IJPSR (2015), Vol. 6, Issue 8 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 18 December, 2014; received in revised form, 13 February, 2015; accepted, 26 April, 2015; published 01 August, 2015

PREPARATION AND EVALUATION OF CONTROLLED RELEASE OF BETAXOLOL HYDROCHLORIDE OCULAR INSERTS

K. B. Kulkarni [*1], Patil Ajaykumar [2], Nagoba Shivappa N.[3] and S.S. Ladde [3]

Channabasweshwar Pharmacy College [*1], Latur, Maharashtra, India
K.R.E.S's Karnataka College of Pharmacy [2], Bidar, Karnataka, India
Shivlingeshwar College of Pharmacy [3], Almala, Latur, Maharashtra, India

Keywords:

Betaxolol Hydrochloride, ocular inserts, HPMCK4m, Ethyl Celluiose

Correspondence to Author:
Dr. Shivappa N. Nagoba

Principal, Shivlingeshwar College of Pharmacy, Almala, Latur (M.S.) India.

E-mail: nshivraj11@rediffmail.com

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 (β1 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 occuserts by diffusion controlled mechanism. Stability studies conducted formulation. The formulation showed satisfactory physical stability at 25^0 C and 40^0C 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.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.6(8).3359-74

Article can be accessed online on: www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.6(8).3359-74

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. [1, 2, 3]

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

concentrations of drug which are not intended for eye.[4, 5] 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 [2, 6] resulting in a bioavailability ranging from 1-10% of total administered dose[7]. 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.[8] 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.[9]

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 [10, 11] 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: [12]

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 solution15 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 file 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 diethylphalate 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 [13, 14, 15]:
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 [16]:** 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 ± 1 ˚C. These vials were placed over hot plate (maintained at room temperature 37 ± 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.[17]**
The cellophane membrane of approximately 25cm^2 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^{0}C±0.5^{0}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 to10 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 (Peppa's double log plots).

Stability Studies:
The selected formulations were stored at 25^0c /60%RH and 40^0c/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 orde*r *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, F11containing 10% of HPMC K4M shows the drug release of 91.00, 96.12% in 4hrs respectively , the formulations F12, F13containing 12% HPMC K4M showes 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 25^0 C and 40^0C 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 25^0C and 40^0C 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) (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 Choloride(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_{10}	11.80 ± 0.10	0.25 ± 0.07	1.35 ± 0.55	99.38 ± 0.21
F_{11}	12.17 ± 1.10	0.30 ± 0.04	1.42 ± 0.24	93.40 ± 0.09
F_{12}	12.33 ± 1.18	0.29 ±0.02	1.96 ± 0.12	91.76 ± 0.01
F_{13}	12.59 ± 1.74	0.31 ± 0.04	2.28 ± 0.53	93.66 ± 0.02
F_{14}	13.70 ± 1.12	0.34 ±0.05	2.32 ± 0.39	99.79 ±0.01
F_{15}	14.20 ± 1.12	0.33 ± 0.06	2.36 ± 0.24	92.87 ± 0.09
F_{16}	13.60 ± 0.10	0.30 ± 0.02	1.06±0.18	98 ± 0.02
F_{17}	14.20 ± 0.15	0.38 ± 0.04	1.59±0.11	98.18 ± 0.01
F_{18}	14.86 ± 0.25	0.44 ± 0.02	1.66±0.14	91.32 ± 0.03
F_{19}	15.16 ± 0.72	0.39 ± 0.01	1.72± 0.18	94.84 ± 0.07
F20	15.66 ± 0.72	0.43 ± 0.04	1.79±1.11	96.60 ± 0.07
F_{21}	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)	√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	1.3869	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)	√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	1.4258	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)	√T	Log T	Abs*	Conc. (µg/ml)	CDR (mg)	CDR (%)	Log % CDR	Cumulative % drug remained	Cumulative Log % Drug remained
30	5.477	1.4771	0.099	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)	√T	Log T	Abs*	Conc. (µg/ml)	CDR (mg)	CDR (%)	Log % CDR	Cumulative % drug remained	Cumulative Log % Drug remained
30	5.477	1.4771	0.104	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)	√T	Log T	Abs*	Conc. (µg/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)	√T	Log T	Abs*	Conc. (µg/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)	√T	Log T	Abs*	Conc. (µg/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)	√T	Log T	Abs*	Conc. (µg/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)	√T	Log T	Abs*	Conc. (µg/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)	√T	Log T	Abs*	Conc. (µg/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	3540	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) mg. hr^{-1}	Regression coefficient (R^2)	Slope	Rate constant (K) mg. hr^{-1}	Regression coefficient (R^2)	Slope	Rate constant (K) mg. hr^{-1}	Regression coefficient (R^2)
F_{10}	-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

	Stored At 25 ^{0}c/ 60 % RH		St0red 40^0 C / 75 % RH	
Time In Weeks	**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^{-1}	Regression coefficient (R^2)	Slope	Rate constant (K) mg. hr^{-1}	Regression coefficient (R^2)	Slope	Rate constant (K) mg. hr^{-1}	Regression coefficient (R^2)
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

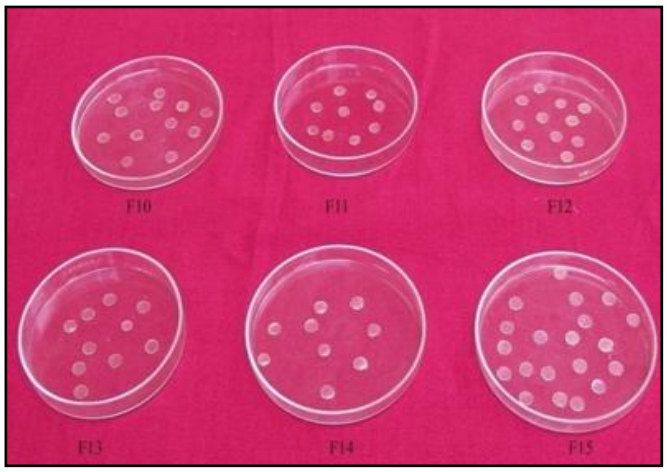

FIG.1: OPHTHALMIC INSERTS OF BETAXOLOL HYDROCHLORIDE USING HPMCK4M AS POLYMER

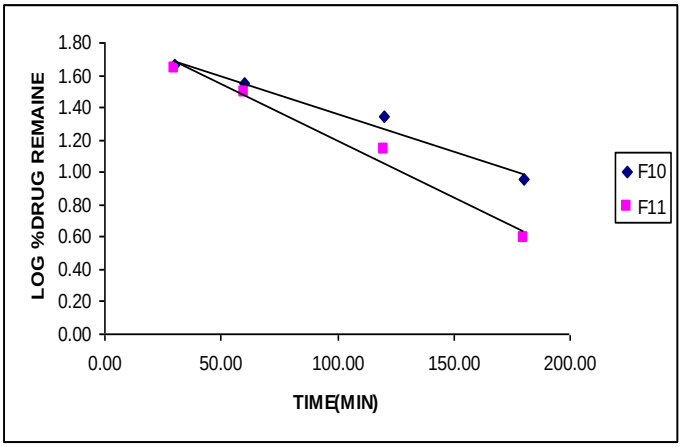

FIG.4: FIRST ORDER PLOTS FOR F10, F11

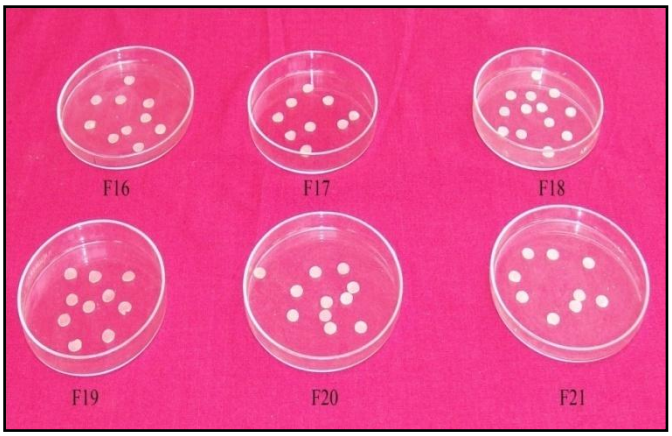

FIG. 2: OPHTHALMIC INSERTS OF BETAXOLOL HYDROCHLORIDE USING ETHYL CELLULOSE AS POLYMER

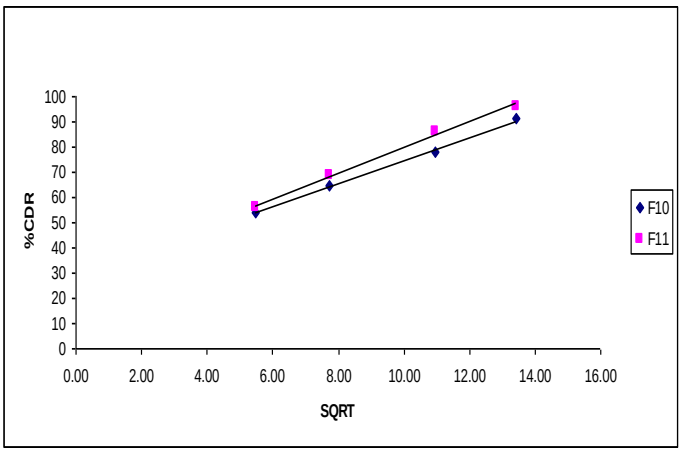

FIG. 5: HIGUCHI'S SQUARE ROOT TIME DEPENDENT PLOTS FOR F10, F11

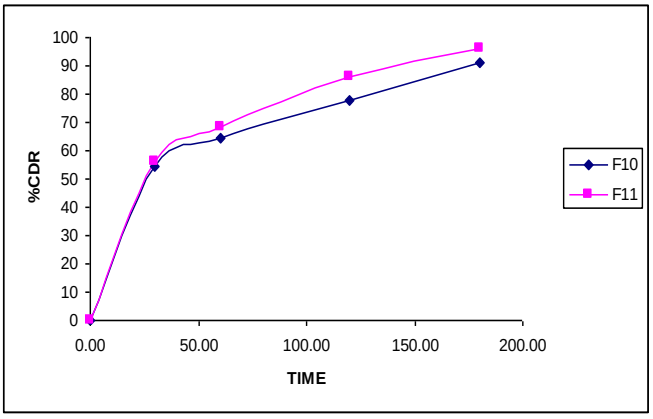

FIGURE 3: *IN-VITRO* DRUG RELEASE PROFILE OF F10, F11

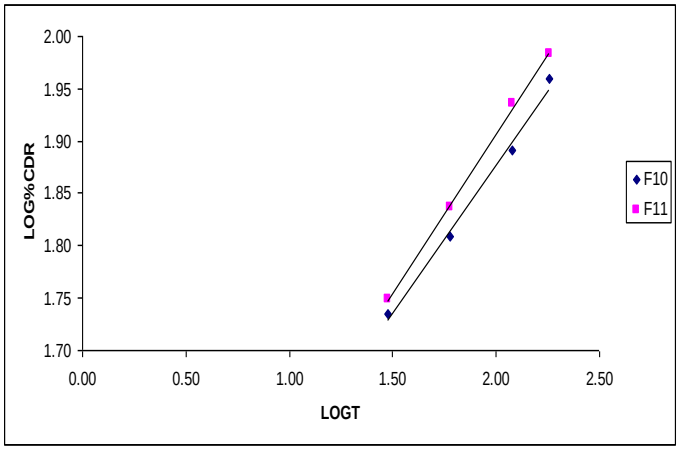

FIG.6: PEPPAS DOUBLE LOG PLOT FOR F10, F11

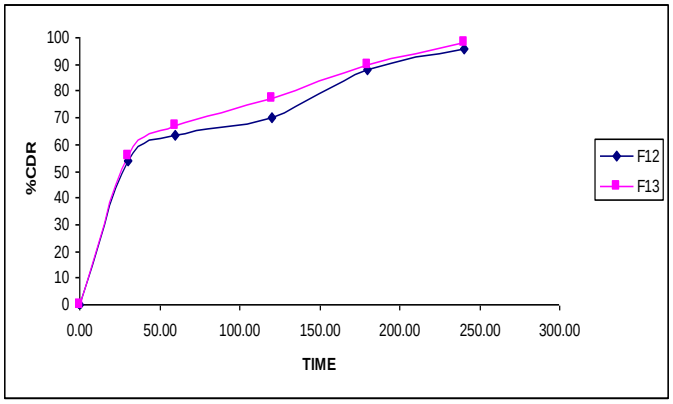

FIG.7: *IN VITRO* DRUG RELEASE PLOT FOR F12, F13

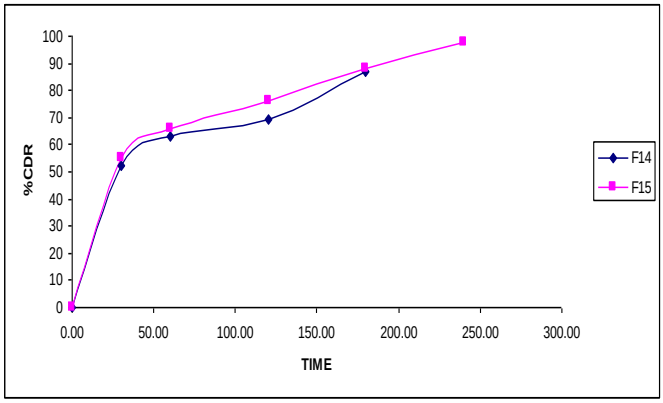

FIG. 11: *IN VITRO* DRUG RELEASE PLOTS FOR F14, F15

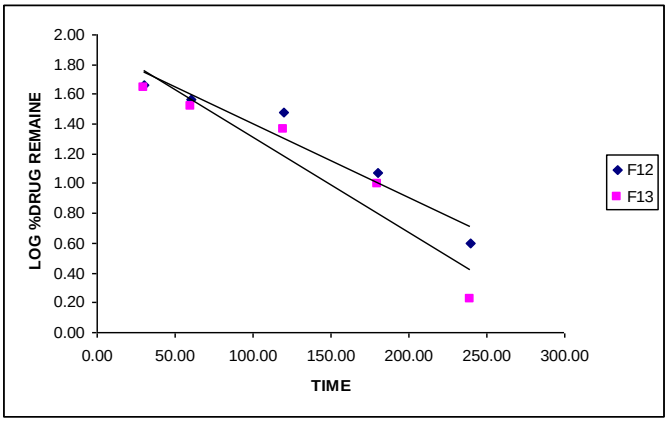

FIG.8: FIRST ORDER PLOTS FOR F12, F13

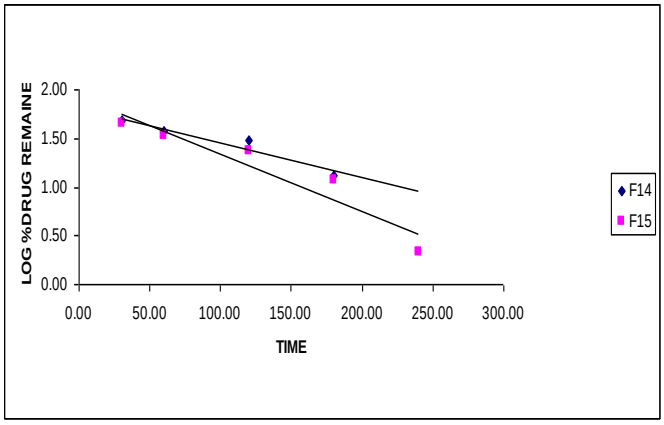

FIG. 12: FIRST ORDER PLOT FOR F14, F15

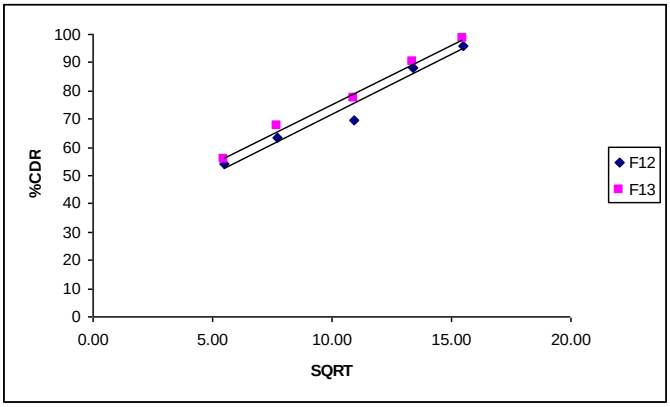

FIG. 9: HIGUCHI'S SQURE ROOT TIME DEPENDENT PLOTS FOR F12, F13

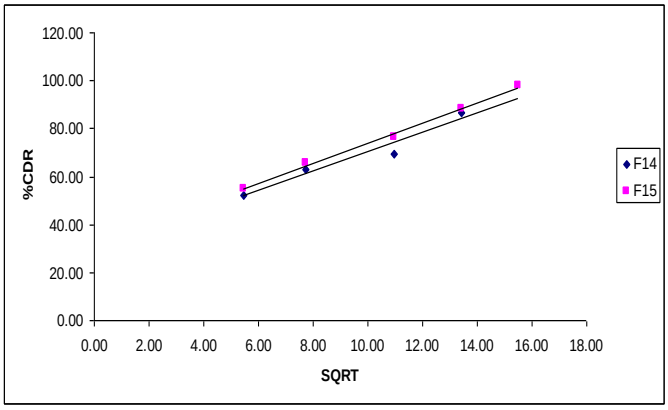

FIG.13: HIGUCHI'S SQUARE ROOT TIME DEPENDENT PLOTS FOR F14, F15

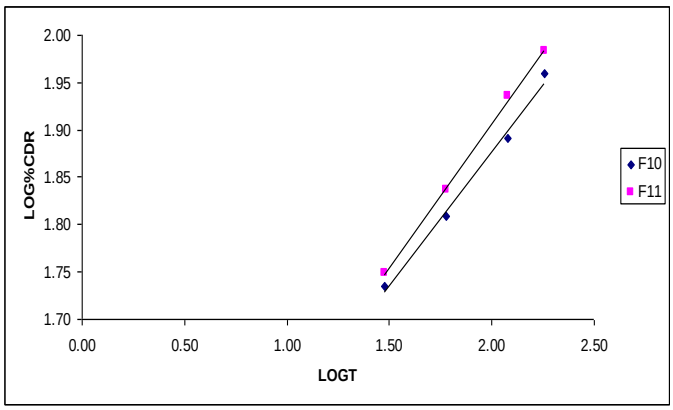

FIG.10: PEPPAS DOUBLE LOG PLOTS FOR F12, F13

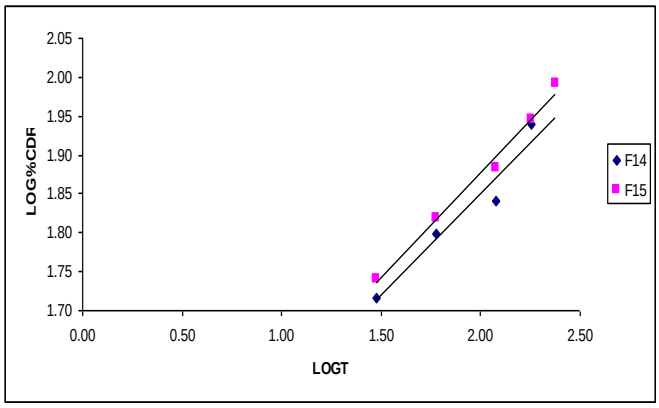

FIG. 14: PEPPAS DOUBLE LOG PLOTS FOR F14, F15

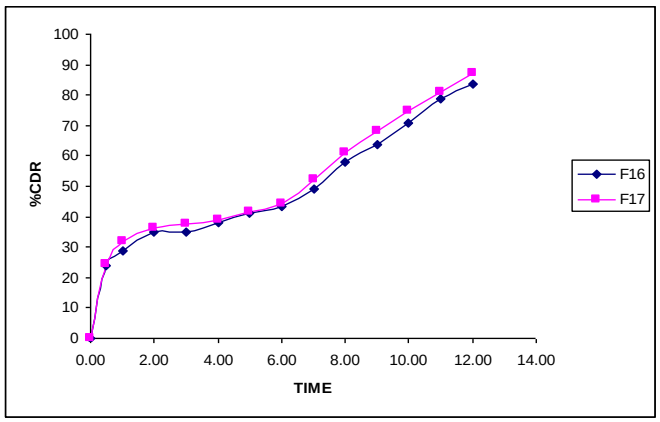

FIG.15: *IN VITRO* DRUG RELEASE PROFILE FOR F16, F17

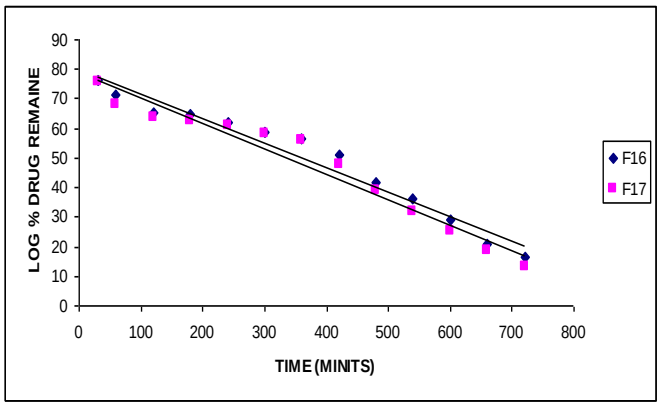

FIG. 16: FIRST ORDER PLOTS FOR F16, F17

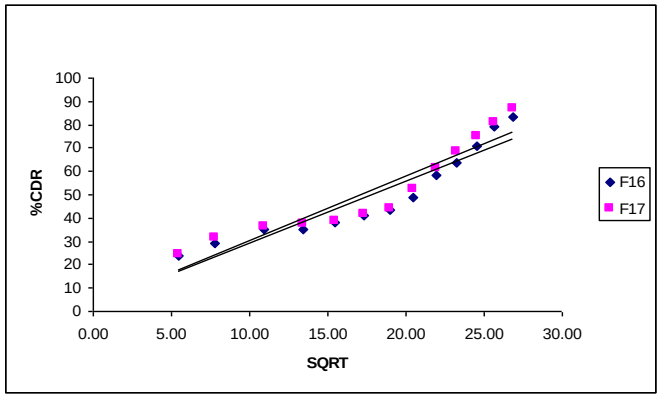

FIG.17: HIGUCHI'S SQUARE ROOT TIME DEPENDENT PLOTS FOR F16, F17

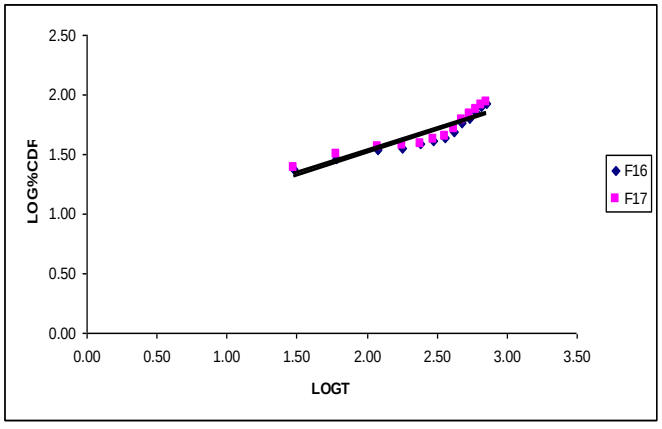

FIG.18: PEPPAS DOUBLE LOG PLOTS FOR F16, F17

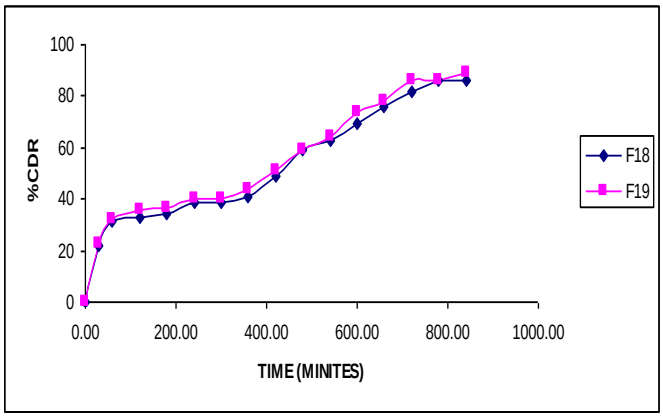

FIG.19: *IN VITRO* DRUG RELEASE PATTERN FOR F18, F19

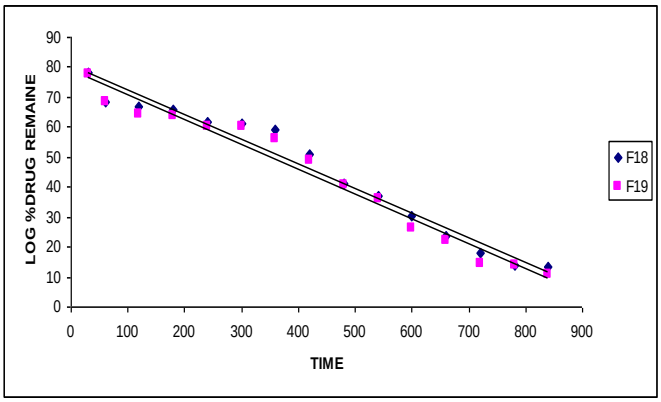

FIG. 20: FIRST ORDER PLOTS FOR F18, F19

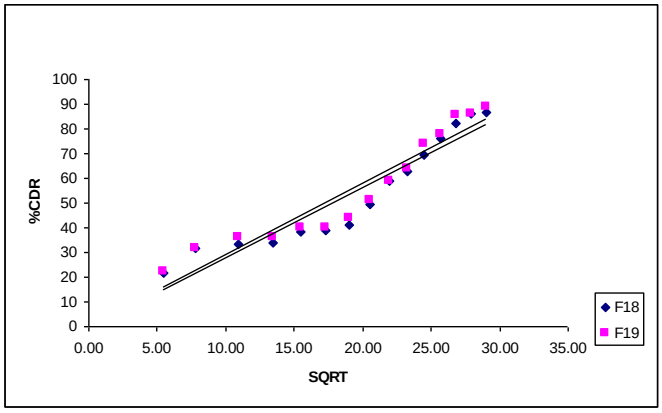

FIG. 21: HIGUCHI'S SQUARE ROOT TIME DEPENDENT PLOTS FOR F18, F19

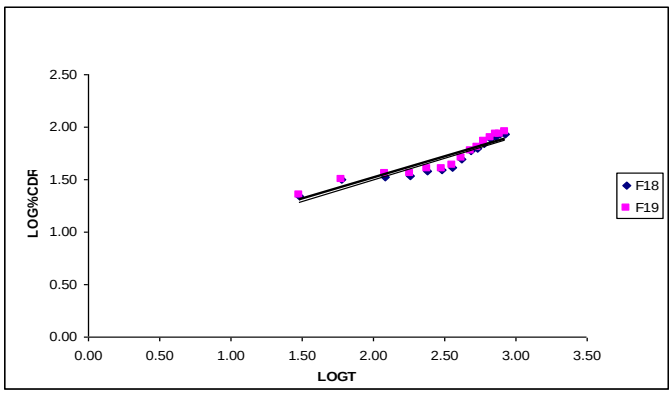

FIG. 22: PEPPAS DOUBLE LOG PLOTS FOR F18, F19

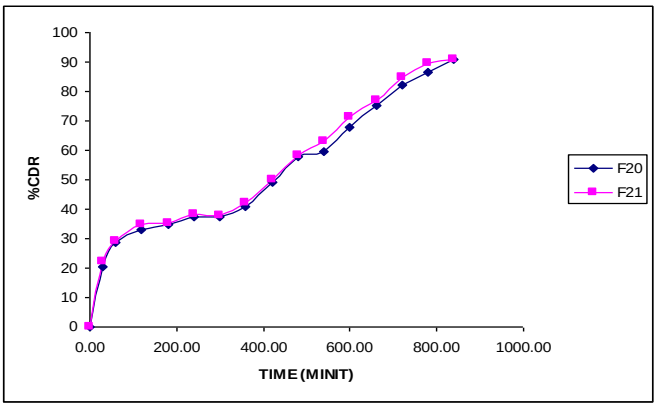

FIG. 23*: IN VITRO* DRUG RELEASE PLOTS FOR F20, F21

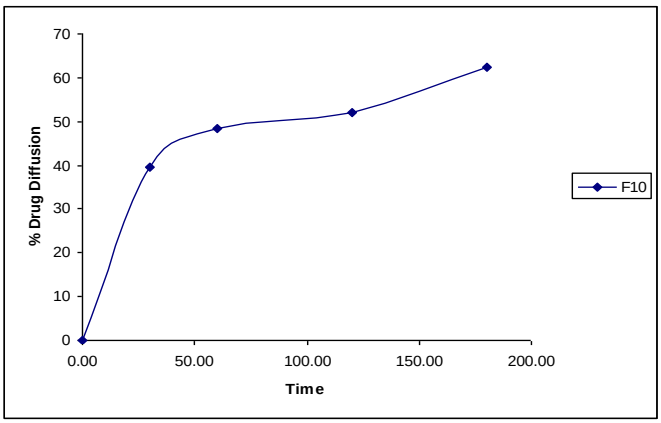

FIG.27: *IN VITRO* DRUG DIFFUSION PLOT FOR F10

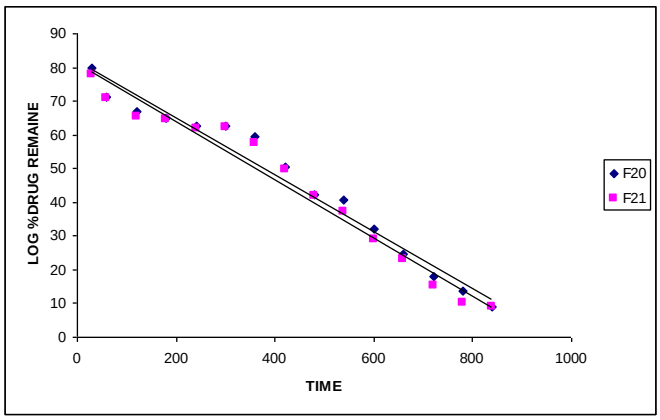

FIG. 24: FIRST ORDER PLOTS FOR F20, F21

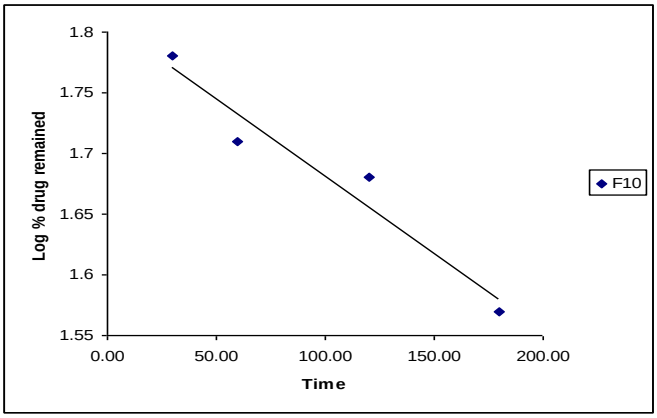

FIG. 28: FIRST ORDER PLOT FOR F10

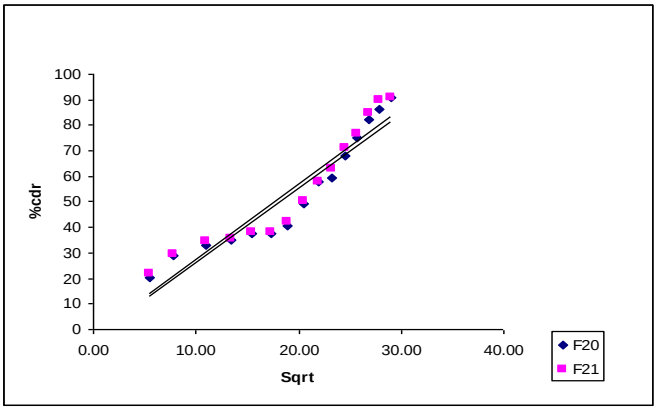

FIG. 25: HIGUCHI'S SQUARE ROOT TIME DEPENDENT PLOTS FOR F20, F21

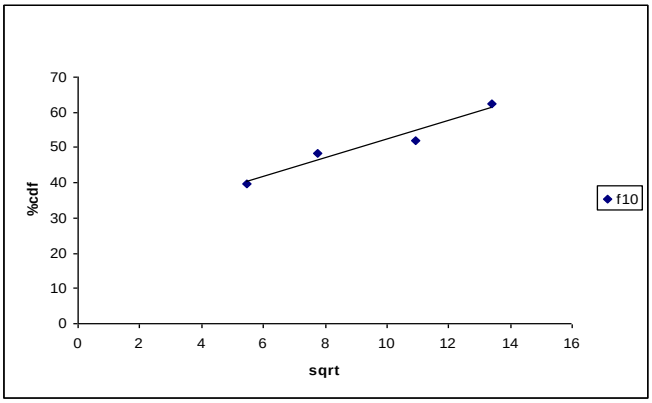

FIG.29: HIGUCHI'S SQUARE ROOT TIME DEPENDENT PLOT FOR F10

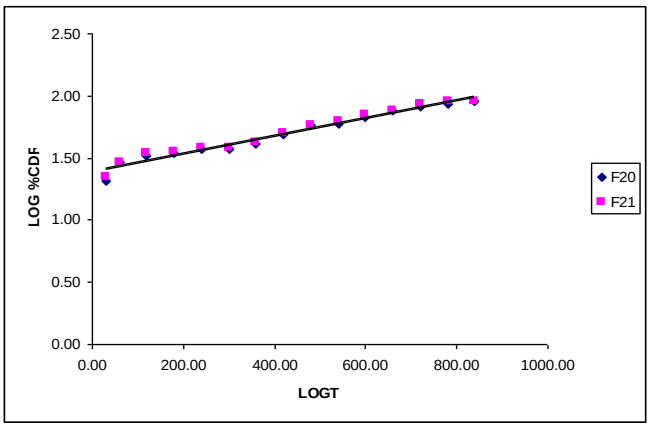

FIG.26: PEPPAS DOUBLE LOG PLOTS FOR F20, F2

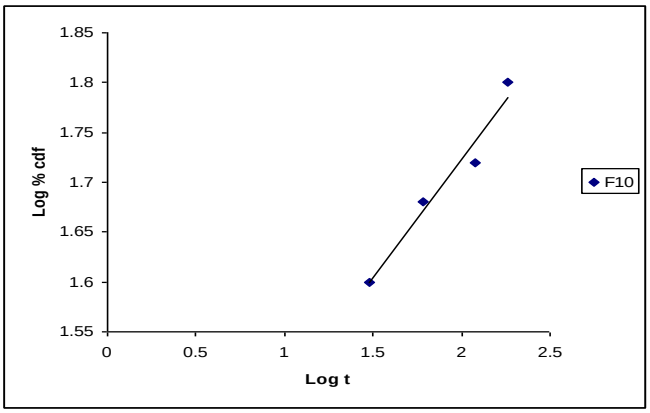

FIG.30: PEPPAS DOUBLE LOG PLOT FOR F10

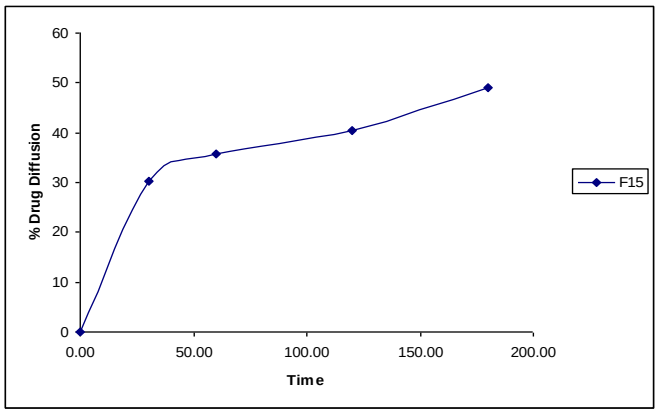

FIG.31: *IN VITRO* DRUG DIFFUSION PLOT FOR F15

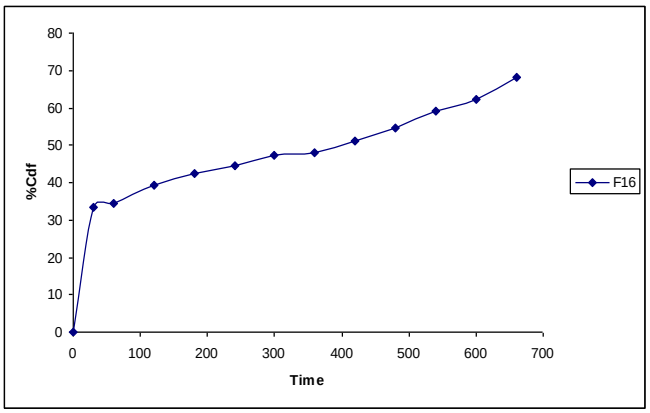

FIG. 35: *IN VITRO* DRUG DIFFUSION PLOT FOR F16

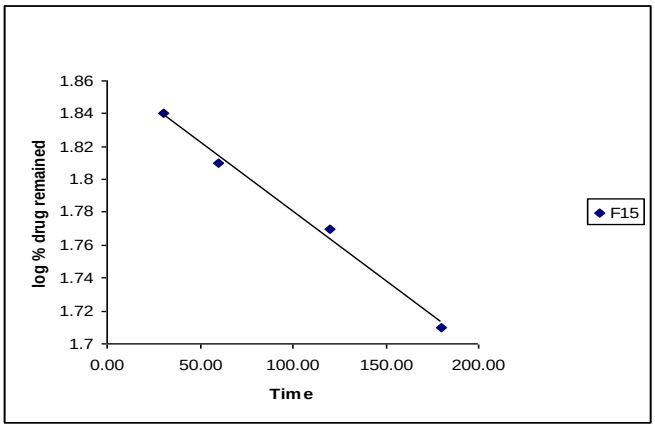

FIG.32: FIRST ORDER PLOT FOR F15

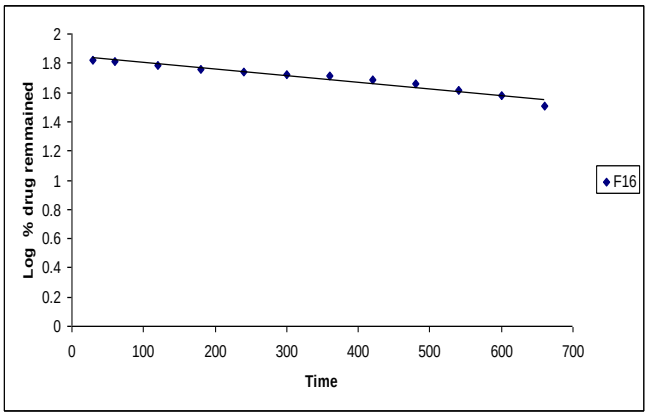

FIG. 36: FIRST ORDER PLOT FOR F16

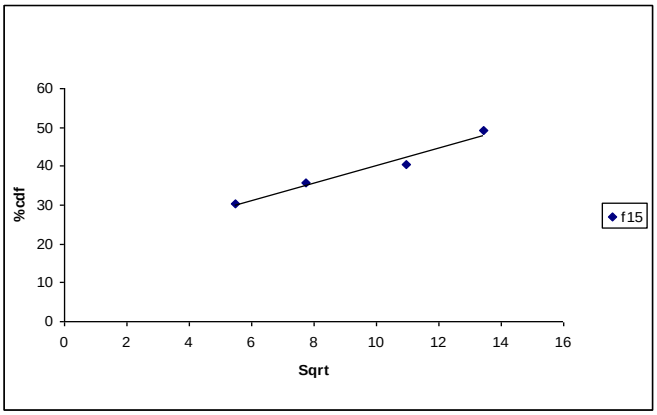

FIG. 33: HIGUCHI'S SQUARE ROOT TIME DEPENDENT PLOT FOR F15

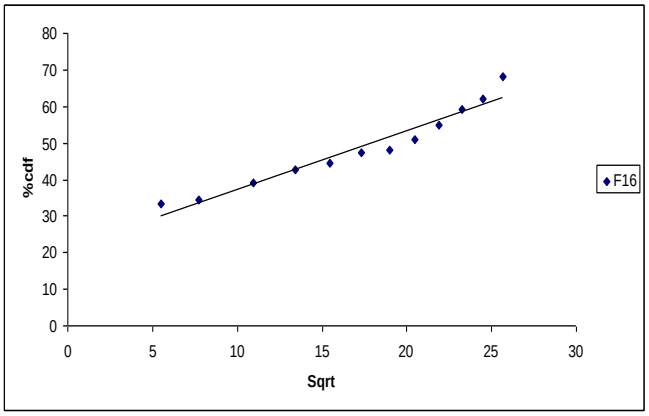

FIG.37: HIGUCHI'S SQUARE ROOT TIME DEPENDENT PLOT FOR F16

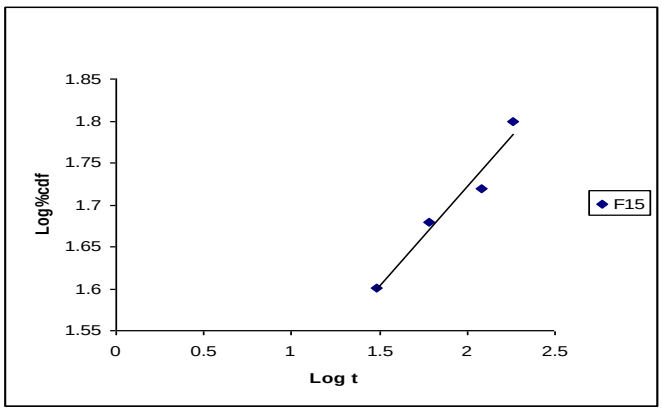

FIG.34: PEPPAS DOUBLE LOG PLOT FOR F15

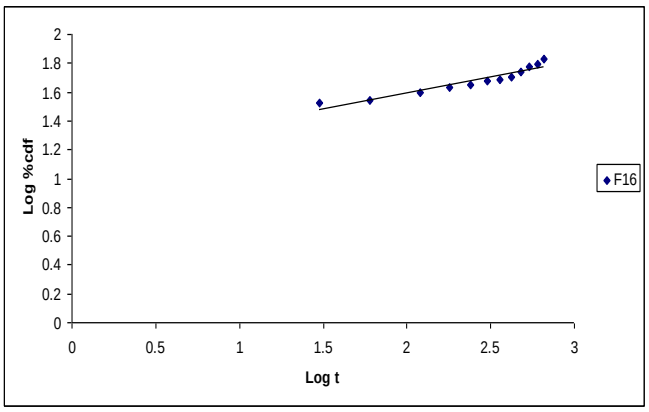

FIG.38: PEPPAS DOUBLE LOG PLOT FOR F16

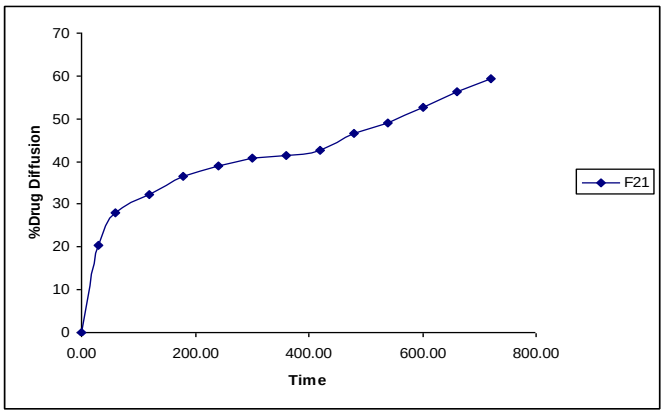

FIG.39: *IN VITRO* DRUG DIFFUSION PLOT FOR F21

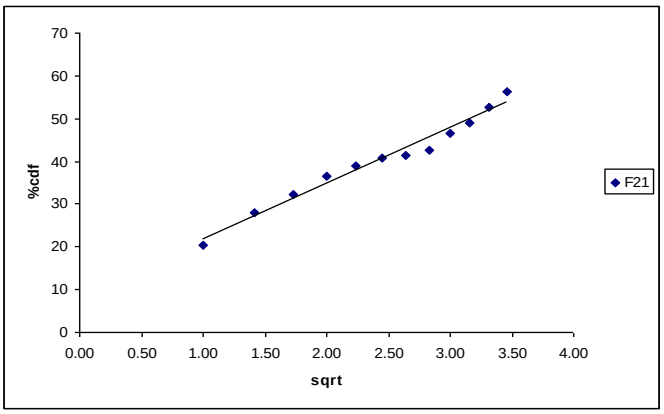

FIG.41: HIGUCHI'S SQUARE ROOT TIME DEPENDENT PLOT FOR F21

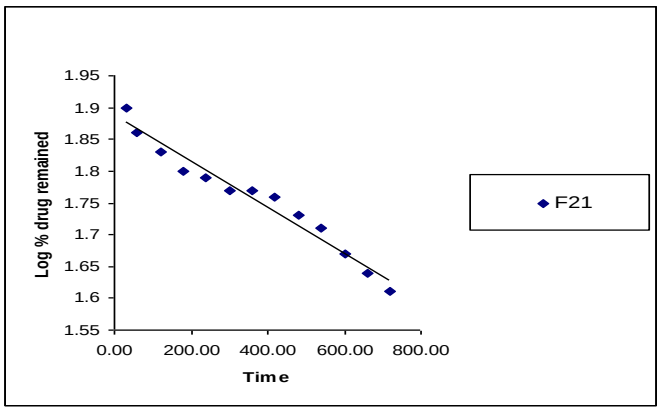

FIG.40: FIRST ORDER PLOT FOR F21

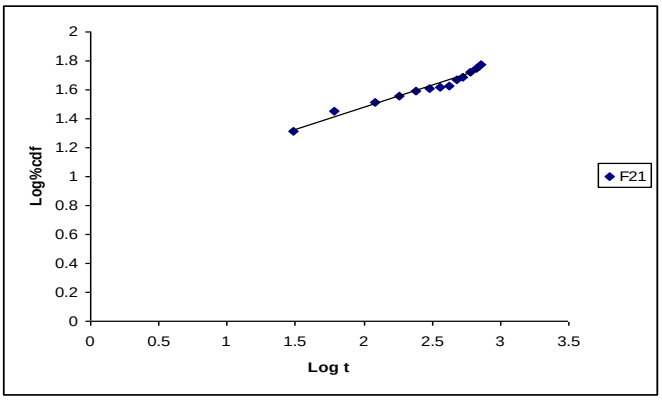

FIG. 42: PEPPAS DOUBLE LOG PLOT FOR F21

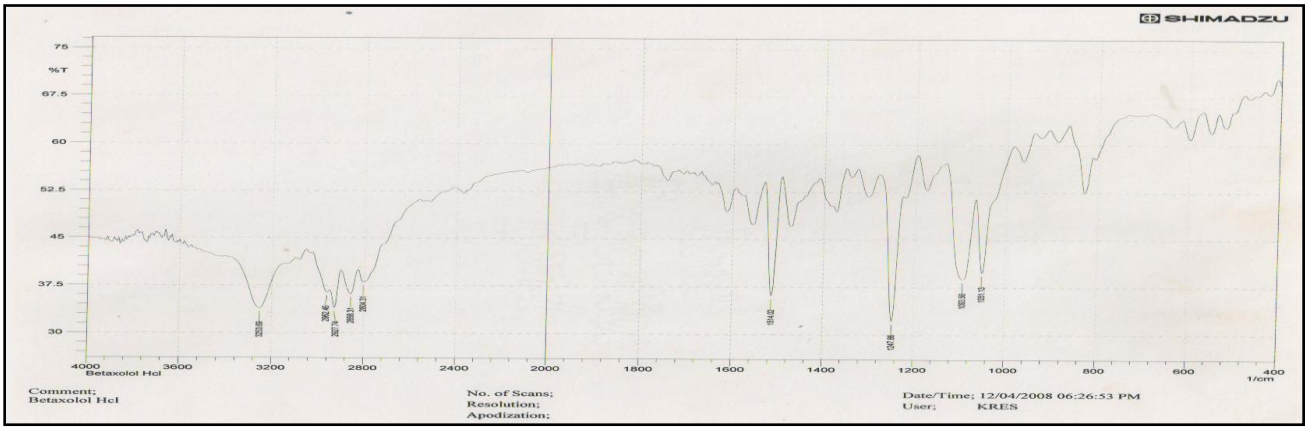

FIG.43: IR STUDY FOR BETAXOLOL HYDROCHLORIDE

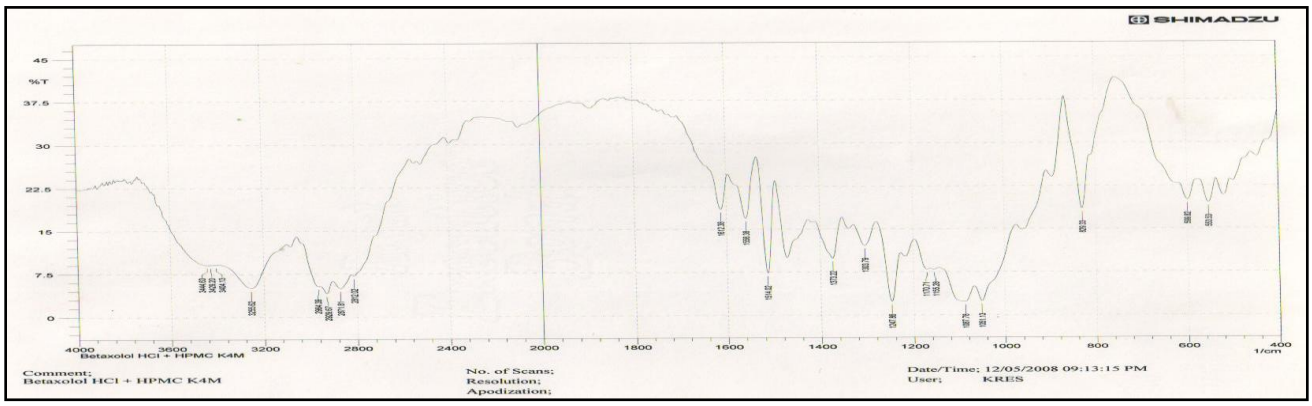

FIG. 44: IR STUDY FOR BETAXOLOL HYDROCHLORIDE + HPMCK4M

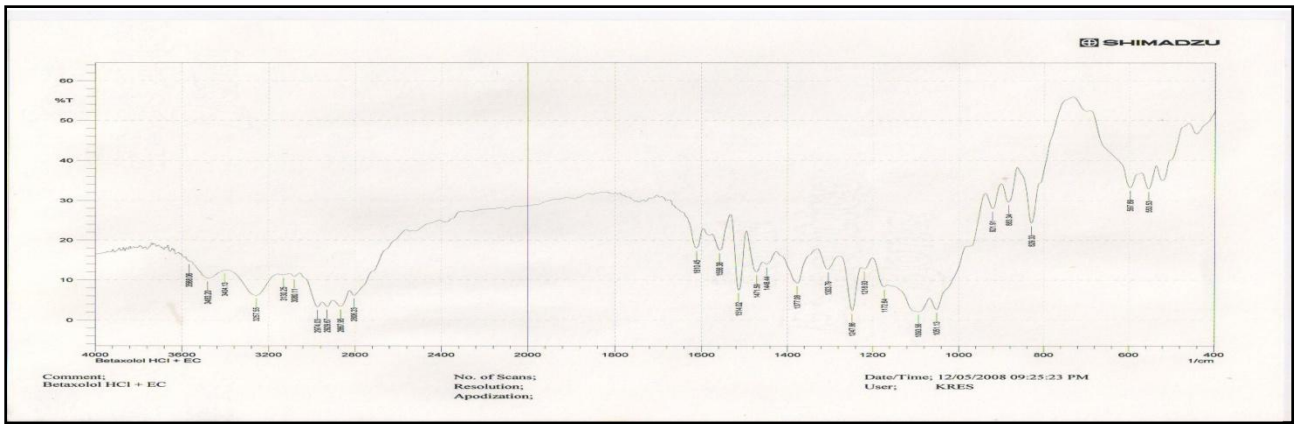

FIG. 45: IR STUDY FOR BETAXOLOL HYDROCHLORIDE + EC

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.

ACKNOWLEDGEMENTS: The authors are thankful to the principal of K.R.E.S's Karnataka College of Pharmacy, Bidar, for providing necessary facilities to carry out this work.

REFERENCES:

1. Hughes PM, Mitra AK. Ophthalmic drug delivery systems. New York; Marcel Dekker. 1993:1-27.
2. Chari SS, Makoid MC, Erikson SP. Robinson JR. Drop size and initial dosing frequency problems of topically applied ophthalmic drugs. J Pharm Sci.1974; 64:333.
3. Robinson JC. Ophthalmic drug delivery systems. Vol-58 New York; Marcel dekker.1993: 29.
4. Gibaldi M, Perrier D. Pharmacokinetics.2nd ed. New York; Marcel dekker.1993: 145.
5. Kaur PI, Kanwar M. Ocular preparations: The formulation approach. Drug Development and Industrial Pharmacy. 2002; 473-93.
6. Zaki I, Fitzerold P, Hardy JG, Wilson CGJ. Dose frequency. Pharm Pharmacol. 1986;38:333
7. Lee VHL, Robinson JR. J Ocul Pharmacol. 1986; 2:67.
8. Baeyens V, Felt O, Zignani M, Buri P, Gruny R,In; Mathiowitzos E Eds. Encyclopedia of controlled drug delivery vol. II. New York, chichester, Weinheim, Brisbane, Singapore, Toronto: John Wiley and sons Inc.1999; 605-626.
9. Lachmann L, Liebermann HA, Knaig JL. Theory and practice of Industrial pharmacy. 3rd ed. Bombay: Varghese publishing house; 1991.
10. Jain NK. Text book of controlled drug delivery, 1st ed. New Delhi; Vallabh Prakashan. 2002: 383-09.
11. Vyas SP, Khar RK. Controlled drug delivery. 1sted.New Delhi: Vallabh Prakashan; 2002.
12. Mundada AS, Shrikhande B. Design and evaluation of soluble ocular drug inserts for controlled release of ciprofloxacin hydrochloride. Indian J Pharm Sci.2004 July-august; 570-7.
13. Allen DJ, Demarco JD, Kwan KL. Free film 1: Apparatus and preliminary evaluation. J Pharm Sci. 1972; 61:106.
14. Bankers GS, Gore AV, Swarbrick J. Water vapour transmission properties of free polymer films. IBID 1996; 18: 458.
15. Knaig JL, Goodmann H. J Pharma Sci. 1962; 5:77.
16. Dandagi PM, Manvi FV, Patil MB, Mastiholimath VS, Rathod R. Development and evaluation of ocular films of cromolyn sodium. Indian J Pharm Sci.2004 May-June; 309-12.
17. Dhachinamoorthi D, Sangeetha K, Dash S, Basak S, Jayaprakash S. Design and evaluation of ofloxacin once a day ocusert. The Pharma Review. 2005 October; 133-35.

How to cite this article:
Kulkarni KB, Ajaykumar P, Shivappa NN and Ladde SS: Preparation and Evaluation of Controlled Release of Betaxolol Hydrochloride Ocular Inserts. Int J Pharm Sci Res 2015; 6(8): 3359-74.doi: 10.13040/IJPSR.0975-8232.6(8).3359-74.