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Design And Development Of Microsponge Gel For Topical Delivery Of Antifungal Drugs

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Abstract: Microsponges are small, porous drug delivery devices. These are small sponge-like spheres with large pores and can alter the release of the drug, increasing stability and reducing side effects. Microsponges were developed using the semi-emulsion solvent diffusion technique as it has a better microsponge formation mechanism. They can also increase stability, reduce side effects, and alter the release process of the drug. Perform preliminary chemical research, melting point and solubility studies, and chemical analysis by FT-IR and DSC to demonstrate drug identification, quality, and stability. Chemical Purity. Evaluate well-designed models and examine drug release patterns. SEM analysis of the optimized F2 formula displaying a rounded and porous structure; The DSC thermogram of F2 shows that the inlet endothermic temperature is 117.12 ℃ & 147.51 ℃. FT-IR and DSC studies indicate that the drug is compatible with the polymer used in the preparation of drug-loaded microsponges and X-ray diffraction studies. It shows that the crystal properties of F2 and F2 do not change after being formulated into microsponges. Safety studies examined F2 and found it to be stable for 3 months

Index Terms - Microsponges**,** stability**,** SEM analysis**,** FT-IR and DSC studies

I. INTRODUCTION

Drug delivery systems are designed to enter the body, where the skin is the gateway to the drug. There are creams, ointments, lotions, TDS, etc. available in the market. Various preparations are available, inc luding: Prasad M.Sc., 2011).
components that control the release of active substances. Effective treatment of this disease is often associated with active drugs, causing skin irritation reported in some studies, as well as uncontrolled evaporation of the active substance and potential conflicts between drugs and carriers. (Prasad MSC, 2011).

For this reason, microsponges must remain under the skin and epidermis for the longest time and release the drug slowly. For these reasons, microsponges must meet the following characteristics (Prasad MSC, 2011):

- Non-collapsible structure, consisting of empty space in many cases Has high shear strength in the void space trapping many components, used mainly in lotions, creams and powders, maximum load (50% ~ 60%)) and is the particle size of the link. The gap area is 5-500 microns.
- It should not be irritating, mutagenic, toxic or oily.
- It must be resistant to high temperature and shear stress.
- We need to make security better.
- It must be able to withstand high oil pressure, that is, it must be able to absorb without drying out upto six times of its weight without drying out..
- Must be exposed continuously for up to 12 hours.

Microsponges have advantages over pharmaceutical models in which the BPO form localizes the active chemical to the skin, causing toxicity and skin irritation. This is avoided by using microsponges, which must associate with the following rules: (Prasad MSC, 2011)

- If the drug is essentially non-polar, it will form a porous structure called a porogen.
- Contain water or generally be very slightly soluble.
- Inert towards monomers and polymers.
- Stable in connection with the polymerization catalyst and polymerization conditions.
- Release can be controlled by exposure or other factors such as humidity, pH, friction, or temperature.

1.1 Advantages of Microsponge Technology (Gupta A, 2016)

- Product performance.
- Continuous release.
- Reduces irritation, thus increasing patient compliance.
- Increase the elegance of your products.
- It improves oil control by absorbing more than six times its weight in oil without drying out.
- Simplifying the formulation.
- Improved thermal, physical and chemical stability.

1.2 Product (Gupta A, 2016)

- It is adhered with microsponges.
- Many liquids or water-soluble substances may remain in the product. Active substances that can be put into microsponges should be meet the following requirements.
- It must be completely miscible with the monomer or soluble by mixing a little amount of water-immiscible solvent.
- There should be no water or no water. It is generally slightly soluble.
- It must be inert towards the monomer.
- It must be stable in contact with the polymerization catalyst and polymerization conditions.

1.3 Advantages of Microsponge (Gupta A, 2016)

- Microcapsules generally cannot control the release of APIs. When the walls are broken, the API contained in the microcapsules is released. Can MDS do this? That's the real question.
- Liposomes have low payload capacity, complex design, lack of chemical stability and microbial instability. MDS is chemically stable and easy to produce
- MDS is stable in the pH range of 1 - 11.
- Microsponges are stable at temperatures up to 130°C.
- The efficiency of micro sponges is between 1 and 11. 50-60%.
- They are free flowing and cost effective.
- Microsponges are small particles that absorb skin secretions, thus reducing the oiliness and shine of the skin.

1.4 Properties of active ingredients capture micro sponges (Gupta A, 2016)

- It must be completely miscible in monomer or miscible by adding a small amount of water-immiscible Solvent.
- It should not contain water or should generally be very slightly soluble.
- It should be inert towards monomers and should not increase the viscosity of the mixture during formulation.
- When used, it must be stable in contact with the polymerization catalyst and polymerization conditions.
- The spherical structure of the microsponge should not be damaged.

2. Formulation Development

Microsponges were prepared using semi-emulsion solvent diffusion technology. The inner phase contains ethylcellulose / Eudragit RS100 as polymer and triethyl citrate (1% w/v) as plasticizer. Dissolve the above internal phase with 5 ml DCM, ethanol (1:1) or 6 ml DCM. External phase PVA used as a surfactant that will completely dissolve in water. The inner phase was added continuously dropwise to the outer phase and magnetic stirring was continued for 180 min at 1000 rpm or 60 min at 500 rpm. The product was filtered, washed three times with distilled water and dried overnight in a desiccator containing calcium chloride.
Preliminary tests were carried out to select polymers like Eudragit RS 100, Eudragit RL 100 and ethylcellulose; microsponges are created with Eudragit RS 100, not Eudragit RL100. The resulting microsponges are soft in nature. Therefore, further research is needed to increase the polymer ratio of the two polymers (ethylcellulose, Eudragit RS 100). Ingredients are listed in the table TableNo:1

Table 1. Composition of Itraconazole Microsponges

Formulation Code	Drug : polymer (mg)	Polymer used	Solvent type (mL)	% PVA (g)	Triethyl citrate (%w/v)	RPM
F1.	1:1	EC	DCM:Alcohol	0.2	1.0	1000
F2.	1:2	EC	DCM:Alcohol	0.2	1.0	1000
F3.	1:3	EC	DCM:Alcohol	0.2	1.0	1000
F4.	1:4	EC	DCM:Alcohol	0.2	1.0	1000
F5.	1:1	ERS-100	DCM	0.2	1.0	500
F6.	1:2	ERS-100	DCM	0.2	1.0	500
F7.	1:3	ERS-100	DCM	0.2	1.0	500
F8.	1:4	ERS-100	DCM	0.2.	1.0	500

*Alcohol95%v/v

Itraconazole microsponges were prepared using semi-emulsion solvent diffusion technology. The inner phase contains 500 mg itraconazole, 1000 mg ethylcellulose as polymer and 1% w/v triethyl citrate as plasticizer. Dissolve the inner phase polymer in 10 ml DCM:alcohol (1:1). The outer phase contains 0.2 g Polyvinyl Acetone in 10 ml of water. The inner phase was mixed into the outer phase with repeated stirring at 1000 rpm about 180 min. The product was filtered, washed three times and dried under a desiccator overnight as shown in Table 2. and Figure 1.

Table 2 Results of Composition of Optimized Formulation

Specification	Optimum values
Drug: polymer	1:2
FP	500 MG
Amount of EC	1000 mg
PVA	0.2 g
phase solvent	Dichloromethane: EC
Qut of internal phase solvent (ml)	10 ml
Qut of water in external phase (ml)	200 ml
Temperature	37 ºC
Mixer type	3 blades
Stirring rate	1000 rpm
Stirring time	180 min
Plasticizer	TEC

FIG: 1 Prepared microsponges of F1-F8

3. Evaluation Studies of Itraconazole

3.1 Visual inspection of Itraconazole

It was determined that the color, appearance and properties of the prepared F1-F8 microsponges were as shown in Table 3. The color, appearance and product of batches F1-F4 are light yellow, non-porous and powdery, and the color is appearance. and the product of batch F5: It is light yellow in nature, not porous and not dusty. -F8, yellow-white, non-porous, dusty, non-hard, as shown in Figure 2 and Table 3. The results showed that microsponges were acceptable according to detection standards.

Table no: 3 Results of Visual Inspection

Formulation code	Color	Appearance	Nature
F1	Pale Yellow	Porous	Powdered
F2	Pale Yellow	Porous	Powdered
F3	Pale Yellow	Porous	Powdered
F4	Pale Yellow	Porous	Powdered
F5	Yellowish white	Non porous	not rigid
F6	Yellowish white	Non porous	not rigid
F7	Yellowish white	Non porous	not rigid
F8	Yellowish white	Non porous	not rigid

3.2 Results of Determination of Percentage Yield

The results of different products of microsponges range from 44.90% ± 1.08 to 68.42% ± 0.118% in F1-F4 and from 43.36% ± 1.96% to 68.16% ± 0.912% in F5-F8 It is changing. has a significant impact on productivity. large In both cases, the results of FF1 and F5 with a chemical:polymer ratio of 1:1 are still low; for example, 44.90% and 43.36%; chemical:polymer ratio 1:8 (F4, F8) 68.42 ± 0.118% and 68.16 ± 0.912% polyvinyl alcohol concentration remains constant, indicating that the polymer has a significant effect on the yield. Solvents used in two different groups due to their solubility in polymers. The drug-to-polymer ratio was found to increase from 57.3 ± 1.5% to 95.2 ± 1.3%. It was concluded that the polymer concentration increased the percentage of microsponges adhering to the structure.

3.3 Encapsulation efficiency percentage

It is lost in the filtrate during the process. The encapsulation efficiency of the two F1-F4 groups ranged from 98.30 ± 0.125% to 86.31 ± 1.53%, and the encapsulation efficiency of F5-F8 ranged from 98.58 ± 0.352% to 89.76 ± 0.49%. The maximum size for microsponges is 5-300 µm. Each batch was visually inspected using a microscope and the size was evaluated for two groups, F1-F4 30.01 to 52.16 µm and F5-F8 30.09 to 45.37 µm. The size of microsponges increases with the increase of the polymer wall. Among the formulations, batch formulation F2 exhibited good spherical shape with large pore surface area compared to other batches. Based on photomicroscopic studies, batch F2 was selected as the final batch of microsponges. The optimized F2 batch and its corresponding particle size is 33.29 µm.

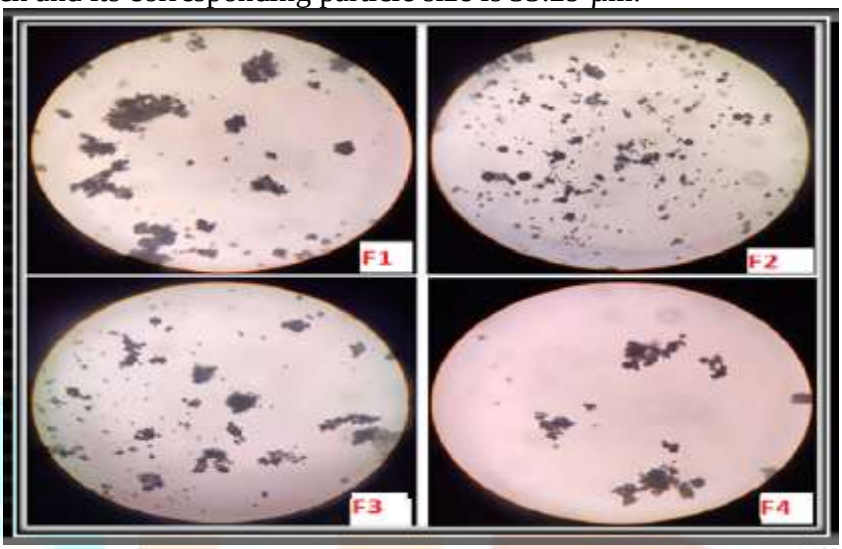


FIG: 2 Results of Photomicroscopic Images of F1-F4

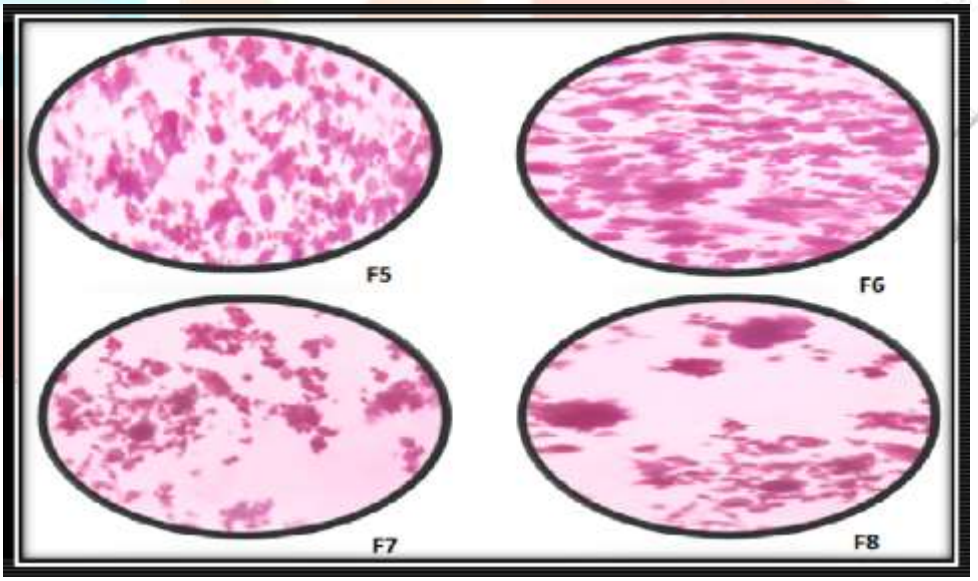
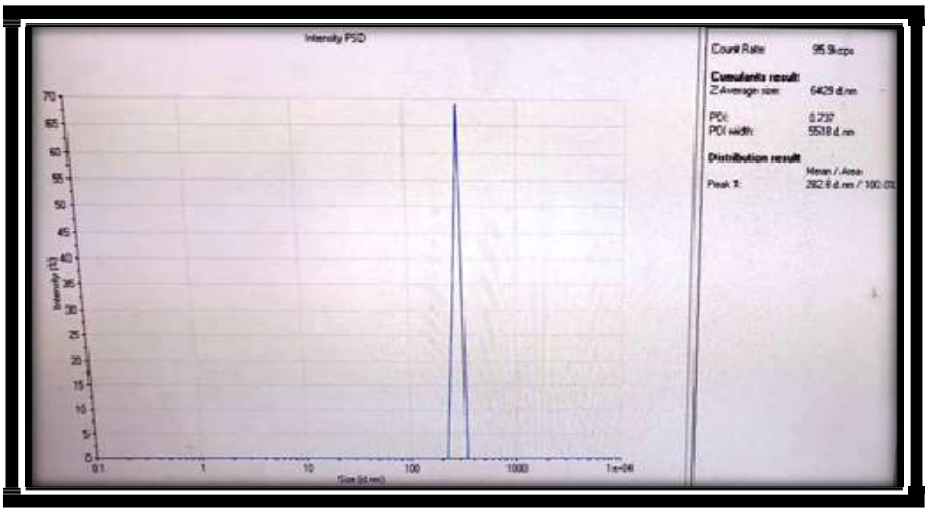


FIG: 3 Results of Photomicroscopic Images of F5-F8

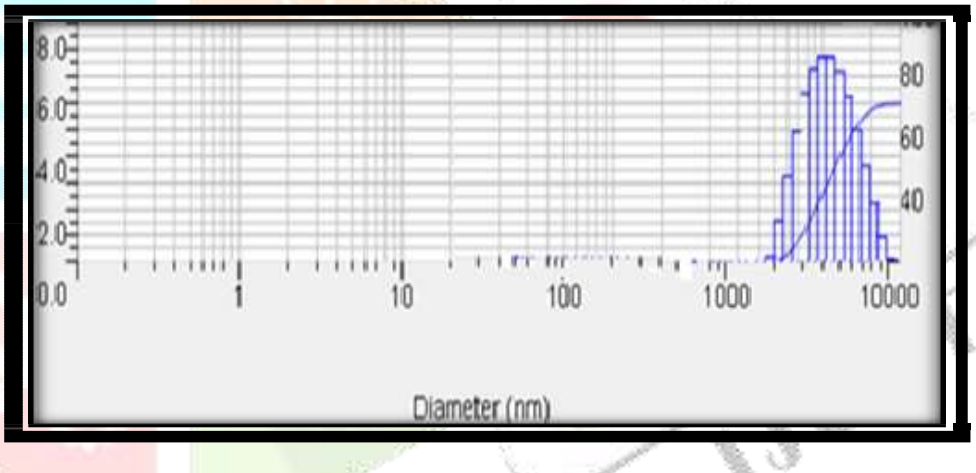
3.4 Particle size analysis by zetasizer

Zeta sizer analysis of the optimized batch (F2) was performed using Zeta sizer (Malvern). The Z-mean size of microsponges In the water diluted sample is 6429 (d) nm and the polydispersity index (PDI)



value is 0.737; this is suitable for particle size estimation as shown in Figure 4. Suitable for particle size estimation.

FIG: 4 mean particle size of optimized formulation F2



3.5 Determination of zeta potential

The created microsponges exhibit electrostatic repulsion between charged particles, preventing the spheres from aggregating. The measurement of zeta potential is as follows: temperature of 24.9°C, viscosity of 0.897 mPa.s, conductivity of 0.815 mS/cm, voltage of 3.3V and electrophoretic mobility of -0.000094 cm2/Vs. The negative of F2 prepared by solvent evaporation process is -12.1 mV, so the preparation process is stable as shown in the figure FIG: 5

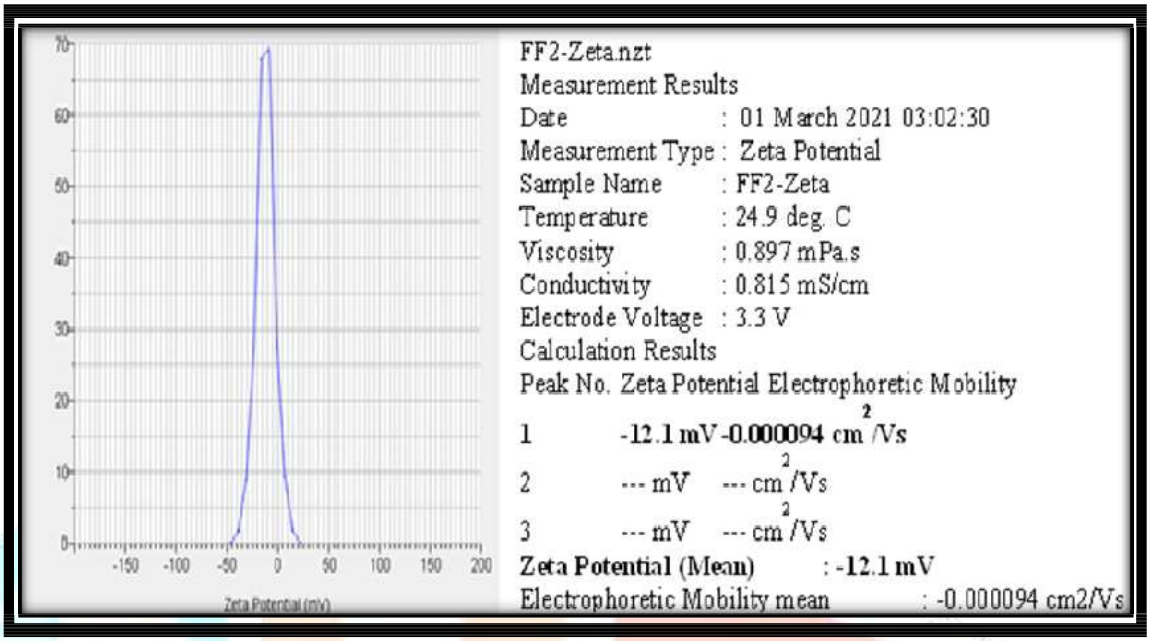


FIG: 5 Results of zeta potential of F2

3.6 Scanning Electron Microscopy (SEM)

Surface morphology analysis showed that microsponges of F2 were porous in nature, resulting from heavy diffusion. Among the SEM tests of all materials, batch FPMF2 was selected as the best structure due to the perfect spherical shape of porous microspheres, as shown in Figure FIG: 6.

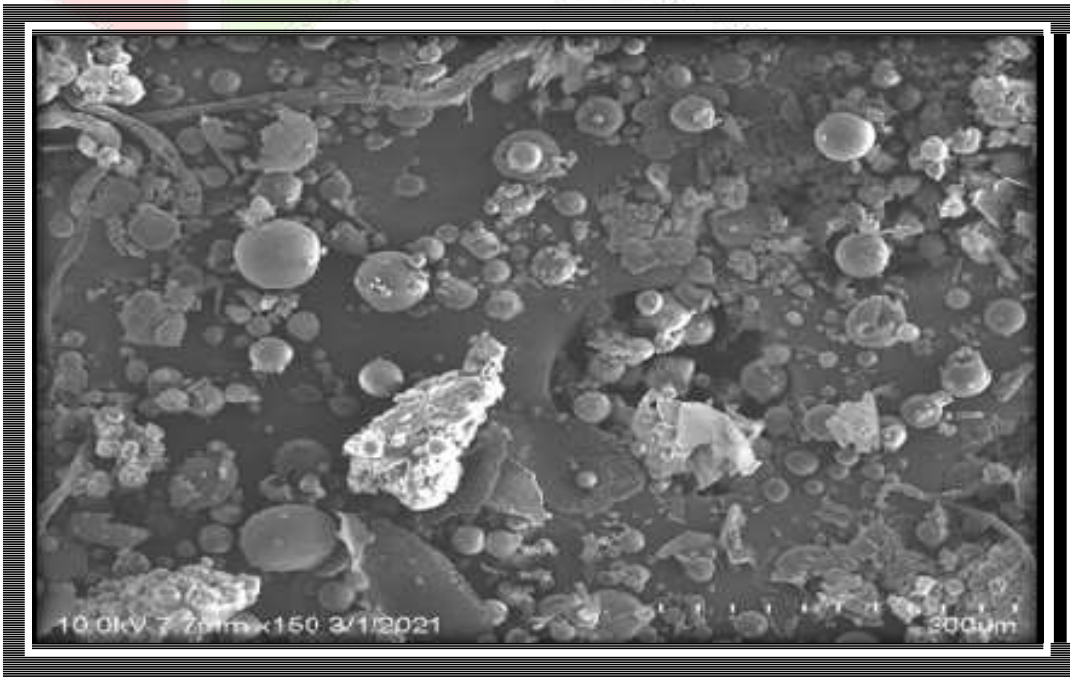


FIG: 6 SEM images of optimized formulation F2

3.7 Differential Scanning Calorimetry (DSC)

Since the DSC thermometer shows the penetrating endotherm peak of 167.12 ℃ found in the final formulation of F2, Corresponding to the melting point of 167.46 ℃ found in pure DSC solution, as shown in Figures 9.6.6 and 9.6.7. but differs slightly from Figures 7 and 8 for pure itraconazole. Temperature did not indicate interaction between the drug and the polymer used to prepare the microsponges; This was also observed.

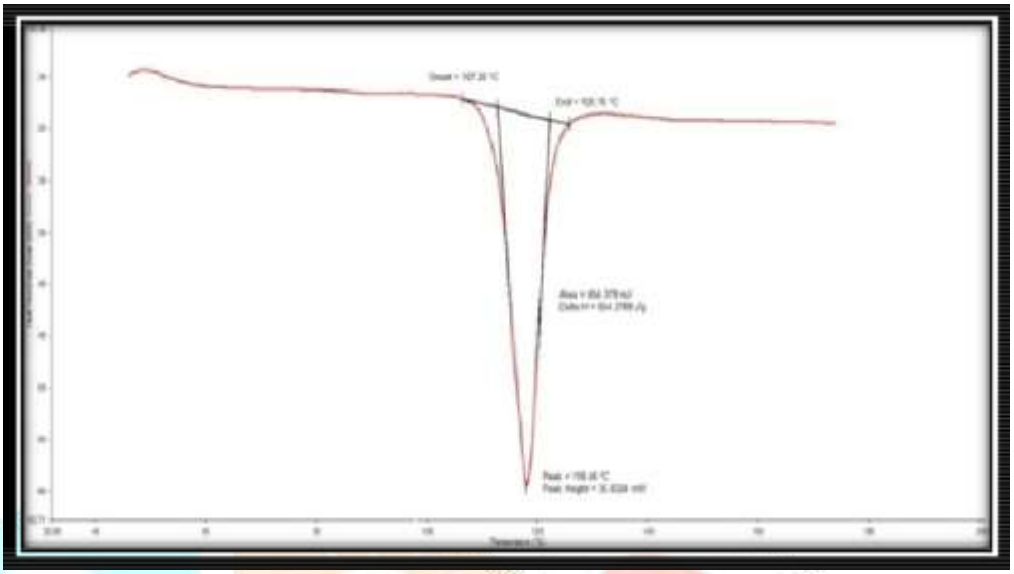


FIG: 7 Results of DSC of Pure drug

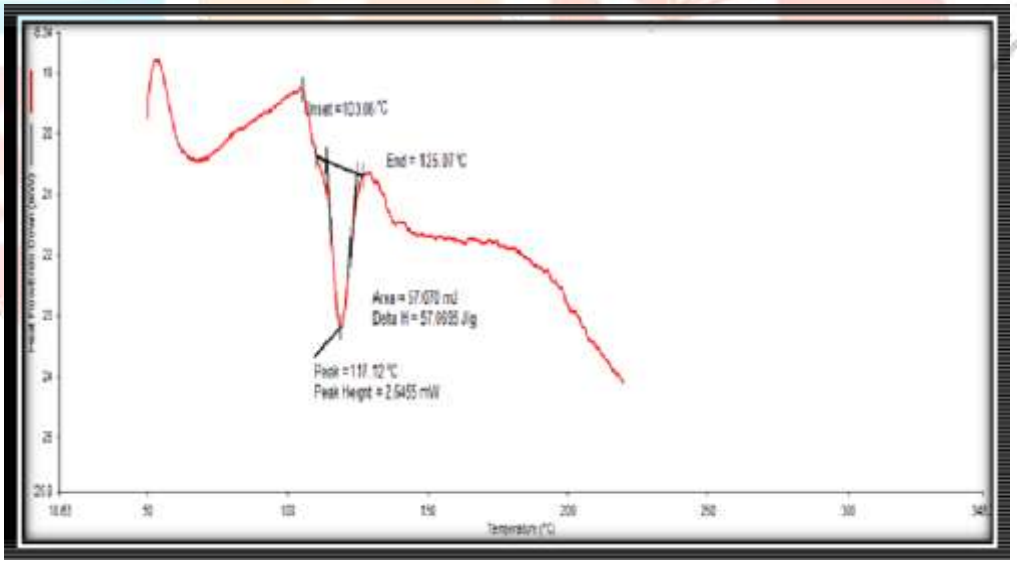


FIG: 8 Results of DSC of optimized formulation F2

3.8 FTIR Spectrum

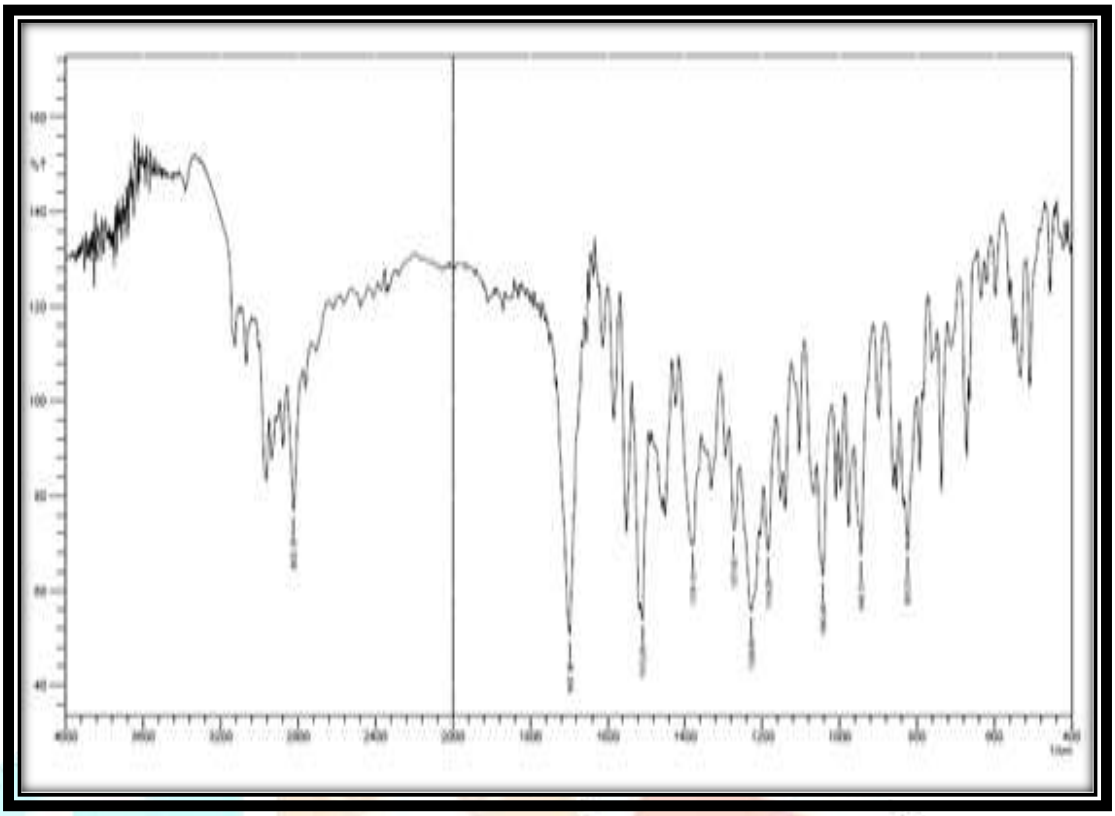


FIG: 9.FTIR of optimized formulation F2

3.9 X-Ray Diffraction Studies

Xray studies are used to determine changes in crystal structure and polymorphism in crystal solutions; Whe n the diffraction patterns of two crystal forms are similar, they indicate that a similar side structure exists wh en the crystal material with different peaks has an internal structure. It has a structure called polymorphic. p aper. The final F2 peak formed in this study is similar to the diffraction angle (2θ) 13° solution, but is less st rong, indicating its crystalline nature. The relative crystallinity (RDC) value was found to be 1.24. As shown in Figures 10 and 11.

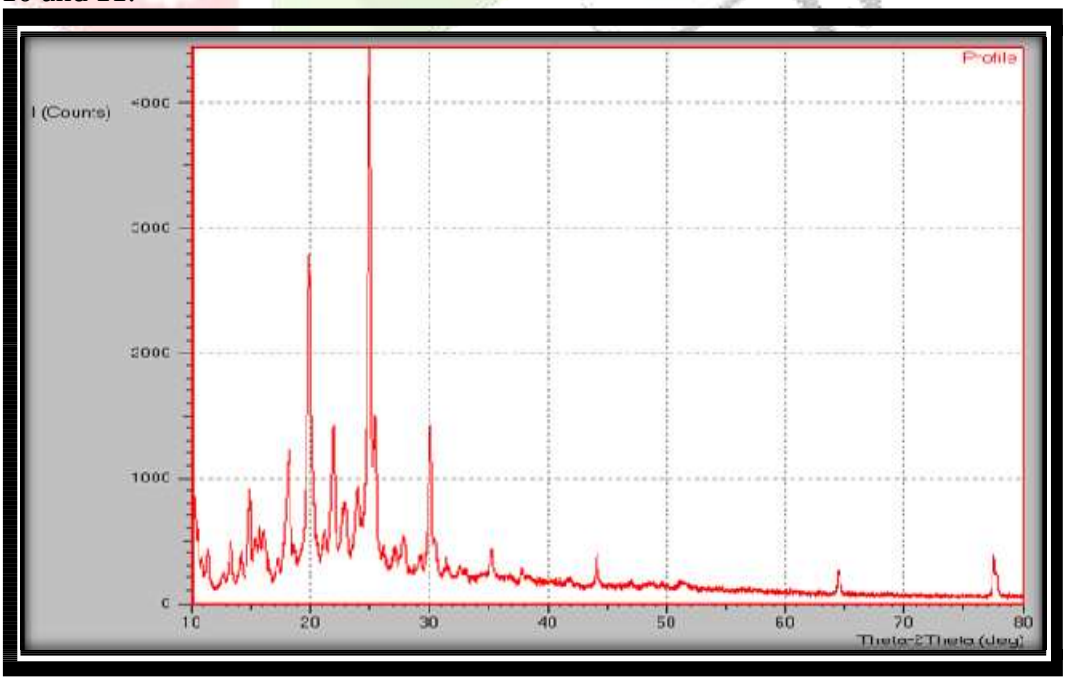


FIG: 10 - Crystalline Structure of Itraconazole

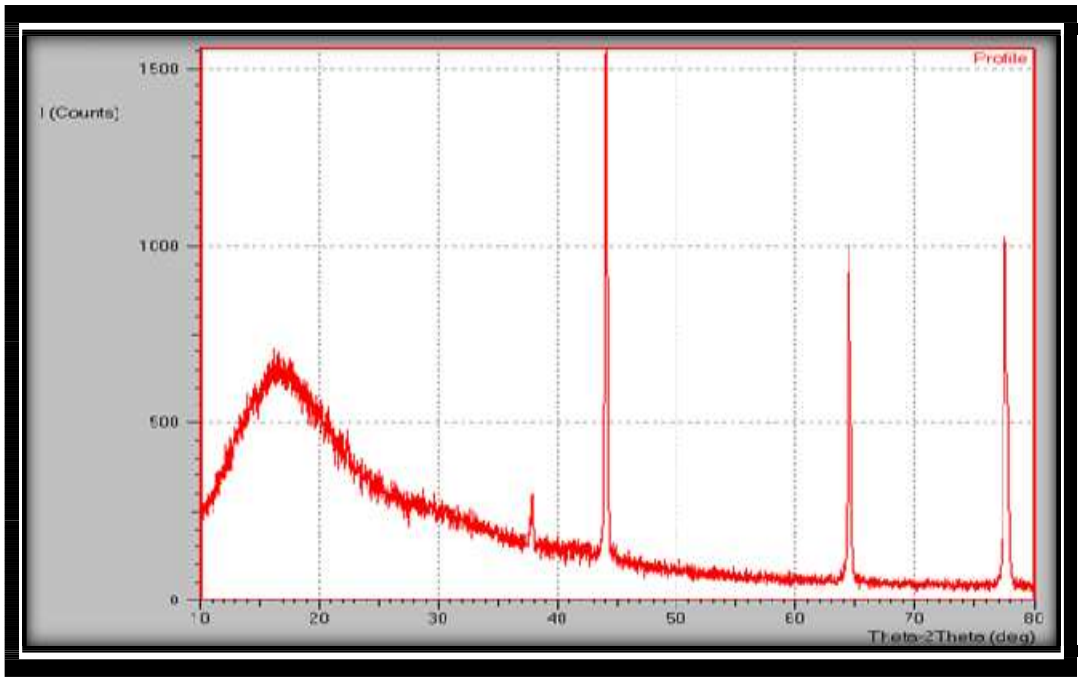


FIG: 11 Results of Crystalline Nature Containing Optimized Formulation F2

3.10 *In-Vitro* Diffusion Studies

Table No. 4 *in vitro* drug diffusion studies

Time (mins)	Cumulative % of drug release							
	F1.	F2.	F3.	F4.	F5.	F6.	F7.	F8.
0	0	0	0	0	0	0	0	0
60	22.34	20.76	19.12	10.22	23.92	20.53	12.68	9.11
120	30.12	30.78	28.69	18.46	31.64	30.27	22.48	17.12
180	39.12	32.69	30.43	22.54	40.74	31.54	28.88	20.56
240	43.42	41.42	38.91	28.99	45.86	40.43	32.48	30.71
300	50.60	52.21	48.34	36.66	53.49	50.66	39.27	35.68
360	60.46	60.12	55.31	42.5	61.52	58.16	43.24	41.92
420	70.19	69.12	62.96	50.99	77.38	66.48	52.38	49.46
480	87.43	77.45	68.16	55.19	87.43	76.81	59.52	55.42

3.11Stability Study

Table No.5 Stability studies

Sr. no.	Properties	Observation
1	Colour (Initial)	Pale White
2	Colour (After two Month)	Pale White
3	PH (initial)	5.56
4	PH (After two Month)	5.56
5	% Drug content at 30± 2ºC 60% RH	96 ± 1.15 %

4. Conclusion

Microsponges are small, porous drug delivery devices. These are small sponge-like spheres with large pores and can alter the release of the drug, increasing stability and reducing side effects. Microsponges were developed using the semi-emulsion solvent diffusion technique as it has a better microsponge formation mechanism. They can also increase stability, reduce side effects, and alter the release process of the drug. Perform preliminary chemical research, melting point and solubility studies, and chemical analysis by FT-IR and DSC to demonstrate drug identification, quality, and stability. Chemical Purity. Evaluate well-designed models and examine drug release patterns. SEM analysis of the optimized F2 formula displaying a rounded and porous structure; The DSC thermogram of F2 shows that the inlet endothermic temperature is 117.12 °C & 147.51 °C. FT-IR and DSC studies indicate that the drug is compatible with the polymer used in the preparation of drug-loaded microsponges and X-ray diffraction studies. It shows that the crystal properties of F2 and F2 do not change after being formulated into microsponges. Safety studies examined F2 and found it to be stable for 3 months

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