



## PREPARATION AND EVALUATION OF PARECOXIB MICROSPONGE HYDROGEL SUSTAINED RELEASED TABLET

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### ABSTRACT:

Microsponges are the polymeric drug delivery systems composed of porous microspheres. They are tiny sponge like spherical particles that consists of myriad of inter-connecting voids within a non-collapsible structure with a large porous surface. The present work is to formulate and evaluate the Parecoxib Microsponge Hydrogel Sustained Release Tablet. The Microsponges of Parecoxib is prepared by Quasi-emulsion solvent diffusion method using Ethyl cellulose and Eudragit RS100 as polymers and Di-butyl phthalate as Plasticizer. And they are characterized for FTIR studies, production yield, particle size analysis, DSC and SEM. The production yields of formulations were from 77.77 to 82.75. FTIR and DSC studies are revealed that the drug and polymer are compatible with each other during preparation. The average diameter of Microsponge is ranged from 536.9 nm to 489.7.

Parecoxib Microsponge hydrogel were prepared as sustained release tablets by using sustained release polymers like MCC, Magnesium stearate, Lactose and talc. Preformulation of Microsponge granules were carried out by various parameters and post formulation were carried out by *In-vitro* dissolution studies, hardness, friability and weight variation tests. Formulation F3 shows good results for the drug release kinetics as controlled release and F6 formulation shows good results for the *in-vitro* dissolution studies for sustained release.

**Key words:** Microsponge hydrogel drug delivery, Parecoxib, Sustained drug release tablets, quasi emulsion solvent diffusion method.

### INTRODUCTION

The term "Drug Delivery" covers a very extensive range of techniques used to deliver therapeutic agents into the human body. Drugs are administered with a main aim of curing patient ailments. Drugs are never administered in their pure form but are converted in a suitable formulation so that its onset and intensity of action as well as total duration of action can be checked. Among the various routes of drug delivery oral route is most widely used route of drug delivery. But conventional dosage form offers few limitations which could be resolved by modifying the existing dosage form.

### Sustained Release Drug Delivery System:

Among the various routes of drug delivery oral route is most preferred route. But conventional dosage form offers few limitations which could be resolved by modifying the existing dosage form. Sustained and controlled drug delivery system helps in constant plasma drug concentration and retards the release rate of drug thereby extending the duration of action. There are various formulation strategies for sustained release tablets among which diffusion system serves as an important tool.

Hence the problem like poor patient compliance, multiple dosing, and see-saw fluctuations can be

easily minimized. They can be formulated by either direct compression or wet granulation method by using a variety of hydrophilic or hydrophobic polymers<sup>1</sup>.

## MATERIALS AND METHODS

### Materials:

Parecoxib was procured from Dr. J Timmasetty, HOD and Professor, Department of Pharmaceutics, Bapuji College of Pharmacy, Davanagere as gift sample, Ethyl cellulose and Di-butyl-phthalate was supplied from Loba Chemie Pvt. Ltd, Dichloromethane was supplied from S.D Fine chemicals Ltd, Mumbai, Eudragit RS 100 was supplied from Yarrow Chemicals Pvt. Ltd. And polyvinyl alcohol was supplied from Fisher Scientific India Pvt. Ltd.

### Method:

#### Preparation of Parecoxib Microsponge by Quasi Emulsion Solvent Method:

Microsponges were prepared by quasi emulsion solvent diffusion method. Various concentrations of polymers (Eudragit RS 100 and Ethyl cellulose) and drug (Parecoxib) was dissolved in 20 ml of Dichloromethane which acts as internal phase. The drug is dissolved under ultra-sonication at 350 C for 15 minutes. Then weighed 1gm of PVA was dissolved in 180 ml of water using water bath or magnetic stirrer not exceeding to 600 C and pour remaining 20 ml of water which acts as an external phase. Internal phase containing drug and polymer is poured to external phase (PVA and water), to this, add 1 ml of Dibutyl Phthalate for the plasticity enhancement. Stirred the above solution using a propeller at 1200 rpm for 2 hrs at room temperature. Microsponges were settled at the bottom. The liquid is poured through Whatman filter paper then the Microsponges were collected on the filter paper then dried at room temperature for 12 hrs<sup>2</sup>.

**Table 1: Composition of the prepared Parecoxib Microsponge hydrogel**

Internal Phase							
SI No		F <sub>1</sub>	F <sub>2</sub>	F <sub>3</sub>	F <sub>4</sub>	F <sub>5</sub>	F <sub>6</sub>
1	Parecoxib	100mg	100mg	100mg	100mg	100mg	100mg
2	Eudragit RS 100	1.6 gm	1.7 gm	1.8 gm	-	-	-
3	Ethyl cellulose	-	-	-	1.6 gm	1.7 gm	1.8 gm
4	Dichloromethane	20ml	20ml	20ml	20ml	20ml	20ml
5	Dibutyl Phthalate	1ml	1ml	1ml	1ml	1ml	1ml
External Phase							
1	PVA	1gm	1gm	1gm	1gm	1gm	1gm
2	Water	200ml	200ml	200ml	200ml	200ml	200ml

### Characterization of Microsponges

#### Percentage Yield

The prepared Microsponges of all batches were accurately weighed. The measured weight of prepared Microsponges was divided by total amount of all the excipients and drug used in the preparation of the Microsponges gives the total percentage yield of Microsponges. It was calculated by using following equation<sup>3</sup>.

$$\text{Percentage yield} = \frac{\text{Actual weight of product}}{\text{Total weight of excipients and drug}} \times 100$$

#### Morphology study using SEM

The morphological studies were carried out by ZEISS EVO. US Scanning Electron Microscope (SEM), connected with fine coat, JEOL JFC-1100E Ion sputter. The sample was loaded on copper sample holder and sputter coated with carbon followed by Gold<sup>4</sup>.

#### Morphological study using DSC

Differential scanning calorimetry (DSC) study was carried out to evaluate thermal behaviour and thermo tropic characteristics of the drug. Nearly 5 mg sample ( Parecoxib pure drug /ethyl cellulose

/formulation F6) were sealed in aluminum pan followed by heating at a rate of 10°C/min over temperature range of 40–300°C under nitrogen atmosphere of flow rate 10 ml/min and thermogram (Mettler-Toledo DSC 821e, Switzerland) was obtained<sup>5</sup>.

### Particle size determination

Particle size determination was done by Zeta potential analyser (Zetasizer) of Malvern Instruments Ltd. The instruments were designed to measure the size, shape and charge of particles. The average particle size was calculated as per the result.

### Drug content studies

The weight equivalent to 100 mg of drug was taken and transferred to a 100 ml standard flask. 25 ml of ethanol and 25 ml of 7.4 pH phosphate buffer were added and shaken for about half an hour and the volume was made up to 100 ml with 7.4 pH phosphate buffer. The above solution was filtered and 5 ml of filtrate was taken and diluted to 100 ml with 7.5 pH phosphate buffer. The absorbance of the resulting solution was measured at 245 nm and the content of Parecoxib was calculated<sup>6</sup>.

### Evaluation of Parecoxib Microsponges

#### Determination of pH

Required quantity of prepared Microsponge was taken in suitable container and measured its pH by using digital pH meter. Microsponges were stable up to the pH range from 1 to 11<sup>7</sup>.

#### Determination of viscosity<sup>8,9</sup>

All formulated Microsponges were subjected to viscosity measurement by using a Brookfield digital viscometer (Analytical Technologies) by using spindle #2 at room temperature. The measurement of consistency of the Microsponge hydrogel was done by dropping a cone attached to a holding rod from distance of 10cm in such a way that, it should fall on centre of the glass cup filled with Microsponge. The distance travelled by the cone was measured.

#### *In vitro* diffusion study<sup>10,11</sup>

Cellophane membrane was used for this study in Frantz Diffusion Cell. 100mg of Microsponge is placed in donor compartment with which is filled phosphate buffer 7.4. The membrane was mounted between the compartments of the Frantz Diffusion Cell. Reservoir compartment was filled with phosphate buffer 7.4. The study was carried out at

37± 1o and speed was adjusted to 100 to 120 rpm and it is carried out for 24 hours. 5 ml of sample was withdrawn from reservoir compartment by the help of hypodermic syringes at half an hour interval for 2 hours, then one hour interval for 10 hours and finally 6 hrs to next 24 hrs. And absorbance was measured spectrophotometrically at 245nm. Each time the reservoir compartment was replenished with the 5 ml fresh volume of phosphate buffer 7.4 pH solution to maintain constant volume.

### Preformulation parameters: Micromeritic properties

#### A. Bulk density and tapped \ true density:

Both bulk density (BD) and Tapped / True density were determined. Powder of Microsponge was taken in a 10ml measuring cylinder and initial volume was write and tapped at height of 2.5cm at 2-second intervals until no further change in volume was noted after tapping. BD and TD calculated using the following formula.

$$BD = \frac{\text{Weight of the powder}}{\text{volume of the powder}}$$

$$TD = \frac{\text{Weight of the powder}}{\text{Tapped volume of the powder}}$$

#### B. Determination of carr's index:

The compressibility index of the powder determined by the Carr's Compressibility index as shown in following formula

$$\text{Carr's index (\%)} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

#### C. Determination of the angle of repose:

Angle of repose was measured for the Microsponge powder, to observe the flow properties of powders. The Funnel method was used; the powder was allowed to pass freely through a funnel and poured onto a horizontal plane, fixed base diameter, free of vibration petri dish to form a cone. The funnel height was maintained at approximately 2- 4 cm from the tip of the powder pile in order to minimize the impact of the falling powder on the tip of the cone. The tan of angle of repose ( $\theta$ ) was calculated after measuring the height (h) of the cone of the powder. This follows following formula

$\tan \Theta = \frac{h}{r}$  where, **h** is the height of the pile in centimetre, **r** is the radius of the pile in centimetre

#### D. Determination of hausner's ratio

Hausner's ratio is a number that is correlated to the flow ability of a powder or granular material. The Hausner ratio is calculated by the formula where the freely settled bulk density of the powder, and the tapped density of the powder. A Hausner ratio greater than **1.25** is considered to be an indication

of poor flowability. The formula is below mentioned<sup>12</sup>.

$$\text{Hausner ratio} = \frac{\text{Tapped density}}{\text{bulk density}}$$

#### Formulation of Parecoxib Microsponge Sustained Release Tablets

The formulated and evaluated Parecoxib Microsponges were prepared as Sustained Release tablets.

**Table 2: Composition of Parecoxib sustained released tablets**

Formulation code	Parecoxib Microsponges (mg)	Micro crystalline cellulose (mg)	Magnesium stearate (mg)	Talc (mg)	Lactose (mg)
F1	90	100	20	10	80
F2	92	100	20	10	78
F3	94	100	20	10	76
F4	92	100	20	10	78
F5	94	100	20	10	76
F6	96	100	20	10	74

#### The Microsponge tablets were prepared as follows:

First weighed all the tablet ingredients according to the required formula. Then prepared 10% starch paste by adding starch to the 100 ml water to 250 ml beaker and heat it until to get a smooth paste. Then blended the ingredients in mortar and pestle and add 100 mg of previously prepared Microsponge hydrogel to above. Then add sufficient quantity of starch paste to above blended powders and finally damp mass is prepared. This prepared mass was passed through sieve no #10 for the granules. This granule were dried under thermostatic ovens like tray drier until the moisture is completely removed. Then the dried granules were proceeded to further sieving (no #22 and #44) to make coarse and fines. Add 15% of fines to that of the total weight of coarse and finally add 2 % of talc. The tablets were compressed into flat-faced punches of 10 mm diameter using Rimek Mini Press-I single sided rotary multiple station tablet compression machine.

#### Post formulation studies of Parecoxib loaded Microsponge tablets

**Weight variation:** 10 tablets are selected randomly and weighed individually and collectively and % of weight variation is calculated by following formula.

$$\% \text{ of weight variation} = \frac{\text{Individual Weight} - \text{Average weight}}{\text{Average Weight}} \times 100$$

**Hardness of tablet:** The mechanical strength of the tablet was determined by using Monsanto hardness tester. This tester has a graduated scale which gives the reading in Kg/cm<sup>2</sup>. The tablet to be tested was placed between the spindle and anvil. The desired pressure needed to hold the tablet in position is applied by moving the screw knob in clockwise direction. The scale was moved so that the indicator rested at zero. The pressure was applied till the tablet breaks. The reading were noted.

**Thickness of tablet:** Thickness of tablet is evaluated by using micrometre screw gauge. Test is carried out randomly on ten tablets and average values are calculated.

**Friability:** 10 tablets are weighed and placed in friabilator. The chamber is rotated for 4 minutes at a speed of 25 r.p.m. the tablets are removed from the chamber and weighed again. Loss in weight

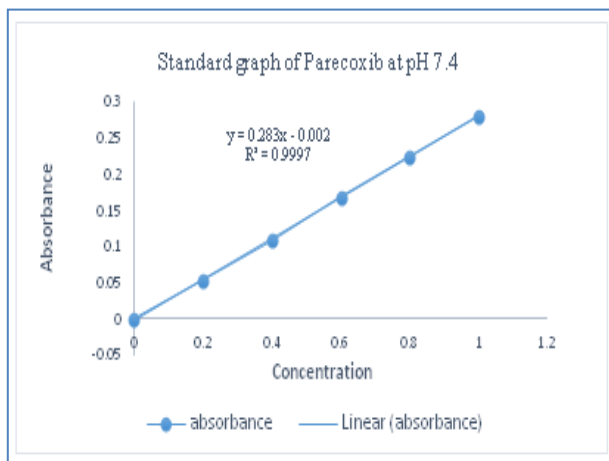
indicates friability. The tablets to be considered of good quality if loss in weight is less than 0.8%.

**In vitro dissolution studies:** In vitro dissolution study of tablets was performed using USP XXIV type II (type II) dissolution apparatus ( $3.7 \pm 0.5$ , 900 mL, 50 rpm) in phosphate buffer pH 7.4 for a period of 24 h. Aliquots were taken out at every 1 hour interval for 24 h, and the volume was replaced with an equivalent amount of aliquots of fresh dissolution medium. The samples were withdrawn and analysed spectrophotometrically at 245 nm respectively<sup>13</sup>.

**RESULTS AND DISCUSSIONS**

**UV spectrometric study**

This Parecoxib showed maximum absorption at wavelength 245nm in phosphate buffer pH 7.4. The standard calibration curve obeys Beer’s law and gives linear curve and the  $R^2$  value is not greater than 0.999<sup>14</sup>.



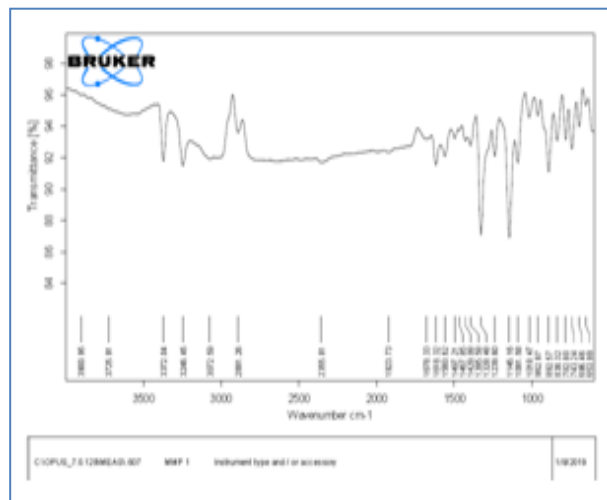
**Figure 1: Calibration curve of Parecoxib in Phosphate buffer 7.4**

**FTIR studies**

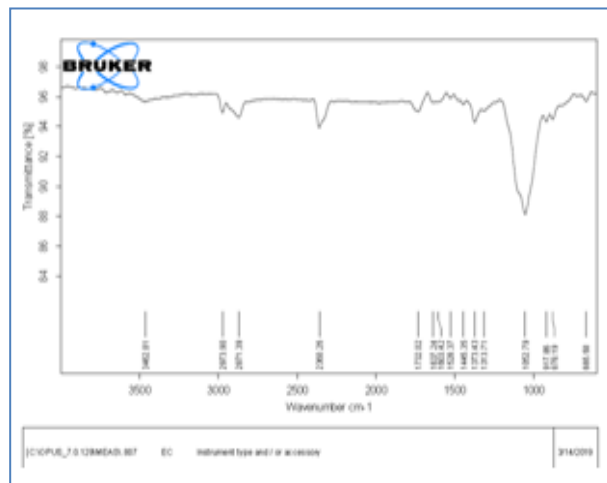
For the compatibility studies between drug and polymer selected are subjected to FTIR studies. IR spectrum of pure drug and polymer and physical mixture of drug and polymer (formulation) was recorded.

The IR spectra shows sharp peak at  $3372\text{ cm}^{-1}$  due to presence of amine group (NH) and it shows the peak at  $1678\text{ cm}^{-1}$  due to the presence of C=O groups corresponding to ketone groups. And presence of alkenes (C=C), the spectra shows peak at  $1618\text{ cm}^{-1}$ . These similar peaks are obtained in formulation also. It indicates that the pure drug

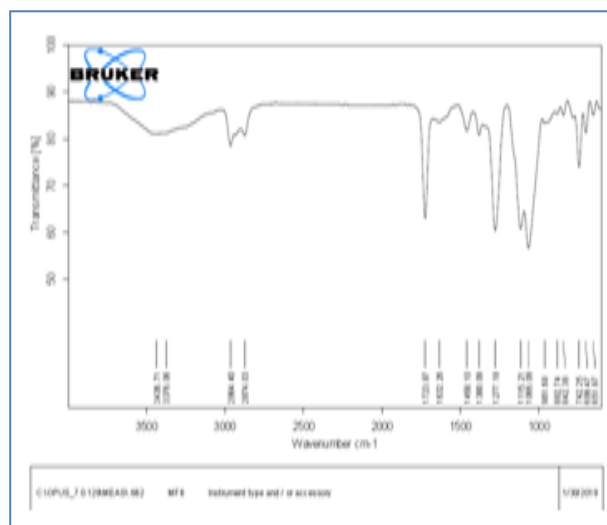
functional groups peaks were present in all the formulations without changes in the peaks position<sup>15</sup>.



**Figure 2: IR spectra of Pure Parecoxib Drug**



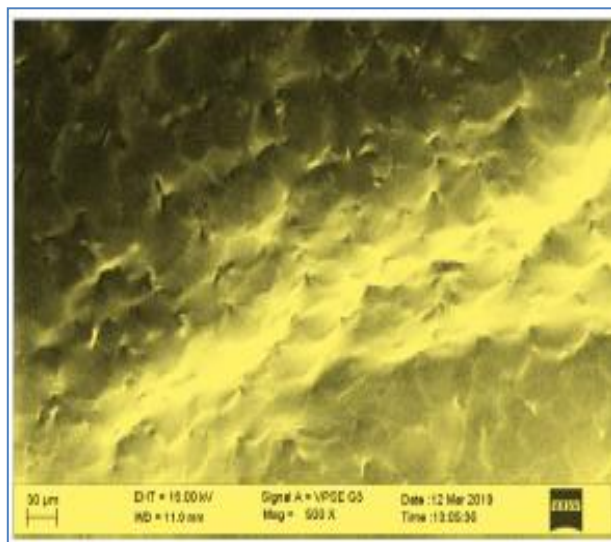
**Figure 3: IR spectra of Ethyl cellulose**



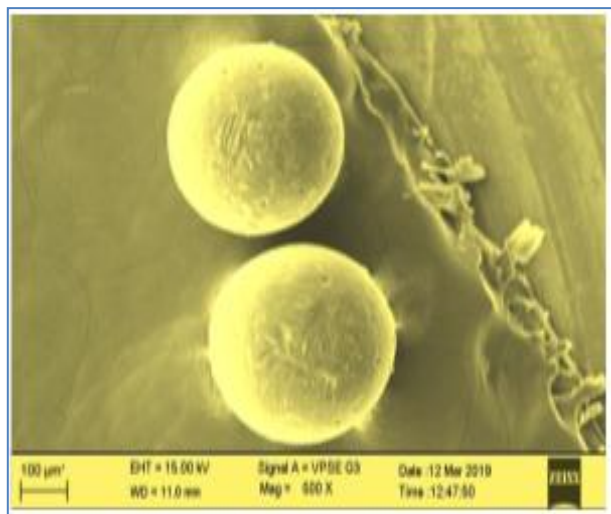
**Figure 4: IR spectra of Microsponge formulation F<sub>6</sub>**

### SEM studies

The SEM images of formulation F3 and F6 reveals that the microsponges were highly porous in nature and pore size is less than  $1\mu$  with discrete spherical and smooth in surface.



(A)



(B)

**Figure 5: Highly porous nature (A) and spherical nature (B) of Microsponges**

### Particle size analysis

The particle size determination of Microsponge formulation was carried out by particle size analyser (Zetasizer, Malvern) and recorded. The average diameter of the Microsponges was found to be **536 nm to 412nm**. Particle size of

Microsponges was increased on increasing in the polymer content and they were mention in **Table No. 3**

### Drug content studies

The drug content study of all Microsponge formulations was carried out by suitable method as mentioned in above methodology. The % drug content was in the range of **82.16 to 92.15 %**. The F6 formulation shows highest drug content compare to other formulation. Different concentrations of two different polymers may changes the drug content. And they are fairly exhibited uniform drug content. The values are shown **Table No. 3**

### DSC studies

DSC thermograms of plain Parecoxib and Microsponges without drug and drug loaded Microsponges was recorded. Drug without Microsponges have shown an endothermic peak at **104.340 C**, whereas Parecoxib loaded Microsponges shows a peak at **103.190 C** and **115.540 C**. The plain Parecoxib has showed an endothermic peaks at **172.360 C** due to the melting of drug. But this peak is not exactly seen in drug loaded formulations. This indicates the drug was amorphously or uniformly distributed in amorphous forms in formulations.

### pH studies

The pH of all six formulations were performed by pH meter and it shown in the pH range of **6.2 to 6.9** as shown in **Table no 3**. The formulation F6 shows highest pH compare to other formulation. By changing different polymers in different concentration in the formulation may lead to changes in the pH of the preparation.

### Viscosity studies

It was performed for all six Microsponge formulations. The viscosity is in the range of **2138 to 2497 cps**. Formulation **F6** shows highest viscosity range. These were free flowing in nature and optimum range. The values are mention in **Table No. 3**

**Table 3: Drug content, particle size analysis, pH and viscosity of Microsponge formulation**

Sl No	Formulation code	Drug content	Particle size analysis (nm)	pH	Viscosity
1	F <sub>1</sub>	82.16%	530	6.2	2355 cps
2	F <sub>2</sub>	86.72%	520	6.3	2364 cps
3	F <sub>3</sub>	90.40%	536	6.5	2165 cps
4	F <sub>4</sub>	85.13%	412	6.6	2255 cps
5	F <sub>5</sub>	89.24%	489	6.2	2138 cps
6	F <sub>6</sub>	92.15%	432	6.9	2497 cps

**Diffusion studies**

The *in vitro* diffusion studies of Microsponge formulations were carried out by using Franz's diffusion cell and using cellophane membrane as barrier. The results of *in vitro* diffusion studies are shown in **Table no 4**. The cumulative percentage of drug diffusion from F1 to F6 ranges from 70.65% to 90.63%. Formulation 'F3' shows second highest percentage drug release (89.2306) and from the graph it shows the drug release in 'controlled manner' compare to other formulations. The release kinetics was evaluated by making use of Zero order, First order, Higuchi's diffusion and Peppas equation.

The drug release through the Microsponge hydrogel of Parecoxib follows Peppas diffusion kinetics with controlled mechanism and the 'n' values are in between 0.51 to 0.7. By fitting in the Korsmeyer- Peppas equation the release kinetics follows non Fickian kinetics. If the 'n' values of Korsmeyer- Peppas equation below 0.5, this indicates Fickian kinetics. If the 'n' values of Korsmeyer- Peppas equation is in between 0.5 to 1, this indicates non-Fickian kinetics. Here the Microsponges of Parecoxib release kinetics are fitted in Korsmeyer- Peppas equation. 'n' values are in between 0.5 to 1, so the release is following non Fickian, diffusion controlled kinetics. The regression co-efficient values are given in **Table 5**

**Table 4: In-vitro drug release kinetics of Microsponge formulation F<sub>1</sub> to F<sub>6</sub>**

Time (hr)	% Drug Release *					
	$\bar{X} \pm SD$					
	F <sub>1</sub>	F <sub>2</sub>	F <sub>3</sub>	F <sub>4</sub>	F <sub>5</sub>	F <sub>6</sub>
0	0	0	0	0	0	0
0.5	7.32±0.015	13.01±0.020	16.23±0.041	10.62±0.035	18.03±0.020	6.23±0.025
1	12.03±0.020	18.33±0.015	24.57±0.035	16.02±0.020	26.13±0.036	13.56±0.021
1.5	16.22±0.017	23.56±0	28.63±0.036	26.68±0.036	36.56±0.040	19.23±0.017
2	23.60±0.025	27.62±0.020	33.63±0.036	32.56±0.036	48.26±0.036	26.15±0.022
3	27.96±0.025	39.52±0.025	39.67±0.026	37.06±0.026	53.15±0.004	28.23±0.040
4	31.67±0.021	47.24±0.020	48.95±0.036	45.36±0.040	65.23±0.045	32.65±0.035
5	45.59±0.026	55.80±0.030	56.63±0.030	50.25±0.035	71.96±0.020	36.58±0.045
6	54.65±0.026	62.64±0.030	67.05±0.040	62.29±0.040	82.13±0.036	41.06±0.026
7	65.34±0.021	77.65±0.020	79.34±0.030	69.32±0.040	80.26±0.022	52.68±0.030
8	72.61±0.00	78.89±0.026	82.61±0.026	75.68±0.040	80.63±0.017	56.12±0.036
9	80.35±0.017	84.74±0.036	85.60±0.050	78.26±0.030	78.23±0.026	62.12±0.035
10	83.65±0.030	82.35±0.036	86.35±0.045	84.26±0.036	85.13±0.025	68.63±0.017
11	85.25±0.026	83.26±0.022	87.61±0.036	80.35±0.030	82.56±0.017	70.62±0.015
12	85.95±0.026	85.25±0.040	89.23±0.035	78.26±0.004	86.26±0.015	72.01±0.036
18	84.25±0.030	89.26±0.030	87.25±0.036	83.16±0.045	85.52±0.030	75.26±0.004
24	82.65±0.020	90.63±0.025	86.64±0.026	70.65±0.053	78.26±0.026	79.26±0.030

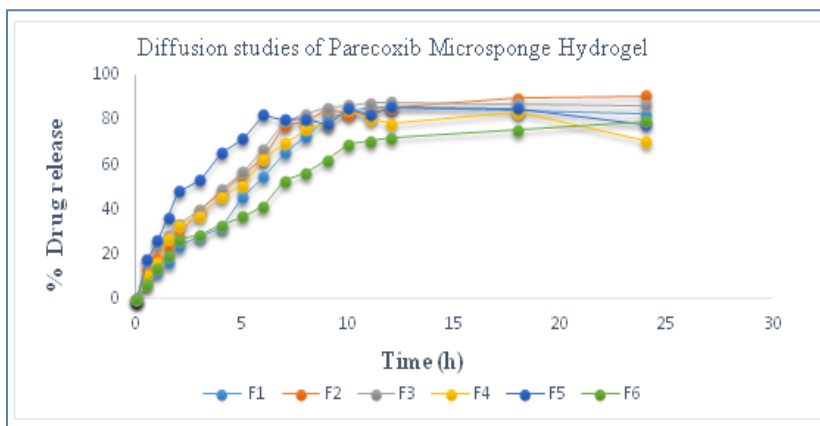


Figure 6: Graph of *in vitro* drug release of Microsponge formulation F<sub>1</sub> to F<sub>6</sub>

Table 5: Regression co-efficient (R<sup>2</sup>) values of Parecoxib Microsponge hydrogel according to different kinetic models

Formulation	Zero order		First order		Higuchi	Peppas	
	R <sup>2</sup>	n	R <sup>2</sup>	n	R <sup>2</sup>	R <sup>2</sup>	n
F <sub>1</sub>	0.6780	3.8896	0.7105	0.096	0.8557	0.9185	0.7032
F <sub>2</sub>	0.6792	3.7541	0.8390	0.111	0.8864	0.9257	0.5662
F <sub>3</sub>	0.6196	3.4856	0.6928	0.101	0.8499	0.9098	0.5398
F <sub>4</sub>	0.5601	3.0688	0.5620	0.071	0.8019	0.8691	0.5134
F <sub>5</sub>	0.4578	2.6588	0.5182	0.071	0.7430	0.8084	0.5652
F <sub>6</sub>	0.7927	3.3755	0.8896	0.072	0.9374	0.9577	0.5890

**Pre formulation studies of Parecoxib loaded Microsponge tablets**

The blended granules with Microsponges were subjected to various preformulation studies like true density, bulk density, angle of repose, carr’s index and finally hausner’s ratio. The results were mentioned in **Table no. 6**. All preformulation studies shows that excellent flow property and they are in within the IP limits.

Table 6: Micromeritic properties of Microsponge hydrogel with granules

Blends	True density (gm/ml) * $\bar{X} \pm SD$	Bulk density (gm/ml) * $\bar{X} \pm SD$	Angle of repose * (°) $\bar{X} \pm SD$	Carr’s index (%) * $\bar{X} \pm SD$	Hausner’s ratio * $\bar{X} \pm SD$
F <sub>1</sub>	0.475±0.023	0.44±0.017	25.6° ±0.001	7.53±0.015	1.08±0.050
F <sub>2</sub>	0.494±0.026	0.46±0.036	26.5° ±0	8.32±0.026	1.04±0.026
F <sub>3</sub>	0.473±0.031	0.44±0.023	26.6° ±0.007	4.25±0.036	1.04±0.021
F <sub>4</sub>	0.515±0.023	0.45±0.021	24.7° ±0.001	5.76±0.021	1.06±0.007
F <sub>5</sub>	0.507±0.050	0.45±0.021	25.6° ±0.005	5.32±0.023	1.04±0.017
F <sub>6</sub>	0.564±0.036	0.53±0.026	24.2° ±0.007	6.19±0.026	1.06±0.026

\* mean of 3 readings

**Post formulation studies of Parecoxib loaded Microsponge hydrogel sustained release tablets**

The formulated Microsponge sustained released tablets were subjected to various post formulation parameters like weight variation, hardness test, friability, diameter and thickness and the results are mentioned in **Table no. 7**. The *In vitro* Dissolution studies were also performed for the sustained release tablets. All the formulations were in IP limits.



**Table 7: Weight Variation, Hardness, Friability, Diameter and Thickness of Parecoxib loaded Microsponge sustained released tablets**

Formulation Code	% weight variation	Hardness test (kg/cm <sup>2</sup> )	Friability (%)	Diameter (mm)	Thickness (mm)
F <sub>1</sub>	2.57±0.026	4.52±0.025	0.466±0.036	8.13±0.022	4.026±0.030
F <sub>2</sub>	3.56±0.030	4.84±0.030	0.360±0.044	8.15±0.040	4.025±0.022
F <sub>3</sub>	2.27±0.044	4.72±0.025	0.498±0.022	7.97±0.036	4.031±0.028
F <sub>4</sub>	2.93±0.025	4.82±0.025	0.380±0.036	8.16±0.025	4.015±0.025
F <sub>5</sub>	2.96±0.030	4.55±0.044	0.465±0.025	8.02±0.027	4.012±0.036
F <sub>6</sub>	2.62± 0.025	4.63±0.036	0.434±0.021	8.18±0.030	4.023±0.036

\*mean of 3 readings

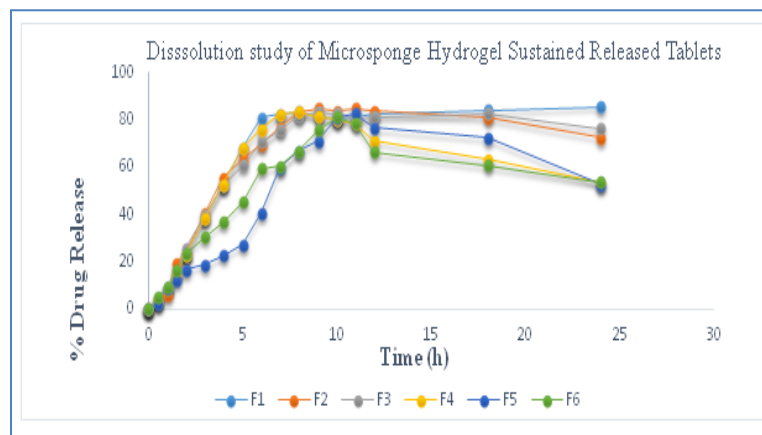
#### ***In vitro* dissolution studies:**

The results of *in vitro* Dissolution studies are shown in **Table no. 8**. The cumulative percentage of drug dissolution from F1 to F6 ranges from 52.69 % to 85.54%. Formulation 'F3' shows second highest percentage drug release (84.6947) and from the graph it shows the drug release in 'Sustained release manner' compare to other formulations. The release kinetics was evaluated by making use of Zero order, First order, Higuchi's diffusion and Peppas equation.

The drug release through the Microsponge hydrogel of Parecoxib follows Peppas dissolution kinetics with sustained release mechanism and the 'n' values are in between 0.61 to 0.76. By fitting in the Korsmeyer-Peppas equation the release kinetics follows non Fickian kinetics, because the 'n' values are in between 0.5 to 1, so the release is following non Fickian, dissolution kinetics. The 'n' values and R<sup>2</sup> values of all six Microsponge formulations are mentioned in **Table no. 9**.

**Table 8: *In- vitro* dissolution studies of Microsponge sustained released tablets F<sub>1</sub> to F<sub>6</sub>**

Time (hr)	% Drug Release *					
	$\bar{X} \pm SD$					
	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
0.5	3.25±0.036	4.35±0.036	3.62±0.040	3.26±0.040	2.36±0.036	5.36±0.022
1	8.62±0.022	6.04±0.036	9.62±0.0360	8.62±0.026	8.63±0.027	9.35±0.031
1.5	15.24±0.040	19.25±0.040	14.69±0.027	15.24±0.036	12.36±0.025	16.23±0.027
2	22.95±0.036	23.64±0.030	25.96±0.036	22.96±0.022	16.69±0.036	23.68±0.022
3	38.16±0.038	40.24±0.036	39.56±0.031	38.18±0.040	18.68±0.040	30.76±0.040
4	52.84±0.040	55.23±0.036	52.31±0.028	52.80±0.036	22.64±0.031	36.96±0.027
5	68.23±0.030	63.25±0.040	60.64±0.036	68.24±0.028	26.96±0.036	45.68±0.031
6	80.64±0.036	69.65±0.040	70.69±0.040	75.65±0.036	40.64±0.040	59.35±0.036
7	82.35±0.040	76.25±0.027	75.62±0.022	82.36±0.031	59.65±0.022	60.56±0.036
8	83.36±0.036	83.02±0.028	81.65±0.030	83.37±0.027	66.56±0.036	66.86±0.040
9	81.13±0.030	84.56±0.036	83.68±0.035	81.13±0.040	70.69±0.022	75.63±0.022
10	80.22±0.025	83.35±0.027	82.96±0.031	80.22±0.022	80.65±0.040	81.65±0.028
11	81.23±0.035	84.64±0.036	84.69±0.036	78.36±0.036	82.63±0.035	78.62±0.040
12	82.34±0.036	83.35±0.036	81.26±0.027	71.12±0.031	76.35±0.031	66.52±0.038
18	83.95±0.036	80.63±0.031	82.86±0.028	63.25±0.040	72.25±0.022	60.65±0.027
24	85.54±0.031	72.32±0.031	76.56±0.036	53.26±0.038	52.69±0.028	53.65±0.036



**Figure 7: Graph of *In-vitro* dissolution study of Microsponge Hydrogel Sustained Released Tablet formulation F<sub>1</sub> to F<sub>6</sub>**

**Table 9: Regression co-efficient ( $R^2$ ) values of Parecoxib Microsponge hydrogel Sustained Tablets according to different kinetic models**

Formulation	Zero order		First order		Higuchi	Peppas	
	$R^2$	n	$R^2$	n	$R^2$	$R^2$	n
F <sub>1</sub>	0.5517	3.5899	0.6345	0.090	0.7794	0.8203	0.7294
F <sub>2</sub>	0.4063	2.5191	0.3220	0.046	0.6480	0.7826	0.6185
F <sub>3</sub>	0.4838	3.1453	0.4640	0.069	0.7318	0.7992	0.6745
F <sub>4</sub>	0.2739	2.3245	0.1839	0.042	0.5225	0.6765	0.6322
F <sub>5</sub>	0.5019	3.1632	0.4145	0.060	0.6830	0.8406	0.7693
F <sub>6</sub>	0.3937	2.865	0.3291	0.060	0.6497	0.7236	0.7027

## Conclusion

The present study was to formulate, and evaluate the Parecoxib loaded Microsponge hydrogel sustained released tablets. To achieve six formulations of Microsponges were prepared by quasi emulsion solvent diffusion method using Eudragit RS 100 and Ethyl cellulose as polymers. Prepared Microsponges were subjected for evaluation for Particle size analysis, Surface morphology, Differential Scanning Calorimetric analysis, Fourier Transform infrared spectroscopy analysis, pH studies, viscosity, Drug content studies and *in vitro* diffusion studies. And evaluated for pre formulation as well as post formulation studies for tablet punching are also performed.

The Microsponges formed have smooth surface and discrete spherical and highly porous in nature as observed in SEM. DSC studies shows the drug is amorphously distributed in formulations. And the FTIR shows the drug and polymers are compatible by incorporating the drug with Eudragit RS 100 and Ethyl cellulose, the same peaks related to

Parecoxib were seen with slight change in their peaks. The *in vitro* diffusion studies of Microsponge hydrogel shows shown maximum amount of drug release in controlled manner. The diffusion studies follows Peppas diffusion and non Fickian kinetics. *In vitro* dissolution studies of prepared Microsponge hydrogel sustained release tablets follows Peppas's dissolution kinetics with sustained release mechanism. And by fitting in Korsmeyer-Peppas's equation it shows non Fickian kinetics.

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