**Bulletin of Environment, Pharmacology and Life Sciences**
Bull. Env. Pharmacol. Life Sci., Vol 10 [5] April 2021 : 60-71
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Online ISSN 2277-1808
Journal's URL:http://www.bepls.com
CODEN: BEPLAD

**ORIGINAL ARTICLE** **OPEN ACCESS**

# Formulation and Evaluation Of Microspheres Loaded with Fenofibrate

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**ABSTRACT**
*The primary objective of the expressed research was to create and test microspheres loaded with Fenofibrate with HPMC K100 M & Pectin polymers. Fenofibrate microspheres were developed utilizing an ionotropic gelation process employing sodium alginate as a crosslinking agent. Designed Fenofibrate microspheres have been characterised for micrometric characteristics, morphology, drug entrapment performance, In vitro drug release, drug and polymer interaction studies such as Fourier Transform Infrared Spectroscopy (FTIR) & Differential Calorimetric Scanning (DSC), X-ray Difference Analysis & Stability Study.The Fenofibrate microsphere having entrapment efficiency ranged from 87% to 98%. The percentage yield of microspheres ranged from 95-99 %. FTIR spectra of Fenofibrate shows that there is no interaction between drug & polymer ratio in the ideal formulation of A4. The stability study was carried out for F4Formulation at 42 ± 2˚C/ 78± 5%. The result obtained in this work demonstrate the use of HPMC K100 M & Pectin polymers for preparation of Fenofibrate microspheres.*
*Keywords:* Fenofibrate, HPMC, Pectin, Mucoadhesive microspheres, Ionic gelation method

Received 23.02.2021 Revised 11.03.2021 Accepted 09.04.2021

## INTRODUCTION

Orally employed drug delivery systems such as mucoadhesive microspheres drug delivery systems are employed to enhance the accommodation period at the site of absorption or application. The micro particles contributes to retain plasma levels over a prolonged period of time there by significantly reducing the medication rate and to lessen the variations in the plasma drug levels at tested and reproductive way by distributing the medication. Bio adhesive micro particles become adhesive on hydration and hence can be located on a fixed target location for a long-term action on gastrointestinal tract (GIT). Administration, no compliance with patients, and versatility in the composition are also simple. The strengths of bio adhesive microphones are
effective absorption, increased medication bioavailability, full drug availability, much more intimate intestinal cell touch, better adherence with patient and an emphasis on clear absorption Site.[1,2,4]
The development of the latest drug delivery system to prolong resistance at an application site and bioavailability was an important topic in the microsphere. In establishing a regulated or sustainable medication distribution system, micro particles have played a significant role. The multiparticulate medication framework for microsphere delivery enhances sustainability and patient enforcement. A new medicinal delivery method was developed with a view to extending the resistance at the site of application and bioavailability is a microsphere. In designing managed or continuous drug provision systems, microspheres played a significant role. A multiparticulate framework for the administration of medication, facilitating continuous action and strengthening patient compliance. [3,4,5]
Fenofibrate is employed in the diagnosis of elevated blood cholesterol and triglycerides. It is also known as antilipemic and fibric acid, which helps the body, extract triglycerides by breaking off grapes.[7, 8]
Fenofibrate is a lipid regulation agent and is a derivative of chemical fibric acid. Fenofibrate is a B.C.S. Type II lipophilic medication with low aqueous solubility. A fenofibric acid drug associated with an isopropyl ester. Therapeutic effects of the fenophibrate are experienced by stimulating the active receptor (PPARα) peroxisome proliferation. This improves lipolysis and the removal of rich plasma particles from triglycerides. The resulting decrease in triglycerides contributes to the alteration of LDL size and compound from tiny, compact particles to larger floating particles. Lipo-lipase activating and decreasing apoprotein development CIII, Due to the decrease in triglycerides, the size and composition of LDLs from tiny, compact particles into large, floating particles are altered. These large particles have a

higher cholesterol affinity, receptor and rapid catabolism. This work was therefore aimed at formulating the fenofibrate microsphere to increase the GIT dose residence, reduce the dose frequency, and improve bio disposability.[7,8,9]

## MATERIAL AND METHODS

Fenofibrate was obtained from Mankind Pharma Ltd, New Delhi, India. HPMC (K100M), Pectin, methanol & calcium chloride were procured from chemical store at Rajgad Dnyanpeeth's College of pharmacy, Bhor, Pune, (India). All chemicals used in the study were of analytical grade & used without further purification.

### Preparation of Microspheres:

The micro particles were formulated by ionic gelation technique. It has been referred as an important method employed in the preparation of microspheres. The HPMC K100 M and pectin solution were dissolved in deionized water employing mild heat at (50°C) with the continuous magnetic stirring. So stirring it constantly then viscous dispersion is developed. To this dispersion, fenofibrate (150 mg) were incorporated and sonicated for 28-30 minutes. The subsequent dispersion was then transferred to the calcium chloride solution (5-10 % w/v) stirring at 100 rpm in a 20 gage hypodermic needle fitted with a 10 ml syringe. Stirring proceeded for one hour to complete the healing of the reaction and to develop the spherical microspheres. Shaped microspheres have been filtered & washed regularly with water to eliminate excess calcium chloride. Deposited on the surface of the microsphere. Then the microspheres were dried at $50^{o}$ under vacuum.[9,10]

**Table 1.Formula and composition with process variables**

| Formulation Code | Amount of Fenofibrate (mg) | Amount of polymer (HPMC K100 + Pectin) (g) | Crosslinking agent ($CaCl_2$) (%) | Distilled water (ml) |
|---|---|---|---|---|
| **A1** | 150 | 1.0 | 5% | 100 |
| **A2** | 150 | 1.5 | 5% | 100 |
| **A3** | 150 | 2.0 | 5% | 100 |
| **A4** | 150 | 1.0 | 7.5% | 100 |
| **A5** | 150 | 1.5 | 7.5% | 100 |
| **A6** | 150 | 2.0 | 7.5% | 100 |
| **A7** | 150 | 1.0 | 10% | 100 |
| **A8** | 150 | 1.5 | 10% | 100 |
| **A9** | 150 | 2.0 | 10% | 100 |

### Experimental Design:

Formula optimizations were performed by $3^2$ factorial designs employing a design expert (Version 9.2; Stat-Ease Inc., Minneapolis, Minnesota, USA) for mathematical modeling and response analysis. The optimum level of the variables was calculated by $3^2$ factorial designs, including the center point. Important factors mentioned were the intensity of HPMC K100 and the cross-linker concentration testing 9 runs.

### Variables for experimental designs:

Independent variable
X1 = concentration of polymer
X2 = cross-linking agent
Dependent variable
Y1 = Particle size
Y2 = Entrapment efficiency
Y3 = t% release

### Evaluation of microspheres:

### Preformulation studies:

Preformulation investigations have described the physical and chemical characteristics of the drug molecule in order to provide a safe, efficient and stable dosage form.

### Physical Appearance:

Physical characteristics of all formulations were tested for color, solubility, homogeneity and consistency. The melting point of the drug was assessed by the use of the melting point apparatus.

### Bulk Characterization:[12,13]

Evaluation of microspheres studied by determining bulk density, tapped density, Carr's index Hausner's ratio, & angle of repose. The properties were determining the following equations,

Bulk density= mass / bulk volume
Tap density= mass/ tapped volume
Carr's index= (Tap density – bulk density / Tap density) × 100

Hausner's ratio= Tapped density/ Bulk density
Angle of repose= Tan ɵ= h/r ---Equation 5

**Process Yield:**[17,19]

Dried microspheres were accurately weighed, and considering the total amount of drug and polymers used for preparing the feed solution, the process yield was calculated, a using following formula.
Entrapment efficiency= Estimated % drug content/ Theorotical % drug content × 100

**Entrapment Efficiency(%):**[14,15]

100 mg of microspheres were powdered & suspended in phosphate buffer solution (pH 6.8). The solution was kept overnight & filtered through whatmann filter 0.45 µm. Drug content was determined by UV-visible spectrophotometer at 290 nm. The percentage entrapment was calculated by following formula,
Encapsulation efficiency = (Actual drug content / Theoretical drug content) × 100

**UV analysis of fenofibrate:[**17,18]

The concentration of Fenofibrate in the samples determined by the UV spectrophotometer (JASCO V-530). A solution of Fenofibrate in methanol gives maximum absorbance at λmax of 286 nm.

**Fourier transforms infrared spectroscopy (FTIR) studies:**[11,12]

In FTIR study mostly potassium bromide pellet method are used. Samples were thoroughly blended with potassium bromide crystals. The mixture was compressed to make a disc. Then this disc was placed in spectrophotometer & spectra of pure drug & drug excipients combination were recorded. Then FTIR spectra of samples were compared with FTIR spectra of pure drug & excipients.

**Differential scanning calorimetric analysis (DSC):**[16,19]

Warm lead of unalterated A.P.I. and fenofibrate microspheres were considered utilizing differential scanning calorimeter (Schimadzu DSC 60) at warming rate of 10˚C/min. Immidiately 5 mg tests were correctly weighed into aluminium dish & after that fixed. The etimtion were performed at a warming extent of 50-400˚C under scrub nitrogen atmosphere.

***In vitro* dissolution:**[23,24,25]

It was done completed utilized USP paddle typeII contraption at 37˚C±5˚C & rotational speed of breaking down gadget was kept in100 rpm. Test in 5ml of sample were withdrawn at predetermined time interval upto 6 hrs& replaced with 5 ml of dissolution media pH 6.8 + 1% S.L.S The absorbance was estimated by UV spectrometry at wavelength of 290 nm & the drug content was resolved.

**Morphology of microspehers: [20, 32]**

The external and internal morphology of the microspheres were studied using scanning electron microscopy in Pune University (Physics Department). The sample was loaded on copper sample holder and sputter coated with platinum.

**Stability Studies:**

The stability study was finished for Fenofibrate definition as indicated by ICH rules. Fenofibrate microspheres definition was fixed in high thickness polyethylene bottles & set away at 40 ±2˚C/75±5% RH in shut for good. The examples were evaluated for capture proficiency for a time of 3 months.

## RESULTS AND DISCUSSION

**Preformulation study:**

**Description:**

The fenofibrate sample was found to be white in colour and odourless solid.

**Solubility:**

The solubility study of Fenofibrate sample can be seen in the following table.

**Table 2. Solubility study of Fenofibrate**

| Solvent | Solubility |
|---|---|
| Methanol | Slightly soluble |
| Ethanol | Slightly soluble |
| Water | Practically insoluble |
| Ether | Soluble |
| Acetone | Soluble |
| Benzene | Soluble |
| Chloroform | Soluble |

**Melting Point:**

The melting point of fenofibrate was found to be 80-81℃.

**Bulk Characterization:**
The bulk density & tapped density was observed to be within the range 0.5 to 0.61 & 0.54 to 0.72. The formulation $A_4$ showed the compressibility index of

**Table 3. Bulk characterization of evaluation of microspheres.**

| Formulation Code | Bulk density | Tapped density | Carr's index | Hausner's ratio |
|---|---|---|---|---|
| A1 | 0.61 | 0.69 | 11.59 | 1.131 |
| A2 | 0.69 | 0.73 | 5.47 | 1.057 |
| A3 | 0.62 | 0.71 | 12.67 | 1.145 |
| A4 | 0.54 | 0.68 | 20.58 | 1.259 |
| A5 | 0.6 | 0.75 | 20 | 1.25 |
| A6 | 0.5 | 0.52 | 3.84 | 1.04 |
| A7 | 0.62 | 0.71 | 12.67 | 1.145 |
| A8 | 0.59 | 0.63 | 6.34 | 1.067 |
| A9 | 0.61 | 0.69 | 11.59 | 1.131 |

**Percentage Yield:**
The highest percentile gain was found of $A_4$ batch & was observed to be 99 percent amongst all the batches. The percentage yield of micro particles has been displayed in table.

**Table 4. Percentage yields**

| Formulation Code | %Yield |
|---|---|
| A1 | 97 |
| A2 | 96 |
| A3 | 94 |
| A4 | 99 |
| A5 | 98 |
| A6 | 97 |
| A7 | 98 |
| A8 | 99 |
| A9 | 95 |

**Entrapment efficiency of Microspheres:**
A rise in the ratio of micro particles encapsulation with an improvement in the concentrations of HPMC & Pectin was found, which may be attributable to an improved lipophilic & hydrophilic ambience that could accommodate more amount of drugs. The 1:2 ratio of HPMC & Pectin was included in the formulation of the micro particles on the basis that this ratio is particularly useful for successful drug encapsulation.

**Table 5. Entrapment efficacy**

| Formulation Code | Entrapment efficacy (%) |
|---|---|
| A1 | 87 |
| A2 | 90.81 |
| A3 | 97.53 |
| A4 | 98.31 |
| A5 | 95.93 |
| A6 | 96.25 |
| A7 | 93.49 |
| A8 | 86.36 |
| A9 | 91.17 |

**Calibration Curve of Fenofibrate:**
10 mg of Fenofibrate was precisely weighed &mixed in methanol in 100 ml of volumetric flask. Sonicated for to form 1000 µg/ml.From the stock solution 1 ml was pipetted out & volume was made upto with 100 ml of methanol which is having the concentration 10 µg/ml. at that point arrangement stock solution concentration of 2 µg/ml - 10 µg/ml.
The absorbance of these arrangement was measured against the methanol as clear at 286 nm using UV-visible double beam spectrophotometer. At that point calibration curve was estimated taking concentration in µg/ml on X axis & absorbance on Y axis.

The linearity of alignment curve was found to be in the scope of 2-10 µg/ml. The regression coefficient value ($R^2$) of 0.9989 was taken note.

**Table 6. Calibration curve of fenofibrate**

| Sr. No. | Concentration (µg/ml) | Absorbance |
|---|---|---|
| **1** | **2** | 0.1721 |
| **2** | **4** | 0.2835 |
| **3** | **6** | 0.4091 |
| **4** | **8** | 0.5412 |
| **5** | **10** | 0.6666 |

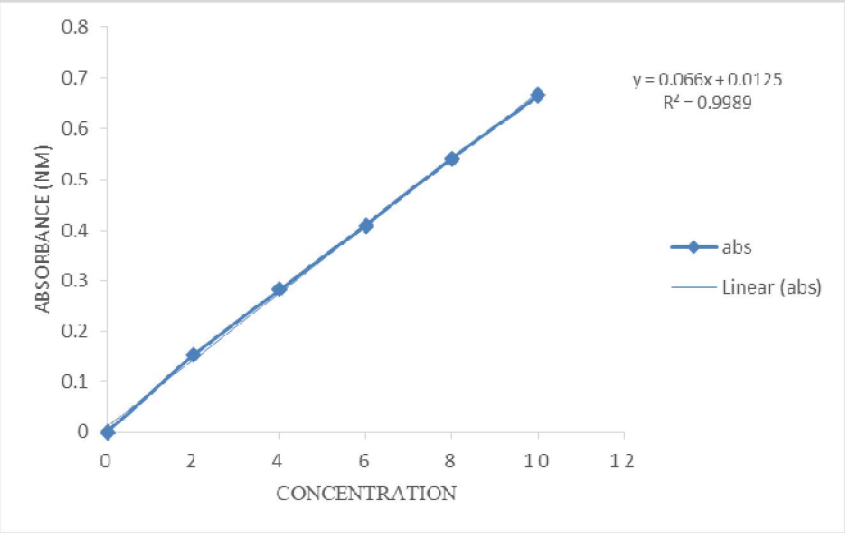


**Fig. 1. Calibration curve of Fenofibrate**

**Compatibility study**

**Fourier transforms infrared spectroscopy (FTIR)**

FTIR spectral data were used to confirm the chemical stability of Fenofibrate in the formulation of microspheres. The FTIR spectra of pure fenofibrate, FTIR spectra of HPMC K100, FTIR spectra of the physical mixture of HPMC K100, pectin and fenofibrate are shown in Fig. 2, 3 and 4 respectively.

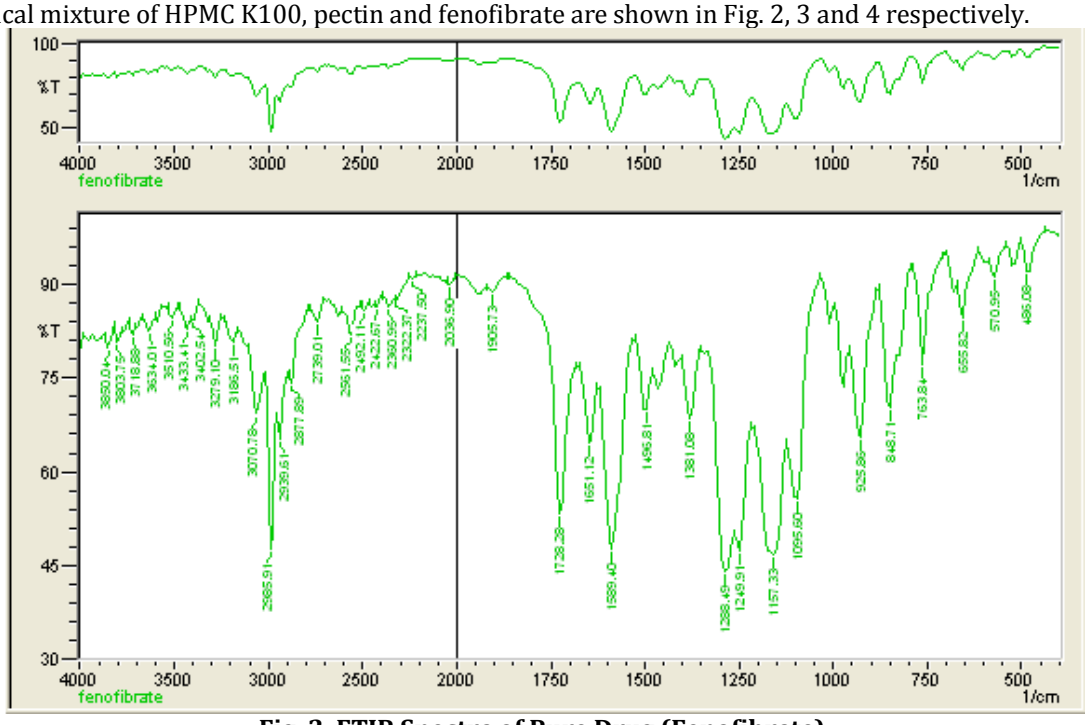


**Fig. 2. FTIR Spectra of Pure Drug (Fenofibrate)**

**Table 7: FTIR Spectrum analysis of Fenofibrate**

| Sr.No | Peak Value(cm-1) | Indication |
|---|---|---|
| 1 | 1651 | -C=C- aromatic stretching vib. Frequency. |
| 2 | 1590 | -C=O stretching vibration frequency. |
| 3 | 1496 | -C-O stretching vibration frequency. |
| | 1728 | -C=O ester stretching vibration frequency. |
| 4 | 1390 | Methyl -CH3 bending vibration frequency. |
| 5 | 763 | -C-Cl stretching vibration frequency. |

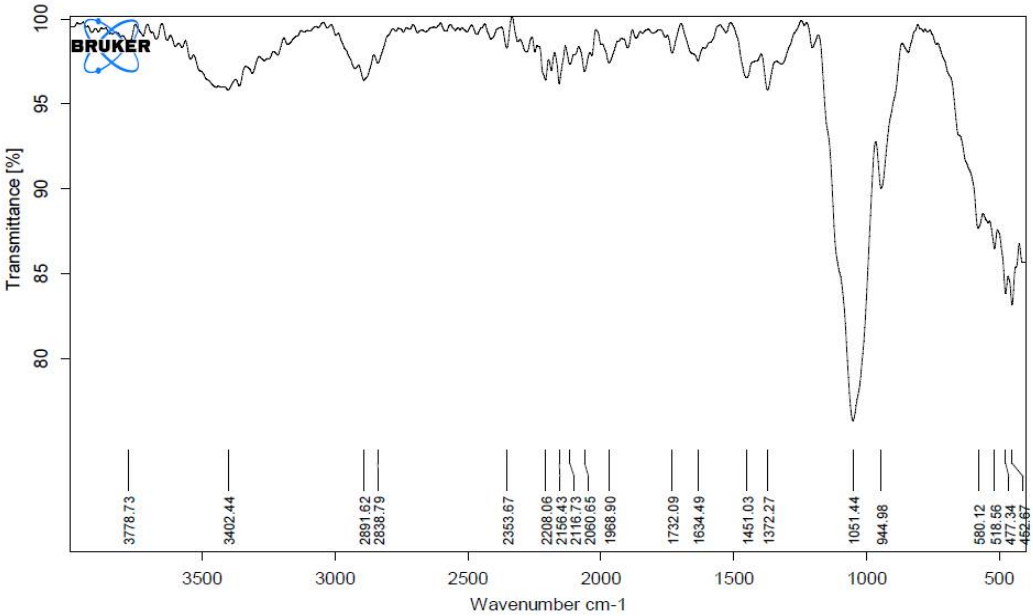


**Fig. 3. FTIR Spectra of HPMC K100M**

**Table 8: FTIR Spectrum analysis of HPMC K100 M**

| Sr. No. | Peak Value(cm-1) | Indication |
|---|---|---|
| **1** | **1051** | -strong vibration frequency for Glucose ring |
| **2** | **1462** | -C-H absorption frequency of cellulose. |
| **3** | **3500** | -OH stretching vibration frequency. |

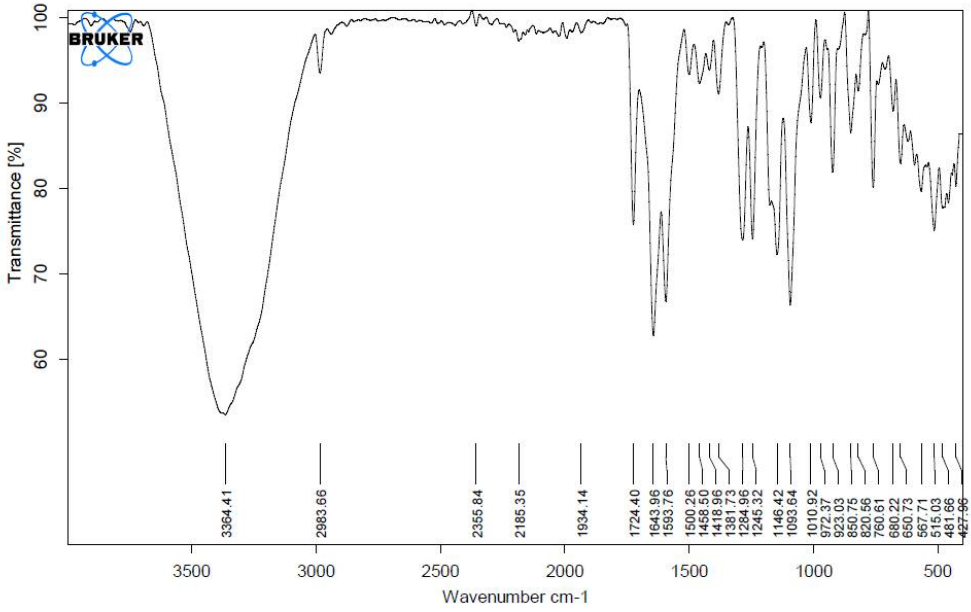


**Fig. 5. FTIR Spectra of Microspheres of Fenofibrate**

**Table 9: FTIR Spectrum Microspheres of Fenofibrate**

| Sr.No | Peak Value(cm-1) | Indication |
|---|---|---|
| 1 | 1651 | -C=C- aromatic stretching vib. Frequency. |
| 2 | 1590 | -C=O stretching vibration frequency. |
| 3 | 1496 | -C-O stretching vibration frequency. |
| | 1728 | -C=O ester stretching vibration frequency. |
| 4 | 1390 | Methyl -CH3 bending vibration frequency. |
| 5 | 763 | -C-Cl stretching vibration frequency. |
| 6 | 1051 | -strong vibration frequency for Glucose ring |
| 7 | 1462 | -C-H absorption frequency of cellulose. |

**Differential Scanning calorimetric analysis (DSC)**

The DSC studies carried out to observe the thermal behavior of drug-loaded Microspheres whether the drug was encapsulated in them or not. The characteristic endothermic peak of Fenofibrate pure drug is appeared at 80.60 °C which was within a range of melting point. Similarly, as for HPMC K100 M peak appeared at 191°C which was within a range of melting point of HPMC K100 M. For sodium alginate the peak was at 252°C. For Pectin the peak was at 147°C. Thermo-gram of the drug and polymer that also shows the thermal stability of the drug. A characteristic peak change in DSC thermo-gram confirmed that Fenofibrate had experienced chemical interaction and had been entrapped into the Microspheres. This explains the molecular Encapsulation of Fenofibrate in the matrix of the polymer used in formulation.

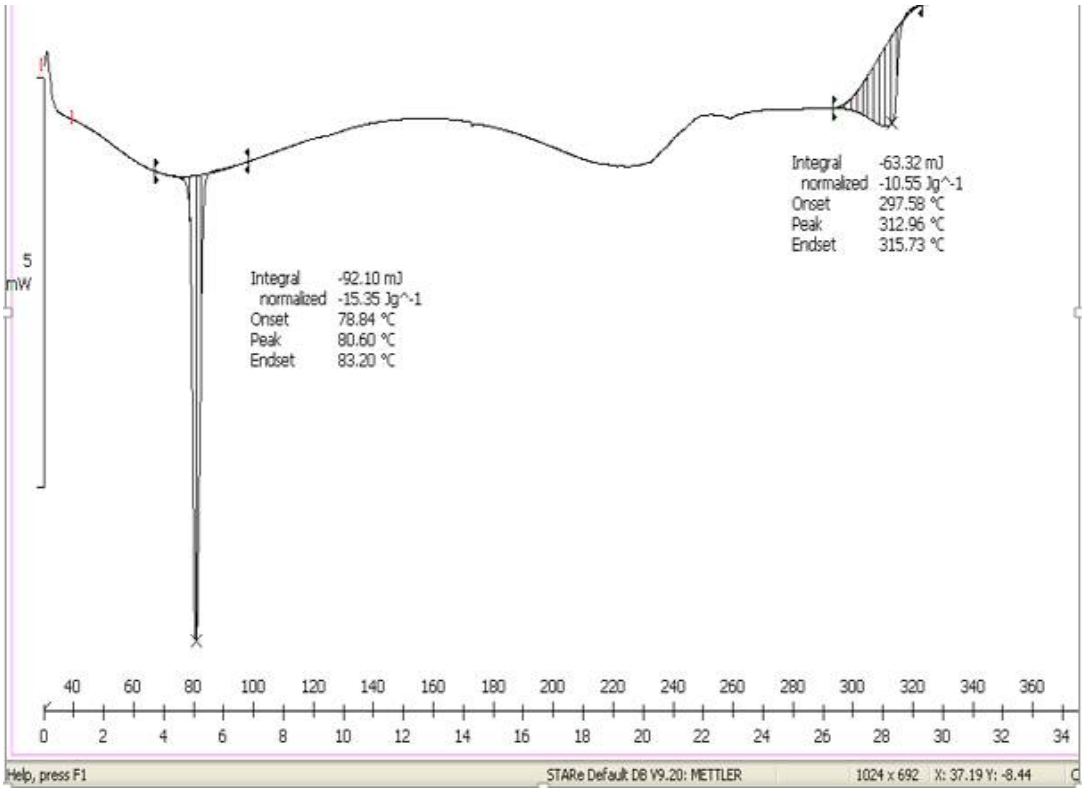


**Fig. 5. DSC analysis of Pure Drug (Fenofibrate)**

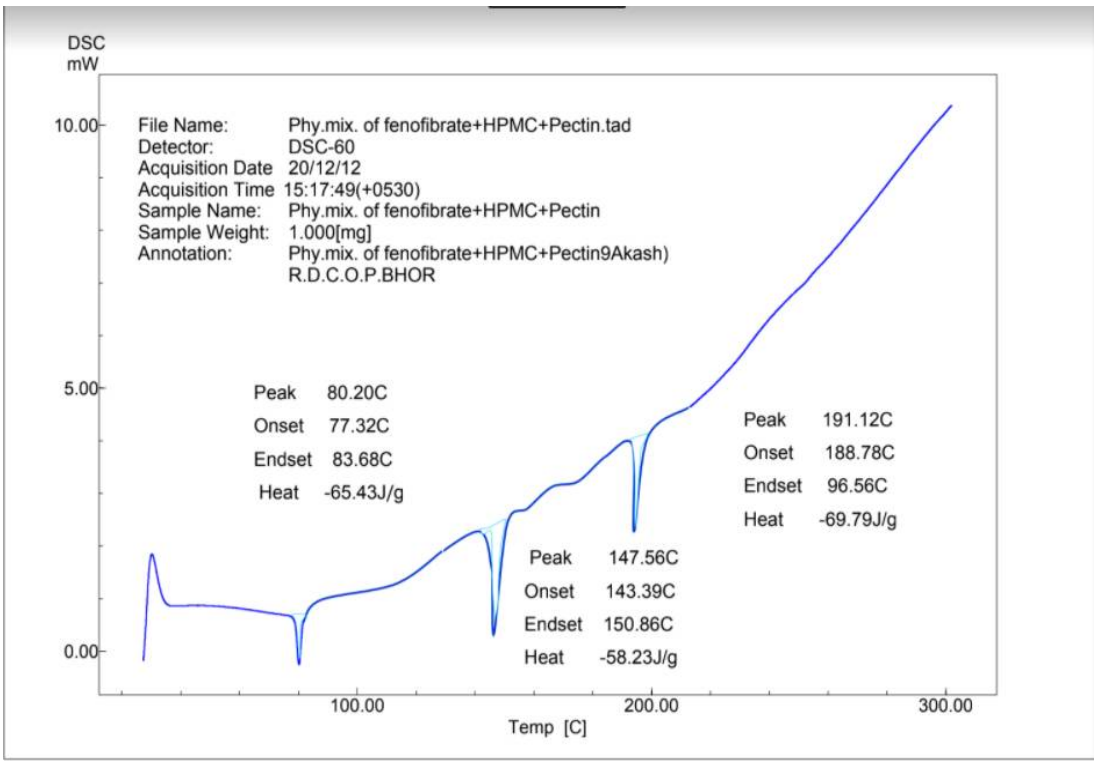


**Fig. 6. DSC analysis of Physical mixture of Pure drug, HPMC K100 & Pectin**

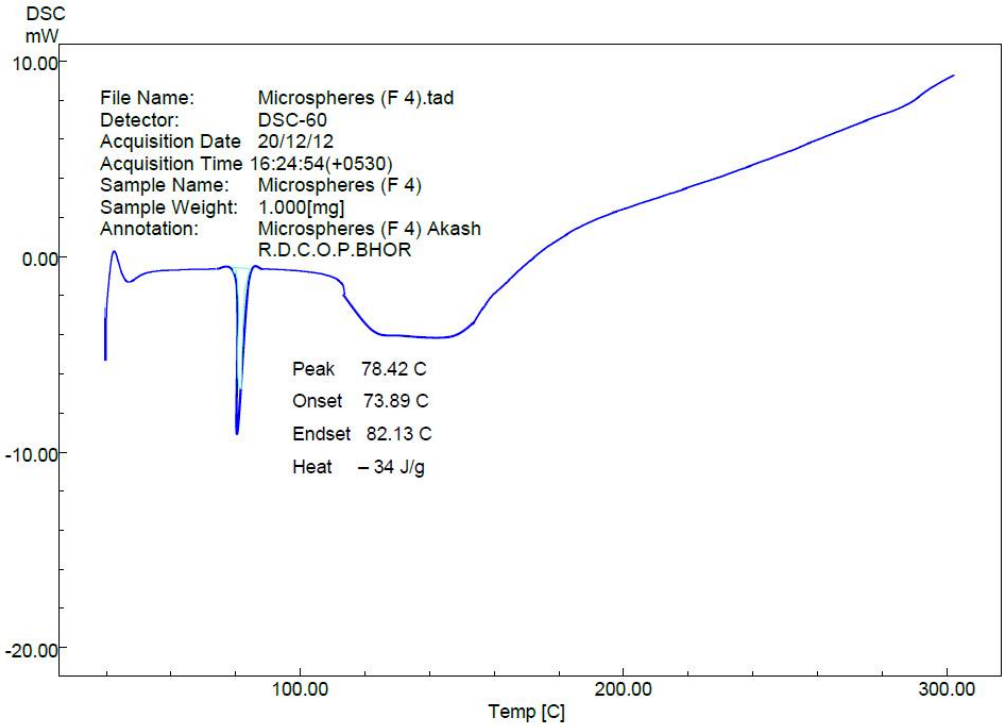


**Fig. 7. DSC analysis of Microspheres of Pure drug (fenofibrate)**

## X-Ray diffraction study (XRD)

The X-ray differentactogram of Fenofibrate displayed a sharp peak illustrating a standard crystalline pattern. The decreased peak shows the conversion of the drug into an amorphous shape. The physical mixture also displayed a less extreme peak. The microparticles of fenofibrate displayed a peak, but a low strength.

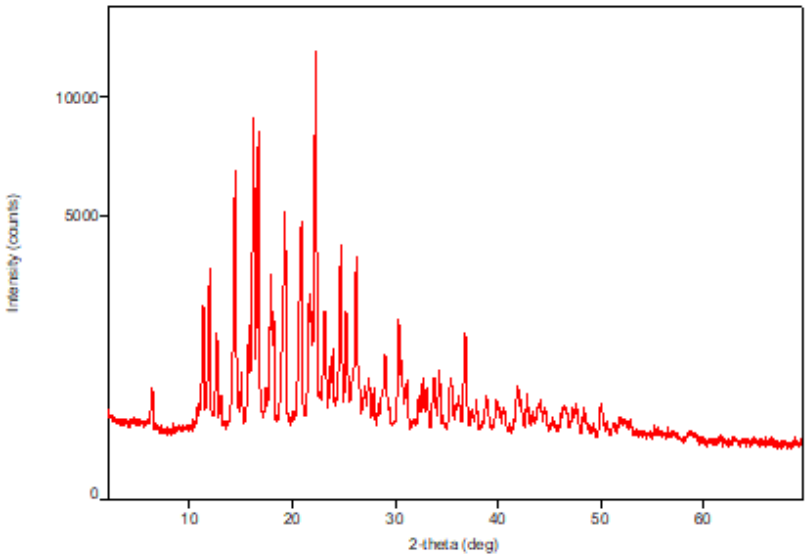


**Fig. 8. XRD of Pure drug (Fenofibrate)**

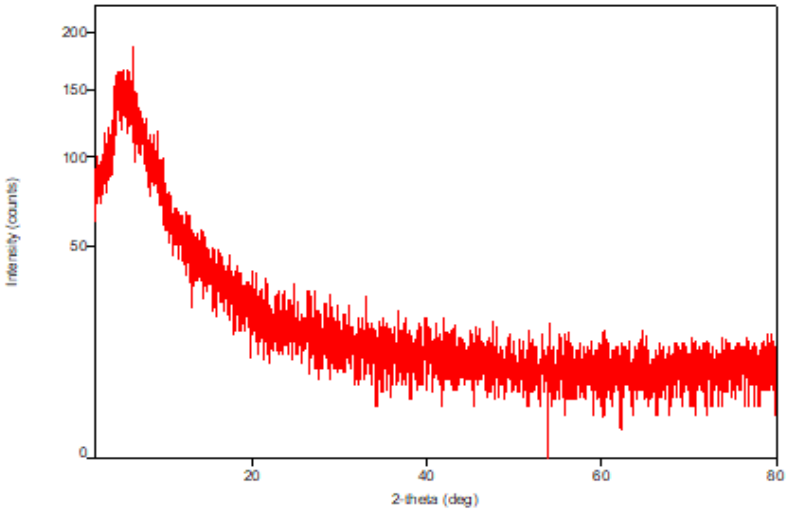


**Fig. 9. XRD of Microspheres of Fenofibrate**

**Scanning electron microscopy:**

The internal and external Morphology of of optimized batch was examined by S. E. M. SEM photographs of optimize formulation $F_4$microspheres were rough nonspherical & shows smooth surface.

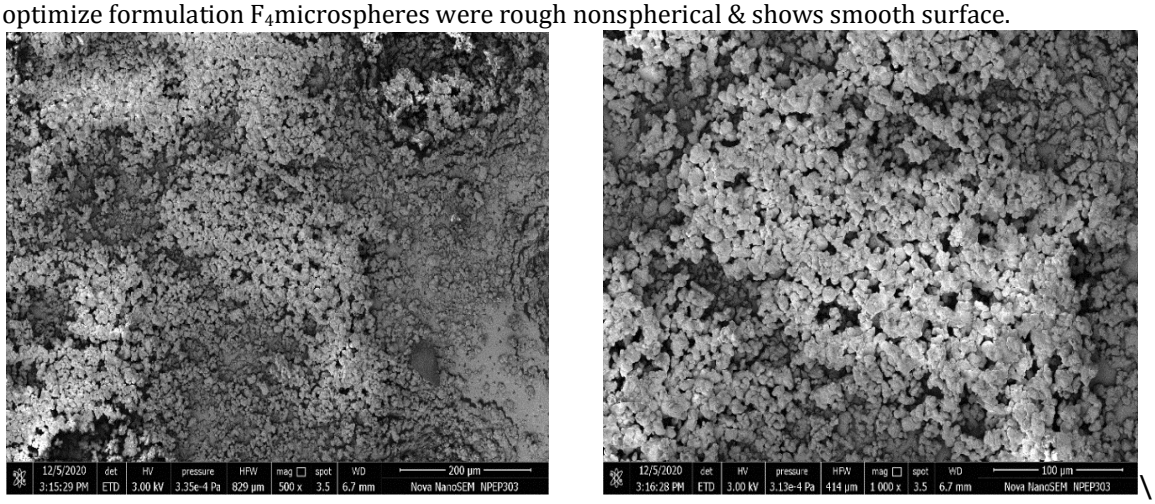


**Fig. 10. SEM of Pure drug (Fenofibrate)**

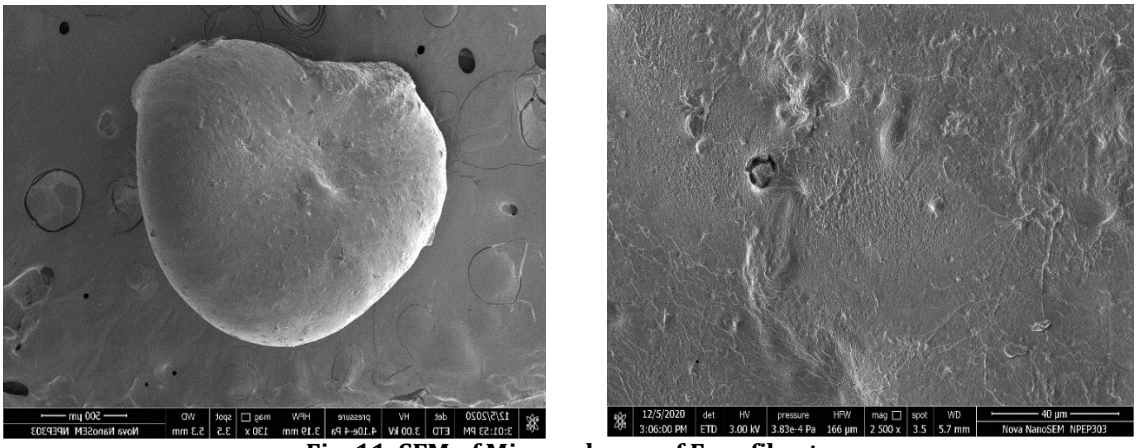

**Fig. 11. SEM of Microspheres of Fenofibrate**

***In vitro* release of fenofibrate microspheres**

The outcomes of the *In vitro* release are displayed in the figure. The research was conducted for pure drug formulations among all F4 batch formulations, there was a strong dissolution pattern with 91.08 percent of drug release in 6 hours. It is also believed to be the best formulation of the microparticles of fenofibrate.

**Table 10. *In vitro* release of fenofibrate microspheres**

| Sr. No. | Time (hr) | 0 | 0.5 | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|---|---|---|
| 1 | **A1** | 0 | 5.93% | 27.24% | 42.52% | 50.8% | 63.27% | 74.14% | 83.05% |
| 2 | **A2** | 0 | 5.51% | 24.4% | 38.48% | 50.46% | 61.89% | 72.98% | 77.5% |
| 3 | **A3** | 0 | 6.87% | 22.19% | 35.68% | 46.37% | 57.93% | 70.47% | 83.96% |
| 4 | **A4** | 0 | 7.09% | 24.12% | 43.74% | 56.91% | 69.00% | 86.21% | 91.8% |
| 5 | **A5** | 0 | 7.84% | 17.69% | 33.95% | 50.64% | 62.08% | 72.29% | 80.96% |
| 6 | **A6** | 0 | 5.85% | 26.34% | 40.69% | 53.57% | 66.68% | 79.23% | 88.84% |
| 7 | **A7** | 0 | 6.68% | 14.06% | 32.69% | 46.57% | 62.76% | 79.23% | 88.84% |
| 8 | **A8** | 0 | 4.15% | 23.18% | 35.58% | 43.60% | 52.77% | 62.76% | 74.47% |
| 9 | **A9** | 0 | 8.38% | 14.58% | 28.07% | 39.75% | 49.27% | 64.16% | 71.40% |

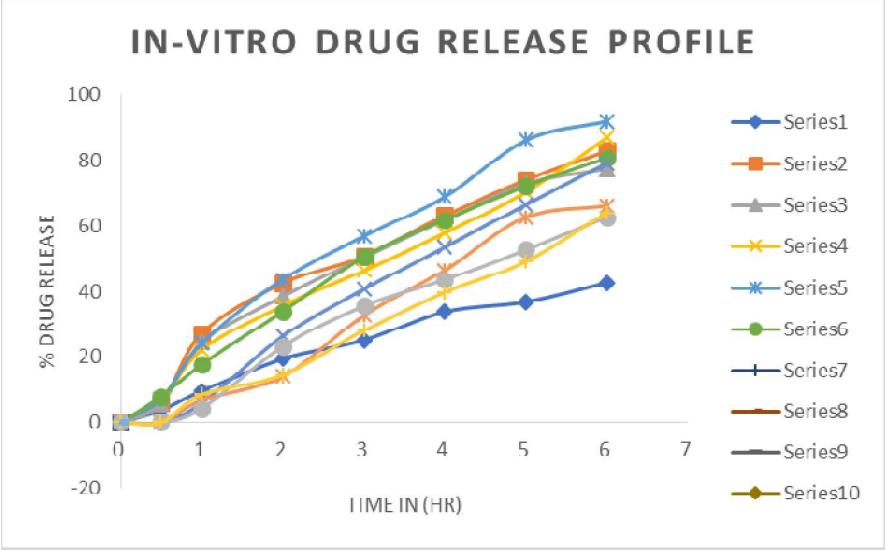


**Fig. 12. Dissolution profile of Microspheres of Fenofibrate**

**Stability study**

Physical description revealed no noticeable variance and color change. Formulation was preserved at a temperature of 40 ± 2 °C and a moisture content of 75 ± 5 per cent for 3 months. After taking and evaluating samples at one month intervals, this formulation was observed to be consistent under the above circumstances.

**Table 11. Stability study of fenofibrate**

| Sr. No. | Duration | Drug Content (%) | *In vitro* dissolution (%) |
|---|---|---|---|
| 1 | 0 Day | 98.31 | 91 |
| 2 | 1 Month | 96 | 89 |
| 3 | 2 Month | 94 | 88 |
| 4 | 3 Month | 93 | 85 |

## CONCLUSION

The bioavailability of the medication can be improved by the preparation of microspheres. Microspheres are becoming increasingly essential for water-soluble drugs. The goal of the present investigation was to improve the micro-particles of fenofibrate to promote solubility and dissolution. Microspheres have been developed utilizing an ionic gel process. HPMC K100M and pectin had an important effect on the effectiveness of drug trapping and medication release. Optimized batch was found to be A4 due to its release profile of action, product yield ability and good drug quality.

## REFERENCES


1. Navneet KV, Gulzar A, Vishwakarma DK, Mishra JN, Wajahat UK, Abhay PS and Asha R: (2015). Recent Advances in Microspheres Technology for Drug Delivery. International Journal of Pharmaceutical Sciences and Nanotechnology ; 8(2): 2799-2813.
2. Stephen OMand Cynthia CU: (2017). Formulation of Domperidone Microspheres Using a Combination of Locally Extracted Chitosan and Hpmc as Polymers. Journal of Chemical Engineering; 11: 65-74.
3. Ramteke KH, Jadhav VB, Dhole SN: (2012). Microspheres: as carriers used for novel drug delivery system. IOSR Journal of Pharmacy; 2(4): 44-48.
4. Sajeev C, Archna R, Gupta V, Sobti A, Saha RN: (2003). Formulation and Evaluation of Parenteral Sustained Release Microspheres of Diclofenac Sodium. Scientia Pharmaceutica ; 71: 101-111.
5. Sarlesh R, Preeti A, Ashish P, Nikhil S, Satyendra, Singh B, Rajendra SR: (2012). A Review on Microspheres: Methods of Preparation and Evaluation. World Journal of Pharmacy and Pharmaceutical Sciences; 1(1): 422-438.
6. Vidya P, Sujith A, (2015). Approaches used for enhancing the bioavailability of Acyclovir: A critical review. International Journal of Institutional pharmacy and life sciences; 5(4): 265-281.
7. Mohsin K, Vaseem AA, Poonam K, Arun K, Juber A: (2015). Mucoadhesive microspeheres for controlled delivery of drugs; 8(4): 17-20.
8. Harsh B, Simar PK, Atul KG, (2011). Microsphere: Methods of preparation and applications; A comparative study. International Journal of Pharmaceutical Sciences Review and Research; 10(1): 69-78.
9. Vishal NG, Gowda DV, Balamuralidhara V and Khan MS: (2013). Preparation and Comparative Bioavailability Studies of Indomethacin- Loaded Cetyl Alcohol Microspheres. Journal of Pharmaceutics; 109837: 1-9.
10. Karan R, Nikhil S. Sahajpal, KS, Harmanpreet S, Harjeet S &Subheet KJ: (2019). Formulation of sustained release microspheres of cefixime with enhanced oral bioavailability and antibacterial potential. Therapeutic Delivery 20-27.
11. Prashant P, Santosh S and Janardhan S: (2018). Praparation and Evaluation of Microspheres of Flurbiprofen. International Journal of Pharmaceutical Sciences and Research; 9(12): 5388-5393.
12. Cheng YZ, Jin YW, Jin H, Guo HH, Yan YJ, Xiang RZ and Dong L: (2019). Preparation and evaluation of gastro-floating hollow adhesive microspheres of carbomer/ethyl cellulose encapsulating dipyridamole. Royal Society of Chemistry.pp89
13. Rahul PG, (2019). Formulation and Evaluation Sustained Release Floating Multi-Particulate. Acta Scientific Pharmaceutical Sciences; 3(5): 128-141.
14. Ankita M, Arti M, Neelesh M: (2018). Formulation and evaluation of chitosan microspheres for the topical delivery of itraconazole. Journal of Pharmacy Research; 12(6): 890-894.
15. Ye Z and Hongming L: (2016). Development of Bioadhesive Microspheres for Oral Bioavailability Enhancement of Berberine Hydrochloride. International Journal of Polymer Science; 4235832: 1-7.
16. Arul B, Kothai R, Sangmeshwaran B and Jayakar B:(2003). Formulation and Evaluation of Chitosan Microspheres. Indian Journal of Pharmaceutical Sciences; 640-642.,
17. Keyur SP, Mandev BP: (2014). Preparation and evaluation of chitosan microspheres containing nicorandil. 4(1): 32-37.
18. Bhavya R, Amit C, Upendra N:(2012).Formulation Development and Evaluation of Aceclofenac Chitosan Microspheres. Journal of Advanced Pharmacy Education & Research; 2(4): 215-220.
19. Meghana KJ, Ashok KP, Suresh VK, Manjunath K: (2019). Formulation and *In vitro* Evaluation of Floating Microspheres of Anti Diabetic Drug. International Journal of Pharma Research and Health Sciences; 7(3): 3007-3012.
20. Munde MR, Anantwar SP, Salunke SS, Sangale B: (2019). Formulation and Characterization of Sustained Release Microspheres of Nitrofurantoin. International Journal of Scientific Research and Reviews; 8(3): 01-09.
21. Mr. Kapil KP, Dr. Navneet G: (2019). Formulation and evaluation of floating microspheres of losartan potassium using sodium alginate and HPMC by solvent evaporation method. Journal of Drug Delivery and Therapeutics ; 9(1-s): 60-66.

*22.* Muthadi RR, SoumyaS: (2019). Design and *In vitro* Characterization of Flutrimazole Microspheres Loaded Topical Emulgel. Asian Journal of Pharmaceutical and Clinical Research; 12(9): 242-251.

*23.* Maina C, ChundawatAV and Chauhan CS: (2017). Development and Characterization of Floating Microspheres of Esomeprazole Magnesium Trihydrate by Solvent Evaporation Method. International Journal of Pharmaceutical Sciences and Research ; 8(2): 686-697.

24. Paroma A, Ikramul H and Selim Reza MD: (2016). Design, characterization and *In vitro* evaluation of HPMC K100 M CR loaded Fexofenadine HCl microspheres. Springer plus; 5-691: 1-11.

25. Syed AA, Syed MP, Omair SA, Omer W, Mohammed M, Mohammed AA, Mohammed AA, Aiyaz A, Syed SB: (2019). Formulation and in vitro evaluation of oral extended release microspheres of aceclofenac using various natural polymers. International Journal of Research in Pharmaceutical Sciences and Technology: 1(2): 58-66.

26. Alalor CA, Agbamu E, Okafo SE: (2018). Evaluation of Mucoadhesive Microspheres of Metronidazole Formulated Using Ionic Gelation Technique. Scholars Academic Journal of Pharmacy; 7(12): 480-487.

27. Dewi MH, Tristiana E, Vita FR: (2019). Experimental Design Approach in Erythropoietin-alginate Microsphere Preparation with Different Concentrations of Drug and Polymer. Journal of Reports in Pharmaceutical Sciences ; 8(1): 78-84.

28. Megha S, Seema K, Agnimitra D: (2015). *In vitro* and In-vivo evaluation of repaglinide loaded floating microspheres prepared from different viscosity grades of HPMC polymer. Saudi Pharmaceutical Journal; 1-8.

29. Phalguna Y, Venkateshwarlu BS, Ganesh KD, Subal D: HPMC Microspheres of zidovudine for sustained release. International Journal of Pharmacy and Pharmaceutical Sciences 2010; 2(4): 41-43.

30. Mulugeta F, Anteneh B and Tsige GM: Formulation of Sustained Release Floating Microspheres of Furosemide from Ethylcellulose and Hydroxypropyl Methylcellulose Polymer Blends. Journal of Nanomedicine & Nanotechnology 2015; 6(1): 1000262.

31. Navid JA, Ikramul H, Md. Shfiqul I and Md. Selim R: Preparation and Characterization of Gliclazide Incorporated Cellulosic Microspheres: Studies on Drug Release, Compatibility and Micromeritics 2014.

32. Surendranath B, Mohan MV, Abbulu K: (2017). Formulation and Evaluation of Sustained Release Microspheres of Metoprolol. International Research Journal of Pharmacy; 8(11): 103-108.

33. Navneet G and Akanksha G: (2012). Preparation and *In vitro* Evaluation of Metformin Microspheres Using Non-Aqueous Solvent Evaporation Technique. Tropical Journal of Pharmaceutical Research; 11 (4): 577-583.,

34. Abdul H, Arun M, Jagpal S, Lakhan R: (2013). *In- vitro* evaluation of floating microspheres of Ketoprofen. Journal of Scientific and Innovative Research ; 2 (3): 714-722.

35. Baby HD, Varsha MG: (2009). Preparation and characterization of mucoadhesive microparticles of sumatriptan succinate for intranasal delivery. Journal of Pharmacy Research 2(9): 1536-1539.

36. Madhuri TD, Shrinivas KM: (2017). Formulation and Characterization of Olanzepine-Loaded Muco-Adhesive Microspheres. Asian Journal of Pharmaceutical and Clinical Research; 10(4): 1-7.

37. Ramya SB and Krishna SA: (2015). Preparation and Evaluation of Floating Microspheres of Omeprazole Microspehers by Solvent Evaporation Method. International Journal of Basic and Applied Sciences ; 5(3): 67-78.

38. Ilaveni PS, Padmapriya, Rajalakshmi AN: (2018).Formulation and evaluation of Mucoadhesive Microspheres of An Anti-Migraine Drug. Journal of drug delivery and Therapeutics ; 8(5): 465-474.

39. Veena SB,Sanjay JS: (2010). Design and Development of Oral Mucoadhesive Multiparticulate System Containing Atenolol: *In vitro*–in Vivo Characterization. Pharmaceutical Society of Japan ; 58(9): 1168-1175.

40. Sreegiri SP, Gupta VM, Devanna N, Jayasurya K: (2014). Microspheres as Drug Delivery Systems. Journal of Global Trends in Pharmaceutical Sciences ; 5(3): 1961-1972.

41. Alagusundaram M, Madhu SC, Umashankari K, Attuluri VB, Lavanya C and Ramkanth S: (2009). Microspheres as a novel drug delivery systems – A Review. International Journal of Chem. Tech. Research; 1(3): 526-534.



**CITATION OF THIS ARTICLE**

A.M. Jadhav, M.T. Deshmukh, A. N. Khopade, S. V. Kilje, R.V. Shete. Formulation and Evaluation of Microspheres Loaded with Fenofibrate. Bull. Env.Pharmacol. Life Sci., Vol10[5] April 2021 : 62-71