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FORMULATION OPTIMIZATION AND *IN-VITRO* EVALUATION OF CEFPODOXIME PROXETILCONTROLLED RELEASE TABLETS

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ABSTRACT

The aim of the present study was to develop Controlled release formulation of Cefpodoxime proxetil and to optimize the suitable polymer to maintain constant therapeutic levels of the drug for over 12 hrs. Methocel E5, PEG6000, and HEC, Methocel K100LV were employed as polymers. Cefpodoxime proxetil dose was fixed as 200 mg. Polymers were used in the concentration of 100, 150 and 200 mg. All the formulations were passed various physicochemical evaluation parameters and they were found to be within limits, whereas from the dissolution studies it was evident that the formulation (F11) showed better and desired drug release pattern i.e., 90.73 %. It contains Methocel K100LV as controlled release material. It followed zero order release kinetics mechanism.

Keywords: Cefpodoxime proxetil, Methocel E5, PEG6000, HEC, Methocel K100LV and Controlled release tablets.

INTRODUCTION

In long-term therapy for the treatment of chronic disease conditions, conventional formulations are required to be administered in multiple doses and therefore have several disadvantages [1-2].

Controlled release (CR) tablet formulations are preferred for such therapy because they offer better patient compliance, maintain uniform drug levels, reduce dose and side effects and increasesthe safety margin for high-potency drugs [3].

Oral controlled release drug delivery system is an oral delivery system thatprovides continuous release of drugs with predictable and reproducible kinetics for apredetermined period, either throughout the course of GI transit or by targeting thedelivery of a drug near/in a specific region within the GI tract for either a local or systemic action [5].

Oral route still remains the most popular for drug administration by virtue of its convenience to the patient. A sizable portion of orally administered dosage forms, so called conventional, are designed to achieve maximal drug bioavailability by maximizing the rate and extent of absorption. Whilesuch dosage forms have been useful, frequent daily administration is necessary, particularly when the drug has a short biological half-life. This may result in wide fluctuation in peak and trough steady-state drug levels, which is undesirable for drugs with marginal therapeutic indices. Moreover, patient compliance is likely to be poor when patients need to take their medication three to four times daily on chronic basis. Fortunately, these short comings have been circumvented with the introduction of controlled release dosage forms. These dosage forms are capable of controlling the rate of drug delivery, leading to more sustained drug levels and hence therapeutic action [6].

Hence the main aim of the present work is to develop the controlled release tablets of cefpodoxime proxetil by optimizing the suitable polymer to treat the chronic bacterial infections [7-8].

MATERIALS AND METHODS

Cefpodoxime proxetil, Methocel E5, PEG 6000, HEC, Methocel K100LV and other excipients were procured from Aurobindopharma ltd.

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Preformulation

Drug and excipients compatability studies were carried out by FTIR. Standardization of the drug was carried out using UV spectrophotometry (UV/Vis Spectrophotometer- Labindia). Preformulation parameters were performed for the powdered blend.

Formulation

Totally 12 formulations each containing 200 mg of drug were prepared using four different polymers, MCC PH 102 as diluent, magnesium stearate and talc as lubricant [Table-1] The average weight of the tablet was 500 mg. Controlled release tablets were prepared by direct compression method using Lab press multi-station machine.

Evaluation

Tablets were evaluated for various parameters such as hardness, friability, weight variation, content uniformity, and *in vitro* drug release. Drug release was carried out using USP Type II apparatus in dissolution medium 0.1 N HCl for 2 hours and then it was replaced with pH 6.8 phosphate buffers. The release was tested at rotational speed of 50 rpm. Samples were withdrawn at appropriate intervals (0.5, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 hours) and after proper dilution the samples of 0.1N HCl were analyzed at 262nm and sample of phosphate buffer were analyzed at 234nm using UV/Vis spectrophotometer.

Stability studies

Accelerated stability studies were conducted at 40±2ºC, 75±5% RH for a period of 3 months. Tablets were evaluated for hardness, weight variation, drug release, and content uniformity.

RESULTS AND DISCUSSION

The results of preformulation studies indicated that the drug was standardized using UV analysis which showed good linearity [Figure-1], [Figure-2].

Drug – excipients compatability studies

The FT-IR spectra, showed that the drug was compatible with all the polymers used [Figure-3], [Figure-4].

The preformulation parameters of powder blends of all twelve formulations were within the limits and showed good flow property [Table-2].

All the quality control parameters such as weight variation, friability, hardness, thickness and drug content were found to be within the limits [Table-3].

The In vitro drug release studies of the formulations F1, F2, F3, F4, F5, F6, F7, F8, F9 showed that the polymer Methocel E5, PEG6000, HEC, were not capable of controlling the drug release for longer period .From the dissolution data of formulations F10, F11, F12 it was found that tablets made of 100 mg of polymer Methocel K100LV failed to control the release of drug for longer period but as the concentration of the polymer increased i.e., 150 mg of polymer in F11 showed required release pattern i.e., retarded the drug release up to 12 hours and showed maximum of 90.73% in 12 hours.

The mechanism of the drug release rate kinetics of the dosage form was analysed by fitting the obtained data into zero-order, first order, Higuchi, and Korsmeyer-Peppa's release model. The highest R^2 value was found in the Zero order release model [Figure-9], [Figure-10], [Figure-11], [Figure-12].

Stability studies

From the stability studies it was observed that there were no significant changes in physicochemical properties [Table-6] and drug release pattern of the formulation during the time course of storage in the accelerated conditions [Table-7], Hence the optimized formulation was found to be stable.

Table 1. Formulation composition for tablets (F1 10 F12 Formulations)

Formulation code	Cefpodoxime proxetil(mg)	Methocel E5 (mg)	PEG6000 (mg)	HEC (mg)	Methocel K100LV (mg)	PVP K30 (mg)	Mag Stearate (mg)	Talc (mg)	MCC PH 102 (mg)
F1	200	100	-	-	-	25	5	5	Q.S
F2	200	150	-	-	-	25	5	5	Q.S
F3	200	200	-	-	-	25	5	5	Q.S
F4	200	-	100	-	-	25	5	5	Q.S
F5	200	-	150	-	-	25	5	5	Q.S
F6	200	-	200	-	-	25	5	5	Q.S
F7	200	-	-	100	-	25	5	5	Q.S
F8	200	-	-	150	-	25	5	5	Q.S
F9	200	-	-	200	-	25	5	5	Q.S
F10	200	-	-	-	100	25	5	5	Q.S
F11	200	-	-	-	150	25	5	5	Q.S
F12	200	-	-	-	200	25	5	5	Q.S

Table 2. Pre-formulation parameters of powder blend

Formulation Code	Angle of Repose	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Carr's index (%)	Hausner's Ratio
F1	26.01	0.49±0.01	0.57±0.04	14.03±0.02	1.16±0.34
F2	24.8	0.56±0.01	0.67±0.02	16.41±0.02	1.19±0.63
F3	22.74	0.52±0.03	0.64±0.01	17.75±0.2	1.23±0.25
F4	25.33	0.54±0.01	0.64±0.01	15.62±0.1	1.18±0.06
F5	26.24	0.53±0.05	0.65±0.06	18.46±0.04	1.22±0.57
F6	26.12	0.56±0.01	0.66±0.02	15.15±0.25	1.17±0.24
F7	27.08	0.58±0.04	0.69±0.03	15.94±0.04	1.18±0.25
F8	25.12	0.48±0.03	0.57±0.03	15.78±0.23	1.18±0.35
F9	25.45	0.54±0.04	0.65±0.01	16.92±0.21	1.2±0.32
F10	25.52	0.56±0.04	0.64±0.02	16.62±0.25	1.0±0.24
F11	26.25	0.52±0.01	0.63±0.01	17.21±0.21	1.12±0.12
F12	26.45	0.55±0.01	0.66±0.01	15.54±0.34	1.21±0.25

Table 3. Quality control parameters for tablets

Formulation code	Weight variation(mg)	Hardness(kg/cm^2)	Friability(% loss)	Thickness (mm)	Drug content (%)
F1	500.5±1.06	4.5±0.32	0.50±0.01	2.8±0.6	99.76±0.32
F2	502.4±1.02	4.5±0.38	0.57±0.04	2.9±0.04	98.45±0.25
F3	500.6±1.05	4.4±0.21	0.57±0.02	2.9±0.03	99.34±0.36
F4	501.0±1.1	4.5±0.32	0.55±0.04	2.9±0.01	97.87±0.21
F5	500.0±1.1	4.4±0.24	0.56±0.01	2.7±0.01	99.14±0.45
F6	500.0±1.2	4.5±0.34	0.45±0.03	2.7±0.02	98.56±0.67
F7	502.3±1.1	4.5±0.37	0.51±0.01	2.4±0.04	98.42±0.38
F8	501.1±1.07	4.3±0.26	0.49±0.07	2.7±0.06	99.65±0.64
F9	498.3±1.05	4.5±0.31	0.55±0.01	2.6±0.03	98.12±0.36
F10	500.2±1.05	4.5±0.14	0.51±0.03	2.5±0.01	99.24±0.74
F11	500.0±1.06	4.5±0.35	0.55±0.01	2.7±0.06	98.46±0.39
F12	500.2±1.02	4.3±0.23	0.51±0.01	2.6±0.05	97.90±0.45

Table 4. Dissolution data of Cefpodoxime proxetil tablets (F1to F6 formulations)

Time(hrs)	Cumulative Percent Drug Dissolved					
	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
0.5	27.51±0.23	20.17±0.05	16.45±0.25	17.25±0.25	20.42±0.24	14.32±0.23
1	48.74±0.52	39.45±0.34	26.73±0.04	38.26±0.34	27.73±0.45	19.12±0.35
2	74.53±0.24	55.33±0.25	34.64±0.37	56.16±0.45	34.63±0.36	23.35±0.04
3	89.48±0.36	75.32±0.24	42.45±0.69	72.01±0.14	40.04±0.87	30.45±0.15
4	96.03±0.15	87.35±0.39	55.43±0.24	85.26±0.35	47.25±0.24	39.07±0.34
5	-	97.37±0.25	67.48±0.78	97.10±0.06	53.33±0.65	46.56±0.37
6	-	-	85.43±0.39	-	60.41±0.26	58.24±0.49
7	-	-	91.55±0.27	-	69.84±0.32	64.42±0.75
8	-	-	98.21±0.18	-	75.80±0.15	76.43±0.49
9				-	84.23±0.27	82.52±0.27
10				-	97.52±0.75	90.23±0.35
11				-	-	99.41±0.46
12						

Table 5. Dissolution data of Cefpodoxime proxetil tablets (F7to F12 formulations)

Time(hrs)	Cumulative Percent Drug Dissolved					
	F7	F8	F9	F10	F11	F12
0	0	0	0	0	0	0
0.5	45.83±0.03	30.23±0.07	26.37±0.04	20.73±0.23	11.82±0.87	7.83±0.75
1	74.65±0.05	52.33±0.04	38.89±0.07	29.61±0.28	17.08±0.92	11.09±0.26
2	98.56±0.17	70.48±0.25	51.92±0.15	36.82±0.34	24.53±1.06	17.34±0.27
3	-	88.88±0.17	65.72±0.27	44.75±0.16	30.61±2.37	24.32±0.24
4	-	99.20±0.63	78.34±0.36	57.64±0.04	35.82±0.56	29.83±0.57
5	-	-	88.96±0.34	63.37±0.25	41.09±0.88	34.56±0.39
6	-	-	99.77±0.24	72.82±0.14	49.18±0.72	38.35±0.14
7				80.91±0.45	54.73±1.35	43.58±0.58
8				88.08±0.36	60.48±0.67	49.21±0.36
9				97.74±0.19	67.50±0.38	55.57±0.25
10				-	75.82±0.12	60.41±0.36
11				-	82.18±0.58	66.47±0.25
12	-			-	90.73±0.47	72.13±0.45

Table 6. Characteristics of Cefpodoxime proxetil Controlled release tablets F11

Initial			After three months		
Hardness (kg/cm^2)	Weight variation(mg)	Content Uniformity (%)	Hardness (kg/cm^2)	Weight variation(mg)	Content uniformity
4.5±0.35	500±1.06	98.46±0.39	4.4±0.65	500±0.95	98.32±0.36

Table 7. Stability studies of Cefpodoxime proxetil Controlled release tablets F11

Time(hr)	Percentage cumulative drug release			
	At 0 day	After 30 days	After 60 days	After 90 days
0	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00
0.5	11.82±0.87	10.95±0.35	9.56±1.05	8.56±0.66
1	17.08±0.92	16.82±0.59	15.52±0.30	14.75±3.4
2	24.53±1.06	23.56±1.05	22.45±0.89	21.86±2.6
3	30.61±2.37	29.84±1.48	28.69±2.60	27.58±0.98
4	35.82±0.56	34.45±0.89	33.25±0.31	32.69±0.51
5	41.09±0.88	39.12±1.02	38.78±0.21	37.56±0.35
6	49.18±0.72	48.23±0.65	47.48±0.68	46.45±0.92
7	54.73±1.35	53.42±0.57	52.79±0.61	51.61±1.20
8	60.48±0.67	59.75±1.24	58.34±2.50	57.26±0.67
9	67.50±0.38	66.27±1.29	65.28±1.16	64.21±0.68
10	75.82±0.12	74.65±1.55	73.46±1.30	72.61±0.65
11	82.18±0.58	81.36±0.56	80.59±1.0	79.57±0.67
12	90.73±0.47	89.57±0.60	88.47±0.36	86.39±0.79

Figure 1. Standard graph of Cefpodoxime proxetil in 0.1N HCl at 262nm

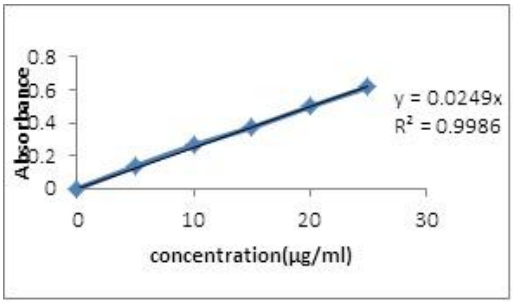


Figure 2. Standard graph of Cefpodoxime proxetil in pH 6.8 phosphate buffer at 234nm

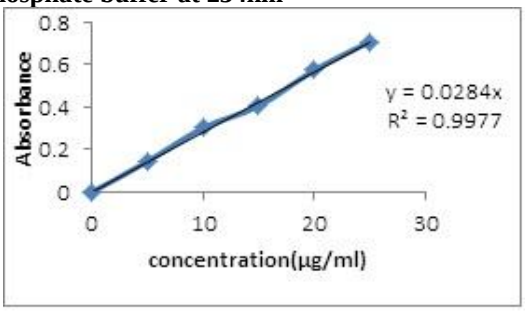


Figure 3: FT-IR Spectrum of cefpodoxime proxetil pure drug

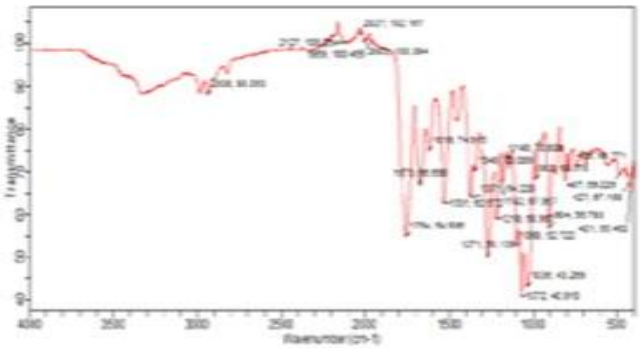


Figure 4: FT-IR Spectrum of Optimized Formulation

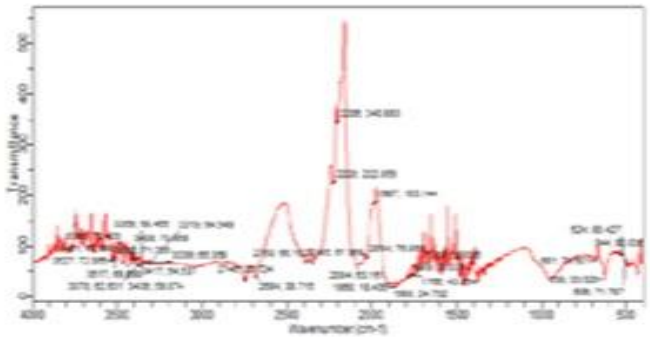
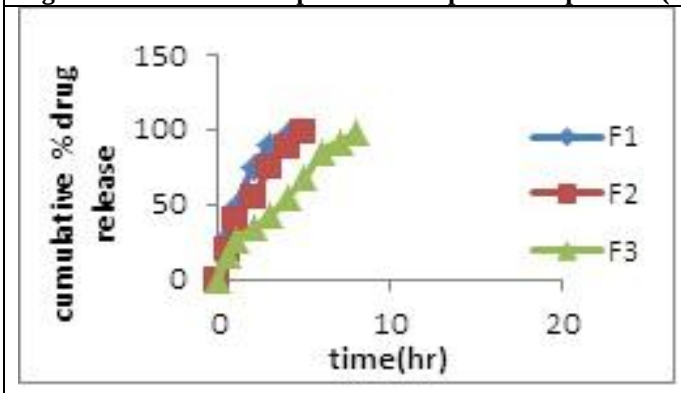


Figure 5&6. Dissolution profile of Cefpodoxime proxetil (F1 to F6 formulations)



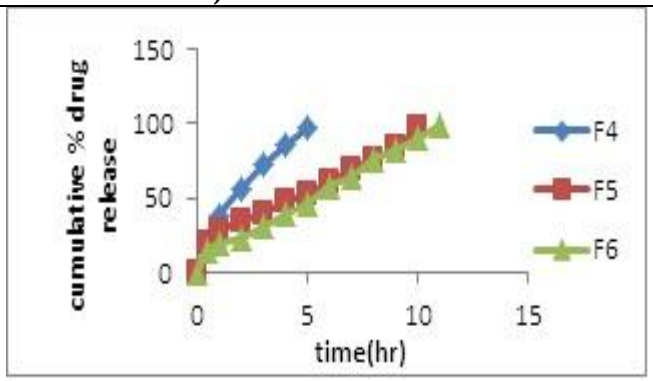
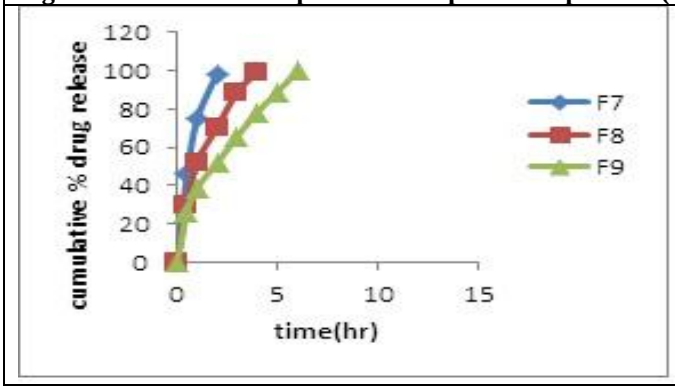


Figure 7&8. Dissolution profile of Cefpodoxime proxetil (F7 to F12 formulations)



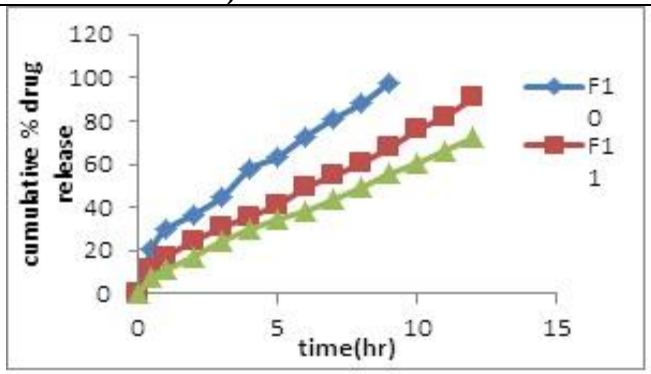


Fig 9. Zero order release kinetics graph

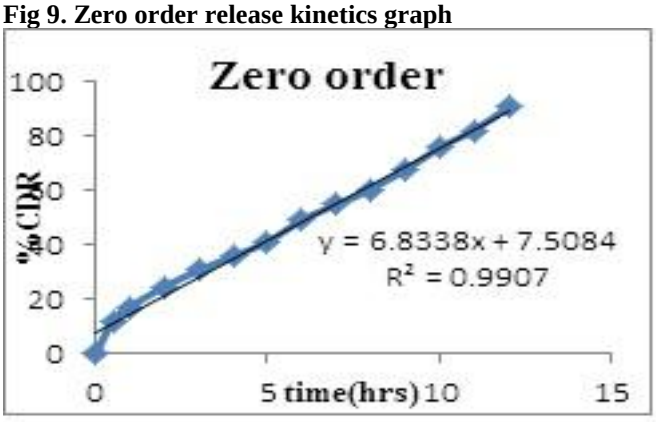


Fig 10. First order release of optimized formulation (F11)

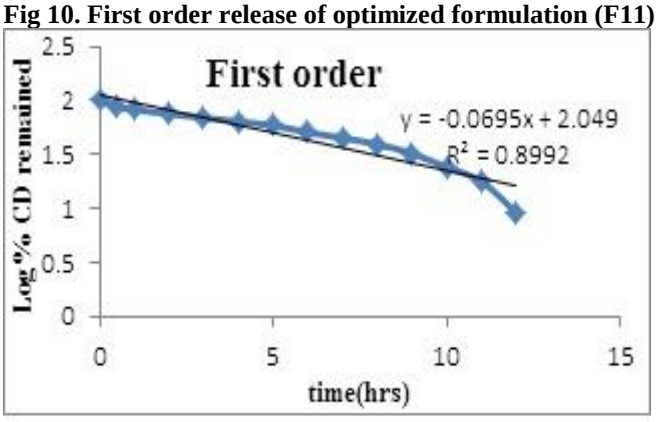


Figure 11. Higuchi release kinetics graph

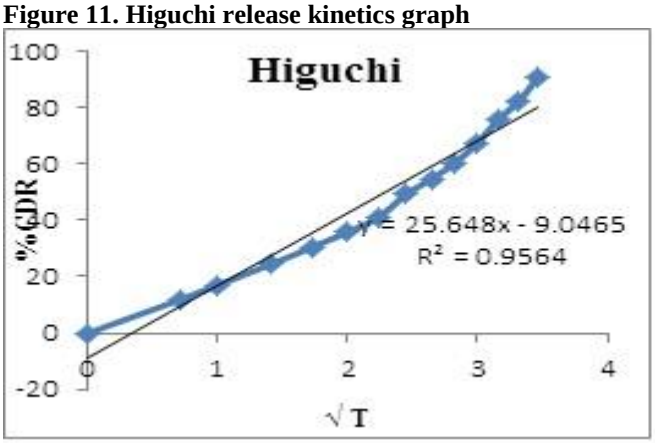
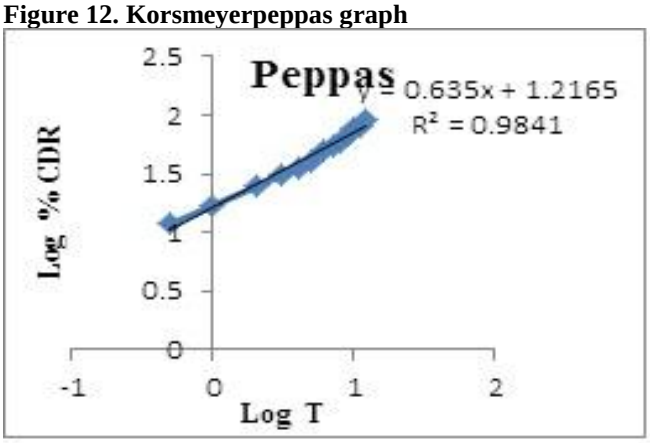


Figure 12. Korsmeyerpeppas graph



CONCLUSION

The formulation was developed with the aim of controlling the drug release for 12 hours by selecting a suitable rate controlling polymer and was achieved successfully by F11 formulation using Methocel K100LV to treat the chronic bacterial infections.

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REFERENCES

1. Chien YW. Controlled Drug Delivery Systems. Novel Drug Delivery Systems, Marcel Dekker, 2nd ed, 1992, 139-196.
2. Banker GS, Rhodes CT. Modern Pharmaceutics. Sustained and Controlled Release Delivery Systems. Marcel Dekker. 4th ed., 2002, 501-528.
3. Nokhodchi, Shaista R, Priya P, Kofi Asare-Addo. The Role of Oral Controlled Release Matrix Tablets In Drug Delivery Systems. *Bioimpacts*, 2(4), 2012, 175-187.
4. Aravind SR, Jat RC, Narendra S, Rahul T. An Overview: Matrix Tablet as Controlled Drug Delivery System. *International Journal of Research And Development In Pharmacy And Life Sciences*, 2(4), 2013, 482-492.
5. Avgoustakis K, Nixon JR. Biodegradable Controlled Release Tablets: Effect of Polymer Characteristics on Drug Release From Heterogeneous Poly (Lactide-co-Glycolide) Matrices. *Int. J. Pharm*, 99, 1993, 247-252.
6. Chidambaram N, Porter W, Flood K, Qiu Y. Formulation and Characterization of New Layered Diffusional Matrices For Zero-Order Sustained Release. *J control release*, 52(1-2), 1998, 149-158.
7. Higuchi T. Mechanism Of Sustained Action Medication, Theoretical Analysis Of Rate Of Release Of Solid Drugs Dispersed In Solid Matrices. *J Pharm Sci*, 52(12), 1983, 1145-1149.
8. Jadhav AS, Tarkase KN. Formulation Aspects with an Comparative Influence of Different Parameters Over Matrix Tablet. *International Journal of Pharmaceutical Review and Research*, 3(2), 2012, 33-42.