and different polymer mixtures and the drug was compatible with all the excipients used in the formulation shown in Figure 1 and 2. Hence these release retarding materials were selected for formulation of extended release tablets.

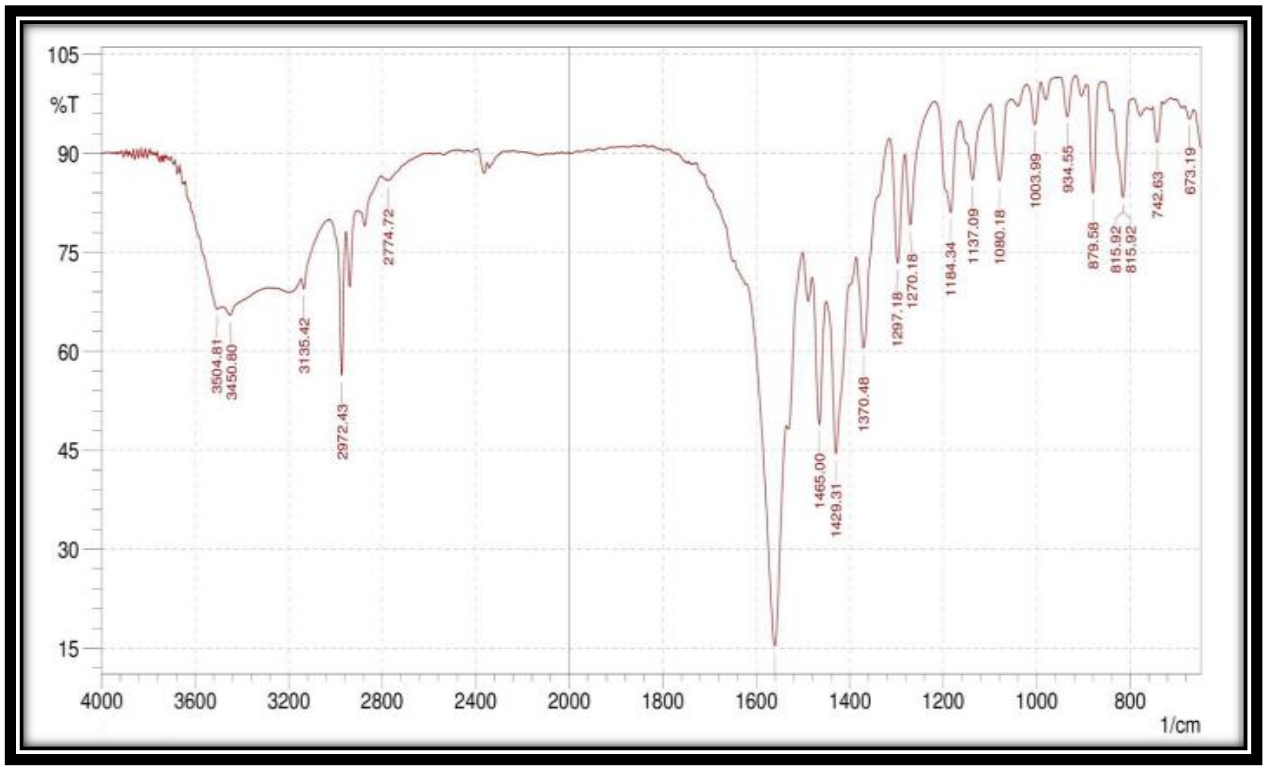


**Fig. 1: FT-IR spectra of Darifenacin Hydrobromide**

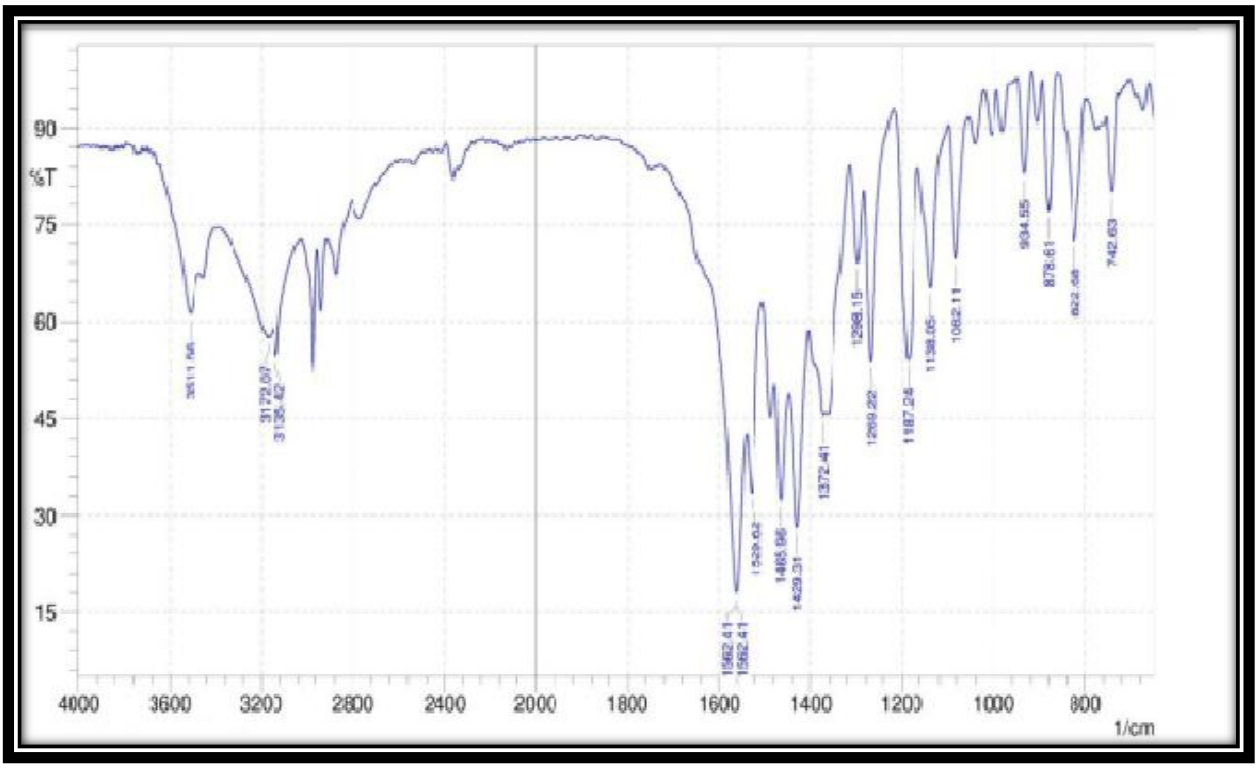


**Fig. 2: FT-IR spectra of Optimized formulation**

**Table No. 3: Evaluation parameters of API**

| S.No. | Characteristics | Results |
|---|---|---|
| 1. | Organoleptic properties | white or almost white colored crystalline powder |
| 2. | Solubility Analysis | 0.10mg/ml in 0.1N HCl,<br>0.13mg/ml in pH 4.5 Acetate buffer,<br>1.08mg/ml in pH6.8 Phosphate buffer,<br>1.91mg/ml in pH7.2 Phosphate buffer,<br>3.10mg/ml in pH8.0 Phosphate buffer,<br>3.03mg/ml in pH9.2 Phosphate buffer,<br>3.03mg/ml in pH10.0 Phosphate buffer,<br>3.10mg/ml in pH12.0 Phosphate buffer,<br>3.00mg/ml in pH9.2 with0.5%SLSbuffer. |
| 3. | Bulk density | 0.372 gm/ml |
| 4. | Tapped density | 0. 465 gm/ml |
| 5. | Compressibility index | 20.00 |
| 6. | Hausner's ratio | 1.25 |
| 7. | Melting point | 228-230ºC |
| 8. | Assay | 99.4% |

**Table No. 4: Pre compression parameters of Darifenacin Hydrobromide Extended release formulations F1 to F12**

| Formulation code | Angle of repose (Θ) | Bulk density ($gm/cc^3$) | Tapped density ($gm/cc^3$) | Carr's index(%) | Hausner's ratio |
|---|---|---|---|---|---|
| F1 | 49.57±0.24 | 0.325±0.31 | 0.456±0.04 | 35.5±0.52 | 1.582±0.02 |
| F2 | 42.14±0.18 | 0.343±0.27 | 0.52±0.42 | 32.4±0.12 | 1.67±0.01 |
| F3 | 51.23±0.33 | 0.296±0.32 | 0.492±0.35 | 36.50±0.34 | 1.701±0.02 |
| F4 | 42.36±0.15 | 0.358±0.41 | 0.468±0.28 | 41.24±0.53 | 1.372±0.01 |
| F5 | 54.52±0.24 | 0.395±0.18 | 0.564±0.4 | 29.42±1.2 | 1.43±0.01 |
| F6 | 43.24±0.08 | 0.320±0.36 | 0.582±0.21 | 38.20±0.62 | 1.625±0.02 |
| F7 | 41.23±0.42 | 0.387±0.54 | 0.481±0.23 | 36.51±0.76 | 1.56±0.01 |
| F8 | 52.12±0.75 | 0.390±0.72 | 0.521±0.61 | 31.72±1.1 | 1.48±0.03 |
| F9 | 39.85±0.38 | 0.295±0.61 | 0.561±0.5 | 40.82±0.12 | 1.633±0.01 |
| F10 | 48.56±0.47 | 0.345±0.4 | 0.486±0.12 | 38.65±0.54 | 1.725±0.02 |
| F11 | 45.72±0.33 | 0.328±0.06 | 0.539±0.19 | 39.45±0.47 | 1.435±0.01 |
| F12 | 51.82±0.23 | 0.356±0.28 | 0.562±0.43 | 35.52±0.26 | 1.61±0.02 |

**Table No. 5: Post compression parameters of Darifenacin hydrobromide Extended release formulations F1 to F12**

| Formulation code | Weight variation (mg) | Thickness (mm) | Hardness ($kg/cm^2$) | Content of uniformity(%) |
|---|---|---|---|---|
| F1 | 207.4±0.20 | 3.67±0.02 | 9-10 | 98.19±0.5 |
| F2 | 210.2±0.23 | 3.69 ±0.08 | 8-9 | 95.23±0.4 |
| F3 | 205.5±0.23 | 3.73±0.05 | 8-9 | 93.7±0.3 |
| F4 | 209.5±0.25 | 3.61±0.12 | 9-10 | 94.76±0.2 |
| F5 | 203.5±0.22 | 3.57±0.02 | 9-10 | 102.47±0.25 |
| F6 | 206.6±0.20 | 3.69±0.14 | 9-10 | 93.10±0.71 |
| F7 | 206.45±0.54 | 3.60±0.12 | 9-10 | 94.56±0.82 |
| F8 | 205.82±0.32 | 3.67±0.05 | 8-9 | 93.88±0.58 |
| F9 | 209.65±0.45 | 3.89±0.07 | 8-9 | 100.43±0.22 |

| | | | | |
|---|---|---|---|---|
| **F10** | 210.43±0.32 | 3.54±0.14 | 9-10 | 104.56±0.41 |
| **F11** | 205.52±0.18 | 3.81±0.04 | 9-10 | 98.59±0.53 |
| **F12** | 208.86±0.26 | 3.45±0.03 | 9-10 | 96.81±0.46 |

**IN VITRO DRUG RELEASE STUDY**

**1. Dissolution profile of Darifenacin Hydrobromide extended release formulations:**

In-vitro drug release studies were carried out by using USP–Type1 (basket) dissolution apparatus at a rotational speed of 100 rpm at 37±0.5°C. The prepared Darifenacin hydrobromide extended release formulations were evaluated for in vitro drug release profile in 0.01M HCl at time intervals of 1, 4, 8, 12, 16, 20 and 24 hrs and Sink conditions were maintained for the whole experiment. Samples (5 ml) were withdrawn at regular intervals and the drug content in each sample was analyzed after suitable dilution by using UV spectrophotometer at 215nm. The data obtained from the in-vitro drug release was plotted between time vs % cumulative drug release. Drug release profiles for all the formulations were shown in figure 3&4.

The percent of Darifenacin Hydrobromide released from the extended release tablets (from F1 to F12) was found to be vary from 9.34±0.22 to 104.45±0.22 in 24 hours. The optimized formulation F12 showed the 97.84±0.23 drug release in 24 hours whereas the marketed extended release tablets (ENABLEX) showed 96.45±0.36 in 24 hours. Thus the F12 was considered better among the other formulations.

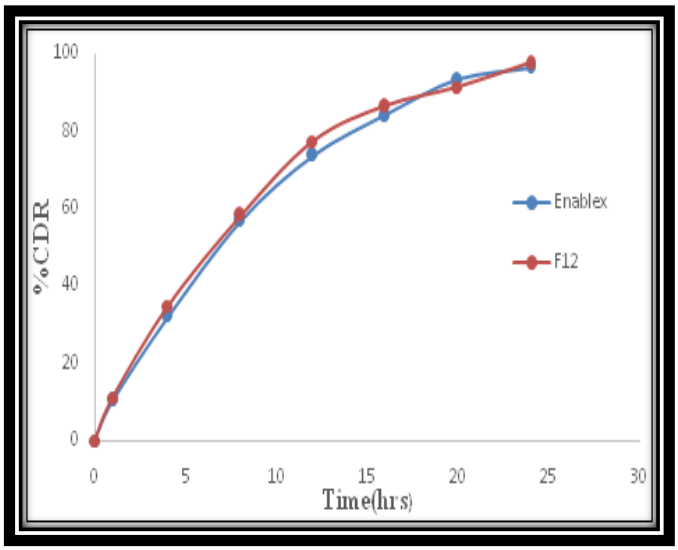


**Fig. 3: In vitro cumulative percentage drug release profile of Darifenacin hydrobromide extended release formulation F12 and innovator (Enablex)**

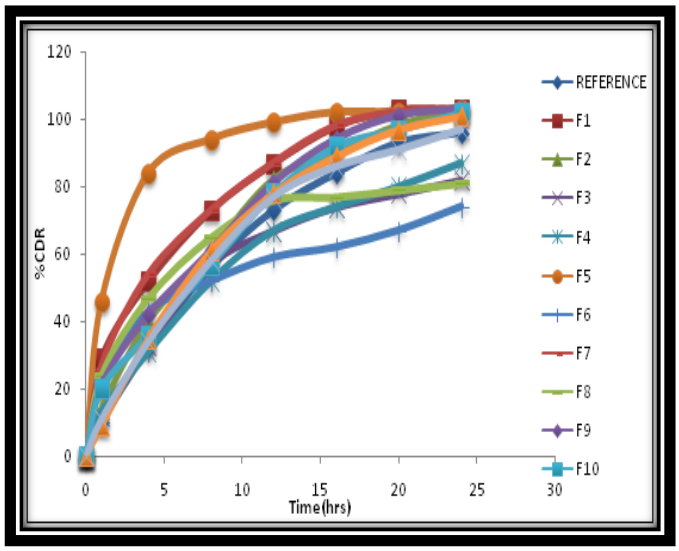


**Fig. 4: In vitro cumulative percentage drug release profile of Darifenacin hydrobromide extended release formulations F1 to F12 and Innovator (Enablex)**

**Release Kinetics:**

The kinetic release data was computed from the drug release data obtained from the in-vitro dissolution study. Kinetic release data obtained for optimized formulation F12 and innovator product was fitted to the mathematical models; Zero order, First order, Higuchi and Korsmeyer Peppas models. The R2 values are shown in Table 6 for optimized formulation. The drug release was found to be first order as R2 value of first order (0.968) was found to be more than R2 value of zero order (0.9115), indicates that the drug release was concentration dependent. To know the mechanism of drug release the data was fitted to higuchi model (R2 value 0.9841) and the drug release was found to be diffusion controlled. Further to know the exact mechanism of drug release the data was fitted to Koresmeyer-peppas model and based on the "n" value (n = 0.971), the mechanism of drug release was found to follow anomalous behavior or non – Fickian transport. (If n = 0.45 it is called Case I or Fickian diffusion, 0.45 < n < 0.89 is for anomalous behavior or non – Fickian transport, n = 0.98 for case II transport and n > 0.89 for Super case II transport).

**Table No. 6: Release Kinetics of Optimized Formulation (F12)**

| Formulation code | Zero order kinetics | Higuchi | Peppaskorsemeyer | First order kinetics | Hixson | n value |
|---|---|---|---|---|---|---|
| F1 | 0.8423 | 0.9785 | 0.9767 | 0.9429 | 0.95 | 0.9916 |
| F2 | 0.9092 | 0.9891 | 0.9722 | 0.9657 | 0.9059 | 0.9871 |
| F3 | 0.8712 | 0.9787 | 0.983 | 0.9721 | 0.9445 | 0.9738 |
| F4 | 0.9198 | 0.992 | 0.9615 | 0.9953 | 0.9844 | 0.9928 |
| F5 | 0.7533 | 0.9262 | 0.9132 | 0.8145 | 0.9594 | 0.9357 |
| F6 | 0.8045 | 0.9605 | 0.9835 | 0.9258 | 0.892 | 0.9861 |
| F7 | 0.8379 | 0.9772 | 0.9854 | 0.9399 | 0.9565 | 0.988 |
| F8 | 0.8388 | 0.978 | 0.9863 | 0.9271 | 0.9556 | 0.9888 |
| F9 | 0.9073 | 0.9914 | 0.9515 | 0.9509 | 0.9287 | 0.9941 |
| F10 | 0.9252 | 0.9899 | 0.9317 | 0.9636 | 0.9077 | 0.9884 |
| F11 | 0.915 | 0.9832 | 0.9757 | 0.9596 | 0.9229 | 0.9744 |
| F12 | 0.9115 | 0.9841 | 0.971 | 0.968 | 0.9947 | 0.9819 |

The different kinetic models were applied to the optimized formula and innovator. The linear nature of the curve obtained for first order demonstrated by very close and higher R2 values. The R2 values are very close in first order model it can be concluded that drug release followed first order and it complies with Innovator as mentioned in Table 7.

**Table No. 7: Comparison of Release Kinetics of Optimized Formulation and Innovator**

| Release kinetics | Correlation coefficient ($R^2$) for Innovator | Correlation coefficient ($R^2$) for optimized formulation |
|---|---|---|
| **Zero order equation** | 0.920 | 0.9115 |
| **First order equation** | 0.970 | 0.968 |

The different kinetic models were applied to the optimized formula. The linear nature of the curve obtained for first order demonstrated by very close and higher R2 values. The release exponent (n) value of korsmeyer peppas plot was found to be 0.971 indicates non-fickian diffusion.

It can be concluded that drug release followed first order and the drug release was controlled by diffusion and erosion.

## CONCLUSION

Darifenacin Hydrobromide is a genitourinary antispasmodic agent, an antimuscarinic agent which is used in the symptomatic treatment of urge incontinence, urinary frequency and urgency as may occur in adult patients with overactive bladder. Darifenacin Hydrobromide extended release matrix tablets were prepared by direct compression method by using hydrophilic matrix polymers such as HPMC and Xanthan gum. All the formulations F1-F12 showed good physico chemical, post compression properties. When compared with the in vitro drug release profiles, formulations F2, F7, F11 and F12 showed good release profile. Among these formulations, Formulation-F12 containing Darifenacin Hydrobromide equivalent to Darifenacin 15mg per tablet and developed employing HPMC K15M and HPMC K100M in varying ratios (40% and 60%) as the matrix former, gave good lag phase values with similar release profile when compared to innovator (ENABLEX) and was confirmed by the similarity factor(f1) value was 86. Based on the results, that the F12 formulation was concluded as optimized formulation. Hence we can conclude that the prepared Darifenacin Hydrobromide extended release tablets were comparable to the innovator product (ENABLEX).

## REFERENCES:


1. 1.Nippani A, Vijendar C, Dindigala A, Kandhula AG, Chandra SK, Alabadri A. Preparation and In-Vitro Evaluation of Mirtazapine Oral Films. Res Rev Pharm Pharm Sci **2016**;5(1):96-103.
2. Shah MS, Shah PB, Patel MS, Patel MR. A review on extended release drug delivery system and Multiparticulate System. World J Pharm Res **2015**; 4990:724-47.
3. Skerjanec A. The clinical pharmacokinetics of darifenacin. Clinical pharmacokinetics. **2006**;45(4): 325-50.
4. Patel P, Ahir K, Patel V, Manani L, Patel C. Drug-Excipient compatibility studies: First step for dosage form development. The Pharma Innovation. **2015**; 4(5, Part A):14.
5. Carstensen JT, Ertell C. Physical and chemical properties of calcium phosphates for solid state pharmaceutical formulations. Drug Develop & Industrial Pharm **1990**; 16(7):1121-33.
6. Tavčar E, Turk E, Kreft S. Simple modification of Karl-Fischer titration method for determination of water content in colored samples. J Analyt Methods in Chem **2012** Jan 1; 2012.

7. Tsume Y, Mudie DM, Langguth P, Amidon GE, Amidon GL. The Biopharmaceutics Classification System: subclasses for in vivo predictive dissolution (IPD) methodology and IVIVC. Eur J Pharm Sci **2014**; 57:152-63.
8. Fagir W, Hathout RM, Sammour OA, ElShafeey AH. Self-microemulsifying systems of Finasteride with enhanced oral bioavailability: multivariate statistical evaluation, characterization, spray-drying and in vivo studies in human volunteers. Nanomed **2015**; 10(22):3373-89.
9. Reddy MR, Reddy MH. Preparation and development of capecitabine microspheres for colorectal cancer. J Pharm Sci & Res **2017**;9(1):37.
10. Zhou ZY, Zou RP, Pinson D, Yu AB. Angle of repose and stress distribution of sandpiles formed with ellipsoidal particles. Granular Matter **2014**; 16(5): 695-709.
11. Wen B, Aydin A, Duzgoren-Aydin NS. A comparative study of particle size analyses by sieve-hydrometer and laser diffraction methods. Geotech Testing J **2002**; 25(4):434-42.

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