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Formulation and Characterization of Rasagiline Mesylate Nanosponges for Parkinson's Therapy

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ABSTRACT

The present study aimed to develop and characterize Rasagiline Mesylate (RM)-loaded nanosponges (NSGs) to enhance the solubility and bioavailability of RM, a poorly water-soluble drug used in the treatment of Parkinson's disease. Nanosponges were prepared using β-cyclodextrin (β-CD) as the polymer and dimethyl carbonate (DMC) as the cross-linker. The nanosponges were synthesized using different molar ratios of β-CD to DMC (1:2, 1:4, and 1:8) and loaded with RM at varying drug-to-polymer ratios (1:5, 1:10, and 1:15). The formulations were characterized for particle size, zeta potential, entrapment efficiency, drug loading, and in vitro drug release. The optimized formulation exhibited a particle size of 400-500 nm, high entrapment efficiency (85-95%), and sustained drug release over 24 hours. The results suggest that RM-loaded nanosponges can significantly improve the solubility and bioavailability of RM, making it a promising approach for the controlled delivery of poorly water-soluble drugs.

INTRODUCTION

Parkinson's disease (PD) is a progressive neurodegenerative disorder affecting millions of people worldwide. Rasagiline Mesylate (RM) is a selective, irreversible monoamine oxidase-B (MAO-B) inhibitor used in the treatment of PD. Despite its therapeutic efficacy, RM suffers from poor aqueous solubility and low oral bioavailability, which limits its clinical effectiveness. To overcome these challenges, nanotechnology-based drug delivery systems, such as nanosponges, have gained significant attention due to their ability to enhance the solubility, stability, and bioavailability of poorly water-soluble drugs.

Nanosponges are porous, nanoscale structures that can encapsulate both hydrophilic and hydrophobic drugs, providing controlled and sustained release. They are typically prepared using cyclodextrins, which are cyclic oligosaccharides that form inclusion complexes with drug molecules, thereby improving their solubility and stability. In this study, we developed RM-loaded nanosponges using β-cyclodextrin (β-CD) as the polymer and dimethyl carbonate (DMC) as the cross-linker. The nanosponges were characterized for their physicochemical properties, drug loading, and in vitro release profile.

MATERIALS AND METHODS

Materials

Rasagiline Mesylate (RM) was obtained from Micro Labs Limited, Bengaluru, India.

β-Cyclodextrin (β-CD) was purchased from Signet Chemical Corporation, Mumbai, India.

Dimethyl carbonate (DMC), dimethylformamide (DMF), and ethanol were procured from Loba Chemie Pvt. Ltd., Mumbai, India.

All other chemicals and solvents used were of analytical grade.

Methods

Synthesis of β-CD Nanosponges

β-CD nanosponges were synthesized by reacting β-CD with DMC in different molar ratios (1:2, 1:4, and 1:8). Briefly, 17.42 g of β-CD was dissolved in 100 mL of anhydrous DMF, and the calculated amount of DMC was added. The reaction mixture was heated at 100°C for 4 hours under continuous stirring. The resulting product was washed with deionized water and purified by Soxhlet extraction with ethanol. The final product was dried and stored for further use.

Preparation of RM-Loaded Nanosponges

RM-loaded nanosponges were prepared by suspending the synthesized β-CD nanosponges in distilled water and adding RM at different drug-to-polymer ratios (1:5, 1:10, and 1:15). The mixture was sonicated for 10 minutes and stirred for 24 hours.

The uncomplexed drug was removed by centrifugation at 2000 rpm for 10 minutes. The supernatant was lyophilized to obtain the RM-loaded nanosponges.

Characterization of Nanosponges

Particle Size and Zeta Potential: The particle size and zeta potential of the nanosponges were determined using a Malvern Zetasizer.

Entrapment Efficiency and Drug Loading: The entrapment efficiency (EE) and drug loading (DL) were calculated using the following formulas:

In Vitro Drug Release: The in vitro drug release study was conducted using a dialysis bag method in phosphate buffer (pH 6.8) at 37°C. Samples were withdrawn at predetermined time intervals and analyzed using UV-Vis spectrophotometry at 265 nm.

Spectral analysis:

UV Spectroscopy:

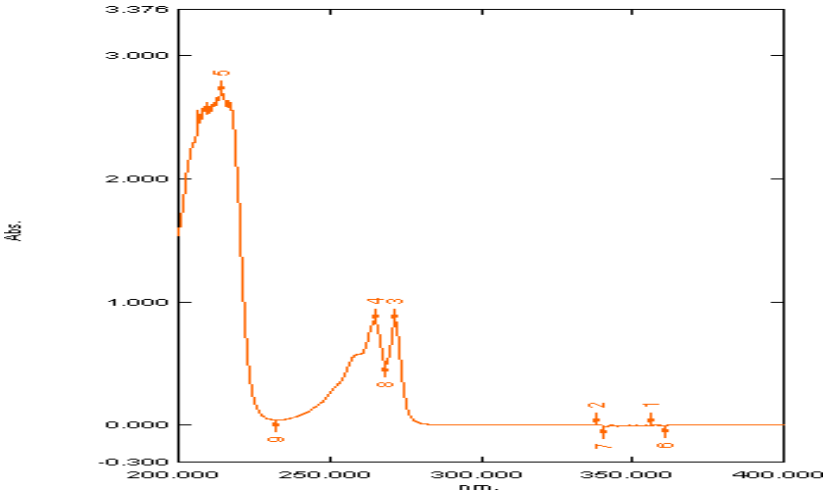

Fig1 : UV-visible spectrum of Rasagiline mesylate.

DSC studies :

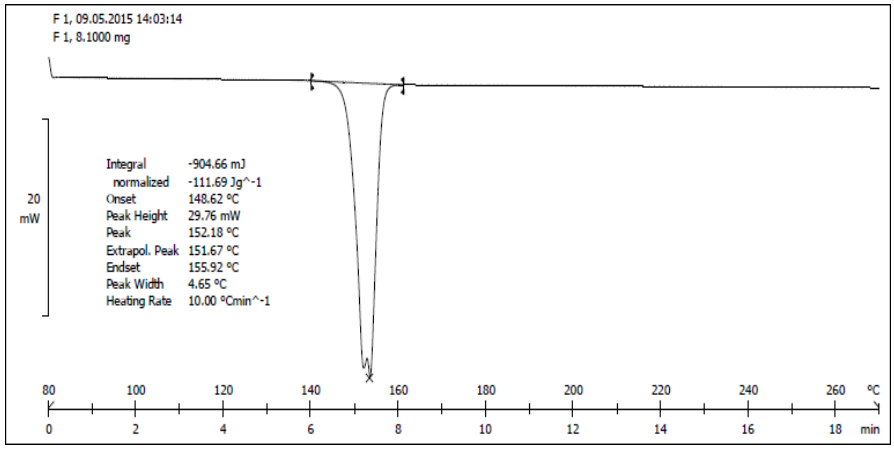

Fig 2: Dsc Of Pure Drug

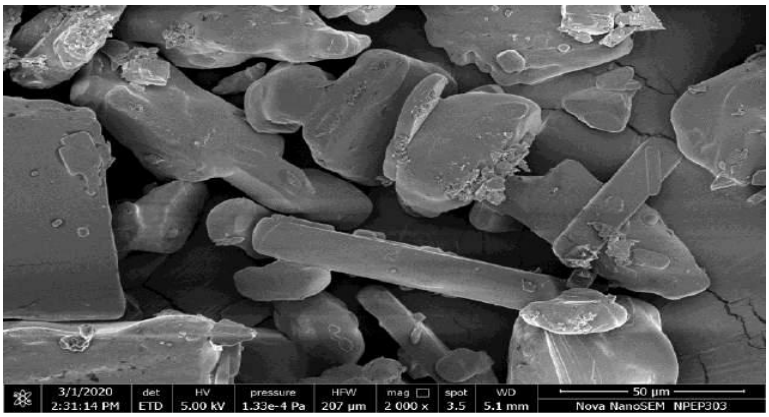

Fig3 : FESEM micrograph of rasagiline mesylate

Fourier Transform Infrared (FTIR) spectroscopy:

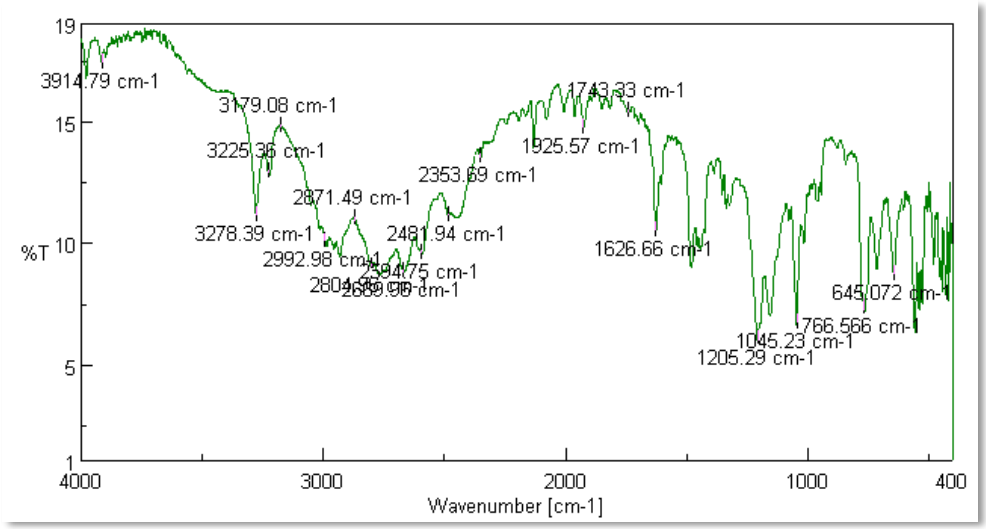

Fig 4: FTIR spectra of Rasagiline mesylate

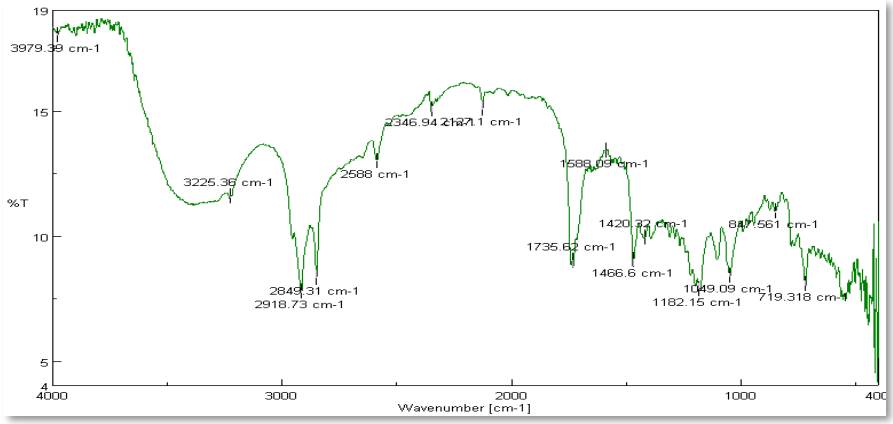

Fig 5: FT-IR spectra of physical mixture

Differential Scanning Calorimetry (DSC) (Melting temperature range):

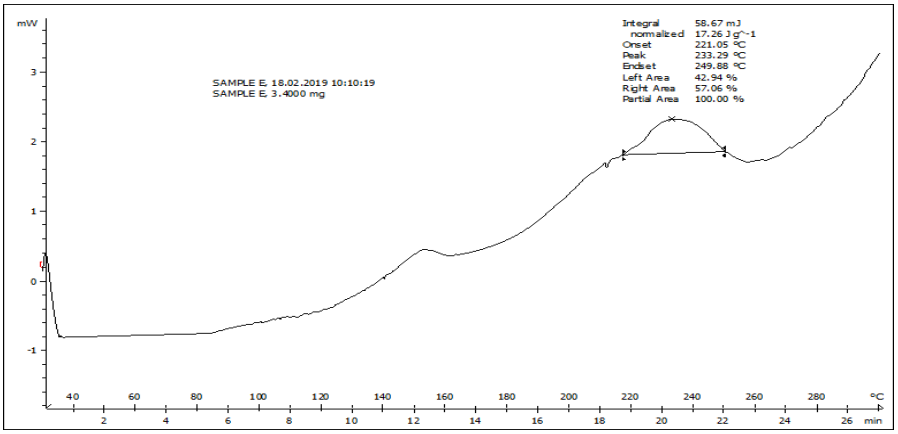

Fig6 : DSC thermogram of Optimized formulation F4

Powder X-ray diffraction (PXRD) analysis:

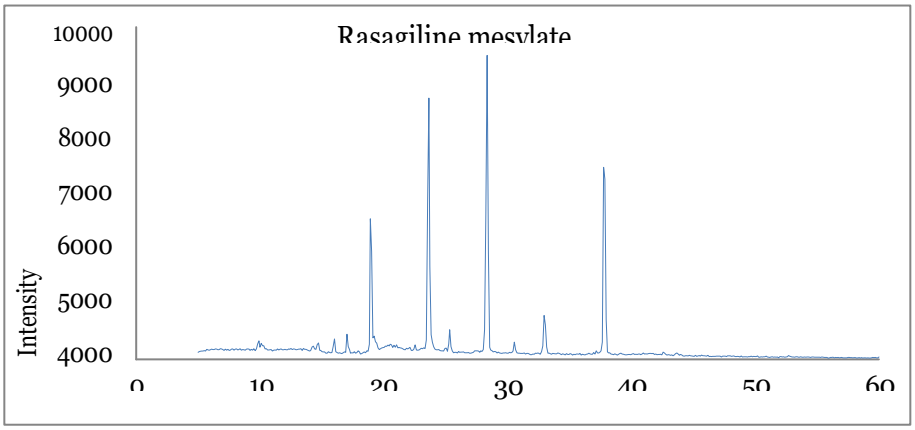

Fig7 : PXRD of Rasagiline mesylate

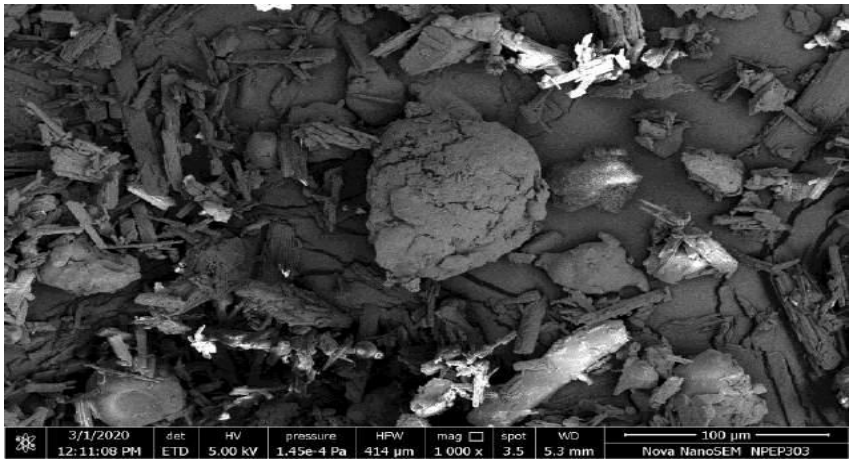

Fig 8 : FESEM micrograph of Physical Mixture

EVALUATION AND CHARACTERIZATION OF NSGS

Saturation solubility study:

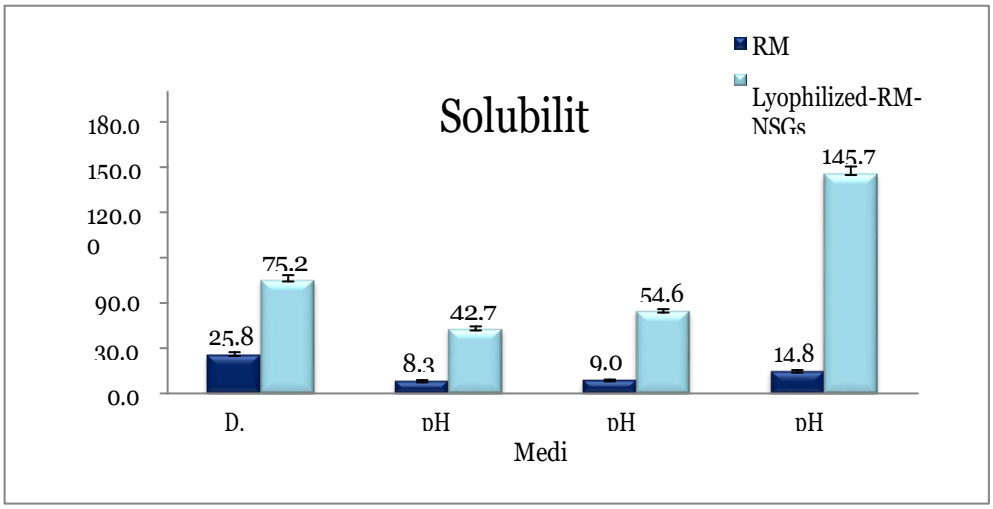

Fig 9. Solubility Comparison of pure RM and lyophilized NSGs in different media.

Entrapment efficiency and Drug loading:

Table1 : Percent drug encapsulation and drug loading of NSGs[a]

Run	RM: EC (% w/w)	Percent drug encapsulation (%)	Unentraped drug (%)	Drug Loading (%)	Solubility (µg/ml)
F1	1: 10	81.76±2.41	18.24±2.41	26.71±0.627	66.99±1.820
F2	1: 10	87.91±1.42	12.09±1.42	29.83±0.281	55.30±1.235
F3	1: 20	86.97±1.89	13.03±1.89	28.19±0.814	70.12±0.284
F4	1: 20	92.49±0.88	7.51±0.88	34.26±1.017	145.74±4.636
F5	1: 15	83.66±1.42	16.34±1.42	25.99±0.516	94.60±1.002
F6	1: 10	77.51±1.90	22.49±1.90	22.65±2.017	85.45±1.912
F7	1: 15	77.34±0.88	21.60±0.88	21.47±1.235	112.21±4.037
F8	1: 20	80.82±1.42	19.18±1.42	25.01±0.918	89.16±1.240
F9	1: 15	73.73±1.89	26.27±1.89	20.66±1.093	98.98±1.288

Table 2: Measurements of particle size by motic microscope

Process Parameters	Actual values
The number of Objects	157
Total Area	76492.2Sq um
Percentage of total area in the whole image	7.01 %
Minimum object Area	3.3 Sq µm
Maximum object area	9852.1 Sq µm
Average object area	294.7 Sq µm
Minimum object Perimeter	2.9 µm
Maximum object Perimeter	4.9µm
Average object Perimeter	3.72 µm

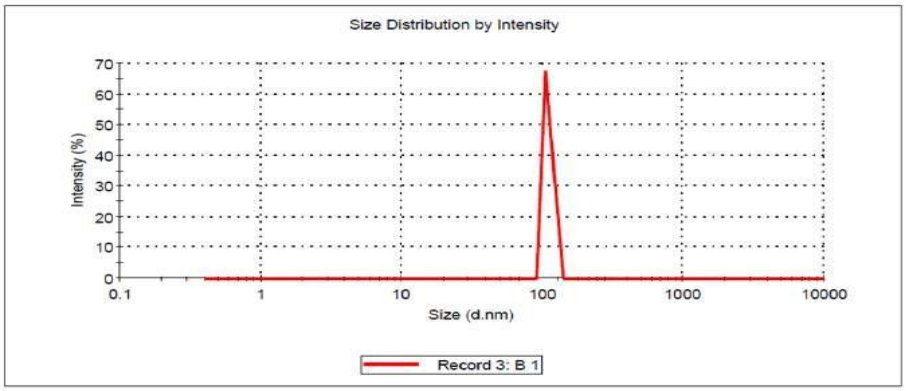

Fig 10: Particle size analysis of formulation (F4)

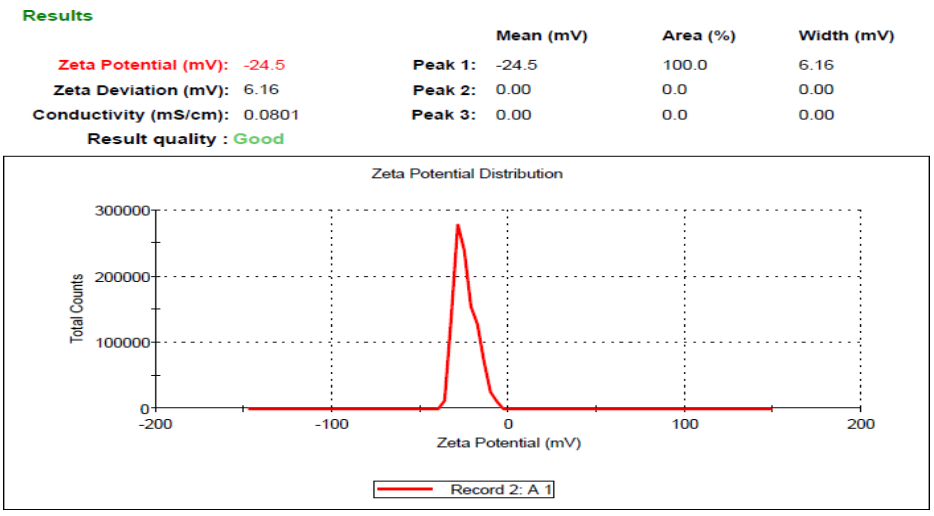

Fig11 : Zeta potential plot of formulation (F4)

Energy dispersive X-ray analysis (EDS):

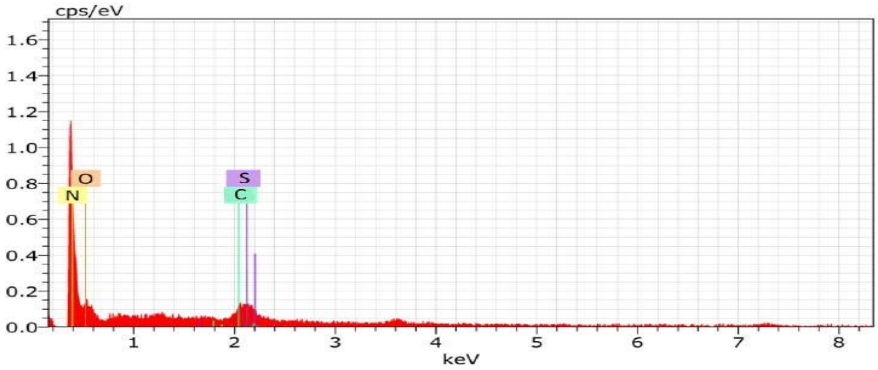

Fig 12: EDS analysis of freeze dried RM-NSGs

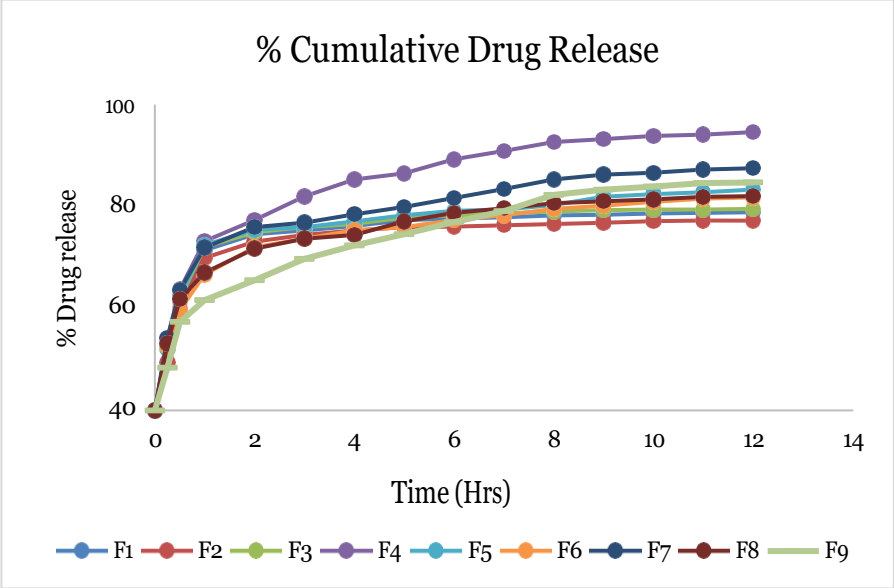

Fig13 : Release profile of different formulations of RM-NSGs.

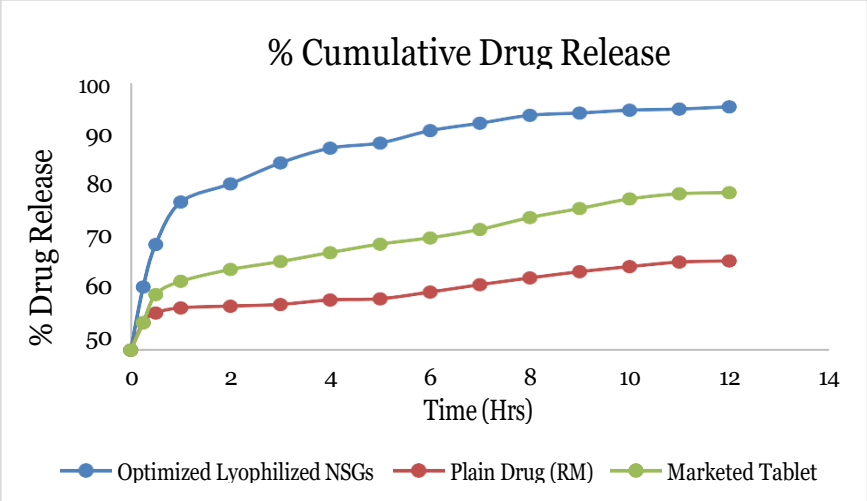

Fig 14 : Release profile of Plain drug-RM, Marketed tablet and optimized lyophilized RM-NSGs

Table 3: 1) Stability study of RM-NSGs

Time (Month/s)	Physical Appearance	Particle size (nm)	Entrapment Efficiency (%)	% CDR	Solubility (µg/ml)
25±2ºC/65± 5% RH					
0	white crystalline powder	108.38±0.25	92.49±1.76	90.77	145.74±0.887
3	white crystalline powder	109.86±0.11	92.20±1.83	90.98	142.85±2.713
6	white crystalline powder	110.01±0.10	92.20±1.83	89.93	141.38±1.296
30±2ºC/70±5% RH					
0	white crystalline powder	108.70±0.27	92.78±1.34	91.19	144.34±0.294
3	white crystalline powder	109.92±0.10	91.90±2.69	91.83	143.40±1.099
6	white crystalline powder	10.58±0.31	91.61±2.33	90.78	141.78±1.898
40±2ºC/ 75±5% RH					
0	white crystalline powder	108.92±0.27	91.61±1.76	90.77	144.41±0.317
3	white crystalline powder	110.39±0.24	91.32±2.21	91.40	143.47±0.871
6	white crystalline powder	110.63±0.21	91.90±1.83	90.98	142.98±0.915

a *Observed values: Mean ±S.D., n=3)*

CONCLUSION

The study successfully developed RM-loaded nanosponges using β-cyclodextrin and dimethyl carbonate. The nanosponges exhibited a narrow particle size distribution, high entrapment efficiency, and sustained drug release. The optimized formulation showed improved solubility and stability of RM, making it a promising candidate for the controlled delivery of poorly water-soluble drugs. Further in vivo studies are warranted to evaluate the pharmacokinetic and pharmacodynamic properties of the RM-loaded nanosponges.

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