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Original Article

Mesalamine-Loaded Microsponges as a Potential Strategy for Colon-Specific Anti-Inflammatory Therapy: Design and Evaluation

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ABSTRACT

Background: This study aimed to develop an efficient drug delivery system targeting the colon to treat inflammatory conditions using mesalamine. The approach involved formulating microsponges with Eudragit polymers, focusing on assessing the *in vitro* drug release patterns. **Materials and Methods:** The quasi-emulsion solvent diffusion method was employed using various Eudragit polymers (S100, L100, RS100 and RL100). Critical parameters, such as entrapment efficiency, particle size and drug release, were systematically examined. Different kinetic models have been used to understand the mechanism of drug release. **Results and Discussion:** The developed microsponges met the desired entrapment efficiency and particle size standards. Drug release from these formulations exhibited a diffusion-based pattern aligned with a zero-order kinetic model. Initial 1-2 hr showed minimal drug release (2-1%), whereas a significant release (92-95%) occurred within 24 hr for formulations F1 and F2. This release behaviour suggests the potential of sustained and pH-dependent drug delivery applications. **Conclusion:** This study contributes to the field by successfully designing a colon-targeted drug delivery system for mesalamines. Using Eudragit polymers and incorporating microsponges showed the potential for sustained drug release, emphasizing their applicability for treating inflammatory colon conditions. This study provides a foundation for future drug-delivery systems targeting specific gastrointestinal regions.

Keywords: Mesalamine, microsponges, colon targeting, drug content, entrapment efficiency, particle size, *in vitro* drug release.

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INTRODUCTION

Inflammatory Bowel Disorder (IBD) is a type of chronic inflammatory condition that affects the digestive tract, with Crohn's Disease (CD) and Ulcerative Colitis (UC) being the most common. The CD is linked to transmural inflammation and ulcers throughout the Gastrointestinal Tract (GIT), fistulas, deep fissuring ulcers and abscesses. In contrast, the mucosa and submucosa of the colon and rectum are vulnerable and are mainly linked to crypt distortion and abscesses. Bloody diarrhoea, fever, weight loss, stomach pain, or vomiting are signs of Crohn's disease. Both disorders can raise the chance of death in extreme circumstances.[1-3]

Conventional oral formulations used in the treatment of Inflammatory Bowel Disease (IBD) have inherent limitations due to their primary emphasis on achieving systemic administration of medicines. However, for the local therapy of inflammatory disorders such as IBD, colonic cancer and other colonic pathologies, targeted drug administration directly into the colon is highly desirable. Delivering medications specifically to the colon minimizes systemic exposure, reduces side effects and enhances localized therapeutic effects, ultimately resulting in improved efficacy and a safer treatment approach. Moreover, targeted drug delivery to the colon offers the advantage of improved patient compliance. Many individuals with IBD and other colonic disorders require long-term medication and conventional oral formulations can be associated with unpleasant side effects. By delivering the medication directly to the colon, targeted therapy reduces the likelihood of systemic side effects, such as nausea or fatigue. It improves patient tolerance and acceptance of the treatment.[4,5]

Colon-specific Drug Delivery Systems (DDSs) offer many advantages over conventional oral formulation, making them a promising approach for treating various colonic disorders. These advantages include maintaining a near-neutral pH,

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prolonging transit time in the colon, reducing enzymatic activity, achieving high local drug concentration with minimal adverse effects, especially for anti-inflammatory medications, avoiding undesired digestion and enhancing overall drug bioavailability. By harnessing these benefits, colon-specific DDSs provide an improved and optimized therapeutic approach for targeted drug delivery to the colon, addressing the limitations of conventional therapy and enhancing patient outcomes.[6]

When these delivery systems are administered orally, they allow medications to be released from the delivery system once they reach the colon. These delayed methods improve the treatment's efficacy by concentrating the drug molecules where they are most needed and reducing the risk of adverse effects and drug instability associated with the drug's premature release.[7-9]

Coating with polymers, coating with pH-sensitive polymers, coating with biodegradable polymers, time-dependent approach, pressure-dependent approach, microbially controlled delivery, osmotically controlled approach, prodrug approach, bioadhesive system, are the approaches for colon targeting via the oral route.[8]

Micro sponges are porous microspheres with several consistent voids ranging from 5 to 300 μm.[9] They are polymeric delivery systems of tiny sponge-like spherical particles with many interconnected gaps within a non-collapsible framework with a porous concrete surface. They may improve medication stability, lessen side effects and positively alter drug release. They are simple to prepare, which makes them attractive in targeted drug delivery systems.[10-14]

Though the non-selective cyclooxygenase inhibitors class links to IBD exacerbation and remission, non-steroidal anti-inflammatory medicines have been studied for their benefits in treating colonic disorders, even though selective Cyclooxygenase-2 (COX-2) inhibitors have improved tolerability and safety in IBD patients, many COX-2 medicines were pulled from the market due to cardiovascular side effects.[15,16]

Mesalamine, a locally acting aminosalicylate utilized in treating inflammatory bowel diseases such as ulcerative colitis and Crohn's disease, faces challenges when administered orally. Using mesalamine orally increases systemic adverse effects and absorption from the upper gastrointestinal tract. Moreover, mesalamine is rapidly and extensively metabolized in the intestinal mucosal membrane and the liver, primarily forming N-acetyl-5-ASA. This extensive metabolism reduces medication bioavailability when administered through traditional oral dose forms. The elimination half-life of Mesalamine is estimated to range between half and 1.5 hr.[17,18]

So, developing colon-targeted formulations using pH-sensitive polymers of mesalamine as microsponges, is expected to have effective localized and controlled drug therapy to colonic tissue and circumvent the limitations of traditional oral formulations. This precise approach of utilizing microsponges demonstrates a targeted and optimized strategy for improving the effectiveness and bioavailability of mesalamine in treating colonic inflammatory conditions.

The focus of this study was to enhance the therapeutic effectiveness of mesalamine by employing a targeted drug delivery system. This system incorporates pH-sensitive polymers of mesalamine, enabling a precise and localized impact on the inflamed tissues of the colon.

MATERIALS AND METHODS

Mesalamine gifted from chemicals Hyderabad. Eudragit S 100, L 100, RS 100 and RL 100 p were gifted from Evonic Industries Mumbai and Polyvinyl Alcohol (PVA) and glycerine were purchased from Loba Chemicals Ltd Mumbai.

Fourier transform infrared spectroscopy (FTIR)

The FTIR spectrophotometer was employed to acquire FTIR spectra for a physical blend comprising the pure drug and polymers. A KBr disc was created by compressing 1-2 mg of material with an equivalent weight of dehydrated potassium bromide. For compatibility verification, the samples underwent scanning using a Shimadzu Model 8400 FTIR spectrometer, covering the range of 500 to 4000 cm^{-1}.[19]

Preparation of drug-loaded microsponges

In developing drug-loaded microsponges, the quasi-emulsion solvent diffusion approach was utilized based on preliminary observations. The polymers Eudragit S-100, Eudragit L-100, Eudragit RL100 and Eudragit RS100 were dissolved in a mixture of dichloromethane and methanol (1:1 ratio) to create an internal phase. Mesalamine, the drug of interest, was incorporated into the internal phase, which was then poured into the external phase consisting of an aqueous solution of surfactant (polyvinyl alcohol) and plasticizer (glycerine) while stirring at a speed of 1000 rpm, as indicated in Table 1. The emulsion was continuously stirred for up to 8 hr. The resulting product was subsequently filtered and subjected to drying at 40°C for 12 hr to obtain microsponges.[19-21]

Evaluation of microsponges

Particle Size

The particle size of the microsponges was determined using optical microscopy. After dispersing in liquid paraffin, the micro sponges and their particle size were measured using an eyepiece micrometre calibrated against a stage micrometre. One hundred particles were measured to ensure accuracy and the average particle size was calculated based on these measurements. The mean particle size and size distribution of the selected formulation were examined using the Horiba SZ-100 nanoparticle Dynamic Light Scattering (DLS) equipment at 25.2°C, sample dispersion

Table 1: Formulation Chart.

Sl. No.	Formulation	Drug (mg)	Polymers(mg)				Org Phase (mL)	Aq. Phase (mL)	PVA (%)	Glycerine (%)
			S-100	L-100	RS-100	RL-100				
1	F1	500	500	-	-	-	10	25	1	0.1
2	F2	500	-	500			10	25	1	0.1
3	F3	500	-	-	500		10	23	1	0.1
4	F4	500	-	-	-	500	10	25	1	0.1
5	F5	500	250	250	-	-	10	25	1	0.1
6	F6	500	-	-	250	250	10	25	1	0.1
7	F 7	500	125	125	125	125	10	25	1	0.1

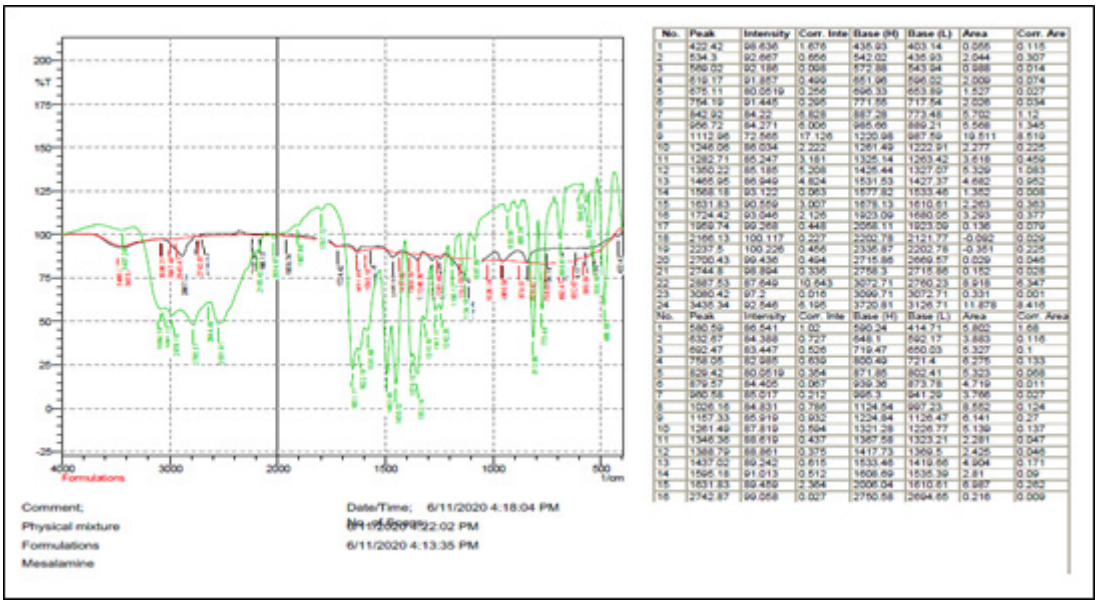

Figure 1: IR spectra of mesalamine, physical mixture and formulation.

was created and particle size was measured three times at a scattering angle of 90°.[22]

Drug entrapment efficiency

To determine the drug concentration in Mesalamine microsponges, 10 mg of microsponges were weighed and dissolved in phosphate buffer solution pH 7.4; after suitable dilutions, the absorbance of the solution was measured at 331 nm using a spectrophotometric technique, with blank microsponges treated in the same manner serving as a reference. To determine free drug concentration, 10 mg of mesalamine microsponges were weighed and mixed with 10 mL of hot water. The mixture was then centrifuged at 2500 rpm for 30 min. The supernatant was collected, filtered and diluted with phosphate buffer solution pH 7.4. The absorbance of the diluted solution was measured at 331 nm using a spectrophotometric technique, using blank microsponges as a control.[23] The drug entrapment efficiency is determined by the formula:

$$\frac{Total\ drug\ content - Free\ drug\ content}{Total\ drug\ content}$$

In vitro drug release studies

In the *in vitro* drug release studies, microsponges were subjected to the USP dissolution apparatus II under simulated physiological conditions. The microsponges were exposed to fluids with different pH values to mimic the pH variations in different gastrointestinal tract regions. Specifically, the microsponges were exposed to Simulated Gastric Fluid (SGF) with a pH of 1.2 for 2 hr. Subsequently, they were exposed to Simulated Intestinal Fluid (SIF) with a pH of 6.8 for 2-4 hr and then to Simulated Colonic Fluid (SCF) with a pH of 7.4 for 10-24 hr at 37°C with agitation at 50 revolutions per minute. Sampling was performed at regular intervals and spectroscopic analysis was carried out at 331 nm using a UV spectrophotometer. Sink conditions were maintained by replacing the withdrawn medium volume. These studies

allowed for assessing the microsponges' drug release profile and kinetics under different pH conditions.[24]

Drug release kinetics

The accuracy and predictability of several kinetic models were examined using R^2 (squared correlation coefficient), utilising KinetDS 3.0 software to fit the release data.[25]

Scanning electron microscopy

A JEOL JSMT-330 Scanning Electron Microscope (SEM) was employed to analyze the morphological characteristics of a specific microsponge formulation. The sample was prepared by placing it on a brass stub and subjecting it to gold sputtering. Gold sputtering, carried out at a pressure of 70 mTorr for 30 sec, involved depositing a thin layer of gold onto the sample's surface. Following this step, the brass stub was removed from the gold sputtering system and transferred to the SEM sample chamber. The SEM imaging was performed under vacuum and at voltages ranging from 1-30 V.[26]

Stability studies

The chosen Formulation (F1) was subjected to a stability study for three months at temperatures of 25±2ºC/60±5% RH and 40±2ºC/75±5% RH, as per ICH recommendations, to assess their stability in terms of physical appearance and drug entrapment efficiency.[27]

RESULTS

FTIR analysis of the physical mixture of Mesalamine and Eudragit revealed characteristic absorption bands corresponding to the functional groups in both components, as shown in Figure 1. In the spectrum, a broad and strong absorption band at 3300-3500 cm^{-1} was observed, indicating the presence of N-H stretching vibrations associated with primary and secondary amines of Mesalamine. Additionally, an intense absorption peak at 1700-1800 cm^{-1} indicated the presence of the Carbonyl (C=O) group in the carboxylic acid functionality of Mesalamine. Furthermore, absorption bands in the range of 1500-1600 cm^{-1} indicated the aromatic rings in Mesalamine. In addition to the characteristic absorption bands observed for Mesalamine, a notable peak corresponding to Eudragit was identified in the FTIR spectrum of the physical mixture. This peak is associated with the ester Carbonyl (C=O) stretching vibration, typically observed in Eudragit based on methacrylic acid derivatives. The peak was observed around 1700-1740 cm^{-1}, indicating the presence of the ester carbonyl group in Eudragit within the physical mixture.[19,20] These results suggest mesalamine's compatibility with various grades of eudragit used in the formations.

Preparation of microsponges

A series of seven formulations were developed using Eudragit L100, S100, RL100 and RS100 polymers in combination with 1% PVA as the surfactant and glycerine, a plasticizing agent. The drug and polymer were mixed in 1:1 to prepare the microsponge formulations. Additionally, the volumes of the internal (organic) and external (aqueous) phases were kept constant, ensuring consistent conditions during the preparation of the micro sponges. This approach allowed for a controlled and comparable evaluation of the different formulations.

Evaluation of microsponges

Particle size

In the study, the particle size of the microsponges was evaluated using optical microscopy. The obtained results are depicted in Table 2. The particle size ranged between 10±0.942 µm and 300±0.8162 µm. The viscosity of various grades of eudragit is the critical factor in maintaining the particle size. Eudragit R100 and S100 have comparatively high viscosity compared to RL and Rs 100 grades. Indicated that it exhibited a larger globule size compared to the other formulations. Increasing the viscosity increases the shear stress and thus breaks down the globule, so there was a reduction in globule size observed when the grade of polymers changed. The distinct properties of different Eudragit grades likely influenced the formation and size of the microsponges, resulting in variations in particle size. Furthermore, Dynamic Light Scattering (DLS) analysis provided a more accurate determination of the particle size of the selected F1 formulation (Figure 2); the particle size was 7.430 µm, which closely aligned with the results obtained through optical microscopy, which is 10 µm (Figure 3). These findings support the reliability of optical microscopy as a method for particle size evaluation and emphasize the impact of Eudragit grades on particle size variations in the microsponge formulations.

Drug entrapment efficiency

The drug entrapment efficiency of the microsponge formulations was assessed and found to be within the range of 62.05±0.42 to 95.23 ±0.59%. The entrapment efficiency was highest for formulations F1 and F2, which used Eudragit L100 and S100, respectively. This may also be due to the viscosity contribution of these formulations compared to the remaining formulation and

Table 2: Particle size and drug entrapment efficiency data.

Formulation	Particle size (µm)	Drug entrapment efficiency (%)
F1	10±0.942	95.23 ±0.59
F2	20±0.471	94.87±0.48
F3	17±0.816	90.12±0.519
F4	70±0.471	91.01±0.438
F5	100±0.816	62.05±0.42
F6	234±0.471	63.11±0.450
F7	300±0.816	70.02±0.435

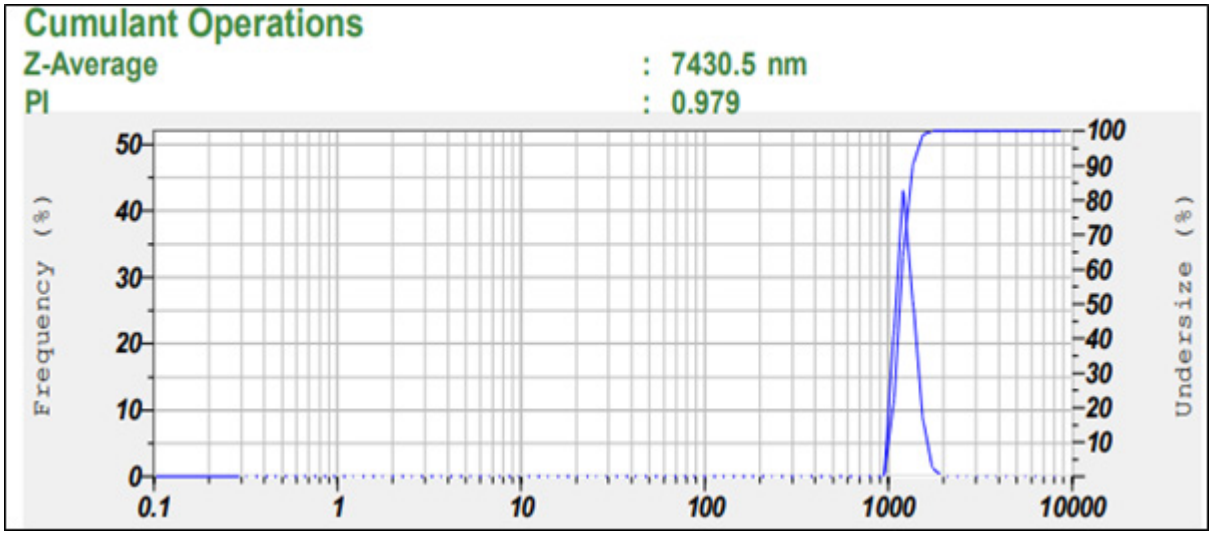

Figure 2: Particle size of F1 formulation by DLS method.

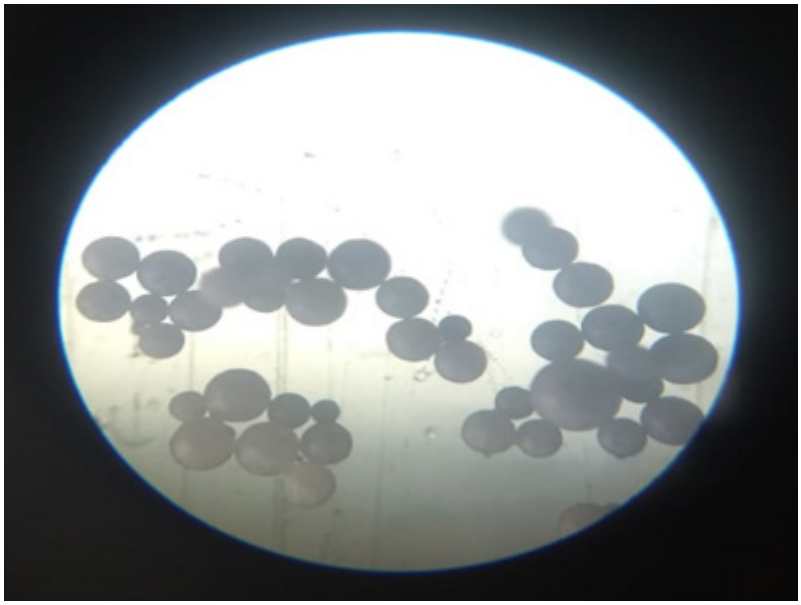

Figure 3: Optical microscopy photograph of F1.

the lower particle size distribution might have helped entrap a large amount of drug into the dispersed globules. Furthermore, F3 and F4 formulations also exhibited high drug loading capacity. However, the drug entrapment efficiency was found to be decreased when a combination of these two polymers was observed in F1 and F6.

In vitro drug release

The *in vitro* drug release profile from the formulations is depicted in Figure 4. As given in the figure, the drug release was found to be in a controlled pattern. In the first two hr, there was no considerable amount of drug release observed from all the formulations. Formulation F3 1.01±0.05% to maximum of 6.12±1.01%. When we see the data for the next 6 hr, a minimum of 40.12±1.12 (F1) to a maximum of 70.45±1.54% is observed. Hereafter, the drug release was slowed down and approximately 40-45% of the drug was released from various formulations for 14 hr. These findings indicate that including Eudragit S100 and Eudragit L100, pH-sensitive polymers with a threshold pH value above 6 and 7, respectively, effectively prevented the premature release of Mesalamine in the upper Gastrointestinal Tract (GIT). Instead, drug release occurred predominantly at pH values above 6, bypassing the upper GIT. Based on these results, it can be concluded that using individual polymers, such as Eudragit S100 or Eudragit L100, yielded relatively higher drug release profiles compared to the combination of polymers, as seen in formulations F5 to F7. These findings highlight the importance of carefully selecting and optimizing polymer combinations to achieve the desired drug release behaviours. Table 3 exemplifies the drug release kinetics of the formulations and it was observed

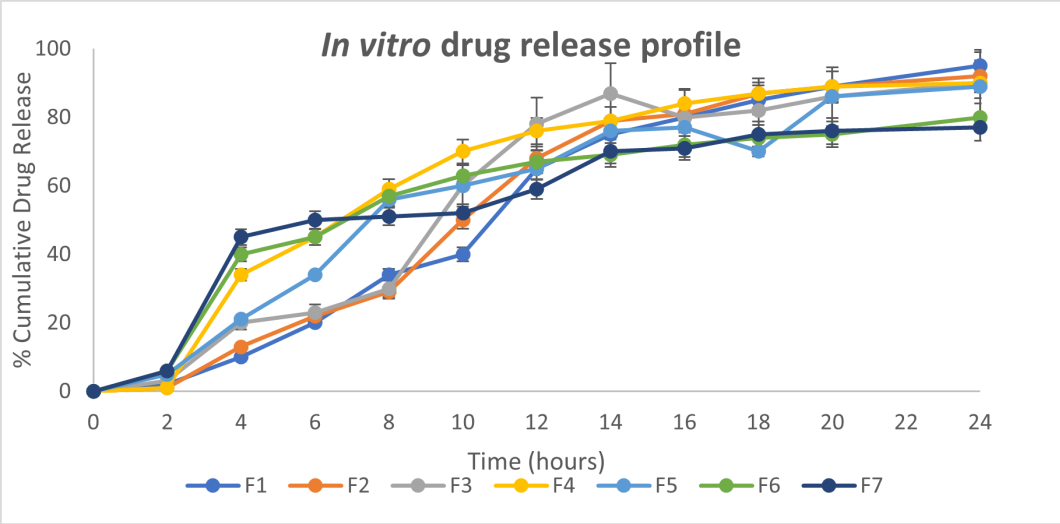

Figure 4: *In vitro* drug release profile of Mesalamine from microsponges.

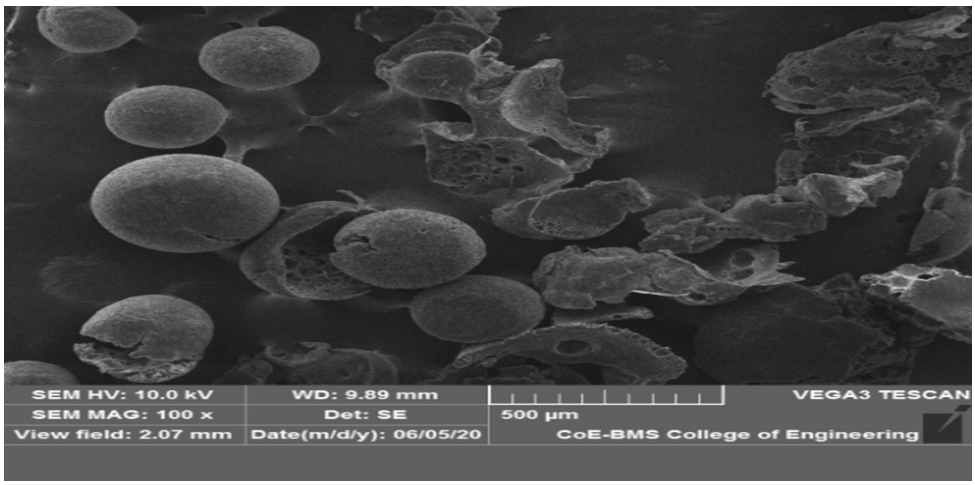

Figure 5: SEM images of F1 formulation.

Table 3: **Drug release kinetics.**

Formulation	Zero order	Korsmeyer - Peppas model	
	R^2	R^2	n
F1	0.9717	0.9837	0.1488
F2	0.9934	0.9949	0.3417
F3	0.9211	0.9765	0.1461
F4	0.7359	0.8738	0.1235
F5	0.9988	0.9897	0.1701
F6	0.9883	0.9863	0.2313
F7	0.9405	0.9732	0.2345

that the drug release followed a zero-order pattern, indicating a zero-order drug release pattern R^2 0.7359-0.9934), and a diffusion-controlled release mechanism (n=0. 0.1235-0.3417) from all the formulations. This also assures a predictable and sustained drug release, ensuring consistent therapeutic effects over an extended period. Drug formulations exhibited maximum particle size and had slower release patterns, which may be the factor of the longer diffusional path to get it released to the outer environment.

Scanning electron microscopy

The formulation F1, which is superior in drug loading, has a smaller particle size and the drug release profile was selected for studying the surface properties. Microsponges exhibited a high

Table 4: Stability studies data of F1 formulation.

Sl. No.	Observation	25±2°C/60% RH±5%	40±2°C/75% RH±5%
1	Entrapment efficiency (%)	93±0.16	85.01±0.23
2	Physical appearance	Buff colored product	Buff colored product

degree of sphericity, as observed in optical microscopy in SEM photographs. They also revealed the presence of minute pores on their surfaces, as depicted in Figure 5. However, there were few with open structures, which depicts the porosity within the particles or spongy structures. The characteristic properties of the microsponges can be attributed to the inclusion of glycerine, a plasticizing agent, in the formulation. The visual inspection confirmed the overall structural integrity of the microsponges; however, the pores appeared more discernible in terms of both size and quantity. This observation suggests a potential detachment of drug molecules from the microsponge surface and a mild erosion phenomenon contributing to drug release properties.

Stability studies

The short-term stability of formulation F1 was assessed over three months under varying temperature and humidity conditions, as represented in Table 4. The physical appearance of F1 remained unchanged throughout the storage period, indicating good physical stability. At 25°C±0.5°C/60% RH, the entrapment efficiency was determined to be 93±0.16%. However, when exposed to a higher temperature of 40°C±2°C/75% RH, the entrapment efficiency slightly decreased. The studies suggest suitable storage conditions for the microsponge formulations.

DISCUSSION

The compatibility study of the drug and excipients revealed no incompatibility. The particle size in the eight formulations ranged from 10±0.942 µm to 300±0.816 µm. The drug entrapment efficiency varied between 62.05±0.42% and 95.23±0.59%. The formulation with the smallest particle size (7.430 µm) and the highest entrapment efficiency was identified through dynamic light scattering. In an acidic environment, the polymers in the microsponges remained intact, resulting in negligible drug release. At pH 6.8, a substantial drug release was observed due to the pH-dependent release properties of Eudragit L 100 and RL 100. Eudragit S 100 and RS100 contributed to a maximum drug release of 40-45% between 10 and 24 hr. The drug release profile followed a zero-order model, indicating a diffusion-controlled mechanism. SEM photographs confirmed the spherical nature of the particles, consistent with optical microscopy findings. Stability studies demonstrated no apparent changes in entrapment efficiency at Room Temperature (RT), with slight alterations observed at elevated temperatures.

CONCLUSION

This investigation aimed to develop and assess microsponges as a localized therapy for inflammatory diseases, specifically Crohn's disease and ulcerative colitis, utilizing Mesalamine. The microsponges were prepared using the quasi-emulsification solvent diffusion method, employing various Eudragit polymers (L100, S100, RL100 and RS100) either alone or in combination. The drug entrapment efficiency of the polymers, both individually and in combination, was found to be satisfactory. *In vitro* drug release studies revealed that utilizing individual polymers, such as Eudragit S100 or Eudragit L100, yielded superior drug release profiles compared to the polymer combinations. Polyvinyl Alcohol (PVA) demonstrated excellent emulsification properties, as evidenced by particle size and drug entrapment efficiency. Overall, the study suggests that Eudragit polymers exhibit promising characteristics for sustained localized drug delivery to the colon, including biocompatibility, non-toxicity, biodegradability and the ability to modulate drug release.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

IBD: Inflammatory Bowel Disease; **CD:** Chron's Disease; **UG:** Ulcerative Colitis; **GIT:** Gastrointestinal tract; **DDS:** Colon specific drug delivery System; **COX:** Cyclooxygenase; **ASA:** Amino Salicylic Acid; **FTIR:** Fourier Transform Infrared Spectroscopy; **DLS:** Dynamic light scattering; **SEM:** Scanning electron microscope.

REFERENCES

1. Danese S, Sans M, Fiocchi C. Inflammatory bowel disease: the role of environmental factors. Autoimmun Rev. 2004;3(5):394-400. doi: 10.1016/j.autrev.2004.03.002, PMID 15288007.
2. Belali N, Wathoni N, Muchtaridi M. Advances in orally targeted drug delivery to colon. J Adv Pharm Technol Res. 2019;10(3):100-6. doi: 10.4103/japtr.JAPTR_26_19, PMID 31334090.
3. Guo Y, Zong S, Pu Y, Xu B, Zhang T, Wang B. Advances in pharmaceutical strategies enhancing the efficiencies of oral colon-targeted delivery systems in inflammatory bowel disease. Molecules. 2018;23(7):1622. doi: 10.3390/molecules23071622, PMID 29973488.
4. Cheng J, Shah YM, Gonzalez FJ. Pregnane X receptor as a target for treatment of inflammatory bowel disorders. Trends Pharmacol Sci. 2012;33(6):323-30. doi: 10.1016/j.tips.2012.03.003, PMID 22609277.

5. Yang L, Chu JS, Fix JA. Colon-specific drug delivery: new approaches and *in vitro/in vivo* evaluation. Int J Pharm. 2002;235(1-2):1-15. doi: 10.1016/s0378-5173(02)00004-2, PMID 11879735.
6. Zhang S, Langer R, Traverso G. Nanoparticulate drug delivery systems targeting inflammation for treatment of inflammatory bowel disease. Nano Today. 2017;16:82-96. doi: 10.1016/j.nantod.2017.08.006, PMID 31186671.
7. Mor J. Recent advances in colon targeted drug delivery systems. Int J Pharm Prof Res. 2011;2(4):413-7.
8. Mathiowitz E. Encyclopedia of controlled drug delivery. 2nd ed. New York: John Wiley & Sons, Inc; 2003.
9. Danda S. Brahma Chandan K. Colon targeted drug delivery: a review on primary and novel approaches. J Glob Trends Pharm Sci. 2013;4(4):1179-83.
10. Veer SU, Gadhve MV, Khedkar AN. Microsponge: A drug delivery system. Int J Pharm Clin Res. 2014;6;Suppl:385-90.
11. Sen S, Sharma A, Kriplani P, Guarve K. Microsponges: A neoteric approach for the effective management of osteoarthritis. Curr Rheumatol Rev. 2023;19(4):385-99. doi: 10.2174/1573397119666230417093138, PMID 37070454.
12. Chauhan S, Harwansh RK. Recent advances in nanocarrier systems for ulcerative colitis: A new era of targeted therapy and biomarker integration. J Drug Deliv Sci Technol. 2024;93:(105466). doi: 10.1016/j.jddst.2024.105466.
13. Abdellatif AA, Zayed GM, Kamel HH, Mohamed AG, Arafa WM, Khatib AM, *et al.* A novel controlled release microsponges containing albendazole against *Haemonchus contortus* in experimentally infected goats. J Drug Deliv Sci Technol. 2018;43:469-76. doi: 10.1016/j.jddst.2017.10.022.
14. Amidon S, Brown JE, Dave VS. Colon-targeted oral drug delivery systems: design trends and approaches. AAPS PharmSciTech. 2015;16(4):731-41. doi: 10.1208/s12249-015-0350-9, PMID 26070545.
15. Ahmed S, Ali M, Ahmed A, Ramzan M. Development and characterization of aceclofenac-loaded microsponges for topical delivery. Arab J Chem. 2017;10:S991-9.
16. Kawashima Y, Niwa T, Takeuchi H, Hino T, Itoh Y, Furuyama S. Characterization of polymorphs of tranilast anhydrate and tranilast monohydrate when crystallized by two solvent change spherical crystallization techniques. J Pharm Sci. 1991;80(5):472-8. doi: 10.1002/jps.2600800515, PMID 1715401.
17. Srivastava R, Kumar D, Pathak K. Colonic luminal surface retention of meloxicam microsponges delivered by erosion-based colon-targeted matrix tablet. Int J Pharm. 2012;427(2):153-62. doi: 10.1016/j.ijpharm.2012.01.036, PMID 22306039.
18. Shahdadi Sardo H, Saremnejad F, Bagheri S, Akhgari A, Afrasiabi Garekani H, Sadeghi F. A review on 5-aminosalicylic acid colon-targeted oral drug delivery systems. Int J Pharm. 2019;558:367-79. doi: 10.1016/j.ijpharm.2019.01.022, PMID 30664993.
19. Kumari A, Jain A, Hurkat P, Tiwari A, Jain SK. Eudragit S100 coated microsponges for Colon targeting of prednisolone. Drug Dev Ind Pharm. 2018;44(6):902-13. doi: 10.1080/03639045.2017.1420079, PMID 29260916.
20. Bhatia M, Saini M. Formulation and evaluation of curcumin microsponges for oral and topical drug delivery. Prog Biomater. 2018;7(3):239-48. doi: 10.1007/s40204-018-0099-9, PMID 30242738.
21. Mandal S, Km Bhumika B, Kumar M, Hak J, Vishvakarma P, Sharma UK. A novel approach on micro sponges drug delivery system: method of preparations, application and its future prospective. Ind J Pharm Educ. 2023;58(1):45-63.
22. Caban M, Lewandowska U. Encapsulation of polyphenolic compounds based on hemicelluloses to enhance treatment of inflammatory bowel diseases and colorectal cancer. Molecules. 2023;28(10):4189. doi: 10.3390/molecules28104189, PMID 37241929.
23. Özdemir S, Üner B, Baranauskaite J, Sümer E, Yıldırım E, Yaba A. Design and characterization of dexamethasone loaded microsponges for the management of ulcerative colitis. Eur J Pharm Biopharm. 2023;187:34-45. doi: 10.1016/j.ejpb.2023.04.007, PMID 37061099.
24. Salunke A, Upmanyu N. Formulation, development and evaluation of budesonide oral nano-sponges using DOE approach: *in vivo* evidences. Adv Pharm Bull. 2021;11(2):286-94. doi: 10.34172/apb.2021.041, PMID 33880350.
25. Adel S, Fahmy RH, Elsayed I, Mohamed MI, Ibrahim RR. Fabrication and optimization of itraconazole-loaded zein-based nanoparticles in coated capsules as a promising colon-targeting approach pursuing opportunistic fungal infections. Drug Deliv Transl Res. 2023;13(12):2982-3002. doi: 10.1007/s13346-023-01365-0, PMID 37270444.
26. Chen Z, Sun XH, Zhou R, *et al.* Oral delivery of curcumin loaded in *Lactobacillus fermentum* for improved systemic bioavailability and colonic anti-inflammatory activity. Colloids Surf B Biointerfaces. 2018;167:356-64.
27. Li R, Wang Y, Xu X, *et al.* Azide-triggered colon-specific drug delivery based on nitroreductase-containing bacteria. J Control Release. 2017;260:54-63.

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