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Formulation and Evaluation of Flurbiprofen Loaded Microsponges in Capsule for Sustained Drug Delivery

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ABSTRACT

The new investigation in this present work is to develop microsponges constructed novel drug delivery system for sustained action of Flurbiprofen. Various techniques are involved, among them, Quai-emulsion solvent diffusion method was engaged using Ethyl cellulose with different drug: polymer ratio for development of microsponges, for optimization purposes, several factors are considered in investigation. Several evaluation studies for the formed microsponges were carried out FT-IR, SEM, particle size analysis, morphology, encapsulation efficiency and *in vitro* drug release studies were carried out. Finally, it was concluded that there is no drug polymer interaction as per FT-IR. Encapsulation efficiency, particle size and drug content showed higher impact on alteration of drug polymer ratio. SEM studies showed that morphological microsponges are spherical and porous in nature and with mean particle size of 30.11 ± 0.14 µm. The capsule loaded with microsponges, were followed by *In vitro* drug release studies and found to release the drug for sustained manner that is 98.12 ±0.63 % of release upto 12 hrs.

Keywords: Microsponges, Flurbiprofen, Capsule, Sustained action

INTRODUCTION

In the current years, the development of new drugs is not sufficient for drug treatment. However, it also involves developing a suitable drug delivery system at the site of action. The *in-vivo* fate of the drug is not only determined by the properties of the drug but it is also determined by the carrier system, which permits a sustained and localized release of the active drug according to the specific need of the therapy. The biggest challenge up to date is to sustain the delivery of the medicaments by various modern technologies met by extensive research.

Carrier technology is the potential solution to these challenges. Microparticles and nanoparticles have been increasingly researched

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to achieve targeted and sustained release of drugs. These include microspheres, liposomes, and nanoparticles etc. Which alters the absorption and release characteristics of the drug from these carriers are unable to sustain the release rate of drug from itself. Once the outer wall is ruptured the drug contained within microspheres will be released from it. The microsponges-based polymeric microspheres uniquely overcome problems associate with above technologies. Microsponges are extremely small, inert, indestructible spheres that do not pass through the skin. Rather, they collect in the tiny nooks and crannies of the skin and slowly release the entrapped drug, as the skin needs it. They are designed to deliver a pharmaceutical active ingredient efficiently at the minimum dose, enhance stability, reduce side effects, and modify drug release.

These products are typically presented to the consumer in conventional forms like creams, gels or lotions and they contain a relatively high concentration of active ingredients. Recently their use is also being investigated for oral drug delivery. This article provides concise information to the various aspects of the structure, development, applications and future of microsponges. Oral route has been the commonly adopted and most convenient route for the drug delivery. Oral route of administration has been received more attention in the pharmaceutical field because of the more flexibility in the designing of dosage form than drug delivery design for the other routes.

MATERIAL AND METHODS

Flurbiprofen was obtained as a gift sample from AET Laboratories Pvt., Ltd. Hyderabad. Ethyl cellulose, Poly vinyl alcohol (PVA) were purchase from S.D fine chemical Pvt., Ltd. Mumbai. Alcohol and Dichloro methane (DCM) were purchased from S.D fine chemical Pvt., Ltd., and Mumbai. All other reagents and solvent used are of analytical grade.

PREFORMULATION STUDIES

Determination of Melting point

The melting point of pure drug (FBD) was determined by melting point apparatus (Bio Technics India). The drug was placed in a capillary tube which is sealed one end and opens other end, then the capillary tube was fitted into the holder containing coil, gradually temperature was increased and identified for melting point of pure drug. Average of three readings was taken and compared with standard melting point of drug.

Determination of λ_{max} : Spectral scanning was done for drug with 10 µg/ml concentration, the maximum absorbance was observed at 248 nm.

Standard curve for Flurbiprofen: 10 mg of Flurbiprofen was weighed and transferred to 100 ml of a volumetric flask the drug was dissolved in 2 ml DMSO and the volume was made up to 100 ml using phosphate buffer pH 6.8 to obtain a stock solution of 100 µg/ml (stock solution), one ml of this stock solution was again diluted with phosphate buffer pH 6.8 up to 10 ml to obtain a solution of 10 µg/ml (stock solution ii). from stock solution ii of 2, 4, 6, 8, 10 ml were transferred to a series of 10 ml volumetric flasks. the volume was made up of phosphate buffer pH 6.8. the absorbances of these solutions were measured at 248 nm against blank.

Solubility Studies of Flurbiprofen

The solubility studies of Flurbiprofen in distilled water, methanol, and phosphate buffer solution pH 6.4 was determined by phase equilibrium method. All excess amount of drug was taken into 20 ml vials containing 10 ml of distilled water, methanol and phosphate buffer pH 6.4. Vials were closed with rubber caps and constantly agitated at room temperature for 24 hrs. using rotary shaker. After 2 hrs. the solution was filtered through 0.2 µm Whatman's filter paper. The amount of drug solubilized was then estimated by measuring the absorbance at 248 nm using UV-Vis spectrophotometer.

Drug-excipient compatibility study: The drug and excipients selected for the formulation are evaluated for chemical compatibility studies.

Chemical Compatibility study: Infrared spectroscopy was conducted using FT-IR spectrophotometer and the spectrum was recorded in the wave number region of 4000 to 400 cm^{-1} the procedure consisted of dispersing the sample (drug alone, mixture of drug and excipients) in potassium bromide and compressed into discs by applying a pressure of 5 tons for 5 minutes in a hydraulic press, the pellet was placed in the light path and the spectrum was recorded.

FORMULATION OF FLURBIPROFEN MICROSPONGES

Flurbiprofen microsponges were prepared by using Quasi emulsion solvent diffusion technique with polymer like ethyl cellulose at different drug to polymer ratios.

Procedure to Formulate Microsponges

Internal phase: Polymer Ethyl Cellulose (EC) was dissolved in 5 ml of dichloromethane and alcohol followed by addition of

Flurbiprofen and mixed well until it gets dissolved completely to which triethyl citrate was added as a plasticizer.

External phase: Accurately weighed PVA is added to distilled water to form clear solution. The internal phase was added to external phase drop by drop stirring upto 3 hours at room temperature. The mixture was filtered to separate microsponges and were dried in a desiccator and stored for subsequent investigation.

Table 1: Composition of Flurbiprofen microsponges.

Formulation Code	Drug: polymer (mg)	Polymer used (mg)	Solvent type (ml)	% PVA (g)	Triethyl citrate (%w/v)	RPM
F1	1:1	EC	DCM: Alcohol	0.2	1	1000
F2	1:2	EC	DCM: Alcohol	0.2	1	1000
F3	1:3	EC	DCM: Alcohol	0.2	1	1000
F4	1:4	EC	DCM: Alcohol	0.2	1	1000

EVALUATION OF PREPARED MICROSPONGES

Production Yield

Percentage yield can be determined by calculating the initial weight of raw materials and the finally obtained weight of microsponges. Percentage yield can be calculated by using the formula:

$$\text{Production yield} = \frac{\text{Practical yield}}{\text{Theoretical yield}} \times 100$$

Actual drug content and theoretical drug content

Samples of all formulated microsponges weighted quantity equivalent to 100 mg of microsponges containing drug were dissolved in 10 ml of phosphate buffer pH 6.4 under sonication for 20min at 25°C followed by membranes filtration of pore size of 0.25 µm and evaluated for drug content spectrophotometrically at 248 nm the actual drug content and encapsulation efficiency were calculated as given formula below (Riyaz et al., 2015).

Actual drug content (%) = [M actual drug / M obtained] × 100

Encapsulation Efficiency

The microsponges was determined spectrophotometrically (λ_{max} = 248 nm). A sample of FBP microsponges (100 mg) was dissolved in 100 ml of phosphate buffer (pH 6.8) and kept for overnight. The drug content was determined and expressed as actual drug content in microsponges. The encapsulation efficiency (%) of the microsponges was calculated according to the following equation.

$$\text{Loading efficiency} = \frac{\text{Actual drug content in microsponges}}{\text{Theoretical drug content}} \times 100$$

Particle size Analysis

Determination of the average particle size of Flurbiprofen loaded microsponges was determined with a binocular microscope using a calibrated ocular and stage micrometer. A minute quantity of microsponges was spread on a clean glass slide with a drop of liquid paraffin and a cover slip is placed on it. The average particle size was calculated by measuring 100 particles of each batch.

$$cf = SMD/EMD \times 10\ \mu m$$

Particle size = EMD division X cf

Where, SMD = stage microscopic division, EMD = Eye piece microscopic division, cf = correction factor.

Surface Morphology

Scanning Electron Microscopy of microsponges formulation was carried to determine the surface morphology. The sample was mounted directly onto the SEM sample holder using double sided sticking tape and images were recorded at different magnifications at acceleration voltage of 10 kv using scanning electron microscope.

EVALUATION OF FLOW PROPERTIES OF MICROSPONGES

The flow properties of powders are critical for an efficient capsule filling operation. A good flow of the powder or granules is necessary to assure efficient mixing and acceptable weight uniformity for the filling into capsules. The flow property measurements include bulk density, tapped density, angle of repose, compressibility index and Hausner's ratio. The flow property measurements of microsponges are determined.

Bulk Density (ρ_b)

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weighed powder into a measuring cylinder and initial weight was noted. This initial volume was called the bulk volume. From this the bulk density was calculated according to the formula mentioned below. It is expressed in g/cc and is given by

$$\rho_b = M / V_b$$

Where, M and Vb are mass of powder and bulk volume of the powder respectively.

Tapped Density(ρ_t)

It is the ratio of weight of the powder to the tapped volume of powder. The powder was introduced into a measuring cylinder with the aid of funnel and tapped for 500 times on a wooden surface at a 2 sec interval and the volume attained is the tapped volume.

$$\rho_t = M / V_t$$

Where, M and Vt are mass and tapped volume of the powder respectively. It is expressed in g/cc.

Angle of Repose (θ)

The flow properties were characterized in terms of angle of repose, Carr's index and Hausner's ratio. For determination of angle of repose (θ), the drug and the blend were poured through the walls of a funnel, which was fixed at a position such that its lower tip was at a height of exactly 2.0 cm above hard surface. The drug or the blends were poured till the time when upper tip of the pile surface touched the lower tip of the funnel. Angle of repose was calculated using following equation.

$$\theta = \tan^{-1} (h/r)$$

Where, h = height of pile in cm; r = radius of pile in cm.

Carr's Index (OR) % Compressibility Index

It indicates powder flow properties. It is measured for determining the relative importance of interparticle interactions. It is expressed in percentage and is given by

$$CI = \frac{\rho_t - \rho_b}{\rho_t} X\ 100$$

Where, ρt and ρb are tapped density and bulk density respectively.

Hausner's Ratio

Hausner's ratio is an indirect index of ease of powder flow. It is calculated by the following formula.

$$HR = \rho_t / \rho_b$$

Where, ρt and ρb are tapped density and bulk density respectively.

PREPARATION OF MICROSPONGES FILLED CAPSULES

The optimized microsponges were filled into "1" size capsule each containing 100 mg equivalent of Flurbiprofen.

Table 2: Composition of Flurbiprofen microsponge capsules.

Ingredients	Quantity (mg)
Flurbiprofen microsponges equ to 100 mg	150 mg
Lactose Monohydrate	55 mg
Magnesium Stearate	5 mg
Total weight	210 mg

EVALUATION OF MICRSPONGES FILLED CAPSULES

Uniformity of Weight

Intact capsule was weighed. The capsule was opened without losing any part of the shell and contents were removed as completely as possible. The shell was washed with ether or other suitable solvent and the shell allowed to stand until the odor of the solvent was no longer detectable. The empty shell was weighed the procedure was repeated with a further 19 capsules. The average weight was determined. Not more than two of the individual weights deviate from the average weight by more than the percentage deviation shown in table 3 and none deviates by more than twice that percentage.

Table 3: Uniformity of weight.

Average weight of capsule contents	Percentage deviation
Less than 300 mg	10
300 mg or more	7.5

Disintegration Test

This test determines whether capsules disintegrate within a prescribed time when placed in a liquid medium under the prescribed experimental conditions. A capsule was placed in each of the six tubes of the apparatus and one disc was added to each tube. The time in minutes taken for complete disintegration of the capsule with no palpable mass remaining in the apparatus was measured.

Drug Content

Five capsules were selected randomly and the average weight was calculated. The powder is removed completely and equivalent amount of powder is made up to 100ml with phosphate buffer pH 6.8. 10ml of solution is diluted to 100ml using phosphate buffer pH 6.8 in separate standard flask. The absorbance of solution was recorded at 248 nm.

In Vitro Drug Release

In-vitro release studies of microsponges were carried out by filling equivalent amount of microsponge along with lubricant in capsules and placed in the basket containing phosphate buffer pH 6.8 was used as medium and rotated at 50 rpm. Samples was withdrawn and determined by spectrophotometrically at 248 nm.

In-vitro Anti-Inflammatory Test

1 ml of sample solution was withdrawn during In-vitro drug release study at every one-hour interval, thereafter subjected to *in-vitro* anti-inflammatory analysis. For the purpose of control, equal volume of distilled water was used. To each reaction mixture, 1 ml of bovine albumin (1% in distilled water) was transferred and pH was adjusted to 6.3 by using small amount of 0.1 N HCl. Samples were incubated for 30 min at 37 ^{0}C in the dark followed by incubation at 57 ^{0}C for 5 min. Reaction tubes were then cooled under running tap water and turbidity of all the samples were recorded spectrophotometrically at 660 nm.

Percentage inhibition of albumin denaturation was calculated by using

$$\text{Percentage inhibition} = \frac{\text{Abs Control} - \text{Abs Sample}}{\text{Abs Control}} \times 100$$

RELEASE KINETIC STUDIES

The mechanism of drug release from the microsponges filled capsules was studied by fitting the dissolution data of optimized formulation in following models:

Zero order: M= $M_0 - K_0 t$

First order: Log$C$ = LogC_0 – $Kt/2.303$

Higuchi square root law: $Q = kt1/2$

Korsmeyer's model: Mt/M_∞= ktn

Where M, C, and Q are the amount of drug released at time t, M_0, and C_0 are total amount of drug, and K_0, Kt, and K are corresponding rate constant.

In case of Korsmeyer's model Mt/M_∞ is the fractional drug release at time t, k is a constant incorporating the properties of the macromolecular polymeric systems and the drug, n is a kinetic constant,

Which is used to characterize the transport mechanism? The value of n for a cylinder is <0.5 for Fickian release, 0.5 < n < 1.0 for Anomalous transport (non-Fickian diffusion), 1.0 for Case-II transport, >1.0 for Super Case-II transport type release.

RESULTS AND DISCUSSION

Determination of Melting Point

The average melting point of pure drug was found to be 118.6 °C, which meets the standards of pure drug as shown in table 4.

Table 4: Results of Melting Point of Flurbiprofen.

S No	Melting point (FP)
1	120 °C
2	118 °C
3	118 °C
Average	118.6 °C

Determination of λ_{max} by Spectrum Scanning

The spectral scanning was done for the test FP in water, methanol and PBS 6.4 pH 10 µg/ml concentrations individually, the maximum absorbance of 0.876 was observed for PBS pH 6.4 at 248 nm.

Standard Graph of Flurbiprofen

Solutions of Flurbiprofen in Phosphate buffer pH 6.8 were suitably diluted to give varying concentrations of 0-9 µg/ml. The absorbance was measured at 248 nm and the values are given in figure 1. It was found that the solutions show linearity (R2=0.9926) in absorbance at a concentration of 0-9 µg/ml and obeys Beer Lambert's law.

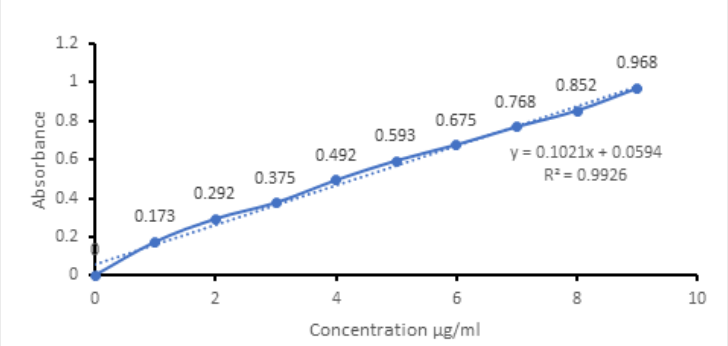

Figure 1: Standard graph of Flurbiprofen in phosphate buffer pH 6.8.

Solubility studies

Solubility is a basic parameter for considering the suitable solvent for an immediate release. FP is considered as highly soluble, as the pH increases to the basic nature, the solubility of FP also increases, when the highest required strength was soluble in various media. Among the above solvents phosphate buffer saline pH 6.4 found to have highest solubility of 88 mg/100ml.

Table 5: Solubility Studies of Flurbiprofen.

Medium	Absorbance	Amount present (µg/100ml)
Distilled water	0.081	8
Methanol	0.867	85
PBS pH 6.4	0.897	87.9

Drug-Excipient compatibility studies

Interaction between the drug and excipients used in the formulation was studied. The results are as follows in figure and table 6.

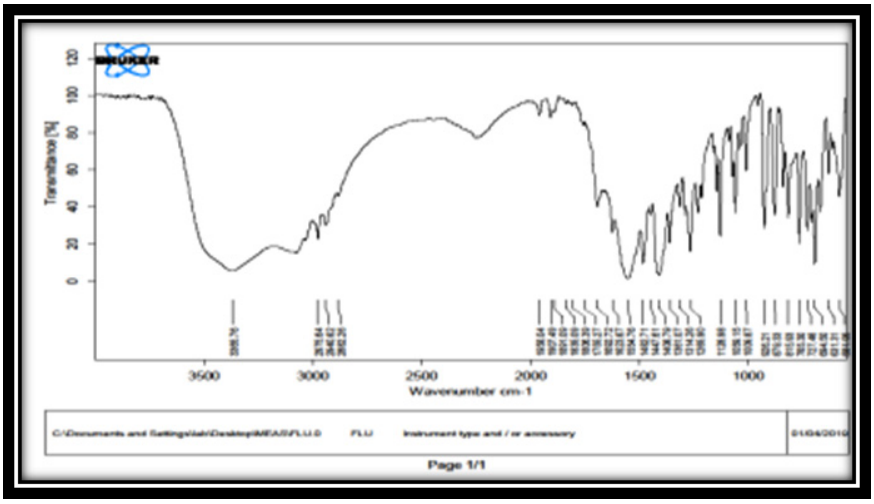

Figure 2: FT-IR of Pure drug Flurbiprofen

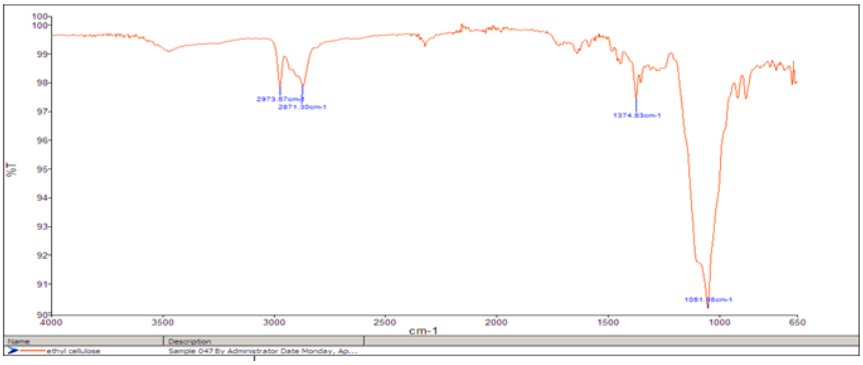

Figure 3: FTIR of Ethyl Cellulose (EC).

Figure 4: FTIR of PVA.

Table 6: FTIR of pure drug and excipient.

Functional groups	Drug	Functional groups	PVP	Functional groups	EC
C-H Stretch (aliphatic)	2882.26	OH Stretching	3424	C-H stretching	2973.34
C-H stretch (aromatic ring)	2975.64	CH2 stretching	2950	OH stretching	3485.55
O-H stretch (carboxylic acid)	3365.76	CH2 wagging	1245.03	C-O-C stretching	1051.98
C-F stretch	1361.07	C-O stretching	1652	C-H Bending	1374.63
C-O stretch	1009.87				

Table 7: Results of Evaluation of Microsponges.

F code	Production yield (%) Avg ± S.D	Theoretical yield (%)	Actual drug content (%) Avg ± S.D	Encapsulation efficiency (%) Avg ± S.D	Particle size (µm) Avg ± S.D
F1	75.29 ± 2.14	73.90	71.85 ± 0.01	97.23 ± 0.02	32.21 ± 0.22
F2	74.17 ± 3.13	78.74	75.83 ± 0.12	96.30 ± 0.02	30.11 ± 0.14
F3	78.10 ± 2.59	81.97	80.08 ± 0.11	97.69 ± 0.03	32.02 ± 0.46
F4	82.10 ± 2.50	80.24	80.00 ± 0.45	96.12 ± 0.02	30.47 ± 0.18

Microsponges were prepared and their production yield was calculated. They were found to be in the range of 75.29 ± 2.14 % to 82.10 ± 2.50 %. It shows increasing drug: polymer ratio increased the production yield. The results correspond to earlier reports done. Encapsulation efficiency ranged from 96.12 ± 0.02 to 98.30 ± 0.02. Highest loading efficiency was found for the formulation F2. This shows that increasing drug: polymer ratio increased encapsulation efficiency. The results correspond to earlier report done.

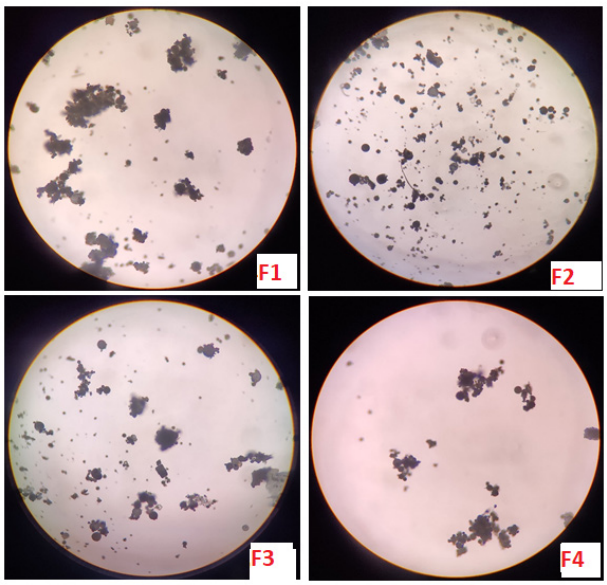

Figure 5: Images of Binocular microscope.

The ideal size range of microsponges was 5-300 µm. Visual inspection of various batches done using binocular microscope, for particle size analysis in the both batches i.e., F1-F4. Due to increase in polymer wall thickness, leads to formulation of larger size of microsponges. Among the formulations batch F2 formulation showed ideal spherical nature with large porous surface area when compare to other batches as shown in Figure no 5. From the photomicroscopic study F2 batch was selected as finalized batch of microsponges.

Surface Morphology by Scanning Electron Microscopy

The shape and surface morphology of optimized microsponges (F2) was observed in SEM. as shown in figure 6 It shows that the microsponges from binocular microscope was spherical, porous and uniform compared to all other formulations, as shown in figure no 5. So, the final optimized formulation F2 is considered for further study.

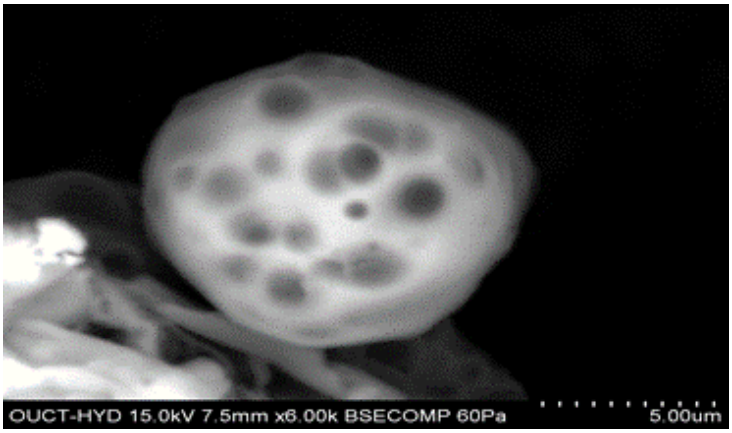

Figure 6: Scanning Electron Microscopy of F2.

Table 8: Evaluation of flow properties of microsponges.

F. Code	Bulk density(g/ml)	Tapped density(g/ml)	Carr's Index(%)	Hausner's ratio	Angle of repose(θ)
Drug	0.299±0.002	0.478±0.001	37.44±0.002	1.564± 0.08	48°57± 0.71
F2	0.394±0.01	0.454±0.00	13.03±3.34	1.151±0.04	30° 03±1.61

*All the values are mean ± SD (n=3)

The flow property of pure drug was found to be very poor. Good flow property was observed for prepared microsponges.

Table 9: Evaluation of Microsponges filled capsules.

F. Code	Weight of capsule (g)	Disintegration Time (min)	Drug Content (%)
F2	0.210 ±0.01	11±1	98.65 ±0.804

*All the values are mean ± SD (n=3)

Table 10: comparative *In-vitro* release of optimized formulation.

Time (hrs)	Cumulative % of drug release Avg ± S.D (n=3)	
	Marketed formulation (MF)	Capsule filled Formulation 2
0	0	0
1	20.76 ± 0.71	20.76 ± 0.41
2	43.90 ± 0.64	42.81 ± 0.71
4	62.11 ± 0.79	51.49 ± 0.01
6	89.54 ± 0.28	62.91 ± 0.12
8	99.91 ± 0.67	76.08 ± 0.14
10		88.28 ±0.015
12		98.12 ± 0.63

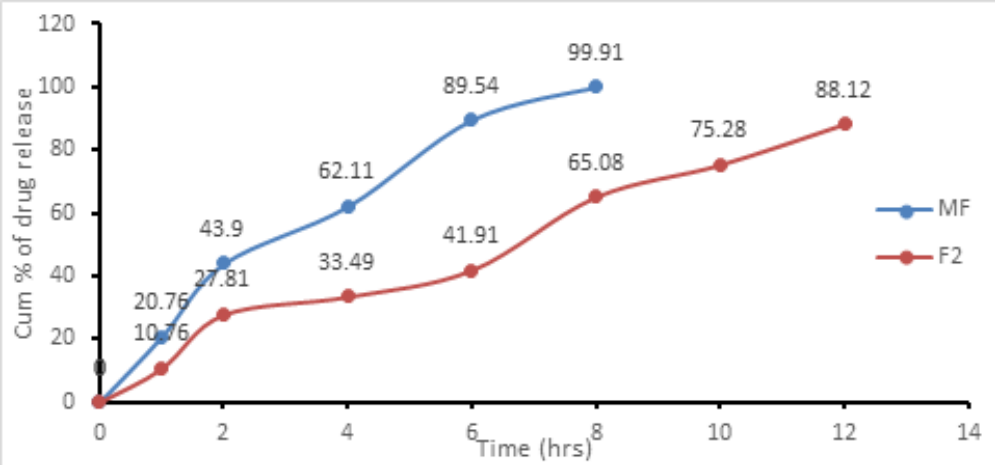

Figure 7: *In-vitro* drug release study of optimized formulation.

Table 11: FTIR study data of FP and Finalized formulation (F2)

Characteristics peak	Frequency (cm^{-1})	
	FP	FP F2
C-H Stretch (aliphatic)	2882.26	2940.45
C-H stretch (aromatic ring)	2975.64	3075.91
O-H stretch (carboxylic acid)	3365.76	3367.65
C-F stretch	1361.07	1361.13
C-O stretch	1009.87	1036.79
C=O Stretch (carboxylic acid)	1725.27	1725.80

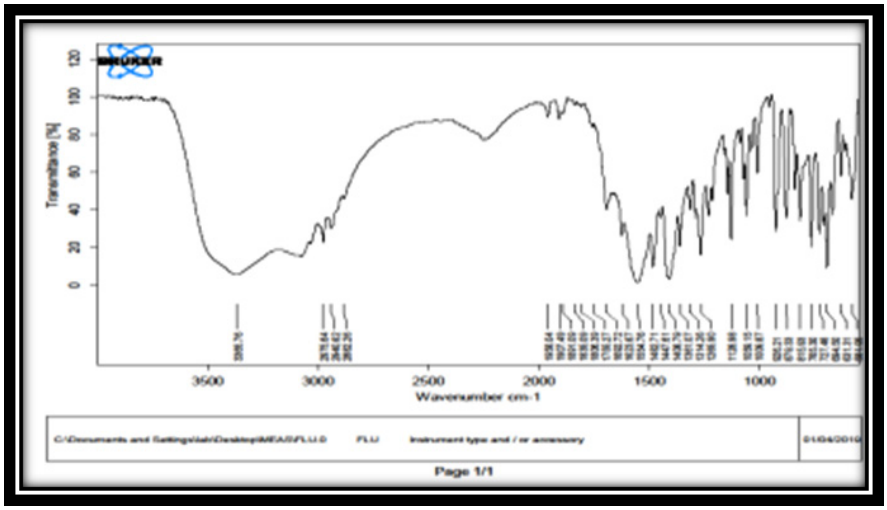

Figure 8: FTIR of pure drug Flurbiprofen.

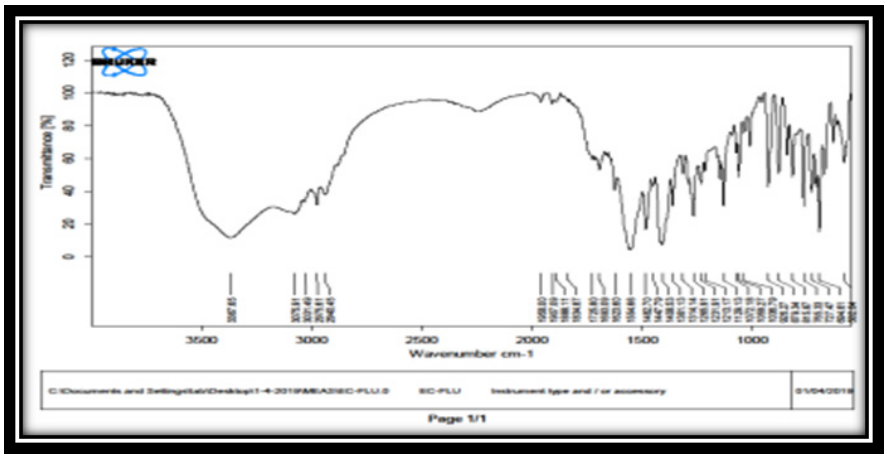

Figure 9: FTIR of optimized formulation F2.

In-vitro anti-inflammatory activity

Table 12: *In-vitro* anti-inflammatory activity of F2.

Time (hrs)	% Inhibition	
	Pure drug	F2
0.5	46.04	-
1	68.35	30.93
1.5	83.87	33.86
2	-	37.01
3	-	39.65
4	-	45.94
5	-	50.60
6	-	53.54
7	-	60.14
8	-	64.60
9	-	70.68
10	-	74.34
11	-	81.54
12	-	83.77

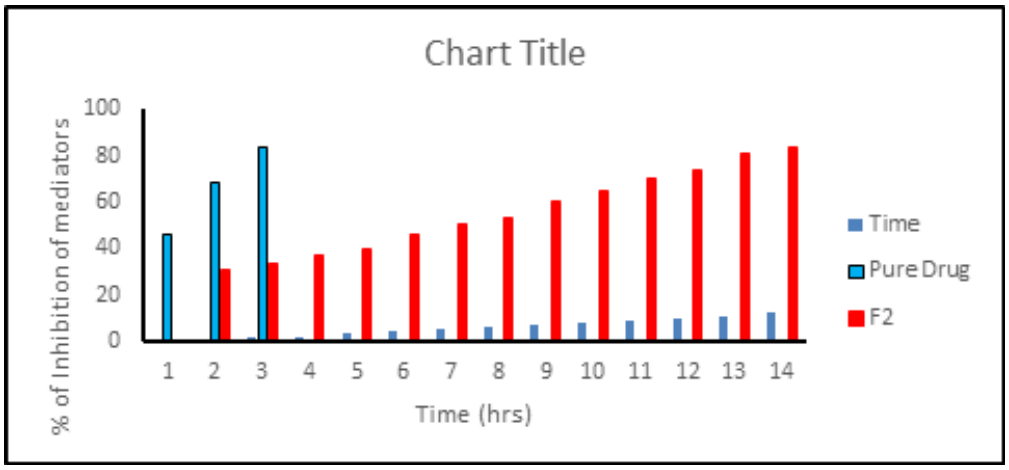

Figure 10: *In-vitro* anti-inflammatory activity.

Results of *in-vitro* anti-inflammatory activity by albumin denaturation method showed that the optimized formulation F2 inhibited approximately 83% within 12 hrs. F2 also exhibits Release Kinetics of the optimized formulation (F2) a satisfactory dose dependent anti-inflammatory activity. As shown in figure 10 & table 12.

Table 13: Release kinetics of the optimized formulation (F2).

Zero order		First order		
Time (hrs)	**Cum % of drug release**	**Time(hrs)**	**Log Cum % of drug remaining**	
1	10.76	1	1.951	
2	27.81	2	1.858	
4	33.49	4	1.823	
6	41.91	6	1.764	
8	65.08	8	1.543	
10	75.28	10	1.393	
12	88.12	12	1.075	
Higuchi		Korsemeyer Peppas		
SQRT Time (hrs)	**Cum % of drug release**	**Log Time (hrs)**	**Log Cum % of drug release**	**"n"**
1.00	10.76	0.00	1.032	0.90
1.41	27.81	0.30	1.444	
2.00	33.49	0.60	1.525	
2.44	41.91	0.78	1.622	
2.82	65.08	0.90	1.813	
3.16	75.28	1.00	1.877	
3.46	88.12	1.08	1.945	

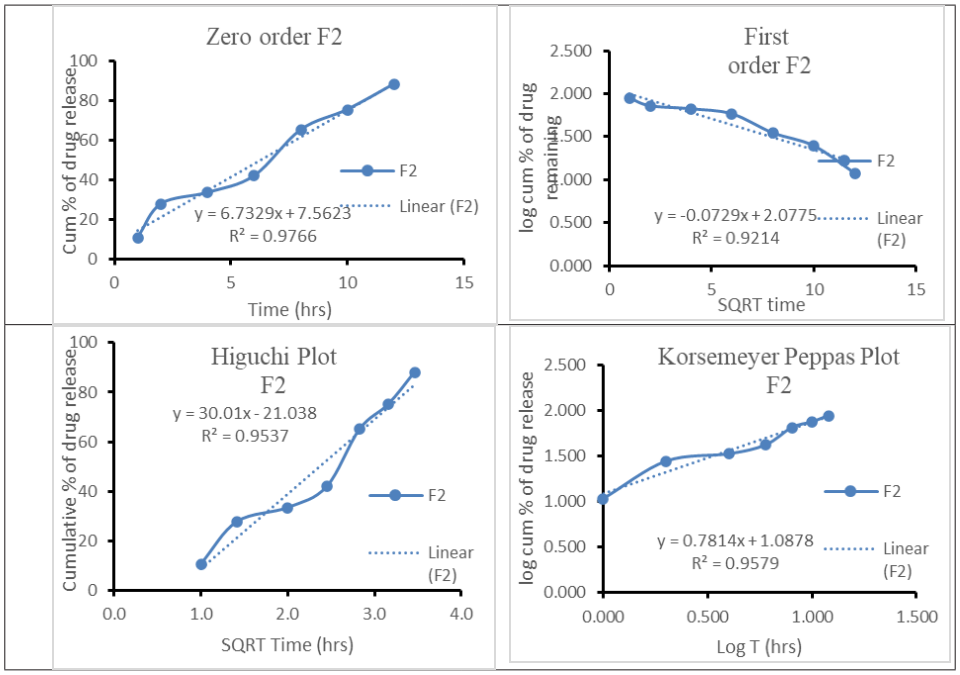

Figure 12: Release kinetic graphs of F2 Formulation.

The *in-vitro* drug release of the optimized formulation F2 was best explained by zero order kinetics as the plots showed linearity (R2=0.9766). As shown in figure 11 & table 13. This Zero order kinetics explains the controlled release of the prepared microsponges over the period of time.

SUMMARY AND CONCLUSION

Flurbiprofen is a poorly soluble drug with short half-life, thus selected as a model drug for MDDS to overcome these problems and to release the drug in a sustained manner. Flurbiprofen is formulated as microsponges by Quasi emulsion solvent diffusion method using different ratios of Drug: polymer (Ethyl cellulose) and finally enclosed in Capsules. Compatibility studies were performed for drug and excipients, Chemical compatibility study (FTIR) was carried out. It revealed no interaction between the drug and formulation as shown in figures 8,9 & table 11. Standard graph was drawn for Flurbiprofen and it was found that the solutions showed linearity (R2=0.9926) and obeyed Beer Lambert's law. Flurbiprofen Microsponges were prepared using two polymers to determine which polymer retards the release better. The *in-vitro* release was carried out for all the formulations. The formulation F2 (containing 1:2 drug: polymer (Ethyl cellulose) ratio released 98.12% at the end of 12th hours. Therefore, F2 was selected as optimized formulations for its sustained action. The effect of stirring rate was studied on optimized formulations for determining production yield, drug content, mean particle diameter and drug release. The stirring rate increases production yield and drug content, while mean particle diameter decreased. No particular pattern was observed for drug release. *In-vitro* anti-inflammatory activity by albumin denaturation method showed that the optimized formulation F2 inhibited approximately 83% within 12 hrs which clearly indicates that F2 also has exhibits a satisfactory dose dependent anti-inflammatory activity. Preformulation study was carried out for drug and F2 microsponges. It revealed that the flow property of pure drug was very poor, but the microsponges has good flow. Post formulation parameters of capsules were evaluated and the results were found to comply with the official specifications. The dissolution data of the optimized formulation were fitted to various kinetic models and the formulation F2 fitted best to Zero order kinetics.

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CONFLICT OF INTEREST

There is no conflict of interest in publishing the article in your

journal.

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