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FORMULATION AND EVALUATION OF COLON TARGETED TABLETS OF KETOPROFEN USING COMBINED pH AND MICROBIAL APPROACH

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ABSTRACT

Objective: The objective of present research work is to drug targeting in colon by using combined pH and microbial triggered approach. **Experimental work*:*** Colon targeted tablets of ketoprofen were prepared by direct compression method using natural polymer sterculia gum and pH dependent polymer Eudragit S 100. Core tablets were formulated then coated with pH dependent polymers. The formulated batches were evaluated for their precompression and post compression properties. Amount of Sterculia gum and % coating level were optimized by 3^2 factorial design. The optimized batch (M5) was subjected for the short-term stability study at 40 ± 2°C with RH of 75% for a period of one month. **Result and discussion*:*** Optimized formulation M5 containing 30% of Sterculia gum and coated with Eudragit S100 at the level of 8% released less amount of drug in 9.18% at the end of 5 hrs and 98.25% at the end of 12 hrs. The drug release from optimized formulation M5 follows Hixon Crowell kinetic (R^2=0.986). the result of stability study indicated no significant changes with respect to drug release. **Conclusion:** Sterculia gum with the coating level of 8% of Eudragit S-100 released the drug in sustained manner over a period of 12 hrs in colonic region. Therefore, combined pH and microbial triggered approach is potential approach for the treatment of rheumatoid arthritis by overcoming the demerits of individual approach.

KEYWORDS: Colon targeted, Microbial flora, Ketoprofen.

INTRODUCTION

Oral administration of different dosage forms is the most common form of administration due to greater patient compliance and flexibility. Targeted drug delivery system is the system in which the dosage form is modified to deliver the drug at the target region or at the disease region. In Colon targeted drug delivery system the drug is targeted to the colon. Colon targeted drug delivery is used to deliver the substances that are degraded by the digestive enzymes in the stomach such as proteins and peptides. Colon targeted drug delivery of drugs reduces the systemic side effects. Colon targeted drug delivery system increases the absorption of poorly absorbable drugs due to the high retention time of the colon.[1-3]

MATERIALS AND METHODS

Ketoprofen was obtained as a gift sample from BEC Chemicals Pvt Ltd. All other excipients were used of analytical grade.

Preparation of core tablet

The core Tablets were prepared by direct compression method. Drug and Excipients were accurately weighed and passed through no.20# mesh sieve separately. Then mixture was blended for 20 min. The uniform blend was compressed to form the tablets.[4]

Preparation of coating solution

The optimized batches of core tablets were coated with Eudragit S100 by dip coating method. Required quantity of Eudragit S100 was dissolve in 100 ml of acetone using magnetic stirrer. After complete solubilisation of polymer, castor oil (0.10% w/w) was added as plasticizer. And the solution was stirred for 15 min. The pre weighted core tablets were dipped for 3-5 times in to the coating solution until when suitable % weight gain occurs on core tablets.[5]

Table 1: Composition of colon targeted tablets.

Ingredients (mg)	M1	M2	M3	M4	M5	M6	M7	M8	M9
Ketoprofen	216	216	216	216	216	216	216	216	216
Sterculia gum	25	25	25	30	30	30	35	35	35
Avicel pH 101	116	76	36	116	76	36	116	76	36
PVP K 30	20	20	20	20	20	20	20	20	20
Talc	4	4	4	4	4	4	4	4	4
Magnesium stearate	4	4	4	4	4	4	4	4	4
Total Wt. (mg)	**400**	**400**	**400**	**400**	**400**	**400**	**400**	**400**	**400**
Coating Level (%)	6	8	10	6	8	10	6	8	10

Evaluation

Hardness

To perform this test, a tablet was placed between two anvils, force was applied to the anvils & the crushing strength that just caused the tablet to break was recorded. The hardness was measured using monseto hardness tester.[6]

Friability Test

The friability of the tablets was determined using friabilator. Approximately 6.5 g (Wo) of dedusted tablets were subjected to 100 free falls of 6 inches in a rotating drum and are then reweighed (W).[7] The friability was given by

$F = 100 \times (1 - Wo/W)$

Weight Variation Test

Twenty tablets were to be weighed individually; average weight was calculated & individual tablet weight was compared to the average weight.

Drug Content

Ten Tablets were weighed and average weight was calculated. All the 10 tablets were crushed in a mortar the powder equivalent to 10 mg was accurately weighed, dissolved in pH 7.4 phosphate buffer and made up to 100ml of pH 7.4 phosphate buffer. The volumetric flask was then shaken for approximately 20 minutes. The solution was filtered and 1 ml of filtrate was diluted to 10ml using pH 7.4 phosphate buffer. Absorbance was measured by UV spectrophometrically at 258 nm using pH 7.4 phosphate buffer as a blank. The amount of drug present in one tablet was calculated.[8-11]

In Vitro Dissolution Studies

The dissolution was performed by using a USP XXII Paddle apparatus. The dissolution studies were performed in 900ml of dissolution medium which was stirred at 50 rpm at 37±0.5°C following a pH progression method. i.e. 1.2 pH for 2hrs, 6.8 pH for next 4hrs and continued in 900 ml of 7.4 pH in the presence of Goat cecal content[12] collected from slaughter house. At every one hour interval, sample of 5 ml was to be withdrawn from the dissolution medium & that amount was replaced with fresh medium to maintain the volume constant. The absorbance of the solutions was measured using UV- Visible double beam spectrophotometer at 258nm.

Release Kinetics

In order to investigate the mode of drug release from tablet the release data wasanalysed with the following mathematical models: zero-order, first-order, Higuchi and Korsmeyer Peppas model.[13]

Stability Study

Stability study was conducted for prepared Tablet optimize formulation batch as per ICH guidelines, kept at 40 ± 2°C with RH of 75% for a period of 30 days in stability chamber. Formulation was evaluated after one-month period for Drug content and Drug release.[14]

Table 2: Pre- compression parameters of formulated batches M1-M9.

Batches	Bulk density (gm/cm^3) n=3	Tapped density (g/cm^3) n=3	Carr's Index (%) n=3	Hausner's Ratio n=3	Angle of Repose (θ) n=3
M1	0.335±0.005	0.440±0.0021	23.86±0.23	1.31±0.013	31.92±0.055
M2	0.345±0.0025	0.445±0.0019	22.47±0.20	1.28±0.017	30.02±0.043
M3	0.341±0.0015	0.443±0.0020	23.02±0.15	1.30±0.020	31.56±0.051
M4	0.377±0.0026	0.457±0.0015	19.66±0.15	1.26±0.012	29.64±0.035
M5	0.363±0.0010	0.460±0.0011	17.50±0.17	1.21±0.010	28.10±0.017
M6	0.368±0.0017	0.462±0.0020	20.34±0.20	1.25±0.015	29.04±0.029
M7	0.383±0.0010	0.471±0.0016	18.68±0.24	1.22±0.019	31.47±0.041
M8	0.380±0.0015	0.473±0.0025	21.08±0.12	1.24±0.022	29.59±0.060
M9	0.381±0.0020	0.476±0.0013	19.95±0.21	1.27±0.027	30.45±0.058

DISCUSSION

An angle of repose of all batches M1- M9 is in range 29.04±0.029 to 31.92± 0.055^{θ} and Carr's index was found in range 17.50±0.17 to 23.86±0.23% while Hausner's ratio of all the batches M1-M9 in range 1.21±0.010 to 1.31±0.013. Thus as per the readings

obtained it shows that the powder mixture of all the optimized batches shows a good to passable flow property.

Table 3: Post compression parameters of formulated batches M1-M9.

Batch	Hardness (kg/cm^2) (n=3)	Friability (%)	Weight variation (mg) (n=20)	Drug Content (%)(n=10)
M1	6.36±0.02	0.34	423.25±0.62	98.36±0.73
M2	6.41±0.02	0.29	433.84±0.47	99.51±0.84
M3	6.53±0.02	0.31	441.40±0.51	100.10±0.51
M4	6.81±0.15	0.18	424.10±0.24	99.95±0.45
M5	7.15±0.01	0.12	432.58±0.15	101.34±0.36
M6	6.98±0.18	0.22	442.04±0.20	100.81±0.63
M7	7.21±0.02	0.15	424.47±0.29	98.74±0.71
M8	6.85±0.02	0.26	432.82±0.34	100.18±0.89
M9	6.91±0.01	0.23	442.76±0.40	99.58±0.75

DISCUSSION

The hardness of formulations M1-M9 tablets was found to be in range of 6.36±0.022 to 7.21±0.024 (kg/cm^2). The friability of formulations M1-M9 was found to be less than 1%. The Uniformity of weight of tablet ranges from 399.3±0.45 to402.51±0.59 with an acceptable standard deviation. The % drug content ranges from 98.36±0.73 to101.34±0.36%.

In-vitro dissolution study

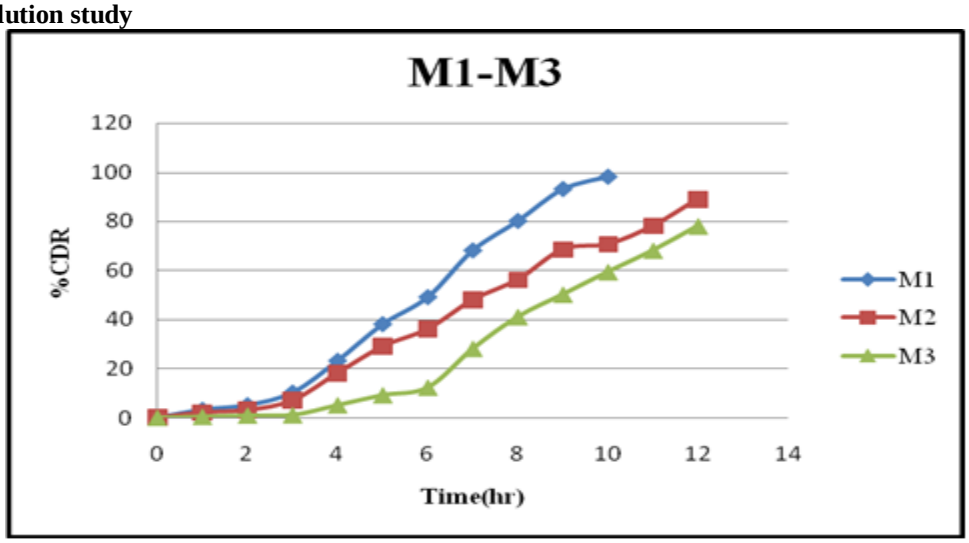


Figure 1: In vitro drug release of formulated batches M1-M3.

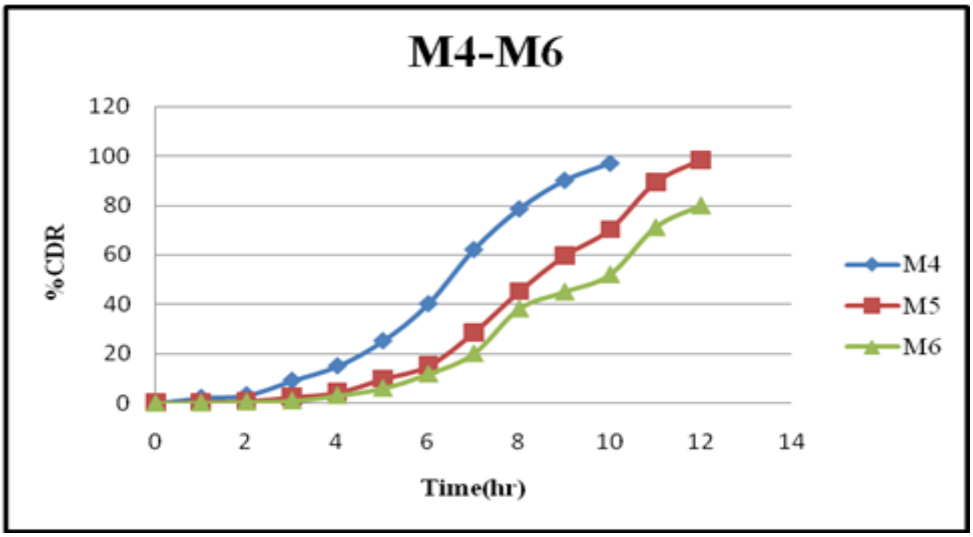


Figure 2: In vitro drug release of formulated batch M4-M6.

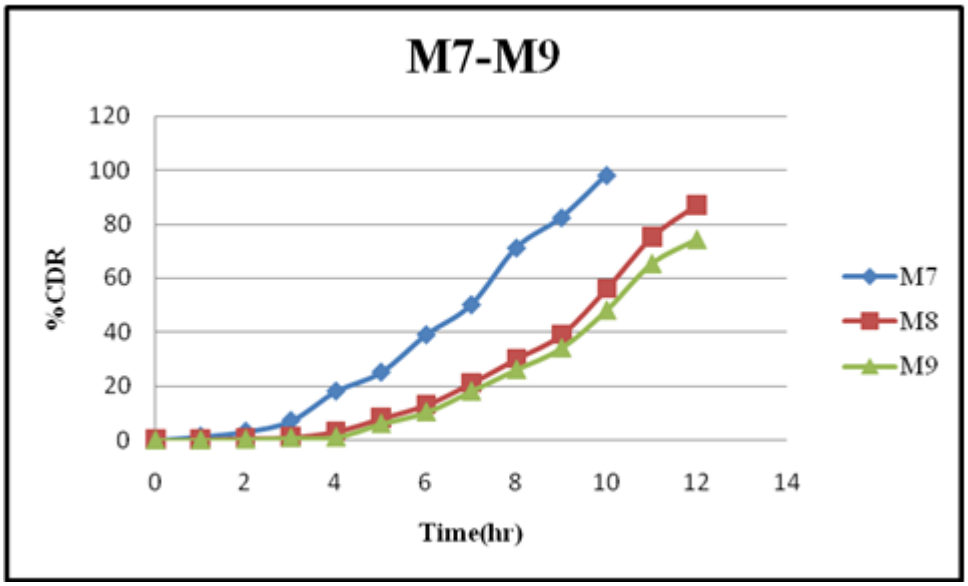
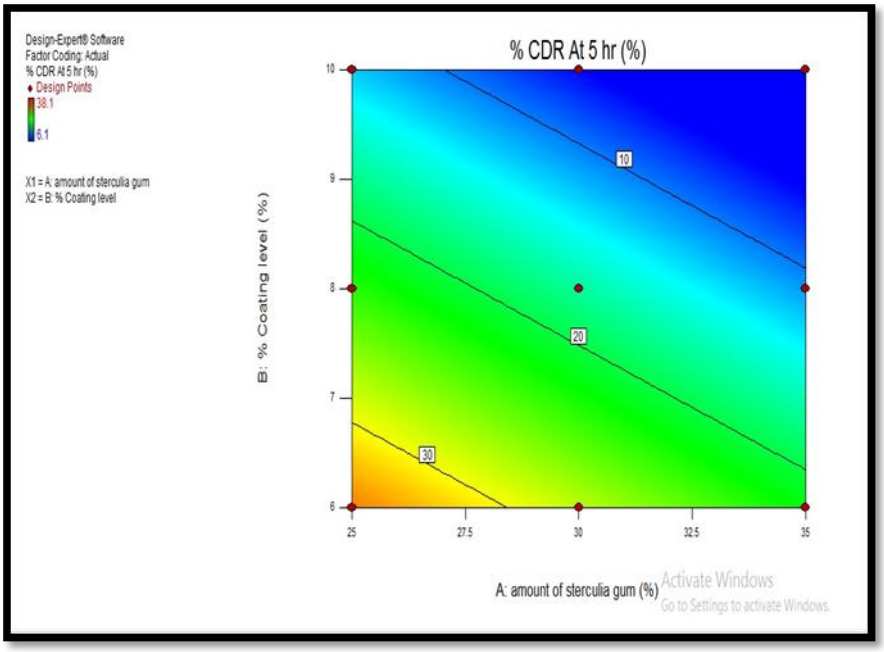


Figure 3: In vitro drug release of formulated batch M7-M9.

DISCUSSION

Core tablet containing 30% Sterculia gumshows higher drug release compared other concentration of sterculia gum and which was coated with 8% of Eudragit S100 pH dependent Polymer. M5 optimized batch which shows the higher drug release up to 98.25% and give the better sustained release action. So, M5 is the best optimized batch for targeting the colon.



Figurea 4: Counter plot showing the effect of amount of Sterculia gum (X1) and % Coating level (X2) on response Y1 (% CDR at 5hrs).

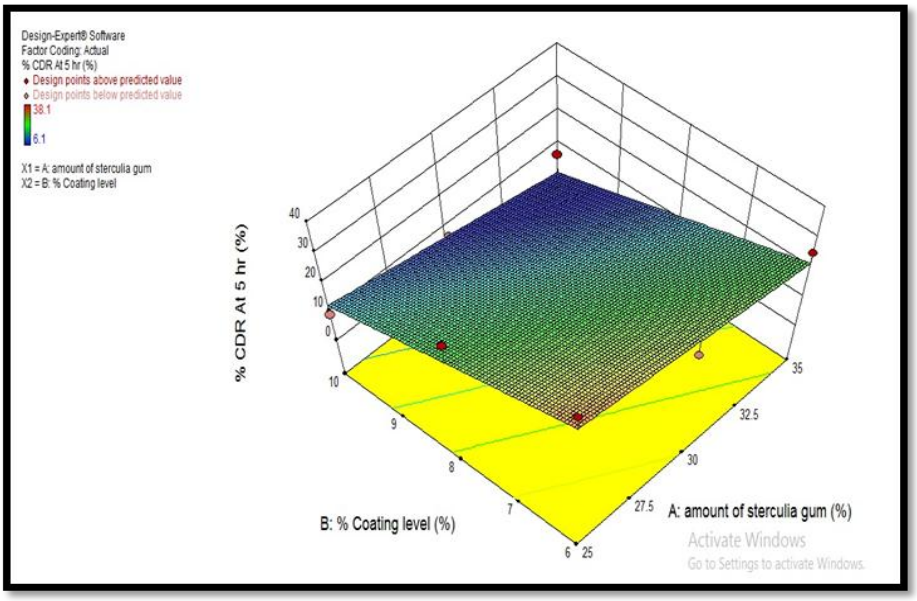


Figure 5: Response surface plot of % CDR at 5hrs.

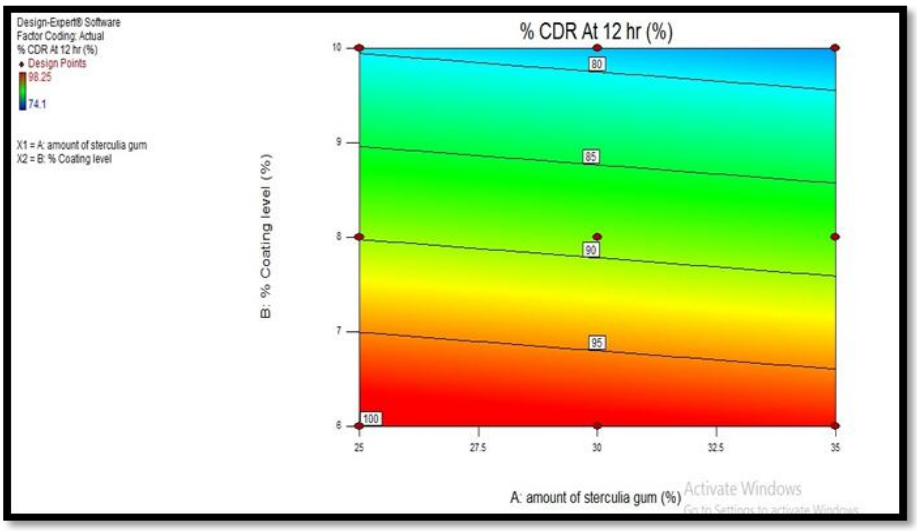


Figure 6: Counter plot showingthe effect of amount of Sterculia gum (X1) and % Coating level (X2) on responseY2 (% CDR at 12hrs).

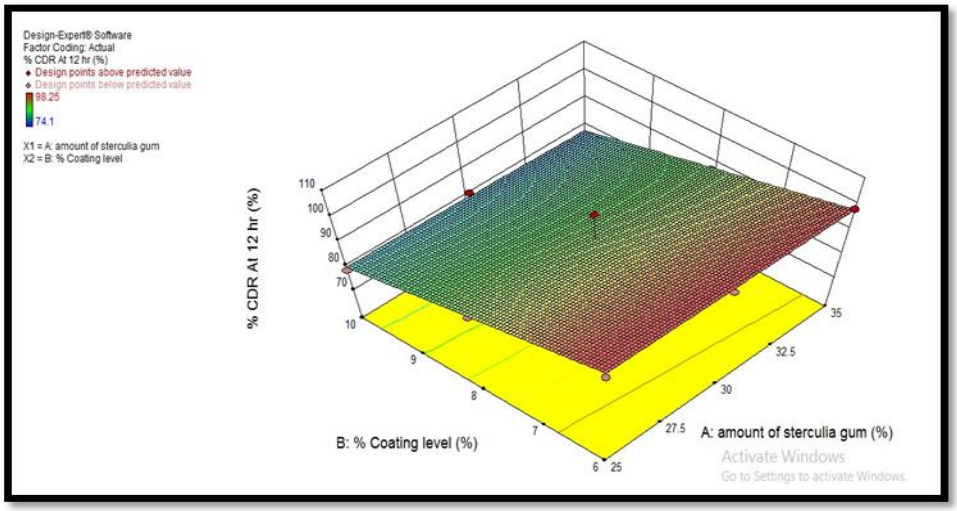


Figure 7: Response surface plot of % CDR at 12 hrs.

Stability Study

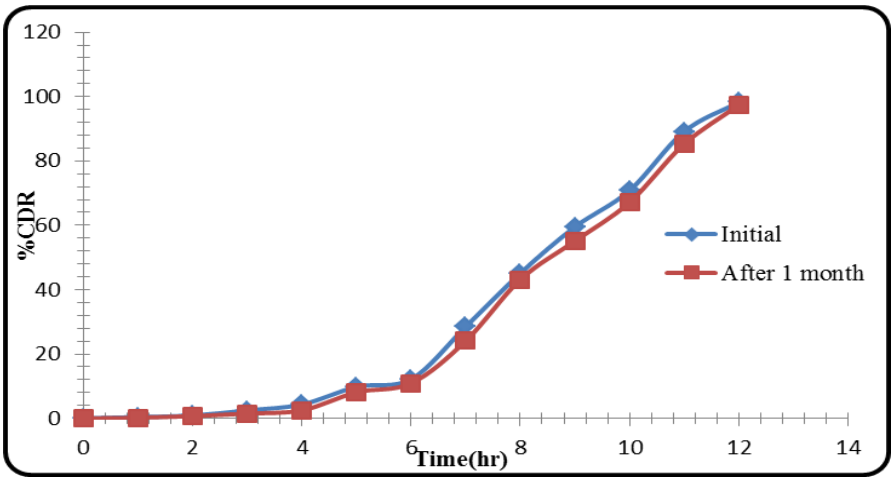


Figure 8: In vitro drug release of M5 after stability study.

CONCLUSION

The core tablets were coated by pH dependent polymer Eudragit S 100 with 8% weight gain by dip coating. Coated tablets were evaluated by thickness, weight variation and in vitro drug release study. From the in vitro release study Eudragit S 100 coated tablet shows higher drug release and gives better sustained action.

From the in vitro drug release study M5 shows higher drug release up to 98.25% for 12 hrs which gives better sustained action compared to other. There was nosignificant changes in drug release after stability study of Batch M5. So, M5 is the optimized batch used for the targeted delivery of Ketoprofen in colonic region for treatment of Rheumatoid arthritis.

REFERENCES

1. Danda S, and Kumar C, "Colon targeted drug delivery – a review on primary and novel approaches" Journal of Global Trend in Pharmaceutical Sciences, 2013; 4(3): 1174-1183.
2. Asija R, Chaudhari B, and Asija S, "Oral colon targeted drug delivery system: a review on current and novel" Journal of Pharmaceutical and Scientific Innovation, 2012; 1(5): 6-12.
3. Gangurde H, and Chordiya M, "Diseases, approaches and evaluation parameters for colon specific drug delivery: a review" International Journal of Drug Research and Technology, 2012; 2(3): 239-262.
4. Pappa R, Helen S, Jancy V, Regitha R, Ajitha D, and Indira S, "Formulation and evaluation of colon targeted tablet of ibuprofen using the combination of microbially triggered and pH sensitive polymers." World Journal of Pharmaceutical Sciences, 2015; 4(8): 1892-1906.
5. Choudhary P, Murthy N, and Tripathy N, "Formulation and development of enteric coated matrix tablet of ornidazole for colonic delivery." Asian Journal of Pharmaceutical and Clinical Research, 2012; 5(3): 86-89.
6. Sharma F, Jain H, Kanzariya V, Upadhyay UM, "Formulation And Evaluation of Controlled Release Osmotic Tablet Of Metoprolol Succinate" Asian Journal Pharmaceutical Clinical Research, 2014; 7(3): 38-43.
7. Jain H, Pasha TY, Bais CS, Bhandari A, "Formulation And Characterization Of Liquisolid Tablets of Valsartan For Improvement Of Dissolution Rate" Asian Journal Pharmaceutical Clinical Research, 2014; 7(4): 21-26.
8. Poptani S, Gohel M, Parikh R, and Patel V, "Preparation and evaluation of osmotic controlled drug delivery system of metoprolol tartarate." International. Bulletin of Drug Research, 1(1): 84-93.
9. Samal H, Sreenivas S, Dey S and Sharma H, "Formulation and evalution of sustained release zidovudine matrix tablets." International Journal of Pharmacy and Pharmaceutical Science, 2011; 3(2): 32-41.
10. Patel H, Patel U, Kadikar H, Bhimani B, Daslaniya D and Patel G, "Formulation and evaluation of controlled porosity osmotic pump tablets of glimepiride." International Journal of Drug Delivery, 2012; 4(1): 113-124.
11. Krishnaiah. YS, Bhaskar R, SatyanarayanaV, Karthikeyan RS. International Journal of Pharmaceutics, 2002; 236(2): 43-55.
12. Ahmad MZ, Akhter S, Ahmad I, Singh A, Anwar M, Shamim M, *et al*. In vitro and in vivo evaluation of Assam Bora rice starch-based bioadhesive microsphere as a drug carrier for colon targeting. Expert Opinion Drug Delivery, 2012; 9(2): 141–9.
13. Dash S, Murthy P N, Nath L and Chowdhury P, "Kinetic Modeling On drug release from controlled drug delivery systems." Acta Poloniae Pharmaceutical and Drug Research, 2010; 67(3): 217-223.
14. Kotwal A. Design and Evaluation of matrix-based controlled release tablets of diclofenac sodium and chondroitin sulfate. AAPS Pharm. Sci. Tech., 2007; 8: 88, E1-E8.