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PREPARATION AND EVALUATION OF CONTROLLED RELEASE TABLETS CONTAINING IBUPROFEN

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Abstract:

The present study aimed at Formulation Development and Evaluation of controlled release tablets of Ibuprofen is nonsteroidal anti-inflammatory drug (NSAID) class that is used for treating pain, fever, and inflammation. This includes painful menstrual periods, migraines, and rheumatoid arthritis. It may also be used to close a patent ductus arteriosus in a premature baby. It can be used by mouth or intravenously.

The matrix tablets of Ibuprofen were prepared using direct compression method. Physical characterization of tablet and powder blends used to form the matrix tablet was under taken using a range of experimental techniques. Granules were evaluated for Bulk density, Tapped density, Compressibility index and Hausner's ratio. Tablets were tested for weight variation, hardness, thickness and friability as per official procedure. The tablets were evaluated for in-vitro drug release profile. Dissolution studies of Ibuprofen controlled release tablets in media with different dissolution media 0.1N HCl, Phosphate buffer pH (6.8) as per US Pharmacopoeia.

The drug release from optimized formulations was controlled for a period of 12 hrs. The kinetic treatment of selected formulation (F3) showed that the release of drug follows Peppas release kinetics mechanism. Results of the present study indicated the suitability of different polymers in the preparation of matrix based controlled release formulation of Ibuprofen. Several kinetic models were applied to the dissolution profiles to determine the drug release kinetics.

Keywords: *Ibuprofen, HPMC K 15M, HEC 2M, HPC 2M and Controlled release tablets.*

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INTRODUCTION:

Controlled release tablets are commonly taken only once or twice daily, compared with counterpart conventional forms that may have to take three or four times daily to achieve the same therapeutic effect. The advantage of administering a single dose of a drug that is released over an extended period of time to maintain a near-constant or uniform blood level of a drug often translates into better patient compliance, as well as enhanced clinical efficacy of the drug for its intended use.

The first Controlled release tablets were made by Howard Press in New Jersy in the early 1950's. The first tablets released under his process patent were called 'Nitroglyn' and made under license by Key Corp. in Florida.

Controlled release, prolonged release, modified release, extended release or depot formulations are terms used to identify drug delivery systems that are designed to achieve or extend therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose.

The goal in designing Controlled or Controlled delivery systems is to reduce the frequency of the dosing or to increase effectiveness of the drug by localization at the site of action, reducing the dose required or providing uniform drug delivery. So, Controlled release dosage form is a dosage form that release one or more drugs continuously in predetermined pattern for a fixed period of time, either systemically or to a specified target organ.

Controlled release dosage forms provide a better control of plasma drug levels, less dosage frequency, less side effect, increased efficacy and constant delivery. There are certain considerations for the preparation of extended release formulations:

- ✓ If the active compound has a long half-life, it is Controlled on its own,
- ✓ If the pharmacological activity of the active is not directly related to its blood levels,
- ✓ If the absorption of the drug involves an active transport and
- ✓ If the active compound has very short half-life then it would require a large amount of drug to maintain a prolonged effective dose.

The above factors need serious review prior to design. Introduction of matrix tablet as Controlled release (SR) has given a new breakthrough for novel drug delivery system in the field of Pharmaceutical technology. It excludes complex production procedures such as coating and Pelletization during manufacturing and drug release rate from the dosage form is controlled mainly by the type and proportion of polymer used in the preparations. Hydrophilic polymer matrix is widely used for formulating an SR dosage form. Because of increased complication and expense involved in marketing of new drug entities, has focused greater attention on development of Controlled release or controlled release drug delivery systems. Matrix systems are widely used for the purpose of Controlled release. It is the release system which prolongs and controls the release of the drug that is dissolved or dispersed.

In fact, a matrix is defined as a well-mixed composite of one or more drugs with gelling agent i.e. hydrophilic polymers. By the Controlled release method therapeutically effective concentration can be achieved in the systemic circulation over an extended period of time, thus achieving better compliance of patients. Numerous SR oral dosage forms such as membrane controlled system, matrices with water soluble/insoluble polymers or waxes and osmotic systems have been developed, intense research has recently focused on the designation of SR systems for poorly water soluble drugs.

Rationale for extended release dosage forms:

Some drugs are inherently long lasting and require only once-a-day oral dosing to sustain adequate drug blood levels and the desired therapeutic effect. These drugs are formulated in the conventional manner in immediate release dosage forms. However, many other drugs are not inherently long lasting and require multiple daily dosing to achieve the desired therapeutic results. Multiple daily dosing is inconvenient for the patient and can result in missed doses, made up doses, and noncompliance with the regimen. When conventional immediate-release dosage forms are taken on schedule and more than once daily, they cause sequential therapeutic blood level peaks and valleys (troughs) associated with the taking of each dose . However, when doses are not administered on schedule, the resulting peaks and valleys reflect less than optimum drug therapy. For example, if doses are administered too frequently, minimum toxic concentrations of drug may be reached, with toxic side effects resulting. If doses are missed, periods of sub therapeutic drug blood levels or those below the minimum effective concentration may result, with no benefit to the patient. Extended-release tablets and capsules are commonly taken only once or twice daily, compared with counterpart conventional forms that may have to be taken three or four times daily to achieve the same therapeutic effect. Typically, extended-release products provide an immediate

release of drug that promptly produces the desired therapeutic effect, followed by gradual release of additional amounts of drug to maintain this effect over a predetermined period.

The Controlled plasma drug levels provided by extended-release products oftentimes eliminate the need for night dosing, which benefits not only the patient but the caregiver as well.

MATERIALS AND METHODS:

Ibuprofen Procured From kind gift from Alkem Pharmaceuticals Ltd, India. Provided by SURA LABS, Dilsukhnagar, Hyderabad, HPMC K 15M fromYarrow chemicals(Mumbai,India), HEC 2M from SD Fine Chem. Ltd. (Mumbai, India), HPC 2M from Arvind Remedies Ltd, Tamil nadu, India, MCC from Merck Specialities Pvt Ltd, Mumbai, India, Aerosil from Chemdyes Corporation (Ahmedabad, India), Magnesium Stearate from Merck Specialities Pvt Ltd, Mumbai, India

Characterization of Ibuprofen:

Organoleptic properties:

Take a small quantity of sample and spread it on the white paper and examine it visually for color, odour and texture.

Determination of Ibuprofen Melting point :

The melting point of Ibuprofen was determined by capillary tube method according to the USP. A sufficient quantity of Ibuprofen powder was introduced into the capillary tube to give a compact column of 4-6 mm in height. The tube was introduced in electrical melting point apparatus and the temperature was raised. The melting point was recorded, which is the temperature at which the last solid particle of Ibuprofen in the tube passed into liquid phase**.**

Determination of Ibuprofen Solubility:

Determination of solubility of drug by visual observation. An excess quantity of Ibuprofen was taken separately and adds in 10 ml of different solutions. These solutions were shaken well for few minutes. Then the solubility was observed and observations are shown in the Table.

Analytical method development:

Determination of Wavelength:

10mg of pure drug was dissolved in 10ml methanol (primary stock solution - 1000 µg/ml). From this primary stock solution 1 ml was pipette out into 10 ml volumetric flask and made it up to 10ml with the media (Secondary stock solution – 100µg/ml). From secondary stock solution again 1ml was taken it in to another volumetric flask and made it up to 10 ml with media (working solution - 10µg/ml). The working solution was taken for determining the wavelength.

Determination of Calibration Curve:

10mg of pure drug was dissolved in 10ml methanol (primary stock solution - 1000 µg/ml). From this primary stock solution 1 ml was pipette out into 10 ml volumetric flask and made it up to 10ml with the media (Secondary stock solution – 100µg/ml). From secondary stock solution required concentrations were prepared (shown in Table 8.1 and 8.2) and those concentrations absorbance were found out at required wavelength.

Preformulation parameters

The quality of tablet, once formulated by rule, is generally dictated by the quality of physicochemical properties of blends. There are many formulations and process variables involved in mixing and all these can affect the characteristics of blends produced. The various characteristics of blends tested as per Pharmacopoeia.

Table : Formulation composition for tablets

Formulation code	API	Polymers			Diluent	Glidant	Lubricant	Total weight
	Ibuprofen	HPMC K 15M	HEC 2M	HPC 2M	MCC	Aerosil	Magnesium Stearate	
F1	100	50	-	-	235	7	8	400
F2	100	100	-	-	185	7	8	400
F3	100	150	-	-	135	7	8	400
F4	100	-	50	-	235	7	8	400
F5	100	-	100	-	185	7	8	400
F6	100	-	150	-	135	7	8	400
F7	100	-	-	50	235	7	8	400
F8	100	-	-	100	185	7	8	400
F9	100	-	-	150	135	7	8	400
All the quantities were in mg								

RESULT AND DISCUSSION:

The present study was aimed to develop controlled release tablets of Ibuprofen using various polymers. All the formulations were evaluated for physicochemical properties and *in vitro* drug release studies.

Organoleptic properties

Table : Organoleptic properties

S NO.	Properties	Results
1	State	Solid
2	Colour	white
3	Odour	Odourless
4	Melting point	75-77.5 °C

Solubility studies

Table : Solubility studies of drug in different solvents

S NO.	Solvents	Solubility of Ibuprofen
1	Water	Insoluble
2	Ethanol	Very soluble
3	Alcohol	Freely soluble

Analytical Method

Graphs of Ibuprofen were taken in 0.1N HCL and in pH 6.8 phosphate buffer at 262 nm and 266 nm respectively.

Table: Observations for graph of Ibuprofen in 0.1N HCL

Concentration (µg/ml)	Absorbance
0	0
2	0.176
4	0.314
6	0.452
8	0.593
10	0.738

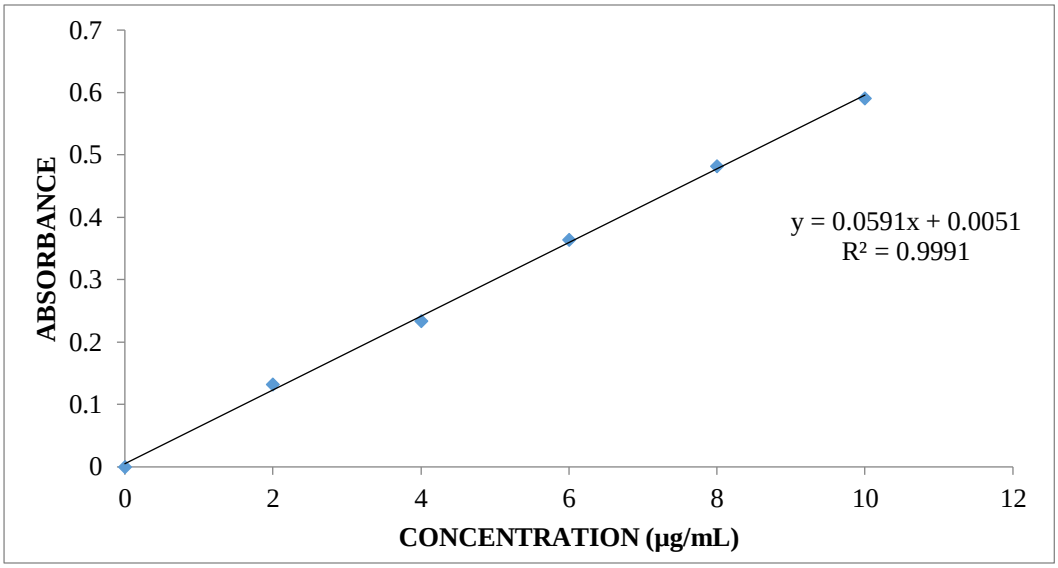

Fig : Standard curve of Ibuprofen

Table : Standard graph values of Ibuprofen at 266 nm in pH 6.8 phosphate buffer

Concentration (µg/ml)	Absorbance
0	0
2	0.132
4	0.234
6	0.364
8	0.482
10	0.591

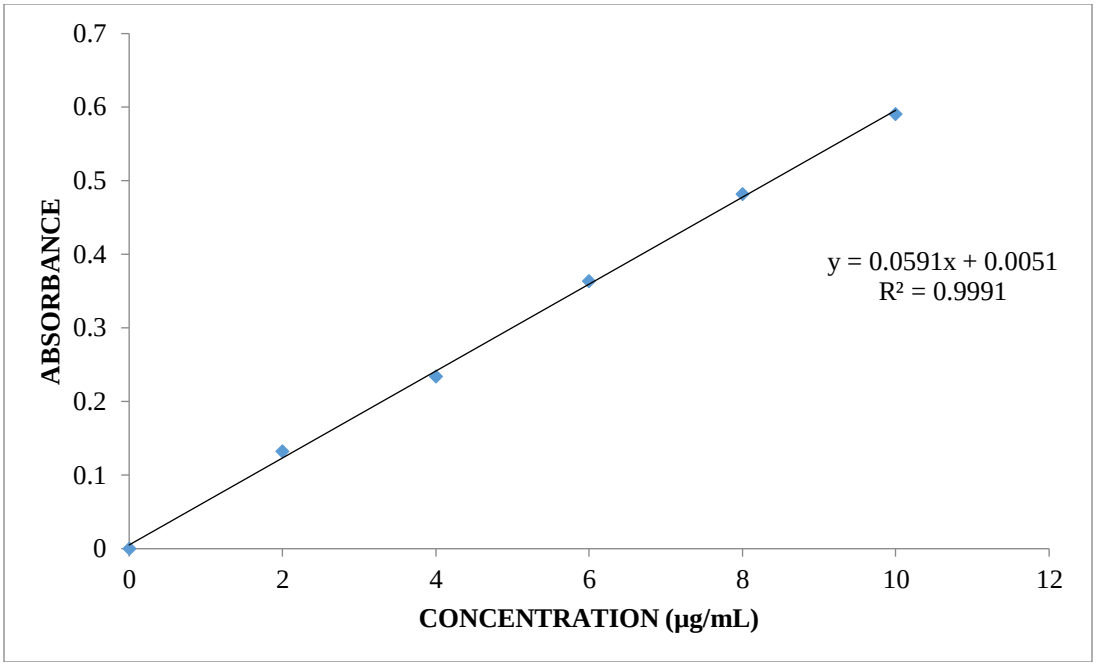

Fig : Standard curve of Ibuprofen

Preformulation parameters of powder blend

Table : Pre-formulation parameters of Core blend

Formulation code	Angle of repose (Θ)	Bulk density (gm/cm^3)	Tapped density(gm/cm^3)	Carr's index (%)	Hausner's ratio
F1	28.46	0.5710	0.6897	17.21	1.121
F2	28.48	0.5698	0.6701	14.96	1.176
F3	28.46	0.5725	0.6909	17.14	1.206
F4	28.40	0.5702	0.6782	15.92	1.189
F5	28.71	0.5620	0.6787	17.99	1.207
F6	28.70	0.5602	0.6698	17.11	1.196
F7	28.65	0.5562	0.6714	16.36	1.207
F8	28.80	0.5665	0.6813	16.85	1.203
F9	28.02	0.5581	0.6775	17.62	1.214

All the values represent n=3

Tablet powder blend was subjected to various pre-formulation parameters. The angle of repose values indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range showing that the powder has good flow properties. The tapped density of all the formulations powders has good flow properties. The compressibility index of all the formulations was found to be below 17.99 which show that the powder has good flow properties. All the formulations have shown the hausner ratio below 1.214 indicating the powder has good flow properties.

Quality Control Parameters for tablets:

Tablet quality control tests such as weight variation, hardness, friability, thickness and drug release studies in different media were performed on the compression tablet.

Table : *In vitro* quality control parameters for tablets

Formulation codes	Weight variation (mg)	Hardness (kg/cm^2)	Friability (%loss)	Thickness (mm)	Drug content (%)
F1	398.15	5.6	0.26	4.92	96.18
F2	400.25	5.3	0.32	4.69	99.82
F3	399.39	5.0	0.46	4.87	97.60
F4	397.52	4.9	0.51	4.35	99.72
F5	400.10	5.2	0.63	4.16	100.05
F6	396.57	4.8	0.72	4.61	98.76
F7	398.61	5.5	0.39	4.38	97.61
F8	399.72	5.7	0.46	4.76	98.27
F9	397.95	5.3	0.62	4.37	99.34

Weight variation test:
Tablets of each batch were subjected to weight variation test, difference in weight and percent deviation was calculated for each tablet. The average weight of the tablet is approximately in range of 396.57 to 400.25 mg, so the permissible limit is ±7.5% (>400 mg). The results of the test showed that, the tablet weights were within limit.

Hardness test:
Hardness of the three tablets of each batch was checked by using Pfizer hardness tester and the data's were shown in Table 8.4. The results showed that the hardness of the tablets is in range of 4.8 to 5.7 kg/cm^2, which was within IP limits.

Thickness:
Thickness of three tablets of each batch was checked by using Micrometer and data shown in Table-8.4. The result showed that thickness of the tablet is raging from 4.16 to 4.92 mm.

Friability:
Tablets of each batch were evaluated for percentage friability and the data were shown in the Table 8.4. The average friability of all the formulations was less than 1% as per official requirement of IP indicating a good mechanical resistance of tablets.

Drug content:
Drug content studies were performed for the prepared formulations. From the drug content studies it was concluded that all the formulations were showing the % drug content values within 96.18 – 100.05 %.
All the parameters such as weight variation, friability, hardness, thickness and drug content were found to be within limits.

***In Vitro* Drug Release Studies:**

Table : Dissolution Data of Ibuprofen Tablets

TIME (H)	CUMULATIVE % OF DRUG RELEASE								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
In dissolution media 0.1 N HCL									
0	0	0	0	0	0	0	0	0	0
0.5	20.89	18.53	15.42	31.28	21.05	16.59	19.61	15.72	13.17
1	28.19	26.10	20.91	40.17	29.79	23.12	25.07	20.91	18.93
2	39.05	34.68	26.25	45.31	36.04	32.53	36.20	26.42	23.55
In dissolution media 6.8 Phosphate Buffer									

3	49.71	43.03	38.85	53.58	43.10	40.28	45.16	30.64	28.47
4	61.14	50.96	42.96	66.76	47.65	45.10	52.92	36.80	32.24
5	68.89	61.24	57.69	72.18	54.96	50.37	59.33	41.16	40.89
6	76.63	69.73	61.52	82.44	63.25	57.05	66.96	49.77	47.51
7	83.56	76.19	76.07	90.16	78.79	62.83	70.05	54.23	51.46
8	96.12	82.88	80.61	98.90	87.91	68.95	75.60	62.15	60.89
9	98.37	87.67	86.40		92.01	74.32	79.81	67.73	65.95
10		92.78	91.31		97.84	88.08	83.37	71.81	67.11
11		97.23	94.57			98.10	93.02	87.22	72.25
12			99.08				95.38	90.64	87.37

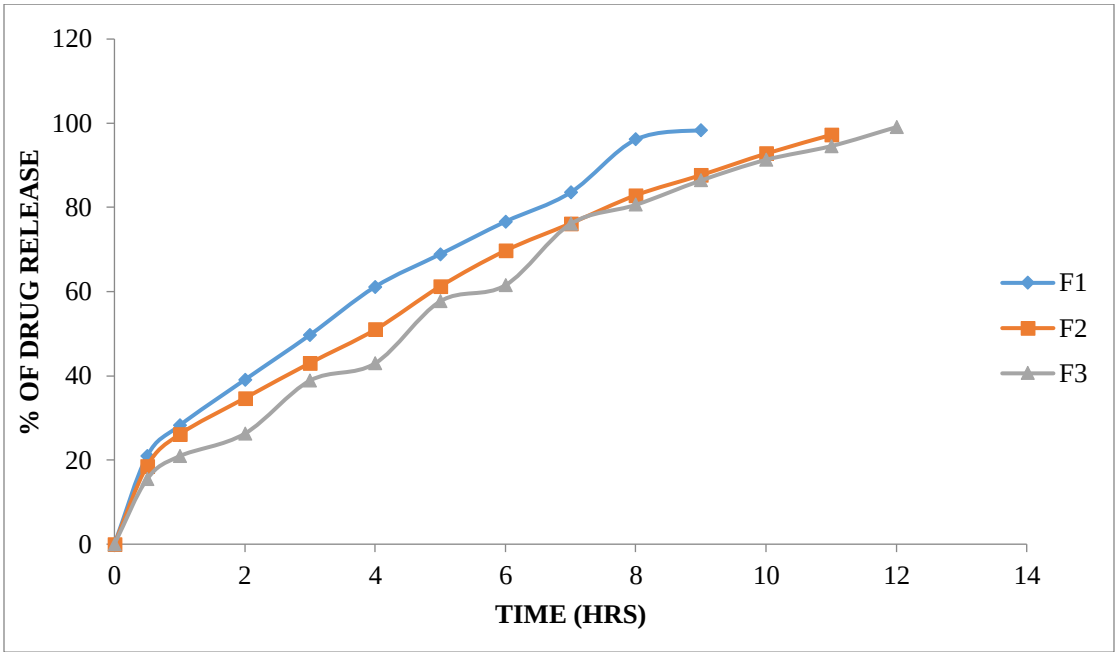

Fig : Dissolution profile of Ibuprofen (F1, F2, F3 formulations)

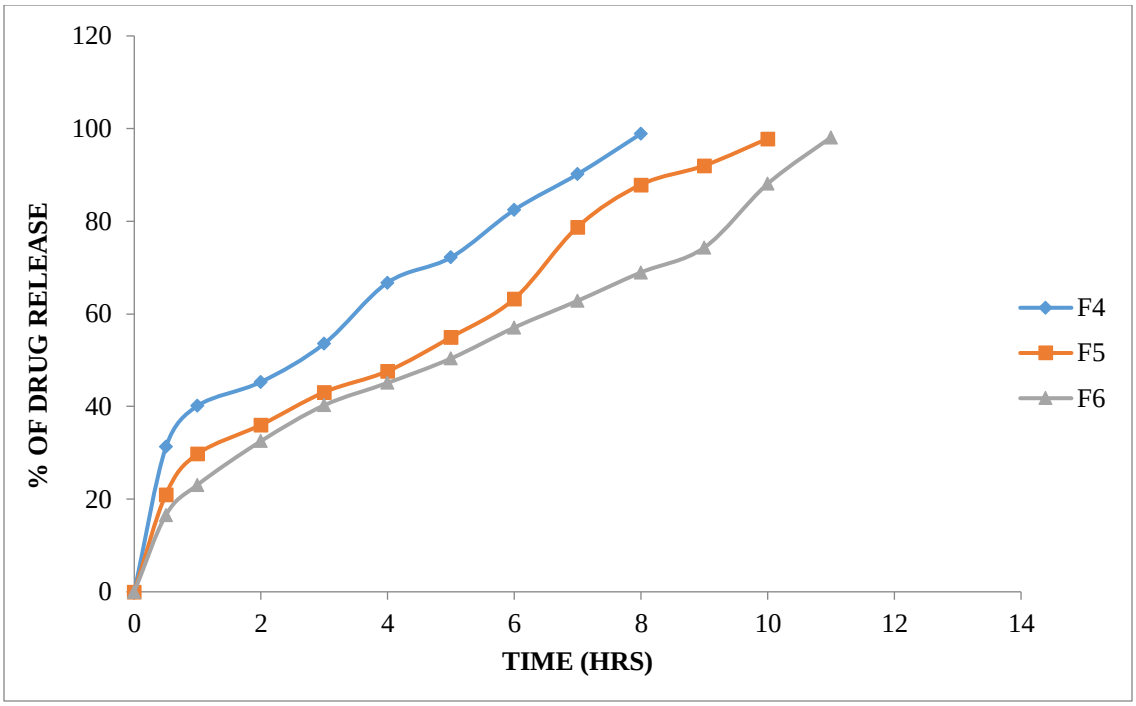

Fig : Dissolution profile of Ibuprofen (F4, F5, F6 formulations)

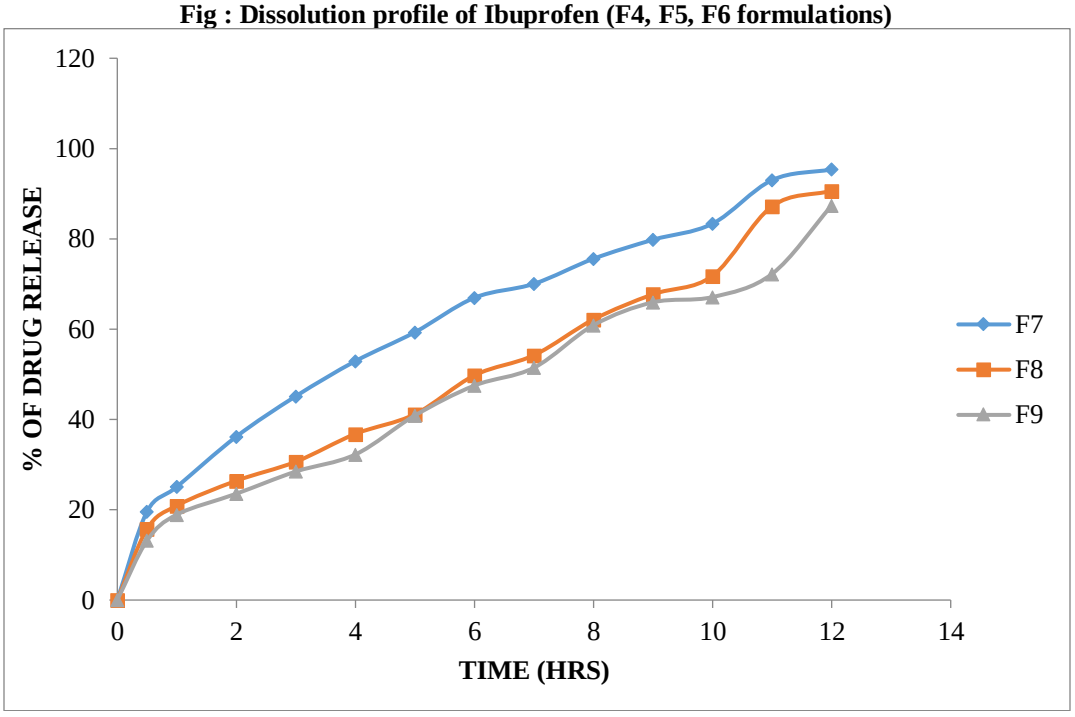

Fig : Dissolution profile of Ibuprofen (F7, F8, F9 formulations)

From the dissolution data it was evident that the formulations prepared with HPMC K 15M as polymer were retarded the drug release Less than 12 hours.

Whereas the formulations prepared with higher concentration of HEC 2M retarded the drug release up to 11 hours in the concentration 150 mg. In lower concentrations the polymer was unable to retard the drug release up to 12 hours.

The formulations prepared with HPC 2M showed good retardation capacity of drug release (95.38%) up to 12 hours in concentration 50 mg whereas high concentrations (100 mg, 150 mg) not retard the drug

release up to 12 hours. Hence they were not considered.

Only HPMC K 15M highest concentrations (150 mg) retards the drug release up to 12 hours and the drug release 99.08 % respectively. In this HPMC K 15M releases the more drug release when compared to HEC 2M and HPC 2M. So F3 Formulation considered as optimised formulation.

Hence from the above dissolution data it was concluded that F3 formulation was considered as optimised formulation because good drug release (99.08 %) in 12 hours.

Table: Release Kinetics:

CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	LOG(%) RELEASE	LOG (T)	LOG (%) REMAIN	RELEASE RATE (CUMULATIVE % RELEASE / t)	1/CUM% RELEASE	PEPPAS log Q/100	% Drug Remaining	Q01/3	Qt1/3	Q01/3-Qt1/3
0	0	0			2.000				100	4.642	4.642	0.000
15.42	0.5	0.707	1.188	-0.301	1.927	30.840	0.0649	-0.812	84.58	4.642	4.390	0.252
20.91	1	1.000	1.320	0.000	1.898	20.910	0.0478	-0.680	79.09	4.642	4.292	0.349
26.25	2	1.414	1.419	0.301	1.868	13.125	0.0381	-0.581	73.75	4.642	4.194	0.448
38.85	3	1.732	1.589	0.477	1.786	12.950	0.0257	-0.411	61.15	4.642	3.940	0.702
42.96	4	2.000	1.633	0.602	1.756	10.740	0.0233	-0.367	57.04	4.642	3.849	0.792
57.69	5	2.236	1.761	0.699	1.626	11.538	0.0173	-0.239	42.31	4.642	3.485	1.157
61.52	6	2.449	1.789	0.778	1.585	10.253	0.0163	-0.211	38.48	4.642	3.376	1.266
76.07	7	2.646	1.881	0.845	1.379	10.867	0.0131	-0.119	23.93	4.642	2.882	1.760
80.61	8	2.828	1.906	0.903	1.288	10.076	0.0124	-0.094	19.39	4.642	2.687	1.955
86.4	9	3.000	1.937	0.954	1.134	9.600	0.0116	-0.063	13.6	4.642	2.387	2.255
91.31	10	3.162	1.961	1.000	0.939	9.131	0.0110	-0.039	8.69	4.642	2.056	2.586
94.57	11	3.317	1.976	1.041	0.735	8.597	0.0106	-0.024	5.43	4.642	1.758	2.884
99.08	12	3.464	1.996	1.079	-0.036	8.257	0.0101	-0.004	0.92	4.642	0.973	3.669

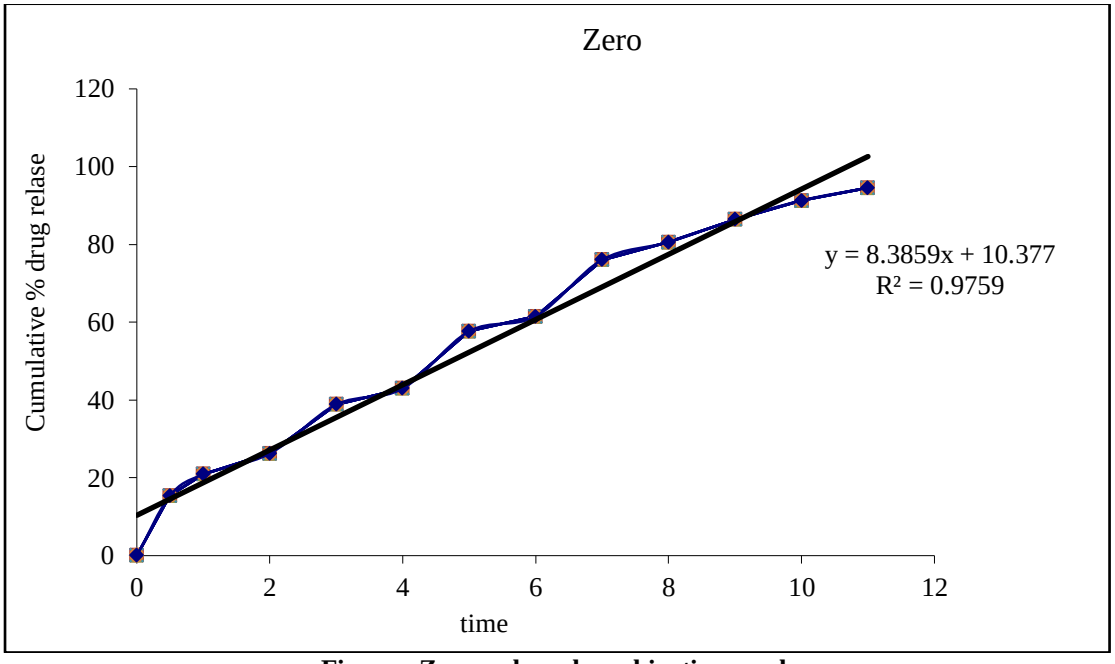

Figure : Zero order release kinetics graph

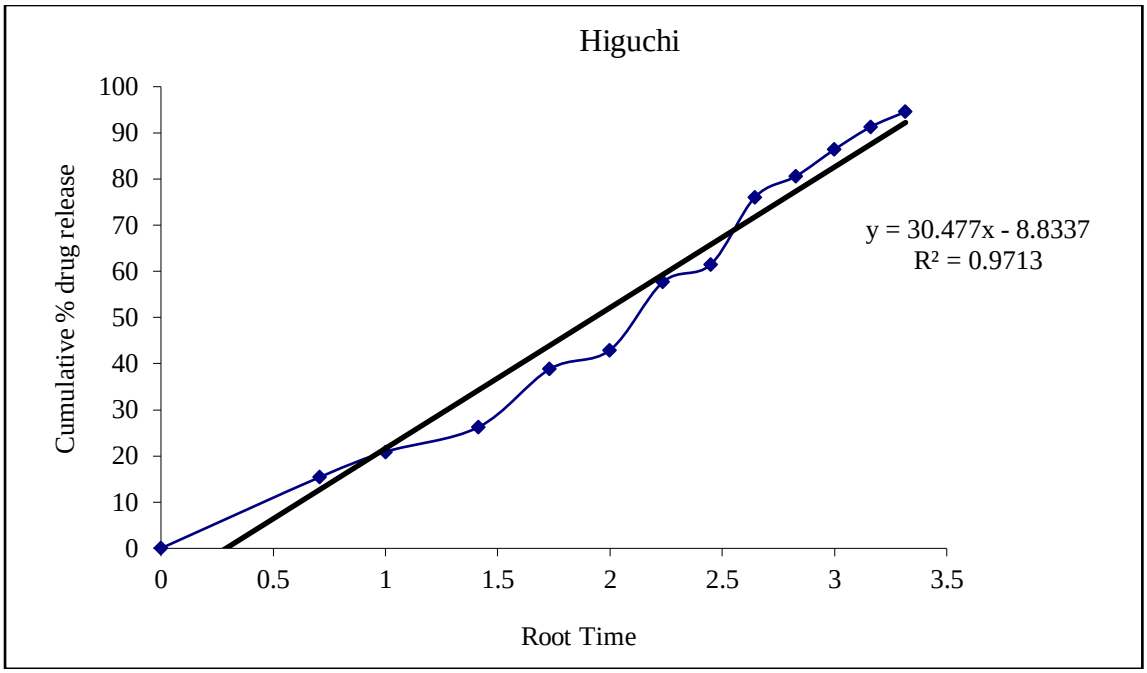

Figure : Higuchi release kinetics graph

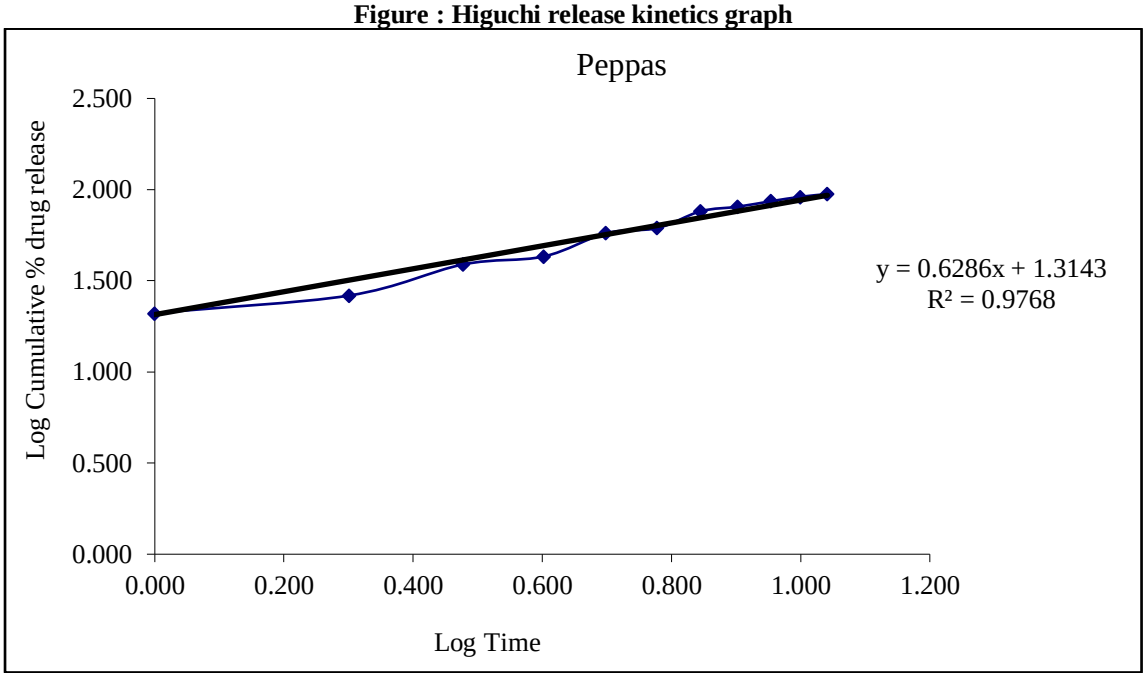

Figure : Peppas release kinetics graph

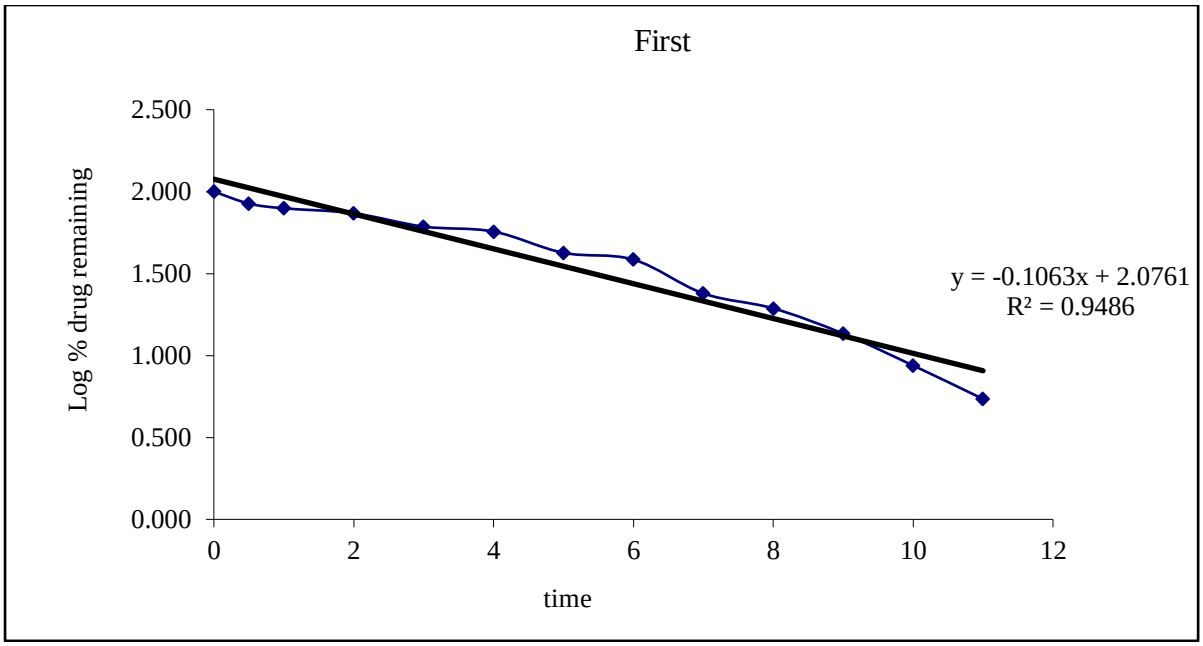

Figure : First order release kinetics graph

Optimised formulation F3 was kept for release kinetic studies. From the above graphs it was evident that the formulation F3 was followed Peppas release kinetics mechanism.

Drug – Excipient compatability studies

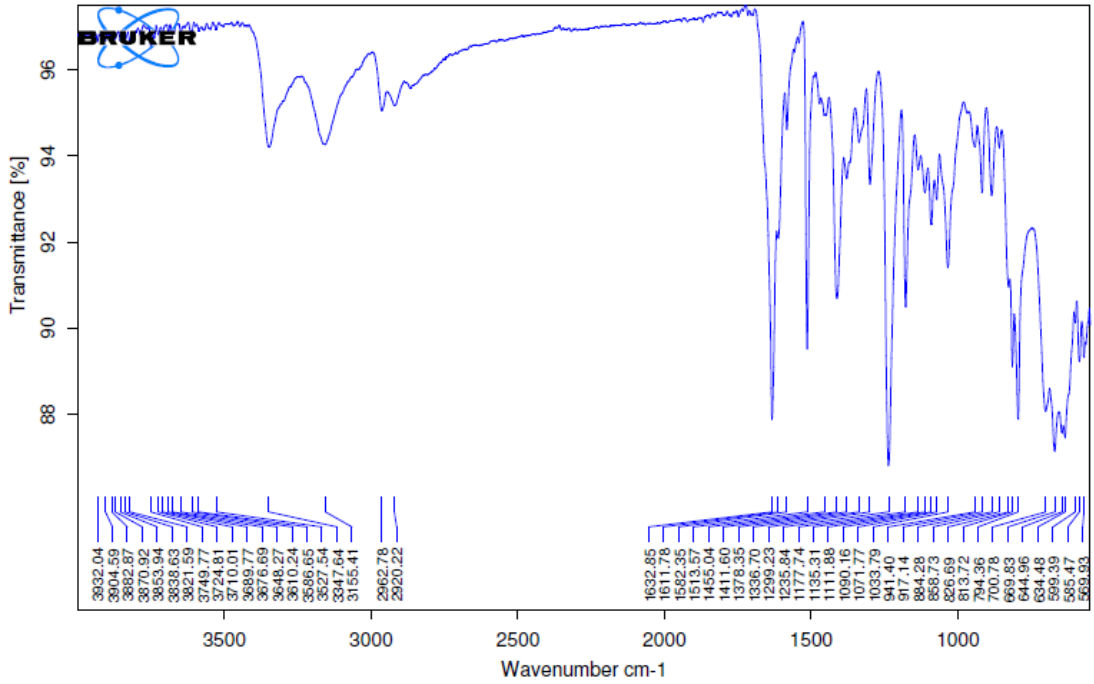

Figure : FT-TR Spectrum of Ibuprofen pure drug

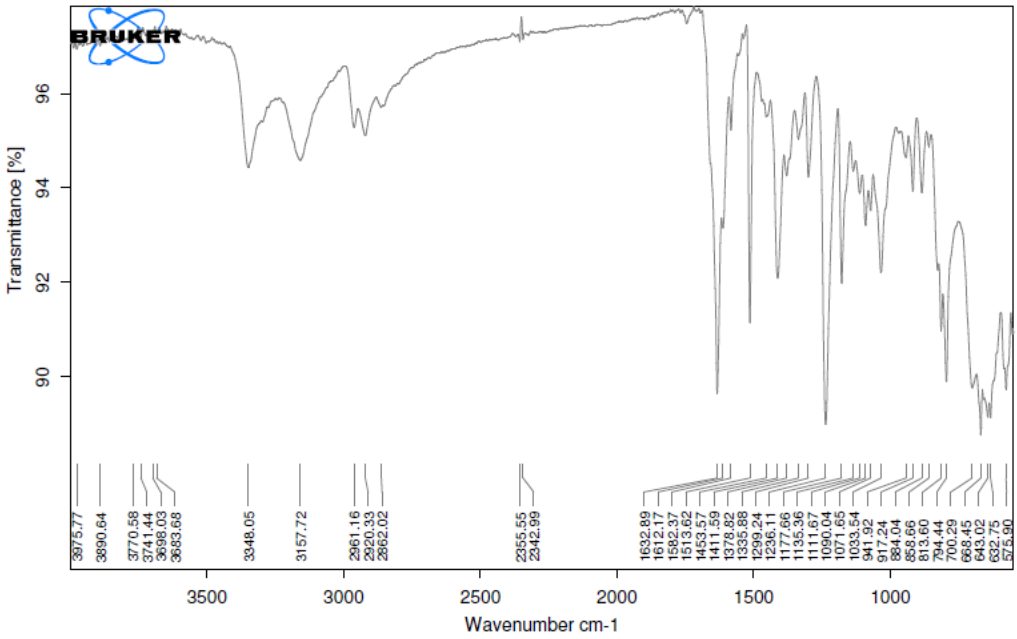

Figure: FT-IR Spectrum of Optimised Formulation

There was no disappearance of any characteristics peak in the FTIR spectrum of drug and the polymers used. This shows that there is no chemical interaction between the drug and the polymers used. The presence of peaks at the expected range confirms that the materials taken for the study are genuine and there were no possible interactions.
Ibuprofen is also present in the physical mixture, which indicates that there is no interaction between drug and the polymers, which confirms the stability of the drug.

CONCLUSION:

Morphological characteristics such as colour, odour, form etc; of Ibuprofen were studied. As the API is found to be white colour and odourless.

The Melting point of Ibuprofen lies in the range between 75-77.5 ˚C, which indicates the purity of the drug.
The solubility of Ibuprofen was analysed in various solvents.

Flow properties of API were studied by performing tests like Angle of repose, bulk density, tapped density, Carr's index, Hausner's ratio. The results indicate that Angle of repose indicating good flow properties. The Carr's index was found to be 17.62% indicating fair to passable. The Hausner's ratio was within the limits indicating free flowability. These results indicated the drug possessed good flow properties and compressible characteristics.

IR spectra of physical mixture of drug and excipients, drug alone showed no significant shift or reduction in intensity of peaks of Ibuprofen. The studies showed that there was no interaction or physical change between the drug and excipients. So the selected excipients were found to be compatible with the drug.

Estimation of Ibuprofen was performed by UV spectrophotometric method. The method obeyed Beer's of drug and law in the concentration range of 0-10µg/ml. Thus the method was found to be suitable for estimation of Ibuprofen content in various products and in vitro dissolution studies.

Ibuprofen along with other excipients was formulated into tablets by direct compression methods as per the formulae given in the table no7.3. HPMC K 15M, HEC 2M and HPC 2M polymers was used in graded amounts as to control the rate of release.

Tablet quality control tests such as weight variation, hardness, friability, thickness and drug release studies in different media were performed on the compression tablet and found within the limits.
Among all the tablets formulated, formulation F3 prepared by direct compression method gave the highest dissolution (99.08%) in a controlled release manner. So formulation F3 was considered as best and optimized for the preparation of tablets of Ibuprofen prepared by direct compression methods.

REFERENCES:

1. Altaf AS, Friend DR, MASRx and COSRx. Sustained-Release Technology in Rathbone MJ, Hadgraft J, Robert MS, Modified Release Drug Delivery Technology, Marcell Dekker Inc., New York, 2003; 1: 102-117.
2. Reddy KR., Mutalik S, Reddy S. AAPS Pharm. Sci. Tech.2003; 4: 19. 121-125.
3. Mohammed AD et al. Release of propranolol hydrochloride from matrix tablets containing sodium carboxymethylcellulose and Hydroxypropyl methyl cellulose. Pharm Dev Tech.1999; 4: 313-324.
4. Salsa T, Veiga F. Drug Develop. Ind Pharm. 1997; 23: 931.
5. Jantzen GM, Robinson JR, Sustained and controlled-release drug delivery systems, inBanker GS, Rhodes CT (Eds.) Modern Pharmaceutics, 3rd Ed, Revised andExpanded, Drugs and the Pharmaceutical Sciences., Marcell Dekker, Inc. NewYork. 1995; 72: 575-609.
6. Jantzen GM, Robinson JR. Sustained and Controlled- Release Drug Delivery systems Modern Pharmaceutics, 4thed; 2003; 121: 501-502.
7. Lee BJ, Ryu SG, Cui JH, Drug Dev. Ind.Pharm.1999; 25: 493-501.
8. Gwen MJ, Joseph RR, In Banker GS and Rhodes CT, Ed. Modern Pharmaceutics, 3rdEd Marcel Dekker Inc. New York. 1996; 72: 575.
9. Vidyadhara S, Rao PR, Prasad JA. Indian J Pharm Sci. 2004; 66: 188-192.
10. Bogner RH. Bioavailability and bioequivalence of extended-release oral dosage forms. US Pharmacist. 1997; 22: 3–12.
11. Rogers JD, Kwan KC. Pharmacokinetic requirements for controlled-release dosage forms. In: John Urquhart, ed. Controlled-release Pharmaceuticals. Academy of Pharmaceutical Sciences. American Pharmaceutical Association. 1979: 95–119.
12. Madan PL. Sustained-release drug delivery systems, part II: Preformulation considerations. Pharm Manu fact. 1985; 2: 41–45.
13. Wani MS, Controlled Release System-A Review, 2008; 6 1: 56-62.
14. Banker GS, Anderson NR. The Theory and Practice of Industrial Pharmacy: Tablet,Lachman, (3rded) Varghese Publishing House, Bombay. 1990; 3: 293-303.
15. Lee VHL, Controlled Drug Delivery Fundamentals and Applications: Influence of drug properties on design, Marcel Dekker, INC, and New York. 1987; 2: 16-29.
16. Manish R, Jayesh P, Siahboomi AR. Hydrophilic Matrices for Oral Extended Release: Influence of Fillers on Drug Release from HPMC Matrices. Pharma Times. 2010; 42(04): 67-73.
17. Kumar KP et al. Innovations in Sustained Release Drug Delivery System and Its Market Opportunities. J Chem Pharm Res. 2010; 2 1: 349-360.
18. Brahmankar DM, Sunil B. Jaishwal. “Controlled release medication” chapter 15th in “Bio pharmaceutics and Pharmacokinetics – A Treatise, 1st ed, 2010; 1: 347- 353.
19. Stanley S. Davis, Formulation strategies for abs windows. Drug Discovery Today, 2005; 10: 249-257.
20. Modi SA et al. Sustained Release Drug Delivery System:A Review.Int J Pharma. Res Dev. 2011; 2 (12): 147-160.