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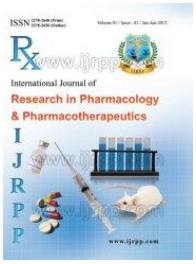

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Research article ***Open Access***

Formulation and Characterization of Aspirin loaded modified release Microsponges by statistical design

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ABSTRACT

Aspirin loaded microsponge can be used to deliver particles to the intestinal region for reducing the side effects and give sustained release effect. Quasi emulsion solvent diffusion method was used to prepare Aspirin loaded microsponge by using Eudragit RS100 as polymer, polyvinyl alcohol as emulsifier, Triethyl citrate as plasticizer, Dichloromethane and methanol as solvent. Optimization of formulation was done by Central Composite design with 15 runs. 3-D surface response plots and contour plots were drawn and optimized formulation was selected by check point batch. Evaluation of formulation were done by Particle size, loading efficiency, production yield, drug content, %CDR at 1 hr, t50%, t90% along with scanning electron microscopy, Residual solvent study, DSC, FTIR also characterized. Spray coating was done by using coater with nozzle spray. Mechanically strong tablets were obtained owing to the plastic deformation of sponge-like structure of microsponges confirmed by resiliency test. All the factors studied had an influence on the physical characteristics of the microsponges. In-vitro dissolution studies were done on all formulations and the results were kinetically evaluated and the release rate of aspirin was found to be modified. This study presents a new approach based on microsponge drug delivery system, drug release in sustained manner with reducing the side effect.

Keywords: Aspirin, Microsponge, Central composite design, Quasi emulsion solvent diffusion method, Sustained drug delivery system.

INTRODUCTION

Aspirin is a non-steroidal anti-inflammatory drug usually used for the treatment of arthritis minor aches and pains and it is known that it has some side effects in gastrointestinal system [1-3]. It is probable that a modified release dosage form would reduce the severity of these side effects [4, 5]

Many of conventional delivery systems require high concentrations of active agents to be incorporated for effective therapy because of their low efficiency as delivery systems. Thus novel drug delivery systems have been increasingly investigated to achieve targeted and controlled release of drugs. Among many multiparticulate drug delivery system microsponge become a good platform for formulate

sustained release dosage form with modifying release rate [6].

Microsponges are patented delivery systems composed of porous microspheres. They are tiny sponge like spherical particles that consist of a myriad of inter connecting voids within a non-collapsible structure with a large porous surface.Microsponges are designed to deliver a pharmaceutically active ingredient efficiently at minimum dose and also to enhance stability, elegance, flexibility in formulation, reduce side effects and modify drug release profiles. [7]

The Microsponge system are based on microscopic, polymer-based microspheres that can bind, suspend or entrap a wide variety of substances and then be incorporated into a formulated product, such as gel, cream, liquid or powder. Advantages of Microsponge Delivery System as compare to other conventional formulations like Microsponges can absorb oil up to 6 times its weight without drying, It provides continuous action up to 12 hours i.e. extended release, Improved product elegancy, Less the irritation and better tolerance leads to improved patient compliance, It can also improve efficacy in treatment, They have better thermal, physical and chemical stability, These are non-irritating, non-mutagenic, non-allergenic and non-toxic, It has wide range of chemical stability, higher payload and are easy to formulate and also improve bioavailability of the drugs. Aspirin an antipyretic and analgesic drug which has been widely used in clinical practice was selected as a model drug. It has a short half life in plasma about 2–4 hours. [8-10]

Commercial pharmaceutical forms of acrylic resins are good candidates for the preparation of sustained release dosage forms due to their inertness, solubility in non-toxic solvents (alcohol) and availability of this polymer with widely different properties.

The present study is aimed at developing microsponge based novel drug delivery system containing aspirin by using polymer Eudragit RL 100 and Eudragit RS 100. The microsponges of aspirin were prepared and characterized. They were formulated as tablets and subjected to in vitro characterization for various attributes. [11]

MATERIALS AND METHODS

Materials

Aspirin was purchased from Yarrow Chem Pvt. Ltd, Rajkot, Eudragit RL 100 and Eudragit RS 100 was provided as a gift sample from Evonik Degussa Industries, Mumbai. All chemicals were used in purified form.

Method

Aspirin microsponges were prepared by a Quasi-emulsion solvent diffusion method. The organic phase was prepared by dissolving the required amount of Aspirin, Eudragit RS100 (ERS 100) in ratio of Dichloromethane (DCM) & Methanol. Triethyl Citrate was added20% of the polymer in order to facilitate the plasticity. In another phase dissolve required amount of polyvinyl alcohol (PVA) in distilled water (External Phase). The above internal phase was gradually added into external phase containing distilled water and polyvinyl alcohol. After emulsification, the mixture was continuously stirred for 2-3 hours. Then the mixture was filtered to separate the microsponges. Then this prepared microsponge was washed with 200 ml distilled water. The product was dried by hot air oven at 40°C for 24 hours. [12]

Central Composite Design (CCD)

Central composite designs are used to statistically optimize the formulation parameter and evaluate main effects, interaction effects and quadratic effects of the formulations

Drug: Polymer(X1), stirring Speed (X2), PVA concentration (X3) were taken as independent variables. Drug content (Y1), %CDR at 1 hrs (Y2), t50% (Y3), t90 %(Y4) were taken as response variables. Variables and their level depicted in below table 1.

Table 1: Variables and their levels in central composite design

Independent Variables	Level of variables				
	-α	**-1**	**0**	**+1**	**+α**
X1= Drug: Polymer	0.159:1	0.5:1	1:1	1.5:1	1.841:1

X2= Speed	454	800	1000	1200	1545
X3=PVA concentration	0.0795%	0.25%	0.5%	0.75%	0.9205%

Dependent variables: Drug content, %CDR at 1 hrs, t50%, t90%

Below table 2 shows that layout of all formulations as per statistical design.

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Table 2: Detail Design layout of central composite design

Batch	Coded value			Actual Value		
	X1	X2	X3	X1 (Drug:Polymer)	X2 (Speed)	X3 (Conc. Of PVA)
F1	-1	-1	-1	0.5:1	800	0.25%
F2	+1	-1	-1	1.5:1	800	0.25%
F3	-1	+1	-1	0.5:1	1200	0.25%
F4	+1	+1	-1	1.5:1	1200	0.25%
F5	-1	-1	+1	0.5:1	800	0.75%
F6	+1	-1	+1	1.5:1	800	0.75%
F7	-1	+1	+1	0.5:1	1200	0.75%
F8	+1	+1	+1	1.5:1	1200	0.75%
F9	-1.682	0	0	0.159:1	1000	0.5%
F10	+1.682	0	0	1.841:1	1000	0.5%
F11	0	-1.682	0	1:1	454	0.5%
F12	0	+1.682	0	1:1	1545	0.5%
F13	0	0	-1.682	1:1	1000	0.0795%
F14	0	0	+1.682	1:1	1000	0.9205%
F15	0	0	0	1:1	1000	0.5%

Assay procedures

Analytical method for the assay of aspirin

In order to determine the standard calibration curve of aspirin, a stock of 1 mg/ml in pH 7.4 phosphate buffer solution was prepared. Then, dilutions were made to prepare a series of solutions containing aspirin in different concentrations. In these solutions, absorbance values at 297 nm were determined UV spectrophotometrically.

Plotting the concentration values (x) versus absorbance values (y) calibration curve of aspirin in pH 7.4 phosphate buffer was determined [13, 14]. Analytical parameters for the assay of aspirin were calculated by using ANOVA test.

LOD and LOQ determination

The limit of detection (LOD) and the limit of quantitation (LOQ) were determined by using the following equations [17/20]:

LOD = 3SD/m LOQ = 10SD/m

Where SD is the standard deviation of the absorbance values (n = 6) of the second smallest concentration, m is the slope of the calibration curve.[15]

Recovery studies

To study the accuracy, reproducibility, precision and to check the interference from excipients used in the formulation of the above method, recovery experiments were carried out. In order know whether the excipients show any interference with the analysis, known amounts of the pure drug were added to the microsponges containing the known amount of aspirin. Mixtures were analyzed by spectrophotometrically. Percentage recovery was calculated after three experiments. [16]

Drug - excipients compatibility studies

Drug excipients compatibility was done by F.T.I.R. and D.S.C.

F.T.I.R. Spectroscopy

Drug and excipients compatibilities were analyzed by IR spectral studies. IR spectra of drug, polymer, drug-polymer physical mixture and the formulation were obtained using FTIR spectrophotometer. Fourier–transformed infrared spectra were obtained on FTIR spectrophotometer (Thermo scientific) using the KBr disk method. 1-2 mg of sample was gently triturated with KBr powder and compress into disc by applying pressure for 10 min in a hydraulic press. The disc was placed in the sample holder and scanned from 4000 to 400cm^{-1} [17, 18]

Differential Scanning Calorimetry (DSC)

The thermal behavior of pure drug and Aspirin loaded microsponge analyzed for differential scanning calorimetry (Shimadzu DSC 60, TSW 60, Japan).The DSC analysis was carried out to identify the compatibility between the drug and excipients. Samples were accurately weighed (2-4 mg) and heated in sealed aluminum pans at a rate of 10°C per min between 30-300°C temperature ranges under nitrogen atmosphere. [18]

Characterization of aspirin loaded microsponge

Production yield

The production yield of the Microsponge can be determined by following equation:

$$\text{Production Yield} = \frac{\text{Practical mass of Microsponge}}{\text{Theoretical mass (polymer + drug)}} \times 100$$

Particle size analysis

The particle size of the microsponges was determined with particle size analyzer. Each determination was carried out in triplicate.

Loading efficiency

The loading efficiency (%) of the microsponges can be calculated by putting the value of Actual drug content and Theoretical drug content in following equation

$$\text{Loading Efficiency} = \frac{\text{Actual drug content}}{\text{Theoretical drug content}} \times 100$$

The weighed amount of drug loaded microsponges (100 mg) was kept in 100 ml phosphate buffer pH 6.8 for 12 h with continuous stirring. The samples were filtered using 0.45_m membrane filter and the samples were analyzed against blank using UV spectrophotometer. [19]

Morphology and Surface topography

For morphology and surface topography, prepared microsponges can be coated with gold-

palladium under an argon atmosphere at room temperature and then surface morphology of the microsponges can be studied by scanning electron microscopy (SEM). [19]

Drug content

Weight accurately 100 mg of Microsponge and dissolved in 25 ml 0.1N NaOH (1000µg/ml). Sonicate this solution for 15 min, and then filtered this solution by using Whattman filter paper No. 42. After that withdraw 1 ml from this solution and add in 100 ml of volumetric flask and then diluted up to the mark (10µg/ml) with 0.1N NaOH. The absorbances of this solution were measured in UV-visible spectrophotometer at 297 nm against blank (0.1N NaOH). [19]

In-vitro dissolution study of uncoated microsponge

This study was performed using USP type-I Dissolution Apparatus (Basket type) at speed 50 rpm. A weighed amount of microsponge was filled in the capsule (00 sized) and put it in the basket. 900 dissolution medium (pH 6.8) was used as dissolution medium. The temperature of medium was maintained at 37 ± 0.5^{o}C.Withdraw 5ml of dissolution medium at specific time intervals (0.5, 1, 2, 3, 4, 5, 6,7, 8, 9, 10, 11 and 12 hour) and equal amount of fresh dissolution medium was replaced immediately after each withdrawal to maintain sink condition. The amount of drug present in each sample was determined by UV-visible spectrophotometer at 297 nm against blank. [20]

Release Kinetic Study

To analyze the in vitro release data various kinetic models will be used to describe the release kinetics. The dissolution profile of batches were fitted to zero order, first order, Higuchi, Korsmeyer-Peppas model, Hixson Crowell to ascertain the kinetic modeling of the drug release. [20]

Residual solvent test

To analyze the amount of Dichloromethane in final formulation was checked by this test. Head Space Gas Chromatography method was applied for this purpose. [21] According to I.C.H. guide line Dichloromethane comes under class II residual solvent and has limitation up to 6oo ppm. Several process parameters which are listed below.

Parameters for gas chromatography:

Inlet temperature: 30 ˚C, Hold time: 5 min, Increasing of temperature: 10˚C/min up to 180˚C
Flow rate 1ml/min.

Parameters for Head Space Auto sampler:

Thermostat time: 20 min.**,** Temperature: 90˚C**,**
Detector: Flame ionization detector

Coating of Microsponge

Aspirin loaded microsponges were coated by spray coating method. Accurately weighed aspirin microsponge were taken in coating pan and allowed to rotate at 50 rpm. Coating solution was sprayed using fine spray nozzle.(table 3) Inlet temperature was maintained at 60 ˚C with the help of blower which allowed rapid evaporation of solvent and drying of the microsponge. It was continues to rotate and hot air sprayed until all the microsponge were completely dried. [22]

Table 3: Preparation and optimization of Coating solution

Batch code	Ingredients (%w/w) of microsponge				(ml)	
	Cellulose acetate phthalate	Dibutyl phthalate	Titanium dioxide	Methyl red	Iso propyl alcohol	Methylene Chloride
CS1	6	2	0.2	0.15	40	60
CS2	4	2	0.2	0.15	40	60

Resiliency test

As the microsponges are claimed to be resilient these should not show any sign of disruption even after compression as tablet. This was verified by SEM micrographs of crushed tablet. It is possible for industrial scale up.

RESULTS

Assay of aspirin

Calibration of aspirin was performed by using the method which was explained earlier Analytical parameters for the determination of aspirin by UV spectrophotometric method were given in below Table 4.

Table 4: Analytical Parameter of Aspirin

Parameter	Result	Confidence limit	
		Lower 95%	Upper 95%
Linearity range (mg/ml)	0.2 - 1.0		
Slope	0.049	0.672	0.032
Intercept	0.011	- 0.009	0.056
RSD of slope (%)	0.69		
RSD of intercept (%)	7.23		
Determination coefficient (r2)	0.9992		
Standard error of slope	0.00069		
LOD (µg/ml)	0.033		
LOQ (µg/ml)	0.192		

Recovery studies

Recovery study results of aspirin microsponges were given in Table 4. Each dose contains 200 mg of aspirin as it can be seen from Table 5

Table 5: Recovery data of Aspirin

Theoretical value (mg)	Practical value (mg)	Recovery (%)	Mean recovery	RSD (%)
210	206.12	98.15		
210	205.18	97.70		
210	208.13	99.10	998.31	0.62

Fourier Transform Infra-Red Spectroscopy (FTIR)

The FTIR spectra of Aspirin, Eudragit RS100, and Aspirin loaded microsponge formulation are depicted in figure 1,2,3.

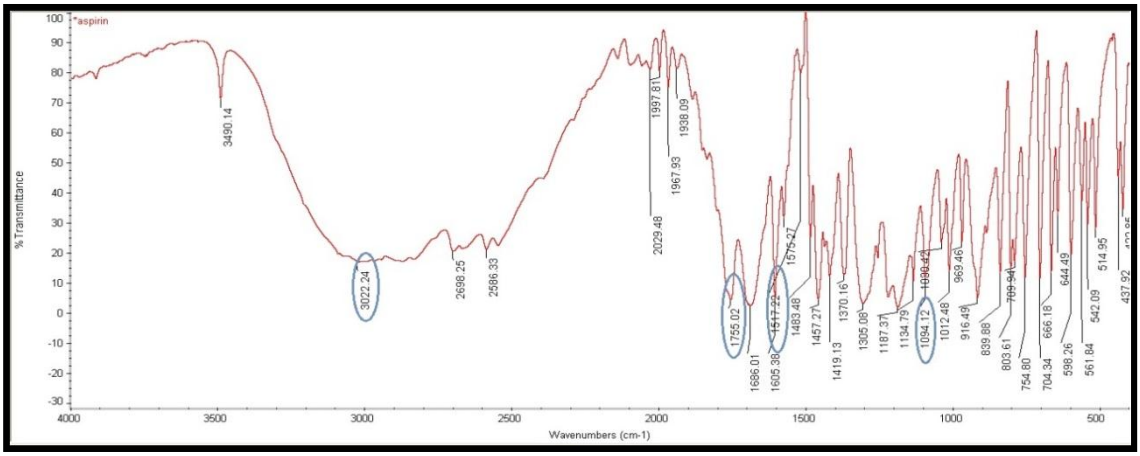

Figure 1: FTIR Spectrum of Aspirin

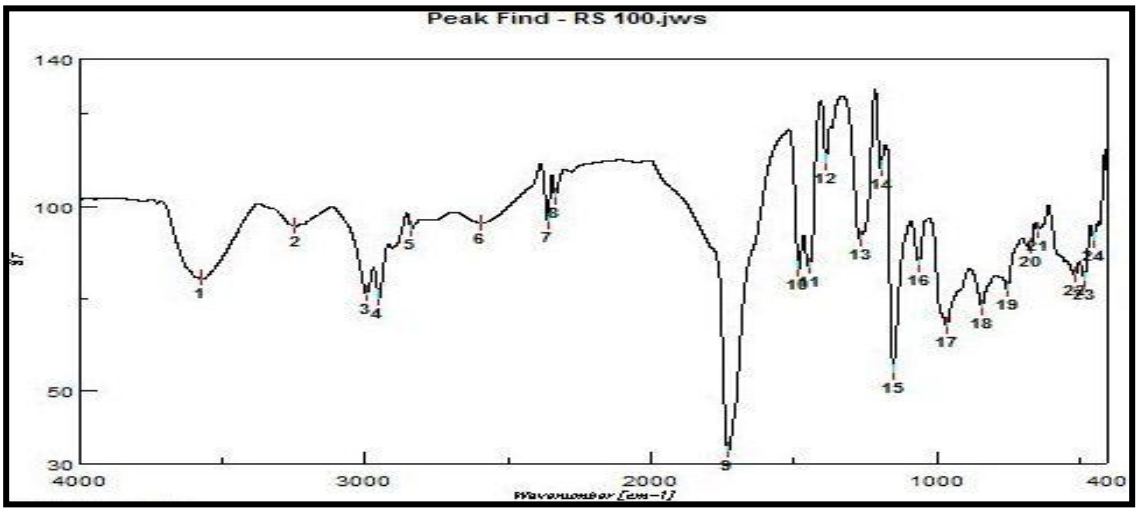

Figure 2: FTIR Spectrum of Eudragit RS 100

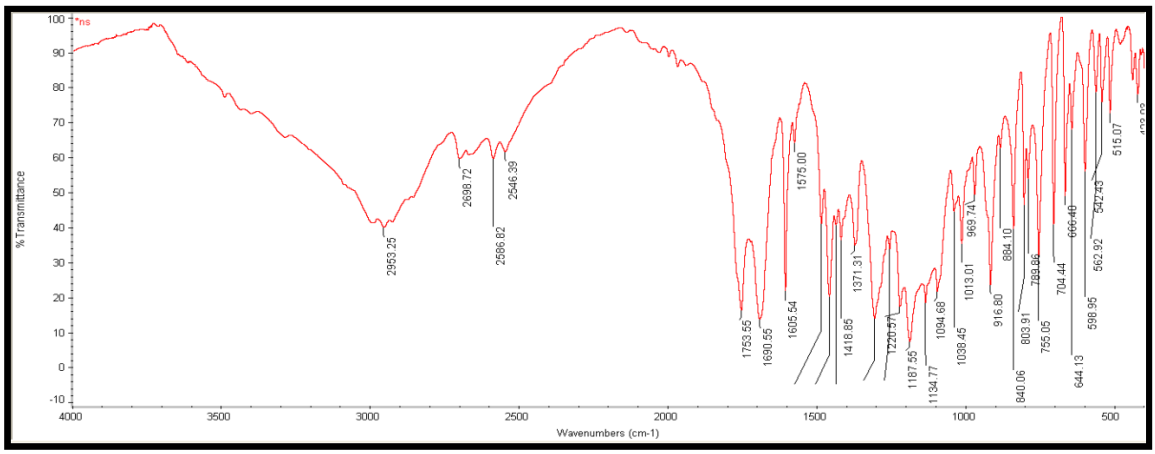

Figure 3: FTIR spectra of Aspirin loaded microsponge formulation.

Differential Scanning Calorimetry (DSC)

The DSC thermogram of Aspirin and Aspirin loaded microsponge were evaluated by DSC and represented in figure 4 and 5.

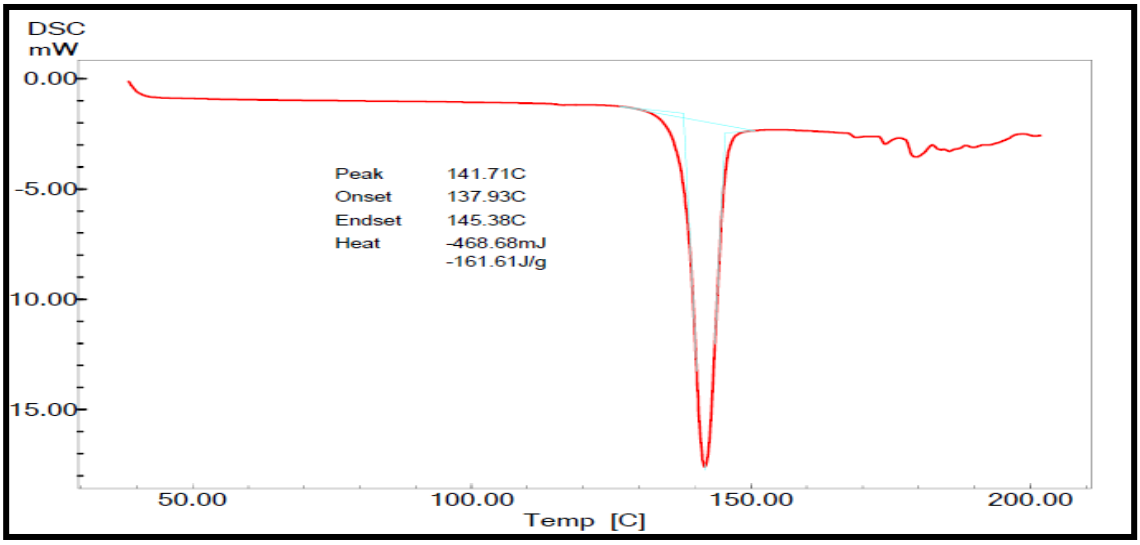

Figure 4: DSC curve of pure Aspirin

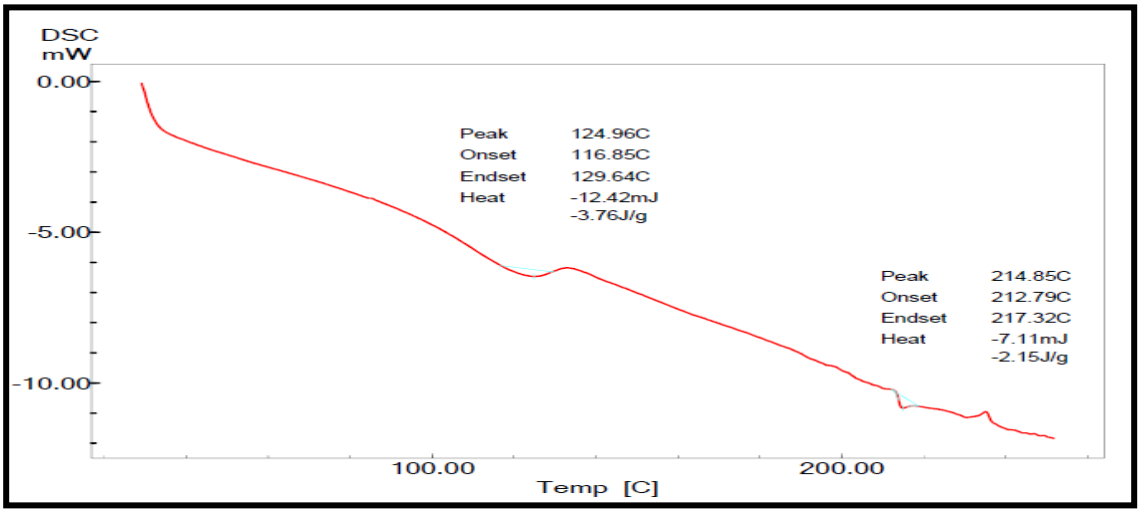

Figure 5: DSC curve of Aspirin loaded microsponge formulation.

Optimization of formulation by Central Composite Design for 2^3(3 factor 2 level)

Results of optimization CCD

As per results depicted in below table 6 loading efficiency were found to be between 25.20 – 64.09 %, Production yield were lies between 27.55 – 64.10 %, Drug content were found between 15.58 - 76.35 % and particle size were lies between 43.14 -298.06 µm.

Table 6: Evaluation data of all batches

Batch	Loading efficiency±S.D. (%) (n=3)	Production yield (%)	Drug content ± S.D. (%) (n=3)	Particle size ± S.D.(µm) (n=50)
F1	47.38±0.2066	48.33	32.71±0.7783	60.04±0.7763
F2	53.29±0.6161	64.12	57.59±0.7145	168.37±0.4688
F3	54.22±0.3798	53.00	34.23±0.2730	180.33±1.2472
F4	55.67±0.6958	61.40	54.68±0.4916	93.07±0.9159

F5	44.92±0.6516	46.10	32.15±0.4163	158.81±0.6059
F6	59.72±0.5159	60.08	59.86±0.4501	171.96±0.5843
F7	30.90±0.6124	33.06	30.68±0.7374	170.66±0.2357
F8	62.42±0.5040	61.24	61.35±0.6291	162.90±0.3012
F9	64.09±0.2080	56.40	15.58±0.4005	86.97±0.4862
F10	62.75±0.1778	53.32	76.35±0.6850	91.22±0.6499
F11	25.20±0.3417	27.55	45.67±0.5450	158.35±1.0464
F12	46.23±0.2759	47.07	49.57±0.7466	298.06±0.4482
F13	50.64±0.5122	53.35	47.66±0.7486	72.07±0.2824
F14	58.58±0.4401	61.00	48.74±0.6143	64.67±0.4619
F15	57.98±0.1385	58.00	49.94±0.6200	43.14±0.3739

Effect of formulation composition on drug content

3D surface and counter plots of drug content for Drug:polymer ratio was shown in figure 6.

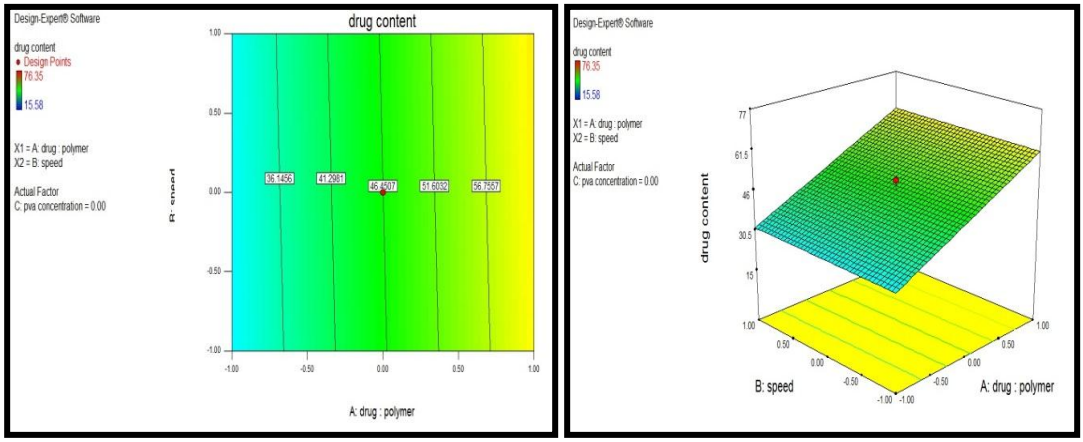

Figure 6: 3D surface and counter plots of Drug content against Drug: Polymer ratio

Table 7: Evaluation data of all batches

Batch	% CDR at 1 hr±S.D(n=3)	t50%±S.D(n=3)	t90%±S.D(n=3)
F1	19.30±0.5632	5.10 ± 0.1471	11.12±0.02512
F2	19.64 ± 1.8703	5.36 ± 0.0163	11.10 ± 0.0336
F3	20.00 ± 0.5034	5.39 ± 0.3894	10.56 ± 0.0090
F4	18.50 ± 2.0915	4.88 ± 0.2160	10.89 ± 0.0376
F5	18.99 ± 2.9844	5.00 ± 0.0339	10.94 ± 0.1253
F6	19.37 ± 1.9036	5.14 ± 0.3080	10.94 ± 0.0799
F7	19.32 ± 1.1649	5.13 ± 0.3080	10.85 ± 0.0489
F8	19.20 ± 2.8037	5.07 ± 0.0408	10.57 ± 0.1177

F9	19.30 ± 0.2262	5.10 ± 0.0216	11.01 ± 0.0067
F10	19.22 ± 0.4105	5.08 ± 0.1489	10.47 ± 0.0123
F11	19.55 ± 0.5605	5.24 ± 0.3080	11.14 ± 0.0168
F12	19.42 ± 0.6231	5.20 ± 0.0509	10.23 ± 0.0186
F13	19.48 ± 0.7349	5.29 ± 0.0418	11.26 ± 0.0073
F14	19.30 ± 0.8173	5.1 ± 0.2160	10.56 ± 0.0408
F15	23.48 ± 0.8043	6.01 ± 0.6940	11.36 ± 0.0241

Effect of formulation composition on %CDR at 1 hrs

3D surface and counter plots of %CDR at 1 hrs against Drug: Polymer ratio was shown in figure 7.

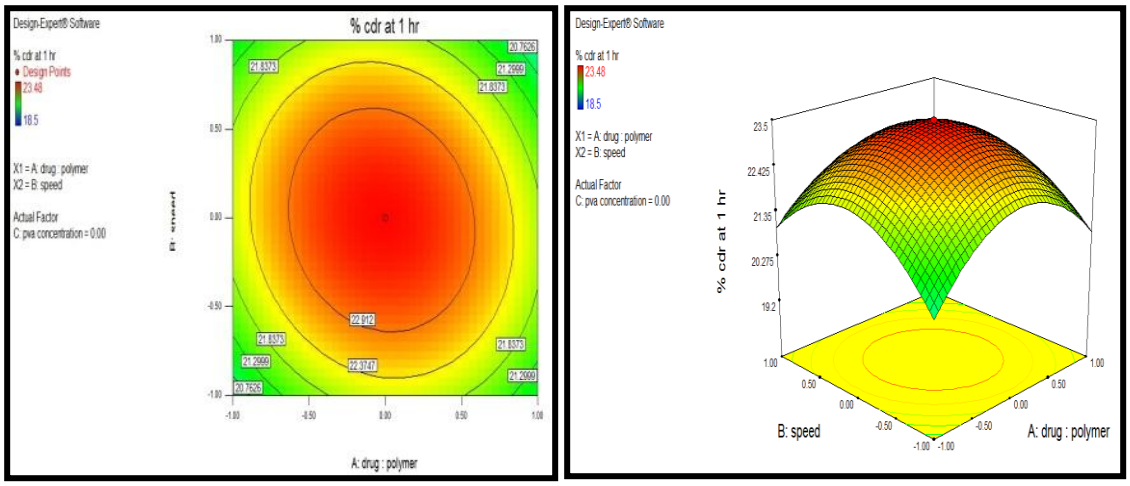

Figure 7: 3D surface and counter plots of %CDR at 1 hrs against Drug : Polymer ratio

Effect of formulation composition on t50%

3D surface and counter plots of t50% against Drug: Polymer ratio Effect of formulation composition on t90% was shown in figure 8.

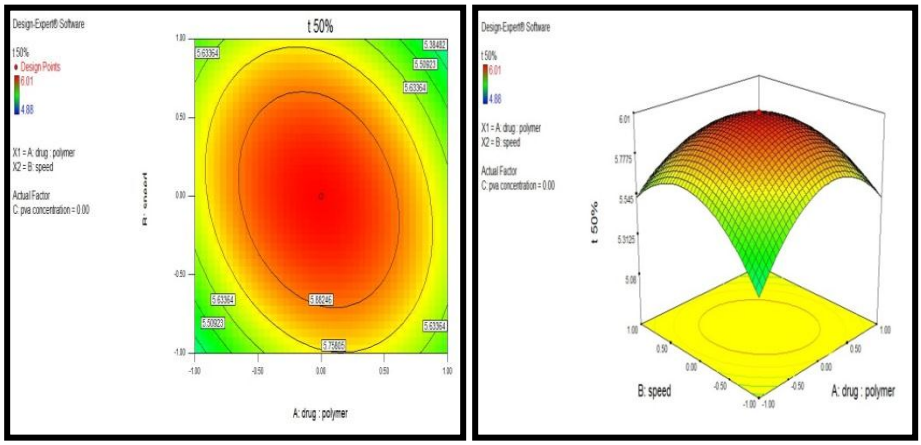

Figure 8: 3D surface and counter plots of t50% against Drug: Polymer ratio

Effect of formulation composition on t90%

Relationship between drug: polymer ratio and t 90% was depicted in figure9.

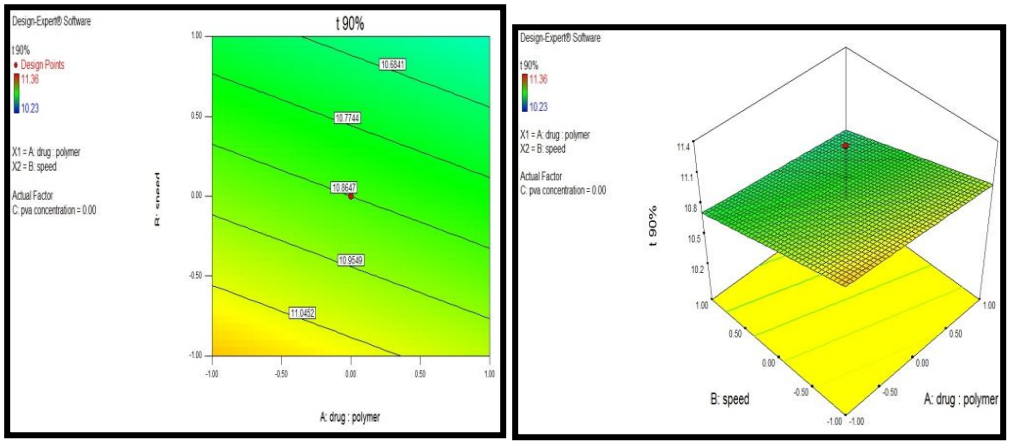

Figure 9: 3D surface and counter plots of t90% against Drug: Polymer ratio

Model Validation and Optimization

The desirability function was probed using Design-Expert software to acquire the optimized formulation. (Table 8) The optimum formulation was selected on based on criteria of drug content, %CDR at 1 hrs, t50%, t90%. Up on trading of various responses variable and comprehensive valuation of feasibility and exhaustive grid search, the formulation composition with speed 1280 rpm, PVA 0.48 %w/v concentration and Drug: Polymer 1.08:1 were found to fulfill the maximum requisite of an optimum formulation

Table 8: Result of check point batch

Responses	Predicted Value	Experimental Value	% Relative Error
Drug content	51.07	47.95 ± 0.93	3.12
%CDR at 1 hrs	21.89	25.67±1.78	3.78
t50%	5.73	4.73±2.12	1.00
t90%	11.08	9.03±2.45	2.05

Check point formulation were obtained from the RSM, the composition and predicted responses confirm the validity of the calculated optimal parameters and predicted responses the optimum formulation were prepared according to values of the factors and subjected to all same studies.

Residual solvent test

In this test the figure 10 shows clear peak in chromatogram of Dichloromethane standard whereas in chromatogram of final formulation the peak of Dichloromethane not appear and it is more confirmed by the area of peak of Dichloromethane in both standard and final formulation 1420944µV.s and 28.34µV.s respectively.

Parts per million calculated by following equation:

Area of standard /Area of sample = Concentration of standard/ Concentration of sample

1420944.16/28.34 = 2800/ Concentration of sample So, Concentration of sample = 0.0558 ppm, Area in µV.s and Concentration in ppm

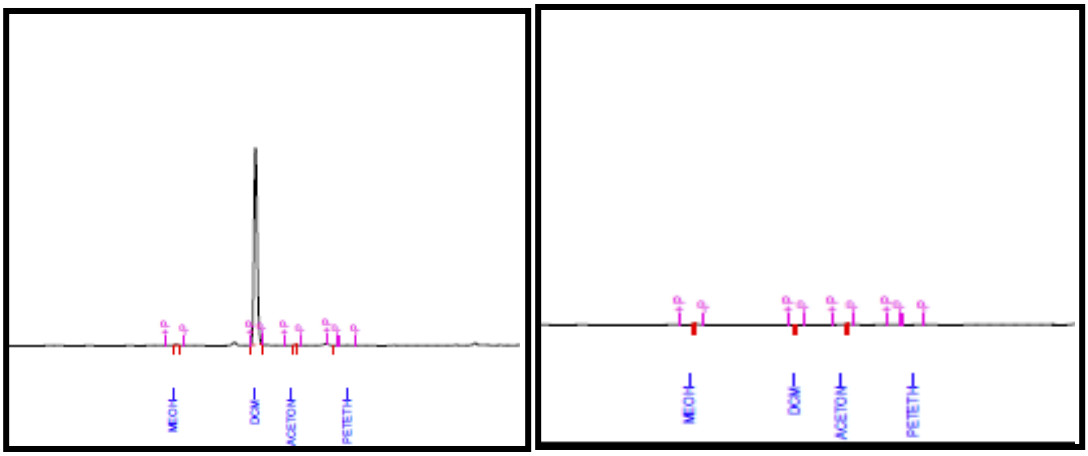

Figure 10: Chromatogram of DCM standard and final formulation

Scanning Electron Microscopy

As shown in SEM photographs figure 11 the

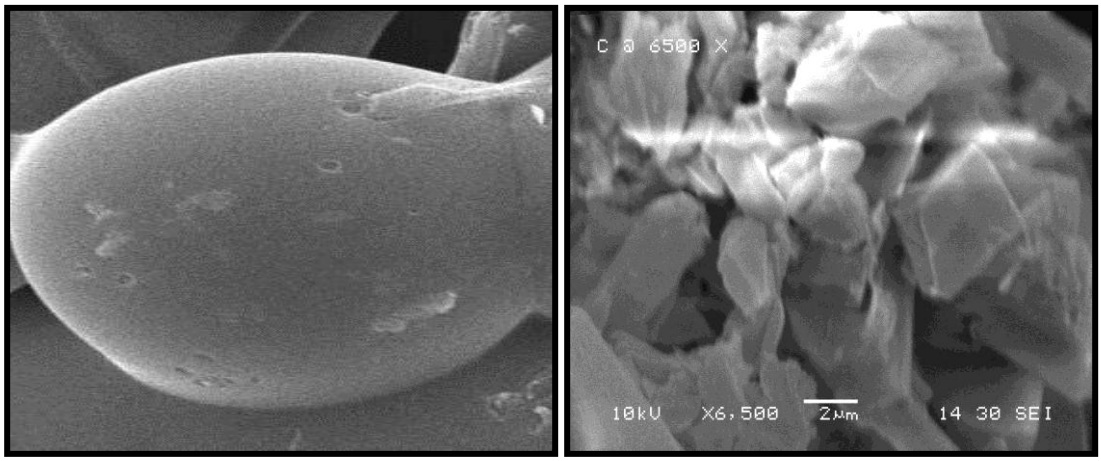

Figure 11: SEM of optimized formulation

Coating of aspirin loaded microsponge

The effects of different concentration of cellulose acetate phthalate and Dibutylphthalate on drug release of enteric coated microsponge in acidic media pH 1.2 were evaluated and the results were given in the Table 9.

Table 9: Drug release from coated microsponge

Batch code	% Drug Release in two hour (acidic buffer pH 1.2)	% Drug release in first hour in pH 6.8
CS1	3.34±0.21	19.70±0.22
CS2	6.12±0.14	25.12±0.42

In-vitro drug release study

Aspirin release from optimized batch of microsponge was performed in different media, in 0.1 N HCL (pH1.2) for initial 2h and phosphate buffer pH6.8 for the period up to 12h and the results are given in the figure 12.

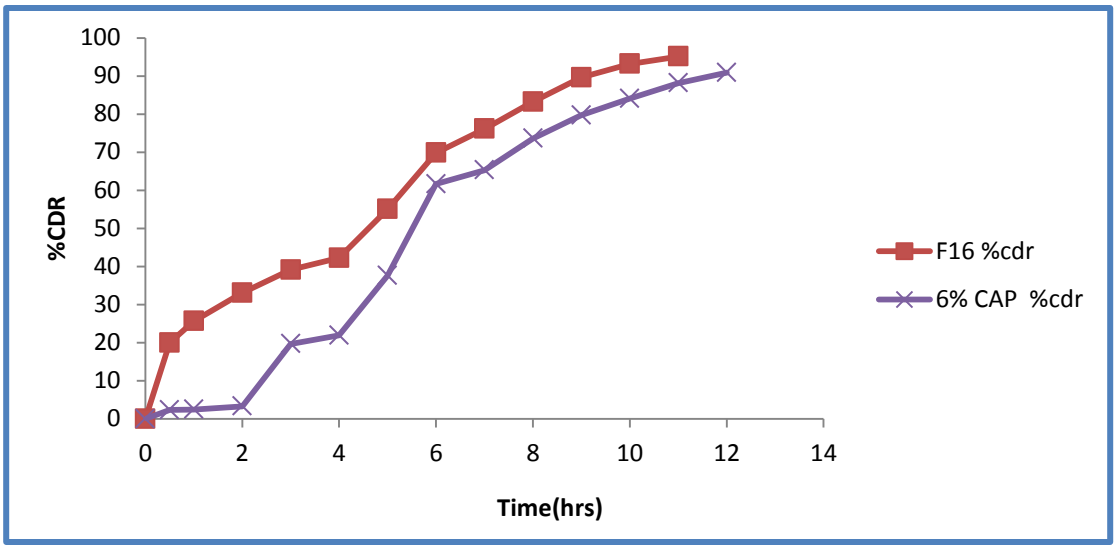

Figure 12: Drug release from F16 batch and 6% Cellulose acetate phthalate

Resiliency test

As the microsponges are claimed to be resilient these should not show any sign of disruption even after compression as tablet. This was verified by SEM micrographs of crushed tablet. Shown in Figure 13.

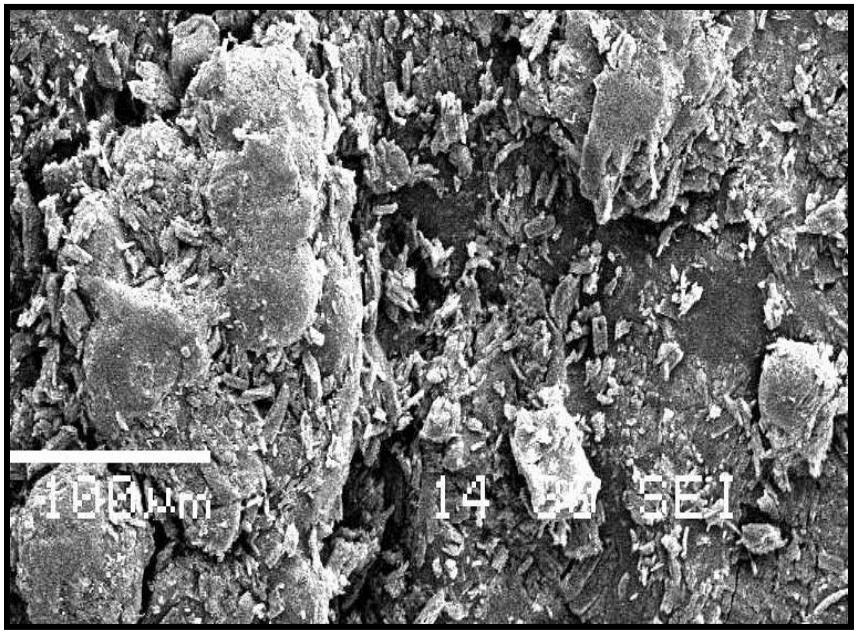

Figure 13: SEM of crushed tablet of formulation

DISCUSSION

Aspirin Microsponge formulated as sustained delivery so reducing the side effects of Aspirin. It was prepared by Quasi emulsion solvent diffusion method using Eudragit RS100 as drug retarding polymer. Central Composite Design was applied for optimizing formulation parameters such as Drug: Polymer, Speed and PVA concentration and study the effect on dependent variables Drug content, %CDR at1 hrs, t50% and t90% and also evaluation parameters were evaluated like particle size, loading efficiency, production yield. Microsponge were

characterized in terms of scanning electron microscopy, Residual solvent test, Resiliency test and Release kinetics models of uncoated and coated microsponge.

By Spectrophotometric method its shows linear relation ship between concentration and absorbance and high percentage recovery results show that the method is free from the interferences of the excipients used in the formulation.

Fourier Transform Infra-Red Spectroscopy (FTIR)

FT-IR spectrum of Aspirin showed characteristic peaks at 1755 cm^{-1} (C=O stretching), 1095 cm^{-1} (C-O stetching), 1516 cm^{-1} (C=C stretching), 2941 cm^{-1} (C-H stretching) whereas, FT-IR spectrum of Eudragit RS100 showed characteristic peaks at 1729 cm^{-1} C=O (ester) stretching, 1448,1482 CH_2 bending were identified, which was same in Aspirin loaded microsponge formulation [23].Thus, there was no any interaction between drug and excipients

Differential Scanning Calorimetry (DSC)

The DSC thermogram of pure Aspirin showed sharp endothermic peak at 141ºC, corresponding to its melting point (135-140 ºC)[24] DSC thermogram of Aspirin loaded microsponge formulation showed endothermic peak at 124ºC which showed complete disappearance of characteristic peaks of Aspirin; a fact that the drug was molecularly dispersed within the polymer matrix and there was no interaction between drug and excipients

Effect of formulation composition on drug content

It was found that drug content increase with increase in the Drug: Polymer ratio as particle size increase more drugs entrapped in the system. But no further increase drug content was found with increase Drug: Polymer ratio above optimum concentration this is due to decrease in particle size.

Effect of formulation composition on %CDR at 1 hrs

It was found that %CDR at 1 hrs increases when Drug: Polymer ratio increases from lower level to middle level but it further reduces when Drug: Polymer ratio increases from middle level to higher level.

Effect of formulation composition on t50%

It was found that t50% increases when Drug : Polymer ratio increases from lower level to middle level but it further reduces when Drug : Polymer ratio increases from middle level to higher level.

Effect of formulation composition on t90%

It was found that when Drug : Polymer ratio increase from lower level to higher level there was no any changes in drug release, it shows the linear relationship between drug: polymer ration and t 90%.Drug release of microsponges can be explained by Higuchi matrix model . All formulations of aspirin microsponges modified the release of ketoprofen when compared drug itself. Among all the formulations of microsponges, it can be said that MS 7 is the best formulation when it is evaluated with all physical parameters and in vitro release profiles. By grid search for check point batches, the predicted error was below 8% indicating that the observed responses were very closed to predicted value.

Residual solvent test

Chromatogram of Dichloromethane standard whereas in chromatogram of final formulation the peak of Dichloromethane not appear and it is more confirmed by the area of peak of Dichloromethane in both standard and final formulation 1420944µV.s and 28.34µV.s respectively.

Scanning Electron Microscopy

Microsponges were porous and spherical. The surface of the microsphere was rough and revealed. The presence of pours in the drug loaded microsponge.

Coating of aspirin loaded microsponge

It was observed that coating solution with 6%w/w concentration of Cellulose acetate phthalate and 2%w/w concentration of Dibutylphthalate (CS1) gave negligible release in gastric pH 1.2 after two hour. Moreover it showed desired percentage release in phosphate buffer pH 6.8.

In-vitro drug release study

It was observed that the drug release from enteric coated microsponge was pH dependent, showed negligible drug release in acidic pH 1.2 due to the stability of cellulose acetate phthalate at lower pH. Drug release of microsponges can be explained by Higuchi matrix model 24. All formulations of aspirin

microsponges modified the release of aspirin when compared drug itself. Among all the formulations of microsponges, it can be said that F16 coating with 6% CAP is the best formulation when it is evaluated with all physical parameters and in vitro release profiles.

Resiliency test

By SEM Study clearly shows the spherical porous particles (microsponges) without any signs of fracture or damage that were structurally similar to fresh microsponges. Thus it can be claimed that the microsponges are resilient enough to withstand the compression force applied during tablet compression, again a favorable manufacturing aspect.

This study presents new approach for the preparation of aspirin loaded modified microsponges. All the factors studied had an influence on the physical characteristics of the microsponges. In vitro dissolution results showed that the release rate of aspirin was modified in all formulations. The unique compressibility of microsponges offers a new alternative for producing mechanically strong tablets. Therefore, one can assume that the aspirin microsponge are promising pharmaceutical dosage forms by providing sustained release drug delivery systems and avoiding the dose related side effects in the entire physiological region.

CONCLUSION

From the present study, it was concluded that quasi emulsion solvent diffusion method can be successfully used for preparation of aspirin microsponge using Eudragit RS100 as drug release modifier. Various formulation variables such as Drug: polymer ratio, Stirring rate and PVA concentration which can influence the loading efficiency, mean particle size, production yield, and drug content, % CDR at 1hrs, t50% and t90%. Out of all other parameters, concentration of polymerhave profound effect to control and sustain the release of Aspirin. Cellulose acetate phthalate was used to prepare enteric coated microsponge which was affected by the pH of the dissolution medium resulted a negligible release in 0.1 N HCL and sustained effect in phosphate buffer (pH 6.8) up to 12 hr. It was concluded that coated as well as uncoated microsponge were following Zero order kinetics for drug release, FT-IR and DSC studies did not reveal any significant drug interactions. Therefore, one can assume that the aspirin microsponge are promising pharmaceutical dosage forms by providing sustained release drug delivery systems and avoiding the dose related side effects in the entire physiological region.

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