CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
SJIF Impact Factor: 7.187

Available online at: http://www.iajps.com Research Article

FORMULATION AND EVALUATION OF XANTHAN GUM MICROSPHERES FOR THE SUSTAINED RELEASE OF FLURBIPROFEN

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Abstract:
The aim of the study was to prepare Flurbiprofen microspheres using Solvent evaporation method using different polymer ratio. FT-IR studies revealed that there was no chemical interaction between the drug and polymer. The average particle size of the optimized formulation was found to be 166 µm. The in-vitro release behavior from all the Nifedipine microspheres was found to be peppas drug release kinetics and produced a sustained release over a period of 12 hours with better entrapment efficiency.
Key words: *Flurbiprofen, Carbopol 934p, Xanthan Gum, Solvent evaporation method and microspheres.*

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Please cite this article in press ***Dhumala Ruthisha*** *et al.,* ***Formulation And Evaluation Of Xanthan Gum Microspheres For The Sustained Release Of Flurbiprofen*** *, Indo Am. J. P. Sci, 2025; 12(10).*

1. INTRODUCTION:

Oral route drug administration is by far the most preferable route for taking medications. However, their short circulating half life and restricted absorption via a defined segment of intestine limits the therapeutic potential of many drugs. Such a pharmacokinetic limitation leads in many cases to frequent dosing of medication to achieve therapeutic effect. Rational approach to enhance bioavailability aSnd improve pharmacokinetic and pharmacodynamics profile is to release the drug in a controlled manner and site specific manner. Microspheres are small spherical particles, with diameters 1 µm to 1000 µm. They are spherical free flowing particles consisting of proteins or synthetic polymers which are biodegradable in nature. There are two types of microspheres; microcapsules and micromatrices, which are described as, Microcapsules are those in which entrapped substance is distinctly surrounded by distinct capsule wall. and micromatrices in which entrapped substance is dispersed throughout the matrix. Microspheres are sometimes referred to as microparticles. Microspheres can be manufactured from various natural and synthetic materials. Microsphere play an important role to improve bioavailability of conventional drugs and minimizing side effects. Ideal characteristics of microspheres: [1,2,3,4,5]

Ideal characteristics of microspheres: [6]

- ✓ The ability to incorporate reasonably high concentrations of the drug.
- ✓ Stability of the preparation after synthesis with clinically acceptable shelf life.
- ✓ Controlled particle size and dispersability in aqueous vehicles for injection.
- ✓ Release of active reagent with a good control over a wide time scale.
- ✓ Biocompatibility with a controllable biodegradability.
- ✓ Susceptibility to chemical modification.

Advantages of microspheres:

1. Particle size reduction for enhancing solubility of the poorly soluble drug.
2. provide constant and prolonged therapeutic effect.
3. provide constant drug concentration in blood there by increasing patent compliance,
4. Decrease dose and toxicity.
5. Protect the drug from enzymatic and photolytic cleavage hence found to be best for drug delivery of protein.
6. Reduce the dosing frequency and thereby improve the patient compliance
7. Better drug utilization will improve the bioavailability and reduce the incidence or intensity of adverse effects.
8. Microsphere morphology allows a controllable variability in degradation and drug release.
9. Convert liquid to solid form & to mask the bitter taste.
10. Protects the GIT from irritant effects of the drug.
11. Biodegradable microspheres have the advantage over large polymer implants in that they do not require surgical procedures for implantation and removal.
12. Controlled release delivery biodegradable microspheres are used to control drug release rates thereby decreasing toxic side effects, and eliminating the inconvenience of repeated injections.

Limitation:

Some of the disadvantages were found to be as follows

1. The costs of the materials and processing of the controlled release preparation, are substantially higher than those of standard formulations.
2. The fate of polymer matrix and its effect on the environment.
3. The fate of polymer additives such as plasticizers, stabilizers, antioxidants and fillers.
4. Reproducibility is less.
5. Process conditions like change in temperature, pH, solvent addition, and evaporation/agitation may influence the stability of core particles to be encapsulated.
6. The environmental impact of the degradation products of the polymer matrix produced in response to heat, hydrolysis, oxidation, solar radiation or biological agents.

MATERIALS AND METHODS:

Flurbiprofen	Provided by SURA LABS, Dilsukhnagar, Hyderabad
Carbopol 934p	Merk specialiities Pvt Limited, Mumbai
Xanthan Gum	Chemical Drug House, New Delhi
Dichloromethane	Chemical Drug House, New Delhi
Methanol	Chemical Drug House, New Delhi
Sodium lauryl sulphate	Chemical Drug House, New Delhi

INSTRUMENTS

UV-Visible spectrophotometer	Lab India, India
Electronic weighing balance	Sartorious
Magnetic stirrer	Remi Laboratories
Dissolution Apparatus	Lab India, Lab India
Ultrasonic cleaner	Remi Laboratories
FT – IR Spectrometer	Bruker Alpha
SEM	SEM(JEOL Ltd.,Japan).

7. METHODOLOGY

PREPARATION OF 0.1N HCl (pH 1.2):

Take 8.5 ml of HCl in a 1000ml volumetric flask and make up the volume with distilled water.

Preparation of 0.2M NaOH Solution:

Dissolve 2g of sodium hydroxide pellets in 250mL of water and mixed well.

Preparation of pH 6.8 Phosphate Buffer:

Weigh and dissolve 6.8g of Potassium dihydrogen orthophosphate and 0.89g of sodium hydroxide pellets to 1000mL of water and mixed well. Adjusted

the pH of this solution to 6.8 with 0.2M NaOH solution.

Preparation of Standard Calibration Curve of Flurbiprofen:

- ✓ 10 mg of Flurbiprofen was accurately weighed and dissolved in 10ml of methanol (Stock Solution –I) to get a concentration of 1000 µg/ml.
- ✓ From the stock solution-I, 1ml of aliquots was taken and suitably diluted with 0.1N HCl (Stock Solution-II) to get concentrations of 100µg/ml.
- ✓ From the stock solution-II, aliquots were taken and suitably diluted with 0.1N HCl (pH 1.2) to get concentrations in the range of 2 to 10µg/ml. The absorbance of these samples were analyzed by using UV-Visible Spectrophotometer at 231nm against reference solution 0.1N HCl (pH 1.2). The procedure repeated to pH 6.8 phosphate buffer and pH 6.8 phosphate buffer.

METHOD OF PREPARATION

Flurbiprofen microspheres were prepared using, Carbopol 934p and Xanthan Gum and distilled water as continuous phase by solvent evaporation technique. Initially dichloromethane (DCM) and methanol was mixed uniformly at room temperature, then Carbopol 934p and Xanthan Gum in various proportions was dissolved in the above solution. To this mixture, a drug solution corresponding was added and mixed thoroughly and injected drop wise in to the continuous phase consisting of 100mL of 0.2% (w/v) SLS (Sodium Lauryl sulphate) at 250 rpm. The microspheres obtained was washed for 2-3 times with distilled water and dried at room temperature. Different concentrations and ratios of polymers used in the formulation of microspheres are mentioned in Table.

Table 7.1: Formulation chart

INGREDIENTS (MG)	FORMULATIONS					
	F1	F2	F3	F4	F5	F6
Flurbiprofen	50	50	50	50	50	50
Carbopol 934p	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%
Xanthan Gum	0.1%	0.15%	0.2%	0.25%	0.3%	0.35%
Dichloromethane (mL)	20	20	20	20	20	20
Methanol (mL)	30	30	30	30	30	30
Sodium lauryl sulphate (mg)	25	25	25	25	25	25

Fourier Transform Infrared (FTIR) spectroscopy:

The physical properties of the physical mixture were compared with those of plain drug. Samples was mixed thoroughly with 100mg potassium bromide IR powder and compacted under vacuum at a pressure of about 12 psi for 3 minutes. The resultant disc was mounted in a suitable holder in Agilent spectrophotometer and the IR spectrum was recorded from 4000 cm-1 to 500 cm-1. The resultant spectrum was compared for any spectrum changes.

SEM (Scanning Electron Microscope) studies:

The surface morphology of the layered sample was examined by using SEM (JEOL Ltd.,Japan). The small amount of powder was manually dispersed onto a carbon tab (double adhesive carbon coated tape) adhered to an aluminum stubs were coated with a thin layer (300A) of gold by employing POLARON - E 3000 sputter coater. The samples were examined by SEM with direct data capture of the images on to a computer.

Powder X-ray Diffraction (PXRD) Studies

The prepared mixtures were also analyzed using X-ray powder diffractometer (PXRD) which confirms the formation of the new solid phases. The difference in the 2 theta lines confirms the formation of the new solid phases as no two solids have same 2 theta lines, thus revealing the formation of new solid phases. It also reveals the information about the crystal structure, chemical composition, and physical properties of the material and also helps in structural characterization. This technique detects changes in the crystal lattice and is therefore a powerful tool for studying polymorphism, pharmaceutical salts, and co crystalline phases. Spectra of PXRD were taken on a sample stage Spinner PW3064. The samples were exposed to nickel filtrate Cukœ radiations (40 KV, 30 mA) and were scanned from 10° to 40° , 2Θ at a step size of 0.045° and step time of 0.5 s.

DIFFERENTIAL SCANNING CALORIMETRY (DSC):

The possibility of any interaction between the drug and the polymer during preparation of tablets was assessed by carrying out thermal analysis of drug and polymer alone as well as physical mixture. DSC analysis was performed using Hitachi DSC 7020, on 5 to 15 mg samples. Samples were heated in sealed aluminum pan at a rate of 10°C/min conducted over a temperature range of 30 to 350°C under a nitrogen flow of 50 mL/min.

Zeta Potential:

Zeta capability becomes anticipated on the premise of electrophoretic mobility under an electric powered field, the use of zeta Sizer Nano ZS (Malvern Instruments, UK). For the Zeta ability measurement, Samples have been diluted as 1:40 ratio with filtered water (v/v) before analysis. zeta potential have been then measured in triplicate.

8. RESULTS AND DISCUSSION:

8.1. PREFORMULATION STUDIES

8.1.1. SPECTROSCOPIC STUDIES

Determination of λmax

A solution of 10µg/ml of Flurbiprofen was scanned in the range of 200 to 400nm. The drug exhibited a λmax at 231 nm in simulated gastric fluid pH 1.2 and pH 7.4 phosphate buffer respectively. Correlation between the concentration and absorbance was found to be near to 0.998, with a slope of 0.028 and intercept of 0.004.

Calibration curve of Flurbiprofen in simulated gastric fluid pH 1.2

Table 8.1 shows the calibration curve data of Flurbiprofen in simulated gastric fluid pH 1.2 at 231 nm Fig.8.1 shows the standard calibration curve with a regression value of 0.997, slope of 0.071 and intercept of 0.015 in simulated gastric fluid pH 1.2.

Table 8.1: Calibration curve data for Flurbiprofen in simulated gastric fluid pH 1.2

CONCENTRATION (µg /ml)	ABSORBANCE
0	0
2	0.167
4	0.306
6	0.459
8	0.579
10	0.718

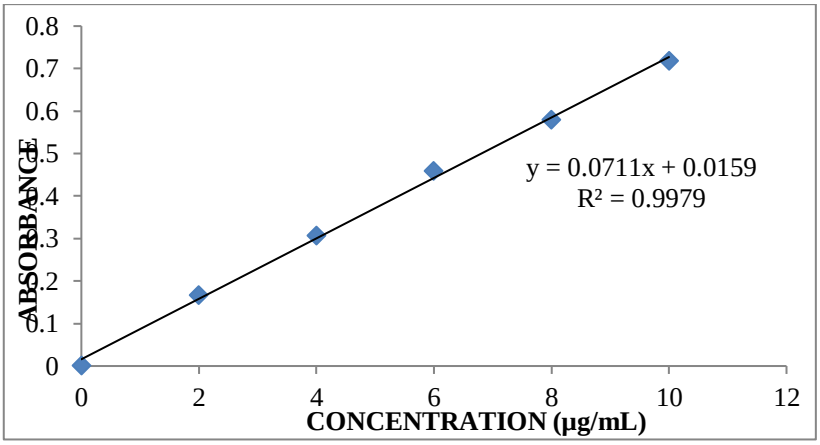


Figure 8.1: Standard graph Of Flurbiprofen in simulated gastric fluid pH 1.2

Calibration curve of Flurbiprofen in pH 6.8 phosphate buffer

Table 8.2 shows the calibration curve data of Flurbiprofen in pH 6.8 phosphate buffer at 232nm. Fig. 8.2 shows the standard calibration curve with a regression value of 0.998, slope of 0.075 and intercept of 0.015 in simulated gastric fluid pH 1.2. The curve was found to be linear in the concentration range of 2-10µg/ml.

Table 8.2: Calibration curve data for Flurbiprofen in pH 6.8 phosphate buffer

CONCENTRATION (µg /ml)	ABSORBANCE
0	0
2	0.185
4	0.319
6	0.471
8	0.622
10	0.769

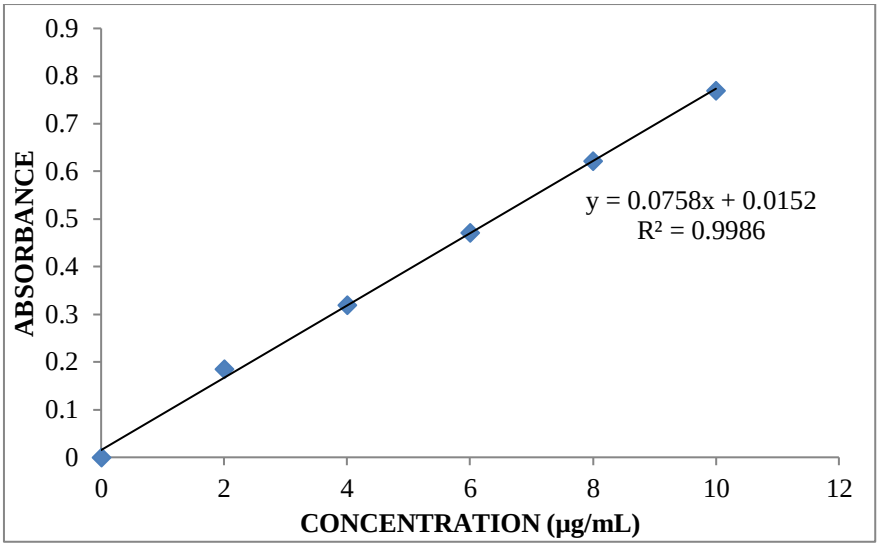


Figure 8.2: Standard graph of Flurbiprofen in pH 6.8 phosphate buffer

Evaluation and characterization of microspheres

Micrometric Properties

The mean size increased with increasing polymer concentration which is due to a significant optimum in the viscosity, thus leading to an increased droplet size and finally a higher microspheres size. Microspheres containing Carbopol 934p and Xanthan Gum as polymer exhibited a size range between 125±0.01µm to 191±0.09µm.

The particle size data is presented in Tables 8.3 and displayed in Figures. The effect of drug to polymer ratio on particle size is displayed in Figure. The particle size as well as % drug entrapment efficiency of the microspheres increased with increase in the polymer concentration.

The bulk density of formulation F1 to F6 containing Eudragit, Carbopol 934p and Xanthan Gum formulation was in the range of 0.50 to 0.59 gm./cm^3 (as shown in table 8.3), tapped density 0.57 to 0.73 and hausners ratio 1.135 to 1.237.

The carr's index of formulation F1 to F6 containing different grades of Carbopol 934p and Xanthan Gum 12.28 to 19.18 respectively. The angle of repose of formulation F1 to F6 containing, Carbopol 934p and Xanthan Gum formulation was in the range <31.45 respectively (as shown in table 8.3) The values of carr's index and angle of repose indicate good flow properties.

Table 8.3: Micromeritic property of microspheres of Flurbiprofen

Formulation code	Mean particle size	Bulk density (gm./cm^3)	Tapped density (gm./cm^3)	Hausner's ratio	Carr's index	Angle of repose
F1	125±0.01	0.59	0.73	1.237	19.18	31.45
F2	171±0.06	0.58	0.71	1.224	18.31	30.64
F3	187±0.05	0.58	0.70	1.207	17.14	30.05
F4	191±0.09	0.50	0.57	1.140	12.28	23.49
F5	166±0.02	0.52	0.59	1.135	11.86	23.82
F6	137±0.08	0.53	0.62	1.170	14.52	24.50

Percentage yield

It was observed that as the polymer ratio in the formulation increases, the product yield also increases. The low percentage yield in some formulations may be due to blocking of needle and wastage of the drug- polymer solution, adhesion of polymer solution to the magnetic bead and microspheres lost during the washing process. The percentage yield was found to be in the range.

Drug entrapment efficiency

Percentage Drug entrapment efficiency of Flurbiprofen ranged from 72.90 to 90.45 % for microspheres containing Carbopol 934p and Xanthan Gum polymer, the drug entrapment efficiency of the prepared microspheres increased progressively with an increase in proportion of the respective polymers. Increase in the polymer concentration increases the viscosity of the dispersed phase. The particle size increases exponentially with viscosity. The higher viscosity of the polymer solution at the highest polymer concentration would be expected to decrease the diffusion of the drug into the external phase which would result in higher entrapment efficiency. The % drug entrapment efficiency of the prepared microspheres is displayed in Table 8.4, and displayed in Figures.

Table 8.4: Percentage yield and percentage drug entrapment efficiency of the prepared microspheres

Formulation code	% yield	Drug Content (mg)	% Drug entrapment efficiency	Zeta Potential (mV)
F1	96.25	96.14	72.90	-22.12
F2	86.21	98.39	84.63	-25.81
F3	90.14	98.50	90.25	-25.52
F4	94.31	97.19	82.70	-24.25
F5	97.35	99.24	89.12	-38.55
F6	97.51	98.76	90.45	-22.83

Swelling studies

The swelling ratio is expressed as the percentage of water in the hydrogel at any instant during swelling. Swell ability is an important characteristic as it affects mucoadhesion as well as drug release profiles of polymeric drug delivery systems. Swellability is an indicative parameter for rapid availability of drug solution for diffusion with greater flux. Swellability data revealed that amount of polymer plays an important role in solvent transfer. It can be concluded from the data shown in Table 8.5 that with an increase in polymer concentration, the percentage of swelling also increases. Thus we can say that amount of polymer directly affects the swelling ratio. As the polymer to drug ratio increased, the percentage of swelling increased from 12.33 to 34.26 %. The percentage of swelling of the prepared microspheres is displayed in Figures. The effect of drug to polymer ratio on percentage swelling is displayed in Table.

Table 8.5: Swelling studies

S.NO.	FORMULATION CODE	INITIAL (Wt)	FINAL (Wt)	PERCENTAGE SWELLING
1	F1	15	16.85	12.33
2	F2	15	18.92	16.13
3	F3	15	20.14	34.26
4	F4	15	17.33	15.53
5	F5	15	18.24	21.6
6	F6	15	20.82	38.8

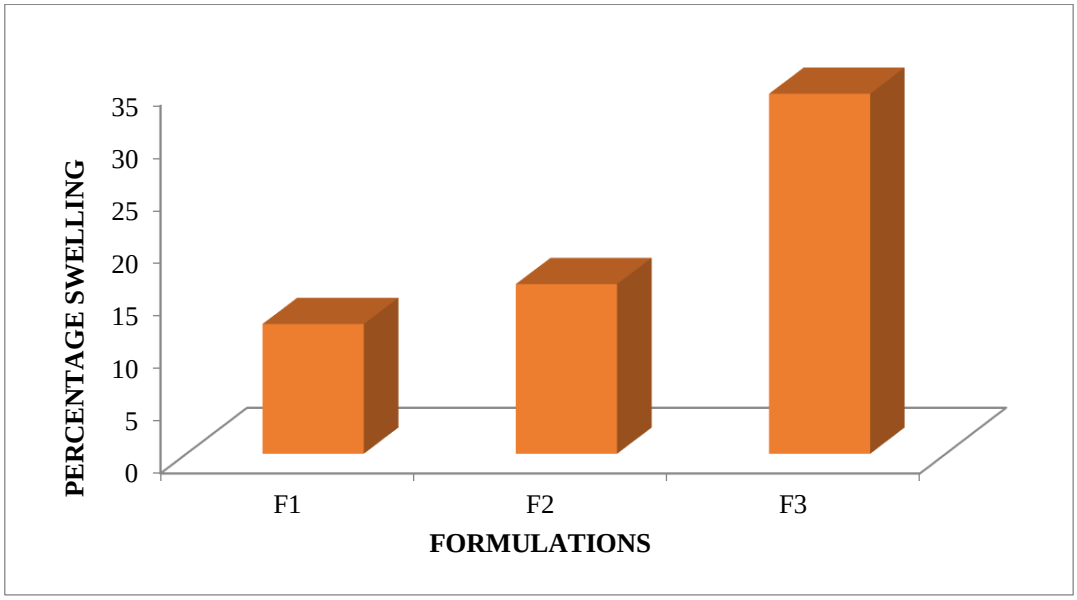


Figure 8.3 : Percentage swelling of microspheres containing Carbopol 934p and Xanthan Gum

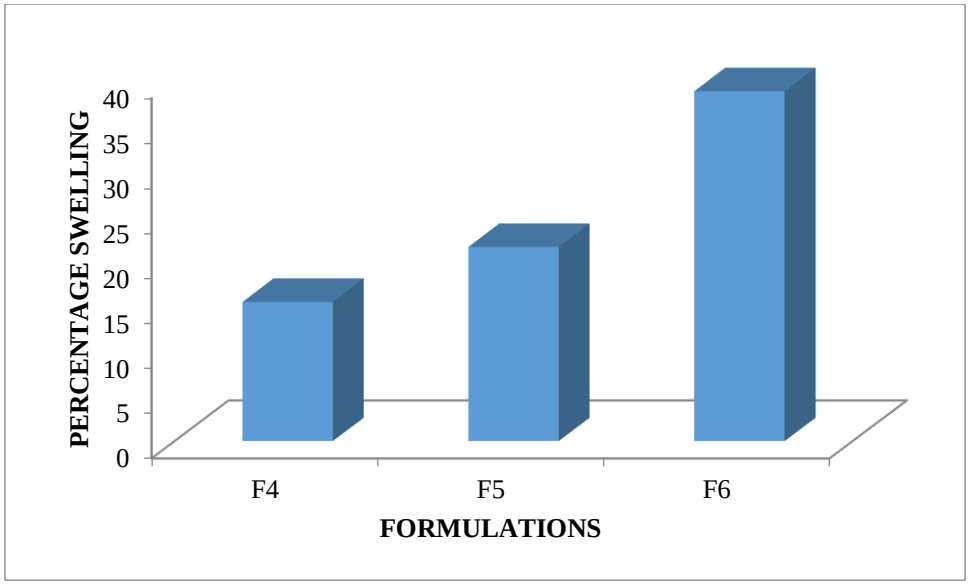


Figure 8.4 : Percentage swelling of microspheres containing Carbopol 934p and Xanthan Gum

***IN VITRO* MUCOADHESION TEST**

As the polymer to drug ratio increased, microspheres containing Eudragit, Carbopol 934p and HPMC exhibited % mucoadhesion ranging from 72.75 to 96.25 %, the results of *in-vitro* mucoadhesion test are compiled in Table 8.6.

Table 8.6: *In Vitro* Mucoadhesion Test of all Formulations

S.NO.	FORMULATION CODE	No. OF MICROSPHERES		PERCENTAGE MUCOADHESION
		INITIAL	FINAL	
1	F1	20	14.55	72.75
2	F2	20	16.12	80.60
3	F3	20	18.14	90.7
4	F4	20	18.92	94.60
5	F5	20	19.25	96.25
6	F6	20	15.72	78.60

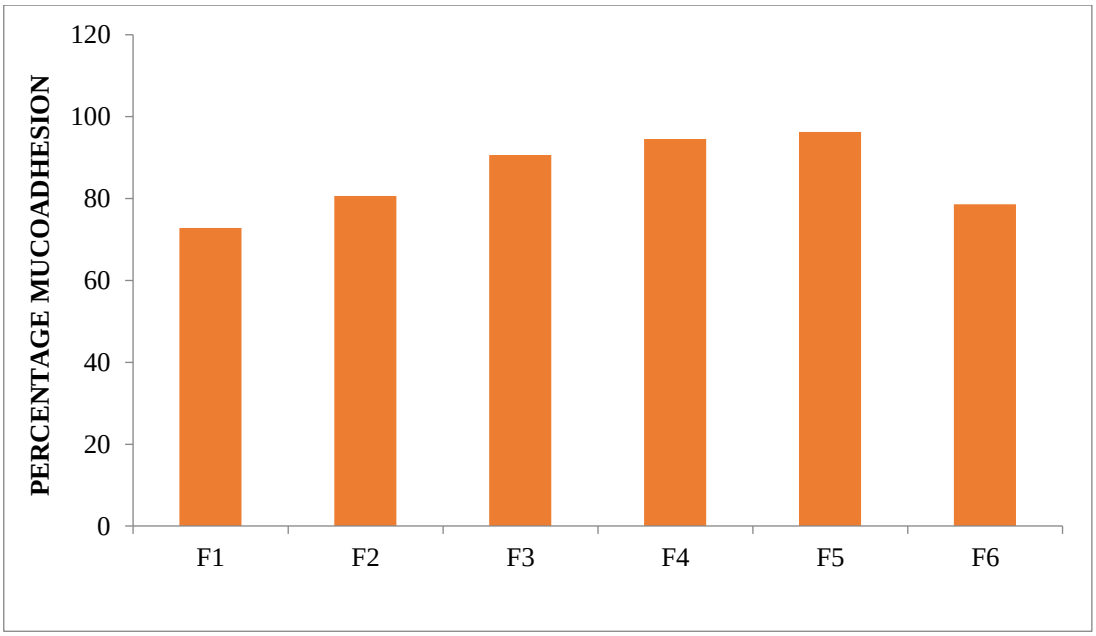


Figure 8.6: Percentage mucoadhesion of microspheres

***IN-VITRO* DRUG RELEASE STUDIES**

Dissolution studies of all the formulations were carried out using dissolution apparatus USP type I. The dissolution studies were conducted by using dissolution media, pH 1.2. The results of the *in-vitro* dissolution studies of formulations F1 to F6 are shown in below table. The plots of Cumulative percentage drug release Vs Time.

The formulations F1, F2, and F3 containing Carbopol 934p and Xanthan Gum showed a maximum release of 79.70 % at 12 hours, 87.91 % after 12 hours, 91.53% 12 hours respectively.

The formulations F4, F5, and F6 showed a maximum release of 97.29 % at 12 hours, 99.72 % after 12 hours, 86.14% 12 hours respectively.

Table 8.7: *In-Vitro* drug release data of Flurbiprofen microspheres

TIME (h)	CUMULATIVE PERCENT OF DRUG RELEASED					
	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
1	12.85	15.75	10.57	12.62	7.82	10.12
2	17.36	20.11	16.31	17.17	13.29	16.72
3	25.17	28.90	20.69	25.34	18.34	21.63
4	30.28	34.71	26.14	32.23	23.71	27.72
5	34.20	40.67	31.52	37.60	27.62	31.34
6	41.63	45.29	37.43	42.57	35.78	37.21
7	47.71	53.75	45.92	47.82	41.83	42.26
8	52.89	59.97	53.21	56.71	56.90	46.33
9	57.40	62.76	60.82	62.22	63.14	52.82
10	65.71	67.34	79.29	77.99	79.57	67.34
11	68.43	74.82	86.32	89.18	86.25	72.21
12	79.30	87.91	91.53	97.29	99.72	86.14

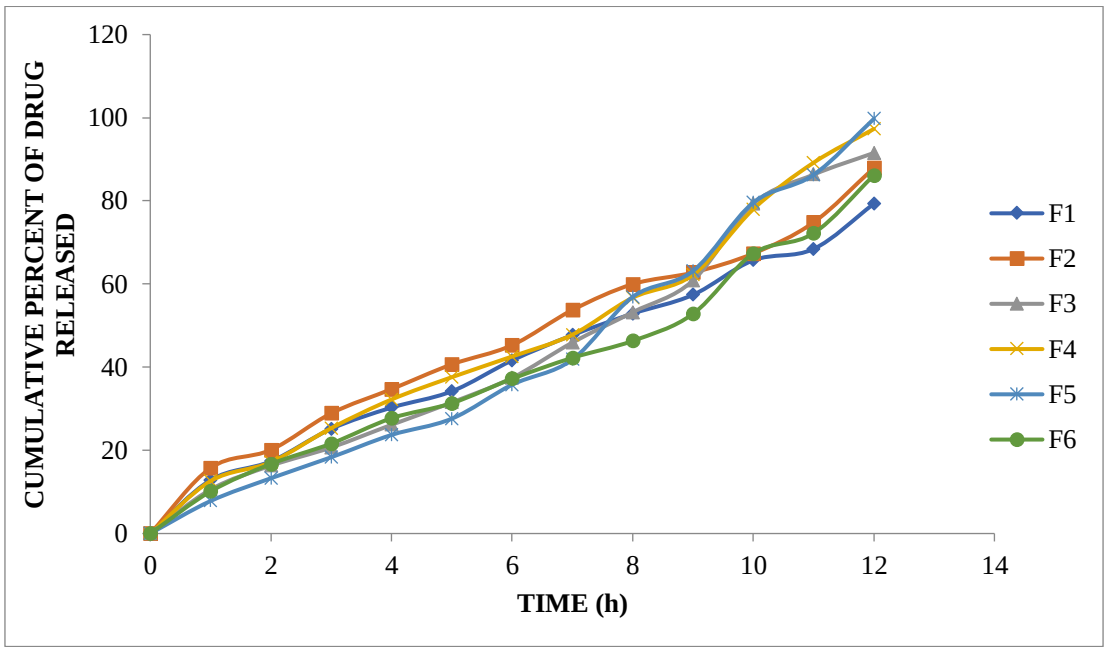


Figure 8.7 : *In-Vitro* drug release profile of Flurbiprofen microspheres

Invitro drug release from all the formulation was found to be slow and sustained over the period of 12 hours, among other formulation F5 showed better sustained release pattern and the cumulative percentage release at the end of 12 hours was found to be 99.72 %.

***In-vitro* drug release kinetics**

For understanding the mechanism of drug release and release rate kinetics of the drug from dosage form, the *in-vitro* drug dissolution data obtained was fitted to various mathematical models such as zero order, First order, Higuchi matrix, and Krosmeyer-Peppas model. The values are compiled in Table 8.8. The coefficient of determination (R^2) was used as an indicator of the best fitting for each of the models considered. The kinetic data analysis of all the formulations reached higher coefficient of determination with the peppas release kinetics whereas release exponent value (n) ranged from 0.970. From the coefficient of determination and release exponent values, it can be suggested that the mechanism of drug release follows peppas release kinetics along with non-Fickian diffusion mechanism which leading to the conclusion that a release mechanism of drug followed combination of diffusion and spheres erosion.

TABLE 8.8: Release kinetics studies of the optimized formulation (F5)

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
7.82	1	1.000	0.893	0.000	1.965	7.820	0.1279	-1.107	92.18	4.642	4.517	0.124
13.29	2	1.414	1.124	0.301	1.938	6.645	0.0752	-0.876	86.71	4.642	4.426	0.215
18.34	3	1.732	1.263	0.477	1.912	6.113	0.0545	-0.737	81.66	4.642	4.338	0.303
23.71	4	2.000	1.375	0.602	1.882	5.928	0.0422	-0.625	76.29	4.642	4.241	0.400
27.62	5	2.236	1.441	0.699	1.860	5.524	0.0362	-0.559	72.38	4.642	4.167	0.474
35.78	6	2.449	1.554	0.778	1.808	5.963	0.0279	-0.446	64.22	4.642	4.005	0.637
41.83	7	2.646	1.621	0.845	1.765	5.976	0.0239	-0.379	58.17	4.642	3.875	0.767
56.9	8	2.828	1.755	0.903	1.634	7.113	0.0176	-0.245	43.1	4.642	3.506	1.135
63.14	9	3.000	1.800	0.954	1.567	7.016	0.0158	-0.200	36.86	4.642	3.328	1.314
79.57	10	3.162	1.901	1.000	1.310	7.957	0.0126	-0.099	20.43	4.642	2.734	1.908
86.25	11	3.317	1.936	1.041	1.138	7.841	0.0116	-0.064	13.75	4.642	2.396	2.246
99.72	12	3.464	1.999	1.079	-0.553	8.310	0.0100	-0.001	0.28	4.642	0.654	3.987

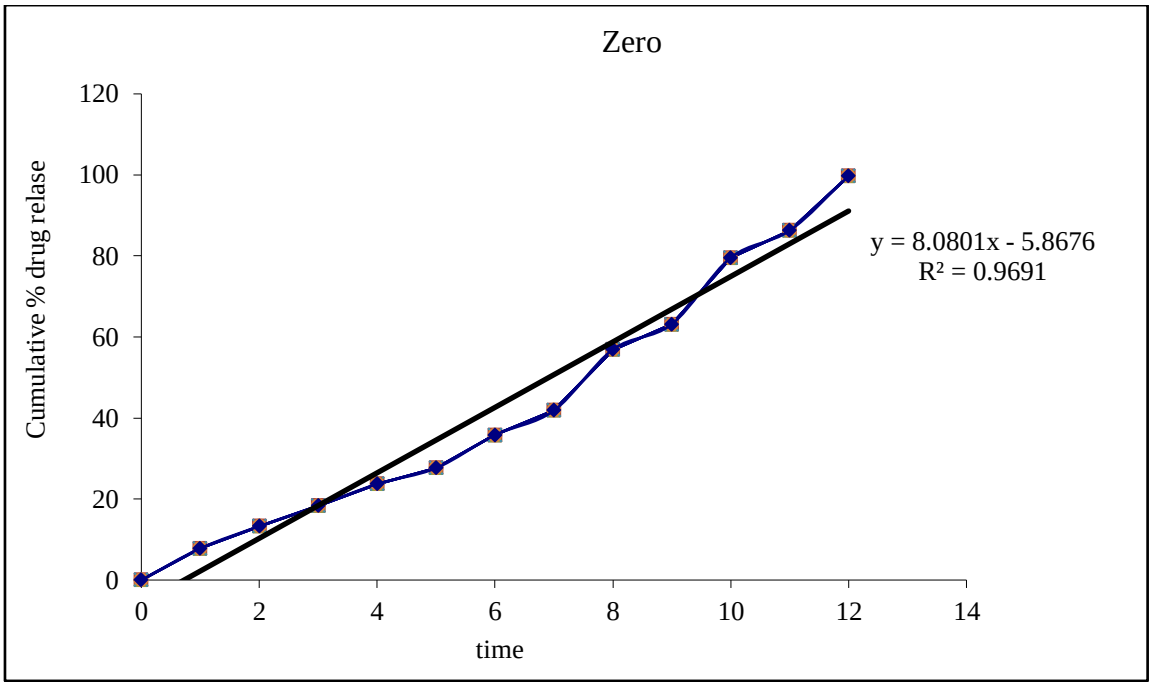


Figure:8.8: Graph of zero order release kinetics of optimized formula

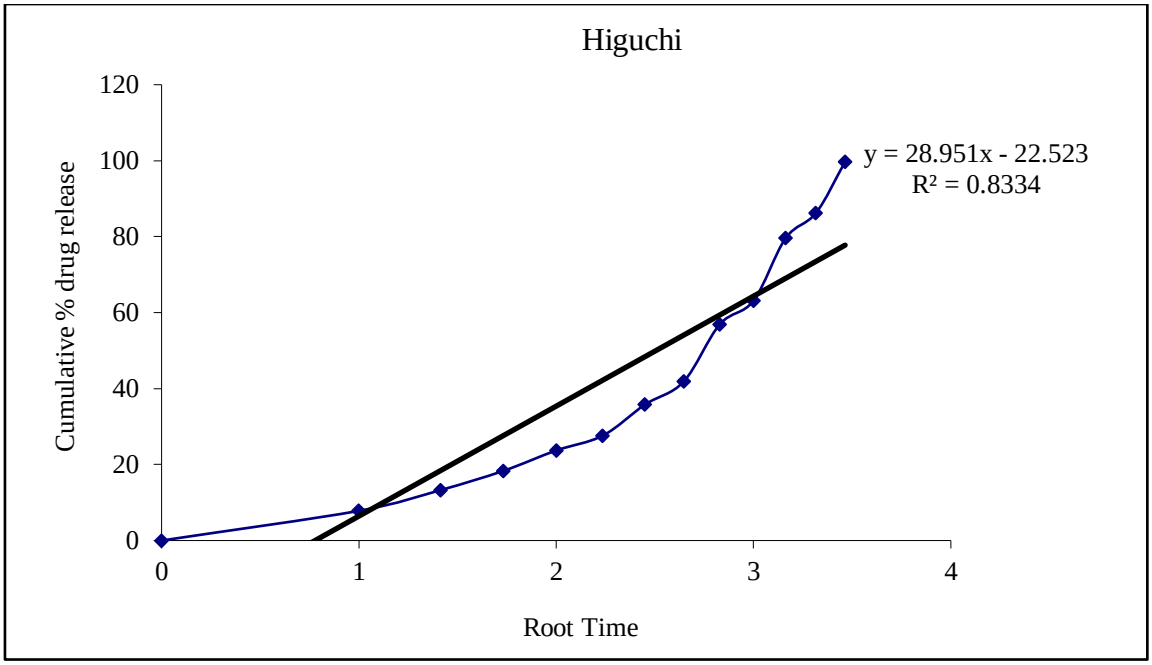


Figure:8.9: Graph of higuchi release kinetics of optimized formula

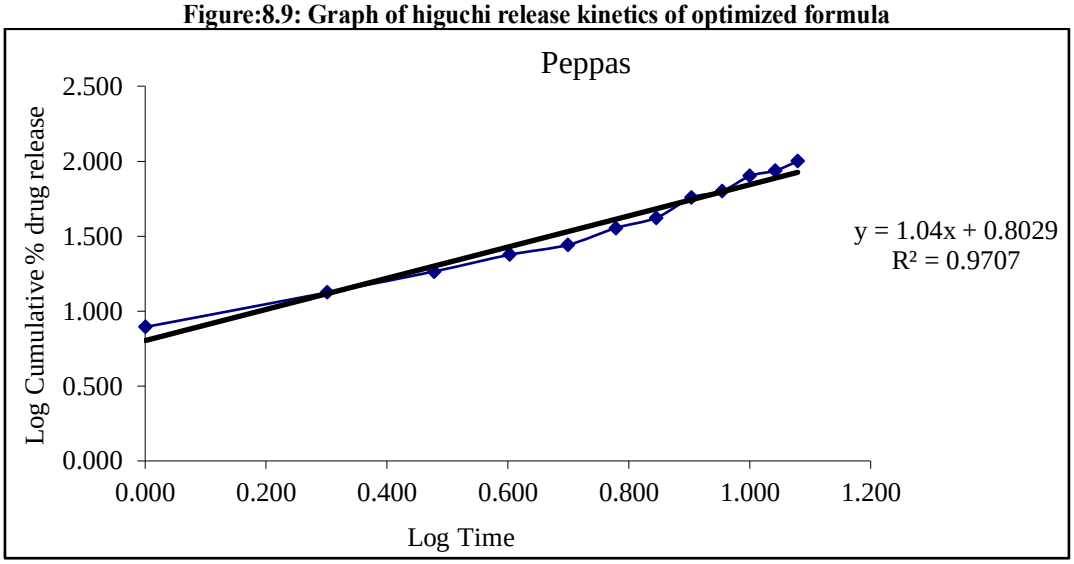


Figure :8.10: Graph of peppas drug release kinetics of optimized formula

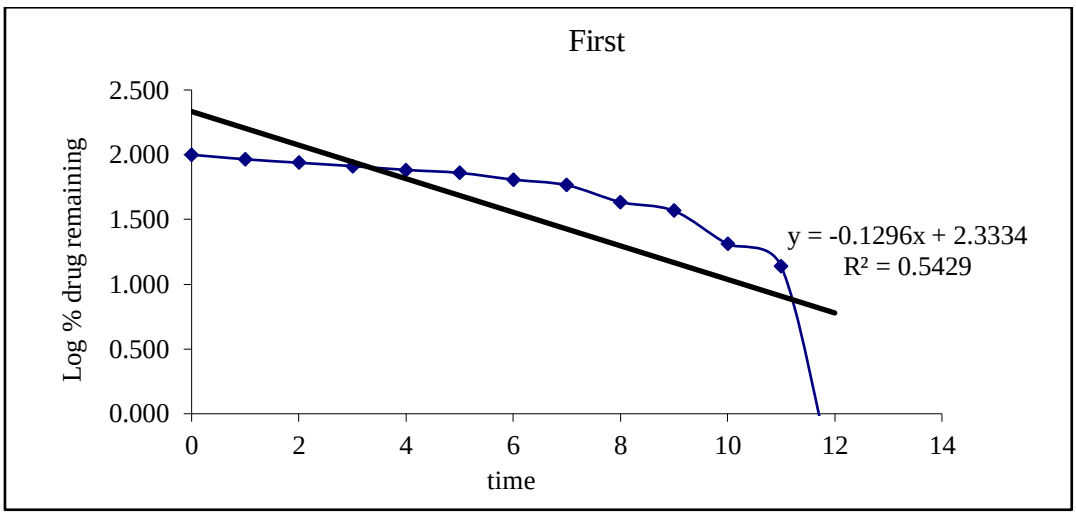


Figure:8.11: Graph of first order release kinetics of optimized formula

Optimised formulation F5 was kept for release kinetic studies. From the above graphs it was evident that the formulation F5 was followed peppas drug release kinetics.

COMPATIBILITY STUDIES

Drug polymer compatibility studies were carried out using Fourier Transform Infra Red spectroscopy to establish any possible interaction of Drug with the polymers used in the formulation. The FT-IR spectra of the formulations were compared with the FTIR spectra of the pure drug.

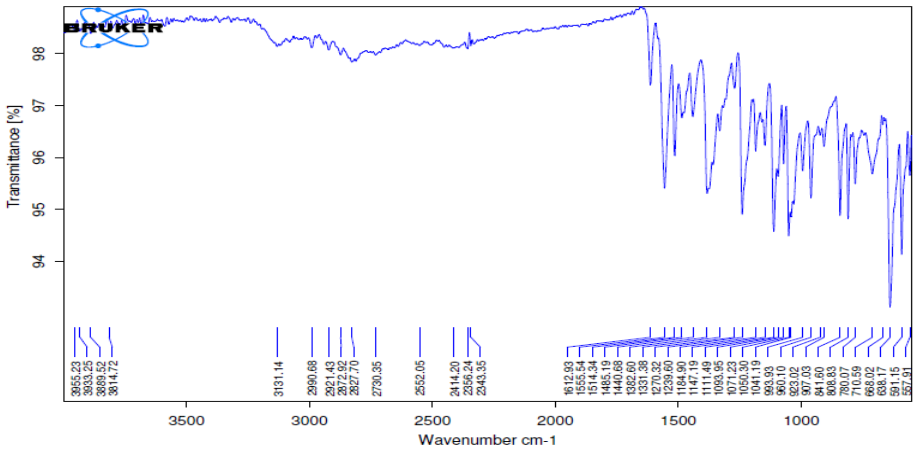


Figure 8.12: FT-IR spectra of Pure drug

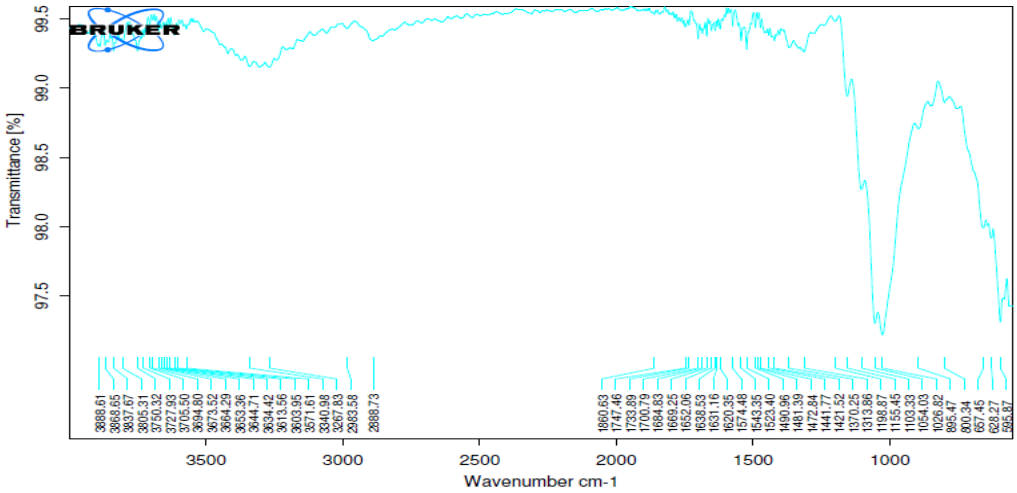


Figure 8.13: FT-IR spectra of Optimised formulation

SEM :

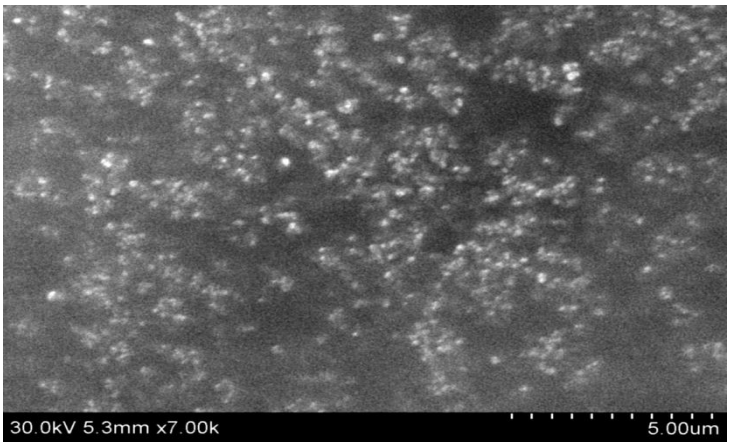


Figure 8.14: SEM of Optimised formulation

SEM was used to examine the morphologies and surfaces of the Flurbiprofen (Fig). The surface morphology of the microspheres was found in plain Eprosartan mesylate powder made up of irregularly shaped crystals with rough surface. The particles of formulation F5 appeared a numerous uniform spherically shaped particles 166±0.02 µm with smooth surfaces of drug-loaded microspheres could be seen with the solvent evaporation technique similar findings have been reported.

XRD:

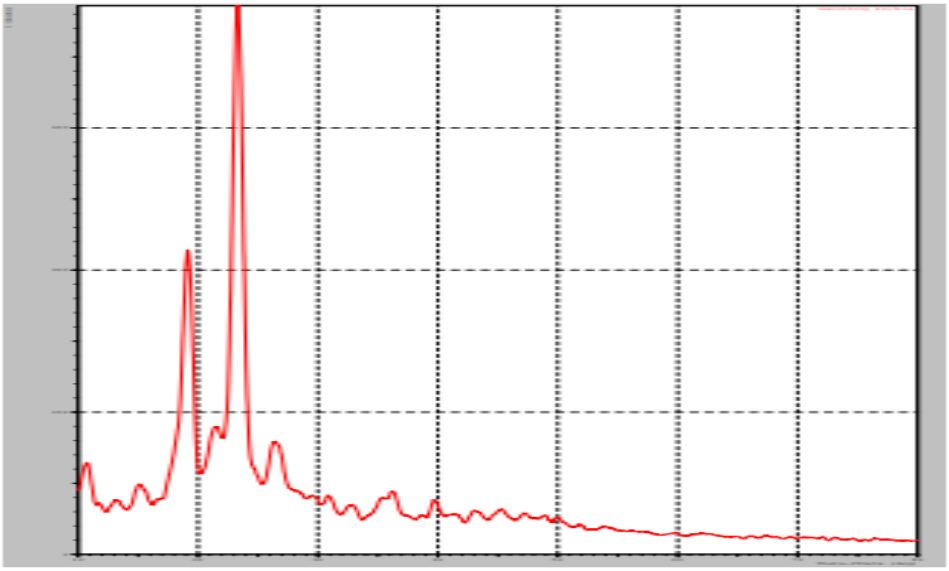


Figure 8.15: Graph: XRD graph of optimised formulations

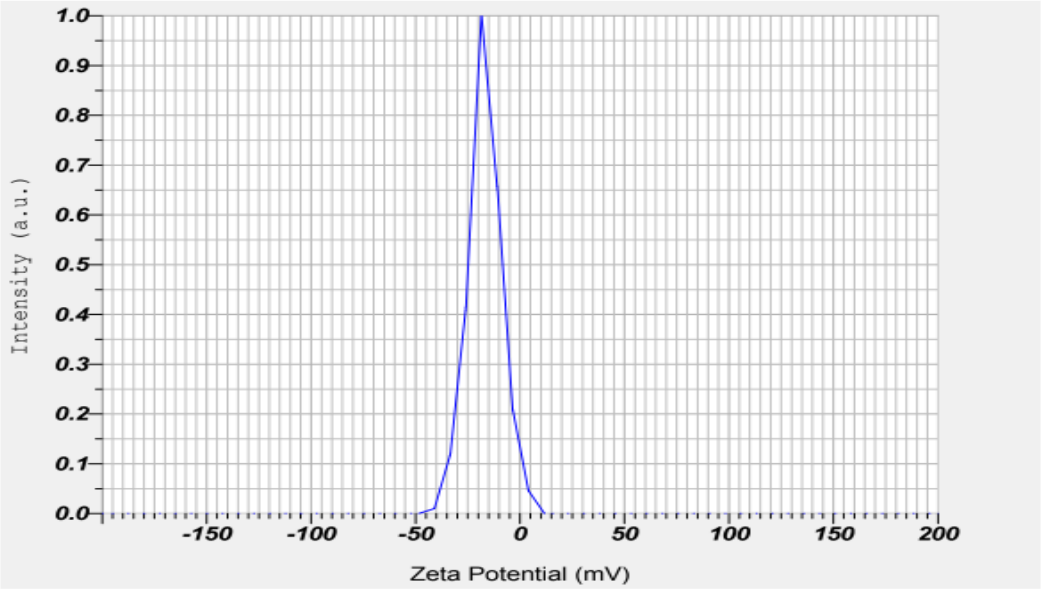
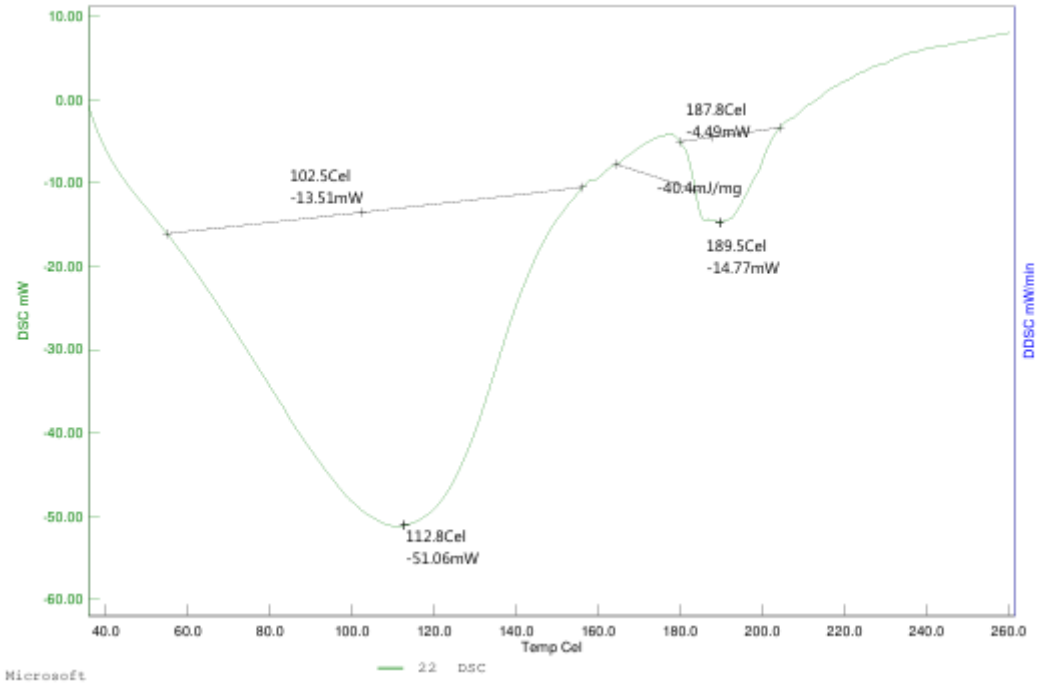


Fig 8.16: Zeta potential of optimised Formulation

The assessment of the zeta potential values (properly related to the double electric layer on the surface of colloidal particles) of a microsphere. Stronger repulsive forces are produced by extreme positive or negative zeta potential values, although repulsion between particles with similar electric charges prevents particle agglomeration and hence simple redispersion. A minimum zeta potential of -38.55 mV is required for simultaneous electrostatic and steric stabilization. The zeta potential study of microsphere formulations F5 were found to be in the range of -38.55 mV) respectively, The zeta potential measurement indicates negatively charged due to double layer repulsion between the droplets and also it depends upon the pH and concentration, which indicates good physical stability of microspheres.



Graph 8.17: DSC graph of pure drug

Upon analysis of the drug Excipient mixture for their physical characteristics no colour change was observed. Based on the chemical evaluation it was found that there was no significant change observed indicating that the drug is compatible with the added ingredients.

10. SUMMARY

- ✓ An attempt was made to formulate Flurbiprofen loaded microspheres using Carbopol 934p and Xanthan Gum as a mucoadhesive polymer by Solvent evaporation method.
- ✓ In the present study F1 to F6 formulations were prepared using Carbopol 934p and Xanthan Gum as a polymer in different ratios.
- ✓ The FTIR study was carried out for the drug, polymer, physical mixture and optimized formulation F5. In FTIR study, all characteristic peaks in the spectra appeared without any remarkable changes showing that there is no chemical interaction between the drug and polymer used in the preparation of microspheres.
- ✓ The mean particle size study was carried out by using microscopic analysis and found that the range for all formulations was varied from 125±0.01 to 191±0.09 µm due to change in drug and polymer ratio.
- ✓ The drug content for all the formulations was found to be in the range of 96.14 to 99.24 %. The formulation F5 had the highest drug content.
- ✓ The entrapment efficiency of all formulations was found to be in the range of 72.90 to 89.12 %.
- ✓ The *in vitro* mucoadhesion study was conducted for all the formulations and the results were found in the range of 72.75 to 96.25%.
- ✓ The *in vitro* drug release study was carried out for all the formulations and the formulation F5 (1:1) showed sustained release of 99.72% at the end of 12 h.
- ✓ The release rate followed peppas drug release kinetics.

CONCLUSION:

The aim of present study is to develop formulation of Flurbiprofen microspheres. Flurbiprofen microspheres were prepared through solvent evaporation technique. In the preliminary screening, from the FTIR spectra, it was observed that similar functional groups appear for the drug and the formulation. Hence it shows that there was no chemical interaction between drug and polymer used. The formulations F1 to F6 prepared by solvent evaporation technique. F5 Selected as an optimized formulation, because of better entrapment efficiency and *in vitro* drug release of about 99.72 % in 12hours. It follows peppas drug release kinetics. Hence it can be concluded that Flurbiprofen can be prepared in the form of microspheres by solvent

evaporation technique to improve the drug targeting efficiency and also to prolong the duration of action.

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