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DESIGN AND EVALUATION OF CONTROLLED RELEASE OF BETAXOLOL HYDROCHLORIDE OCULAR INSERTS

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ABSTRACT

The main aim of this study is to develop ocular drug delivery system for Betaxolol is a cardio selective (β1 adrenergic) receptor blocking agent. Ocular betaxolol may be especially useful in the treatment of glaucoma in patient with pulmonary disease. In the present study, an attempt was made to formulate ocular drug delivery system films for Betaxolol. In matrix, type formulations for Betaxolol containing 10%, 12%, and 14% w/v of Gelatin 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. Gelatin F 09, (14%) w/v exhibited maximum average weight 15.16 mg and thickness of F 09 is 0.29 mm respectively .The drug content of F 09 is 99.48%. The In-vitro studies of selected formulations F1, F2, F3 containing 10% Gelatin shows the release of 96.16, 97.12 and 98.98% respectively, The formulation F4,F5, F6 containing 12% Gelatin shows the release of 95.18, 96.25, 97.73% respectively and the formulations F7, F8, F9 containing 14% Gelatin shows the release of 91.00, 97.79 and 99.23 % respectively. It showed that the gelatin films release of drug. Over 3hrs period was selected as an ideal formulation. In vitro diffusion studies of selected formulations i.e., lower and higher concentrations of Gelatin formulation F1 and F9 were 78.79 & 68.50% at 3hrs 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 shows flexibility more as the concentration increases Stability studies conducted for F 09 formulation. 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.

KEYWORDS: Betaxolol Hydrochloride, ocular inserts, Gelatin.

INTRODUCTION

Ophthalmic drug delivery is one of the most interesting and challenging endeavors 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.[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 instill 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.

Experimental Section

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

METHOD

Preparation of Ocular Inserts[12]

The required quantity of gelatin and glycerin were weighed and dissolved in water and the mixture was heated at 60^0C on a water bath until the entire gelatin was dissolved. The weighed amount of Betaxolol Hydrochloride (passed through sieve # 400) was added and

stirred for 6 hrs at 40^0C on magnetic stirrer to get uniform dispersion. After complete mixing the casting solution (15ml) was poured in clean petridish. The petridish was cooled at 10^0C by placing on ice until the films were gelled. The gelled films were taken out from ice and allowed to dry at room temperature for 24 hours. The dried films thus obtained were cut into required size (8mm diameter) by cork borer and stored till used. The formulas used in preparation are shown in the 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 Presoaked 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 adonor 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^{0}c /60%RH and 40^{0}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 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 F09 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 Gelatin is hydrophilic 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. In vitro studies were carried out using procedure as mentioned in section IV methods the release profile of the formulations F1, F2, F3 containing 10% Gelatin shows the release of 96.16, 97.12 and 98.98% drug in 3hrs respectively, The formulation F4,F5, F6 containing 12% Gelatin shows the release of 95.18, 96.25, 97.73% respectively and the formulations F7, F8, F9 containing 14% Gelatin shows the release of 91.00, 97.79 and 99.23 % respectively. It showed that the gelatin films release of 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 the drug from the Gelatin formulation F1 and F9 was 78.79 & 68.50% at 3hrs 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 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 25^0 C 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	F1	F2	F3	F4	F5	F6	F7	F8	F9
		10% w/v			12% w/v			14% w/v		
1	Drug (mg)	50	50	50	50	50	50	50	50	50
2	Gelatin (gm)	1.5	1.5	1.5	1.8	1.8	1.8	2.1	2.1	2.1
3	Glycerin (ml) (40% w/w of polymer)	0.47	-	-	0.57	-	-	0.67	-	-
4	Glycerin (ml) (50% w/w of polymer)	-	0.59	-	-	0.71	-	-	0.83	-
5	Glycerin (ml) (60% w/w of polymer)	-	-	0.7	-	-	0.85	-	-	1.0
6	Water (ml)	15	15	15	15	15	15	15	15	15
7	Benzyl Alkonium Choloride(ml)	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_1	11.10 ± 1.10	0.19±0.01	1.30 ± 0.20	98.68 ± 0.03
F_2	11.40 ± 0.17	0.26±0.01	1.85 ± 0.53	95.33 ± 0.07
F_3	11.80 ± 0.83	0.22 ± 0.07	1.98 ± 0.11	99.00 ± 0.05
F_4	12.10 ± 0.18	0.27 ± 0.05	2.14 ± 0.58	98.30 ± 0.05
F_5	12.76 ± 0.05	0.28±0.05	2.18 ± 0.63	99.41 ± 0.02
F_6	13.33 ± 1.09	0.30 ± 0.03	2.29 ± 0.58	97.74 ± 0.04
F_7	14.26 ± 1.34	0.31 ± 0.03	2.40 ± 0.44	93.49 ± 0.05
F_8	14.73 ± 1.03	0.28 ± 0.02	2.83 ± 0.13	98.55 ± 0.03
F_9	15.16 ± 1.48	0.29 ± 0.01	2.86 ± 0.48	99.48 ± 0.02

*Mean ± SD, n =3.

Table -3: *In vitro* Dissolution of Betaxolol Hydrochloride from formulation -1(F 1)(Drug:Gelatin 10%).

Time (min)	√T	Log T	Abs*	Conc. (µg/ml)	CDR (mg)	CDR (%)	Log % CDR	Cumulative % drug remained	Cumulative Log % Drug remained
30	5.477	1.477	0.116	1.570	0.235	61.353	1.7878	38.64	1.5871
60	7.745	1.778	0.131	1.776	0.266	69.409	1.8414	30.59	1.4855
120	10.954	2.079	0.182	2.461	0.369	96.162	1.98300	3.83	0.5840

*Each reading is an average of three determinations

Table 4: *In vitro* Dissolution of Betaxolol Hydrochloride from formulation -2 (F 2) (Drug: Gelatin 12%).

Time (min)	√T	Log T	Abs*	Conc. (µg/ml)	CDR (mg)	CDR (%)	Log % CDR	Cumulative % drug remained	Cumulative Log % Drug remained
30	5.4772	1.4771	0.121	1.6486	0.2473	64.39	1.8088	35.603	1.551
60	7.7459	1.7781	0.133	1.8151	0.2723	70.90	1.8506	29.097	1.463
120	10.954	2.0791	0.184	2.4865	0.3730	97.12	1.9873	2.872	0.458

*Each reading is an average of three determinations.

Table 5: *In vitro* Dissolution of Betaxolol Hydrochloride from F formulation-3 (F3) (Drug: Gelatin 14%).

Time (min)	√T	Log T	Abs*	Conc. (µg/ml)	CDR (mg)	CDR (%)	Log % CDR	Cumulative % drug remained	Cumulative Log % Drug remained
30	5.4772	1.4771	0.129	1.745	0.261	68.192	1.8337	31.8072	1.5025
60	7.7459	1.7781	0.144	1.977	0.296	77.260	1.887	22.7395	1.3567
120	10.954	2.0791	0.188	2.534	0.380	98.984	1.995	1.0156	0.0067

*Each reading is an average of three determinations.

Table 6: *In vitro* Dissolution of Betaxolol Hydrochloride from formulation -4 (F 4) (Drug: Gelatin 10%).

Time (min)	√T	Log T	Abs*	Conc. (µg/ml)	CDR (mg)	CDR (%)	Log % CDR	Cumulative % drug remained	Cumulative Log % Drug remained
30	5.4772	1.4771	0.108	1.4571	0.2186	56.9188	1.7552	43.081	1.6342
60	7.7459	1.7781	0.126	1.7049	0.2557	66.59	1.8234	33.40	1.5237
120	10.954	2.0791	0.180	2.4368	0.3655	95.18	1.9785	4.812	0.6823

*Each reading is an average of three determinations.

Table 7: *In vitro* Dissolution of Betaxolol Hydrochloride from formulation -5 (F 5) (Drug: Gelatin 12%).

Time (min)	√T	Log T	Abs*	Conc. (µg/ml)	CDR (mg)	CDR (%)	Log % CDR	Cumulative % drug remained	Cumulative Log % Drug remained
30	5.4772	1.4771	0.113	1.532	0.2298	59.855	1.777	40.1449	1.60363
60	7.7459	1.7781	0.134	1.81	0.2720	70.825	1.850	29.1745	1.46500
120	10.954	2.0791	0.182	2.46	0.3696	96.259	1.983	3.740	0.57299

*Each reading is an average of three determinations.

Table 8: *In vitro* Dissolution of Betaxolol Hydrochloride from formulation -6 (F 6) (Drug: Gelatin 14%).

Time (min)	√T	Log T	Abs*	Conc. (µg/ml)	CDR (mg)	CDR (%)	Log % CDR	Cumulative % drug remained	Cumulative Log % Drug remained
30	5.4772	1.4771	0.123	1.6589	0.2488	64.7992	1.8115	35.200	1.54655
60	7.7459	1.7781	0.144	1.9505	0.2926	76.1894	1.8818	23.810	1.37676
120	10.954	2.0791	0.185	2.5020	0.3753	97.733	1.9900	2.266	0.3553

*Each reading is an average of three determinations.

Table 9: *In vitro* Dissolution of Betaxolol Hydrochloride from formulation -7 (F 7) (Drug: Gelatin 10%).

Time (min)	√T	Log T	Abs*	Conc. (µg/ml)	CDR (mg)	CDR (%)	Log % CDR	Cumulative % drug remained	Cumulative Log % Drug remained
30	5.4772	1.4771	0.107	1.4455	0.2168	56.4648	1.75177	43.535	1.6388
60	7.7459	1.7781	0.123	1.6612	0.2492	64.889	1.8121	35.110	1.5454
120	10.954	2.0791	0.175	2.349	0.3755	91.009	1.9627	8.2215	0.9149

*Each reading is an average of three determinations.

Table 10: *In vitro* Dissolution of Betaxolol Hydrochloride from formulation -8 (F 8) (Drug: Gelatin 12%).

Time (min)	√T	Log T	Abs*	Conc. (µg/ml)	CDR (mg)	CDR (%)	Log % CDR	Cumulative % drug remained	Cumulative Log % Drug remained
30	5.4772	1.4771	0.110	1.492	0.223	58.300	1.7656	41.699	1.6201
60	7.7459	1.7781	0.131	1.771	0.265	69.186	1.8400	30.813	1.4887
120	10.954	2.0791	0.178	2.406	0.361	94.009	1.9731	5.990	0.77747
180	13.416	2.255	0.185	2.503	0.375	97.796	1.9903	2.204	0.3432

*Each reading is an average of three determinations.

Table 11: *In vitro* Dissolution of Betaxolol Hydrochloride from formulation -9 (F 9) (Drug: Gelatin 14%).

Time (min)	√T	Log T	Abs*	Conc. (µg/ml)	CDR (mg)	CDR (%)	Log % CDR	Cumulative % drug remained	Cumulative Log % Drug remained
30	5.4772	1.4771	0.120	1.6190	0.2428	63.24	1.80100	36.758	1.5653
60	7.7459	1.7781	0.139	1.8773	0.2816	73.33	1.8652	26.667	1.4259
120	10.954	2.0791	0.182	2.4620	0.3693	96.17	1.9830	3.828	0.5829
180	13.416	2.255	0.188	2.5403	0.3810	99.23	1.9966	0.7684	-0.1144

*Each reading is an average of three determinations.

Table 12: 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_1	-0.702	2.0379	0.9428	6.486	23.363	0.959	0.324	1.294	0.936
F_2	-0.7683	2.0543	0.9333	6.121	28.141	0.945	0.296	1.355	0.913
F_3	-1.0476	2.1776	0.9412	5.698	35.558	0.9821	0.268	1.427	0.965
F_4	-0.0111	2.055	0.9493	7.114	15.565	0.968	0.370	1.192	0.952
F5	-0.0119	2.0497	0.9569	7.927	9.422	1	0.342	1.260	0.972
F_6	-0.0138	2.0573	0.96	6.059	30.739	0.994	0.296	1.367	0.985
F_7	-0.0084	1.9541	0.9547	5.509	25.636	0.953	0.3206	1.2684	0.9554
F_8	-0.009	1.9342	0.9839	5.351	29.525	0.954	0.3103	1.3035	0.9709
F_9	-0.0117	2.0068	0.9873	4.885	37.077	0.950	0.2711	1.3971	0.9685

Table 13: Stability study for F- 9 formulations.

	Stored at 25^0c/ 60 % rh		St0red 40^0 c / 75 % rh	
Time in weeks	Physical appearance	% drug content	Physical appearance	% drug content
0	+++	95.14	+++	97.12
2	+++	96.54	+++	94.26
4	+++	99.78	+++	96.48
6	+++	98.20	++	95.28
8	++	96.47	++	94.91

Table 14: *In vitro* Diffusion of Betaxolol Hydrochloride from formulation -1 (F 1) (Drug: Gelatin 10%).

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	0.09	1.21	0.20	52.27	1.72	47.73	1.68
60	7.75	1.78	0.11	1.44	0.24	62.64	1.80	37.36	1.57
120	10.95	2.08	0.12	1.61	0.27	69.63	1.84	30.37	1.48
180	13.42	2.26	0.13	1.82	0.30	78.79	1.90	21.21	1.33

Table 15: *In vitro* Diffusion of Betaxolol Hydrochloride from formulation -9(F 9) (Drug: Gelatin 14%).

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	0.08	1.03	0.17	44.82	1.65	55.18	1.74
60	7.75	1.78	0.08	1.14	0.19	49.28	1.69	50.72	1.71
120	10.95	2.08	0.09	1.25	0.21	53.98	1.73	46.02	1.66
180	13.42	2.26	0.12	1.58	0.26	68.50	1.84	31.50	1.50

Table 16: Curve Fitting Data For Diffusion.

Batches	First order Equation			Higuchi' s Equation			Peppas Equation		
	Slope	Rate Constant (k) Mg. hr^{-1}	Regression coefficient	Slope	Rate Constant (k) Mg. hr^{-1}	Regression coefficient	Slope	Rate Constant (k) Mg. hr^{-1}	Regression coefficient
F01	0.0015	1.8029	0.9214	3.1754	35.984	0.9821	0.2186	1.3982	0.987
F09	-0.0015	1.8029	0.9214	2.7838	27.979	0.8969	0.2211	1.3074	0.859

Table 17: Selected comparative study for dissolution and diffusion.

Time (min)	F1		F9	
	Dissolution	Diffusion	Dissolution	Diffusion
30.00	61.35	52.27	63.24	44.82
60.00	69.41	62.64	73.33	49.28
120.00	96.16	69.63	96.17	53.98
180.00		78.79	99.23	68.50

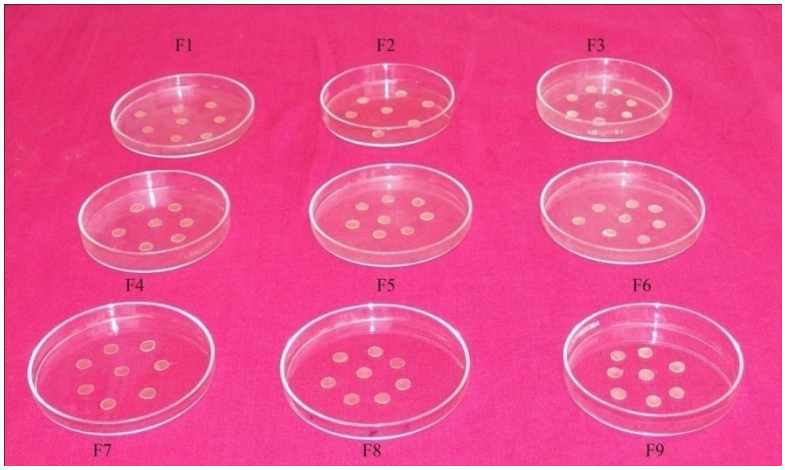

Figure 1: Ophthalmic Inserts of Betaxolol hydrochloride using Gelatin as polymer.

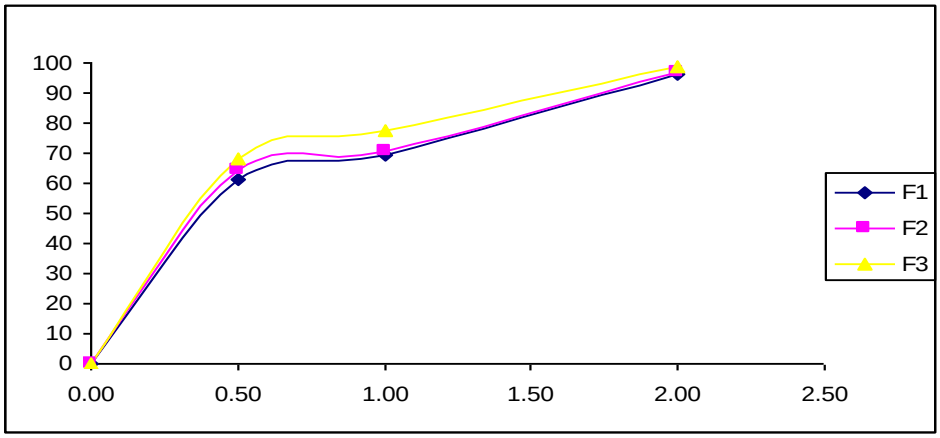

Figure 2: *In vitro* Drug release profile F1, F2, F3.

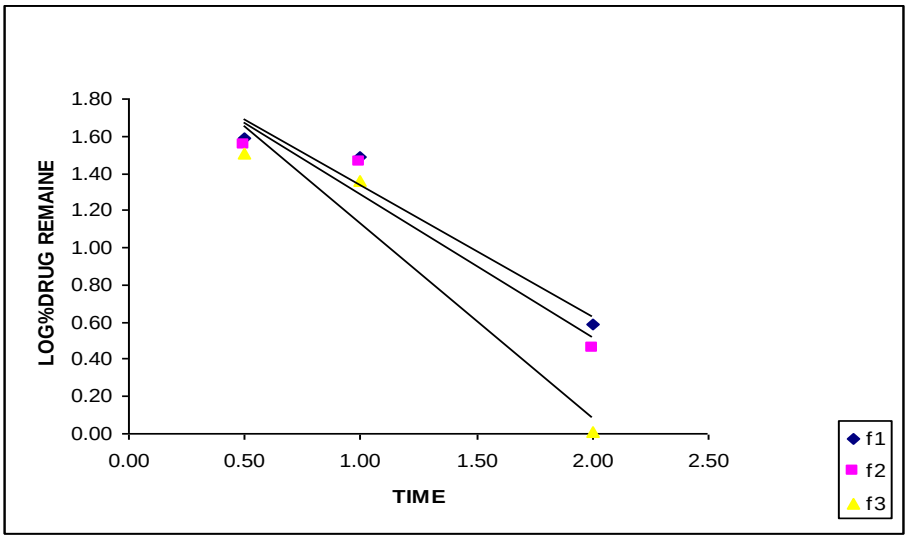

Figure 3: First order drug release plots F1, F2, F3.

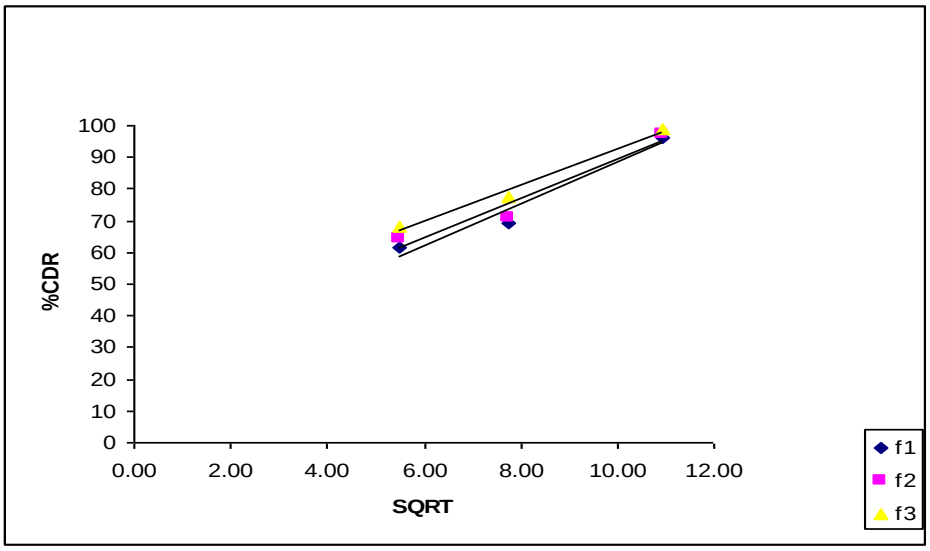

Figure 4: Higuchi's square root time dependent plots for F1, F2, F3.

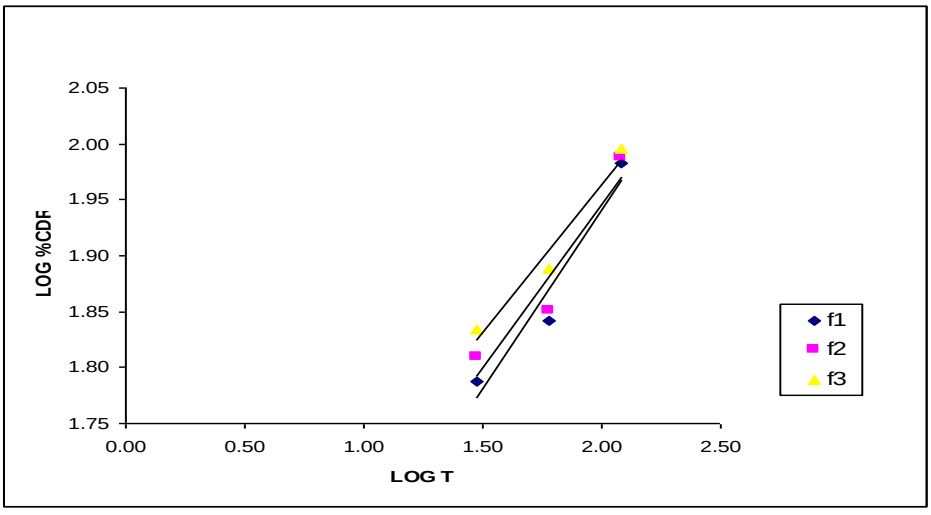

Figure 5: Peppas double log plots for F1, F2, F3.

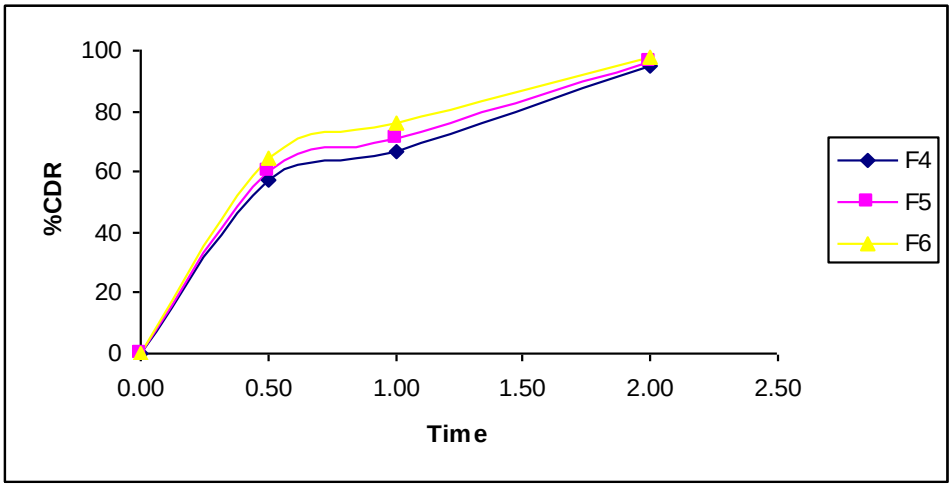

Figure 6: *Invitro* release profile for F4, F5, F6.

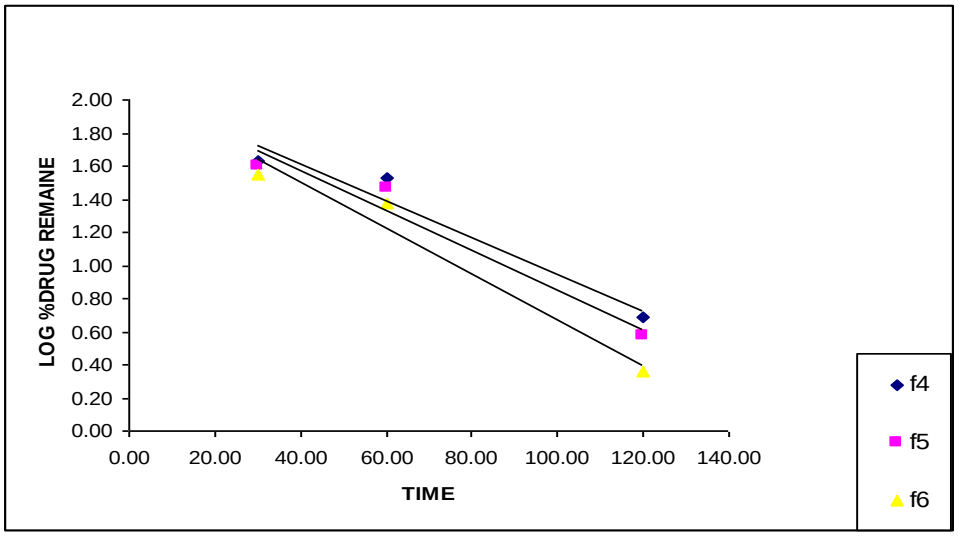

Figure 7: First order plots for F4, F5, F6.

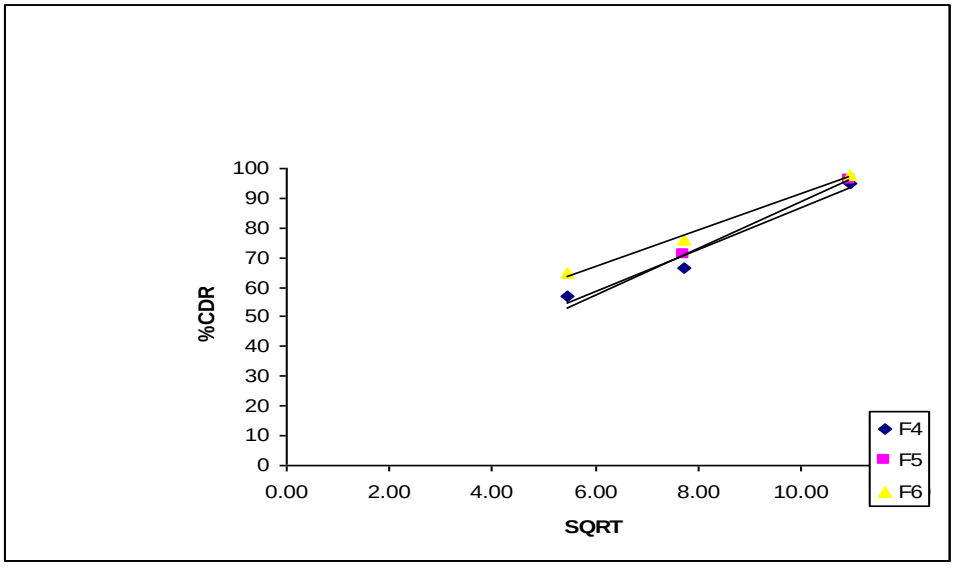

Figure 8: Higuchi's square root time dependent plots for F4, F5, F6.

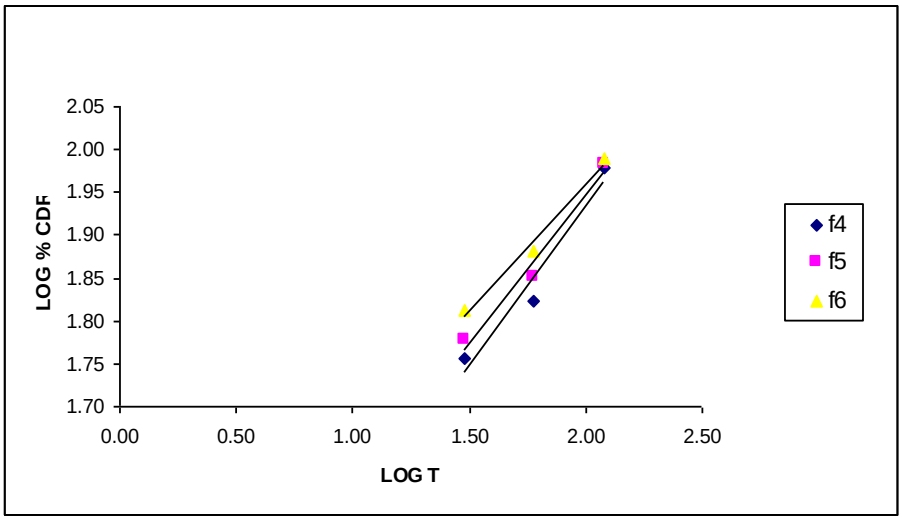

Figure 9: peppas double log plots for F4, F5, F6.

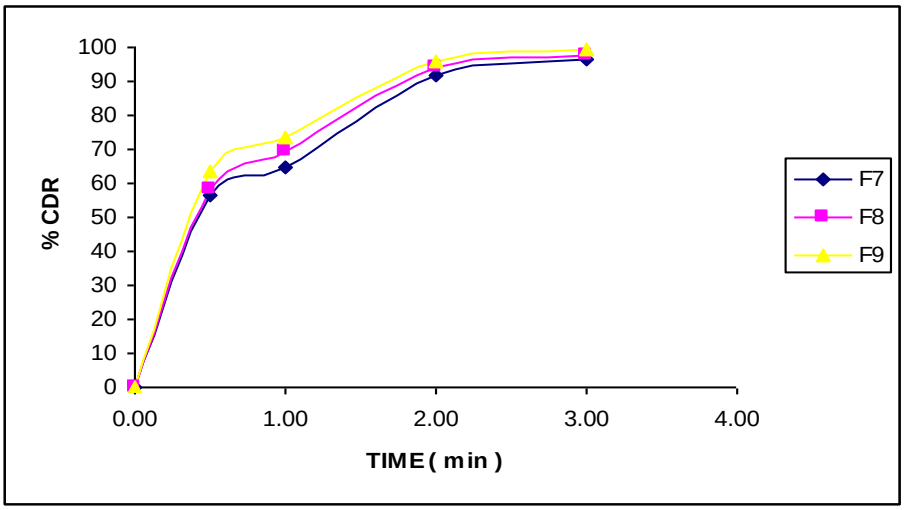

Figure 10: *Invitro* drug release profile for Betaxolol Hydrochloride.

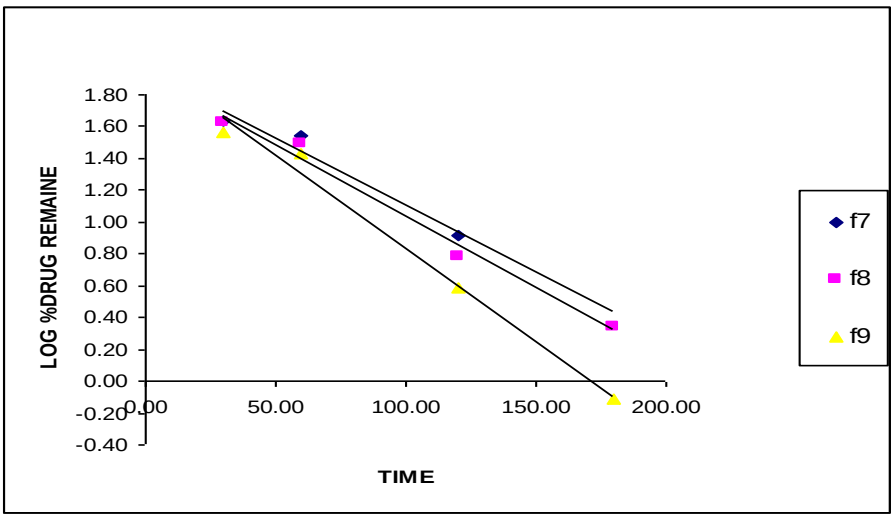

Figure 11: First order plots for F7, F8, F9.

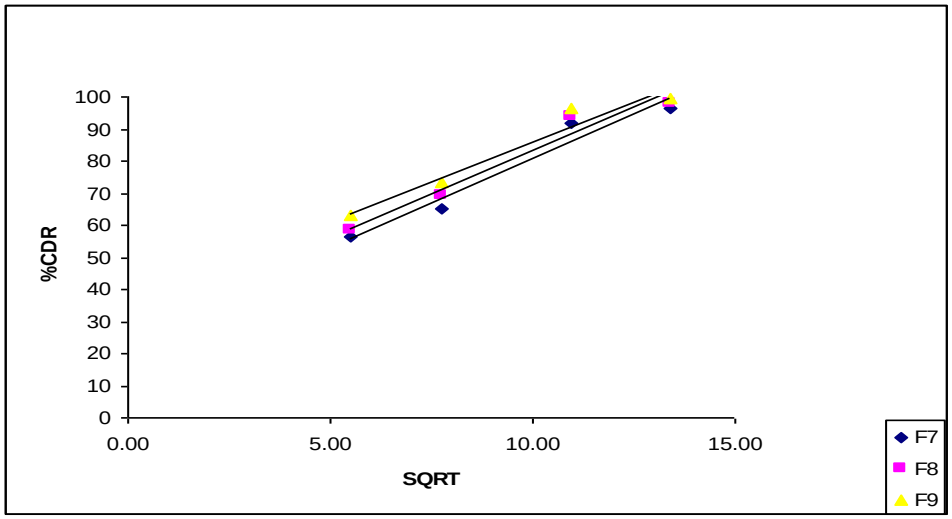

Figure 12: Higuchi's squre root time dependent plots for F7, F8, F9.

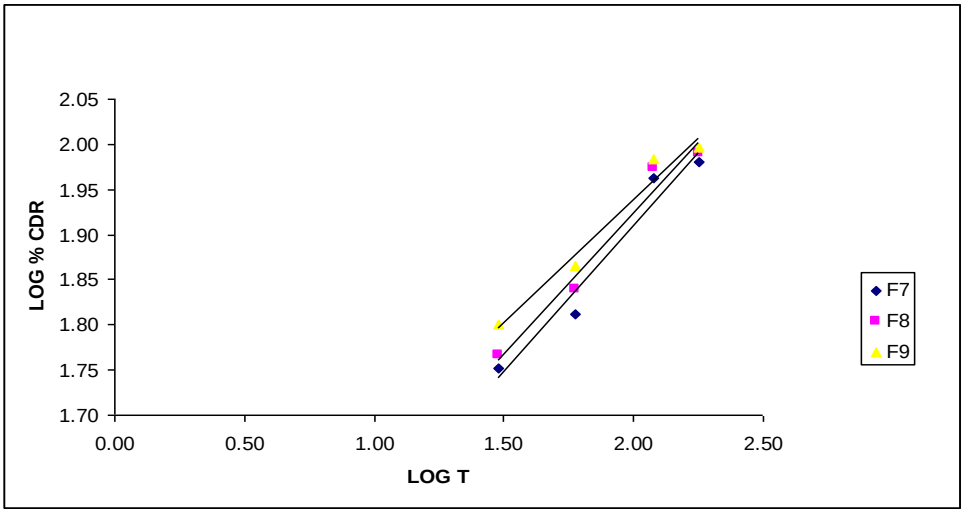

Figure 13: Peppas double log plots for F7, F8, F9.

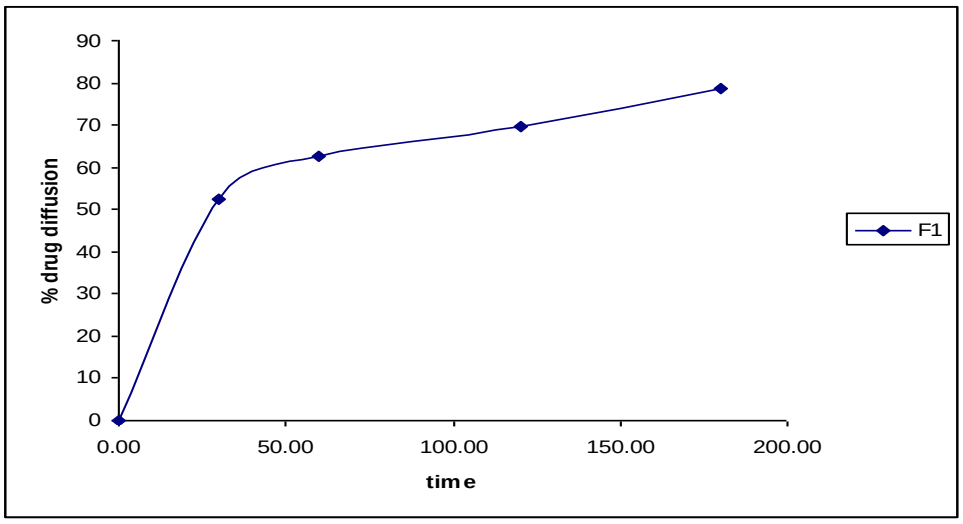

Figure 14: *In vitro* drug diffusion plot for F 1.

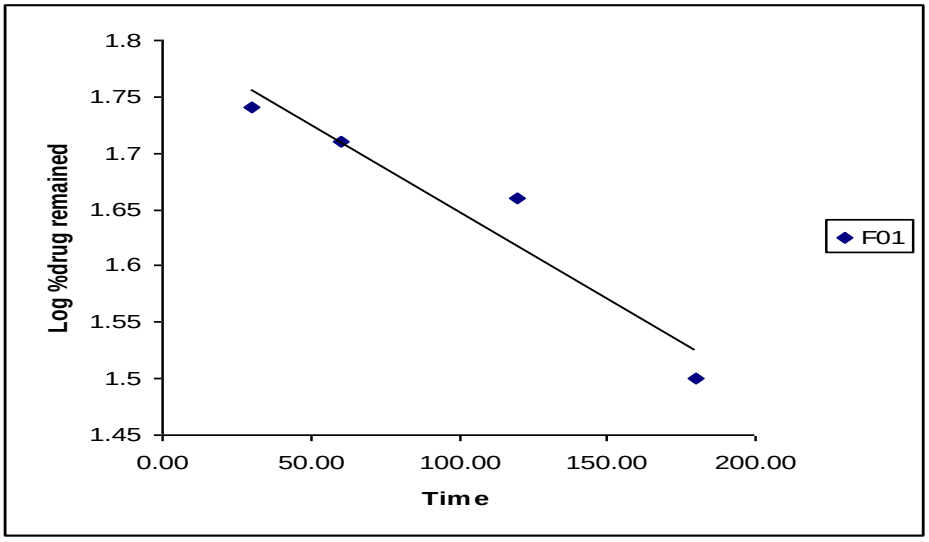

Figure 15: First order plots for F 1.

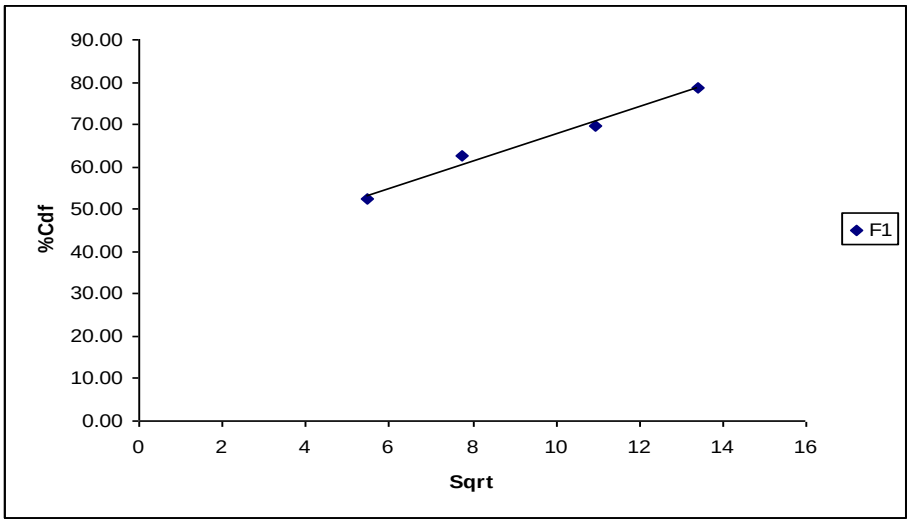

Figure 16: Higuchi's square root time dependent plot for F 1.

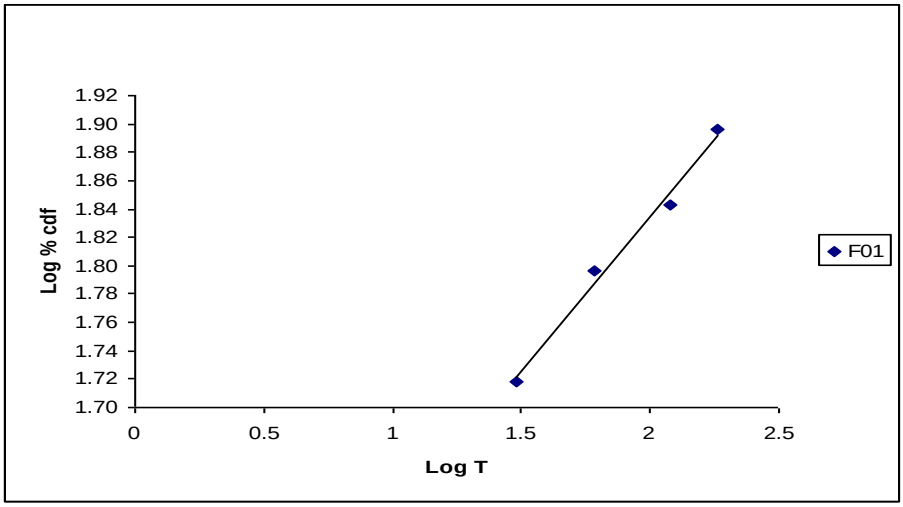

Figure 17: Peppas double log plot for F 1.

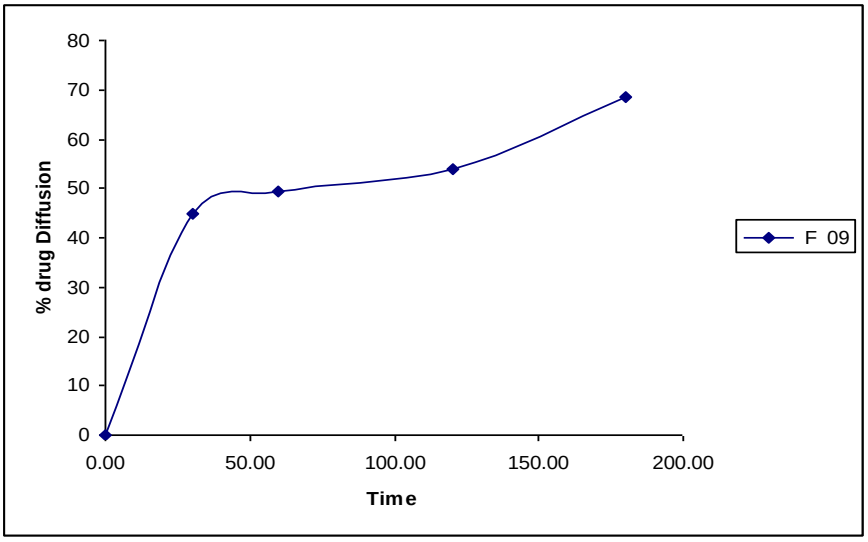

Figure 18: *In vitro* drug diffusion plot for F 9.

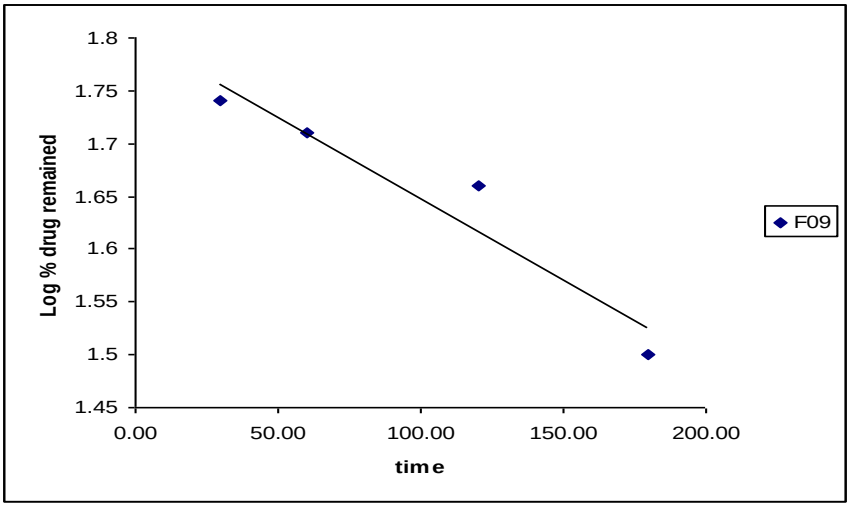

Figure 19: First order plot for F 9.

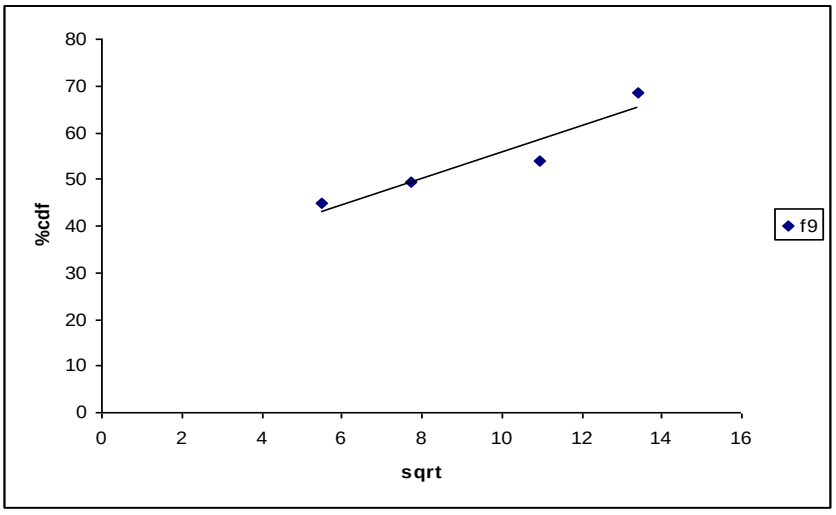

Figure 20: Higuchi's square root time dependent plot for F 9.

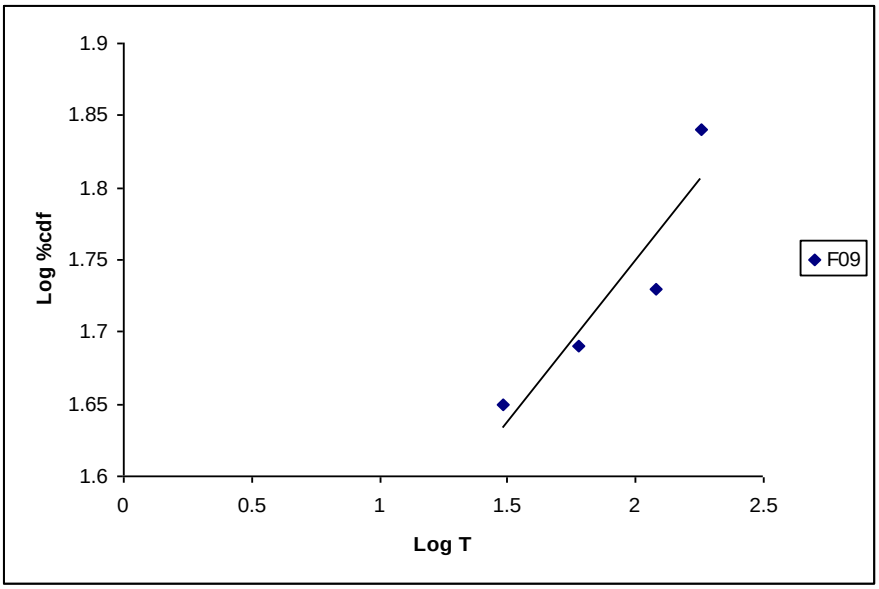

Figure 21: Peppas double log plot for F9.

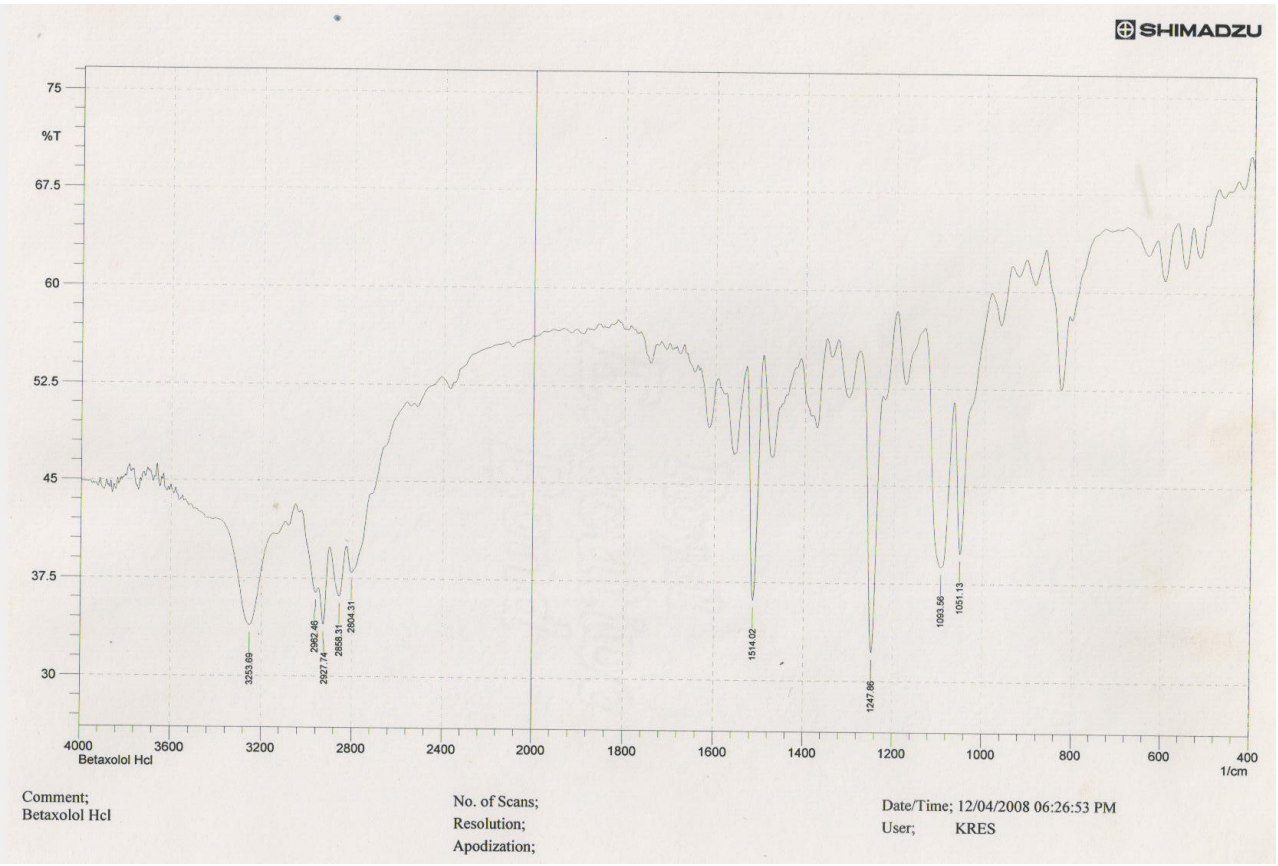

Figure 22: IR Study for Betaxolol Hydrochloride.

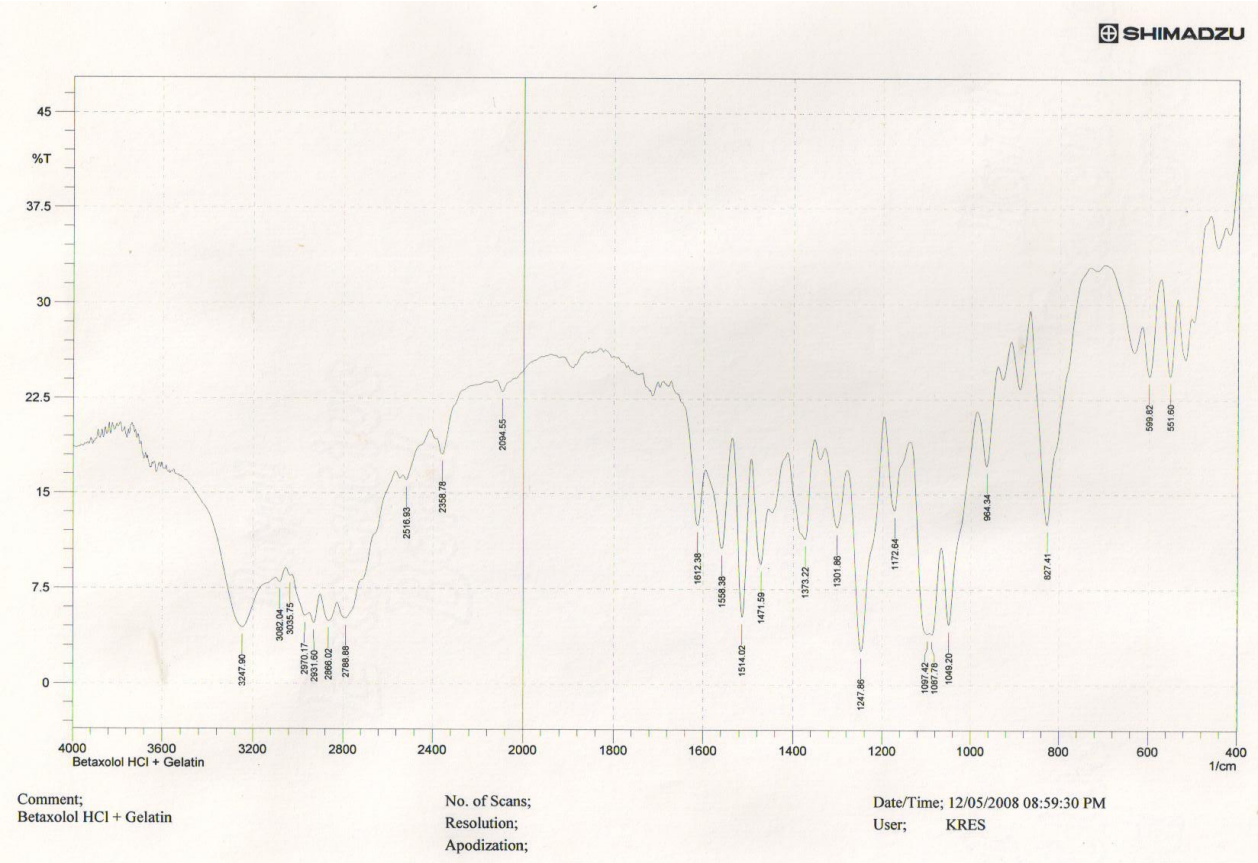

Figure 23: IR Study for betaxolol Hydrochloride + Gelatin.

CONCLUSION

The methodology adopted in present study was simple and re producible. The polymers used were inexpensive and easily available. The Betaxolol Hydrochloride ocular inserts were prepared by using Gelatin. Among the different formulations the best formulation was Drug: Gelatin 14% since it showed retarded release of drug up to 3 hrs. They were also 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: Gelatin in the 10%, 12 % and 14%.

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