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FORMULATION AND EVALUATION OF SUSTAINED RELEASE DICLOFENAC SODIUM MICROSPHERES USING EUDRAGIT RS100.

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ABSTRACT

The objective of the current investigation is to formulate Eudragit RS100 based sustained release microspheres, containing Diclofenac sodium as a model drug. Diclofenac sodium is a type II anti-inflammatory agent. When administered together shows synergistic effect in their action. Microspheres were prepared by O/O emulsion solvent evaporation method with different stabilizer concentration and at different speeds of emulsification while maintaining constant amounts of Diclofenac sodium. Drug excipient compatibility study was performed prior to formulation development and only compatible excipients were used in the fabrication of microspheres. Prepared microsphere formulations were characterized by percentage yield, particle size analysis, entrapment efficiency, in vitro release behavior, differential scanning calorimetry (DSC) and scanning electron microscopy (SEM). SEM studies showed that the microspheres were spherical with rough surface morphology. The drug loaded microspheres showed 50-80% entrapment efficiency. The in vitro release profile showed a slow and steady release pattern for Diclofenac sodium. A 100% Diclofenac sodium was released within a period of 12 hrs during this time. The drug release was found to be diffusion controlled mechanism. The n value of Korsmeyer Peppas equation indicated non Fickian type of diffusion. DSC results indicated that the physical state of the drug was changed upon fabrication. As a result of these experiments, it was concluded that, novel sustained release oral microspheres comprising a combination of diclofenac sodium was successfully prepared using eudragit RS100 as the polymer and using emulsion solvent evaluation methods.

KEYWORDS: Microspheres, Diclofenac sodium, Eudragit RS100, O/O Emulsion solvent evaporation method, FTIR, SEM and DSC.

INTRODUCTION

The sustained release of drugs is still one of the main objectives of drug delivery systems, which are designed to achieve a prolonged therapeutic effect by continuously releasing the drug over a prolonged period of time after administration of a single dose.[1] Microspheres are defined as homogeneous, monolithic particles in the size range of about 0.1- 1000µm and are widely used as drug carriers for controlled release. Polymeric microspheres and microcapsules have received much attention as drug delivery systems in recent years to modify and retard drug release.[2] Microspheres preparation involves the coating of individual drug particles by inert polymeric material, through which the drug diffuse at a controlled and predictable rate in the surrounding medium and thus improves the treatment by providing the localization of active substance at the site of action and by sustaining release of drugs.[3,4] Eudragit RS100 is an anionic copolymer based on meth acrylic acid and methyl methacrylate and is non-toxic, biocompatible, and biodegradable. It is insoluble in an acid medium and dissolves above neutral pH. Dissolution occurs as a result of structural change of the polymer association with ionization of the carboxylic functional groups.[5] It is a solid substance in the form of a white powder with a faint characteristicodour. Granulation of drug substances in powder form for controlled release Effective and stable enteric coatings with a fast dissolution in the upper Bowel Site specific drug delivery in intestine by combination with other Eudragit RS100 grades.[6] 1 g Eudragit RS 100 7g dissolves in methanol, ethanol, aqueous isopropyl alcohol and acetone (containing approx. 3% water). In 1 N sodium hydroxide to give clear to slightly cloudy solutions.[7] Eudragit RS 100 is practically insoluble in ethyl acetate, methylene chloride, petroleum ether and water. Important characteristics of Eudragit RS 100 to be considered in the pharmacy.[8] Diclofenac sodium is a natural product belonging to anti inflammatory activity. The main aim of the present study was to investigate the possibility of obtaining sustained release Eutragit microspheres designed for simultaneous delivery of the two drugs by using Double emulsion solvent diffusion method.

MATERIALS

Diclofenac sodium was obtained as a gift sample from Cipla Pharma. Pvt. Ltd. Mumbai. Eudragit RS 100 generously donated by Arabindo Pharma, Hyderabad, India. All other chemicals and solvents used were of analytical grade.

METHODS

Pre-Formulation Studies

Solubility analysis

Pre-formulation solubility analysis was done to select a suitable solvent system to dissolve the drug as well as various excipients used in formulation of microspheres. The solubility of the material is usually determined by the equilibrium solubility method, which employs a saturated solution of the material, obtained by stirring an excess of material in the solvent for a prolonged time until equilibrium achieved.[9]

Melting point determination

Melting point determination of the obtained drug sample was done; as it is a first indication of purity of the sample. The presence of relatively small amounts of impurity can be detected by lowering as well as widening in the melting point range.[10]

Compatibility studies of drug and polymer

FTIR spectrum of drug, polymer and physical mixture of drug with polymers were obtained on FTIR instrument. Sample about 5 mg was mixed thoroughly with 100 mg potassium bromide IR powder and compacted under vacuum at a pressure of about 12 Psi for 3 minutes. The resulting disc was mounted in a suitable holder in Perkin Elmer IR spectrophotometer and the spectrum was scanned over the wave number range of 4000-400 cm^{-1}. IR helps to confirm the identity of the drug and to detect the interaction of the drug with the carriers.[11]

Analytical Method Development

Preparation of buffer pH 6.8

50ml of the potassium dihydrogen phosphate (0.2M) was placed in 200ml volumetric flask and to it 22.4ml of sodium hydroxide solution (0.2M) was added and the volume was made up to 200ml with distilled water.[12]

Preparation of standard solution of Diclofenac sodium

Accurately weighed 50 mg of Diclofenac sodium was dissolved in 50 ml of methanol (Conc. 1000 µg/mL). From this solution, 10 ml was pipette out into 100 ml volumetric flask and volume was made up to with ethanol. (Conc. 100 µg/ml). Further 10ml aliquot was taken from this solution (100µg/ml) and diluted to 100ml with ethanol to give 10µg/ml standard solution of drug. Similarly, standard stock solution was prepared in phosphate buffer pH 6.8.[13]

Determination of absorption maxima (λ_{max}) for Diclofenac sodium

The solution containing 10 µg/ml of Diclofenac sodium was scanned over the range of 275 nm against suitable blank using double beam UV spectrophotometer. The maximum obtained in the graph was considered as λ_{max} for the pure drug.[14]

Standard Calibration Curve of Diclofenac sodium

Aliquots of 2,4,6,8,10 and 2 ml of Diclofenac Sodium standard solution (100µg/ml) were transferred to a series of 10 ml volumetric flask and volume was made up to mark with methanol to get serial dilution 2-20 µg/ml of the drug. The absorbance of the solutions was determined at 275nm against methanol as blank and a calibration curve was obtained. Similarly, standard calibration curve was prepared in phosphate buffer pH 6.8 and methanol.[15]

Preparation of Microspheres

The EudragitS100 microspheres were prepared by o/o emulsion solvent evaporation method. Drug(100mg) and the polymer (200mg) were taken and dissolved in a mixture of 10ml of acetone and 5ml of ethanol. 1% span 80 was taken in 100ml of liquid paraffin and kept under propeller stirrer. Solution of the drug and polymer mixture was added drop by drop to liquid paraffin containing Span 80 while stirring continued for 3-4 hours for complete removal of solvent. After that microspheres were collected by filtration with Whatsmman filter paper.[16]

Characterization of Microspheres

Percentage Yield

Percentage practical yield is calculated to know about percentage yield or efficiency of any method, thus it helps in selection of appropriate methods of production. The prepared microspheres of all batches were accurately weighed. The measured weight of prepared microspheres was divided by the total amount of all the excipients and drug used in the preparation of the microspheres, which give the total percentage yield of floating microspheres. It was calculated by using the following equation.[17]

% Yield = actual weight of product/total weight of excipients and drug × 100

Particle Size Determination

The mean particle size was determined by using an optical microscope. In this method 25 particles size was determined by using stage micrometer. The average particle size was determined by this method. The eye piece was adjusted and the stage micrometer was

adjusted according to the eye piece. Calibration factor was calculated by the following formula:

Calibration factor =Stage micrometer/Eye piece

A minute quantity of prepared microspheres was spread on a clean glass slide. Then the particle size of the microspheres was measured, from which average particle size was calculated which was then multiplied with the obtained calibration factor. In this way, the average particle size was calculated for all the six batches.[18]

Drug Entrapment Efficiency

Microspheres equivalent to 50 mg of the drug were taken for evaluation. Microspheres formulation was dissolved in an aliquot amount of methanol by continuous shaking, in a 10 ml volumetric flask and the volume was made up to the mark. The solution was filtered and the absorbance was measured after suitable dilution. The amount of drug entrapped was estimated spectrophotometrically (UV 1700, Shimadzu, Japan) at Diclofenac Sodium of wavelength i.e., 275nm and against appropriate blank. The amount of drug entrapped in the microspheres was calculated by the following formula:[19]

% Drug entrapment = Amount of drug actually present Actual Drug Content/ Theoretical drug load expectedX100

Scanning Electron Microscopy (SEM)

The most widely used procedures to visualize microparticles are conventional light microscopy (LM) and scanning electron microscopy (SEM). It images the sample surface of a solid specimen by using a focused beam of high-energy electrons. The signal contains information about surface topography, texture, external morphology of fractured or sectioned surface, chemical composition, crystallographic information, and electrical conductivity. In order to examine the particle surface morphology and shape, Scanning Electron Microscopy (SEM) was used. Microspheres were scanned and examined under Electron Microscope. Dry microspheres were spread over a slab. The sample was shadowed in a cathodic evaporator with gold layer 20 nm thick. Photographs were taken using an S-3700N Scanning Electron Microscope (Hitachi) operated at 20 kV.[20]

***In-vitro* release study**

The drug release rate from microspheres was determined by using USP dissolution apparatus Type II (basket-type). A weighed amount of microspheres equivalent to 25 mg of the drug

(Diclofenac Sodium) was weighed and placed in a non reacting mesh that had a smaller mesh size than the microspheres. Dissolution medium used was 0.1 N Hcl (pH 1.2, 750 ml) for first 2 hours and maintained at 37 ± 0.5°C at a rotation speed of 100 RPM. 5 ml of sample was withdrawn at each 15 min interval for the first hour, followed by 30 min interval, later this interval was extended to 1 h. Sample was then passed through a 5 µm membrane filter and analyzed spectrophotometrically at 275 nm determine the concentration of Diclofenac Sodium present in the dissolution medium respectively. The initial volume of dissolution medium was maintained by adding 5 ml of fresh dissolution media after each withdrawal. The dissolution study was continued with using phosphate buffer (pH 6.8 ± 1, 900ml) for the next 10 hours. The cumulative % drug release was calculated using standard calibration curve.[21]

Release Kinetics

The matrix systems were reported to follow the Peppas release rate and the diffusion mechanism for the release of the drug. To analyze the mechanism for the release and release rate kinetics of the dosage form, the data obtained was fitted in to, Zero order, First order, Higuchi matrix and Peppas model. In this by comparing the r-values obtained, the best-fit model was selected.[22]

Differential Scanning Calorimetry (DSC)

Differential Scanning Calorimetry is used to determine drug excipient compatibility studies, and also used to observe more phase changes such as glass transition, crystallization, amorphous forms of drugs and polymers. The physical state of drugs and the polymer was analyzed by Differential Scanning calorimeter (Schimadzu). Approximately 10 mg of sample was analyzed in an open aluminum pan and heated at a scanning rate of 10°C/min between 0°C and 400°C. Magnesia was used as the standard reference material.[23]

RESULTS AND DISCUSSION

In the present investigation an attempt has been made to formulate microspheres of Diclofenac sodium by using polymer like Eudragit RS100 as a carrier for sustained release. Microspheres were prepared by O/O emulsion solvent evaporation method. Prepared microspheres are subjected for characterization and evaluation studies.

Preformulation Studies

Preformulation study for Diclofenac sodium has been performed to know the drug physical properties so as to design it to a suitable formulation as shown in Table 1.

Table 1 Description data of Diclofenac sodium

Physical property	Pure Diclofenac sodium
Empirical Formula	$C_{14}H_{11}Cl_2NO_2$
Molecular Weight	296.149 g/Mol
Color and odour	White, odourless powder
Taste	Slightly bitter in taste
Appearance	Crystalline powder

Solubility

The solubility of pure drug Diclofenac in 10 mg/10 ml of solvent was carried out and it reveals that it is freely soluble in water, slightly soluble in ethanol, chloroform and dichloromethane. It is soluble in methanol.

Melting Point

The melting point of the pure drug (Diclofenac sodium) was determined at 283-285°C.

Compatibility studies by FTIR

Drug polymer compatibility studies were carried out by using FTIR spectral studies to establish the possible interaction in the formulations. The FTIR spectrum of Diclofenac sodium shown in Figure 1, Eudragit RS100 shown in Figure 2 and their physical mixture is shown in Figure 3.The following characteristic peaks were observed with Diclofenac sodium as well as the physical mixture containing. As the identical principle peaks were observed in all the cases, hence it shall be confirmed that interactions do not exist between the drug and polymer. The physical mixture retained the integrity of drugs and as a reason these polymer were selected for further studies. From the above spectra of Diclofenac sodium, physical mixture and polymers and formulation F5, it was observed that all characteristic peaks of Diclofenac sodium were present in the combination spectrum and there is no shift in peaks, thus indicating compatibility of the diclofenac sodium and polymer. There is no physical and chemical interaction of drug and polymers. Hence there is no drug and excipient incompatibility, Thus, drug and excipients are compatable shown in Figure 4.

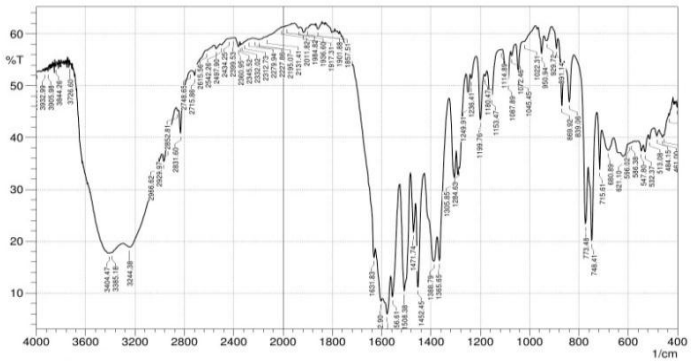


Figure 1 FTIR Spectra of pure drug (Diclofenac sodium)

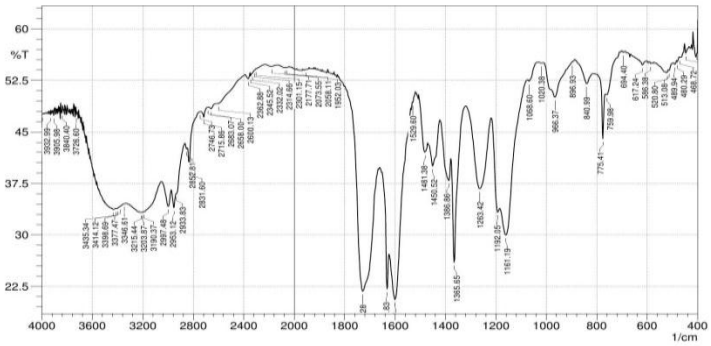


Figure 2 FTIR Spectra of Excipient (Eudragit RS100)

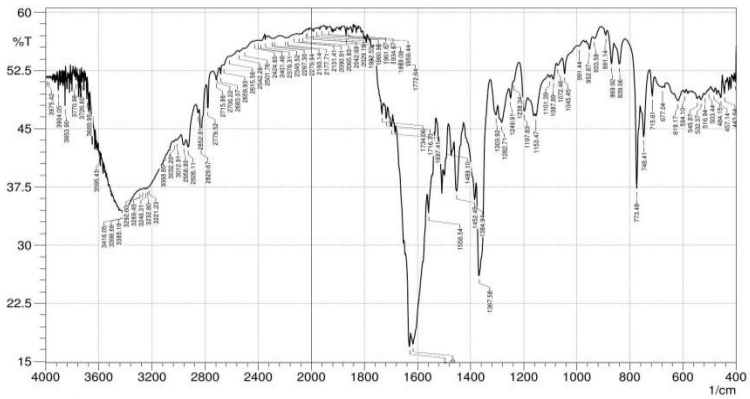


Figure 3 FTIR Spectra of Mixture (Diclofenac sodium and Eudragit RS100)

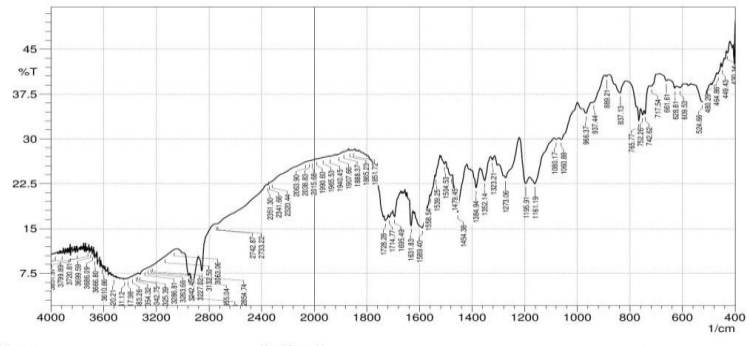


Figure 4 FTIR Spectra of optimized Formulation F5

Analytical Method Development

Standard calibration curve of Diclofenac sodium in UV-spectrophotometer

The UV absorbance of Diclofenac sodium in the range of 0-20µg/ml of the drug pH 6.8(PBS) buffers showed linearity at lambda max of 275nm. The lineartiy was plotted for absorbance againest concetration. The absorbance values and standard graph shown in table 2 and figure 5.

Standard calibration curve of Diclofenac sodium in methanol

The UV absorbance of Diclofenac sodium in the range of 0-50µg/ml of the drug in methonol showed linearity at lambda max of 275nm. The lineartiy was plotted for absorbance againest concetration. The absorbance values and standard graph shown in table 10 and figure 13.

Table 2 Data for standard graph of Diclofenac sodium

Concentration (ug/ml)	Absorbance
0	0
10	0.104
20	0.206
30	0.314
40	0.413
50	0.516

Average reading of n=3.

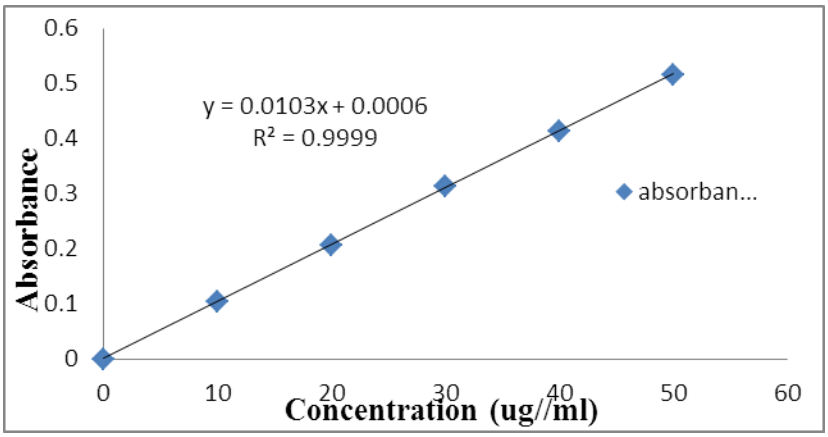


Figure 5 Standard graph of Diclofenac sodiumin Ph 6.8 buffer

Preparation of Microspheres

Microspheres were prepared by O/O emulsion solvent evaporation method. A mixed solvent system (MSS) of acetonitrile and dichloromethane and distilled water were used for the preparation of microspheres as internal organic phase and an aqueous phase. Liquid paraffin and Span80 were used as external oily phase and surfactant. N-hexane was added as a non-

solvent to the processing medium to solidify the microspheres. This method for preparation of microspheres was reported to overcome the problem of low encapsulation efficiency of water soluble drugs prepared by conventional o/o emulsion solvent evaporation method. The composition and ratio of compounds was shown in the following table 3.

Table 3 Formulation design of Microspheres

Formulation code / Materials	F1	F2	F3	F4	F5	F6
Diclofenac sodium (mg)	50	25	25	25	**25**	25
Eutragit (mg)	100	100	100	50	**50**	50
Span-80 (%)	0.5	1	2	0.5	**1**	2
Acetone	10	10	10	10	**10**	10
Petrolieum ether	4	4	4	4	**4**	4
Liquid Paraffin (ml)	50	50	50	50	**50**	50
Stirring Speed (rpm)	750	750	750	1000	**1000**	1000

Particle size and Percentage Yield of Microspheres

The mean particle size of the developed formulations of microspheres was found to be in the range of 88.62 to 296 µm for F5. Minimum size was obtained from batch F5 has 1% span 80 concentration at a stirring speed of 1000 RPM. It was found that the mean particle size was decreased with an increase in the stirring speed and stabilizer concentration. Percentage yield of all the formulations was calculated and reported in the table. Percentage yield in the range of 42% to 80% was observed for the formulations F1-F6. Maximum yield was obtained from formulation F5 with a yield of 80. The Particle size and Percentage yield of all the formulations were shown in the table 4.

Table 4 Particle size and Percentage yield Data of microspheres

Formulation	Particle size(µm)	Percentage (%)Yield
F1	184.56±3.78	67.5
F2	98.35±4.25	42
F3	230±2.32	54
F4	296±4.28	74.2
F5	88.62±3.69	80
F6	170.33±2.51	72.5

Percentage Drug Entrapment Efficiency

The drug entrapment efficacy of microspheres for F1 to F6 was in the range of 8-33%. Highest entrapment efficacy was observed with F5 formulation, with a percentage entrapment of 80% for Diclofenac sodium. The results of percentage drug entrapment efficiency are shown in the table 5 From the encapsulation efficiency values it was observed that an

increase in the speed of rotation from 750 to 1000 RPM at constant surfactant concentration, resulted in higher encapsulation efficiency. This may be due to the formation of larger emulsion droplets at low speed, ensuring enough drug diffusion out of the microspheres before they harden. From the encapsulation efficiency values it was observed that by keeping the speed of rotation constant, there was a significant decrease in encapsulation efficiency of the drugs to increase in concentration of surfactant for the secondary emulsion. This may be due to the fact that the increase in surfactant concentration proportionally increases miscibility of acetone with light liquid paraffin (processing medium) which may increase the extraction of the drug into the processing medium.

Table 5 Drug entrapment efficiency Data of all the formulations

Formulation	Entrapment efficiency
F1	60%
F2	50%
F3	50%
F4	63%
F5	80%
F6	56%

Dissolution Studies of Microspheres

The cumulative present drug release of F1 to F6 formulations at various time intervals was calculated and tabulated in table 6, the cumulative present drug release in all formulations was plotted against time in figure 6, among all the batches slow and constant release was observed with all formulations. But F5 was considered the optimized formulation and was used further because it produced ideal sustained release. It was observed that Diclofenac sodium release was at the end of the release study, this may be due to reasons that release from the microspheres depends on the core: coat ratio i.e., drug: polymer ratio which resulted in low cumulative percentage drug release of Diclofenac sodium from the microspheres.

Table 6 In-vitro cumulative percentage drug release data of Diclofenac sodium

Time(hours)	Cumulative % drug release					
	F1	F2	F3	F4	F5	F6
0	0	0	0	0	**0**	0
1	2.80	0.3	0.8	6.1	**8.01**	3.14
2	6.74	2.94	2.15	8.2	**15.26**	13.78
3	9.36	4.55	5.10	11.69	**27.61**	22.32
4	12.68	6.98	7.58	15.08	**35.95**	34.78
5	17.12	10.89	9.98	19.76	**52.22**	45.32
6	21.64	12.72	11.32	22.91	**64.89**	54.28

7	23.03	13.82	13.25	27.61	**78.59**	64.72
8	23.80	15.05	14.59	31.79	**93.49**	71.54
9	23.97	17.48	15.12	32.43	**98.32**	82.86
10	24.22	18.54	16.36	33.78	**100**	84.32
12	25.39	18.92	17.12	34.54	**100**	85.12

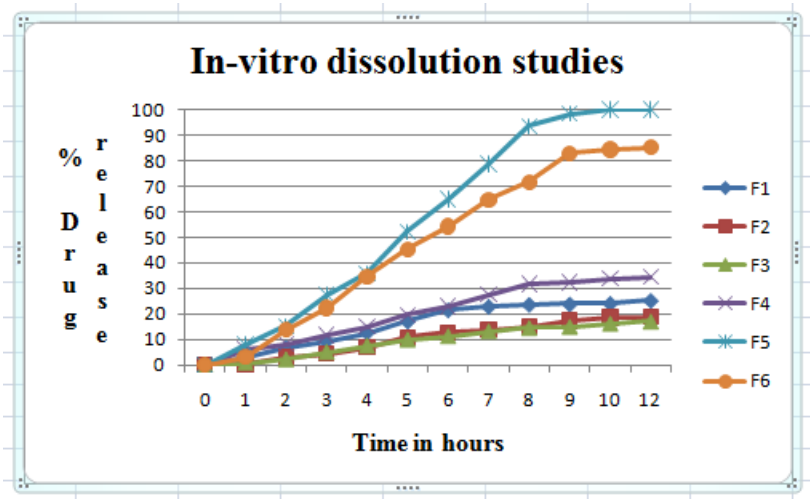


Figure 6 Comparison of cumulative percentage drug release (Diclofenacsodium) of all the formulation

Preferred Formulation

Among the different formulations prepared using different surfactant concentration and at different speed of rotation, it has been observed that the formulation prepared using 1% span 80 concentrations at a speed of 1000 RPM resulted in maximum entrapment efficiency and desired cumulative percentage drug release therefore, this formulation was considered as the optimized formulation. This formulation was characterized for in-vitro drug release kinetics, surface morphology by SEM and solid state analysis by DSC.

Data of Release Kinetics

The in vitro release data obtained from optimized Formulation F5 was fitted in various kinetic dissolution models such as zero order, first order, Higuchi model and Korsmeyer-Peppas model. The Peppas model is widely used to confirm whether the release mechanism is Fickian diffusion, non-Fickian diffusion or zero order. 'n' value could be used to characterize different release mechanisms. Optimized formulation F5 is following Higuchi model release mechanism for both the drugs (Diclofenac sodium), with first order release kinetics and it follows a non Fickian diffusion when it applied to the Korsmeyer-Peppas model for mechanism of drug release. The results are shown in table7-8 and figures 7-10.

Table 7 Release kinetics data of Diclofenac sodium from optimized formulation F5

Time (h)	Cumulative(%) Release Q	Root (T)	Log (t)	Log (%) Release	Log (%) Remain
0	0	0			2.000
0.25	5.45	0.500	-0.602	0.736	1.976
0.5	10.09	0.707	-0.301	1.004	1.954
0.75	16.53	0.866	-0.125	1.218	1.922
1	20.46	1.000	0.000	1.311	1.901
2	30.28	1.414	0.301	1.481	1.843
3	33.57	1.732	0.477	1.526	1.822
4	36.87	2.000	0.602	1.567	1.800
5	39.95	2.236	0.699	1.602	1.779
6	45.42	2.449	0.778	1.657	1.737
7	52.2	2.646	0.845	1.718	1.679
8	57.04	2.828	0.903	1.756	1.633
9	64.21	3.000	0.954	1.808	1.554
10	69.75	3.162	1.000	1.844	1.481
11	73.97	3.317	1.041	1.869	1.415
12	77.02	3.464	1.079	1.887	1.361

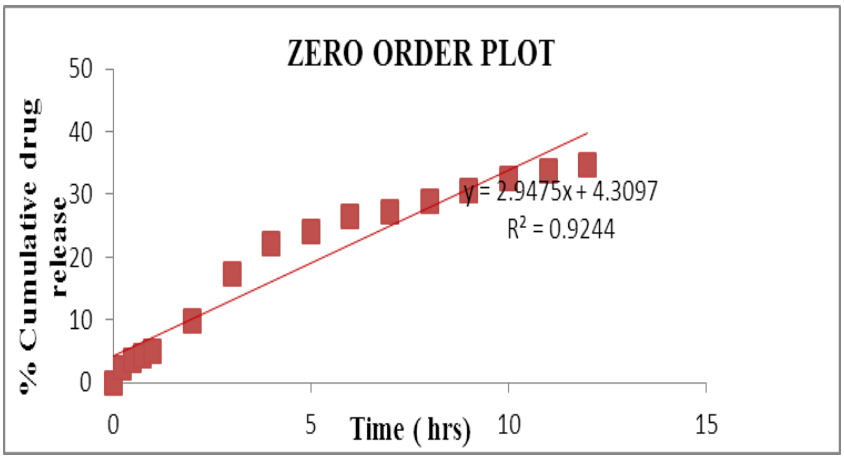


Figure 7 Zero Order Release kinetics of optimized formulation F5

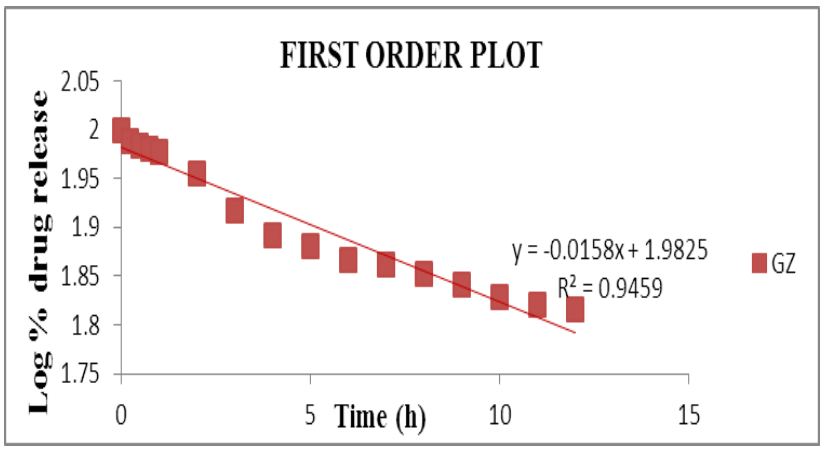


Figure 8 first Order Release kinetics of optimized formulation F5

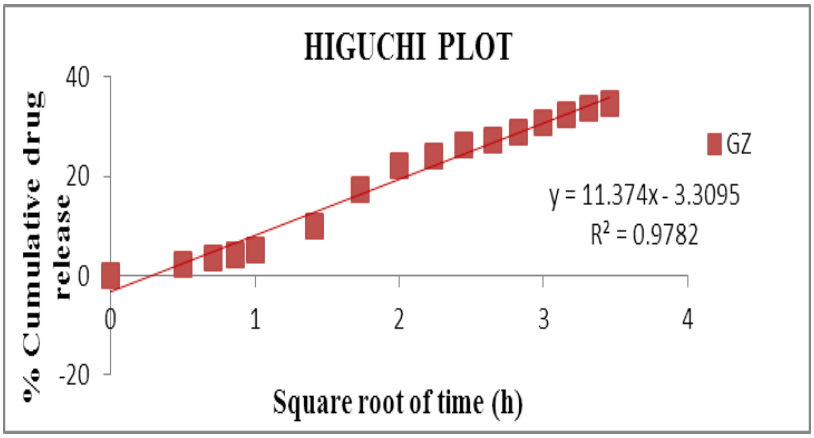


Figure 9 Higuchi model Release Studies for optimized formulation F5

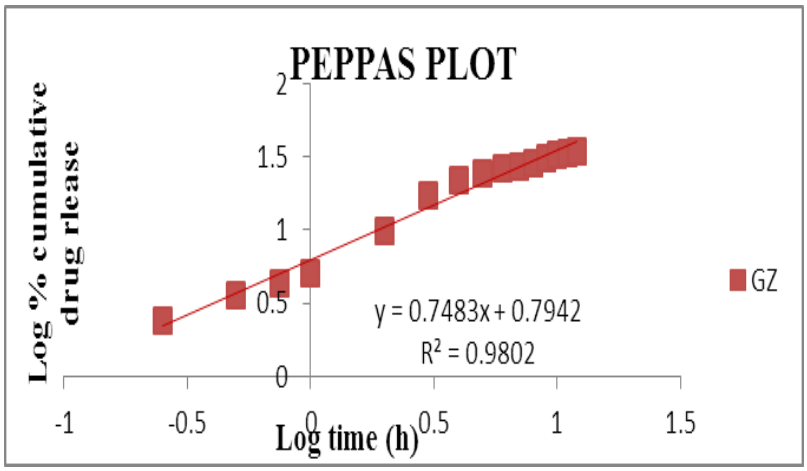


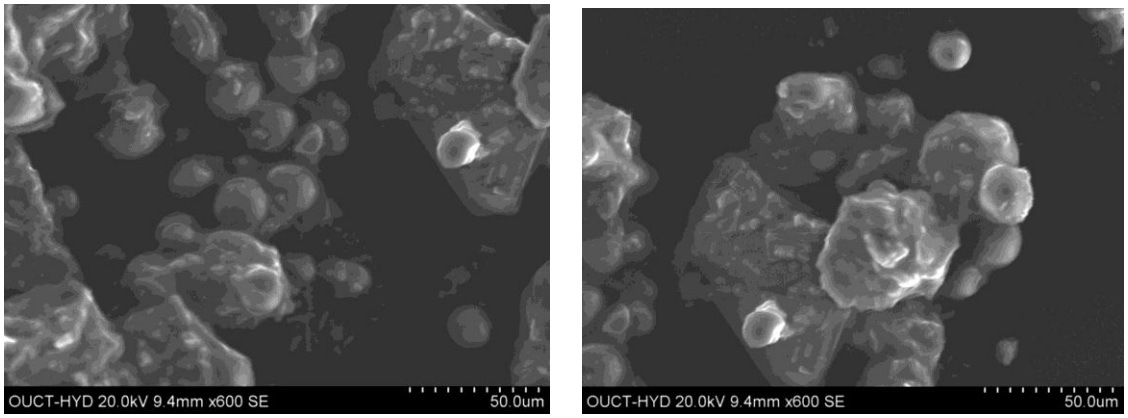
Figure 10 Korsmeyer Peppas model Release Studies for optimized formulation F5

Table 8 Regression coefficient (r^2) values of different kinetic models and diffusion exponent (n) of Peppas model for Diclofenac sodium.

Formulation code	Zero order	First order	Higuchi	Peppas	
	R^2	R^2	R^2	R^2	n
F5(Diclofenac sodium)	0.9608	0.9671	0.9819	0.9504	0.684

Surface Morphology by SEM

The surface morphology of the microspheres was examined by scanning electron microscopy (SEM). The microspheres of optimized formulation were examined. The SEM results showed that the microspheres were spherical in nature with rough surface morphology. In addition, micropores were observed on the surface of microspheres at higher magnifications. SEM pictures are shown in figure 11 and it was concluded that the average particle size was found to be in a micron range (µm).



Spherical microparticles **Particles in micron range**

Figure 11 SEM photographs of microspheres of optimized formulation

DSC Results

DSC studies were performed to understand the nature of the encapsulated drug in the matrix. The physical state of drug in the polymer matrix would also influence its release characteristics. To probe this effect, DSC analysis was performed Diclofenac sodium F5 as shown in the Figure 12. The DSC thermogram of diclofenac sodium exhibits an endothermic peak at 230^{o}C., corresponding to its melting transition point. There was no peak detected in the temperature ranges of both the drugs in the optimized formulation (Diclofenac sodium, Eutragit, formulation microspheres) as shown in figure 13. The absence of drug peak may be due to conversion of drugs from crystalline state to semicrystalline or amorphous state. The absence of detectable crystalline domains in the optimized formulation clearly indicates that the drug Diclofenac sodium in amorphous or disordered-crystalline form of a molecular dispersion in the polymer matrix.

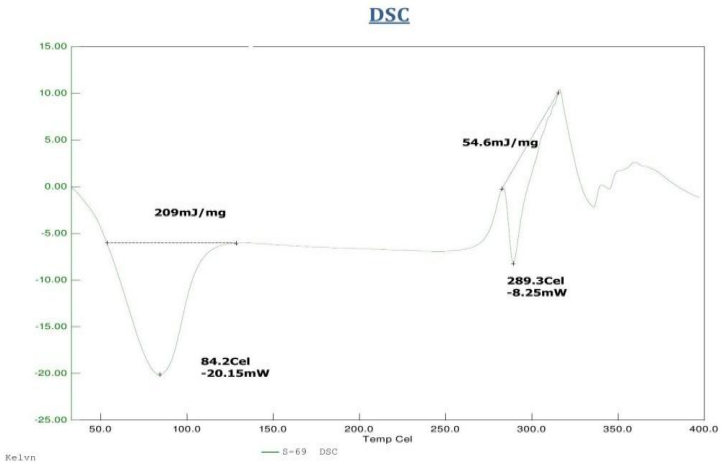


Figure 12 Thermogram of pure drug of Diclofenac Sodium

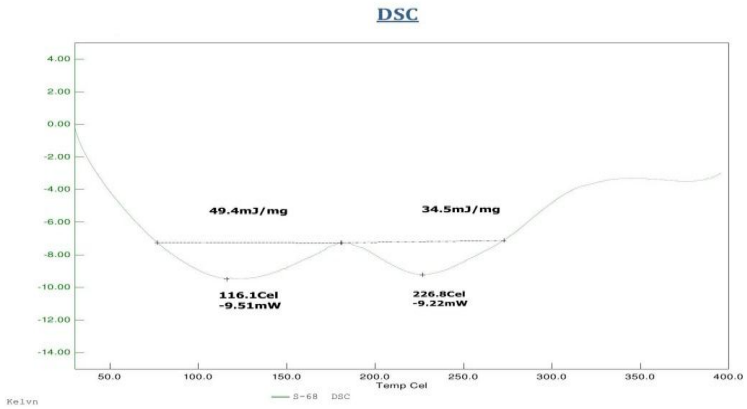


Figure 13 DSC thermogram of optimized formulation (F5).

CONCLUSION

The preformulation studies, like melting point, solubility and UV analysis of Diclofenac sodium were complied with IP standard. Compatibility studies carried out by IR spectroscopy studies revealed that there is no significant interaction between the drug and polymer. Microspheres were prepared by varying the concentrations of surfactant and speed. Particles were abundantly found and they were spherical in their shape. Thus, emulsifier produced better surface characteristics. Increment in particle size was observed with increased concentrations of emulsifying agent (span 80). The smaller size was obtained with increasing stirring speed. Interestingly, it was observed that the particle size had no significant influence on the *in vitro* drug release. Highest entrapment efficacy was observed with F5 formulation, with a surfactant concentration of 1% at a speed of 1000 rpm and thus it was selected as best formulation. Increase in the encapsulation efficiency was observed to increase in the speed of rotation at constant surfactant concentration. An increase in the concentration of surfactant at a constant speed of rotation resulted in decreased encapsulation efficiency of the drugs. The in *vitro* release profile indicated sustained release of both the drugs Diclofenac sodium, which may be attributed to the use of EudragitRS100 polymer. Based on mathematical data revealed from kinetic models, it was concluded that the release of the drug followed first order. Higuchi equation explains the diffusion controlled release mechanism, the diffusion exponent 'n' values were found to be more than 0.5 for the Diclofenac Sodium indicating Non-Fickian diffusion. The DSC data indicates that there is no interaction between the drug and polymer, and it also indicates that the drug is dispersed in the polymer in an amorphous state. From the study it is evident that promising sustained release microspheres of Diclofenac sodium may be developed by O/O emulsion solvent evaporation technique by using Eudragit RS100 polymer.

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