



## Preparation and Evaluation of Flurbiprofen Based Microsponges

Vaibhavkumar Bhagwat<sup>1</sup>, Onkar Doke<sup>2</sup>, Chaitali Dhale<sup>3</sup>, Uniket Gosavi<sup>4</sup>, Pranita S. Kavitate<sup>5\*</sup>

<sup>1</sup>\*Assistant Professor, Vidya Niketan College of Pharmacy, Lakhewadi

<sup>2</sup>Associate Professor, Vidya Niketan College of Pharmacy, Lakhewadi

<sup>3</sup>Associate Professor, Vidya Niketan College of Pharmacy, Lakhewadi

<sup>4</sup>Assistant Professor, Vidya Niketan College of Pharmacy, Lakhewadi <sup>5\*</sup>Assistant Professor, Vidya Niketan College of Pharmacy, Lakhewadi

**\*Corresponding author:** Vaibhavkumar Bhagwat

<sup>\*</sup>Assistant Professor, Vidya Niketan College of Pharmacy, Lakhewadi

### Abstract :

Flurbiprofen (FP) is a medicine belonging to class of Non-Steroidal Anti-Inflammatory Drugs and is classified in class II of BCS having high permeability and low solubility. The end of present study was to formulate the flurbiprofen as a micro sponge technology. Microsponges is used to increase the drug release. Flurbiprofen is the class II drug of BCS class having the High Permeability and Low solubility activity. In this Microspongal patented Drug Delivery System, Flurbiprofen drug loaded in cross linked polymers pore. The Quasi emulsion solvent diffusion method introduced for preparation of Flurbiprofen Microsponges. In this method, the internal and external phases employed. Where drug dissolved in mixture of Eudragit RS 100 and dichloromethane as a internal phase and this internal phase add in poly vinyl alcohol as a external phase. Throughout the process ultrasonication, stirring and filtration used to achieve microsponges. The percentage yield, FTIR, entrapment efficiency, dissolution test carried and to increase the entrapment efficiency and percentage yield drug polymer ration used.

**Keywords:** Microsponges, Flurbiprofen, Low Solubility, Surfactant, External- Internal Organic Phase.

### I. INTRODUCTION:

An a topical dosage forms contain drugs which shows the systemic action mainly called as a Transdermal Drug Delivery Systems (TDDS) also known as a transdermal therapeutic systems (TTS). Transdermal drug delivery is defined as the delivery of a drug moiety through the 'intact' skin and reaches in to the systemic circulation in adequate quantity which is to advantageous after the administration of therapeutic dose. Transdermal delivery systems are typically suited for chronic diseases treatment. Hence, anti-inflammatory agents of therapeutic usage subjected to the transdermal examination<sup>[1]</sup>.

### MICROSPONGES DRUG DELIVERYSYSTEM:

Drug delivery systems (DDS) can sustained release rate sand target drugs to a specific body site. Due to their targeting the specific body site it gives effect on the health care system. Carrier technology is important because they regulate the absorption as well as release characteristics of the drug. Microsponges are important part of drug delivery system due to their smaller size and efficient carrier characteristics <sup>[2]</sup>.

Microsponges are polymeric based` delivery system composed of porous microspheres. They are small sponge-like spherical particle and having porous nature. Microsponge system entrap wide variety of ingredient and improve stability, reduced side effects as well as systematic exposure, minimizes the local skin reaction, increase elegance, and enhanced flexibility of formulation. Microsponge systems are the microscopic, polymer-based microspheres that can entrap or suspend a wide variety of substances, and can be incorporated into a formulated product such as gel, cream, liquid or powder. So that microsponges are unique area to carry active pharmaceutical ingredient at the minimum dose and also stability enhances, reduce side effects and modify drug release <sup>[3]</sup>.

### Definition:

A Microsponge Delivery System (MDS) is patented, highly(extremely) cross-linked and porous, polymeric based microspheres that can entrap wide range of active ingredient and response to trigger, the active ingredient release onto the skin in desired rate<sup>[4]</sup>. The size of the microsponges ranges from 5-300µm in diameter and a typical 25µm sphere will have up to 250000 pores <sup>[5]</sup>.

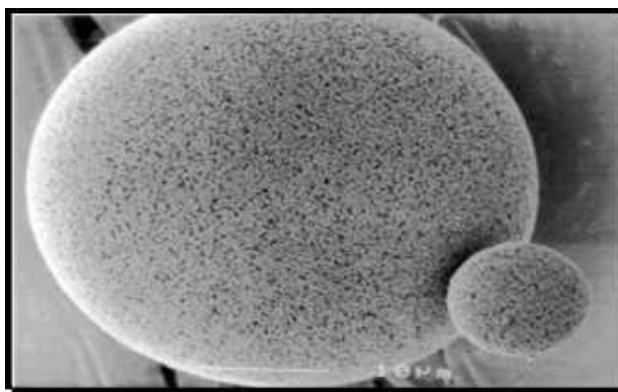


Figure 1. Microsponges [6]

**Characteristics:** [7]

- Monomers and polymer would not work without the increasing in viscosity.
- Immiscible in water or slightly soluble.
- To avoid cosmetics problems incorporation should not be more than 10-12% w/w microsponges.
- Rate of release is controlled by diffusion or moisture, pH and temperature.
- Release is extended in nature.

**Advantages:** [3]

- Microsponges are biologically safe and release drug in programmable manner.
- They entrap variety of ingredients and enhanced formulation flexibility.
- They have the capacity to absorb active materials into the particle or load a high degree of active material onto its surface.
- Microsponges are stable at pH range of 1- 11 and up to temperature of 130°C.
- Bacteria cannot penetrate because microsponges are self-sterilizing as average pore size is 0.25 m.
- Microsponges having ability of absorbing skin secretions so reducing the oiliness of the skin up to 6 times of its weight.
- The size 10 to 25 microns in diameter it is capable of entrapping the various ingredients in a single microsphere.
- The drug releases in microsponges by the external mechanism like pH, temperature, and rubbing.
- Microsponge are non-allergic, non-toxic, non-irritant and non-mutagenic.
- These are compatible with the majority of vehicles and ingredients.
- These systems have higher payload up to 50 to 60%.
- Microsponges are thermal, physical and chemically stable.
- They provide continuous action up to 12 hrs. i.e. extended release and improved product elegance.

**Microsponges Preparation Method:**

There are 2 methods for preparation of microsponges, these are:

- Liquid liquid suspension polymerization method.
- Quasi emulsion solvent diffusion method.

**Liquid-liquid suspension polymerization (1 step process):** [7]

Immiscible monomers and active ingredient are dissolved in suitable solvent monomers.



Dispersed in aqueous phases which consist of additives like surfactant, suspending agent.



Polymerization is activated by adding catalyst or by increasing the temperature.



Polymerization process is continues the formation of spherical structure.



At the end of process the solvent evaporates and forms spherical porous microsponges.

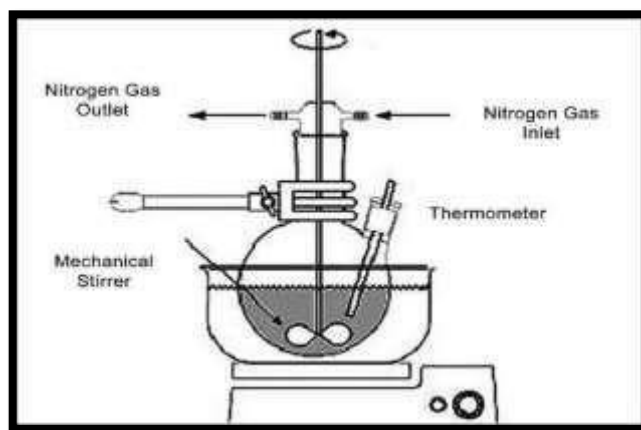


Figure 2. Liquid-liquid suspension polymerization<sup>[35]</sup>

#### Quasi-emulsion solvent diffusion: (2 step process) <sup>[7]</sup>

Immiscible monomers and active ingredient are dissolved in suitable solvent monomers.



Dispersed in aqueous phases which consist of additives like surfactant, suspending agent.



Polymerization is activated by adding catalyst or by increasing the temperature.



Polymerization process is continues the formation of spherical structure.



At the end of process the solvent evaporates and forms spherical porous microsponges.

#### Mechanism of Action: <sup>[3]</sup>

The topical formulation by using microsponges system can be prepared in many different forms such as a gel, cream, or lotion. The active ingredients diffuse from spheres into the vehicle and then onto the skin, when the formulation is applied topically to the desired area of the skin. The release can be initiated by many release triggers, including temperature, change pressure and moisture. Due to the smaller size of microsponges, they cannot pass through the stratum corneum, so microsponges are retained on the skin surface, releasing slowly the active pharmaceutical ingredients in controlled manner.

#### Mechanism of Drug Release: <sup>[8, 9, 10]</sup>

**Pressure release:** When pressed or squeezed the microsponges, then it releases active ingredient or fluid, thereby entrapped active ingredient onto the skin.

**Temperature release:** The release of drug from microsponges can be activated by temperature. As the skin temperature increases, flow rate is also increased and hence release is also enhanced.

**pH triggering:** The release of drug from the microsponges will be achieved by modifying the coating on the microsphere.

**Solubility:** The release of the drug activated by diffusion but taking into consideration, the partition coefficient ingredient between microsponges and external system.

#### Physical Characterization of Microsponges: <sup>[11]</sup> Particle Size Determination:

Particle size analysis of loaded and unloaded microsponges can be performed by using laser light diffractometer or any other suitable method. The values can be expressed for all formulation as mean size range. Cumulative percentage drug release from microsponges of different particle size must be plotted against time to review effect of particle size on drug release. Particle larger than 30 μm can impart gritty feeling and hence particles of size between 10 and 25 μm are preferred to use in final topical formulation.

#### Morphology and surface topography of Microsponges:

The morphology and surface topography, prepared microsponges can be coated with gold- palladium under an argon atmosphere at room temperature and then the surface morphology of the microsponges can be studied by using scanning electron microscopy (SEM). SEM of a fractured microsponges particle can also be taken to illustrate its ultra-structure.

#### Determination of Entrapment efficiency and Production yield:

The entrapment efficiency (%) of the micro-sponges can be calculated according to following equation:

$$\text{Entrapment Efficiency} = \frac{\text{Actual drug content in Micro-sponges}}{\text{Theoretical Drug Content}} \times 100$$

The production yield of micro-sponges can be determined by following equation:

$$\text{Production yield} = \frac{\text{Practical mass of Micro-sponges}}{\text{Theoretical mass of micro-sponge}} \times 100$$

#### Dissolution Studies:

Dissolution profile of microsponges can be studied by use of dissolution apparatus equipment USP XXIII with a modified basket of 5 $\mu$ m stainless steel mesh. The speed of the rotation is 150rpm. The dissolution medium is selected while considering solubility of actives to ensure sink conditions. Samples from the dissolution medium can be analyzed by suitable analytical method at various interval.

#### In-vitro Diffusion studies:

The in vitro diffusion studies of prepared microsponges can be carrying out in Franz diffusion cell. 25ml of Phosphate buffer use as dissolution media and then sample taken on cellophane membrane. The receptor compartment is kept in contact with donor compartment with maintained temperature at 37 $\pm$ 0.5 $^{\circ}$ C.

The drug concentration on the receptor fluid was determined spectrophotometrically against appropriate blank.

#### Marketed Formulation Based On Microsponges: [12, 13, 14]

- Retinolcream
- Dermalogica oil controllotion
- Oil free matte block spf2o
- Carac cream0.5%
- Salicylic peel 20 and30
- Sports cream RS andXS
- Micro peelplus
- EpiQuinmicro
- Lactrex™ 12% Moisturizingcream
- NeoBenzmicro, NeomicroSD, NeoBenzmicrowash.
- Glycolic acid moisturizer w/SPF15
- Line Eliminator Dual Retinol Facial treatment
- Retinol 15nightcream
- Ultra guard.

## 2. NEED AND OBJECTIVE:

- Microsponges are polymeric based drug delivery system which consists of non- collapsible structure with porous surface through which variety of active ingredients are entrapped and released drug in a controlled manner and better patient compliance. So this system is employed for topically applieddrugs.
- Microsponges are designed to deliver a pharmaceutically active ingredient efficiently at minimum dose and also to enhance the stability, reduce the side effect and modify the drug releaseprofile.
- Comparisons to another dosage form it remain in the skin for longer period oftime.
- Microsponges enhanced product performance, extended release, reduced drug irritation and hence it can improve patient compliance, product elegancy, formulation flexibility, Thermal, physical and chemicalstability.
- It is also known to be:
  - i. Nonirritating
  - ii. Nonallergic
  - iii. Nontoxic
- Flurbiprofen is a non-steroidal anti-inflammatory drug (NSAID) is a derivative of propionic acid, and phenylalkanoic acid derivatives. It binds to and inhibits cyclooxygenase (COX). This resulting that an arachidonic acid reduction is conversion in to the prostaglandins and that are involved in the regulation of inflammation, fever and pain. According to literature survey non-steroidal anti-inflammatory drug inhibits cyclooxygenase (COX). This resulting that an arachidonic acid reduction is conversion in to the prostaglandins and that are involved in the regulation of inflammation, fever and pain. Hence, to fulfill this objective there is a need to develop the topical controlled drug delivery system such as microsponges topical drug delivery.

### 3. MATERIAL AND METHOD:

#### Materials:

The Active Pharmaceutical Ingredient drug obtained from Swapnroop Drugs and Pharmaceutical from Aurangabad. Polymer like Eudragit RS-100 received from Evonik pvt. Ltd. Mumbai and PVA, Dichloromethane obtained from Mumbai.

#### Method:

##### Quasi-emulsion solvent diffusion: (2 step process) <sup>[7]</sup>

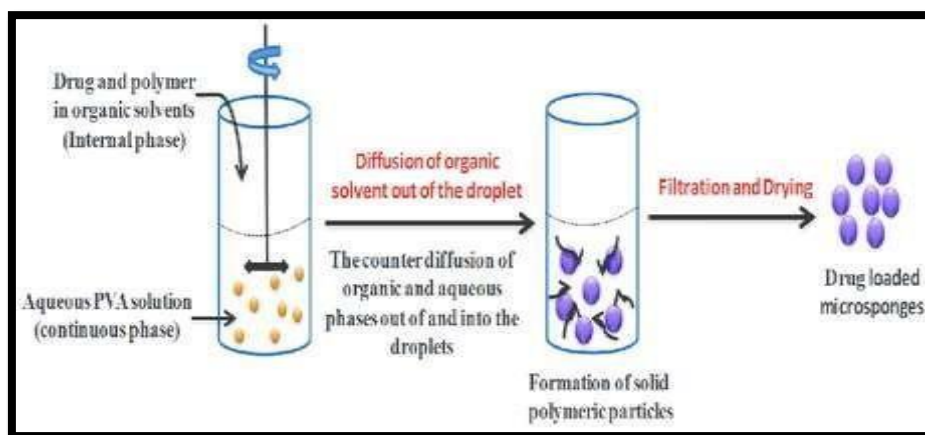
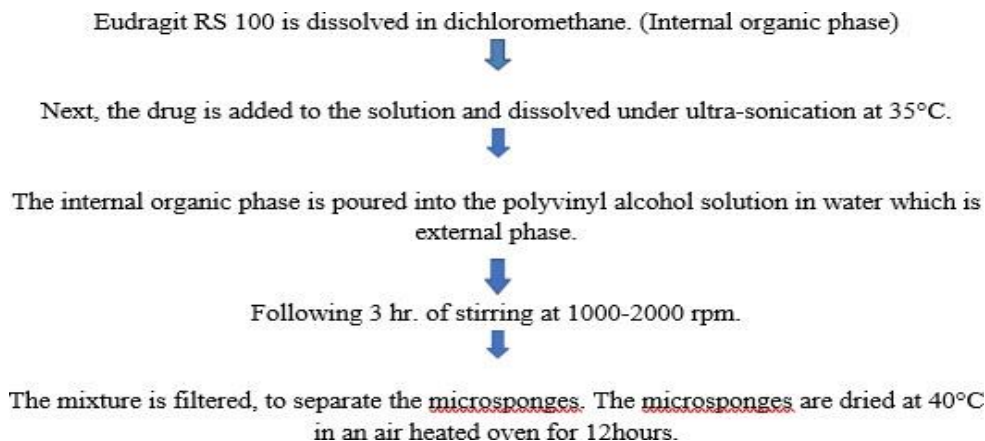


Figure 3. Quasi emulsion solvent diffusion method <sup>[15]</sup>

#### FORMULATION OF FLURBIPROFEN MICROSPONGE BATCHES: <sup>[16, 17]</sup>

The microsponges containing Flurbiprofen were prepared by quasi emulsion solvent diffusion method by using eudragit RS-100 as a polymer. An accurately weighed Eudragit RS-100 was dissolved in internal phase dichloromethane. This solution was then sonicated in ultrasonic bath for 5min. Once the clear solution obtained, the drug was added to above solution, this solution was then sonicated in ultrasonic bath for 3min. The inner phase was added drop wise with the help of syringe into the PVA solution in water (external phase) for 2h stirring at 1500 rpm, the mixture is filtered to separate the microsponges. The microsponges were dried in a heated oven at 40°C for 12hr.

#### Formulation of preliminary batches of Flurbiprofen Microsponges:

Various formulation were prepared by using different compositions of polymer and emulsifying agent. Preliminary trial batches with different concentrations of Eudragit RS-100 and PVA are formulated. The formulation were evaluated for production yield, particle size and other parameter

##### ❖ Preliminary Batches of Microsponge:

Table no.1-Preliminary batches of microsponges

Ingredient	Quantity		
	R1	R2	R3
Flurbiprofen(g)	0.5	0.5	0.5
Eudragit RS- 100(g)	10	12.5	15
Dichloromethane(mL)	50	50	50
PVA (g)	5	5	5
Purified Water	1000ml	1000ml	1000ml

**CHARACTERIZATION AND EVALUATION OF FLURBIPROFEN DRUG:****Determination of Melting Point:**

Approximate amount of Flurbiprofen drug fill in capillary tube. One end of capillary is seal. Capillary tube is attached to the thermometer and that thermometer is place in to the thieles tube. With the help of burner heat supply to the tube meanwhile the temperature of oil increased the drug present in capillary is start to melting and note down the melting point of drug <sup>[18]</sup>.

**Solubility Studies:**

Solubility studies were performed by solid dispersion method, in various solvent systems distilled water, 0.1 N hydrochloric acid and pH 7.4 phosphate buffers. Excessive quantities of drug were placed in flask containing 10 ml of each solvent. The flask was sonicated at 25 °C for 1 h, stirred and agitated for 2 days at 25 °C. The suspension was filtered using a 0.45 µm filter paper, diluted suitably with respected solvents and analyzed at 247 nm using UV spectrophotometer <sup>[19, 20]</sup>.

**Spectrofluorometric and UV System:**

Spectral was runs on a Shimadzu Ultra Violet (UV)-Visible spectrophotometer and the spectral bandwidth of 0.5 nm and wavelength accuracy of ± 0.3 nm with wavelength 247 nm with 10 mm quartz cells<sup>[21]</sup>.

**Preparation of phosphate buffer pH 7.4:**

Dissolve 2.38gm of disodium hydrogen phosphate, 0.19gm of potassium dihydrogen phosphate and 8gm of sodium chloride in sufficient water to produce 1000ml. Adjust the pH if necessary.

**Preparation of the Solutions:**

The stock standard solution of flurbiprofen was prepared in Phosphate Buffer 7.4 pH to a concentration of 100 µg/ml and stored at -20 C in volumetric flasks. Sample solutions prepared from the stock standard solutions. Sample solutions were prepared as 2, 4, 6, 8, 10 µg/ml for the UV method and took absorbance at the 247 nm wavelength <sup>[22]</sup>.

**Calibration plot of Flurbiprofen in Methanol:**

Calibration plot of Flurbiprofen was prepared in methanol by dissolving the drug (10mg) in methanol and volume was made to 100 ml with the methanol from this stock solution concentration ranging from 4-20 ug/ml were prepared and analysed spectrophotometrically at 249nm.

**Fourier Transform Infrared Spectroscopy:**

Fourier Transform Infrared (FTIR) spectroscopy was conducted. The procedure consists of placing the drug's sample in FTIR sample holder. It was placed in the light path and scanned in the range of 4000-400cm<sup>-1</sup> on Jasco FTIR-4100. The spectrum was recorded <sup>[23]</sup>.

**CHARACTERIZATION AND EVALUATION OF FLURBIPROFEN MICROSPONGES:****Determination of production Yield:**

The production yield of the microsponges was determined by calculating accurately the initial weight of the raw materials and the final weight of the microsponges obtained.

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

**Particle Size Analysis:**

The particle size was determined using an optical microscope. The microscope was fitted with a stage micrometer to calibrate the eyepiece micrometer.

One division of stage micrometer = 0.01mm = 10µm.

$$C = \frac{SM \times 10}{EM}$$

Where, C=correction factor

SM=reading of stage micrometer which coincides with reading of eyepiece micrometer.

A minute quantity of microsponges was spread on a clean glass slide with a drop of liquid paraffin and covered with a cover slip. The average particle size was determined using following formula:

$$D_{\text{mean}} = \frac{\sum nd}{\sum n}$$

Where, n= number of microsp sponge observed and d = mean size range.

**Particle size analyzer:**

Particle size analysis of prepared optimized microsponges was carried out using particle size analyzer (Malvern Master sizer). Microsponges were dispersed in double distilled water before running sample in instrument to ensure that light scattering signal is within sensitivity range of instrument.

**Entrapment efficiency:**

Flurbiprofen loaded microsponges theoretically equivalent to specific amount of Flurbiprofen weighed. Crushed and extracted with 10 ml of methanol by vortexing. Sample was centrifuged at 2000 rpm for 10 min. Filtered and assayed spectrophotometrically at 249nm after appropriate dilution.

$$\text{Entrapment Efficiency} = \frac{\text{Practically entrapped drug}}{\text{Total amount of drug}} \times 100$$

**4. RESULT AND DISCUSSION:  
PRE-FORMULATION STUDIES:**

**Melting Point:**

Melting point of Flurbiprofen was found to be 112°C which complies with the value mentioned in the literature.

**Solubility:**

Solubility studies of were done in various solvent systems. Solubility of FLB is higher in 7.4 pH phosphate buffer compared to 0.1N HCl and distilled water. The solubility of flurbiprofen in Phosphate buffer 7.4 pH were found to be 1.289µg/ml. in case of distilled water and 0.1N HCL, the solubility were found 1.219 µg/ml and 0.63. µg/ml respectively. From this result, FLB showed greater solubility in pH 7.4 phosphate buffer.

**Determination of wavelength of maximum absorbance (λmax value):**

The wavelength of maximum absorbance i.e. lambda max was found to 249 nm as shown in fig.4

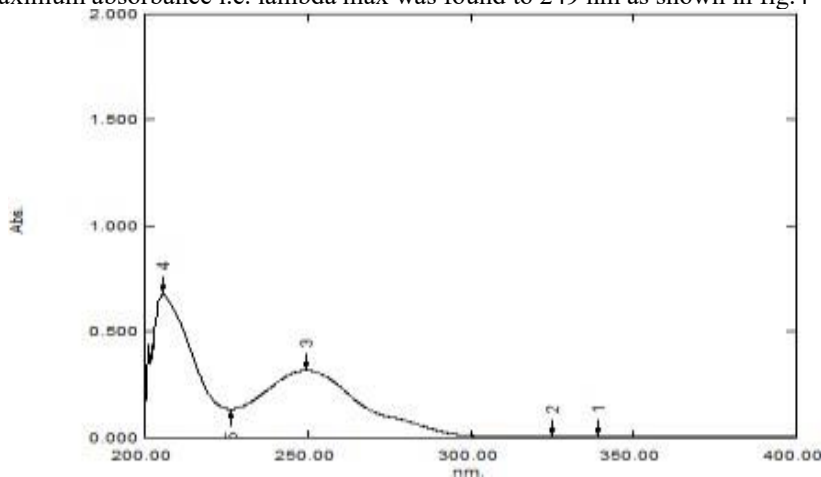


Figure 4- UV spectra of Flurbiprofen Drug

**Calibration Curve of Flurbiprofen Drug:**

For the calibration study of Flurbiprofen drug, prepared different concentrations like 2, 4, 6,8,10 µ/ml respectively from the stock solutions and took the absorbance at 249 nm wavelength. It gives the absorbance values which helps in plotted the calibration curve graph as concentration verses absorbance.

**Calibration Readings of FLB**

Concentrations (µ/ml)	Absorbance (nm)
0	0
2	0.3
4	0.69
6	1.01
8	1.37
10	1.69

Table 2 - Calibration Readings of FLB

After plotting the graph concentrations verses absorbance we got straight line equation which is  $y = 0.173x - 0.026$  and value of  $R^2$  is 0.999.

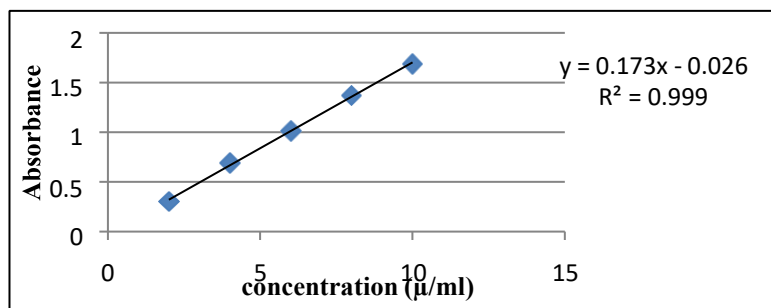


Figure 5- Calibration Curve of Flurbiprofen Drug

**Calibration plot of Flurbiprofen in Methanol:**

Calibration plot of Flurbiprofen was prepared in methanol with regression value of 0.9984 at 238nm. The figure showed calibration curve with regression value of 0.9984, slope of 0.1197 and intercept of 0.1171 in concentration range 4 -20 µg/mL.

Table 3 - Construction of calibration curve using different Concentration in methanol

Conc (µg/mL)	Absorbance
4	0.231
8	0.368
12	0.468
16	0.601
20	0.713

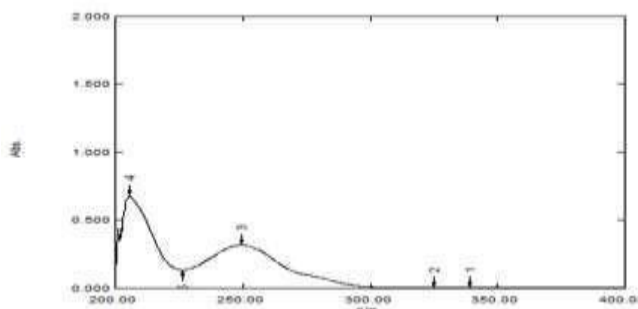


Figure 6- Calibration curve of Flurbiprofen in methanol.

**FTIR:**

The compatibility study of drug, physical mixture of drug and polymer, polymer and PVA carried out by using FTIR to establish any possible interaction between drug and polymer used in formulation. Resulting there is no chemical interaction between drug and polymer as showed in following figure.

**Drug- Excipient comparative studies:**

Drug and Excipient comparative studies carried by FTIR analysis (Jasco-4100). IR spectrum of Flurbiprofen Drug compared with IR spectrum of Drug and excipients respectively. It was found that no any interaction between the drug and excipients.

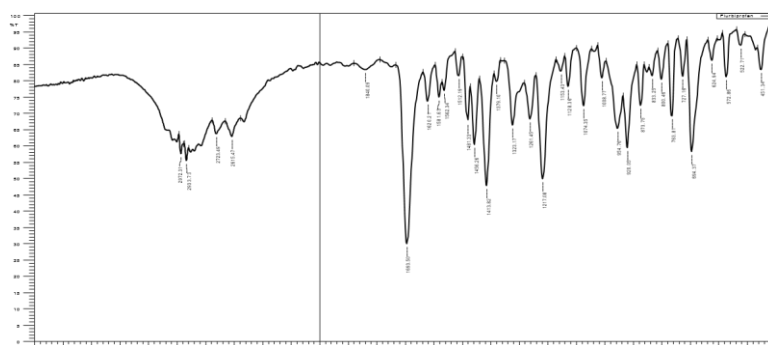


Figure 7 - IR spectrum of Flurbiprofen Drug

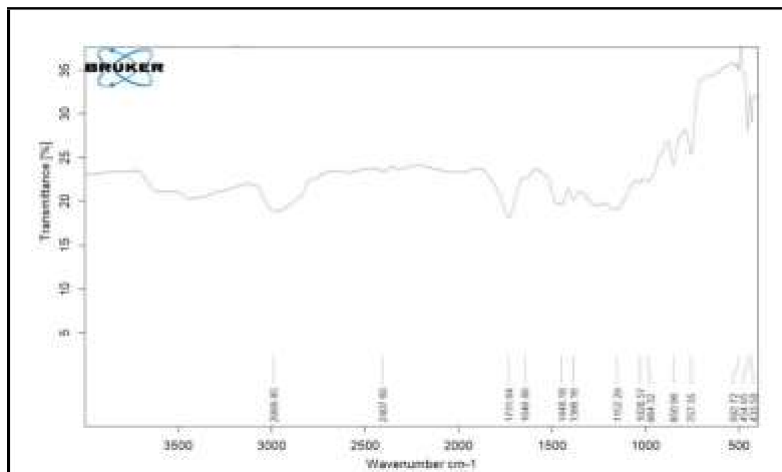


In figure no. 4, the IR spectrum shows the presence of methyl group (CH<sub>3</sub>) at 1456.26 cm<sup>-1</sup>. Similarly at peak we can observed the IR values at 1693.5 cm<sup>-1</sup> stands for carbonyl group (=O), 2972.49 cm<sup>-1</sup> is for hydroxyl group (OH) and 1413.82 cm<sup>-1</sup> is for fluorine group (F).and observed values are expressed in Table no-4 with the standard reported values.

**Table 4 - Characteristic IR peaks of Flurbiprofen Drug**

Functional Group	Standard Range (cm <sup>-1</sup> )	Observed Frequency (cm <sup>-1</sup> )
— CH <sub>3</sub>	1450-1375	1456.26
= O	1725-1700	1693.5
– OH	3400-2400	2972.49
— F	1400-1000	1413.82

**1. Eudragit RS-100:**



**Figure no.8-** IR Spectrum of Eudragit RS-100

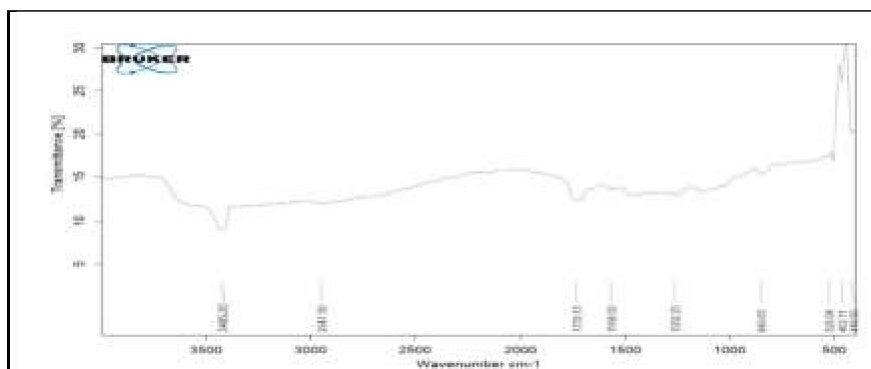
All the major peak of Eudragit RS-100 was found at wave number and showed presence of functional group such as, CH<sub>3</sub> and CH<sub>2</sub> bending, aliphatic C-H Stretching, C=O Stretching, bending CH<sub>2</sub> and Amines (C-N) etc. which confirmed the molecule was Poly(ethyl acrylate-co- methylmethacrylate-co trimethylammonioethyl methacrylate chloride).

The interpretation obtained from the IR is given in table no.5 All the major peak of Eudragit RS-100 was found at wave number and showed presence of functional group such as, CH<sub>3</sub> and CH<sub>2</sub> bending, aliphatic C-H Stretching, C=O Stretching, bending CH<sub>2</sub> and Amines (C-N) etc. which confirmed the molecule was Poly(ethyl acrylate-co- methylmethacrylate-co trimethylammonioethyl methacrylate chloride). The interpretation obtained from the IR is given in table no.5-

**Table no.5-** the functional groups along with their wave numbers of Eudragit RS-100.

Functional Group and bond	Peak observed(cm <sup>-1</sup> )
Aliphatic C-H Stretching	2989.85
C=O stretching	1731.64
Presence of C-O stretching	1448.18
CH <sub>2</sub> -CH <sub>3</sub> bending	1368
C-O bending	1028.
Amine C-N	1152.29

**1. PVA:**

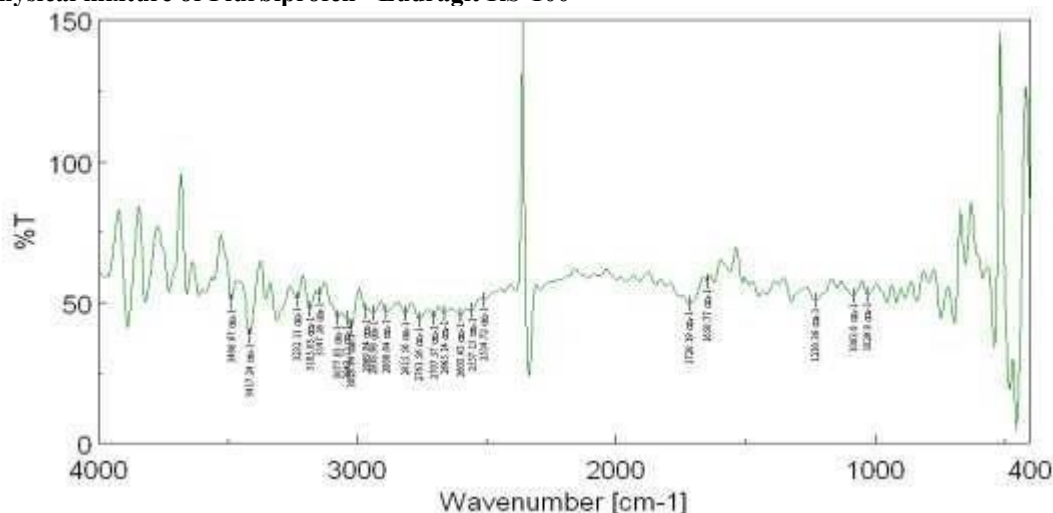


**Figure no.9- IR Spectrum of PVA**

All the major peak of PVA was found at wave number and showed presence of functional group such as, Hydroxyl group -OH, aliphatic C-H group, C-O and CH<sub>2</sub> bending, which confirmed that molecule was polyvinyl alcohol. The interpretation obtained from the IR is given in table no.6.

**Table no.6-** The functional groups along with their wave numbers of PVA

Functional group and bond	Peak observed (cm <sup>-1</sup> )
hydroxyl-OH	3529.09
Methyl -CH	2965.08
Presence of C-O Bending	1262.23
CH <sub>2</sub> Bending	849.63

**2. Physical mixture of Flurbiprofen +Eudragit RS-100****Figure no.10-** IR Spectrum of Physical mixture of Flurbiprofen and Eudragit RS-100

The FTIR spectra of physical mixture of Flurbiprofen and Eudragit RS-100 is shown in figure 10, There is no chemical interaction or significance changes in peak pattern observed. The interpretation obtained from the IR is given in table no.7

**Table no.7-** The functional groups along with their wave numbers of physical mixture.

Functional group and bond	Peak observed(cm <sup>-1</sup> )
Aliphatic C-H Stretching	2842.56
Methyl -CH	2962.08
Aromatic ester C=O	1707.89
Aromatic C=C	1458.12
Aromatic ester C=O	1382.35
Secondary alcohol C-O	1060.8
Presence of C-O stretching	1458.01
CH <sub>2</sub> -CH <sub>3</sub> bending	1267.40
- F	1413.82

**5. PREPARATION OF PRELIMINARY BATCH BY QUASI EMULSION SOLVENT DIFFUSION METHOD:**

The Quasi emulsion solvent diffusion method was selected for preparation of microsponges due to their flexibility to formulate Microsponge's formulation.

**Evaluation of Preliminary batches:****• Physical Evaluation:**

All batches of formulation were white in colour and free flowing in nature as compared with pure drug.

**• Production Yield:**

Production yield of all preliminary formulations ranged from 62.00%-82.00%. It was found that the production yield was affected by concentration of polymer as well as by concentration of polyvinyl alcohol. It was indicated that production yield increased by increasing polymer concentration because higher amount of polymer present resulting in increase in yield. As increasing concentration of polyvinyl alcohol decreased production yield because some big droplet formed that to form the aggregate around the mechanical stirrer result production yield decreased

#### • Particle Size:

Particle Size of microsponges varied from 46.60 $\mu$ m-56.40 $\mu$ m .It was found that the particle size increased by increasing polymer concentration because higher viscosity of the internal phase formed the larger size emulsion droplets and hence larger the microsponges .As the concentration of polyvinyl alcohol increased, the droplets could not be easily divided into smaller droplets particle resulted larger the microsponges

#### • Effect of drug to polymer ratio:

It was found that, the production yield, and the particle size gradually increased with increasing drug polymer ratio. The drug release decreases may be due to porosity or thickening wall of Microsponge's drug release decreases with increasing polymer concentration.

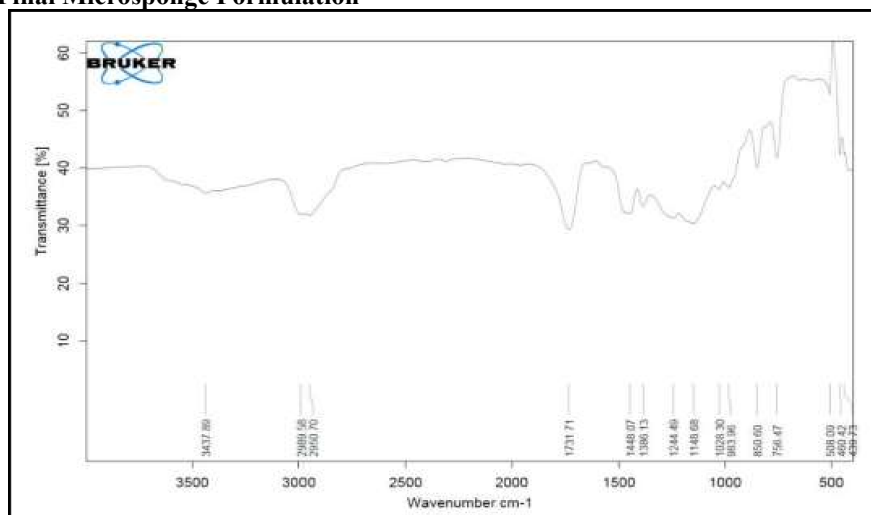
Batches	Polymer (g)	Production Yield %	Particle Siz $\mu$ m
R1	10	62.40	46.6
R2	12.5	78.90	52
R3	15	81.10	56.4

**Table No 8-** Result of Preliminary trial batches R1 to R3

#### • Effect of Surfactant (emulsifier) Concentration:

The surfactant or emulsifier plays an important role in the preparation of microsponges. In absence of surfactant there is no microspunge formation. It was found that when the concentration of surfactant was increased, the particle size of microsponges increased, production yield decreased.

#### FTIR Spectra of Final Microsponge Formulation



**Figure no.11-** IR Spectrum of Final microsponge Formulation

#### 6. SUMMARY AND CONCLUSION:

Microsponge's technology is patented, highly cross linked, porous and polymeric in nature. They entrap wide variety of active ingredient and release them in controlled manner. Microsponge's drug delivery system is non-irritating, non-allergic, non-biodegradable because of using biologically inert polymer. This system have higher payload, are free flowing as well are as cost effective. The microsponges delivery system is a unique technology for the controlled release of microporous beads, loaded with active agent, reduction in side effects, while maintaining their therapeutic efficacy, hence decided to formulate Flurbiprofen microsponge. On UV Scanning lambda max of drug was found to be 249nm and it is matching with reported value. Evaluation of Physicochemical Property and FTIR were confirm that drug is Flurbiprofen. Spherical and bunches of microsponge particle was seen under the microscope. Microsponges containing different polymer ratio were prepared and evaluated and it is concluded that as polymer concentration increases, production yield and particle size of the microsponges also increases. It was found that when the concentration of surfactant was increased, the particle size of microsponges increased, production yield decreases.

#### 6. REFERENCES:

1. Kanitakis JA. Histology and Immune Histochemistry of Normal Human Skin. European Journal of Dermatology. 2002; 12(4): 390-401.doi.org /10.1684/ejd.2012.1871
2. Chowdary KPR. Rao YS. Mucoadhesive microspheres for controlled drug Delivery. Biological Pharmaceutical Bulletin.2004; 27(11): 1717-1724.doi.org /10.1248/bpb.27.1717
3. Joshi G. Kaur R. Microsponges: A Novel Drug Delivery System. International Research Journal Of Pharmaceutical and Bioscience. 2016; 3(1):01-11

4. Patil Rahul. Kemkar Vishnu. Patil SS. Microsponge Drug Delivery System: A Novel Dosage Form. *American Journal Pharmaceutical Technology Research*.2012;2(4):227-251
5. Charde MS. Ghanawat PB. Welankiwar AS. Kumar J. Chakole RD. Microsponge A Novel New Drug Delivery System: A Review. *International Journal of Advances in Pharmaceutics*.2013; 2 (6):63-70
6. Namrata Jadhav. Vruti Patel. Siddesh Mungekar. Gaurav Bhamare. Manisha Karpe. Vilasrao Kadams. Microsponge Delivery System: An updated review, current status and future prospects. *Journal of Scientific and Innovative Research*.2013;2(6):1097-1110.[doi.org/0.31254/jsir](https://doi.org/0.31254/jsir)
7. Verma Pratibha. Dhyani Archana. Juyal Divya. A brief review on microsponges use in chronopharmacology. *The Pharma Innovation Journal*.2018; 7(6):538-543. [doi.org/10.22271/tpi](https://doi.org/10.22271/tpi)
8. Christensen MS. Hargens CW. Nacht S. Gans EH. Viscoelastic properties of intact human skin instrumentations, hydration effects and contribution of the stratum corneum. *J Invest Dermatol*.1977; 69:282–286.[doi.org/10.1111/1523-1747.ep12507500](https://doi.org/10.1111/1523-1747.ep12507500)
9. Sato T. Kanke M. Schroeder G. Deluca P. Porous biodegradable microspheres for controlled drug delivery.I. Assessment of processing conditions and solvent removal techniques. *Pharmaceutical Research*. 1988; 5(1): 21-30. [doi: 10.1023/a:1015855210319](https://doi.org/10.1023/a:1015855210319)
10. Guyot M. Fawaz F. Nifedipine loaded-polymeric microspheres: Preparation and Physical Characteristics. *International Journal Pharmaceutics*.1998;175(1): 61-74. [doi.org/10.1016/S0378-5173\(98\)00253-1](https://doi.org/10.1016/S0378-5173(98)00253-1)
11. Parikh BN. Gothi GD. Microsponges as novel Topical drug delivery system. *Journal of Global pharma technology*. 2010;2(1):17-29
12. Kaity S. Maiti S. Ghosh A. Pal D. Banerjee A. Microsponges: A novel strategy for drug delivery system. *Journal Advanced Pharmaceutical Technology Research*. 2010;1(3):283-290. [doi.org/10.4103/0110-5558.72416](https://doi.org/10.4103/0110-5558.72416)
13. Shyam SM. Vedavathi T. Novel approach: microsponge drug delivery system. *International Journal Pharmaceutical Science Research*. 2012; 3(4): 967-980.[doi.org/10.13040/IJPSR.0975-8232.3\(4\).967-80](https://doi.org/10.13040/IJPSR.0975-8232.3(4).967-80)
14. Srivastava R. Pathak K. Microsponges: a futuristic approach for oral drug delivery. *Expert Opinion Drug Delivery*. 2012; 9(7): 863-878. [doi.org/10.1517/17425247.2012.693072](https://doi.org/10.1517/17425247.2012.693072)
15. Amrita Kumari. Ankit Jain. Pooja Hurkat. Amit Verma. Sanjay KJ. Microsponges: A Pioneering Tool for Biomedical Applications. *Department of Pharmaceutical Sciences*. 2016; 33(1): 77-105. [doi.org/10.1615/CritRevTherDrugCarrierSyst.v33.i1.40](https://doi.org/10.1615/CritRevTherDrugCarrierSyst.v33.i1.40)
16. Manoj Kumar Mishra. Optimization, Formulation development and characterization of eudragit RS-100 loaded microsponges and subsequent colonic delivery. *International Journal of Drug Discover and herbal Research*. 2011;1(1):8-13
17. Maiti Sabyasachi. Biswanath SA. Kaity S. Ray S. Development and Evaluation of xanthum gum- facilitated ethyl cellulose microsponges for controlled percutaneous delivery of diclofenac sodium. *Acta Pharmaceutica*. 2011;61(3):257-270. [doi.org/10.2478/v10007-011-0022-6](https://doi.org/10.2478/v10007-011-0022-6)
18. Sawant SD. Baravkar AA. Kale RN. FT- IR Spectroscopy: Principle, Technique and Mathematics. *International Journal of Pharma and Bio Sciences*. 2011; 2(1): 513-519.[doi.org/10.22376/ijpbs](https://doi.org/10.22376/ijpbs)
19. Mutalik S. Anju P. Manoj K. Enhancement of Dissolution Rate and Bioavailability of Aceclofenac: A Chitosan- Based Solvent Change Approach. *Indian Journal of Pharmaceutical Education and Research*. 2010; 45(4): 146–252.[doi.org/10.5530/ijper.45.4](https://doi.org/10.5530/ijper.45.4)
20. Daravath B. Naveen C. Vemula SK. Solubility and Dissolution Enhancement of Flurbiprofen by Solid Dispersion using Hydrophilic carriers. *Brazilian Journal of Pharmaceutical Sciences*. 2018; 53(4): ISSN 2175-9790.[doi.org/10.1590/s2175-9790201700040001012](https://doi.org/10.1590/s2175-9790201700040001012)
21. Adepu V. Nagoji KE. Girijasastry V. Simultaneous Determination of Flurbiprofen and Pantoprazole in Bulk and Pharmaceutical Dosage Form by UV Spectrophotometer. *International journal of pharmacy and pharmaceutical sciences*. 2014; 6(9):31-33
22. Yilmaz B. Alkan E. Spectrofluorometric and UV Spectrophotometric Methods for the Determination of Flurbiprofen in Pharmaceutical Preparations. *Research & Reviews: Journal of Pharmaceutical Analysis*.2015; ISSN: 2320-0812
23. Kokotailo GT. Fyfe CA. Zeolite Structure Analysis with Powder X-Ray Diffraction and Solid-State NMR Techniques. *The Rigaku Journal*. 1995;12(1):3-10