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## PREPARATION AND EVALUATION OF CONTROLLED RELEASE OF BETAXOLOL HYDROCHLORIDE OCULAR INSERTS

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Betaxolol Hydrochloride, ocular inserts, HPMCK4m, Ethyl Cellulose

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**ABSTRACT:** The present work focuses on treatment of glaucoma by formulating ocular inserts of different polymeric combination and Betaxolol to enhance therapeutic effect through prolonging contact time with corneal surface, Betaxolol is a cardio selective ( $\beta_1$  adrenergic) receptor blocking agent. Ophthalmic betaxolol may be especially useful in the treatment of glaucoma in patient with pulmonary disease. Sustained drug therapies have more advantages than conventional. In the present study, an attempt was made to formulate sustained drug delivery system films for Betaxolol. In matrix type formulations for Betaxolol containing 10%, 12%, and 14% w/v of HPMCK4m and 14%, 16% and 18% w/v for Ethyl cellulose were Prepared by solvent casting method. And evaluated for their average weight variation, thickness, Drug content, In-vitro drug release and stability studies. An increase in average weight and thickness is due to increase in polymer concentration. IR spectral studies were performed to confirm the interaction of drug with excipients. IR spectrum revealed that there is no compatibility and no drug interaction. In vitro drug release Studies were performed by vial and pre hydrated cellophane membrane method. HPMCK4m F15 (14%) & F 21(18%) EC w/v exhibited maximum average weight (14.20 & 15.90 mg) and thickness of F15, F21, is 0.33, 0.43mm respectively. The drug content was ranging from 90% to 100%. The In vitro drug release studies showed that increase in polymer content decreases the drug release from ocular films. Formulations 16 % and 21% w/v EC showed sustained and almost complete drug release and diffused (91.10%) over 14 hrs period was selected as an ideal formulation. Drug release from the occusers by diffusion controlled mechanism. Stability studies conducted formulation. The formulation showed satisfactory physical stability at 25<sup>0</sup> C and 40<sup>0</sup>C at 60.

**INTRODUCTION:** Ophthalmic drug delivery is one of the most interesting and challenging endeavours facing the pharmaceutical scientists. The anatomy-physiology and biochemistry of the eye render this organ exquisitely impervious to foreign substances.

The challenge to the formulator is to circumvent the protective barriers of the eye without causing permanent tissue damage. The development of newer, more sensitive diagnostic techniques and therapeutic agents renders urgency to the development of maximum successful and advanced ocular drug delivery systems. <sup>1, 2, 3</sup>

The goal of pharmacotherapeutics is the attainment of an effective drug concentration at the intended site of action for a desired period of time. Eye, as a portal for drug delivery is generally used for the local therapy as against systemic therapy in order to avoid the risk of eye damage from high blood

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concentrations of drug which are not intended for eye.<sup>4, 5</sup> The conventional ocular dosage forms for the delivery of drugs are i) Liquids as eye drops-solutions, suspensions, sol to gel systems. ii) Semisolids-eye ointments, eye gels. Liquids are the most popular and desirable type of dosage forms for the eye.

This is because the drug absorption is fastest from these types. The slow release of the drug from the suspended solids provides a sustained effect for a short duration of time. The eye drop dosage form is easy to in still but suffers from the inherent drawback that most of the instilled volume is eliminated from the pre-corneal area<sup>2, 6</sup> resulting in a bioavailability ranging from 1-10% of total administered dose<sup>7</sup>. The rapid pre-corneal elimination of drugs given in eye drops is mainly due to conjunctival absorption, solution drainage by gravity, induced lacrimation and normal tear turnover. Because of poor ocular bioavailability, many ocular drugs are applied in high concentrations.

This causes both ocular and systemic side effects, which are often related to high peak drug concentrations in the eye and in systemic circulation. The frequent periodic instillation of eye drops becomes necessary to maintain a continuous sustained level of medication. This gives the eye a massive and unpredictable dose of medication.<sup>8</sup> Solutions are the pharmaceutical forms most widely used to administer drugs that must be active on the eye surface or in the eye after passage through the cornea or the conjunctiva. The drug in the solution is in the dissolved state and may be immediately active. This form also has the disadvantage of instability of the dissolved drug and the necessity of using preservatives.<sup>9</sup>

Suspension types of pharmaceutical dosage forms are formulated with relatively water insoluble drugs to avoid the intolerably high toxicity created by saturated solutions of water-soluble drugs. However, the rate of drug release from the suspension is dependent upon the rate of dissolution of the drug particles in the medium, which varies, constantly in its composition with the constant inflow and outflow of lachrymal fluid. Ophthalmic inserts<sup>10, 11</sup> are sterile preparations with a solid or a semisolid consistency, whose

shape and size are designed for ophthalmic application. They are composed of polymeric support with or without drugs, the latter being incorporated as dispersion or a solution in the polymeric support. Ocular inserts can overcome the disadvantage reported with traditional ophthalmic systems like aqueous solutions, suspensions and ointments. The typical pulse entry type drug release behavior observed with ocular aqueous solutions (eye drops), suspensions and ointments is replaced by more controlled, sustained and continuous drug delivery using a controlled release ocular drug delivery system.

In the recent years, there has been explosion of interest in the polymer based delivery devices, adding further dimension to topical drug delivery thereby promoting the use of polymers such as collagen and fibrin fabricated into erodible inserts for placement in cul-de-sac. Ocular inserts also offer the potential advantage of improving patient compliance by reducing the dosing frequency. They may be used for topical or systemic therapy with the main objective, in addition to increasing the contact time, being to ensure a sustained release suited for topical or systemic treatment.

#### **MATERIAL AND METHODS:**

Betaxolol Hydrochloride was received a gift sample from FDC Pharmaceuticals Pvt. Ltd., Mumbai, HPMCK4m, Ethyl cellulose, Glycerin and Benzyl alkonium chloride were obtained from SD fine Chemicals Pvt. Ltd., Mumbai., All other chemicals and solvents were of analytical reagent grade.

#### **Preparation of ocular inserts:<sup>12</sup>**

##### **Preparation of HPMCK4m films:**

The required quantity of HPMC were weighed and dissolved in distilled water by gentle stirring on Magnetic stirrer. The required amount of Glycerin was added as plasticizer to above solution under stirring condition. Weighed amount of Betaxolol Hydrochloride, previously passed through sieve # 400, was added and stirred for 6hrs to get clear solution. After complete mixing, the casting solution 15 ml was poured in clean anumbra Petri dish of area 63.64sq.cm. Then the Petri dish was dried at room temperature for 24hrs. The dried films thus obtained were cut into size of mm

diameter by cork borer, wrapped in aluminum foil and stored till used. The formulas used in the preparation are shown in the **Table 1**

#### **Preparation of Ethyl cellulose films:**

Accurately weighed quantity of polymer was dissolved in alcohol containing diethylphthalate as plasticizer 40 w/w% of polymer. Weigh and transfer required quantity of Ethyl cellulose to this solution and stir for about 2 hours. Allow to stand overnight and then placed under vacuum to remove air bubbles. The polymeric drug solution 15 ml was then poured into prelubricated glass mould and allows to get dried at 50°C for 6 hours in hot air oven. After drying, the films were removed and cut into circular disc of 8 mm diameter. The formulas used in the prepared are shown in **Table 1**.

#### **Evaluation of the prepared formulations**<sup>13, 14, 15</sup>: **Uniformity of thickness:**

Five films were taken and their individual thickness was measured using micrometer screw gauge.

#### **Uniformity of weight:**

Five films were taken and their individual weights were determined by using electronic balance.

#### **Uniformity of drug content:**

Three films were taken and individually dissolved or crushed in 5 ml of Phosphate buffer in a beaker and filter it into the beaker 0.5 ml of the filtered solution was taken in 20ml beaker and diluted to 15 ml with Phosphate buffer. Three reading were taken using Shimadzu-160A UV spectrophotometer at 233 nm.

#### **Water absorption character:**

Three films were weighed and placed separately in beakers containing 4ml of distilled water. After a period of 5 minutes, the films were removed and the excess water on their surface was removed using a filter paper and then again weighed till there was no increase in the weight. The swelling index was then calculated by dividing the increase in weight by the original weight and was expressed as percentage.

***In vitro* dissolution studies of formulations using the vial method**<sup>16</sup>: The *in vitro* dissolution of drug from the different ophthalmic inserts was studied

using the vial method. Each insert was placed in 10 ml capacity vials containing 5 ml of phosphate buffer that was previously warmed at  $37 \pm 1$  °C. These vials were placed over hot plate (maintained at room temperature  $37 \pm 1$  °C) that was positioned on a sieve shaker. Shaker was kept at minimum shaking speed to simulated the blinking of eye. Aliquots of 5 ml samples at specific interval of time were withdrawn carefully using pipette and equivalent amount of fresh dissolution fluid was replaced. The aliquots withdrawn were suitably diluted with pH 7.4 phosphate buffer solution and was analyzed at 233 nm using Shimadzu-160A UV Spectrophotometer against blank.

#### ***In vitro* diffusion studies of formulations using the pre-soaked Cellophane membrane.**<sup>17</sup>

The cellophane membrane of approximately 25cm<sup>2</sup> was taken and washed in running water. It was soaked in distilled water for 24 hrs before being used for diffusion study to remove glycerin present in it. The *in vitro* diffusion of drug from the different ophthalmic inserts was studied using the classical standard cylindrical tube fabricated in the laboratory i.e. simple modification of the cell is a glass tube of 15 mm internal diameter and 100mm height. The diffusion cell membrane was tied to one end of open cylinder which acted as a donor compartment. The diffusion cell membrane acted as corneal epithelium. The entire surface of the membrane was in contact with the receptor compartment containing 25ml of phosphate buffer pH 7.4 in 100 ml beakers.

#### ***In vitro* diffusion studies:**

An ophthalmic inserts was placed inside this compartment. The content of receptor compartment was stirred continuously using a magnetic stirrer and temperature was maintained at  $37^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$ . At specific interval of time, 1.5 ml of sample solution was withdrawn from the receptor compartment and replaced with 1.5 ml fresh buffer solution. The samples were analyzed for the drug content using Shimadzu-160A at 233nm after diluted up to 10 ml of phosphate buffer. Phosphate Buffer used as a Blank.

#### **Comparison with various models:**

The release rate obtained are tabulated and graphed according to the following modes of data treatment:

- a) Percentage cumulative drug released v/s time (*In-vitro* diffusion plots).
- b) Percentage cumulative drug released v/s square root of time (Higuchi's plots).
- c) Log percentage drug remained v/s time (first order rate plots).
- d) Log percentage drug released v/s log time (Peppas's double log plots).

### Stability Studies:

The selected formulations were stored at 25<sup>0</sup>c /60%RH and 40<sup>0</sup>c/75/RH for 2 months and evaluated for their physical appearance drug content and drug excipient compatibility at specific period of time.

### RESULTS AND DISCUSSION:

The formulation were also subjected to model fitting analysis to know the mechanism of drug release from the formulation by treating the data according to *first order Higuchi's and peppas equation*. The results shown in the table. The linearity and slope indicates that the release of drug from the films have followed *Higuchi diffusion model* and non fickian nature. The *Hguchi* plots reveled that the release of drug to be by diffusion controlled mechanism. Based on results obtained the formulation showing the best drug release and appearance were selected namely F15 and F21 was subjected to stability studies. The IR spectra of pure drug were also seen in the IR spectra of prepared formulations indicating that there was no interaction between drug and formulation components.

The thickness of the formulation was determined by micrometer screw gauge. The results are shown in the **Table 2**. The weight of film is important and so this parameter was also determined for films. The weights of formulation were determined by electronic balance. The results are shown in the **Table 2**. The drug content of the formulations was determined according to procedure described in methods. The values are shown in **Table 2**. The HPMC K4m is hydrophilic polymer, EC is hydrophobic polymer but water permeable due to their nature, the polymer can be expected to absorb

water. So to verify this fact, a water absorption test was carried out. The results are shown in **Table 2**. The results showed that there was no much variation in the water absorption properties of formulation. The values of water absorb ion test are encouraging.

*In vitro* studies were carried out using procedure as mentioned in section IV methods the release profile of the formulations F10, F11 containing 10% of HPMC K4M shows the drug release of 91.00, 96.12% in 4hrs respectively, the formulations F12, F13 containing 12% HPMC K4M shows the drug release of 96.06, 98.32 in 4hrs respectively and the formulations F14, F15, containing 14 % HPMC K4M shows the release 86.87, 97.87% in 4hrs respectively. Similarly the formulations F16, F17 containing 14% EC shows the drug release of 83.58, 86.96% in 12 hrs respectively, the formulations F18, F19 containing 16 % EC shows the drug release of 86.43, 88.96 in 14hrs respectively and the formulations F20, F21 containing 18% EC shows the release of 91.00, 91.00% 14 hrs respectively.

It showed that the EC films sustain the release of the drug. *In vitro* diffusion studies of selected formulations i.e., lower and higher concentrations of polymer were carried out using procedure as mentioned section in V of methods. The release of drug from HPMC K4m formulation F10 was found to be 62.46% at the end of 3hrs, F15 was found to be 49.15% at the end of 3hrs. The release of drug from the formulation F16 and F21 were found to be 68.16 % and 59.33% at the end of 12 hrs respectively. From the diffusion study it is concluded that as the concentration of polymer increases drug release from the formulation decreases.

The addition of plasticizer like Glycerin, Diethyl phthalate shows flexibility more as the concentration increases. The stability studies of selected formulation was tested for eight weeks at storage condition of 25<sup>0</sup> C and 40<sup>0</sup> C at 60% RH and it was analyzed for their drug content. The results are shown in Table. The residual drug content of selected formulation were found to be within the permissible limits. The formulation was also subjected to IR study to determine compatibility of



drug with the components used in formulation. The IR study showed that the no interaction between the drug and components. The formulation showed

satisfactory physical stability at 25°C and 40°C at 60% and 75% RH respectively. The physical appearance had not changed considerably.

**TABLE 1: FORMULA FOR THE PREPARATION OF OCULAR INSERT:**

| Sl. No. | Ingredient                            | F10     | F11     | F12     | F13     | F14     | F15     | F16    | F17    | F18    | F19    | F20    | F21    |
|---------|---------------------------------------|---------|---------|---------|---------|---------|---------|--------|--------|--------|--------|--------|--------|
|         |                                       | 10% w/v | 12% w/v | 14% w/v | 14% w/v | 16% w/v | 18% w/v |        |        |        |        |        |        |
| 1       | Drug (mg)                             | 50      | 50      | 50      | 50      | 50      | 50      | 50     | 50     | 50     | 50     | 50     | 50     |
| 2       | HPMC(gm)                              | 1.5     | 1.5     | 1.8     | 1.8     | 2.1     | 2.1     | -      | -      | -      | -      | -      | -      |
| 3       | EC (gm)                               | -       | -       | -       | -       | -       | -       | 2.1    | 2.1    | 2.4    | 2.4    | 2.7    | 2.7    |
| 4       | Glycerin (ml)<br>(40% w/w of polymer) | 0.47    | -       | 0.57    | -       | 0.67    | -       | -      | -      | -      | -      | -      | -      |
| 5       | Glycerin (ml) (50% w/w of polymer)    | -       | 0.59    | -       | 0.7     | -       | 0.83    | -      | -      | -      | -      | -      | -      |
| 6       | Glycerin (ml) (60% w/w of polymer)    | -       | -       | -       | -       | -       | -       | -      | -      | -      | -      | -      | -      |
| 7       | DEP (ml) (40% w/w of polymer)         | -       | -       | -       | -       | -       | -       | 0.75   | -      | 0.86   | -      | 0.96   | -      |
| 8       | DEP (ml) (50% w/w of polymer)         | -       | -       | -       | -       | -       | -       | -      | 0.93   | -      | 1.07   | -      | 1.20   |
| 9       | Water (ml)                            | 15      | 15      | 15      | 15      | 15      | 15      | -      | -      | -      | -      | -      | -      |
| 10      | Alcohol (ml)                          | -       | -       | -       | -       | -       | -       | -      | -      | -      | 15     | 15     | 15     |
| 11      | Benzyl Alkonium Chloride(ml)          | 0.0012  | 0.0012  | 0.0012  | 0.0012  | 0.0012  | 0.0012  | 0.0012 | 0.0012 | 0.0012 | 0.0012 | 0.0012 | 0.0012 |

**TABLE 2: PHYSICO-CHEMICAL EVALUATION OF OCULAR INSERTS**

| Formulations    | Weight in (mg) ± SD | Thickness in (µm) ± SD | Swelling Index (%) | % Drug content |
|-----------------|---------------------|------------------------|--------------------|----------------|
| F <sub>10</sub> | 11.80 ± 0.10        | 0.25 ± 0.07            | 1.35 ± 0.55        | 99.38 ± 0.21   |
| F <sub>11</sub> | 12.17 ± 1.10        | 0.30 ± 0.04            | 1.42 ± 0.24        | 93.40 ± 0.09   |
| F <sub>12</sub> | 12.33 ± 1.18        | 0.29 ± 0.02            | 1.96 ± 0.12        | 91.76 ± 0.01   |
| F <sub>13</sub> | 12.59 ± 1.74        | 0.31 ± 0.04            | 2.28 ± 0.53        | 93.66 ± 0.02   |
| F <sub>14</sub> | 13.70 ± 1.12        | 0.34 ± 0.05            | 2.32 ± 0.39        | 99.79 ± 0.01   |
| F <sub>15</sub> | 14.20 ± 1.12        | 0.33 ± 0.06            | 2.36 ± 0.24        | 92.87 ± 0.09   |
| F <sub>16</sub> | 13.60 ± 0.10        | 0.30 ± 0.02            | 1.06 ± 0.18        | 98 ± 0.02      |
| F <sub>17</sub> | 14.20 ± 0.15        | 0.38 ± 0.04            | 1.59 ± 0.11        | 98.18 ± 0.01   |
| F <sub>18</sub> | 14.86 ± 0.25        | 0.44 ± 0.02            | 1.66 ± 0.14        | 91.32 ± 0.03   |
| F <sub>19</sub> | 15.16 ± 0.72        | 0.39 ± 0.01            | 1.72 ± 0.18        | 94.84 ± 0.07   |
| F <sub>20</sub> | 15.66 ± 0.72        | 0.43 ± 0.04            | 1.79 ± 1.11        | 96.60 ± 0.07   |
| F <sub>21</sub> | 15.90 ± 1.51        | 0.43 ± 0.02            | 1.87 ± 1.01        | 90.26 ± 0.03   |

\*Mean ± SD, n=3.

**TABLE 3: IN VITRO DISSOLUTION OF BETAXOLOL HCL FROM FORMULATION -10 (F 10) (DRUG: HPMCK4M10%)**

| Time (min) | √T     | Log T  | Abs*  | Conc. (µg/ml) | CDR (mg) | CDR (%) | Log % CDR | Cumulative % drug remained | Cumulative Log % Drug remained |
|------------|--------|--------|-------|---------------|----------|---------|-----------|----------------------------|--------------------------------|
| 30         | 5.477  | 1.4771 | 0.103 | 1.3895        | 0.2084   | 54.2787 | 1.7346    | 45.7212                    | 1.6601                         |
| 60         | 7.745  | 1.7781 | 0.122 | 1.6470        | 0.2470   | 64.3344 | 1.8084    | 35.6655                    | 1.5522                         |
| 120        | 10.954 | 2.0791 | 0.148 | 1.9943        | 0.2991   | 77.9016 | 1.8915    | 22.0983                    | 1.34435                        |
| 180        | 13.416 | 2.2552 | 0.172 | 2.3296        | 0.3494   | 91.0012 | 1.9590    | 8.9988                     | 0.9541                         |

\*Each reading is an average of three determinations

**TABLE 4: IN VITRO DISSOLUTION OF BETAXOLOL HCL FROM FORMULATION-11(F11)(DRUG: HPMC10K4M%)**

| Time (min) | √T     | Log T  | Abs*  | Conc. (µg/ml) | CDR (mg) | CDR (%) | Log % CDR | Cumulative % drug remained | Cumulative Log % Drug remained |
|------------|--------|--------|-------|---------------|----------|---------|-----------|----------------------------|--------------------------------|
| 30         | 5.477  | 1.4771 | 0.106 | 1.4365        | 0.2155   | 56.1114 | 1.7490    | 43.8885                    | 1.6423                         |
| 60         | 7.745  | 1.7781 | 0.130 | 1.7557        | 0.2634   | 68.5836 | 1.8362    | 31.4163                    | 1.4971                         |
| 120        | 10.954 | 2.0791 | 0.163 | 2.2087        | 0.3313   | 86.2787 | 1.9359    | 13.7212                    | 1.1373                         |
| 180        | 13.416 | 2.2552 | 0.182 | 2.4609        | 0.3691   | 96.129  | 1.9828    | 3.871                      | 0.58782                        |

\*Each reading is an average of three determinations

**TABLE 5: IN VITRO DISSOLUTION OF BETAXOLOL HCL FROM FORMULATION-12(F12)(DRUG : HPMCK4M12%)**

| Time (min) | $\sqrt{T}$ | Log T  | Abs*  | Conc. ( $\mu\text{g/ml}$ ) | CDR (mg) | CDR (%) | Log % CDR | Cumulative % drug remained | Cumulative Log % Drug remained |
|------------|------------|--------|-------|----------------------------|----------|---------|-----------|----------------------------|--------------------------------|
| 30         | 5.477      | 1.4771 | 0.103 | 1.3869                     | 0.2080   | 54.1765 | 1.7338    | 45.8234                    | 1.6610                         |
| 60         | 7.745      | 1.7781 | 0.120 | 1.6199                     | 0.2430   | 63.2787 | 1.8012    | 36.7212                    | 1.5649                         |
| 120        | 10.954     | 2.0791 | 0.132 | 1.7879                     | 0.2682   | 69.8410 | 1.84411   | 30.1589                    | 1.4794                         |
| 180        | 13.416     | 2.2552 | 0.167 | 2.2554                     | 0.3383   | 88.1023 | 1.94498   | 11.8977                    | 1.07546                        |
| 240        | 15.491     | 2.3802 | 0.182 | 2.4593                     | 0.3689   | 96.0678 | 1.98257   | 3.9322                     | 0.59463                        |

\*Each reading is an average of three determinations

**TABLE 6: IN VITRO DISSOLUTION OF BETAXOLOL HCL FROM FORMULATION-13(F13) (DRUG : HPMCK4M12%)**

| Time (min) | $\sqrt{T}$ | Log T  | Abs*  | Conc. ( $\mu\text{g/ml}$ ) | CDR (mg) | CDR (%) | Log % CDR | Cumulative % drug remained | Cumulative Log % Drug remained |
|------------|------------|--------|-------|----------------------------|----------|---------|-----------|----------------------------|--------------------------------|
| 30         | 5.477      | 1.4771 | 0.106 | 1.4258                     | 0.2139   | 55.69   | 1.7458    | 44.3048                    | 1.6464                         |
| 60         | 7.745      | 1.7781 | 0.128 | 1.7231                     | 0.2585   | 67.30   | 1.8280    | 32.6917                    | 1.5144                         |
| 120        | 10.954     | 2.0791 | 0.146 | 1.9755                     | 0.2963   | 77.16   | 1.8874    | 22.8327                    | 1.3585                         |
| 180        | 13.416     | 2.2552 | 0.171 | 2.3042                     | 0.3456   | 90.00   | 1.9542    | 9.9933                     | 0.9997                         |
| 240        | 15.491     | 2.3802 | 0.186 | 2.5171                     | 0.3776   | 98.32   | 1.9926    | 1.6755                     | 0.2241                         |

\* Each reading is an average of 3 readings

**TABLE 7: IN VITRO DISSOLUTION OF BETAXOLOL HCL FROM FORMULATION -14(F 14) (DRUG: HPMCK4M14%)**

| Time (min) | $\sqrt{T}$ | Log T  | Abs*  | Conc. ( $\mu\text{g/ml}$ ) | CDR (mg) | CDR (%) | Log % CDR | Cumulative % drug remained | Cumulative Log % Drug remained |
|------------|------------|--------|-------|----------------------------|----------|---------|-----------|----------------------------|--------------------------------|
| 30         | 5.477      | 1.4771 | 0.099 | 1.3341                     | 0.2001   | 52.11   | 1.7169    | 47.8885                    | 1.68023                        |
| 60         | 7.745      | 1.7781 | 0.119 | 1.6136                     | 0.2420   | 63.02   | 1.7995    | 36.9704                    | 1.56785                        |
| 120        | 10.954     | 2.0791 | 0.131 | 1.7750                     | 0.2662   | 69.33   | 1.8409    | 30.6655                    | 1.4866                         |
| 180        | 13.416     | 2.2552 | 0.165 | 2.2240                     | 0.3336   | 86.87   | 1.9388    | 13.1255                    | 1.1181                         |

\* Each reading is an average of 3 readings

**TABLE 8: IN VITRO DISSOLUTION OF BETAXOLOL HCL FROM FORMULATION -15(F15) (DRUG: HPMCK4M14%)**

| Time (min) | $\sqrt{T}$ | Log T  | Abs*  | Conc. ( $\mu\text{g/ml}$ ) | CDR (mg) | CDR (%) | Log % CDR | Cumulative % drug remained | Cumulative Log % Drug remained |
|------------|------------|--------|-------|----------------------------|----------|---------|-----------|----------------------------|--------------------------------|
| 30         | 5.477      | 1.4771 | 0.104 | 1.4093                     | 0.2114   | 55.05   | 1.7407    | 44.9474                    | 1.6527                         |
| 60         | 7.745      | 1.7781 | 0.125 | 1.6826                     | 0.2524   | 65.72   | 1.8177    | 34.2753                    | 1.5349                         |
| 120        | 10.954     | 2.0791 | 0.145 | 1.9563                     | 0.2935   | 76.41   | 1.8832    | 23.5802                    | 1.3725                         |
| 180        | 13.416     | 2.2552 | 0.167 | 2.2555                     | 0.3384   | 88.11   | 1.9450    | 11.8865                    | 1.0750                         |
| 240        | 15.491     | 2.3802 | 0.185 | 2.5056                     | 0.3758   | 97.87   | 1.9906    | 2.1257                     | 0.3275                         |

\* Each reading is an average of 3 readings

**TABLE 9: IN VITRO DISSOLUTION OF BETAXOLOL HCL FROM FORMULATION-16(F16) (DRUG: EC14%)**

| Time (min) | $\sqrt{T}$ | Log T | Abs*  | Conc. ( $\mu\text{g/ml}$ ) | CDR (mg) | CDR (%) | Log % CDR | Cumulative % drug remained | Cumulative Log % Drug remained |
|------------|------------|-------|-------|----------------------------|----------|---------|-----------|----------------------------|--------------------------------|
| 30         | 5.4772     | 1.477 | 0.045 | 0.6072                     | 0.0911   | 23.720  | 1.3751    | 76.279                     | 1.8824                         |
| 60         | 7.7459     | 1.778 | 0.055 | 0.7400                     | 0.1110   | 28.904  | 1.4609    | 71.095                     | 1.8518                         |
| 120        | 10.954     | 2.079 | 0.066 | 0.8915                     | 0.1337   | 34.823  | 1.5418    | 65.176                     | 1.8140                         |
| 180        | 13.416     | 2.255 | 0.066 | 0.8954                     | 0.1343   | 34.975  | 1.5437    | 65.024                     | 1.8130                         |
| 240        | 15.491     | 2.380 | 0.072 | 0.9763                     | 0.1464   | 38.136  | 1.5813    | 61.863                     | 1.7914                         |
| 300        | 17.320     | 2.477 | 0.078 | 1.0500                     | 0.1575   | 41.015  | 1.6129    | 58.984                     | 1.7707                         |
| 360        | 18.973     | 2.556 | 0.082 | 1.1063                     | 0.1659   | 43.215  | 1.6356    | 56.784                     | 1.7542                         |
| 420        | 20.493     | 2.623 | 0.093 | 1.2553                     | 0.1883   | 49.037  | 1.6905    | 50.962                     | 1.7072                         |
| 480        | 21.908     | 2.681 | 0.110 | 1.4880                     | 0.2232   | 58.123  | 1.7643    | 41.876                     | 1.6219                         |
| 540        | 23.237     | 2.732 | 0.121 | 1.6356                     | 0.2453   | 63.890  | 1.8054    | 36.109                     | 1.5576                         |
| 600        | 24.494     | 2.778 | 0.135 | 1.8179                     | 0.2727   | 71.012  | 1.8513    | 28.988                     | 1.4622                         |
| 660        | 25.690     | 2.819 | 0.150 | 2.0219                     | 0.3033   | 78.982  | 1.8975    | 21.017                     | 1.3225                         |
| 720        | 26.832     | 2.857 | 0.158 | 2.1397                     | 0.3210   | 83.581  | 1.9221    | 16.419                     | 1.2153                         |

\* Each reading is an average of 3 readings

**TABLE 10: IN VITRO DISSOLUTION OF BETAXOLOL HCL FROM FORMULATION-17(F17) (DRUG: EC14%)**

| Time (min) | $\sqrt{T}$ | Log T | Abs*  | Conc. ( $\mu\text{g/ml}$ ) | CDR (mg) | CDR (%) | Log % CDR | Cumulative % drug remained | Cumulative Log % Drug remained |
|------------|------------|-------|-------|----------------------------|----------|---------|-----------|----------------------------|--------------------------------|
| 30         | 5.4772     | 1.477 | 0.046 | 0.625                      | 0.0938   | 24.42   | 1.3878    | 75.5726                    | 1.87836                        |
| 60         | 7.7459     | 1.778 | 0.060 | 0.813                      | 0.1220   | 31.77   | 1.5021    | 68.2204                    | 1.8339                         |
| 120        | 10.954     | 2.079 | 0.068 | 0.924                      | 0.1387   | 36.12   | 1.5577    | 63.8777                    | 1.8053                         |
| 180        | 13.416     | 2.255 | 0.071 | 0.957                      | 0.1437   | 37.41   | 1.5730    | 62.5874                    | 1.7964                         |
| 240        | 15.491     | 2.380 | 0.074 | 0.997                      | 0.1496   | 38.95   | 1.5905    | 61.05                      | 1.7856                         |
| 300        | 17.320     | 2.477 | 0.079 | 1.067                      | 0.1601   | 41.68   | 1.6199    | 58.3133                    | 1.7657                         |
| 360        | 18.973     | 2.556 | 0.084 | 1.128                      | 0.1693   | 44.07   | 1.6442    | 55.9215                    | 1.7475                         |
| 420        | 20.493     | 2.623 | 0.099 | 1.334                      | 0.2001   | 52.11   | 1.7169    | 47.8871                    | 1.6802                         |
| 480        | 21.908     | 2.681 | 0.116 | 1.568                      | 0.2352   | 61.25   | 1.7871    | 38.7479                    | 1.5882                         |
| 540        | 23.237     | 2.732 | 0.129 | 1.749                      | 0.2624   | 68.32   | 1.8345    | 31.6761                    | 1.5007                         |
| 600        | 24.494     | 2.778 | 0.142 | 1.917                      | 0.2876   | 74.90   | 1.8744    | 25.0971                    | 1.3996                         |
| 660        | 25.690     | 2.819 | 0.154 | 2.076                      | 0.3114   | 81.10   | 1.9090    | 18.8938                    | 1.2763                         |
| 720        | 26.832     | 2.857 | 0.165 | 2.227                      | 0.3341   | 86.99   | 1.9394    | 13.004                     | 1.1140                         |

\* Each reading is an average of 3 readings

**TABLE 11: IN VITRO DISSOLUTION OF BETAXOLOL HCL FROM FORMULATION-18(F18) (DRUG: EC16%)**

| Time (min) | $\sqrt{T}$ | Log T | Abs*  | Conc. ( $\mu\text{g/ml}$ ) | CDR (mg) | CDR (%) | Log % CDR | Cumulative % drug remained | Cumulative Log % Drug remained |
|------------|------------|-------|-------|----------------------------|----------|---------|-----------|----------------------------|--------------------------------|
| 30         | 5.4772     | 1.477 | 0.041 | 0.5605                     | 0.0841   | 21.89   | 1.3402    | 78.107                     | 1.8926                         |
| 60         | 7.7459     | 1.778 | 0.060 | 0.8045                     | 0.1207   | 31.42   | 1.4972    | 68.574                     | 1.8361                         |
| 120        | 10.954     | 2.079 | 0.063 | 0.8483                     | 0.1272   | 33.13   | 1.5203    | 66.863                     | 1.8251                         |
| 180        | 13.416     | 2.255 | 0.065 | 0.8729                     | 0.1309   | 34.09   | 1.5327    | 65.902                     | 1.8189                         |
| 240        | 15.491     | 2.380 | 0.073 | 0.9818                     | 0.1473   | 38.35   | 1.5838    | 61.6465                    | 1.7899                         |
| 300        | 17.320     | 2.477 | 0.074 | 0.9942                     | 0.1491   | 38.83   | 1.5892    | 61.1628                    | 1.7864                         |
| 360        | 18.973     | 2.556 | 0.078 | 1.051                      | 0.1577   | 41.05   | 1.6133    | 58.9445                    | 1.7704                         |
| 420        | 20.493     | 2.623 | 0.093 | 1.260                      | 0.1891   | 49.23   | 1.6922    | 50.7652                    | 1.7055                         |
| 480        | 21.908     | 2.681 | 0.112 | 1.510                      | 0.2266   | 59.00   | 1.7708    | 40.9979                    | 1.6127                         |
| 540        | 23.237     | 2.732 | 0.119 | 1.612                      | 0.2419   | 62.98   | 1.7992    | 37.0138                    | 1.5683                         |
| 600        | 24.494     | 2.778 | 0.132 | 1.783                      | 0.2675   | 69.66   | 1.8430    | 30.3302                    | 1.4818                         |
| 660        | 25.690     | 2.819 | 0.144 | 1.949                      | 0.2925   | 76.15   | 1.8817    | 23.8407                    | 1.3773                         |
| 720        | 26.832     | 2.857 | 0.155 | 2.099                      | 0.3150   | 82.02   | 1.9139    | 17.9739                    | 1.2546                         |
| 780        | 27.928     | 2.892 | 0.163 | 2.1986                     | 0.3298   | 85.88   | 1.9338    | 14.1189                    | 1.1498                         |
| 840        | 28.982     | 2.92  | 0.164 | 2.212                      | 0.3319   | 86.43   | 1.9366    | 13.568                     | 1.1325                         |

\* Each reading is an average of 3 readings

**TABLE 12: IN VITRO DISSOLUTION OF BETAXOLOL HCL FROM FORMULATION-19(F19) (DRUG: EC16%)**

| Time (min) | $\sqrt{T}$ | Log T | Abs*  | Conc. ( $\mu\text{g/ml}$ ) | CDR (mg) | CDR (%) | Log % CDR | Cumulative % drug remained | Cumulative Log % Drug remained |
|------------|------------|-------|-------|----------------------------|----------|---------|-----------|----------------------------|--------------------------------|
| 30         | 5.4772     | 1.477 | 0.042 | 0.5699                     | 0.0855   | 22.26   | 1.3475    | 77.7367                    | 1.8906                         |
| 60         | 7.7459     | 1.778 | 0.060 | 0.8143                     | 0.1221   | 31.80   | 1.5025    | 68.1926                    | 1.8337                         |
| 120        | 10.954     | 2.079 | 0.068 | 0.9205                     | 0.1381   | 35.95   | 1.5557    | 64.0435                    | 1.8064                         |
| 180        | 13.416     | 2.255 | 0.069 | 0.9295                     | 0.1394   | 36.30   | 1.5600    | 63.6909                    | 1.8040                         |
| 240        | 15.491     | 2.380 | 0.076 | 1.0226                     | 0.1534   | 39.94   | 1.6014    | 60.0532                    | 1.7785                         |
| 300        | 17.320     | 2.477 | 0.076 | 1.0235                     | 0.1535   | 39.98   | 1.6018    | 60.0179                    | 1.7782                         |
| 360        | 18.973     | 2.556 | 0.083 | 1.1209                     | 0.1681   | 43.78   | 1.6413    | 56.2166                    | 1.7498                         |
| 420        | 20.493     | 2.623 | 0.097 | 1.3079                     | 0.1962   | 51.09   | 1.7083    | 48.9084                    | 1.6893                         |
| 480        | 21.908     | 2.681 | 0.112 | 1.5141                     | 0.2271   | 59.14   | 1.7719    | 40.8536                    | 1.6112                         |
| 540        | 23.237     | 2.732 | 0.121 | 1.6390                     | 0.2459   | 64.02   | 1.8063    | 35.976                     | 1.5560                         |
| 600        | 24.494     | 2.778 | 0.140 | 1.8917                     | 0.2838   | 73.89   | 1.8686    | 26.1039                    | 1.4167                         |
| 660        | 25.690     | 2.819 | 0.148 | 1.9968                     | 0.2995   | 78.001  | 1.8921    | 21.999                     | 1.3424                         |
| 720        | 26.832     | 2.857 | 0.163 | 2.1961                     | 0.3294   | 85.78   | 1.9334    | 14.215                     | 1.1527                         |
| 780        | 27.928     | 2.892 | 0.163 | 2.2052                     | 0.3308   | 86.14   | 1.9352    | 13.858                     | 1.1417                         |
| 840        | 28.982     | 2.92  | 0.169 | 2.2776                     | 0.3416   | 88.96   | 1.9492    | 11.0306                    | 1.0425                         |

\* Each reading is an average of 3 readings

**TABLE 13: IN VITRO DISSOLUTION OF BETAXOLOL HCL FROM FORMULATION-20(F20) (DRUG: EC18%)**

| Time (min) | $\sqrt{T}$ | Log T | Abs*  | Conc. ( $\mu\text{g/ml}$ ) | CDR (mg) | CDR (%) | Log % CDR | Cumulative % drug remained | Cumulative Log % Drug remained |
|------------|------------|-------|-------|----------------------------|----------|---------|-----------|----------------------------|--------------------------------|
| 30         | 5.4772     | 1.477 | 0.039 | 0.5213                     | 0.0782   | 20.36   | 1.3088    | 79.635                     | 1.9011                         |
| 60         | 7.7459     | 1.778 | 0.055 | 0.7399                     | 0.1110   | 28.90   | 1.4609    | 71.099                     | 1.8518                         |
| 120        | 10.954     | 2.079 | 0.063 | 0.8478                     | 0.1272   | 33.11   | 1.5200    | 66.884                     | 1.8253                         |
| 180        | 13.416     | 2.255 | 0.066 | 0.8933                     | 0.1340   | 34.89   | 1.5427    | 65.105                     | 1.8136                         |
| 240        | 15.491     | 2.380 | 0.071 | 0.9613                     | 0.1442   | 37.55   | 1.5746    | 62.448                     | 1.7955                         |
| 300        | 17.320     | 2.477 | 0.071 | 0.9609                     | 0.1441   | 37.53   | 1.5744    | 62.464                     | 1.7956                         |
| 360        | 18.973     | 2.556 | 0.077 | 1.0409                     | 0.1561   | 40.66   | 1.6091    | 59.338                     | 1.7733                         |
| 420        | 20.493     | 2.623 | 0.093 | 1.2632                     | 0.1895   | 49.34   | 1.6932    | 50.657                     | 1.7046                         |
| 480        | 21.908     | 2.681 | 0.110 | 1.4822                     | 0.2223   | 57.89   | 1.7626    | 42.100                     | 1.6242                         |
| 540        | 23.237     | 2.732 | 0.113 | 1.5231                     | 0.2285   | 59.49   | 1.7744    | 40.504                     | 1.6075                         |
| 600        | 24.494     | 2.778 | 0.128 | 1.7355                     | 0.2603   | 67.79   | 1.8311    | 32.206                     | 1.5079                         |
| 660        | 25.690     | 2.819 | 0.142 | 1.9242                     | 0.2886   | 75.16   | 1.8760    | 24.835                     | 1.3950                         |
| 720        | 26.832     | 2.857 | 0.156 | 2.1021                     | 0.3153   | 82.11   | 1.9144    | 17.888                     | 1.2525                         |
| 780        | 27.928     | 2.892 | 0.164 | 2.2103                     | 0.3315   | 86.34   | 1.9362    | 13.658                     | 1.1354                         |
| 840        | 28.982     | 2.92  | 0.172 | 2.3296                     | 0.3494   | 91.00   | 1.9590    | 8.998                      | 0.9541                         |

\* Each reading is an average of 3 readings

**TABLE 14: IN VITRO DISSOLUTION OF BETAXOLOL HCL FROM FORMULATION-21(F 21) (DRUG: EC18%)**

| Time (min) | $\sqrt{T}$ | Log T | Abs*  | Conc. ( $\mu\text{g/ml}$ ) | CDR (mg) | CDR (%) | Log % CDR | Cumulative % drug remained | Cumulative Log % Drug remained |
|------------|------------|-------|-------|----------------------------|----------|---------|-----------|----------------------------|--------------------------------|
| 30         | 5.4772     | 1.477 | 0.042 | 0.5621                     | 0.0843   | 21.95   | 1.3415    | 78.0419                    | 1.8923                         |
| 60         | 7.7459     | 1.778 | 0.056 | 0.7512                     | 0.1127   | 29.34   | 1.4675    | 70.6567                    | 1.8491                         |
| 120        | 10.954     | 2.079 | 0.066 | 0.8871                     | 0.1331   | 34.65   | 1.5397    | 65.347                     | 1.8152                         |
| 180        | 13.416     | 2.255 | 0.067 | 0.9063                     | 0.1359   | 35.40   | 1.5490    | 64.597                     | 1.8102                         |
| 240        | 15.491     | 2.380 | 0.072 | 0.9750                     | 0.1463   | 38.08   | 1.5807    | 61.9139                    | 1.7917                         |
| 300        | 17.320     | 2.477 | 0.072 | 0.9709                     | 0.1456   | 37.92   | 1.5789    | 62.0743                    | 1.7929                         |
| 360        | 18.973     | 2.556 | 0.080 | 1.0843                     | 0.1627   | 42.35   | 1.6269    | 57.6432                    | 1.7607                         |
| 420        | 20.493     | 2.623 | 0.095 | 1.2835                     | 0.1925   | 50.13   | 1.7001    | 49.8628                    | 1.6977                         |
| 480        | 21.908     | 2.681 | 0.110 | 1.4862                     | 0.2229   | 58.05   | 1.7638    | 41.9468                    | 1.6226                         |
| 540        | 23.237     | 2.732 | 0.119 | 1.6086                     | 0.2413   | 62.83   | 1.7982    | 37.163                     | 1.5701                         |
| 600        | 24.494     | 2.778 | 0.135 | 1.8227                     | 0.2734   | 71.19   | 1.8524    | 28.1457                    | 1.4594                         |
| 660        | 25.690     | 2.819 | 0.146 | 1.9675                     | 0.2951   | 76.85   | 1.8856    | 23.1457                    | 1.3644                         |
| 720        | 26.832     | 2.857 | 0.161 | 2.1740                     | 0.3261   | 84.92   | 1.9290    | 15.08                      | 1.1784                         |
| 780        | 27.928     | 2.892 | 0.170 | 2.2969                     | 0.3445   | 89.72   | 1.9528    | 10.2791                    | 1.0119                         |
| 840        | 28.982     | 2.92  | 0.172 | 2.3297                     | 0.3495   | 91.00   | 1.9590    | 8.9952                     | 0.9540                         |

\* Each reading is an average of 3 readings

**TABLE 15: CURVE FITTING DATA FOR ALL FORMULATIONS**

| Formulations | First order Equation |  |                                  | Higuchi's Equation |  |                                  | Peppas Equation |  |                                  |
|--------------|----------------------|--|----------------------------------|--------------------|--|----------------------------------|-----------------|--|----------------------------------|
|              | Slope                | Rate constant (K) $\text{mg. hr}^{-1}$ | Regression coefficient ( $R^2$ ) | Slope              | Rate constant (K) $\text{mg. hr}^{-1}$ | Regression coefficient ( $R^2$ ) | Slope           | Rate constant (K) $\text{mg. hr}^{-1}$ | Regression coefficient ( $R^2$ ) |
| F10          | -0.0046              | 1.8279                                 | 0.9737                           | 4.5726             | 28.903                                 | 0.9976                           | 0.2842          | 1.3092                                 | 0.9923                           |
| F11          | -0.007               | 1.8986                                 | 0.983                            | 5.1024             | 28.821                                 | 0.9956                           | 0.3046          | 1.298                                  | 0.9988                           |
| F12          | -0.0049              | 1.8973                                 | 0.9256                           | 4.1931             | 29.774                                 | 0.964                            | 0.2713          | 1.3203                                 | 0.9469                           |
| F13          | -0.0063              | 1.9452                                 | 0.9058                           | 4.1845             | 33.273                                 | 0.994                            | 0.2677          | 1.3479                                 | 0.9903                           |
| F14          | -0.0035              | 1.8049                                 | 0.9173                           | 4.0475             | 29.797                                 | 0.946                            | 0.2617          | 1.3275                                 | 0.9435                           |
| F15          | 0.0059               | 1.9302                                 | 0.9005                           | 4.1861             | 32.193                                 | 0.996                            | 0.2701          | 1.337                                  | 0.9905                           |
| F16          | -0.0828              | 80.058                                 | 0.9615                           | 2.6543             | 2.5779                                 | 0.8842                           | 0.3759          | 0.7573                                 | 0.8666                           |
| F17          | -0.0862              | 78.973                                 | 0.957                            | 2.7583             | 3.0099                                 | 0.8786                           | 0.3725          | 0.7851                                 | 0.8541                           |
| F18          | -0.0815              | 80.36                                  | 0.9693                           | 2.8221             | -0.3508                                | 0.9036                           | 0.407           | 0.6842                                 | 0.8687                           |
| F19          | -0.0828              | 79.134                                 | 0.9687                           | 2.8761             | 0.4039                                 | 0.9077                           | 0.4055          | 0.703                                  | 0.8816                           |
| F20          | -0.0842              | 82.057                                 | 0.9703                           | 2.9105             | -2.5875                                | 0.9001                           | 0.0007          | 1.3844                                 | 0.9649                           |
| F21          | -0.0861              | 81.36                                  | 0.9695                           | 2.9731             | -2.3089                                | 0.8982                           | 0.0007          | 1.3996                                 | 0.9695                           |



**TABLE 16: STABILITY STUDY**

| Time In Weeks | Stored At 25 <sup>o</sup> c/ 60 % RH |                | Stored 40 <sup>o</sup> C / 75 % RH |                |
|---------------|--------------------------------------|----------------|------------------------------------|----------------|
|               | Physical Appearance                  | % Drug Content | Physical Appearance                | % Drug Content |
| 0             | +++                                  | 96.34          | +++                                | 98.22          |
| 2             | +++                                  | 96.94          | +++                                | 97.96          |
| 4             | +++                                  | 99.78          | +++                                | 96.88          |
| 6             | +++                                  | 98.50          | ++                                 | 96.08          |
| 8             | ++                                   | 97.77          | ++                                 | 95.51          |

**TABLE 17: IN VITRO DIFFUSION OF BETAXOLOL HCL FROM FORMULATION-10(F10) (DRUG: HPMCK4M10%)**

| Time (min) | √T    | Log T | Abs* | Conc. (µg/ml) | CDR (mg) | CDR (%) | Log % CDR | Cumulative % drug remained | Cumulative Log % Drug remained |
|------------|-------|-------|------|---------------|----------|---------|-----------|----------------------------|--------------------------------|
| 30         | 5.48  | 1.48  | 0.07 | 0.92          | 0.15     | 39.69   | 1.60      | 60.31                      | 1.78                           |
| 60         | 7.75  | 1.78  | 0.08 | 1.11          | 0.19     | 48.33   | 1.68      | 51.67                      | 1.71                           |
| 120        | 10.95 | 2.08  | 0.09 | 1.20          | 0.20     | 52.05   | 1.72      | 47.95                      | 1.68                           |
| 180        | 13.42 | 2.26  | 0.11 | 1.44          | 0.24     | 62.46   | 1.80      | 37.54                      | 1.57                           |

**TABLE 18: IN VITRO DIFFUSION OF BETAXOLOL HCL FROM FORMULATION-15(F15) (DRUG: HPMCK4M14%)**

| Time (min) | √T    | Log T | Abs* | Conc. (µg/ml) | CDR (mg) | CDR (%) | Log % CDR | Cumulative % drug remained | Cumulative Log % Drug remained |
|------------|-------|-------|------|---------------|----------|---------|-----------|----------------------------|--------------------------------|
| 30         | 5.48  | 1.48  | 0.05 | 0.70          | 0.12     | 30.26   | 1.48      | 69.74                      | 1.84                           |
| 60         | 7.75  | 1.78  | 0.06 | 0.83          | 0.14     | 35.87   | 1.55      | 64.13                      | 1.81                           |
| 120        | 10.95 | 2.08  | 0.07 | 0.94          | 0.16     | 40.56   | 1.61      | 59.44                      | 1.77                           |
| 180        | 13.42 | 2.26  | 0.08 | 1.13          | 0.19     | 49.15   | 1.69      | 50.85                      | 1.71                           |

**TABLE 19: IN VITRO DIFFUSION OF BETAXOLOL HCL FROM FORMULATION -16 (F 16) (DRUG: EC 14%)**

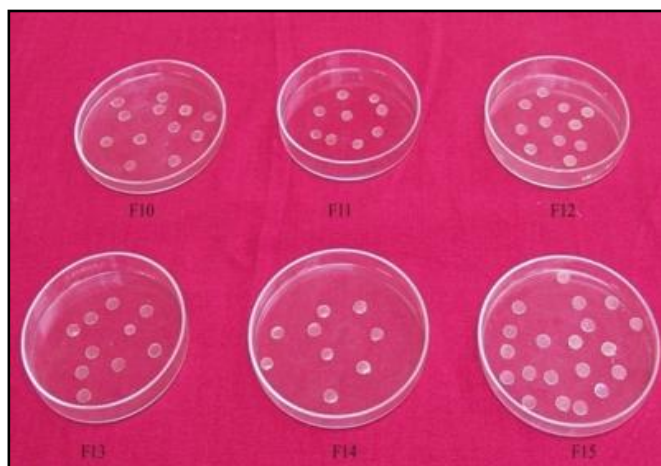
| Time (min) | √T       | Log T    | Abs*     | Conc. (µg/ml) | CDR (mg) | CDR (%)  | Log % CDR | Cumulative % drug remained | Cumulative Log % Drug remained |
|------------|----------|----------|----------|---------------|----------|----------|-----------|----------------------------|--------------------------------|
| 30         | 5.477226 | 1.477121 | 0.057056 | 0.771021      | 0.128375 | 33.431   | 1.524149  | 66.569                     | 1.823272                       |
| 60         | 7.745967 | 1.778151 | 0.059063 | 0.798143      | 0.132891 | 34.607   | 1.539164  | 65.393                     | 1.815531                       |
| 120        | 10.95445 | 2.079181 | 0.06693  | 0.904464      | 0.150593 | 39.217   | 1.593474  | 60.783                     | 1.783782                       |
| 180        | 13.41641 | 2.255273 | 0.072639 | 0.98161       | 0.163438 | 42.562   | 1.629022  | 57.438                     | 1.759199                       |
| 240        | 15.49193 | 2.380211 | 0.076134 | 1.028843      | 0.171302 | 44.61    | 1.649432  | 55.39                      | 1.743431                       |
| 300        | 17.32051 | 2.477121 | 0.080727 | 1.090906      | 0.181636 | 47.301   | 1.67487   | 52.699                     | 1.721802                       |
| 360        | 18.97367 | 2.556303 | 0.082132 | 1.109887      | 0.184796 | 48.124   | 1.682362  | 51.876                     | 1.714966                       |
| 420        | 20.4939  | 2.623249 | 0.08705  | 1.176355      | 0.195863 | 51.006   | 1.707621  | 48.994                     | 1.690143                       |
| 480        | 21.9089  | 2.681241 | 0.093493 | 1.263418      | 0.210359 | 54.781   | 1.73863   | 45.219                     | 1.655321                       |
| 540        | 23.2379  | 2.732394 | 0.100966 | 1.364411      | 0.227174 | 59.16    | 1.772028  | 40.84                      | 1.611086                       |
| 600        | 24.4949  | 2.778151 | 0.106058 | 1.433221      | 0.238631 | 62.14356 | 1.793396  | 37.85644                   | 1.57814                        |
| 660        | 25.69047 | 2.819544 | 0.116335 | 1.572094      | 0.261754 | 68.165   | 1.833561  | 31.835                     | 1.502905                       |

**TABLE 20: IN VITRO DIFFUSION OF BETAXOLOL HCL FROM FORMULATION -21(21) (DRUG: EC 18%)**

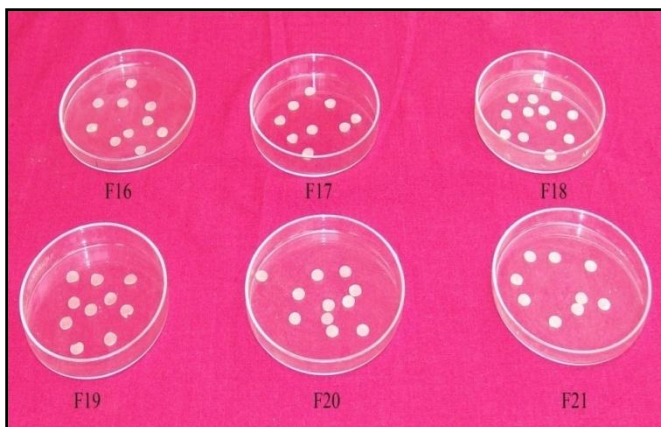
| Time (min) | √T    | Log T | Abs* | Conc. (µg/ml) | CDR (mg) | CDR (%)  | Log % CDR | Cumulative % drug remained | Cumulative Log % Drug remained |
|------------|-------|-------|------|---------------|----------|----------|-----------|----------------------------|--------------------------------|
| 30         | 5.48  | 1.48  | 0.04 | 0.47          | 0.08     | 20.53861 | 1.31      | 79.46                      | 1.90                           |
| 60         | 7.75  | 1.78  | 0.05 | 0.65          | 0.11     | 28.14312 | 1.45      | 71.86                      | 1.86                           |
| 120        | 10.95 | 2.08  | 0.06 | 0.74          | 0.12     | 32.27495 | 1.51      | 67.73                      | 1.83                           |
| 180        | 13.42 | 2.26  | 0.06 | 0.84          | 0.14     | 36.38267 | 1.56      | 63.62                      | 1.80                           |
| 240        | 15.49 | 2.38  | 0.07 | 0.90          | 0.15     | 38.89717 | 1.59      | 61.10                      | 1.79                           |
| 300        | 17.32 | 2.48  | 0.07 | 0.94          | 0.16     | 40.86177 | 1.61      | 59.14                      | 1.77                           |
| 360        | 18.97 | 2.56  | 0.07 | 0.96          | 0.16     | 41.46629 | 1.62      | 58.53                      | 1.77                           |
| 420        | 20.49 | 2.62  | 0.07 | 0.98          | 0.16     | 42.6271  | 1.63      | 57.37                      | 1.76                           |
| 480        | 21.91 | 2.68  | 0.08 | 1.08          | 0.18     | 46.7107  | 1.67      | 53.29                      | 1.73                           |
| 540        | 23.24 | 2.73  | 0.08 | 1.13          | 0.19     | 49.0403  | 1.69      | 50.96                      | 1.71                           |
| 600        | 24.49 | 2.78  | 0.09 | 1.22          | 0.20     | 52.75894 | 1.72      | 47.24                      | 1.67                           |
| 660        | 25.69 | 2.82  | 0.10 | 1.30          | 0.22     | 56.2557  | 1.75      | 43.74                      | 1.64                           |
| 720        | 26.83 | 2.86  | 0.10 | 1.37          | 0.23     | 59.3329  | 1.77      | 40.67                      | 1.61                           |

**TABLE 21: CURVE FITTING DATA FOR DIFFUSION**

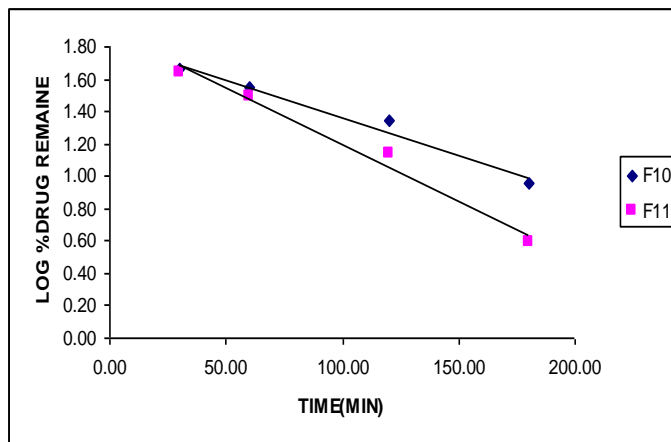
| Formulations | First order Equation |  |  | Higuchi's Equation |  |  | Peppas Equation |  |  |
|--------------|----------------------|--|--|--------------------|--|--|-----------------|--|--|
|              | Slope                | Rate constant (K) mg. hr <sup>-1</sup> | Regression coefficient (R <sup>2</sup> ) | Slope              | Rate constant (K) mg. hr <sup>-1</sup> | Regression coefficient (R <sup>2</sup> ) | Slope           | Rate constant (K) mg. hr <sup>-1</sup> | Regression coefficient (R <sup>2</sup> ) |
| F10          | -0.0013              | 1.8095                                 | 0.9451                                   | 2.6308             | 25.902                                 | 0.9505                                   | 0.2381          | 1.2476                                 | 0.9615                                   |
| F15          | -0.0008              | 1.8646                                 | 0.9928                                   | 2.2553             | 17.759                                 | 0.9726                                   | 0.2568          | 1.0946                                 | 0.9745                                   |
| F16          | -0.0004              | 1.8495                                 | 0.9517                                   | 1.5873             | 21.616                                 | 0.9394                                   | 0.2192          | 1.1549                                 | 0.8989                                   |
| F21          | -0.0004              | 1.8874                                 | 0.9629                                   | 12.96              | 8.9065                                 | 0.9764                                   | 0.2979          | 0.8842                                 | 0.9709                                   |



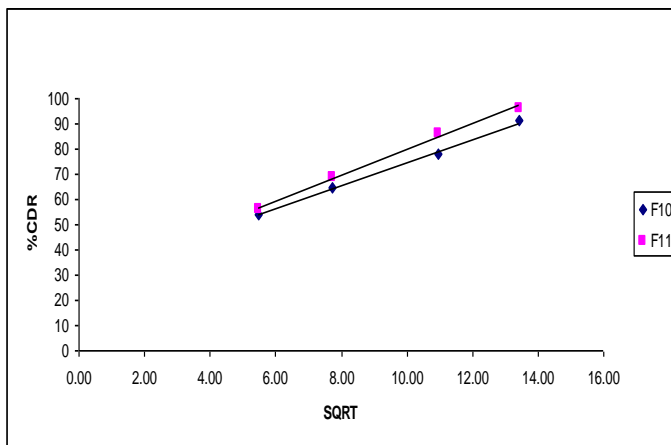
**FIG.1: OPHTHALMIC INSERTS OF BETAXOLOL HYDROCHLORIDE USING HPMCK4M AS POLYMER**



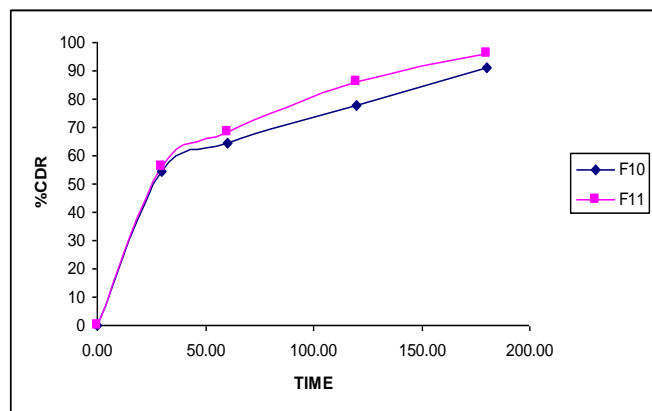
**FIG. 2: OPHTHALMIC INSERTS OF BETAXOLOL HYDROCHLORIDE USING ETHYL CELLULOSE AS POLYMER**



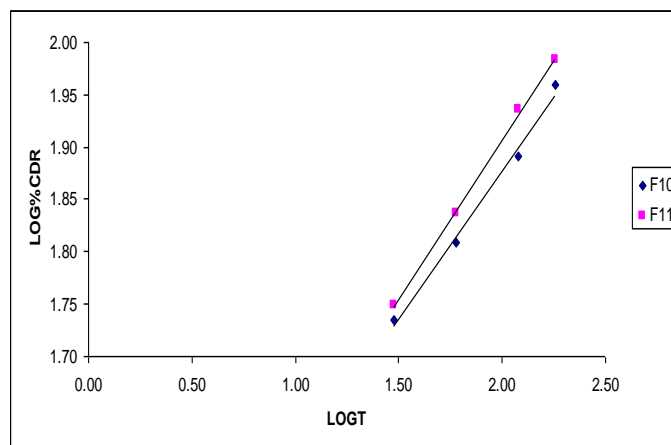
**FIG.4: FIRST ORDER PLOTS FOR F10, F11**



**FIG. 5: HIGUCHI'S SQUARE ROOT TIME DEPENDENT PLOTS FOR F10, F11**



**FIGURE 3: IN-VITRO DRUG RELEASE PROFILE OF F10, F11**



**FIG.6: PEPPAS DOUBLE LOG PLOT FOR F10, F11**

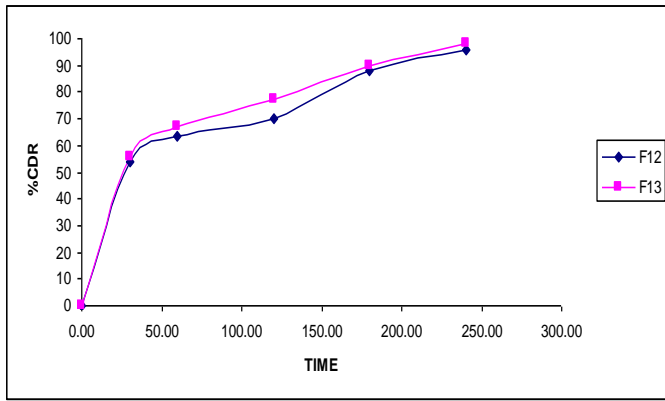


FIG.7: IN VITRO DRUG RELEASE PLOT FOR F12, F13

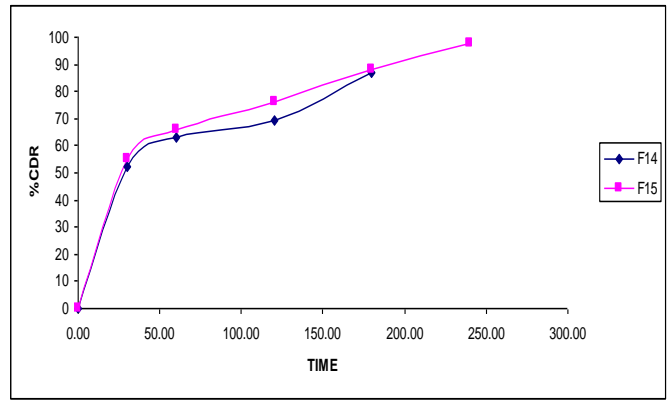


FIG. 11: IN VITRO DRUG RELEASE PLOTS FOR F14, F15

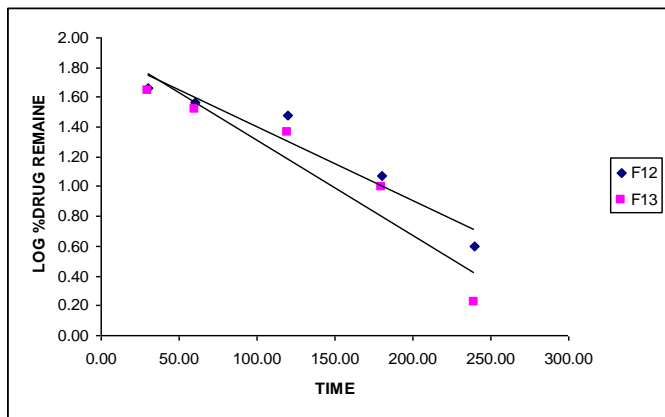


FIG.8: FIRST ORDER PLOTS FOR F12, F13

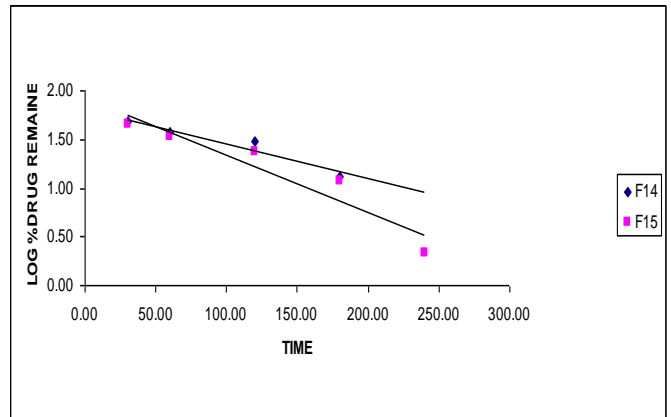


FIG. 12: FIRST ORDER PLOT FOR F14, F15

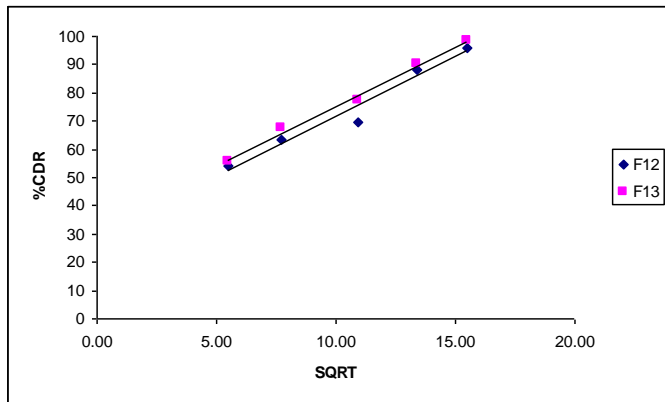


FIG. 9: HIGUCHI'S SQUARE ROOT TIME DEPENDENT PLOTS FOR F12, F13

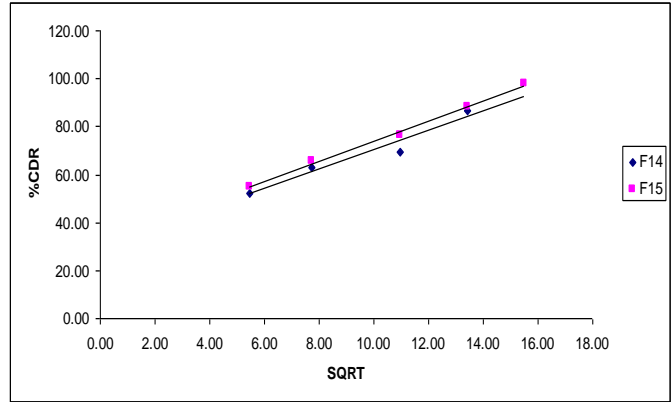


FIG.13: HIGUCHI'S SQUARE ROOT TIME DEPENDENT PLOTS FOR F14, F15

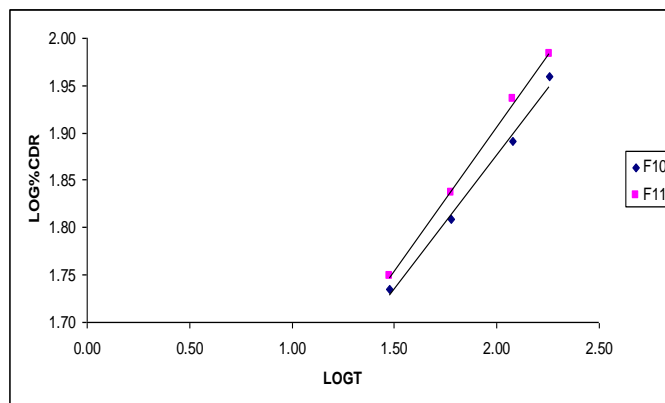


FIG.10: PEPPAS DOUBLE LOG PLOTS FOR F12, F13

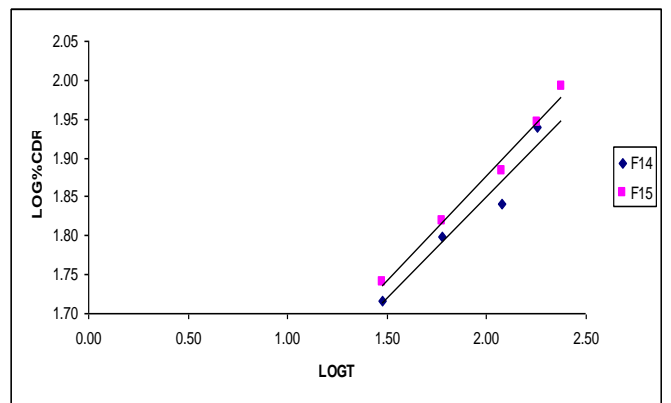


FIG. 14: PEPPAS DOUBLE LOG PLOTS FOR F14, F15

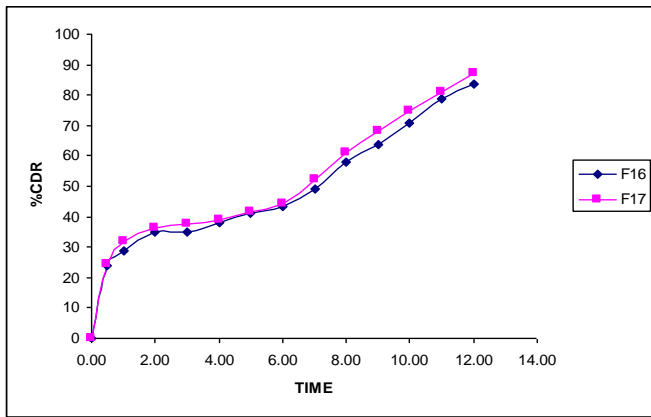


FIG.15: IN VITRO DRUG RELEASE PROFILE FOR F16, F17

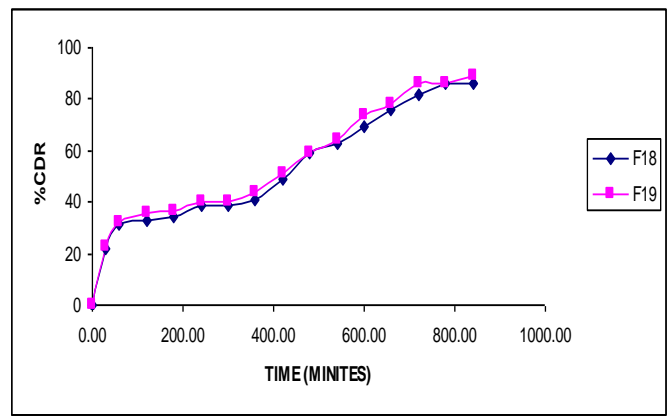


FIG.19: IN VITRO DRUG RELEASE PATTERN FOR F18, F19

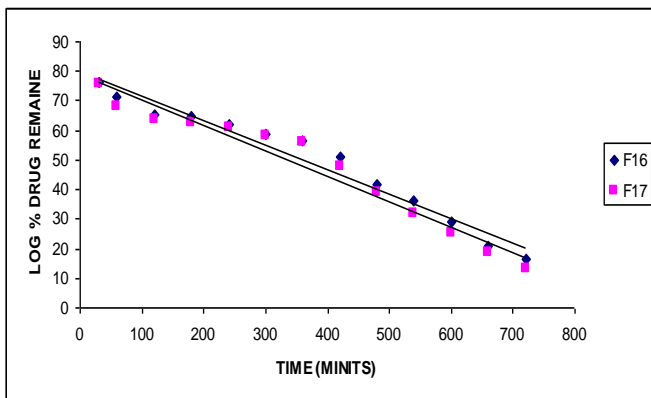


FIG. 16: FIRST ORDER PLOTS FOR F16, F17

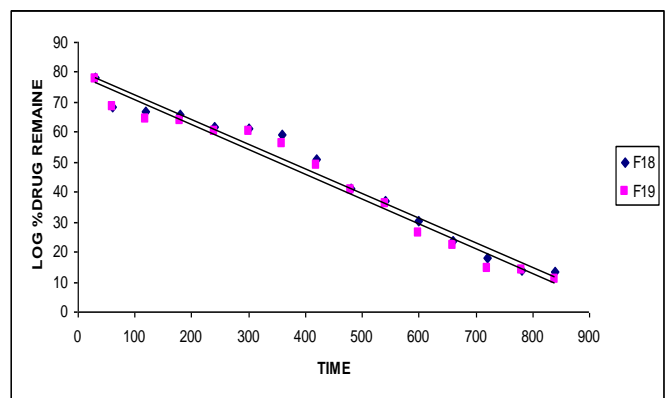


FIG. 20: FIRST ORDER PLOTS FOR F18, F19

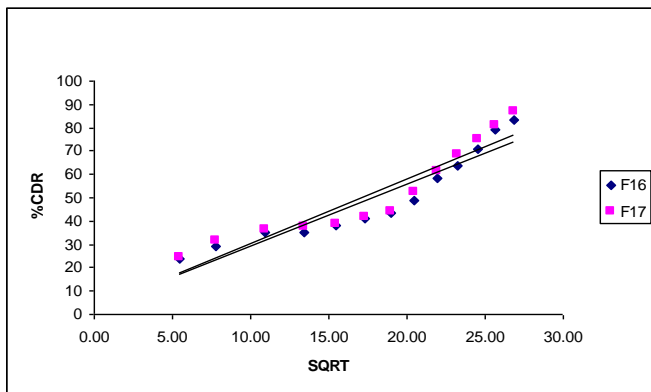


FIG.17: HIGUCHI'S SQUARE ROOT TIME DEPENDENT PLOTS FOR F16, F17

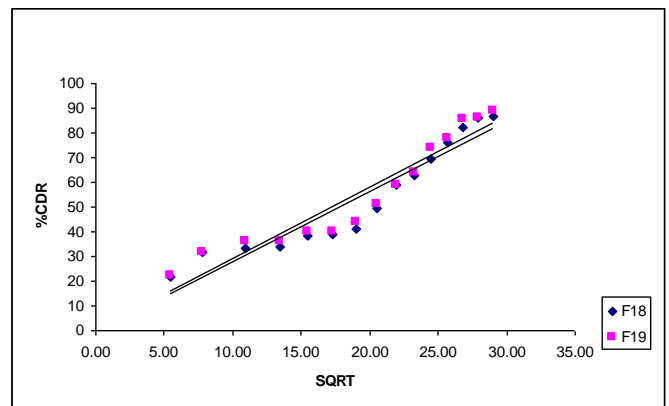


FIG. 21: HIGUCHI'S SQUARE ROOT TIME DEPENDENT PLOTS FOR F18, F19

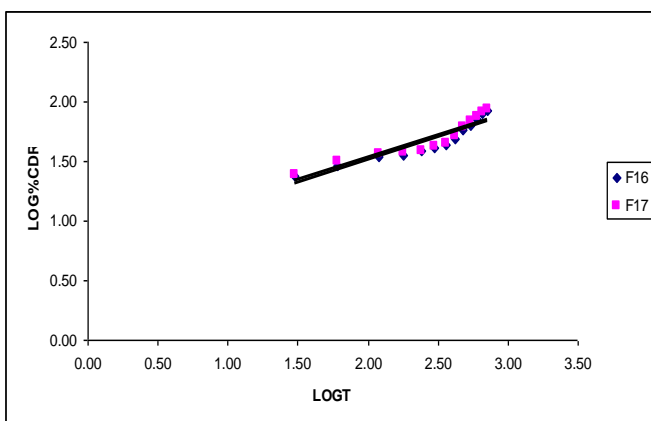


FIG.18: PEPPAS DOUBLE LOG PLOTS FOR F16, F17

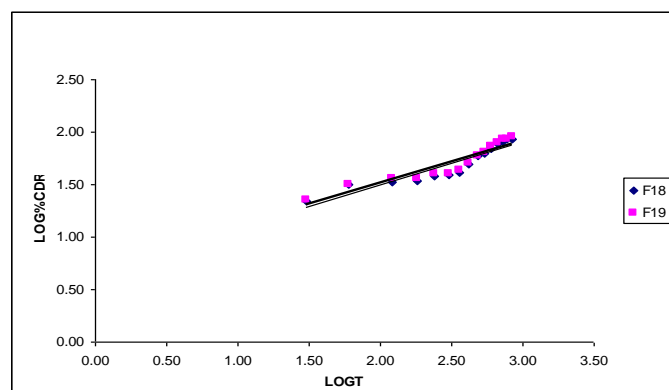


FIG. 22: PEPPAS DOUBLE LOG PLOTS FOR F18, F19

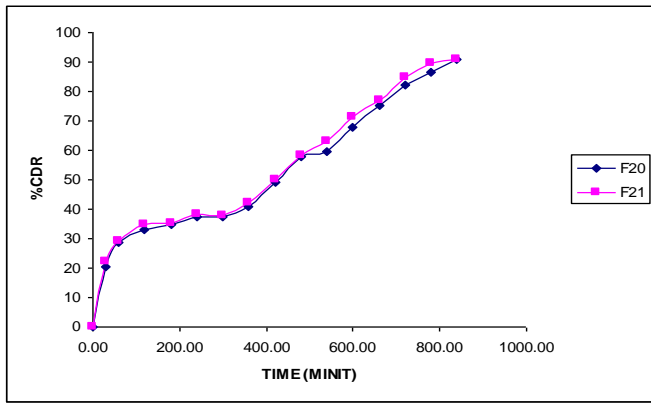


FIG. 23: IN VITRO DRUG RELEASE PLOTS FOR F20, F21

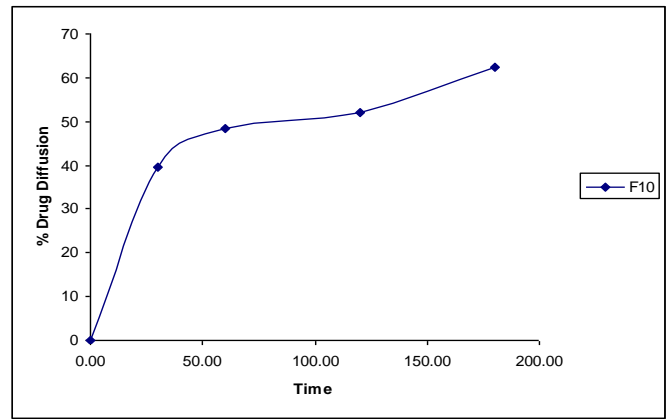


FIG. 27: IN VITRO DRUG DIFFUSION PLOT FOR F10

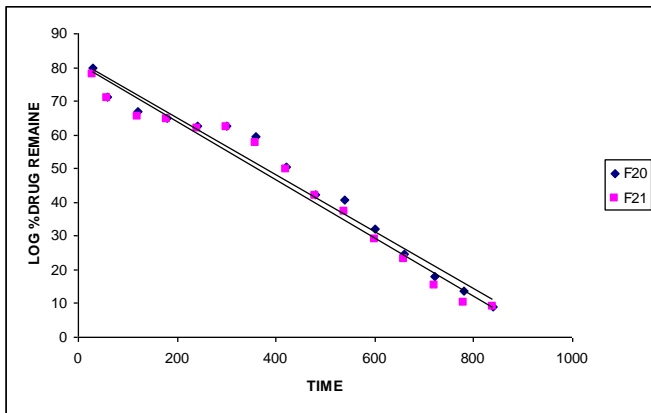


FIG. 24: FIRST ORDER PLOTS FOR F20, F21

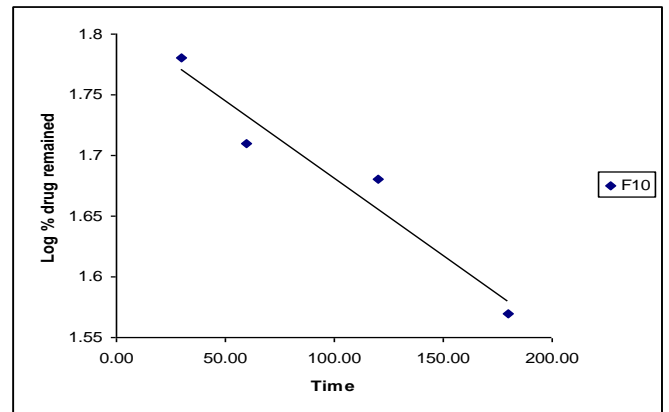


FIG. 28: FIRST ORDER PLOT FOR F10

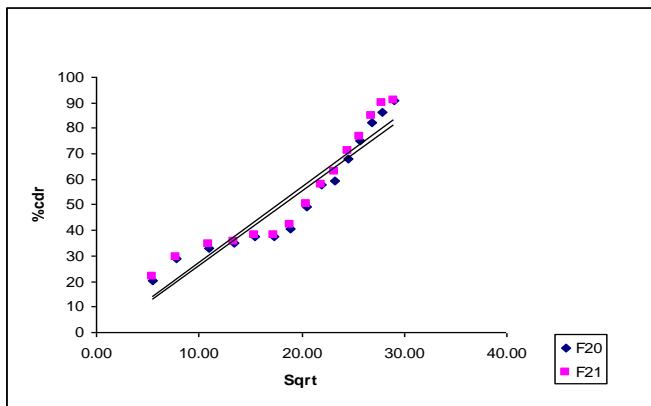


FIG. 25: HIGUCHI'S SQUARE ROOT TIME DEPENDENT PLOTS FOR F20, F21

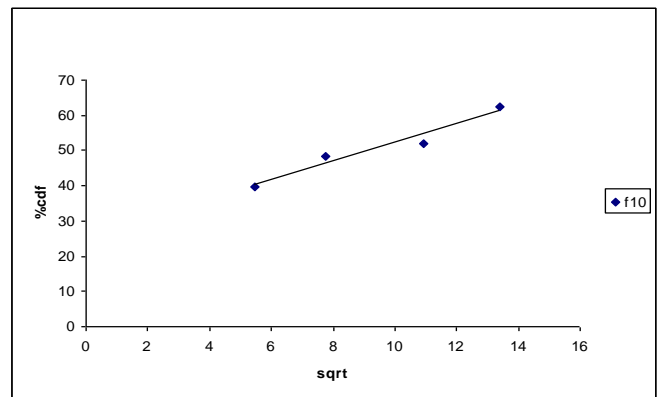


FIG. 29: HIGUCHI'S SQUARE ROOT TIME DEPENDENT PLOT FOR F10

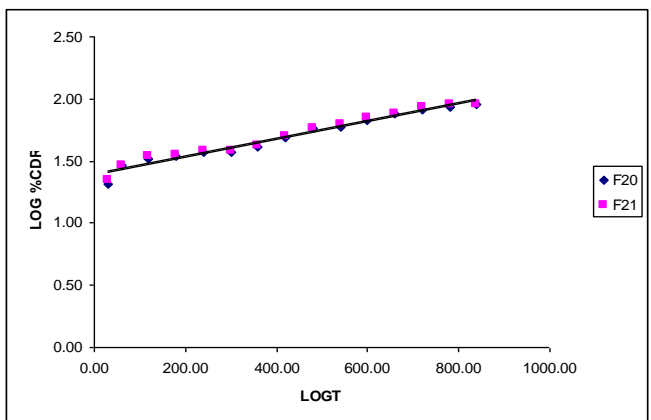


FIG. 26: PEPPAS DOUBLE LOG PLOTS FOR F20, F21

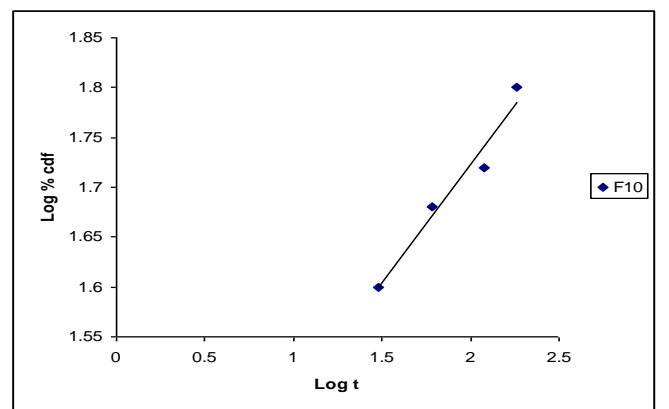


FIG. 30: PEPPAS DOUBLE LOG PLOT FOR F10



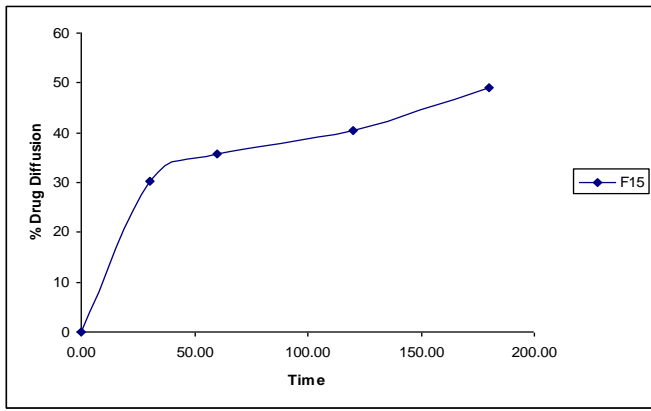


FIG.31: IN VITRO DRUG DIFFUSION PLOT FOR F15

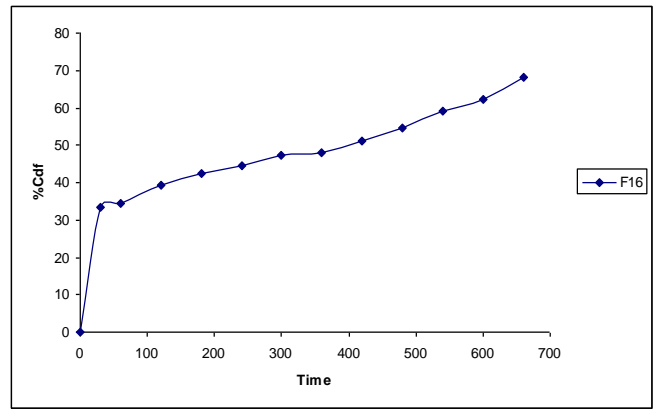


FIG. 35: IN VITRO DRUG DIFFUSION PLOT FOR F16

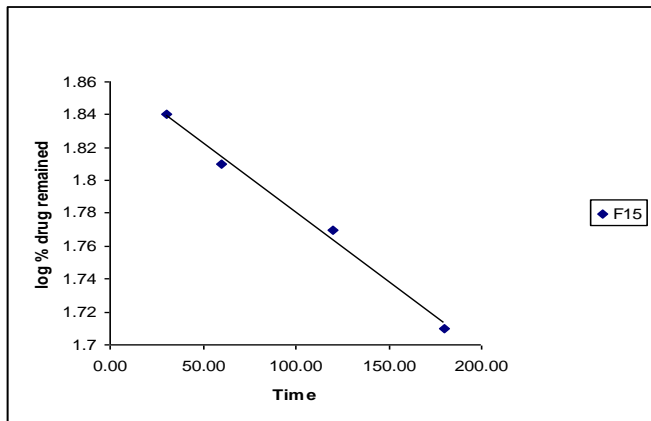


FIG.32: FIRST ORDER PLOT FOR F15

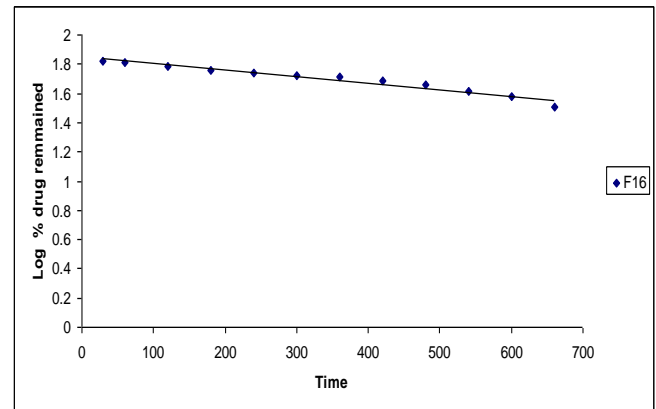


FIG. 36: FIRST ORDER PLOT FOR F16

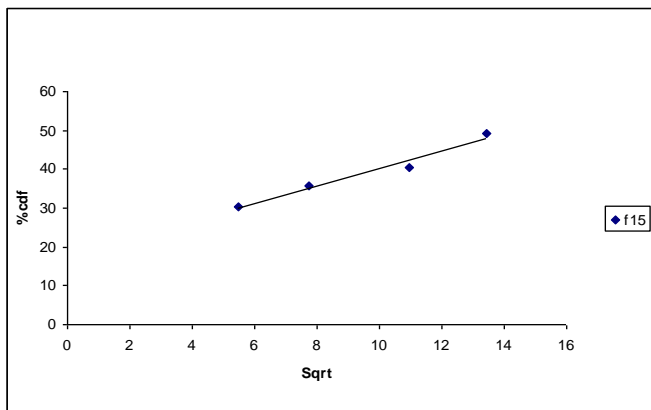


FIG. 33: HIGUCHI'S SQUARE ROOT TIME DEPENDENT PLOT FOR F15

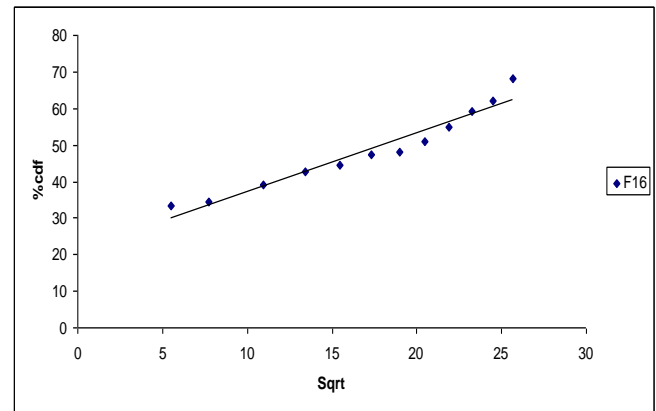


FIG.37: HIGUCHI'S SQUARE ROOT TIME DEPENDENT PLOT FOR F16

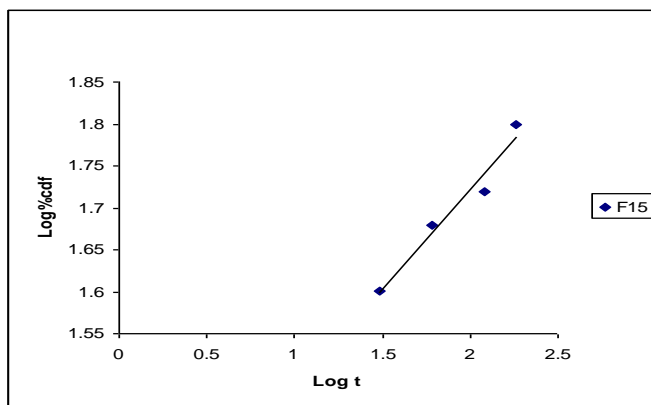


FIG.34: PEPPAS DOUBLE LOG PLOT FOR F15

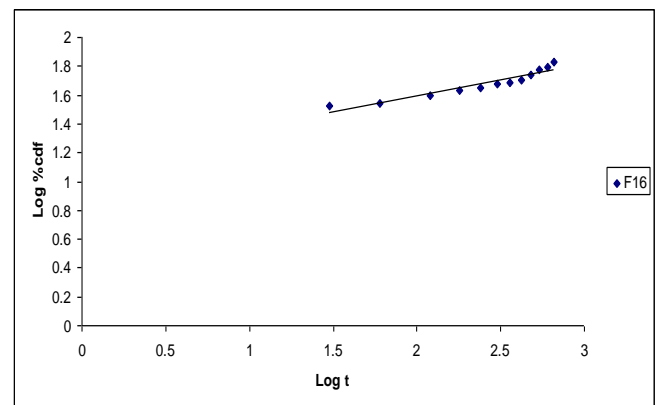


FIG.38: PEPPAS DOUBLE LOG PLOT FOR F16

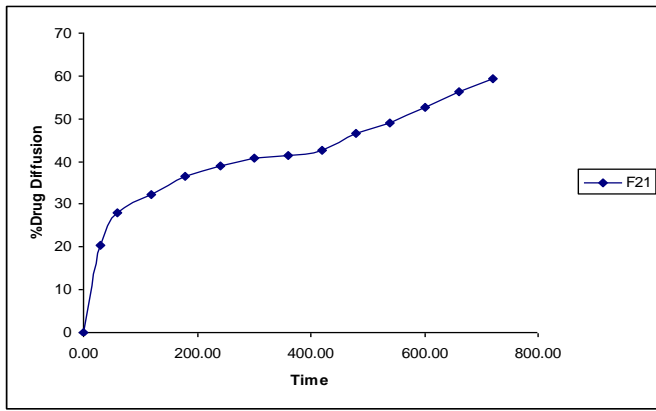


FIG.39: IN VITRO DRUG DIFFUSION PLOT FOR F21

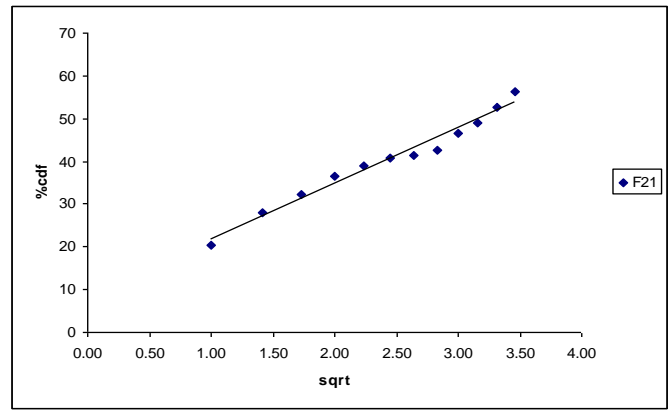


FIG.41: HIGUCHI'S SQUARE ROOT TIME DEPENDENT PLOT FOR F21

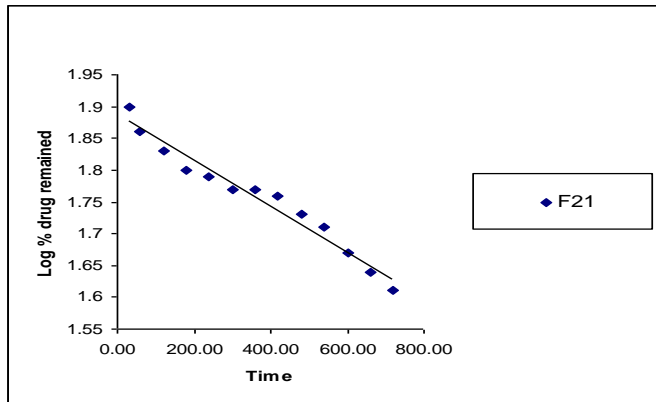


FIG.40: FIRST ORDER PLOT FOR F21

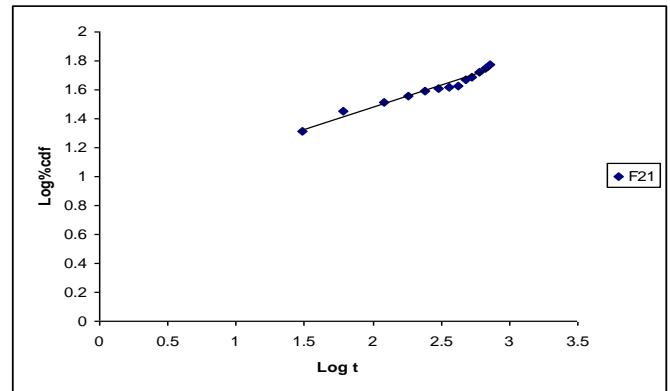


FIG. 42: PEPPAS DOUBLE LOG PLOT FOR F21

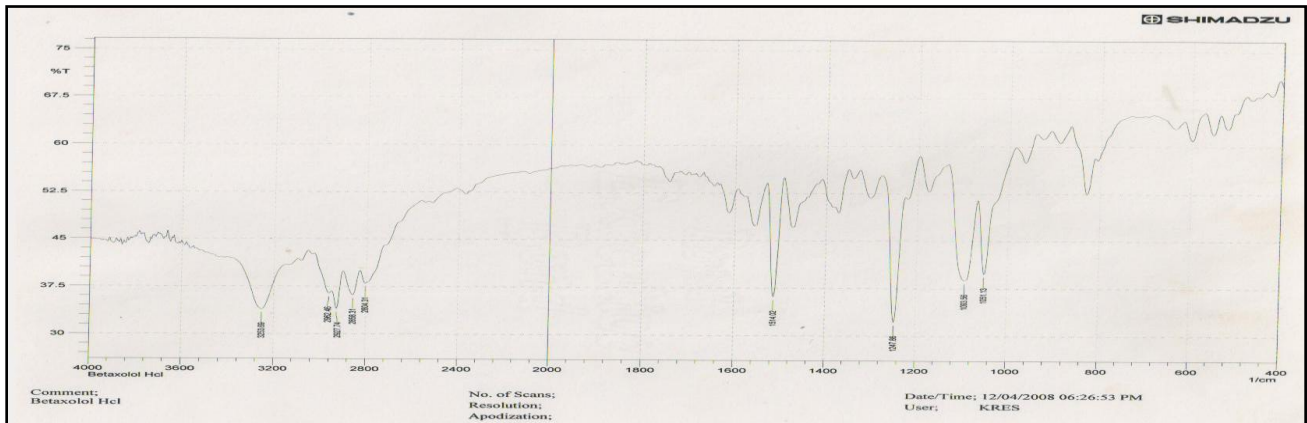


FIG.43: IR STUDY FOR BETAXOLOL HYDROCHLORIDE

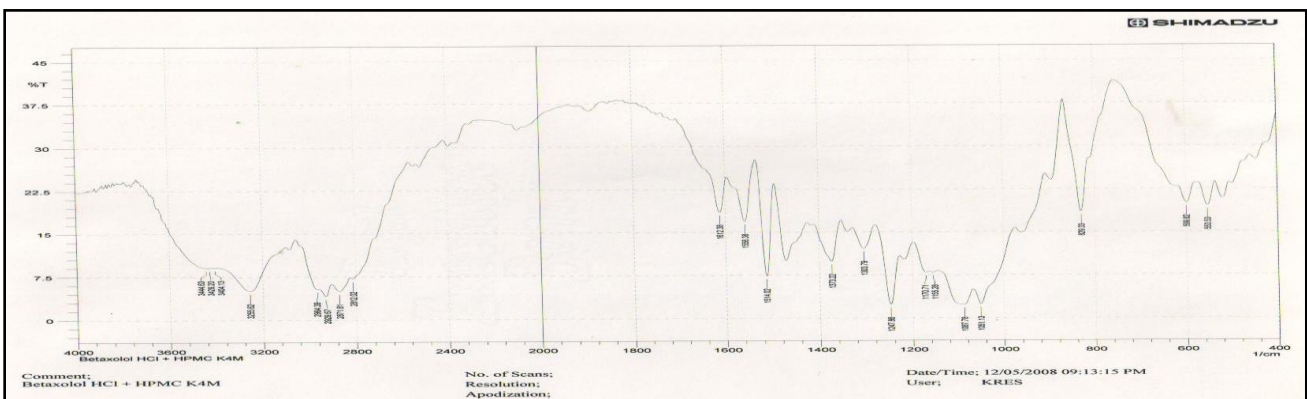


FIG. 44: IR STUDY FOR BETAXOLOL HYDROCHLORIDE + HPMCK4M

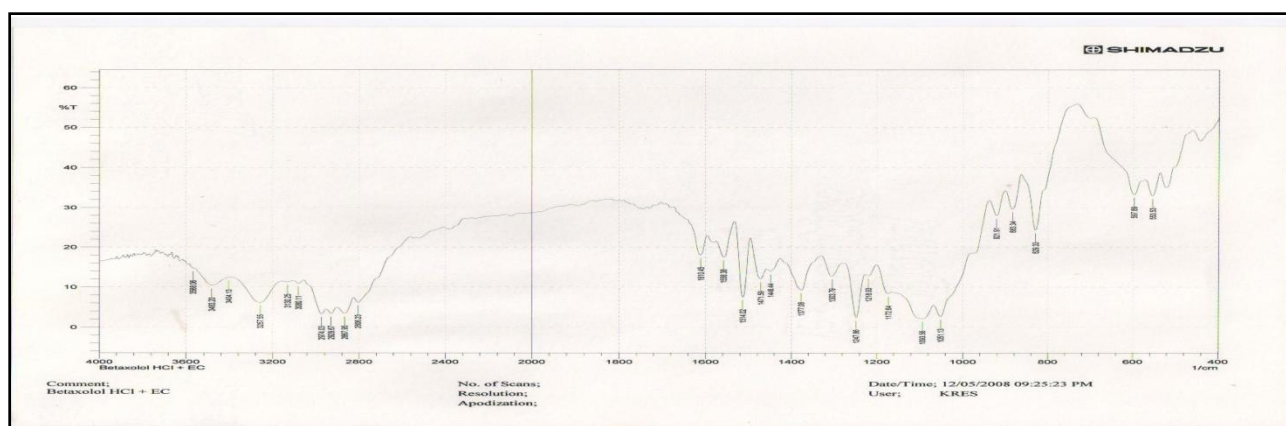


FIG. 45: IR STUDY FOR BETAXOLOL HYDROCHLORIDE + EC

**CONCLUSION:** The methodology adopted in present study was simple and re producible. The polymers used were inexpensive and easily available. The Betaxolol Hydrochloride ophthalmic inserts were prepared by using polymers such as HPMCK4m and EC. Among the different formulations the best in terms of physical appearance and uniformity of the drug content in comparison to all other formulation. In conclusion, it can be stated that inserts using Drug: HPMCK4m, Drug: EC in the 14 % HPMCK4m and 18% EC.

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