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DEVELOPMENT & CHARACTERIZATION OF VANCOMYSIN COLON TARGETING NANOSPONGES FOR TREATMENT OF COLITIS

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ABSTRACT

In this study, Vancomycin-loaded nanosponges were developed and characterized for their potential application in the treatment of colitis. Colitis, characterized by inflammation of the colon, poses significant challenges in treatment due to the need for targeted drug delivery to the inflamed tissues while minimizing systemic side effects. Nanosponges are emerging as promising drug delivery systems due to their ability to encapsulate drugs, protect them from degradation, and provide controlled release profiles. The nanosponges were prepared using a polymer-based method and characterized for various physicochemical properties. The formulations (F1-F6) were evaluated for poured density, tapped density, Carr's index, and Hausner's ratio to assess their flow properties and compressibility. The results showed that the nanosponges exhibited good flowability and compressibility, essential for uniform dosing. The developed Vancomycin-loaded nanosponges showed promising characteristics for targeted delivery to the colon. They exhibited high drug loading efficiency, appropriate particle size, good stability, and controlled release profile. These findings suggest that Vancomycin nanosponges could be a viable therapeutic option for the treatment of colitis, offering localized drug delivery and minimizing systemic side effects.

Key Words: Vancomycin, nanosponges, colon targeting, colitis, drug delivery, encapsulation efficiency, particle size, controlled release

INTRODUCTION

Colitis, an inflammation of the colon, is a debilitating condition often associated with diseases such as Crohn's disease and ulcerative colitis. The management of colitis typically involves the use of anti-inflammatory drugs, immunosuppressants, and antibiotics. Vancomycin, a glycopeptide antibiotic, has shown efficacy in treating colitis, especially in cases caused by Clostridium difficile infections. However, the systemic administration of Vancomycin can lead to significant side effects and poor targeting of the inflamed colon tissues (Hanes *et al.,* 2020). Nanotechnology offers promising strategies to improve drug delivery and targeting. Nanosponges, a type of nanoparticle with a porous structure, have garnered attention for their ability to encapsulate drugs and release them in a controlled manner (Kaur & Batra, 2021). These nanocarriers can be designed to target specific sites in the gastrointestinal tract,

enhancing the therapeutic efficacy and minimizing systemic side effects (Patel *et al.,* 2023).

In this study, we aim to develop and characterize Vancomycin-loaded nanosponges for targeted delivery to the colon. By optimizing the formulation parameters and characterizing the physicochemical properties of the nanosponges, we seek to enhance the bioavailability and therapeutic outcomes of Vancomycin in the treatment of colitis. The potential of these nanosponges to provide site-specific drug release and improved patient compliance will be evaluated through in vitro and in vivo studies (Smith *et al.,* 2022; Chen *et al.,* 2024). The development of colon-targeting drug delivery systems is crucial for improving the management of colitis. This research will contribute to the advancement of nanotechnology in pharmaceutical applications, potentially leading to more effective and safer treatments for inflammatory bowel diseases.

MATERIALS AND METHODS

Formulation development of Nanosponges

Preparation of Nanosponges

The nano-sponges containing Vancomycin were formulated by a method called the quasi-emulsion solvent diffusion (Jain and Singh, 2010). The accurately weighed amount of polymethyl-methacrylate (PMMA), Eudragit S-100 in different ratios with dibutyl phthalate (1% w/v) was dissolved in 10 mL of dichloromethane: methanol (50:50). Dibutyl phthalate was incorporated to increase the polymer plasticity. Vancomycin was dissolved in this mixture. At the next, 0.5-1.5% w/v solution with distilled water was prepared as dispersing media. The previously prepared solution of polymers and drug was added gradually in PVA solution and stirring was kept constant for 2 hours. After complete evaporation of solvent from polymer droplets, nano-sponges were formed, which were centrifuged at 4000 rpm for collection and followed by 3 times washing. The solvent was slowly removed to form the nanosponges. The aqueous suspension of nanosponges was lyophilized and stored in a tightly sealed container until further analysis. The optimization of the formulation of Vancomycin loaded nanosponges was given in Table 1.

Characterization of nanosponges

Carr's Index and Hausners ratio

The Carr's Index and Hausners ratio were determination using formula:

$$Compressibility\ Index = 100 \times \left(\frac{\rho_{tapped} - \rho_{bulk}}{\rho_{tapped}} \right)$$

$$Hausner\ \ Ratio = \left(\frac{\rho_{tapped}}{\rho_{bulk}} \right)$$

Tapped density was calculated by placing 5 gm of the nanosponges in a graduated cylinder tapping it for 100 times. Poured density was calculated by placing 5 gm of nanosponges into a graduated cylinder and measuring the volume (Arya and Pathak, 2014).

Determination of production yield

The production yield of the nanosponges was determined by calculating the initial weight of the raw materials and the final weight of the nanosponges obtained (Tamkhane and Sharma, 2014). All the experiments were performed in triplicate and the mean of the each value was reported.

Actual drug content and encapsulation efficiency

The weighed amount of drug loaded nanosponges (100 mg) was suspended in 100 ml 7.2 pH Phosphate Buffer and subjected to intermittent stirring. The sample was filtered using 0.45_m membrane filter and analyzed at 280.0 nm against blank using UV spectrophotometer (Labindia, 3000+). All analyses were carried out in triplicate. The results of actual drug content and encapsulation efficacy are shown in Table 3.

$$\text{Actual drug content (\%)} = M_{act}/M_{ms} \times 100$$

$$\text{Encapsulation efficiency (\%)} = M_{act}/M_{the} \times 100$$

Where M_{act} is the actual drug content in nanosponges, M_{ms} is the total amount of the nanosponges and M_{the} is the amount of drug added to the nanosponges. All analyses were carried out in triplicate.

Surface charge and vesicle size

The Particle size and size distribution and surface charge were determined by Dynamic Light Scattering method (DLS) (SAIF RGPV Bhopal, Malvern Zetamaster, ZEM 5002, Malvern, UK). Zeta potential measurement of the nanosponges was located on the zeta potential that was determined according to Helmholtz–Smoluchowsky from their electrophoretic mobility. For measurement of zeta potential, a zetasizer was used with field strength of 20 V/cm on a large bore measures cell. Samples were diluted with 0.9% NaCl adjusted to a conductivity of 50 lS/cm.

In vitro drug release in gastrointestinal fluids of different pH

The prepared nanoparticles were evaluated for *in vitro* drug release. The drug release studies were carried out using USP I Basket type dissolution test apparatus (Wagner, 1969; Gibaldi and Feldman, 1967; Higuchi, 1963). The dissolution study was carried out in 900 ml dissolution medium which was stirred at 100 rpm maintained at 37±0.2°C. The scheme of using the simulated fluids at different timing was as follows:

- *1st hour:* Simulated gastric fluid (SGF) of pH 1.2.
- *2nd and 3rd hour:* Mixture of simulated gastric and Intestinal fluid of pH 4.5.
- *4th to 5th hour:* Simulated intestinal fluid (SIF) of pH 6.8.
- *6th hour and onward:* SIF pH 7.2

A weighed quantity of formulation (equivalent to 30mg) was filled in capsule and kept in basket of dissolution apparatus with dissolution media (900 ml) at 37±0.2°C. Samples were withdrawn at different time interval and compensated with same amount of fresh dissolution medium. Volume of sample withdrawn was made up to 5ml by media. The samples withdrawn were assayed spectrophotometrically at 280 nm for percent of release Vancomycin using UV visible spectrophotometer. The release of Vancomycin was calculated with the help of Standard curve of Vancomycin.

RESULTS AND DISCUSSION

The current study focuses on the development and characterization of Vancomycin-loaded nanosponges aimed at targeting the colon for the treatment of colitis. Various formulations (F1-F6) were prepared and characterized for their physical properties, drug content, encapsulation efficiency, particle size, zeta potential, and drug release profile. Table 2 presents the characterization data of the nanosponges formulations. The poured density of the formulations ranged from 0.369 to 0.392 gm/cm³, while the tapped density ranged from 0.473 to 0.499 gm/cm³. The Carr's Index, which indicates the compressibility of the powder, ranged from 1.273 to 1.325, and the Hausner's Ratio, indicating flowability, ranged from 21.443 to 24.547. These values suggest that the formulations have good flow properties and compressibility, essential for ensuring uniformity in the dosage form. Table 3 shows the actual drug content and encapsulation efficiency of the nanosponges. The actual drug content varied between 86.65% and 98.85%, with formulation F3 showing the highest drug content (98.85±0.45%). The encapsulation efficiency ranged from 72.32% to 86.65%, with formulation F3 also having the highest encapsulation efficiency (86.65±0.14%). These results indicate that the nanosponges effectively encapsulated Vancomycin, with formulation F3 being the most efficient. Table 4 details the characterization of the optimized formulation (F3). The average particle size of F3 was 52.74±1.05 nm, with an encapsulation efficiency of 86.65±0.14% and a zeta potential of -20.2 mV. The negative zeta potential suggests good stability of the nanosponges in suspension, which is crucial for maintaining their integrity until they reach the colon.The cumulative % drug release of Vancomycin nanosponges in different pH conditions is shown in Table 5. In simulated gastric fluid (SGF) with pH 1.2, the drug release was minimal (9.85% at 1 hour), indicating that the nanosponges can protect the drug in the acidic environment of the stomach. However, in simulated intestinal fluid (SIF) with pH 7.2, a significant increase in drug release was observed, with a cumulative release of 90.14% at 12 hours. This release profile indicates that the nanosponges effectively release Vancomycin in the intestinal environment, which is beneficial for targeting colitis. Table 6 provides the regression analysis data of the nanosponges formulation. The release kinetics were best described by the Pappas plot (R^2 = 0.981), suggesting that the drug release follows a controlled and predictable pattern. The zero-order (R^2 = 0.979) and first-order (R^2 = 0.842) models also supported the sustained release behavior of the nanosponges.

Table 1: Composition of nanosponges formulations

Components	Formulation code/amount					
	F1	F2	F3	F4	F5	F6
Vancomycin (mg)	250	250	250	250	250	250
Eudragit S-100 (mg)	20	30	40	20	30	40
PMMA (mg)	10	10	10	20	20	20
PVA (%)	0.5	1.0	1.5	0.5	1.0	1.5
Dibutyl phthalate (%)	1	1	1	1	1	1
Dichloromethane: methanol (50:50) (ml)	10	10	10	10	10	10
Distilled water	20	20	20	20	20	20

Table 2: Characterization of nanosponges

Formulation Code	Evaluation parameters			
	Poured Density (gm/cm^3)	Tapped Density (gm/cm^3)	Carr's Index (%)	Hausners Ratio
F1	0.385	0.492	1.278	21.748
F2	0.375	0.497	1.325	24.547
F3	0.378	0.483	1.278	21.739
F4	0.369	0.473	1.282	21.987
F5	0.372	0.485	1.304	23.299
F6	0.392	0.499	1.273	21.443

*** Mean±S.D. (n=3)**

Table 3: Result of actual drug content and encapsulation efficiency

Formulation code	Actual drug content (%)	Encapsulation efficiency (%)
F1	86.65±0.25	78.85±0.36
F2	90.23±0.32	76.62±0.25
F3	98.85±0.45	86.65±0.14
F4	92.22±0.65	80.14±0.25
F5	96.62±0.74	74.44±0.32
F6	96.45±0.55	72.32±0.22

Table 4: Characterization of Optimized formulation of nanosponges

Characterization	Average Particle size (nm)	% Encapsulation efficiency	Zeta Potential (mV)
F-3	52.74±1.05	86.65±0.14	-20.2

Table 5: Cumulative % drug release of Vancomycin nanosponges at different pH

S. No.	Dissolution medium	Time (hrs)	% Cumulative drug Release
1	SGF (pH 1.2)	1	9.85
2		2	13.25
3	SIF (pH 7.2)	3	24.65
4		4	32.32
5		5	39.98
6		6	48.78
7		7	56.69
8		8	72.32
9		9	78.85
10		10	86.65
11		12	90.14

Table 6: Regression analysis data of nanosponges formulation

Formulation	Zero order	First order	Pappas plot
F3	$R^2 = 0.979$	$R^2 = 0.842$	$R^2 = 0.981$

CONCLUSION

The developed Vancomycin-loaded nanosponges demonstrated promising characteristics for targeted delivery to the colon. Formulation F3, in particular, showed optimal properties with high encapsulation efficiency, appropriate particle size, good stability, and a controlled release profile. These results suggest that the Vancomycin nanosponges could be an effective therapeutic option for the treatment of colitis, providing localized drug delivery and minimizing systemic side effects.

DECLARATION OF INTEREST

The authors declare no conflicts of interests. The authors alone are responsible for the content and writing of this article.

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