RESEARCH PAPER

Formulation and Evaluation of Febuxostat Loaded Polymeric Microballoons as a Gastro Retentive Drug Delivery System

K.V. Ratnamala[1*], Vasumathi Pole[2], Sangeetha Chowdary[2]

[1*]Professor, RBVRR Women's College of Pharmacy, Barkatpura, Hyderabad, Telangana, Barkatpura, Hyderabad-500027, India

[2]M. Pharm (Pharmaceutics), RBVRR Women's College of Pharmacy, Barkatpura, Hyderabad, Telangana, India

***Corresponding author: K.V. Ratnamala, Professor, RBVRR Women's College of Pharmacy, Barkatpura, Hyderabad, Telangana, India**

Email: ratnakolapalli@gmail.com

ABSTRACT

Febuxostat is a xanthine oxidase inhibitor used in the management of gout. However, its poor aqueous solubility and limited gastric residence time reduce its oral bioavailability. Gastroretentive polymeric microballoons offer a promising strategy to prolong gastric retention and provide sustained drug release. The present study aimed to formulate and evaluate Febuxostat-loaded polymeric microballoons using Eudragit S100 and HPMC K100 to improve gastric retention and sustain drug release. Polymeric microballoons were prepared by solvent evaporation/emulsion diffusion technique using varying concentrations of Eudragit S100 and HPMC K100. The formulations were evaluated for particle size, entrapment efficiency, percentage buoyancy, and in-vitro drug release. Surface morphology was examined using scanning electron microscopy (SEM). The UV analytical method exhibited good linearity at 315 nm with a regression coefficient of 0.993. Among all formulations F11 showed better results. The optimized formulation demonstrated desirable particle size distribution, high buoyancy, and sustained drug release characteristics. SEM analysis confirmed spherical hollow microballoons responsible for prolonged floating behaviour. Febuxostat-loaded polymeric microballoons successfully prolonged gastric residence time and provided controlled drug release, indicating their potential as an effective gastroretentive drug delivery system for gout therapy.

Keywords: Febuxostat; Polymeric Microballoons; Gastroretentive Drug Delivery System; Floating Microspheres; Eudragit S100; HPMC K100; Sustained Release.

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1. Introduction[1-5]

Gout is a chronic metabolic disorder characterized by elevated serum uric acid levels and deposition of monosodium urate crystals in joints. Febuxostat is a selective xanthine oxidase inhibitor widely prescribed for long-term management of hyperuricemia and gout. Despite its therapeutic effectiveness, Febuxostat exhibits poor aqueous solubility, which limits dissolution and oral bioavailability. Furthermore, rapid gastrointestinal transit may reduce drug absorption in the upper gastrointestinal tract where absorption is optimal.

Gastroretentive drug delivery systems (GRDDS) have gained considerable attention due to their ability to prolong gastric residence time and improve absorption of drugs exhibiting a narrow absorption window. Polymeric microballoons are hollow microspheres capable of floating on gastric fluids, thereby maintaining prolonged gastric retention and sustained drug release. Such systems improve bioavailability, reduce dosing frequency, and enhance patient compliance.

The present investigation focuses on the formulation and evaluation of Febuxostat-loaded polymeric microballoons using Eudragit S100 and HPMC K100 to develop a sustained-release gastroretentive delivery system.

2. Materials and Methods[6-8]

2.1 Materials

Febuxostat was used as the model drug. Eudragit S100 and HPMC K100 were employed as release-retarding polymers. Span 80 served as surfactant, while methanol and liquid paraffin were utilized during formulation development.

2.2 Analytical Method

The maximum absorption wavelength (λmax) of Febuxostat was determined using UV-visible spectrophotometry and was found to be 315 nm.

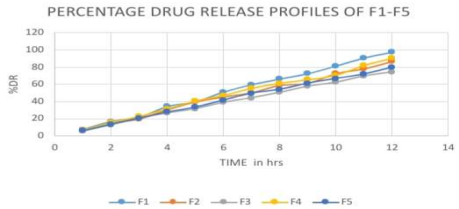
A calibration curve was prepared over concentrations ranging from 2–12 µg/mL, demonstrating linearity with a regression coefficient of 0.993.

2.3 Solubility study

Solubility studies were performed to estimate the solubility of drug in various solvents

Table 1: Solubility of drug in various solvents:

Solvents	Solubility (µg/ml)
CCL4	0.09
Distilled water	0.03
Methanol	0.86
Ethanol	0.58
DMSO	1.29
0.1 N HCL	4.06
PH 4.5 acetate buffer	1.9



PH 6.8 phosphate buffer	2.69
PH 7.4 phosphate buffer	0.04

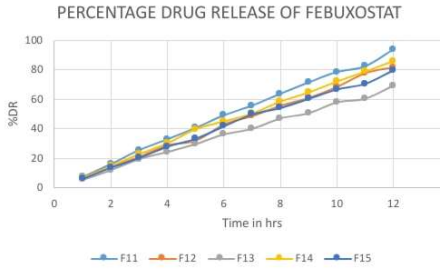
2.4 Preparation of Polymeric Microballoons[9-12]

Microballoons were prepared using the solvent evaporation method. Febuxostat was dissolved in methanol and dispersed into liquid paraffin containing Span 80 under controlled stirring. Continuous stirring facilitated solvent evaporation and formation of hollow microballoons.

2.5 Formulation Design

Table 2. Composition of Febuxostat Polymeric Microballoons

Formulation code	Drug (mg)	Amount of Eudragit S 100 (mg)	Amount of HPMC K 100 (mg)	Amount of surfactant (ml)	Stirring speed(rpm)
F1	100	500	100	1	500
F2	100	300	500	1	300
F3	100	500	300	1	500
F4	100	100	300	1	500
F5	100	300	300	1	300
F6	100	300	500	1	500
F7	100	100	300	1	500
F8	100	100	500	1	500
F9	100	300	300	1	300
F10	100	300	100	1	700
F11	100	300	500	1	500
F12	100	500	300	1	700



F13	100	300	500	1	700
F14	100	100	300	1	300
F15	100	100	100	1	500

2.6 Evaluation Parameters[13-20]

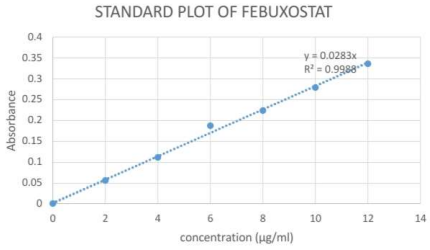
Prepared formulations were evaluated for:

- Particle size
- Percentage yield
- Drug entrapment efficiency
- In-vitro buoyancy
- In-vitro drug release
- Surface morphology by SEM

3. Results and discussion:

3.1 Calibration Curve

The developed UV spectrophotometric method showed satisfactory linearity over the concentration range studied with a correlation coefficient of 0.993, indicating suitability for quantitative estimation of Febuxostat.



3.2 Solubility Studies

Solubility studies revealed maximum solubility of Febuxostat in carbon tetrachloride, followed by ethanol and phosphate buffer pH 6.8, confirming its poor aqueous solubility**.**

3.3 Formulation Optimization[21-25]

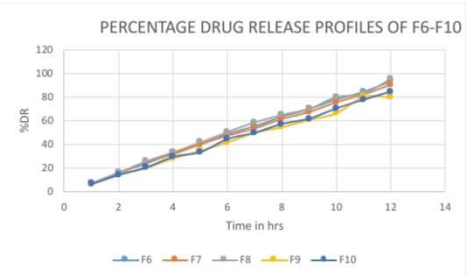
Fifteen formulations were prepared using varying polymer concentrations and stirring speeds. The formulations demonstrated significant differences in particle size, entrapment efficiency, buoyancy, and drug release characteristics.

Invitro Drug Release of Formulations (F1-F5)

- These formulations show that, the influence of polymer concentration on early phase drug release.
- Lower polymer levels allow faster hydration and diffusion, resulting in comparatively higher initial % drug release.
- The release pattern gradually increases with time, indicating controlled but moderately sustained delivery.
- Microballoons integrity and buoyancy contribute to uniform drug diffusion through 12 hrs study.
- Among these formulations, the release rate reflects the balance between polymer viscosity and matrix stability.

Invitro Drug Release of Formulations (F6-F10)

- These formulations demonstrate enhanced sustained-release behavior due to higher levels of Eudragit/HPMC polymers.
- Increased polymer viscosity forms a thicker diffusion barrier, slowing the release rate compared to earlier formulations.
- The gradual rise in drug release over time indicates strong gel formation and controlled diffusion.
- These formulations show improved gastro-retentive properties, contributing to prolonged drug availability.
- Differences between F6-F10 highlight the effect of polymer ratio adjustments on long release efficiency.



Invitro Drug Release of Formulations (F11-F15)

- These formulations show the strongest sustained-release characteristics due to maximum polymer content.
- High polymeric density restricts water penetration, resulting in slower but more consistent drug release.
- These formulations maintain microballoons stability for an extended period, ensuring prolonged buoyancy.
- Drug release progression over 12 hrs. reflects a highly controlled diffusion mechanism.
- F11-F15 represents the most sustained formulations, ideal for long-duration gastro-retentive delivery applications.

Table 3: Various parameters evaluated for prepared formulations

No of formulations	Percentage yield	Drug entrapment efficiency	Invitro buoyancy	
			Lag time (s)	Floating time (h)
F1	85.7%	40.0	14	9
F2	84.4%	76.0	12	11
F3	87.8%	79.0	18	10
F4	82.0%	41.0	15	12
F5	82.9%	58.0	14	11
F6	91.1%	43.0	17	9
F7	86.0%	62.0	19	12
F8	88.6%	60.5	20	11
F9	85.4%	38.0	13	12
F10	76.0%	83.0	15	10
F11	92.2%	79.0	17	12
F12	85.7%	60.0	11	11
F13	90.0%	90.0	10	12
F14	80.0%	40.0	14	9
F15	70.0%	21.0	16	12

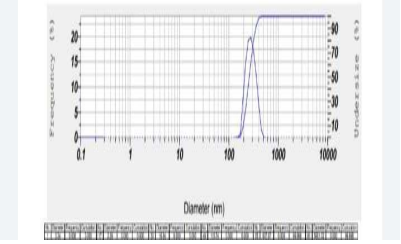
- The optimization study evaluates how variations in polymer concentration and formulation composition affect percentage yield, drug entrapment, buoyancy, and drug release of microballoons.
- Percentage yield values ranging from 70%-92% indicate efficient production, with higher yields observed in formulations containing optimal polymer ratios that enhance microballoons formation.
- Drug entrapment efficiency shows significant variability, suggesting that polymer viscosity and drug-polymer interaction strongly influence encapsulation performance.
- In-vitro buoyancy parameters, including lag time and floating duration, reveal that most formulations achieve rapid floatation and prolonged gastric retention.
- Floating times 9-12 hrs confirm stable microballoons structure and adequate density for gastro-retentive delivery.
- The in-vitro drug release values demonstrate sustained-release behavior,

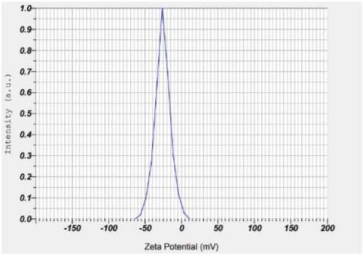
with optimized formulations showing higher release due to improved polymer swelling and diffusion characteristics.

- Overall, the combined evaluation of all parameters helps identify the most efficient formulation that balances buoyancy, entrapment efficiency, and controlled drug release for effective gastro-retentive therapy.
- From all the above results it can be concluded that F 11 formulation showed better results and stable formulation

3.4 Particle size analysis

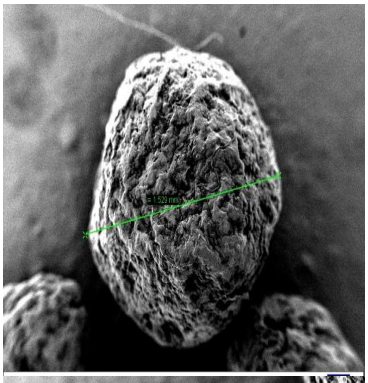
The optimized formulation showed a particle size of be 330.8 nm and zeta potential value of −25 mV indicating the F11 formulation is stable. The optimized formulation exhibited a zeta potential of approximately **−25 mV**, indicating adequate surface charge and colloidal stability. The negative zeta potential suggests the presence of ionized functional groups on the particle surface, contributing to electrostatic repulsion between particles and minimizing aggregation.

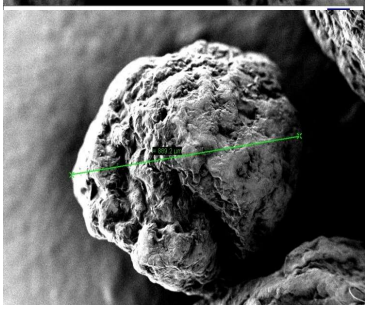




3.5 Morphological Characterization

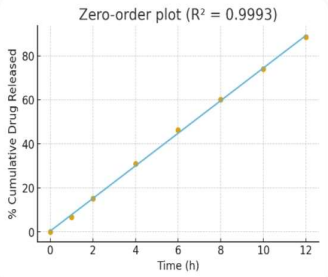
Scanning electron microscopy revealed discrete spherical microballoons with smooth external surfaces and hollow internal cavities. The hollow nature of the particles contributed significantly to floating behavior and prolonged gastric retention.

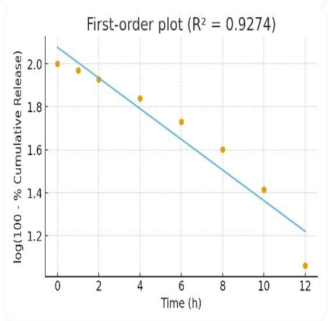


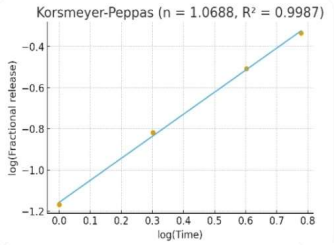


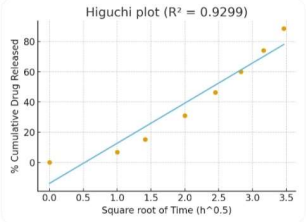
4. Drug release kinetics and mechanism:

The drug release kinetics and mechanism of the optimised formulation (F11) were evaluated using various mechanical models.The correlation coefficient R^2 values indicates that the formulation followed Zero order kinetics (R^2=0.9993) suggesting a concentration-independent release pattern. The Higuchi model (R^2=0.9987). with n value of 0.898 further conformed as a non-fickian (anomalous) diffusion mechanism indicating that the drug release occurred through a combination of diffusion and erosion process.









5. Discussion

The polymeric microballoons demonstrated excellent floating properties due to their hollow structure. Increased polymer concentration enhanced entrapment efficiency and prolonged drug release. Formulations containing balanced concentrations of Eudragit S100 and HPMC K100 exhibited superior sustained-release characteristics.

Among all formulations, F9 showed the highest drug entrapment efficiency (95.67%), F7 demonstrated maximum buoyancy (96.45%), and F12 exhibited the highest cumulative drug release (98.89%). These findings confirm the effectiveness of polymeric microballoons as gastroretentive carriers.

6. Stability studies:

Stability studies were performed for optimized formulation F11.The drug content and invitro drug release values indicate that the formulation was stable after 3-month time.

6. Conclusion

The study successfully developed Febuxostat-loaded polymeric microballoons using Eudragit S100 and HPMC K100 through a solvent evaporation technique. The prepared formulations exhibited satisfactory particle size distribution, high drug entrapment efficiency, prolonged buoyancy, and sustained drug release. SEM analysis confirmed the formation of hollow spherical structures essential for gastroretentive performance.

The optimized formulations demonstrated the potential to improve gastric retention, enhance oral bioavailability, reduce dosing frequency, and increase patient compliance. Therefore, Febuxostat-loaded polymeric microballoons represent a promising gastroretentive delivery system for the long-term management of gout.

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