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FORMULATION AND EVALUATION OF ACECLOFENAC BILAYER TABLETS

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ABSTRACT

The goal of the work described in the passage was to develop bi-layer tablets of Aceclofenac, a strong non-steroidal anti-inflammatory medication, with both immediate and sustained release characteristics. The ultimate aim was to achieve quick drug release in the stomach for immediate symptom relief and a steady release in the intestine to maintain the intended therapeutic effect. Dry granulation method is used for first layer for formulations F1 - F4 contains cross carmellose sodium and F5 - F8 contains sodium starch glycolate for immediate release. Second layer was made by wet granulation method for formulations F1 - F4 with ethyl cellulose & for formulations F5 - F8 with HPMCK100M. Various formulations are prepared to obtain desired release profile to show first layer Aceclofenac release in stomach and second layer 98% for 10 h sustained release layer. Pre-compression tests are done to all the formulation and all are passed. Formulations (F1-F8) are tested for hardness, thickness, friability, weight variation and drug content. Goal of this is to optimise the formulation that bi-layer tablet to be released immediately in the stomach and second layer to be released for 10 h in the intestine. Optimized formulation F4 contains cross carmellose sodium as super disintegrants in the first layer and ethyl cellulose in the second layer.

Keywords: Aceclofenac bi-layer immediate release (IR) sustained release (SR) *in vitro* studies release kinetics

1. INTRODUCTION

Aceclofenac sodium is a non-Steroidal anti-inflammatory COX-2 Inhibitor **[1]**. It is widely used in osteoarthritis, rheumatoid arthritis, ankolysing spondylitis. Physico chemical properties, biological properties of aceclofenac help us to making formulation of sustained release easily. The plasma half-life of aceclofenac is 3-4 h **[2]** so it is suitable candidate for sustained release. Ethyl cellulose and HPMC are the sustained release polymers, which gives the release upto10 h **[3-4]**.

2. MATERIALS AND METHODS

Aceclofenac, active pharmaceutical ingredient was procured from local vendor. Ethylcellulose (SD fine chem Pvt. Ltd., Mumbai, India), HPMC (Qualigens Fine Chemicals, Mumbai, India), were procured and used in this investigation.the entire chemicals of analytical grade and double distilled water used throughout the experiment.

2.1. Development of standard calibration curve

2.1.1. Determination of λ max of aceclofenac solution

Using a UV spectrophotometer, aceclofenac solution of 10 µg/ml was produced and scanned against 0.1N HCl as a reference solution over the wavelength range of 200 - 400 nm **[5]**. A plot was created by taking concentration and absorbance. Graph's tallest peak was designated as ''max''

2.1.2. Standard stock solution preparation

Aceclofenac should be carefully weighed and dissolved in 100 ml of ethanol **[6].** This results in a standard stock solution of 1000 µg/ml.

2.1.3. Working stock solution preparation

10 ml of the first stock solution was taken, and it was then filled with 0.1N HCl to make 100 µg/ml. This results in a working stock solution with a 100 µg/ml concentration **[6]**.

2.1.4. Preparation of working dilutions with 0.1N HCl

0.2, 0.4, 0.6, 0.8, 1.0 & 1.2 ml are taken from the working solution and it was make up with 10 ml of 0.1N HCl to produce 2, 4, 6, 8, 10 and 12 µg/ml concentrations **[7]**.

2.1.5. Phosphate buffer pH 7.4 of working dilutions

0.2, 0.4, 0.6, 0.8, 1.0 and 1.2 ml are taken from working standard stock solution volume was make up to 10 ml with pH 7.4 to form 2, 4, 6, 8, 10 and 12 µg/ml concentrations **[8]**.

2.2. Formulation of aceclofenac bilayer tablets

2.2.1. Formulation design: Dry granulation method and wet granulation method are used in preparing aceclofenac bilayer tablets. Super disintegrants cross carmellose sodium and sodium starch glycolate in first layer, ethyl cellulose & HPMC K100M are used in second layer.

Table 1: Formulation trials of aceclofenac immediate release layer

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8
Aceclofenac	100	100	100	100	100	100	100	100
Cross carmellose sodium	10	12	16	18	-	-	-	-
Sodium starch glycolate	-	-	-	-	10	12	16	18
Lactose	33	26	12	15	33	26	12	15
PVPK 30	5	10	20	15	5	10	20	15
Magnesium stearate	2	2	2	2	2	2	2	2
Total weight	150	150	150	150	150	150	150	150

Table 2: Formulation trials of aceclofenac sustained release layer

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8
Aceclofenac	100	100	100	100	100	100	100	100
Ethyl cellulose	10	15	20	25	-	-	-	-
HPMC K100M	-	-	-	-	10	15	20	25
Lactose	36	31	26	21	36	31	26	21
Isopropyl Alcohol	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Magnesium stearate	2	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2	2
Total weight	150	150	150	150	150	150	150	150

Procedure

Dry granulation method and wet granulation method is used for preparing. First layer is prepared as immediate release layer and second layer is prepared as sustained layer **[9]**. First layer by dry granulation method and second layer by wet granulation method, in dry granulation method Cross carmellose sodium and SSG are used, trails were done using different concentration of super disintegrants. Second layer was prepared employing varying ethyl cellulose concentrations and the wet granulation process. HPMCK100M. They are assigned with formulation codes. First layer by direct compression method as in Table 1 Second layer, is prepared by wet granulation technique **[10]**. HPMCK100 M and Ethyl cellulose are used in different amounts as shown in **Table 2**.

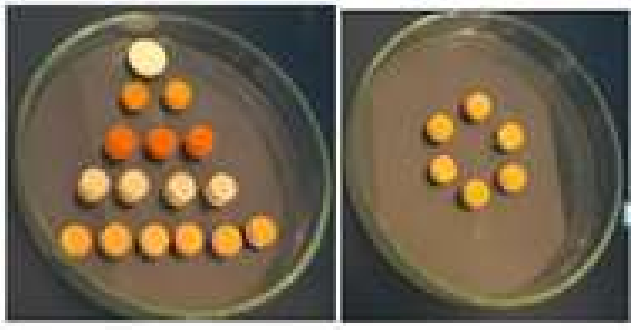

Figure 1: Formulation of bilayer tablets

3. RESULTS

3.1. Preformulation studies

3.1.1. Melting point determination

Substance transforming from a solid to a liquid state is melting point. Pure crystals are distinct and have well defined melting point

Capillary method is used to determine aceclofenac melting point. In this method, a high accuracy thermometer is placed close to a heated stand (a metal block or liquid bath) that consists of glass capillary tube with a compact column of the drug to be estimated **[11]**.

Table 3: Melting point of aceclofenac

Trials	Melting point observed	Average melting point	Reference melting point
1	149		
2	153	150.3	149 - 153^{0}c
3	149		

3.1.2 Solubility

Most important parameter to prepare formulations

1. It shows how the drug dissolves.
2. Oral administration and drug dissolution have a direct impact on a drug's bioavailability. During formulation Particle size, shape and surface area should be determined because they may affect the way a drug dissolves.

Method: The solubility of aceclofenac was assessed after required quantity was added to the appropriate volume of solvent **[12]**.

Table 4: Melting point of aceclofenac

S. No.	Solvents	Observed
1	Ethanol	Soluble Freely
2	PBS- 7.4(PH)	Soluble Freely

3.1.3. Analytical methodology

3.1.3.1. Determination of absorption maximum (λ) of aceclofenac

Using a UV spectrophotometer, aceclofenac solution of 10 µg/ml was produced and scanned against two, 0.1N HCl and phosphate buffer pH 7.4 as a reference solution under the wavelength range of 200 - 400 nm. A plot is created by taking concentration and absorbance. Plot's tallest peak was designated as 275 nm.

3.1.3.2 Development of calibration curve

The absorbance for various concentrations measured at 275 nm is as follows

Table 5: Standard graph of aceclofenac

S.no	Concentration	Absorbance
1	0	0
2	2	0.046
3	4	0.092
4	6	0.135
5	8	0.185
6	10	0.229

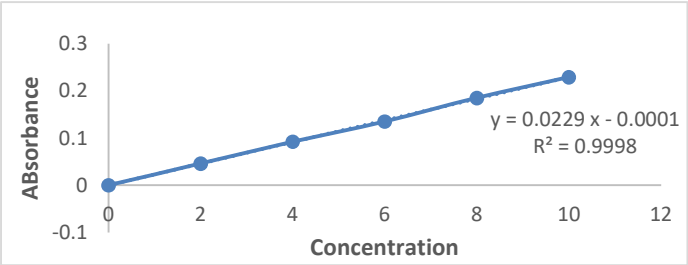

Figure 2: Aceclofenac standard graph

Aceclofenac shows good linearity with the range 2 - 10 µg / ml concentration ranges in 0.1N HCl. with $R^2 = 0.999$, Slope = 0.022.R^2 value was closer to 1 follow's Beer-lamberts law.

Table 6: Aceclofenac in phosphate buffer pH 7.4

S.No.	Conc. (µg/mL)	Absorbance
1	**0**	**0**
2	2	0.153
3	4	0.321
4	6	0.519
5	8	0.645
6	10	0.828
7	12	0.971

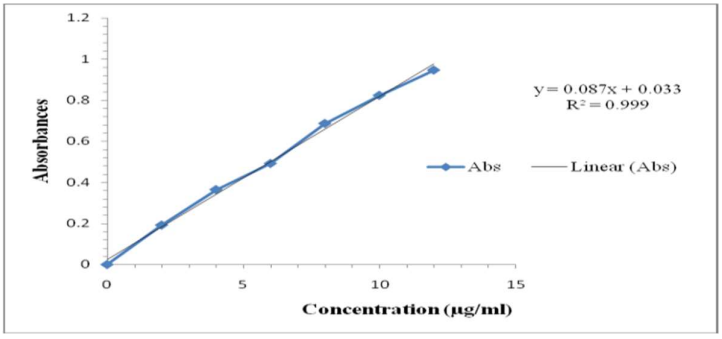

Figure 3: Aceclofenac in phosphate buffer pH 7.4

Aceclofenac shows good linearity with the range 2-12 µg / ml concentration ranges in 0 phosphate Buffer pH 7.4. With $R^2 = 0.999$, Slope = 0.087. R^2 is near to ''1'' follows Beer-lamberts law.

4.2. Compatability studies

4.2.1. Compatibility study between aceclofenac and excipient

To find out the chemical interaction between drug and excipient, in tablet formulation drug is in intimate contact with excipients, drug excipient compatibility study was performed by FTIR. FTIR spectra of aceclofenac and optimised formulation are analysed in the range of 400 to 4000cm^{-1}

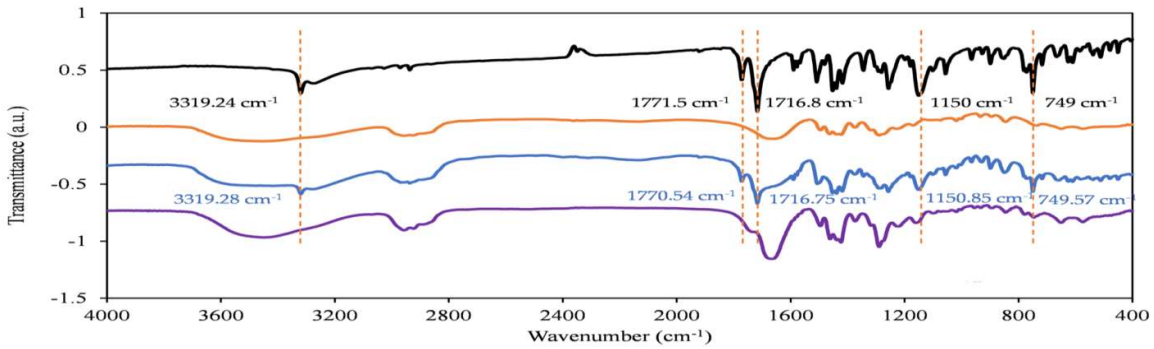

Figure 4: Pure drug aceclofenac (black), cross carmellose sodium (orange), ethyl cellulose (blue), and the aceclofenac-formulation (purple).

Table 7: Interpretation of Drug & optimised formulations

Functional groups	Wave number(cm^{-1})
N-H Stretching	3319.24
carbonyl stretching	1771.5 & 1716.7
Alkyl Amine	1150
Aromatic C=H stretching	749

Discussion

The FTIR spectral analysis of optimised formulation showed that the peaks observed were N - H Stretching, carbonyl stretching, Alkyl Amine and Aromatic C = H stretching, which are similar pure drug and drug with excipients which has showed in figures. This indicates no drug excipient interaction.

3.3. Preformulation studies

Table 8: Preformulation studies of different formulation of aceclofenac

Formulation	Angle of repose (θ)	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Carr's Index (I)%	Hausner's ratio
F1	25.47	0.454	0.563	17.12	1.24
F2	26.78	0.461	0.559	17.78	1.21
F3	25.85	0.459	0.564	17.97	1.22
F4	26.47	0.455	0.558	17.64	1.22
F5	24.27	0.459	0.564	17.62	1.22
F6	25.47	0.455	0.563	17.97	1.24
F7	26.47	0.558	0.559	17.64	1.21
F8	24.27	0.564	0.564	17.62	1.22

Discussion

Pre-formulation studies were carried out to all the formulation and all are passed. Formulations F1 - F8, angle of repose falls in the range of 24.27 ± 0.25 to 26.78 ± 0.34, follows the good flow properties, Formulations F1- F8, bulk density from 0.454 to 0.564. Formulations F1 - F8 Carr's index from 17.12 to 17.97. Formulations F1-F8, tapped density from 0.55 - 0.56. All parameters were found to be within the limits.

3.4. Evaluation of aceclofenac bilayer tablets Aceclofenac bilayer tablets are tested for their *in vitro* dissolution studies, uniformity of weight, thickness, hardness, friability and disintegration. All evaluations are done in triplicate.

Table 9: Evaluation properties of different formulation F1-F8 of aceclofenac bilayer tablets

Formulation	Weight variation (mg)	Thickness (mm)	Hardness	Friability (%)	Drug Content (%)
F1	298 ± 1.2	7.0 ± 0.03	5.0 ± 0.6	0.53	92.1
F2	298 ± 1.2	5.4 ± 0.03	5.5 ± 0.7	0.51	90.4
F3	301 ± 1.2	6.1 ± 0.03	5.2 ± 0.6	0.52	91.4
F4	300 ± 1.3	5.0 ± 0.03	5.0 ± 0.1	0.50	90.5
F5	299 ± 1.2	6.0 ± 0.03	5.5 ± 0.6	0.54	96.6
F6	298 ± 1.2	7.0 ± 0.03	5.0 ± 0.6	0.53	92.1
F7	299 ± 1.3	5.4 ± 0.03	5.5 ± 0.7	0.50	90.5
F8	300 ± 1.3	5.0 ± 0.03	5.0 ± 0.1	0.54	95.5

Discussion: All formulations (F1-F8) are tested for thickness, hardness, friability, weight variation and drug content. All formulations had average tablet weight within 298 - 300 mg and thickness was within 5.0 mm. The tablet hardness was within 5.0 - 5.5 kg/cm2. The friability was in range of 0.51 - 0.54 which was within the limits and all formulations (F1-F8) drug content is in the range of 90.5 - 96.6%

4.4.1. Aceclofenac bilayer tablets *in vitro* dissolution studies

Table 10: Aceclofenac bilayer tablets of all formulation F1-F8 *in vitro* dissolution studies

Time	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	0	0	0
0.5	9.93±10.12	10.21±0.12	12.0±0.12	14.23±0.12	12.34±0.12	11.45±0.22	12.09±0.12	13.41±0.12
1	14.89±0.61	15.54±0.16	16.88±0.32	17.89±0.12	15.59±0.12	14.2±0.02	15.78±0.88	16.45±0.12
2	22.34±0.57	21.09±0.17	20.44±0.12	27.86±0.12	20.45±0.12	21.5±0.27	21.89±0.54	23.45±0.12
4	35.4±0.56	38.36±0.12	40.87±0.33	43.96±0.12	36.56±0.12	37.45±0.65	40.46±0.54	42.22±0.54
6	52.5±0.90	58.12±0.25	69.14±0.45	72.22±0.12	58.47±0.12	60.12±0.12	61.77±0.12	70.21±0.67
8	82.2±0.48	79.21±0.49	80.12±0.74	89.55±0.12	65.1±0.12	67.11±0.1	70.56±0.76	85.78±0.56
10	90.31±0.43	93.4±0.61	95.23±0.14	98.89± 0.12	80.55±0.12	81.25±0.12	85.24±0.12	92.54±0.12

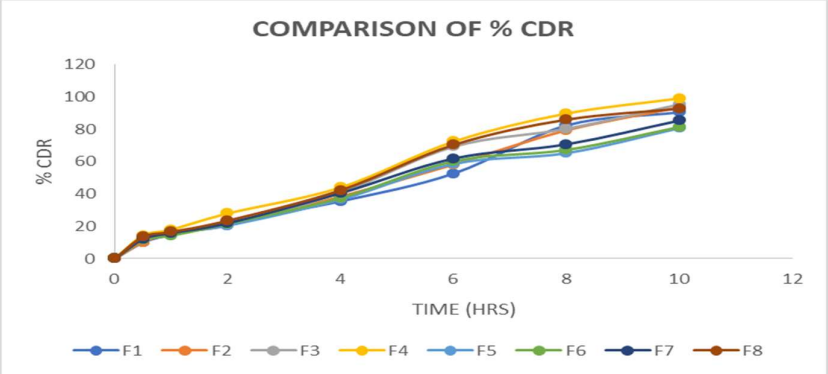

Figure 5: Aceclofenac bilayer tablets of all formulation F1-F8 cumulative percentage drug release

Discussion

In vitro percentage drug release studies are done by 0.1N HCl and phosphate buffer pH 7.4 of aceclofenac bilayer tablets formulated in two layers first layer to be released in stomach and second layer to be released in the intestine for 10 h. Percentage drug release for formulation F4 which contains 18 mg of cross carmellose sodium and 25 mg of ethyl cellulose 98.89% of drug release up to 10hours. F4 formulation is considered as best formulation containing 18 mg of ethyl cellulose and 25 mg of ethyl cellulose showed maximum drug release of 98.89%

up to 10 h. So Formulation F4 is chosen for release kinetics and evaluated.

4.4. Model dependent kinetics for the optimized formulation

Kinetics of the aceclofenac bilayer best tablet, in vitro dissolution study of best formulation are shown in different kinetics model. It follows the zero order release kinetics.

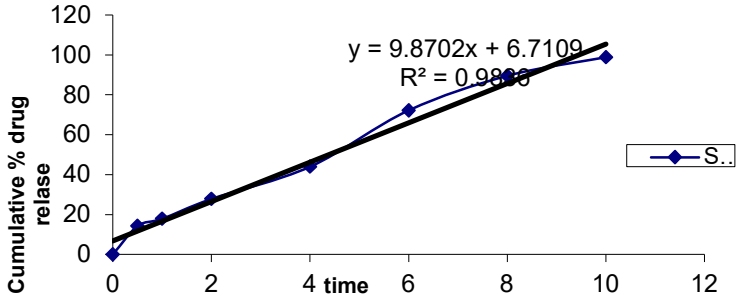

Figure 6 a: Zero order kinetics

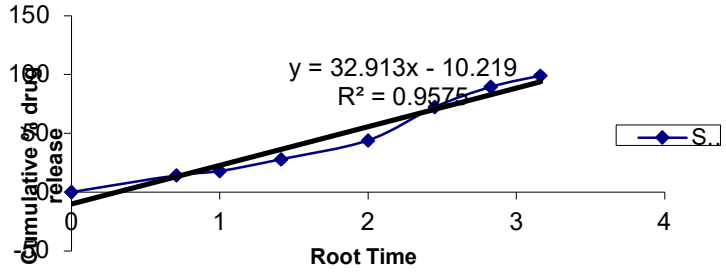

Figure 6 b: Higuchi

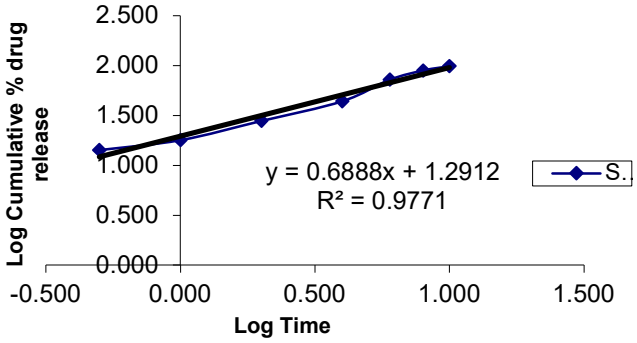

Figure 6 c: Korsmeyer peppas model

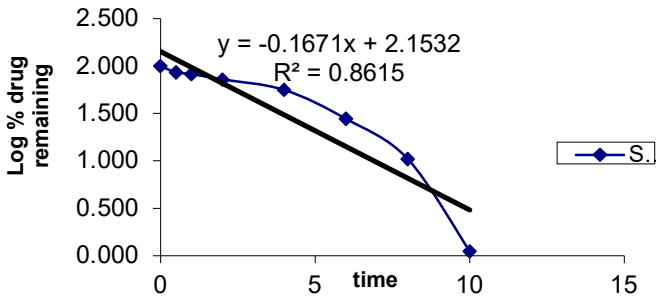

Figure 7: First order kinetics

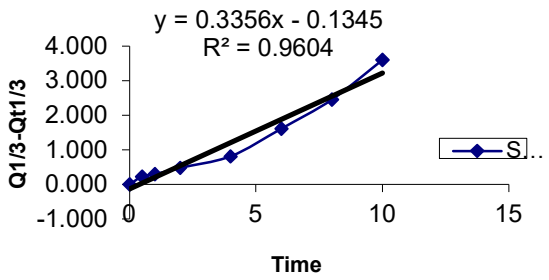

Figure 8: Hixson Crowell

DISCUSSION

R^2 value for zero order are obtained as 0.98 which are close to '1' based on that we confirm the optimised formulation F4 follows zero order release kinetics. From the zero order release kinetics the release component 'n' value was found to be 0.911 which is greater than <0.89 it was known as non fickian diffusion.

CONCLUSION

Aceclofenac is non steroidal anti inflammatory drug, mainly used for the treatment of pain inflammation in osteoarthritis, rheumatoid arthritis. Aceclofenac is asuitable for controlled release administration due to its short elimination time 4 h.The goal of work to formulate aceclofenac to decrease dosing frequency and improve patient acceptance by using different superdisintegrant cross carmellose sodium and sodium starch glycolate in first layer and polymers in second layer like HPMCK100M & ethyl cellulose along with suitable excipients. Drug exicipent compatability studies were conducted between pure drug and optimized formulations were carried out by FTIR spectroscopy. Cumulative percentage drug was seen, F4 formulation is optimized formulation containing sodium carboxy methyl cellulose as superdisinegrant and ethyl cellulose in second layer is consider as the optimized with respect to *in vitro* drug release. F4 formulation showed satisfactory results with immediate release and sustained release upto 10 h in the intestine.

REFERENCES

[1] Leon Lachman and Schwartz, B. 'Compression coated and layer Tablets'. Pharmaceutical dosage forms: Tablets, Mumbai: Varghese Publishing House. 1989, 2: pp-273-274

[2] India, Ministry of Health and Family Welfare. Indian Pharmacopeia. Ghaziabad: The Indian Pharmacopoeia Commission. 2007, 2: 662.

[3] Banker, S. and Anderson R. 'Tablets'. In: Leon Lachman and Liberman, A. Eds. The theory and practice of industrial pharmacy.

Mumbai: Varghese Publishing House, 1987, 3: pp-329-335, 430.

[4] Pradeep Reddy. Bilayer technology – An Emerging trend: A Review, International Journal of Research and Development in Pharmacy and Life Sciences, Vol. 2, April - May, 2013, pp 404-411 ISSN: 2278-023.

[5] Hemanth Kumar A. Novel approach of bilayer tablet technology – A Review, International Journal of pharmaceutical, chemical, biological sciences, 2013, 3(3), 887- 893 ISSN: 2249-9504.

[6] Arvind Mishraet. Review: Bilayer tablet and Evaluation, International Journal of Drug Research and Technology, 2013, Vol. 3 (2), pp-21-30 ISSN 2277 – 1506.

[7] Utsav Patel. A Review on Immediate release Drug delivery system, International Journal of pharmaceutical Research and Bioscience,2012; Volume 1(5), pp-37-66 ISSN: 2277-8713.

[8] Jain, N.K. (Ed). Advances in controlled and novel drug delivery system. New Delhi: CBS Publisher and distributors.2008, 4:11-21.

[9] Clive G, Wilson, Patrick J and Crowley. Controlled Release in Oral Drug Delivery, pp-111- 112.

[10] Deepika, K.L. 'Design, Development and evaluation of Domperidone maleate bilayer tablets'. International Journal of Pharmacy and Pharmaceutical Science, 2013, 5(4): pp-701 – 710.

[11] Nabin Karna. 'Design, development and evaluation of novel sustained release bilayer tablets of Lornoxicam based on the combination of hydrophilic matrix formers and basic PH modifiers'. International Journal of Pharma and Bio Science, 3(4): 392 – 402.

[12] Malpani Amol. 'Formulation of Lisinopril dehydrate tablet and study effect of extent of granulation on response variables'. International Journal of Pharmaceutical Sciences, 2009, 1(1): 132 – 139.