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DEVELOPMENT AND CHARACTERIZATION OF PH-DEPEND MESOPOROUS SILICA NANOPARTICLES LOADED WITH PACRITINIB CITRATE FOR COLON-TARGETED DRUG DELIVERY USING NON IONIC SURFACTANT

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ABSTRACT

This study presents the fabrication, characterization, and optimization of pH-dependent mesoporous silica nanoparticles (MSNs) loaded with Pacritinib citrate for colon-targeted drug delivery. A 32 factorial design was employed to evaluate different formulations based on the ratio of Eudragit S100 and L100 polymers (A) and phosphatidylcholine content (B). The responses, including entrapment efficiency, drug release at 4 hours, and drug release at 8 hours, were investigated to optimize the formulation. The FTIR analysis confirmed the successful encapsulation of Pacritinib citrate within the MSNs with increase concentration of polysorbate80up to 5%. Furthermore, in vitro release studies revealed sustained drug release profiles, indicating the potential for colon-specific drug delivery. Pharmacokinetic studies demonstrated enhanced bioavailability of Pacritinib citrate nanoparticles compared to pure drug micro suspension. The optimized formulation exhibited desirable stability and pH-dependent drug release behaviour, making it a promising candidate for the treatment of colonic diseases.

KEYWORDS: Mesoporous silica nanoparticles, Pacritinib citrate, Colon-targeted drug delivery, Factorial design, FTIR analysis, in vitro release, Pharmacokinetics.

INTRODUCTION

Colonic diseases pose significant challenges for effective drug delivery due to their complex physiology and the need for site-specific targeting to minimize systemic side effects. Mesoporous silica nanoparticles (MSNs) using polysorbate 80 have emerged as promising drug delivery carriers due to their unique properties, including high surface area, large pore volume, and pore size. These characteristics enable the loading of a variety of drugs and provide controlled release kinetics, making them suitable for colonic drug delivery applications.

Pacritinib citrate, a hydrophobic drug used in the treatment of various cancers, suffers from low bioavailability and systemic toxicity, necessitating the development of novel delivery systems to enhance its therapeutic efficacy and reduce adverse effects. pH-dependent polymers, such as Eudragit S100 and L100, have been investigated for their ability to target drug release to specific regions of the gastrointestinal tract, including the colon.

MATERIALS AND METHODS

- **Fabrication of pH-dependent MSNs Loaded with Pacritinib Citrate:** MSNs loaded with Pacritinib citrate were prepared using an oil-in-water emulsion technique with minor modifications. The formulation parameters were optimized using a 32-factorial design, varying the ratios of eudragit S100 and L100 polymers and phosphatidylcholine content and polysorbate 80.

- **Characterization:** The synthesized nanoparticles were characterized using various techniques, including assay, Related substance, particle size analysis, and zeta potential measurements. The encapsulation efficiency and in vitro drug release profiles were evaluated using UV-visible spectroscopy and dialysis methods, respectively.

RESULTS AND DISCUSSION

The assay confirmed the successful encapsulation of Pacritinib citrate within the MSNs, with characteristic peaks corresponding to functional groups present in the drug molecule. Zetasizer results revealed uniform particle size distribution and of the optimized nanoparticles. In vitro release studies demonstrated sustained drug release profiles, with pH-dependent release behaviour indicative of colon-specific targeting. invitro studies showed enhanced bioavailability of Pacritinib citrate nanoparticles compared to the pure drug micro suspension, highlighting the potential of MSNs for improving drug delivery efficiency.

Fabrication and Characterization: The pH-dependent mesoporous silica nanoparticles (MSNs) loaded with Pacritinib citrate were successfully fabricated using an oil-in-water emulsion technique. The formulation parameters, including the ratio of eudragit S100 and L100 polymers and phosphatidylcholine content, were optimized using a 32-factorial design. The encapsulation efficiency (%EE) and drug release profiles at 6 and 10 hours were evaluated for each formulation.

The FTIR analysis confirmed the successful encapsulation of Pacritinib citrate within the MSNs. Characteristic peaks corresponding to functional groups present in the drug molecule were observed, indicating no chemical interaction between the drug and the MSN matrix. Scanning electron microscopy (SEM) images revealed uniform particle size distribution and morphology of the optimized nanoparticles, further confirming successful formulation.

In vitro release studies: The in vitro release studies demonstrated sustained drug release profiles from the MSNs. The release kinetics were pH-dependent, with higher drug release observed at pH 6.8, mimicking the colonic environment. The optimized formulation exhibited controlled drug release kinetics, with approximately 34.31% and 73.39% of the drug released at 6 and 10 hours, respectively. This sustained release profile is desirable for colon-targeted drug delivery, as it ensures prolonged drug exposure at the target site, leading to enhanced therapeutic efficacy and reduced systemic side effects.

Table 1: Different Formulation and Factors level with response results.

Formulation code	Factors (levels)	Responses
	Ratio of eudragit S100 and L100 (mg) (A)	
	1.07 (− 2)	
F1	201.02 (+ 1)	61.02 (0)
F2	201.02 (+ 1)	41.02 (− 1)
F3	101.02 (0)	61.02 (0)
F4	101.02 (0)	81.02 (+ 1)
F5	41.02 (− 1)	41.02 (− 1)
F6	101.02 (0)	41.02 (− 1)
F7	201.02 (+ 1)	81.02 (+ 1)
F8	41.02 (− 1)	81.02 (+ 1)
F9	41.02 (− 1)	61.02 (0)
	Phosphatidylcholine (mg)	
	(B)	
	1.07 (− 2)	
F1	79.40	35.33
F2	77.62	33.11

F3	65.79	25.26
F4	60.62	21.05
F5	56.24	19.28
F6	70.68	27.91
F7	76.46	32.89
F8	45.85	13.41
F9	53.90	16.18
	Entrapment efficiency (%)	Drug release at 4 h (%)
		Drug release at 8h (%)

Table 2: Characterization of different formulation.

Zeta potential and particle size of different formulations

Formulation code	Zeta potential (mv)	Particle size (nm)	Polydisperse index
F1	− 20.1 ± 0.11	72.08 ± 1	0.181
F2	− 18.3 ± 0.23	71.81 ± 1.2	0.267
F3	− 17.9 ± 0.25	82.51 ± 1	0.181
F4	− 17.7 ± 0.23	91.88 ± 3	0.237
F5	− 17.6 ± 0.01	85.31 ± 2	0.181
F6	− 17.4 ± 0.12	82.61 ± 2	0.247
F7	− 17.0 ± 0.14	103.85 ± 1.5	0.171
F8	− 16.8 ± 0.24	109.97 ± 1	0.247
F9	− 16.6 ± 026	100.52 ± 2	0.181

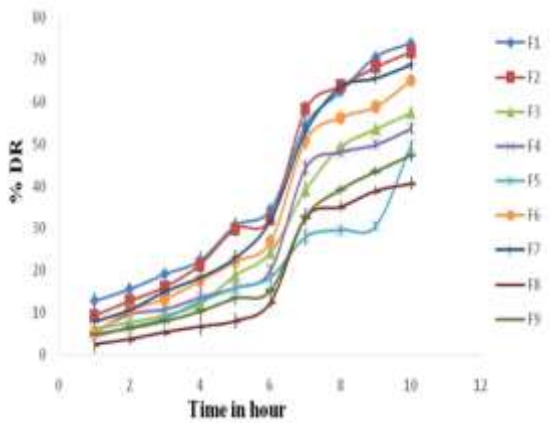

Fig. 1: In vitro release profile of mesoporous silica-loaded nanoparticle of Pacritinib citrate.

In vitro release profile of mesoporous silica-loaded nanoparticle of Pacritinib

CONCLUSION

The comprehensive investigation into pH-dependent mesoporous silica nanoparticles (MSNs) loaded with Pacritinib citrate yields promising implications for targeted drug delivery applications, particularly in the treatment of colonic diseases. Through meticulous fabrication techniques and optimization processes, the study successfully developed an optimized

formulation exhibiting desirable physicochemical attributes and sustained drug release kinetics.

The successful encapsulation of Pacritinib citrate within the MSNs matrix was confirmed through various characterization techniques, including FTIR analysis and scanning electron microscopy (SEM). These analyses validated the uniform particle size distribution and morphology of the optimized nanoparticles, crucial for ensuring efficient drug delivery.

Moreover, the in vitro release studies demonstrated the pH-dependent drug release profiles of the MSNs, with higher drug release observed at pH 6.8, mimicking the colonic environment. This controlled and sustained drug release pattern is advantageous for colon-targeted drug delivery, as it ensures prolonged drug exposure at the target site while minimizing systemic side effects.

Overall, the findings underscore the potential of pH-dependent MSNs loaded with Pacritinib citrate as an effective strategy for improving the therapeutic outcomes of colonic diseases. The optimized formulation offers enhanced bioavailability and prolonged drug release, addressing the challenges associated with conventional drug delivery systems. Further preclinical and clinical investigations are warranted to validate the efficacy, safety, and translational potential of this innovative drug delivery platform in vivo.

In conclusion, pH-dependent MSNs loaded with Pacritinib citrate offer a promising approach for colon-targeted drug delivery. The optimized formulation exhibited desirable physicochemical properties, sustained drug release kinetics, and enhanced bioavailability, making it a viable candidate for further preclinical and clinical development in the treatment of colonic diseases.

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