DESIGN, DEVELOPMENT AND EVALUATION OF NANOSPONGES USING MODEL DRUG

Payal Malekar[1], Dr. A. Chandewar[2], Dr. B. V. Bakde[2], Gaurav Magar[3], Mayuri Raut[4]

ABSTRACT

The present study focuses on the design, development and evaluation of nanosponges using Pioglitazone HCl through nanosponges technology followed by capsule formulation. Pioglitazone HCl, known for its potent anti-diabetic properties, and nanosponges via the quasi-emulsion solvent diffusion technique, employing ethyl cellulose as the polymer and polyvinyl alcohol as the stabilizer. The prepared nanosponges were characterized for particle size, surface morphology, entrapment efficiency, and thermal stability using techniques such as, scanning electron microscopy (SEM), and the optimized nanosponges were then incorporated into a capsule formulation. The capsule was evaluated for physicochemical parameters, in-vitro drug release, and release kinetics. Results indicated conventional release of the active constituents. This nanosponge-based capsule system offers a promising approach for the effective oral delivery, providing a conventional and targeted therapeutic effect with minimal side effects.

Keywords: Pioglitazone HCl, conventional release, nanosponges, quasi emulsion solvent diffusion method, capsule formulation and in vitro diffusion study.

1. INTRODUCTION:

The development of a wide range of nanoscale technologies is the first step toward altering the fundamentals of illness prevention, diagnosis, and treatment. Numerous nanodevices have significantly improved the effectiveness of many current medications and made it possible to develop whole new therapeutic modalities, which has had a profound impact on medical technology. Nanosponges are a novel kind of material that can encapsulate a wide variety of chemicals in cavities that are only a few nanometers in size. These particles have the ability to transport hydrophilic and lipophilic materials and improve the solubility of molecules that are not very soluble in water. They revolutionize the treatment of many illnesses, and preliminary experiments show that this technology is five times more effective than standard techniques in delivering medications to breast cancer cells.

These tiny sponges can circulate throughout the body, where they encounter the precise target spot and attach to the surface, allowing the medicine to be released in a controlled and predictable manner. Nanosponges are a type of nanoparticle, about the size of a virus, and are typically made from a carbon-containing polymer. They are threedimensional structures formed by hyper cross-linkage cyclodextrins, either alone or in combination with significant amounts of linear dextrin cross-linked with an acceptable crosslinking agent. Because of their small size and porous structure, they can bind poorly soluble medications inside the matrix and boost their bioavailability. These can be produced into dose forms for topical, parenteral, oral, or inhalation application and have a solid consistency

2. AIM, OBJECTIVE AND NEED OF STUDY:

The aim of the study is to "design, development and evaluation of nanosponges using model drug"

Objective:

- To achieve controlled and sustained release capabilities.
- To overcome issues with drug toxicity, decreased bioavailability and drug release over a wide area by formulating nanosponges.
- To increase drug holding capacity of nanosponges.
- To formulate nanosponges with 3-dimensional network having a porous cavity by crosslinking with different compound.

3. DRUG PROFILE

3.1 PIOGLITAZONE HCl:

Synonym Name: Actos, glustin, piogla, piozone, zactos.
Molecular formula: $C_{19}H_{21}ClN_2O_3$
Molecular Weight:392.90. g/mol
Category of Drug: Antidiabetic
Iupac Name: 5- [[4- [2- (5-Ethyl-2-pyridinyl) ethoxy] phenyl] methyl]-2,4-thiazolidinedione monohydrochloride.

Chemical Structure:

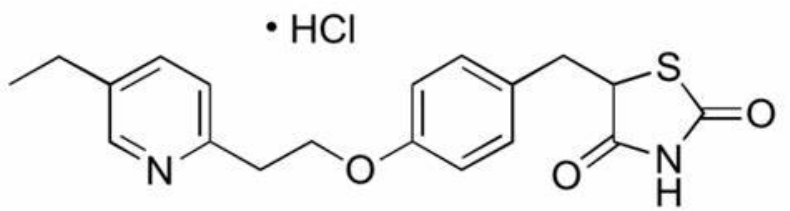


Fig No:1 Pioglitazone Hcl Structure.

Uses:

Pioglitazone is commonly used to help lower blood sugar levels in people with type 2 diabetes. Pioglitazone may also be used for other conditions as determined by your healthcare provider. Pioglitazone is not used to treat type 1 diabetes.

EXCIPIENTS PROFILE:

Sr no.	Excipient name	Role
1	Ethyl cellulose	Coating
2	Polyvinyl alcohol	Stabilizer

4. MATERIALS AND METHODS:

4.1 Analytical characterizationof drug sample:

25 mg of drug pioglitazone hcl was dissolved in 0.1 N HCl and volume was make up to 25 ml to make stock solution of concentration 100µg/ml. Then 0.1ml of stock solution was taken and diluted upto 10ml with the buffer of 0.1 N HCl to get concentration of 0.1 µg/ml and in similar way dilutions were made as 0.1, 0.2, 0.3, 0.4, 0.5 µg/ml respectively and absorbance was measured at 268 nm by UV visible spectrophotometer. The absorbance values were plotted against concentration (µg/ml) to obtain the standard calibration curve.

4.2 FT-IR spectroscopy:

Before formulating a drug substance into dosage form, it is essential that it should be chemically and physically compatible. Compatibility studies give information needed to define the nature of the drug substance and provide a frame work for the drug combination with pharmaceutical excipients in the fabrication of a dosage form. This study was carried out by using infrared spectrophotometer to find if there is any possible chemical interaction between the silymarin and polymers.

4.3 Scanning electron microscopy (SEM):

SEM analysis was performed to determine their microscopic characters (shape & morphology) of prepared Pioglitazone hcl nanosponges. Nanosponges were prepared and dried well to remove the moisture content and images were taken using scanning electron microscopy (Hitachi X650, Tokyo, Japan) in different magnifications. Samples were placed on glass slide kept under vacuum and then by using sputter coater unit,samples were coated with a thin gold layer, operated at 15kv acceleration voltage.

4.4 Prepartion of nanosponges:

Two phases were used, one is organic and the other is the aqueous phase. The organic phase, containing drug and polymer mixture in 20 ml DCM and the aqueous phase containing PVA and in 100 ml distilled water. The aqueous phase was added in a dropwise manner in the organic phase on a magnetic stirrer at 5000 rpm. After two hours of stirring, nanosponges were collected by filtration method and dried in an oven at 40 °C for 24 hours. Nanosponges are stored in a vacuum desiccator for removal of moisture.

Table no. 1: Formulation of Nanosponges containing Pioglitazone HCl

Sr No.	Ingredients	F1	F2	F3	F4	F5	F6
1	Pioglitazone HCl (mg)	100	100	100	100	100	100
2	Polyvinyl alcohol (mg)	0.5	0.5	0.5	0.5	0.4	0.4

3	Ethyl cellulose (mg)	0.2	0.3	0.4	0.5	0.3	0.4
5	Dichloromethane (ml)	20	20	20	20	20	20
6	Distilled water (ml)up to	100	100	100	100	100	100

5.4.1 Determination of Percentage Yield

Pioglitazone HCl loaded nanoosponges were weighed after drying. Percentage yield was calculated by:

$$\% \text{ Yield} = \frac{\text{Actual weight of product}}{\text{theortical weight drug and excipients}} \times 100$$

5.4.2 Particle size determination:

The average mean diameter and size distribution of loaded nanosponges is found by Dynamic Light Scattering method using Malvern zeta sizer at 25°c. The dried nanosponges were dispersed in water to obtain proper light scattering intensity for Pioglitazone hcl nanosponges.

5.4.3 Determination of Zeta potential:

Zeta potential is a measure of surface charge. The surface charge (electrophoretic mobility) of nanosponge can be determined by using Zeta sizer (Malvern Instrument) having zeta cells, polycarbonate cell with gold plated electrodes and using water as medium for sample preparation. It is essential for the characterization of stability of the nanosponges.

5.4.4 Determination of Entrapment Efficiency:

The entrapment efficiency of nanosponges were determined by adding 10 ml of 0.1 N HCl and sonicated in a bath sonicator and filtered. 1ml of filtrate is made up to 10 ml with phosphate buffer and was assayed spectrophotometrically at 268 nm (UV visible spectrophotometer, model UV1601 PC, Shimadzu). The amount of entrapped drug was calculated from the equation.

$$\% \text{ DEE} = \frac{\text{actual loading}}{\text{therotical loading}} \times 100$$

5.5 Preparation of Nanosponges loaded capsule:

Pioglitazone HCl nanosponges equivalent to 15 mg were added to the empty hard gelatine capsule shell.

5.6. Evaluation of capsule:

5.6.1 Disintegration test:

The capsules are placed in the basket-rack assembly, which is repeatedly lowered 30 times per minute into a thermostatically controlled bath of fluid at 37 +2°C and observed over the time described in the individual monograph.

5.6.2. Content uniformity test:

This test is performed only when the content is specified in the individual monographs and when capsules fail weight variation test. If the weight of capules is completely filled no need of this test. Unless otherwise stated in the monograph for an individual capsule, the amount of drug substance, determined by assay, is within the range of 85.0% to 115.0% of the label claim for nine (9) of ten (10) dosage units assayed, with no unit outside the range of 75.0% to 125.0% of the labelled drug content. Additional tests are prescribed when two or three dosage units are outside of the desired range but within the stated extremes.

5.6.3. Weight variation test:

20 capsules are selected or taken at randomly and weighed individually, take average and compare each capsule weight with average. Then test passes if none of the individual weights are less than 90% and more than 110% of average. If test requirements are not met we have to remove the powder, net content of powder can be weighed individually. They have to be averaged. Test requirements are met if not more than 2 of the individual's difference is not greater than 10 of average. In any case difference should not be more than or equal to 25%. If more than 2 and less than 6 net weights determined, they deviate 10% Then we go for additional 40 capsules.

5.6.4. Stability testing:

To evaluate stability at different physical and chemical conditions, the optimized nanosponges was subjected to a short-term stability study. The samples were kept in clean, dry, air tight glass vials at condition of storage (refrigerator). The samples were checked for appearance, temperature of gelation, drug content, cumulative % drug release and pH after 30 day

5.6.5. In vitro release studies

In vitro drug release studies of pioglitazone hcl NS formulations were carried out for using an eight station USP dissolution apparatus II. The dissolution studies were carried out in 600 ml of 0.1N HCl for 1. The study was carried out at 37 ± 0.5 °C and 75 rpm. Five ml samples were withdrawn from the dissolution medium at each time intervals, passed through Whatman filter paper (45 µ) and analyzed Spectro photometrically at 268 nm after suitable dilution. The experiment was carried out in triplicate and the mean values were plotted versus time. The results were expressed as percentage of the cumulative amount of drug released as a function of time.

6. Result:

6.1 Preparation of standard calibration curve of Pioglitazone HCl in pH 0.1 N HCl.

Table No. 2: conc vs absorbance of pioglitazone HCl in 0.1 N HCl buffer

Conc in ug/ml	Absorbane
10	0.215
20	0.380

30	0.575
40	0.805
50	1.003

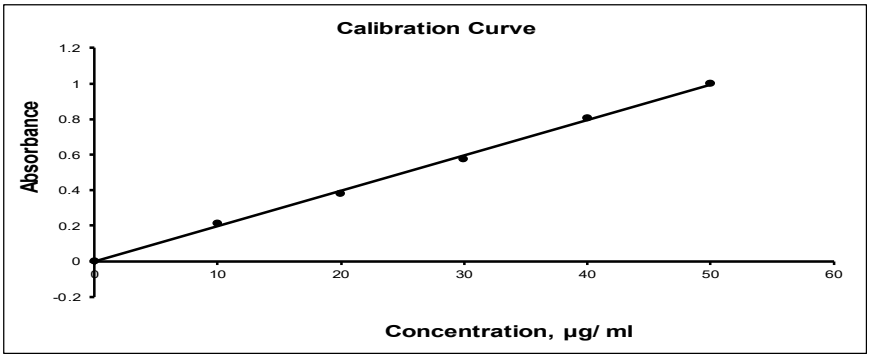
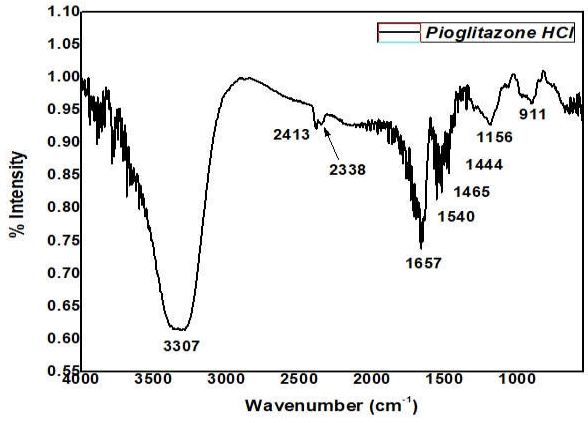


Figure no. 2: Standard calibration curves of Pioglitazone HCl in 0.1N HCl

6.2 Drug – Excipient Interaction Study :

The FTIR studies were performed to observe any interaction between drug and polymers inthe formulation. FTIR study of optimized nanosponges (F5 batch) was carried out. The FTIR spectra of optimized nanosponges were shown in Figure 8. The FTIR spectra indicate that there is no interaction between ethyl cellulose and drug within nanosponges. The spectrum of optimized nanosponges was found to be similar to pure Pioglitazone HCl drug. FT-IR spectra of prepared formulation showed there are significant changes in the fingerprint region i.e. 600 to 1500 cm-1. This confirmed the formation of a bond between ethyl cellulose and pioglitazone HCl. There is a significant change in downshift and upshift in the formulation due to cross linking, seen in a condition such as S-O, and C-N stretching. Thus, it can be concluded that no major chemical interaction is taking place between the drug and carrier.



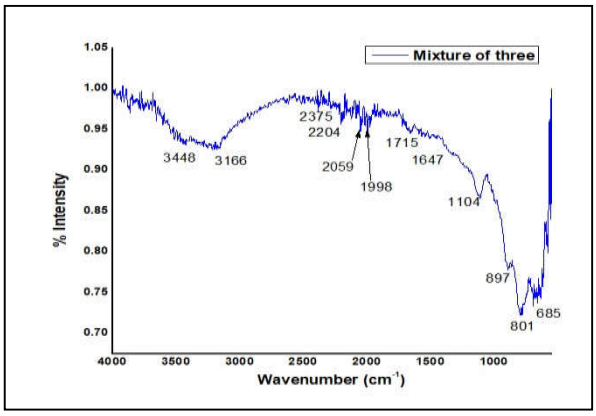


Fig no. 3,4: IR Spectra of Pioglitazone HCl Nanosponges

6.4 Evaluation of nanosponges:

6.4.1. Determination of Percentage Yield:

Table No.3: Percentage Yield

Sr.No	Formulation code	Percentage yield (%)
1	F1	60.0
2	F2	56.0
3	F3	61.0
4	F4	52.0
5	F5	62.0
6	F6	59.0

6.4.2. Content uniformity Nanosponges:

Table No. 4: Content uniformity of Nanosponges.

Sr.no	Formulation code	Percentage yield (%)
1	F1	80.64
2	F2	90.43
3	F3	77.00
4	F4	70.16
5	F5	105.00
6	F6	68.59

6.4.3. Solubility of Nanosponges

Table No. 5: Solubility of Nanosponges

Solubility before Nanosponges	Formulation code	Solubility after Nanosponges
0.029	F1	0.042
	F2	0.046
	F3	0.051
	F4	0.078
	F5	0.183
	F6	0.167

Human taste panel method

To evaluate the taste, a scale with the following numerical value was used to following code:

A= Verry Bitter B=Tasteless

Table No. 5 Sensory evaluation of Nanosponges formulation F1 To

F6

Formulation code	HUMAN VOLOUNTER		
	V1	V2	V3
Pure drug	A	A	A
F1	A	B	B
F2	B	A	A
F3	A	B	A
F4	B	A	B
F5	B	B	B
F6	A	B	B

6.4.4. Scanning electron microscopy (SEM):

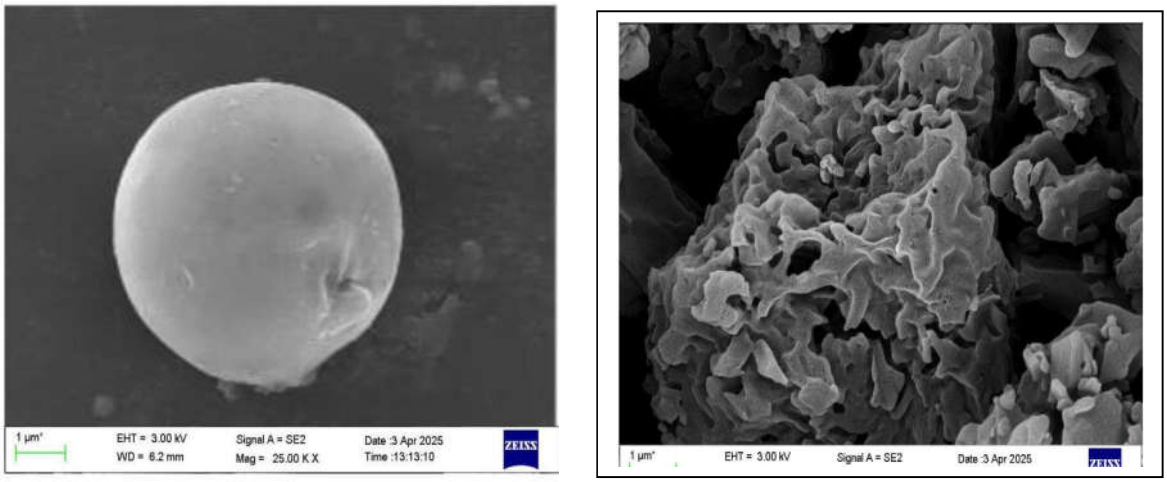


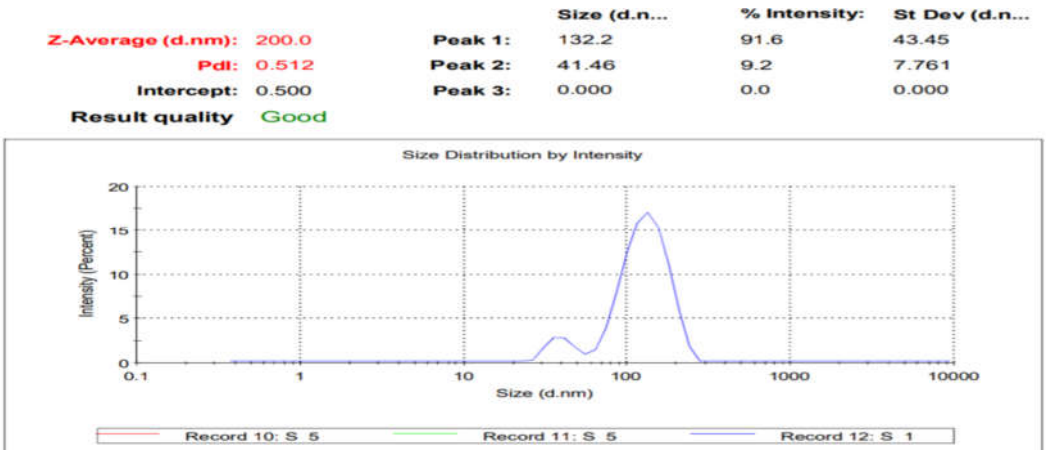
Fig No.5: SEM F5 Batch Result

SEM images showed the nanosponge was porous with a smooth surface morphology and spherical in shape.

6.4.5. Particle size determination.

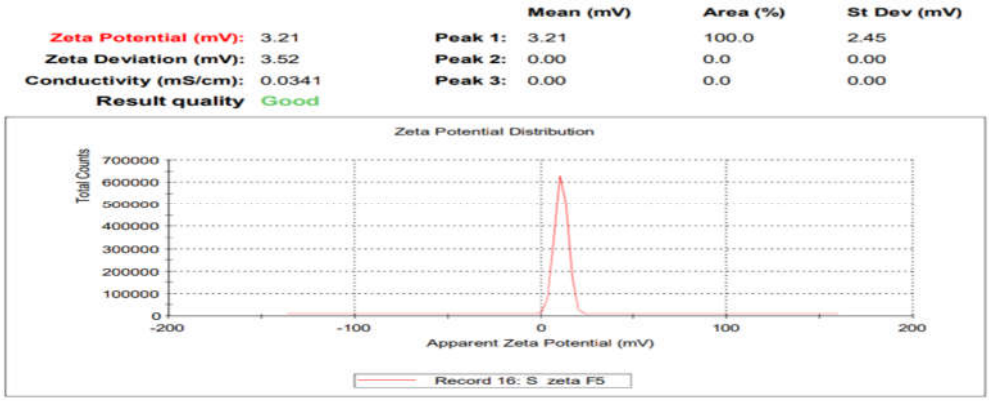
Particle size analysis showed that the average particle size of Pioglitazone HCl nanosponges formulated using ethyl cellulose (F5) was found to be 200.0 nm with polydispersity index (PDI) value 0.512 and with intercept 0.500. The zeta size distribution of ethyl cellulose - Pioglitazone HCl nanosponges is depicted in Figure no.7.

Figure No.7: Zeta size distribution of Pioglitazone HCl nanosponges (F5)



6.4.6. Determination of Zeta potential

For Pioglitazone HCl nanosponges using ethyl cellulose zeta potential was found to be 3.21 mV with peak area of 100% intensity. These values indicate that the formulated Pioglitazone HCl nanosponges (F5) are stable. Zeta potential distribution of Pioglitazone HCl nanosponges prepared using ethyl cellulose is depicted in the Figure 8.



6.4.7. Determination of Entrapment Efficiency

Table No. 6: Entrapment efficiencies of Pioglitazone HCl nanosponges

Sr no	Formulation code	Entrapment Efficiency (%)
1	F1	91.61
2	F2	97.45
3	F3	88.41
4	F4	92.89

5	F5	98.00
6	F6	97.50

6.4.8. Evaluation of Capsule:

6.4.8.1. In vitro release studies:

In vitro drug released of Pioglitazone HCl nanosponges by using dissolution apparatus was carried out. From theresults it was concluded that the initial release rate was very rapid.

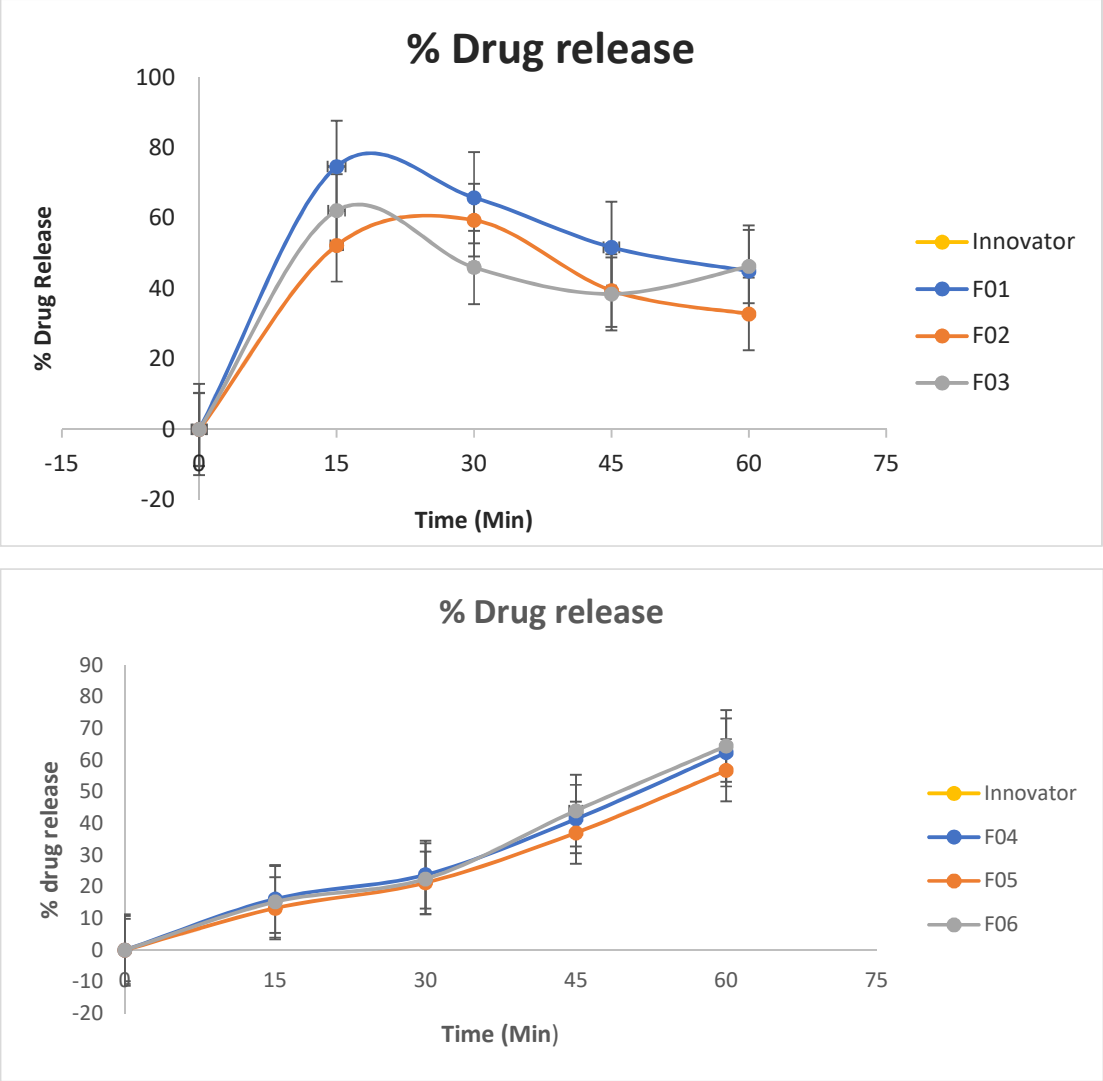


Fig No. 9: In vitro release profile of drug formulation

Table No. 7: In vitro release profile of drug formulation

Time (min)	% Cumulative drug release					
	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
15	74.4±8	53.08±7	62.33±1	28.57±2	78.78±2	52.49±2
30	66.96±9	59.72±6	46.75±9	28.57±2	102±9	52.49±3
45	52.08±2	39.81±3	38.96±4	40±2	42.75±3	26.24±1
60	44.64±8	33.17±4	46.75±4	45.57±2	25.65±1	34.99±4

6.4.8.2. Disintegration test:

Table No. 8. Disintegration table

Sr.no	Disintegration time (Min)
1	6 min
2	7.2 min
3	9.5 min

6.4.8.3. Weight variation test:

Table No.9.Weight variation

Sr.no	Capsule weight variation	Average
1	113.6 mg	
2	116.6 mg	115.7 mg
3	116.3 mg	
4	114.9 mg	
5	117.1 mg	

6.4.8.4. Stability testing:

The following data were recorded as follows to identify the change in optimized formulation (F5). No significant change in drug content was observed hence the formulation was found to be stable at low and high temperature condition.

Table No.10: Stability data for in pioglitazone HCl nanosponges formulation.

Sr. no	Time	Storage condition	Colour	% Drug content
1.	Initial	Room Temperature	White	100%
2.	One month	40^0C	White	100%

7. Summary and Conclusion.

The study successfully developed a nanosponge capsule system using the emulsion solvent diffusion method. Formulation F5 demonstrated the best results, with 98% entrapment efficiency, 105% drug content, and controlled drug release for up to 1 hour. FTIR confirmed minimal drug-polymer interaction, PDI indicated mid-range monodispersity, and a zeta potential of 3.21 mV suggested moderate stability. SEM images validated nanosponge formation.

8. Reference:

1. V Ravi Shankar, Y Dastagiri reddy, G Hanumantha reddy, G Sudheer Kumar reddy, Formulation and in- vitro characterization of sustained release metronidazole cocoa butter suppository, Inventi impact pharm tech, 2012, Vol. 4, 275-280.

2. Subhash Chandra Bose penjuri, Nagaraju ravouru, Saritha damineni, Sailakshmi bns, Srikanth Reddy poreddy, Formulation and Evaluation of Lansoprazole Loaded Nanosponges, Turk J Pharm Sci., 2016, Vol. 13 issue 3, 304-310.

3. Swarupa Arvapally, M. Harini, G. Harshaitha, A. Arun Kumar, Formulation and in-vitro evaluation ofglipizide nanospoges, Am.j. pharma tech res, 2017, Vol. 7 issue 3, 341-361.

4. Anjali S. Kumar, Sheri P.S., M.A.Kuriachan, formulation and evaluation of nanosponge
5. loaded hydrogel for topical delivery, Ijppr, 2018, Vol. 13 issue1, 362-379.

6. Nirosha Manyam, Kishore Kumar Reddy Budideti, Surendra Mogili, Formulation and

in-vitro Evaluation of Nanosponge Loaded Extended Release Tablets of Trimethoprim, UPI Journal of Pharmaceutical, Medical and Health Sciences 2018, Vol.1 issue 1, 78-86.

7. Rahul S, Solunke, Uday R. Borge, Krishna Murthy, Madhuri T. Deshmukh, Rajkumar V. Shete, Formulation and evaluation of gliclazide nanosponges, Int J App Pharm, 2019, Vol 11, Issue 6,181-189.
8. Shrishali M. Ghurghure, Kamalapurkar Ka, Thorat Ys, Pathan Ma, Preapartion and in-vitro evaluation of itraconazole loaded nanosponges for topical drug delivery, Indo american journal of pharmaceutical research, 2019, Vol. 9 issue 4, 1999-2013.
9. Khanderao Rajaram Jadhav, Shivraj Popat jadhav, Deepak Devidas sonawani, Formulation and evaluation of nanosponge based topical gel preparation of fluconazole, Ijppr, 2020, Vol. 19 issue 3, 597-616.
10. Mane P. K, Alookar N. H., Development, characterization and evaluation of nanosponge gel containing flurbiprofen as a now steroidal anti- inflammatory drug, Pharm Res,2021, Vol. 3, issue 2, 80-92.
11. Mohammed Muqtader Ahmed, Farhat Fatima, Md. Khalid Anwer Elmutasim Osman Ibnouf, Mohd Abul Kalam, Aws Alshamsan, Mohammed F. Aldawsari Ahmed Alalaiwe, and Mohammad Javed Ansari, Formulation and in vitro evaluation of topical nanosponge-based gel containing butenafine for the treatment of fungal skin infection, Saudi pharm j, 2021, Vol. 29 issue 5, 467-477.
12. Pushpalatha D, Abdul Waris Khan, Manjunath K and Brunda S, Formulation and evaluation of lovastatin loaded nanosponges, World Journal of Advanced Research and Reviews, 2021, Vol.11 issue 3, 041–056.
13. Shrivansh Srivastava, Alok Mahor, Gyanedra Singh, Kuldeep Bansal, Prem Prakash Singh, Rishikesh Gupta, Rohit Dutt, Amer M Alanazi, Azmat Ali Khan, Prashant Kesharwani, Formulation development, in-vitro and in-vivo evaluation of topical hydrogel formulation of econazole nitrate-loaded β-cyclodextrin nanosponges, J pharma sci, 2021, Vol. 10 issue 11, 3702-3714.
14. Abhishek Soni, Nishant Sharma, Sunaina Rana, formulation and evaluation of luliconazole suppositories for the treatment of candida infection (vulvovaginal candidiasis), Journal of pharma and drug regulatory affairs, 2022, Vol. 4 issue 2, 31-39.
15. Ashish Y Pawar , Khanderao R Jadhav, Sharayu P Rathod , Ashwini S Sanap , Milind J Umekar, Formulation and Evaluation of Nanosponges Loaded Hydrogel of Metformin Hydrochloride, Indian Journal of Pharmaceutical Education and Research , 2023,Vol. 57 Issue 1, 53-61.
16. Dalia A. Gaber, Mahasen A. Radwan, Danah A. Alzughaibi, Jenan A. Alail, Rafa S. Aljumah, Reema M. Aloqla, Sara A. Alkhalifah & Siham A. Abdoun, Formulation and evaluation of Piroxicam nanosponge for improved internal solubility and analgesic activity, Drug Delivery 2023, Vol. 30, NO. 1-10.
17. Sri Charan, K. Kishore, G. Vijay Kumar, Design development and characterization of clotrimazole nanosponges gel, International journal of pharmacy Res. & tech, 2023, Vol.13 issue 2, 2250-0944.
18. Chetana Kapadne, Sourabh Birari, Vishal Gulecha, Anita Shinde, Aishwarya Sambare

and Sanjay Kshirsagar, Formulation and Evaluation of Budesonide-loaded Nanosponges for Colon-specific Drug Delivery Systems, BIOI 2024, Vol. 5 issue 19,1-12.

19. Priya Kumari, Navneet Kumar Upadhyay, Rahul Varma, Shivam Kumar, Laxmi Gharti , Hemlata Kaurav, Formulation and evaluation of famotidine-loaded nanosponges for the treatment of peptic ulcer: and evaluation, Journal of Applied Pharmaceutical Science,2025, Vol. 15 issue 3,260-269.