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Research Article

Formulation and Evaluation of Sustained Release Floating Microspheres of Doxofylline

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The present study aimed to develop and evaluate sustained release floating microspheres of Doxofylline for prolonged gastric retention and controlled drug delivery. Floating microspheres were prepared using the emulsion solvent diffusion technique with polymers such as HPMC K100LV, HPMC K4M, HPMC K15M, and Ethylcellulose. The prepared formulations were evaluated for micromeritic properties, percentage yield, buoyancy, drug entrapment efficiency, in-vitro drug release, stability studies, and characterization by FTIR, SEM, XRD, HPLC, GC, Mass spectroscopy, and NMR studies. Among all formulations, batch A5 showed the best performance with 74.42% yield, 79.65% drug entrapment, 47.50% buoyancy, and 99.25% cumulative drug release over 12 hours. Release kinetics followed the Higuchi model and Korsmeyer-Peppas model indicating anomalous non-Fickian diffusion. Stability studies confirmed good stability with estimated shelf life of 1.9 years. The developed floating microspheres can therefore be considered a promising gastroretentive sustained release drug delivery system for Doxofylline.

Keywords: Floating microspheres, Doxofylline, Gastroretentive drug delivery system, Sustained release, HPMC, Ethylcellulose.

INTRODUCTION

Gastroretentive drug delivery systems (GRDDS) are designed to prolong gastric residence time and improve bioavailability of drugs absorbed mainly in the stomach or upper gastrointestinal tract. Floating microspheres represent an important multiparticulate gastroretentive system due to their low density and prolonged gastric retention. Doxofylline is a xanthine derivative used in the treatment of asthma and chronic obstructive pulmonary disease (COPD). Because of its short biological half-life, sustained release formulations are required to reduce dosing frequency and improve patient compliance. The objective of the present work was to formulate and evaluate sustained release floating microspheres of Doxofylline using hydrophilic polymers.

MATERIALS AND METHODS

2.1 MATERIALS

- Drug: Doxofylline
- Polymers: HPMC K100LV, HPMC K4M, HPMC K15M, Ethylcellulose
- Solvents: Ethanol and Dichloromethane
- Stabilizer: Polyvinyl alcohol (PVA)

2.2 Preparation of Floating Microspheres

Floating microspheres were prepared by emulsion solvent diffusion technique using ethanol and dichloromethane (1:1) as solvent system. The polymer-drug solution was added to aqueous PVA solution under stirring at controlled temperature (30–40°C). Microspheres formed were filtered, washed, and dried.

2.3 Evaluation Parameters

The prepared microspheres were evaluated for:

- Particle size
- Bulk density
- Tapped density
- Carr's index
- Hausner ratio
- Angle of repose
- Percentage yield
- Buoyancy
- Drug entrapment efficiency
- In-vitro drug release
- Release kinetics
- Stability studies

RESULTS AND DISCUSSION

3.1 Physical Characterization of Doxofylline

Table 1: Physical Properties of Doxofylline

Parameter	Observation
Nature	Crystalline powder
Color	White
Odor	Odorless
Taste	Bitter
Melting Point	142–145°C
Solubility in Water	11.4 mg/ml
Solubility in Ethanol	3.50 mg/ml
Loss on Drying	0.499%

The drug sample complied with standard physicochemical characteristics and showed purity of 99.65%.

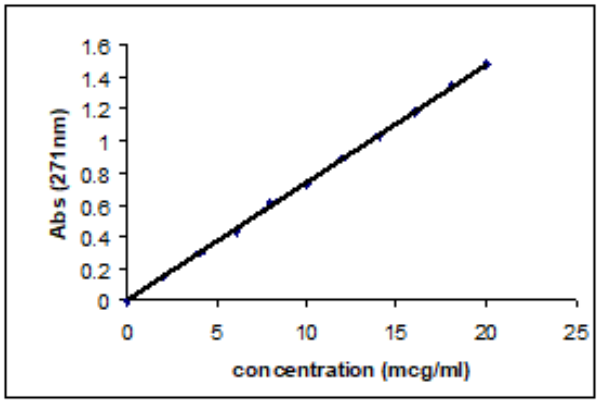
3.2 Calibration Curve

The calibration curve of Doxofylline in 0.1 N HCl obeyed Beer-Lambert's law at 271 nm.

Y=0.0735x+0.0054Y = 0.0735x + 0.0054Y=0.0735x+0.0054

Correlation coefficient:

R=0.9998R = 0.9998R=0.9998



3.3 Micromeritic Properties

Table 2: Micromeritic Evaluation of Microspheres

Batch	Particle Size (µm)	Carr's Index (%)	Angle of Repose
A1	237.2	15.2	24°19'
A5	340.7	10.2	15°82'
B1	219.0	12.6	22°78'

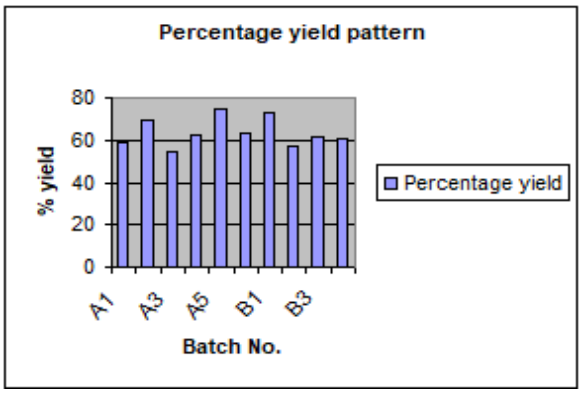
All formulations showed good flow properties suitable for capsule filling.

3.4 Percentage Yield

Table 3: Percentage Yield

Batch	% Yield
A1	58.86
A5	74.42
B1	73.25

Batch A5 showed maximum percentage yield.

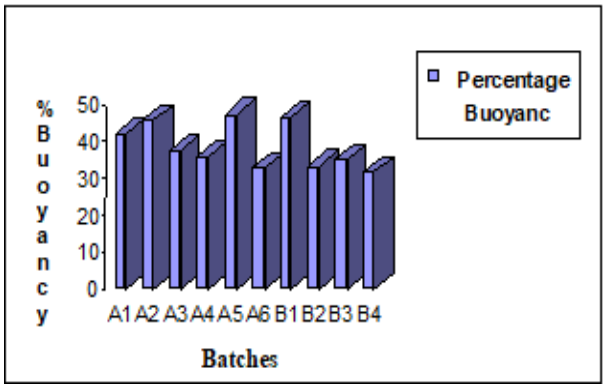


3.5 Buoyancy Studies

Table 4: Percentage Buoyancy

Batch	% Buoyancy
A1	42.20
A5	47.50
B1	46.65

The optimized formulation remained buoyant for more than 12 hours due to hollow internal structure.

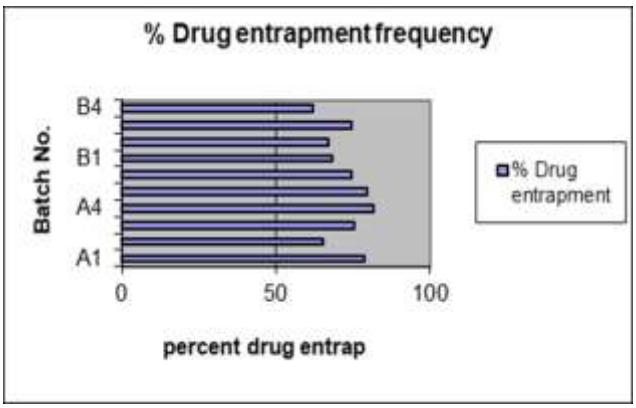


3.6 Drug Entrapment Efficiency

Table 5: Drug Entrapment Efficiency

Batch	% Drug Entrapment
A1	78.55
A5	79.65
B4	62.15

Higher polymer concentration improved drug retention.

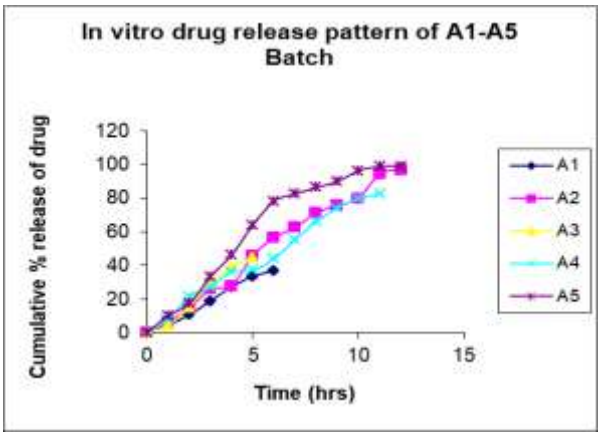


3.7 In-vitro Drug Release

Table 6: Drug Release Profile of Optimized Batch A5

Time (hrs)	% Drug Release
1	10.24
4	46.31
8	86.38
12	99.25

The formulation exhibited sustained release over 12 hours with initial burst release followed by controlled release.



3.8 Release Kinetics

The optimized formulation followed Higuchi diffusion kinetics and Korsmeyer-Peppas non-Fickian diffusion mechanism.

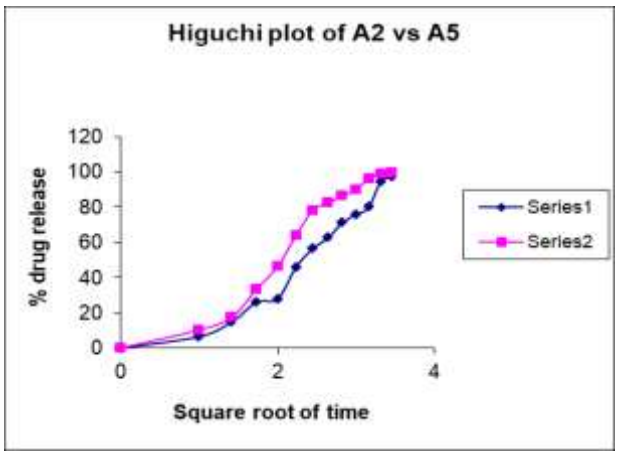
Higuchi Model

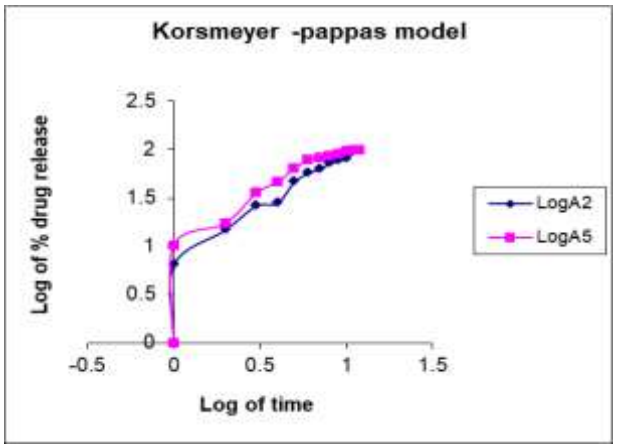
Q=Kt0.5Q = Kt^{0.5}Q=Kt0.5

Korsmeyer-Peppas Equation

MtM∞=Ktn\frac{M_t}{M_\infty}=Kt^nM∞Mt=Ktn

The diffusion exponent value indicated anomalous transport.





3.9 Stability Studies

Table 7: Stability Study of Optimized Batch A5

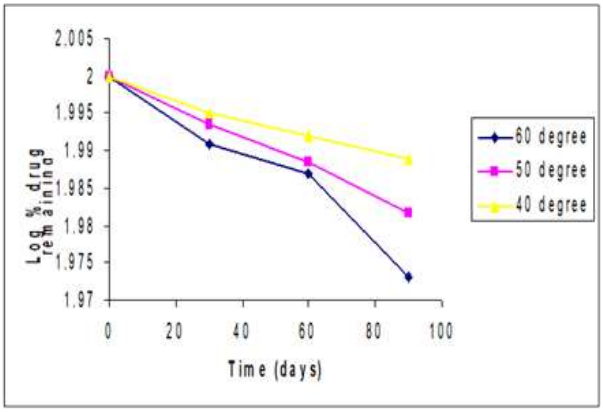
Time (Days)	% Drug Remaining
0	100
30	99.92
60	99.84
90	99.77

The optimized formulation remained stable under accelerated conditions.

Estimated shelf life:

T0.9=0.1054K25T_{0.9}=\frac{0.1054}{K_{25}}T 0.9=K250.1054

Shelf life was found to be approximately 1.9 years.



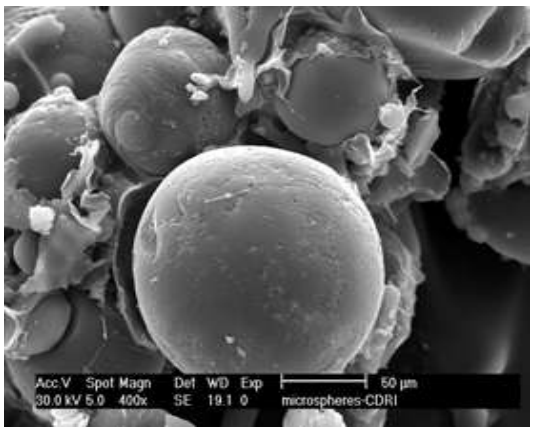
3.10 SEM Studies

SEM studies revealed:

- Smooth outer surface
- Hollow internal cavity

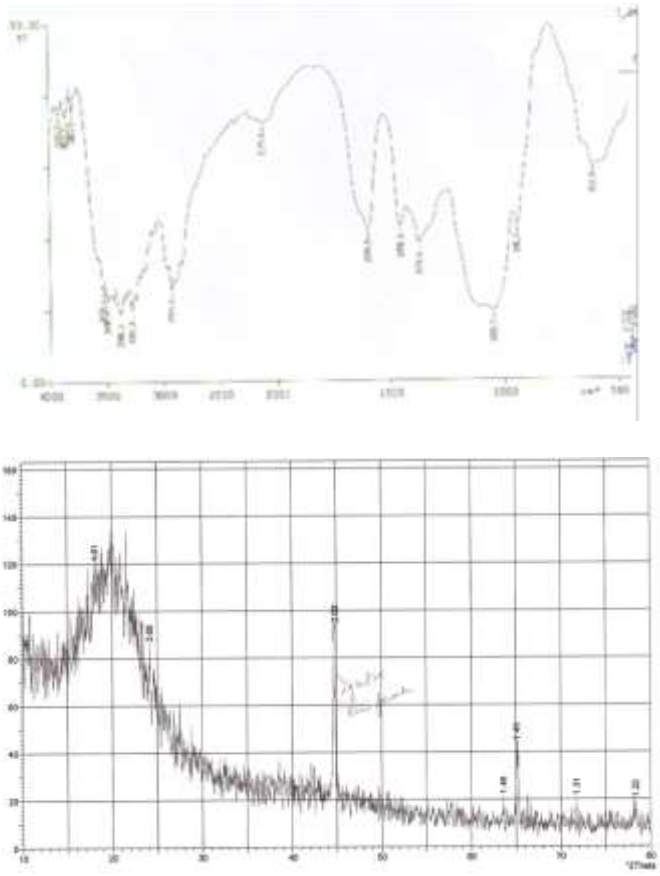
- Porous structure
- Spherical morphology

These characteristics were responsible for floating behavior and sustained release.



3.11 FTIR and XRD Studies

FTIR studies confirmed absence of drug-polymer interaction. XRD studies indicated the crystalline nature of Doxofylline remained intact in the optimized formulation.



CONCLUSION

Sustained release floating microspheres of Doxofylline were successfully formulated using HPMC and Ethylcellulose polymers by emulsion solvent diffusion technique. Optimized formulation A5 demonstrated excellent buoyancy, high drug entrapment, controlled drug release for 12 hours, and good stability characteristics. The developed floating microspheres can improve gastric residence time, enhance bioavailability, reduce dosing frequency, and improve patient compliance.

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