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Formulation and Evaluation of Sustained Release Microspheres of Fexofenadine Hydrochloride by Ionotropic Gelation Method

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Abstract: ***This research paper is based on the formulation and evaluation of sustained release polymericmicrospheres of the second-generation,anti-histaminic drug Fexofenadine Hydrochloride. Though fexofenadine hydrochloride is an effective and safer option compared to other antihistaminic drugs available in the market still it is not commonly used in the treatment of seasonal allergic rhinitis due to its less bioavailability and higher cost. The aim of this research was to formulate a novel, effective, efficient and safe drug delivery system for Fexofenadine HCL so that this drug can be made more efficient and cost-effective. The ionotropic gelation method was applied to formulate the microsphere formulations, where sodium alginate, HPMC and pectin were used (in different combinations and ratios) as polymers and calcium chloride was used as a crosslinking agent. Total 6 formulations (FX-1 to FX-6) were formulated and evaluated. Among all the formulations prepared FX-3 was selected as the optimized and final formulation based on the evaluation of all the important parameters. In the final formulation drug: polymer ratio was 1:7 and sodium alginate and HPMC were used as polymers in 1:1 ratio.***

Keywords: Fexofenadine Hydrochloride, Microspheres, Ionotropic gelation, Sodium Alginate, HPMC

1. Introduction

Traditional forms of medication like tablets and capsules can result in significant changes in the amount of drug in the bloodstream. Patients need to remember when to take their medication to avoid these fluctuations. Sometimes, patients may accidentally miss a dose, which prevents the drug from reaching an effective level in the bloodstream. Additionally, traditional forms of medication can lead to unwanted side effects or ineffective treatment. These forms also require more frequent dosing, making it harder for patients to stick to their treatment plan. To ensure the desired effect of the medication, it is important to maintain the appropriate level of the drug in the bloodstream. The development of oral extended-release drug delivery systems, which is a comparatively very novel idea, is driven by the need to reduce the number of times a patient has to take a drug and the uncertainty in how the drug is absorbed.

Recently, new methods of drug delivery have become more popular, replacing traditional dosage forms. Sustained and Controlled release formulations have become very widely used methods in recent years. Sustained release systems work by releasing the drug at a steady rate over time, ensuring consistent levels of the drug in the bloodstream. This helps reduce the risk of side effects and improves patient adherence to the treatment plan.

Microspheres have become valuable tools for controlled or sustained drug delivery in various medical applications. Compared to traditional delivery systems, biodegradable microspheres offer several advantages. Unlike conventional systems where drugs are quickly released and their effects diminish within a short period, biodegradable polymers enable sustained release over an extended duration. This eliminates the need for frequent doses and ensures controlled drug delivery for up to 7 days or more. The utilization of degradable microspheres helps minimize potential toxicity concerns, although it does result in the production of byproducts that must be well-tolerated without causing adverse reactions.

Microspheres are an innovative method of delivering drugs, either through sustained release or controlled release. These microspheres are made up of biodegradable or synthetic polymers and have particle sizes of 100 to 1000µm. They are also known as microparticles and have a powdery consistency.

Polymeric microspheres can be classified mainly into two types.

- **Biodegradable polymeric microspheres:**

Polymers derived from natural sources, such as starch, are utilized based on their inherent biodegradability, biocompatibility, and bioadhesive properties. These biodegradable polymers exhibit a prolonged residence time upon contact with mucous membranes due to their significant swelling capacity in aqueous environments, resulting in gel formation. The amount of polymer plays a crucial role in governing both the release rate and extent of total drug release, ensuring sustained release patterns. Despite their numerous advantages, one of the primary challenges associated with the clinical use of biodegradable microspheres is achieving efficient drug loading and controlling drug release. However, these microspheres offer multiple applications in various treatments.

- **Synthetic polymeric microspheres:**

Microspheres which are made up of synthetic polymers have gained significant popularity in clinical applications and are commonly employed as bulking agents, fillers, embolic particles, and drug delivery vehicles. These microspheres have demonstrated their safety and biocompatibility. However, it is important to note that their main drawback lies in their tendency to migrate away from the injection site,

which poses potential risks such as embolism and subsequent organ damage.

There are different methods available for the preparation of polymeric microsphere such as Spray drying technique, double emulsion technique, single emulsion technique, solvent evaporation technique, ionotropic gelation technique gelation and Phase separation coacervation technique. Among these techniques, ionotropic gelation technique is selected for this microsphere formulation.

Fexofenadine Hydrochloride is the hydrochloride salt form of Fexofenadine, which is a carboxylate metabolite derived from terfenadine. It belongs to the second generation of selective, long-acting histamine H1 receptor antagonists, possessing antihistaminic properties. When administered, fexofenadine competitively binds to peripheral H1 receptors located in the gastrointestinal tract (GI), blood vessels, and bronchial smooth muscles. This binding hinders the attachment of histamine to peripheral H1 receptors, thereby preventing their activation and subsequent allergic reactions caused by histamine. Another added advantage of fexofenadine is it does not penetrate the blood-brain barrier (BBB).

Fexofenadine alleviates all the symptoms of allergic reactions in the body by counteracting the effects causes by the histamine.Due to its prolonged duration of action (around 24 hours), fexofenadine can be administered once or twice daily, providing convenience for patients. Additionally, its fast absorption results in a quick onset of action within 1-3 hours.

2. Literature Review

1) **Suzanne G Meeves** et al: (The Journals of Allergy and clinical immunology/Vol.112(4), S69-S77, October 2003/) This literature demonstrates the anti-allergic characteristics of fexofenadine, classified as a second-generation antihistamine. Histamine induces pro-inflammatory responses, that can further promote the long-lasting progression of allergic inflammation. Fexofenadine effectively inhibits peripheral H1-receptors, reducing allergic inflammatory reactions mediated by mast cells, basophils, epithelial cells, eosinophils, and lymphocytes. Alongside its antihistaminergic effects, fexofenadine also diminishes the release and activity of inflammatory mediators, contributing to its unique pharmacological profile. Fexofenadine exhibits exceptional safety, non-sedating effect, even at high doses. Its selectivity for H1-receptors as well as its noninteractive character with muscarinic receptors provides significant advantages over newly used second-generation antihistamines. Further exploration of fexofenadine's anti-allergic effects is underway, with ongoing research in allergic-mediated diseases.
2) **Peter H. Howarth** et al: (The Journals of Allergy and clinical immunology/Vol.104(5), P927-933, November 1999/) This study compared the effectiveness and safety of fexofenadine HCL at quantities of 120 and 180 mg daily, along with cetirizine at 10 mg once daily, versus placebo for seasonal allergic rhinitis. Both fexofenadine HCl doses showed superior effectiveness in reducing symptoms compared to the placebo, with sustained efficacy throughout the 24-hour dosing interval. No significant differences were observed between the fexofenadine HCl doses or between fexofenadine HCl and cetirizine. Fexofenadine HCl had minimal side effects, with lower effects of drowsiness compared to cetirizine. So daily one dose of fexofenadine HCl is a better option for seasonal allergic rhinitis treatment.
3) **James Halliday Day** et al: (Annals of Allergy, Asthma & Immunology/Vol.79(6), P533-540, December 1997/) This study investigated the efficacy of different doses of fexofenadine HCl in providing relief to ragweed-sensitive subjects. One hundred forty-six subjects were primed with ragweed pollen and 99 subjects were randomized to receive placebo or 120mg of fexofenadine HCl daily after 1 hour of ragweed exposure. The study found that both doses of fexofenadine provided relief faster than placebo, with a median time to onset of 60 minutes. The proportion of subjects with relief was 82% at 60 mg, 85% at 120 mg, and 64% for placebo. The study concluded that fexofenadine is a safe and effective option in terms of daily doses of 60 mg or 120 mg.
4) **David I Bernstein** et al: (Annals of Allergy, Asthma & Immunology/ Vol.79(5), P443-448, November 1997/) In a 14-day trial, patients with moderate to severe ragweed seasonal allergic rhinitis were given fexofenadine HCl at different doses or a placebo. The study found that all doses of fexofenadine HCl provided significant improvement in symptoms compared to placebo. Any kind of dose-related negative trends or sedation symptom was detected. It was concluded that fexofenadine HCl is a very safe and effective drug for the treatment of seasonal allergic rhinitis caused by ragweed or similar kind of allergens, and the optimal therapeutic dosage is 60 mg twice a day.
5) **Paroma Arefin** et al: (International Journal of Applied Pharmaceutics/Vol 14, Issue 1,2022/) The article discusses the use of Fexofenadine HCl, a commonly recommended antihistamine drug, in the treatment of allergic rhinitis. While intranasal corticosteroids are more effective, antihistamines are considered safer globally. However, antihistamines have limitations such as longer onset of action. Allergen immunotherapy is an option for disease modification, but it has its own challenges. Fexofenadine HCl is often formulated as sustained-release tablets or capsules to improve convenience for patients. Microspheres, which are small particles containing the drug, can enhance dosage efficiency and minimize side effects. By using Fexofenadine HCl-loaded polymeric microspheres, the absorption profile and bioavailability of the drug can be improved. This approach also reduces the risk of dose bursts and allows for individualized dosing based on the patient's needs. Using microspheres can lower the amount of drugs required and reduce production costs, making medications more affordable for patients. By balancing the polymer content, the long half-life of Fexofenadine HCl can be maintained while increasing its absorption. Ultimately, this can lead to a lower total dose and higher bioavailability. The goal is to provide

effective treatment for allergic rhinitis while minimizing side effects and improving cost-effectiveness.

6) **Paroma Arefin** et al:(Springerplus/Vol 5,691/May 2016/) While there are existing extended-release matrix tablets of Fexofenadine HCl on the market, microspheres offer distinct advantages in terms of drug distribution and dose stability. Matrix tablets release the drug gradually through a matrix system, but the distribution of the drug within the tablet may not always be uniform. This non-uniform drug distribution can lead to dose dumping, where a large amount of the drug is released at once, potentially causing adverse effects or reduced efficacy.

On the other hand, microspheres provide a more consistent drug distribution throughout the formulation. These small spherical particles encapsulate the drug, allowing for controlled release over an extended period. The drug is uniformly dispersed within the microspheres, ensuring a more predictable and controlled release profile. This improved drug distribution minimizes the risk of dose dumping and enhances the overall efficacy and safety of the medication.

Physiochemical Properties of Fexofenadine Hydrochloride:

IUPAC name: 2-[4-[1-hydroxy-4-[4-[hydroxy(diphenyl)methyl]piperidin-1-yl]butyl]phenyl]-2-methylpropanoic acid.

Solubility profile: It is partially soluble in water and freely soluble in Ethanol and Methanol.

Melting point: 191^{o} Celsius

Physical appearance: White crystalline powder.

3. Materials and Methods

Ingredients: Fexofenadine HCL received from Lupin Ltd, India as a gift sample. Sodium alginate, HPMC, Pectin and Calcium chloride were procured from ipca laboratories Ltd, India.

Instruments Used:

Hot air oven (Servewell instruments), Magnetic stirrer (Remi), U.V spectrophotometer (Shimadzu), Dissolution apparatus (EFFEM Technologies), Electronic weighing balance (EFFEM Technologies), Fourier-transform infrared spectrophotometer (PerKinElmer).

Preparation of Fexofenadine Microspheres:

These are the following steps done for the preparation of microsphere.

The Fexofenadine HCL microspheres were prepared with the help of the ionotropic gelation method. In this process, a measured amount of Fexofenadine HCL was taken and diluted in 5 ml of ethanol and shaken it so that the drug solubilize properly. Polymers mentioned in Table 5 were added to a 100 ml of distilled water and mixed properly, then the Crud drug solution (Fexofenadine HCL and Ethanol) was added to it and further mixed with the help of a magnetic stirrer. The resulting solution was then taken into a syringe and extruded drop by drop using the syringe and needle into a 100 ml calcium chloride aqueous solution, while stirring at 100 rpm. After stirring for 10 minutes, the microspheres obtained were washed properly with distilled water, dried at 60 degrees Celsius for 2 hours in a hot air oven, and stored in a suitable airtight container.[1]

Table 1: Composition of Formulations

Formulation Code	Drug: Polymer	Polymer: polymer	Fexofenadine HCL	Sodium Alginate (P1)	HPMC (P2)	Pectin (P3)
FX1	1:10	-	180mg	1800mg	-	-
FX2	1:7	-	180mg	1260mg	-	-
FX3	1:7	P1 : P2 =1:1	180mg	630mg	630mg	-
FX4	1:7	P1 : P2 =1:2	180mg	420mg	840mg	-
FX5	1:7	P1 : P3 =1:1	180mg	630mg	-	630mg
FX6	1:7	P1 : P3 =1:2	180mg	420mg	-	840mg

Evaluation of microspheres:

1) Percentage yield:

All the dried microsphere formulations were weighted one by one and then the % yield of the microsphere formulations was calculated with the help of the formula mentioned below.

$$\% \text{ Yield} = \frac{\text{Total weight of microspheres}}{\text{Total weight of drug and polymer used to prepare the formulation}} \times 100 \quad [2]$$

2) Drug entrapment efficiency:

100 mg Microspheres were taken and crushed properly with the help of a mortar pestle. The crushed residue of the microsphere was then dissolved in 10 ml of methyl alcohol and the volume of the solution adjusted up to 100 ml by adding 6.8 phosphate buffer. The solution was then sonicated for 20 minutes and left to stand overnight for 24 hours to extract the API out of the microspheres. After 24 hours the remaining solution was filtered using Whatman filter paper. 1 ml filtrated solution was then taken out and diluted to 10 ml with 6.8 phosphate buffer solution. The absorbance of the solution was then measured at 259 nm with the help of a UV spectrophotometer, with 6.8 phosphate buffer as the blank.

Drug entrapment efficiency = (Actual drug content/Theoretical drug content) x 100[2]

3) Swelling index:
The swelling capacity of microspheres in physiological media was evaluated by immersing 50 mg of accurately weighed microspheres in an excess amount of 6.8 phosphate buffer. The swelling index was then calculated with the help of the following formula:

Swelling ratio (SR) = (We - W0) / W0
Where,
W0 = Total weight of microspheres before swelling
We = Total weight of microspheres after swelling.[2]

4) Particle Size analysis:
The particles were visually observed with an optical microscope and their size was analyzed with the help of a stage micrometer scale. The microspheres were placed upon a glass slide, and the size of the microsphere was noted, then the mean size of the microspheres was obtained after analyzing the particle size of total 50 microspheres carefully measured by a calibrated ocular micrometer. [2]

5) IR spectroscopy (Drug compatibility studies):
Infrared spectroscopy is a technique that focuses on the infrared region of the electromagnetic spectrum. FTIR (Fourier Transform Infrared) spectroscopy is a valuable tool for identifying both organic and inorganic chemicals by analyzing the types of chemical bonds present, known as functional groups. To assess the drug and polymer compatibility, FTIR spectroscopy was performed. The FTIR spectroscopy reports of Fexofenadine HCL and final formulation (FX-3) were obtained using the KBr dice method with the FTIR instrument by Shimadzu, Japan. The characteristic peak wave numbers of the drug and polymers in the mixture were compared to determine their compatibility.

6) In-vitro drug release study:
In vitro dissolution studies were conducted using a USP Type II Basket-type tablet dissolution test apparatus. A weighed amount of drug-loaded microspheres, equivalent to 100 mg of the drug, was filled into a capsule and placed in the basket. The dissolution medium used was phosphate buffer with a pH of 6.8, maintained at a temperature of 37°C ± 10°C and a rotation speed of 50 RPM.[2]At a 60-minute of time interval, 5 ml of solution was taken out, and an equal volume of fresh 6.8 phosphate buffer was added to maintain a sink condition. Then, 1 ml of each sample was taken out and diluted with 6.8 phosphate buffer to make a 5 ml of solution. The concentration of the drug present in the samples was analyzed spectroscopically at 259 nm.

7) Drug release kinetics mechanism:
Various kinetic models were used to analyze the drug release data collected from the dissolution test conducted with all the fexofenadine HCL microsphere formulations prepared. The analyzed models are like Zero order release kinetics (Eq.1), First order release kinetics (Eq.2), Higuchi's square root of time model (Eq.3), Korsemeyer and Peppas model (Eq.4), and Hixson-Crowell cube root law (Eq. 5).

$$C=K_0t \quad (1)$$

Where $\mathbf{K_0}$ is representing the zero-order rate constant expressed as concentration/ time and **t** is time.

$$LogC_0 - LogC = k_1t / 2.303 \quad (2)$$

Where $\mathbf{C_0}$ is representing the initial concentration of the drug and $\mathbf{K_1}$ is the first-order constant.

$$Q = K_ht \quad (3)$$

Where $\mathbf{K_h}$ is representing the constant reflecting the design variables of the system.

$$M_t/M_\infty = K_{kp}\, t^{n} \quad (4)$$

Where $\mathbf{M_t/M_\infty}$ is representing the fraction of drug release, $\mathbf{K_{kp}}$ is the release rate constant, n is the diffusion release exponent indicative of the drug release mechanism, and t is the dissolution time.[3]

$$Q_0^{1/3} - Q_t^{1/3} = K_{HC}t \quad (5)$$

Where $\mathbf{Q_t}$ is representing the amount of drug released in time t and $\mathbf{Q_0}$ is representing the initial amount of the drug in the microsphere and $\mathbf{K_{HC}}$ is the rate constant for the Hixson-Crowell rate equation.[4]

4. Result and Discussion

A calibration curve (Standard curve) Data of Fexofenadine HCL in Phosphate buffer pH 6.8 at λ max 259nm:

Table 2

S.N.	Concentration(µg/ml)	Absorbance(λmax259nm)
1.	02	0.160
2.	04	0.268
3.	06	0.392
4.	08	0.522
5.	10	0.708

From the standard Fexofenadine solution (100ug/ml), 02, 04, 06, 08, and 10 ml is taken out and transferred to the volumetric flask (100 ml) and the final volume was adjusted by adding 6.8 phosphate buffer up to 100 ml. The standard curve was made from the samples with previously selected concentrations by drawing the absorption vs. concentration graph.

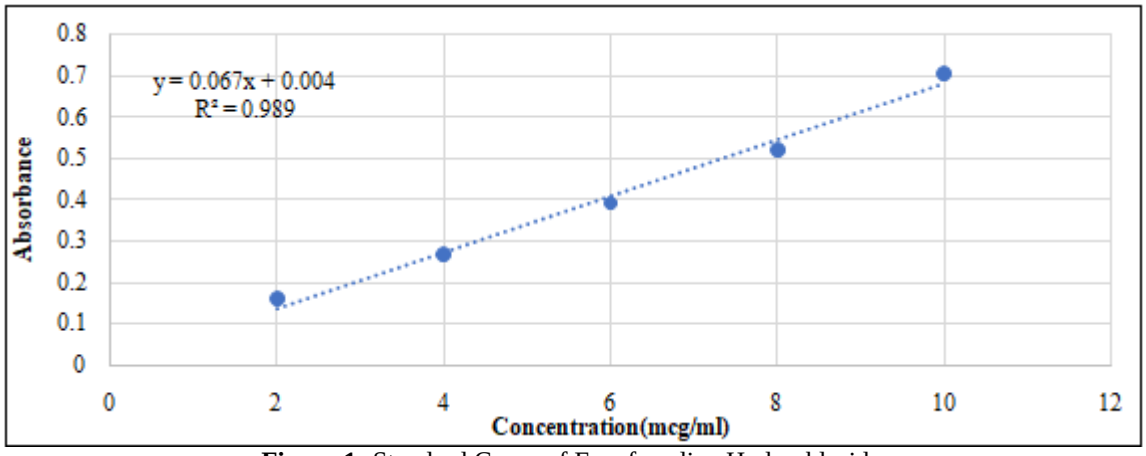

Figure 1: Standard Curve of Fexofenadine Hydrochloride

1) % Yield of microspheres:

The table (Table 3) displays the percentage yield of various microsphere formulations. The concentrations of HPMC and pectin were found to be crucial factors affecting the yield of FX-3, FX-4 and FX-5, FX-6 microsphere formulations. An increase in HPMC concentration resulted in higher viscosity of the polymer mixture. This higher viscosity led to reduced process loss and increased percentage yield of the microspheres. On the other hand, formulations FX-5 and FX-6 exhibited lower percentage yields, which can be attributed to the higher concentration of pectin in combination with sodium alginate.

2) Swelling Index:

No significant change in the swelling index was found in formulations FX-1, FX-2, FX-3 and FX-4. In the case of formulation FX-5 and FX-6 there was a decrease in the swelling index observed may be due to the presence of pectin in combination with sodium alginate.swelling index data is shown in Table3.

3) Particle size of microspheres:

The particle size of the Fexofenadine HCL microspheres was measured with the help of an optical microscope. No significant change was observed in different formulations. Particle size data is shown in Table3.

4) Drug entrapment efficiency:

The measurement of Fexofenadine HCL content in different microsphere formulations was performed through entrapment efficiency determination. The percentage of drug entrapment efficiency was found to be dependent on the concentration of Sodium Alginate and pectin. The FX-1 formulation, with a drug-to-sodium alginate ratio of 1:10, exhibited the highest entrapment efficiency. (Table-3)

As the concentration of Sodium Alginate increased in the formulation, the entrapment efficiency also increased. A similar trend was observed with an increase in the pectin concentration, indicating that higher drug entrapment occurred when the polymer concentration increased in the formulation, especially sodium alginate and pectin.

Table 3: % Yield, Swelling index, Particle size, Drug entrapment efficiency of total 6 formulations of microsphere:

Formulation	% yield	Swelling Index	Particle size (µm)	% Drug entrapment efficiency	Sphericity
FX1	81.21%	30.6	993	75%	Irregular spherical
FX2	83.18%	30.2	979	69%	Irregular spherical
FX3	107.63%	32.3	946	72%	Spherical
FX4	110.38%	31.5	952	68%	Spherical
FX5	67.72%	22.1	992	69%	Spherical
FX6	65.42%	20.6	989	70%	Spherical

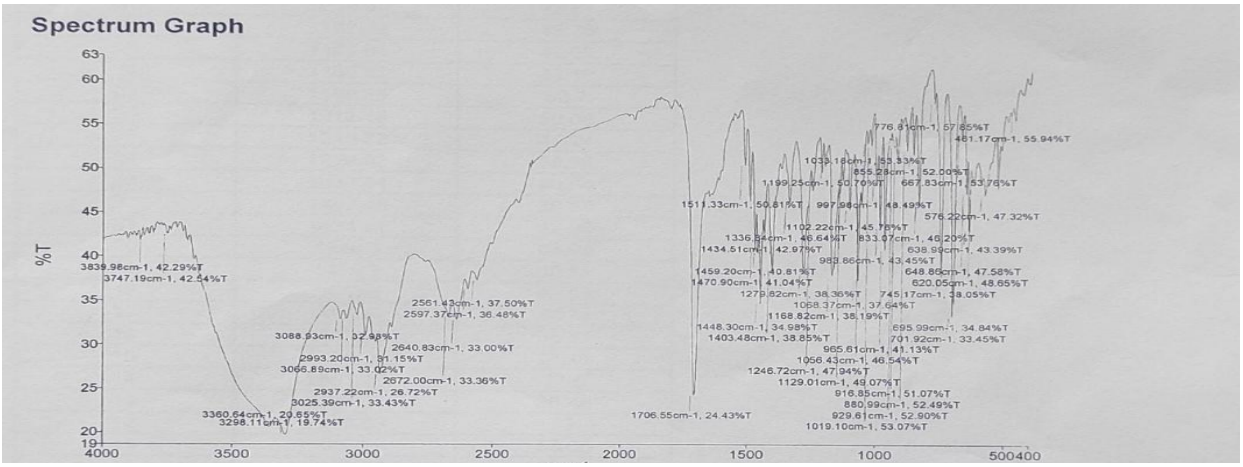

Figure 2: FTIR -Spectroscopy of Fexofenadine HCL

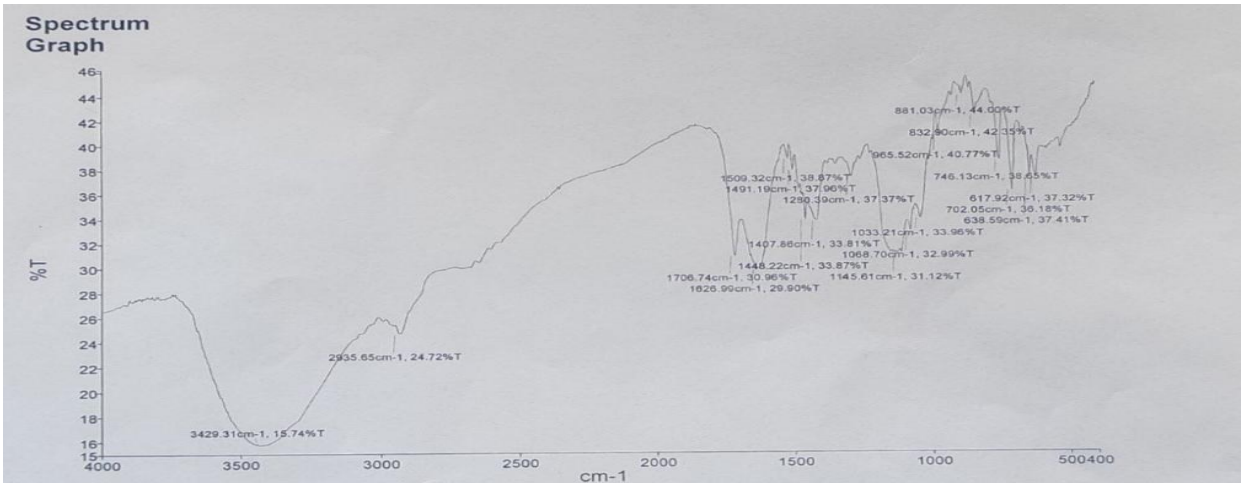

Figure 3: FTIR -Spectroscopy of FX-3

5) Fourier transform infrared spectroscopy (FTIR) compatibility study:

FT-IR (Fourier transforms infrared spectroscopy) of the pure drug (Fexofenadine HCL) and Fexofenadine HCL microspheres prepared with sodium alginate and HPMC were done and carefully observed (Figure- a and b). The IR spectra report of API (Fexofenadine HCL) shows the peak at 3360.64 cm-1 (O-H stretching vibrations), 1706.55 cm-1 (C=O stretching of Carboxylic acid), 1448.30 cm-1 (aromatic C=C stretching) and 1168.82 cm-1 (C-O stretching vibration of tertiary alcohol)

On the other hand, the IR spectra report of the final microsphere formulation (FX-3) shows the peak at 3429.31 cm-1 (O-H stretching vibrations), 1706.74 cm-1 (C=O stretching of Carboxylic acid), 1448.22 cm-1 (aromatic C=C stretching) and 1145.61 cm-1 (C-O stretching vibration of tertiary alcohol)

Comparison of both the FT-IR report suggests no incompatibility between Fexofenadine HCL and polymers (sodium alginate and HPMC) as no change of functional groups was detected during the process of formulation.

6) In-vitro drug release studies:

In-vitro drug release studies of all Fexofenadine microsphere formulations (FX-1 – FX-6) were done and the data showed the drug release range of 61% to 86% in 12 hours of study. Drug release data indicate that the release rate decreases with the increased concentration of sodium alginate and pectin. On the other hand, in the case of formulation FX-3, FX-4 when the ratio of HPMC increases and sodium alginate decreases the in the polymer ratio release rate increases gradually. The cumulative % drug release data is shown in Table4.

Table 4: In-vitro cumulative drug release percentage

Time (min)	FX-1	FX-2	FX-3	FX-4	FX-5	FX-6
0	0	0	0	0	0	0
60	14.48	13.12	21.49	20.88	13.18	13.75
120	18.22	22.67	29.65	29.85	20.87	21.85
180	20.66	26.25	33.84	34.14	23.88	24.76
240	29.89	31.7	38.05	39.64	25.46	26.3
300	37.62	38.85	42.28	46.35	27.05	27.84
360	46.9	44.48	46.54	50.73	29.73	30.43
420	54.84	57.54	51.39	56.91	31.71	32.34
480	61.5	66.87	55.69	60.75	33.69	34.61
540	68.9	73.2	61.2	67.5	39.5	41.2
600	73.2	76.5	65.3	71.3	45.6	48.7
660	77.5	81.2	69.8	74.5	54.7	54.3
720	82.3	86.4	74.5	78.8	62.3	61.4

7) Drug release kinetics mechanism:

The in-vitro drug release data of all the Fexofenadine HCL microsphere formulations (FX-1 to FX-6) were fitted to zero order, first order, Higuchi model, Korsemeyer-Peppas model and Hixson- Crowell model to find out the appropriate drug release kinetic model for all the formulations prepared.

The drug release kinetic data indicates the best-fitted model was Zero order kinetic model for the formulation FX-1(R^2 = 0.989), FX-2(R^2 = 0.987), FX-5(R^2 = 0.928) and FX-6(R^2 = 0.935).

On the other hand, Korsemeyer-Peppas model was the best-fitted model for formulation FX-3(R^2 = 0.983) and FX-4(R^2 = 0.991).

All the Drug release kinetic data and graphs are shown below.

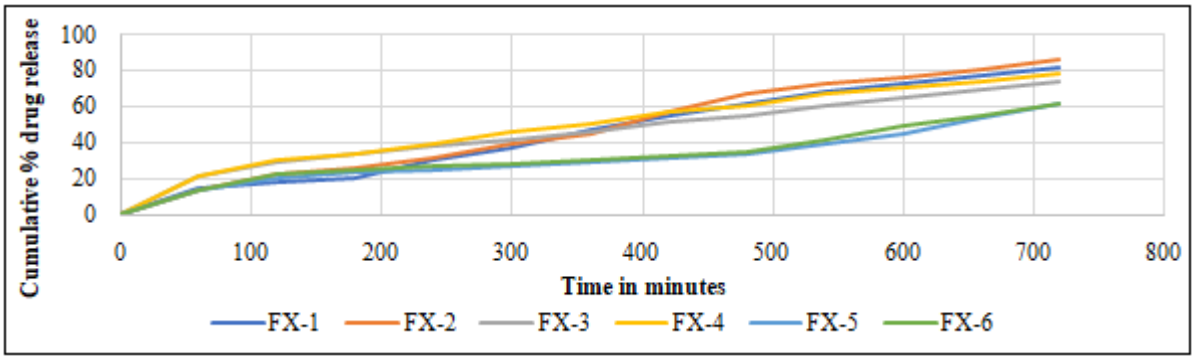

Figure 4: Drug release rate of all formulations

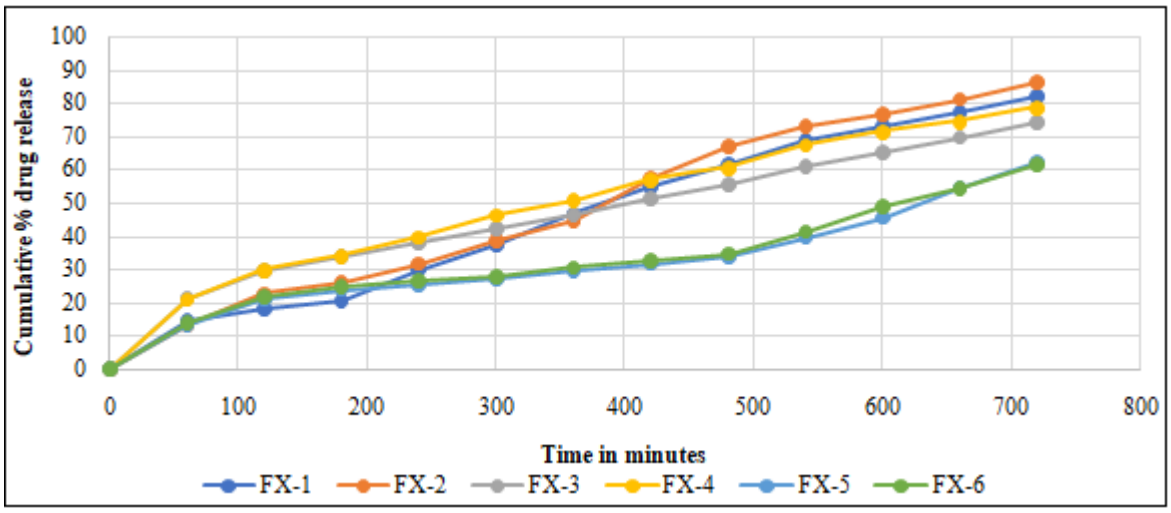

Figure 5: Zero order kinetics graph of all formulations

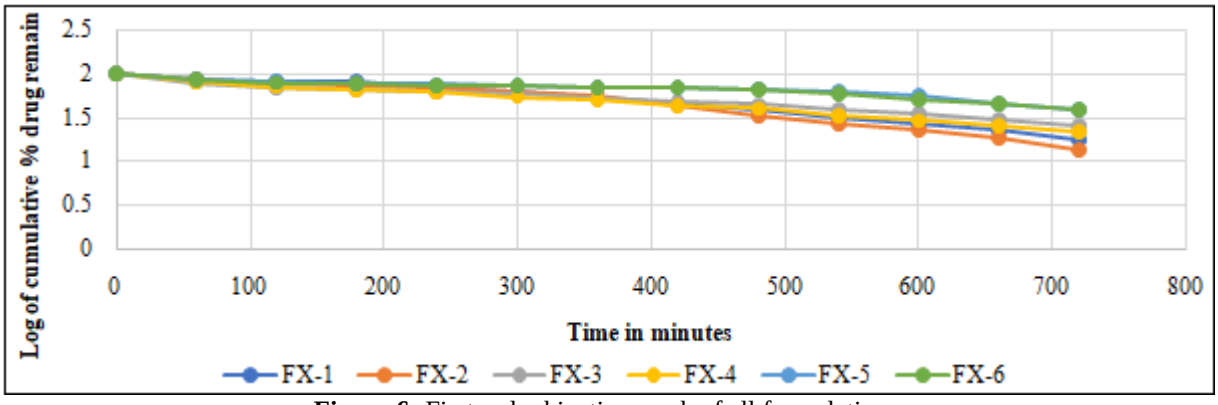

Figure 6: First order kinetics graph of all formulations

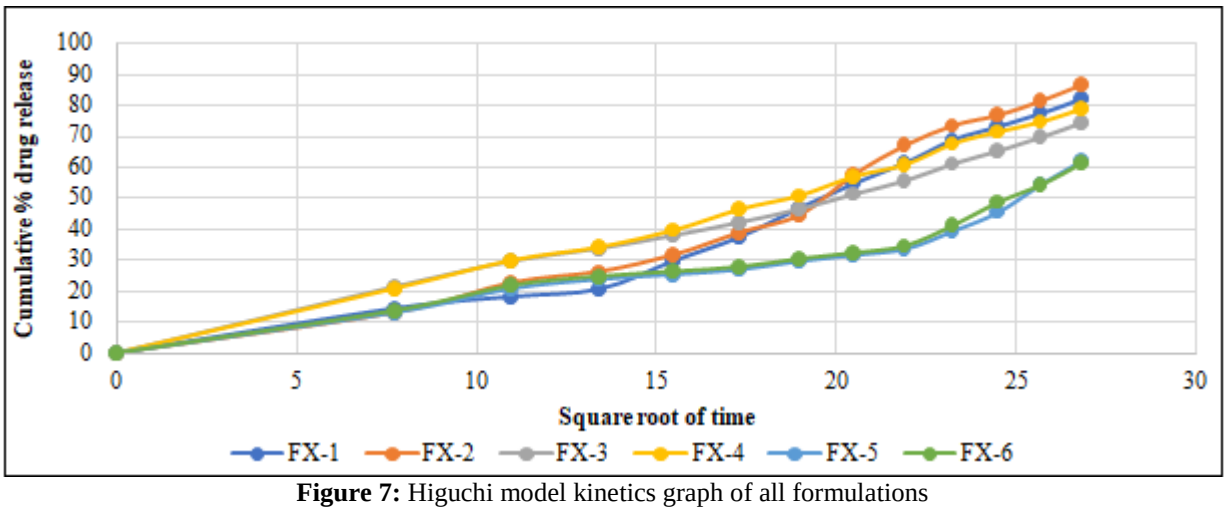

Figure 7: Higuchi model kinetics graph of all formulations

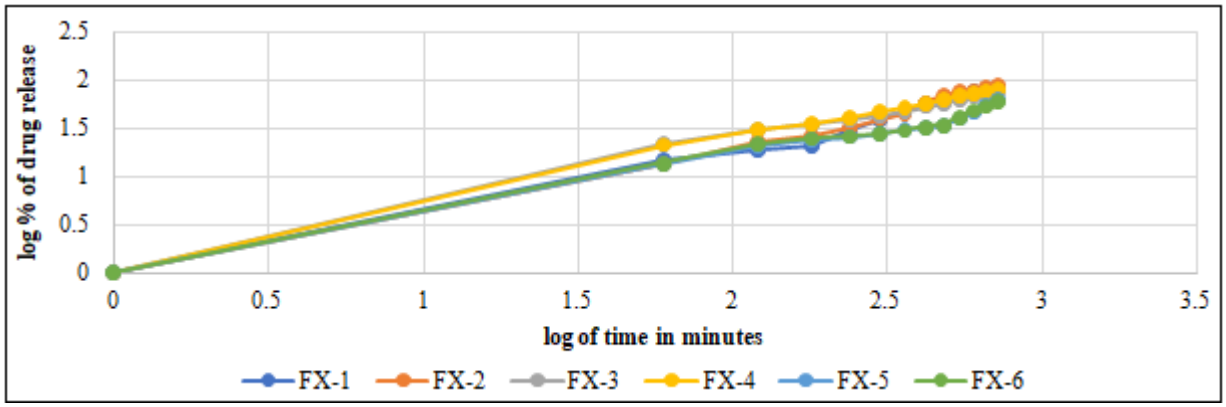

Figure 8: Korsmeyer- Peppas model kinetics graph of all formulations

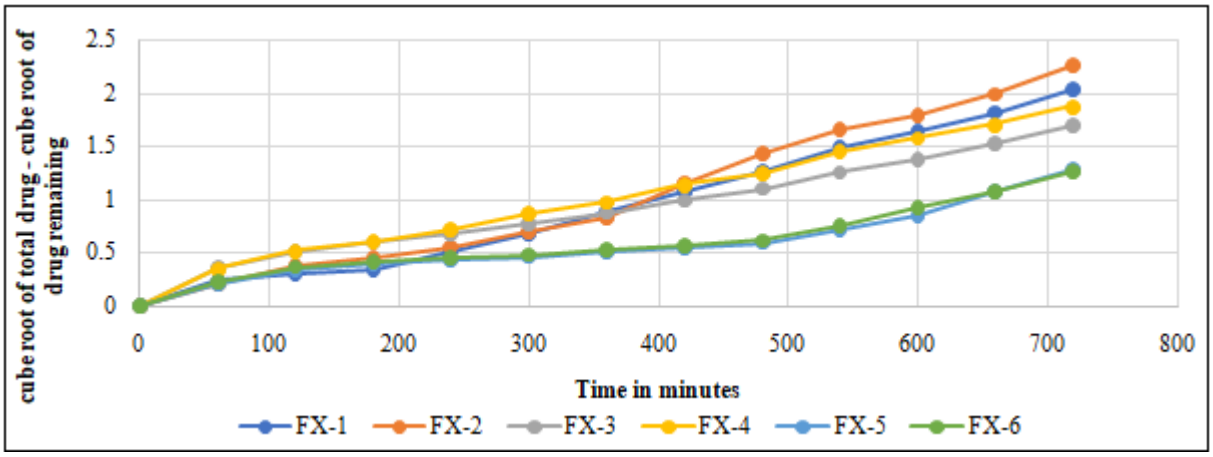

Figure 9: Hixson-Crowell kinetics graph of all formulations

Table 5: Drug release kinetics mechanism data

Formulations	Zero-order		First order		Higuchi model		Korsemeyer-peppas model		Hixson-crowell model	
	K_0	R^2	K_1	R^2	K_H	R^2	K_{KP}	R^2	K_{HC}	R^2
FX-1	0.114	0.989	-0.0024	0.971	9.961	0.917	0.706	0.958	0.0006	0.987
FX-2	0.119	0.987	-0.0027	0.958	10.173	0.914	0.7334	0.981	0.0007	0.980
FX-3	0.087	0.949	-0.0017	0.980	8.870	0.903	1.530	0.9834	0.0004	0.9805
FX-4	0.097	0.955	-0.0020	0.989	9.302	0.906	1.395	0.991	0.0005	0.990
FX-5	0.068	0.928	-0.0011	0.889	7.962	0.885	1.144	0.911	0.0003	0.908
FX-6	0.068	0.935	-0.001	0.911	7.938	0.887	1.196	0.916	0.0003	0.924

Table 6: The best-fitted model and mechanism of drug release from all the formulations:

Formulation	Best fitted model	n value	Release mechanism
FX-1	Zero-order	0.788	Anomalous Transport
FX-2	Zero-order	0.783	Anomalous Transport
FX-3	Korsemeyer-peppas model	0.495	Fickian Diffusion
FX-4	Korsemeyer-peppas model	0.542	Anomalous Transport
FX-5	Zero-order	0.543	Anomalous Transport
FX-6	Zero-order	0.531	Anomalous Transport

Selection of final formulation (Optimization): After analyzing all the important evaluation parameters of 6 different microsphere formulations,it has been concluded that FX-3 is selected as the optimized and final formulation.

5. Conclusion

The polymeric fexofenadine HCL microspheres were prepared successfully. The ionotropic gelation method was applied to prepare total 6 different formulations, where Calcium chloride was considered as a crosslinking agent and sodium alginate, HPMC and Pectin were used as polymers. Polymers were used in different combinations and ratios to prepare the formulations.

Various microsphere evaluation methods were performed on all 6 formulations. After analyzing all the study results FX-3 formulation was found as the optimized formulation.

So, it is concluded that the FX-3 formulation can be used as sustained release fexofenadine hydrochloride microsphere formulation as it demonstrated the best sustained release effect among all the formulations prepared.

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Author Profile

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