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Development and characterization of mesalamine loaded mucoadhesive microspheres for effective treatment of inflammatory bowel disease

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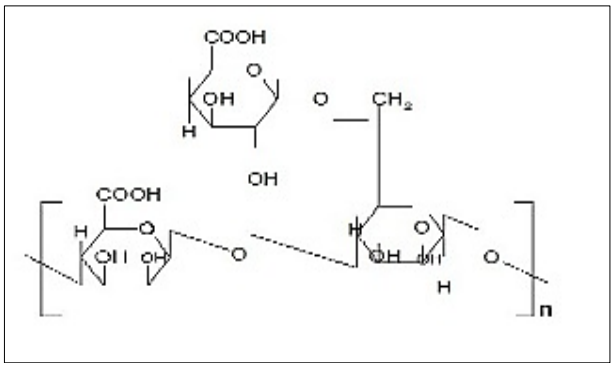
Abstract
This study aimed to develop and evaluate Eudragit-S100 coated guar gum microspheres for delivering mesalamine hydrochloride specifically to the colon. Guar gum was produced using an emulsion dehydration technique, varying mesalamine hydrochloride and starch ratios (0.5 to 2.0 w/v), stirring speeds (300 to 1200 rpm), and emulsifier concentrations (0.5% to 2% v/v). All microspheres containing mesalamine hydrochloride exhibited high preparation yield and encapsulation efficiency. The best formulation utilized a 40:100 w/w drug to polymer ratio, 600 rpm stirring speed, and 1.5% w/v span 80 as the emulsifying agent. Starch microspheres were coated with Eudragit-S100 using a dip coating method, with a 1:10 core to coat ratio. Both mesalamine hydrochloride microspheres and Eudragit-S100 coated microspheres were analyzed for surface morphology, particle size and distribution, swell ability, drug entrapment percentage, and in vitro drug release in simulated gastrointestinal fluids (SGF). The optimized formulation underwent an in vitro drug release study in simulated colonic fluid with 4% rat cecal content. An organ distribution study in albino rats assessed the formulation's colon-targeting potential. Mesalamine hydrochloride release from Eudragit-S100 coated guar gum microspheres was pH-dependent, with slower release in acidic conditions and faster release at pH 7.4. The study concludes that Eudragit-S100 coated guar gum microspheres show promise as effective controlled release carriers for colon-targeted delivery of 5-mesalamine hydrochloride.

Keywords: Mesalamine hydrochloride, guar gum microspheres, Eudragit- S100 coating, colon targeting, colon specific drug delivery

Introduction
In the United States, colorectal cancer is the second most deadly form of cancer, with the Indian subcontinent reporting over 66,000 new colon cancer cases each year. Traditional cancer chemotherapy often proves ineffective in treating colorectal cancer due to the inability of drug molecules to reach the target area in sufficient concentrations. Consequently, successful treatment using conventional methods requires high doses to compensate for drug loss in the upper gastrointestinal (GI) tract, potentially causing severe side effects. This problem can be addressed through targeted, site-specific drug delivery to the colon. Various approaches have been explored for targeted colonic drug delivery, including prodrugs, pH-sensitive polymer coatings, and time-dependent formulations. Furthermore, existing literature has documented the use of biodegradable polymers such as azopolymers and polysaccharides (e.g., pectin, starch, and dextrin) for colon targeting. Among the numerous strategies for achieving colon-selective drug delivery, the use of polymers specifically degraded by colonic bacteria shows significant promise. pH-dependent systems are founded on the established understanding that pH levels in the human GI tract progressively increase from the stomach (pH 2-3) to the small intestine (pH 6.5-7.0) and finally to the colon (pH 7.0-8.0). The most commonly used pH-dependent coating polymers are methacrylic acid copolymers (such as Eudragit L100-55, Eudragit L100, and Eudragit S100), which dissolve at pH levels of 5.5, 6.0, and 7.0, respectively. Guar gum, extracted from the ground endosperms of Cyamposis tetragonolobus, is primarily composed of high molecular weight hydro colloidal polysaccharides, consisting of galactan and mannan units connected by glycosidic bonds, and is broken down in the large intestine by microbial enzymes. The structure of guar gum consists of a linear chain to single α-D-galactopyranosyl units, which

act as side branches. It is composed of roughly 80% galactomannan, 12% water, 5% protein, 2% acid-soluble ash, and 0.7% fat. With a molecular weight of approximately 1 million, guar gum exhibits high viscosity in solution. This gelling property decelerates drug release from the dosage form, and it is susceptible to degradation in the colonic environment.

This research aimed to develop a mucoadhesive drug delivery system for the targeted administration of mesalamine hydrochloride, utilizing natural guar gum and the pH-sensitive polymer Eudragit-S100, to treat inflammatory bowel diseases. The system is designed to reduce drug loss in the upper gastrointestinal tract, leveraging the properties of Eudragit S100, and to ensure the specific delivery of mesalamine hydrochloride to the colon. By applying enteric polymers as a protective coating on the microspheres, the drug can be released at the specific pH level found in colonic fluid. The proposed mechanism combines the targeted biodegradability of the polymer with pH-sensitive drug release from the coated microspheres.



Chemical structure of guar gum

Mesalazine is believed to function primarily at the local level rather than systemically. Individuals suffering from chronic inflammatory bowel disease exhibit increased production of arachidonic acid metabolites in the mucosa. This occurs through both cyclooxygenase pathways, resulting in prostanoids, and lipoxygenase pathways, yielding leukotrienes and hydroxyl eicosatetraenoic acids. One hypothesis suggests that mesalazine reduces inflammation by inhibiting cyclooxygenase and subsequently decreasing prostaglandin production.

This research aimed to create a mucoadhesive drug delivery system for targeted release of mesalamine hydrochloride. The system utilizes natural polysaccharides like guar gum and the pH-sensitive polymer Eudragit to treat colon cancer. By leveraging Eudragit's inherent properties, this approach is expected to minimize drug loss in the upper gastrointestinal tract and ensure specific release of mesalamine hydrochloride in the colon. The application of enteric polymers as a protective coating on the microspheres enables drug release at the specific pH of colonic fluids. The proposed mechanism for drug release is twofold, combining the polymer's specific biodegradability with pH-dependent release from the coated microspheres.

Materials

Mesalamine Hydrochoride were purchased from CDH New Delhi, India. Guar Gum were received from Loba Chemie Pvt. Ltd. Mumbai, India. All polymers and chemicals used were of analytical grade.

Preparation of Guar microspheres (GGM)

An emulsification method followed by cross-linking with a calcium chloride solution (5%, m/V, in IPA) was employed to produce guar gum microspheres (GGM). The core microspheres were fabricated using varying drug-to-polymer ratios. A predetermined quantity of guar gum was dissolved in heated distilled water, after which the drug was dispersed in this aqueous solution. This dispersion was then emulsified in light liquid paraffin containing Span 80 (2%, V/V) using a mechanical stirrer (propeller type) (Remi Instrument Ltd, Mumbai, India) operating at 400 rpm for one hour. To solidify the formed microspheres, a calcium chloride solution (5%, m/V in IPA) was added drop by drop to the emulsion at a rate of 1 mL per minute, with stirring continued for an additional 20 minutes to ensure effective cross-linking. The microspheres were collected through filtration and washed three times with petroleum ether to remove any residual liquid paraffin. The collected microspheres were then frozen for 10 hours and subsequently stored in vacuum desiccators for 12 hours.

Preparation of Eudragit S-100 coated microspheres

The guar gum microspheres were optimized and subsequently coated with Eudragit S-100. The core microspheres were combined with a 5% (W/V) solution of Eudragit S-100, prepared in a mixture of acetone and isopropyl alcohol at ambient temperature. This composite was then emulsified in light liquid paraffin containing 2% (V/V) Span 80 in a beaker using a mechanical stirrer (propeller type) at a speed of 400 rpm. The stirring process was maintained for 3 hours at room temperature to promote the evaporation of the solvent. Ultimately, the encapsulated microspheres were filtered, washed with petroleum ether to remove any residual oil, and dried in a vacuum desiccator for 24 hours.

Characterization of Guar Gum and Eudragit-S100 coated Guar Gum microsphers.

Sem for surface morphology

The surface morphology was examined utilizing a scanning electron microscope (SEM). For the preparation of samples for SEM analysis, nanoparticles were gently applied onto double-sided adhesive tape mounted on an aluminum stub. Subsequently, these stubs underwent a gold coating process to achieve a thickness of approximately 300 Å, accomplished using a sputter coater. All samples were analyzed with a scanning electron microscope (LEO 435 VP, Eindhoven, Netherlands) at an acceleration voltage of 25 kV, and photomicrographs were obtained at suitable magnifications.

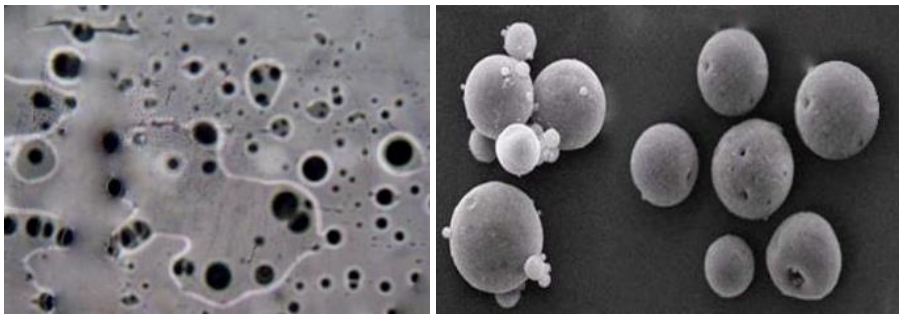


Fig 1: (A) Phase contrast photograph (100X) (B) SEM Photomicrograph of Eudragit-S100 coated guar gum microspheres (650X)

Average particle size, surface charge and polydispersity index

The average particle size was evaluated using photon correlation spectroscopy with a Zetasizer (Malvern Instruments, UK). The particle size distributions are represented by the average size. The polydispersity index (PDI) is a dimensionless parameter that indicates the breadth of the particle size distribution and is useful for assessing the formulation of nanoparticles. The zeta potential of a particle reflects the overall charge that the particle acquires in a specific medium, also measured using a Zetasizer (Malvern Instruments, UK). The magnitude of the measured zeta potential denotes the repulsive forces at play and can be utilized to anticipate the long-term stability of the product. The polydispersity index (PDI), a dimensionless measure representing the spread of a particle size distribution, was calculated using the following formula:

$$PDI = \frac{\text{Standard deviation}}{\text{Average particle size}} \quad (1)$$

In principle, the polydispersity index (PDI) for a monodisperse colloidal suspension is zero. However, a typical particle dispersion exhibiting a PDI of around 0.05 is considered monodisperse, whereas a PDI exceeding 0.5 indicates a more extensive size distribution.

Drug encapsulation and *in vitro* release study

Estimation of surface drug in microspheres

A total of 100 mg of microspheres was suspended in 10 ml of PBS (pH 7.4) and subjected to vigorous agitation for 10 minutes, after which the supernatant was collected. The sediment underwent the same treatment, and the resultant second supernatant was merged with the first supernatant. The mesalamine hydrochloride concentration in the combined supernatants was assessed using spectrophotometry at a wavelength of 266 nm. The quantity of mesalamine hydrochloride detected in the aggregated washings reflected the amount of drug that had adhered to the microsphere surfaces.

Table 1: Characterization of Guar Gum microspheres and Eudragit-S100 coated starch microspheres formulation.

S. No.	Formulation Code(s)	Particle size (µm)	Zeta Potential (mV)	PDI	% EE
1.	GGM	29.2±2.1	-18.3±0.9	0.083	90. 2 ± 1.7%
2.	E-GGM-1(1:5)	61±3.4	-13.1±1.3	0.153	86. 7 ± 2.1%
3.	E-GGM-2(1:10)	72±2.6	-9.38±1.6	0.283	88. 4 ± 1.9%

* Guar gum conc. (1% w/v): Drug conc. (40% w/w): Span 80 conc. (1.5% w/v): Volume of gluteraldehyde 0.8 ml: Stirring speed: 600 rpm and Stirring time: 4 hr. Values are expressed as mean ±SD, n=3.

Estimation of entrapped drug in microspheres

A total of 100 mg of microspheres was dispersed in 10 ml of distilled water and allowed to sit for 1 hour. Subsequently, 50 ml of PBS (pH 7.4) was introduced. The resulting digested homogenate was centrifuged at 3000 rpm for 5 minutes and then filtered through a 0.2 µm filter (Millipore, USA). Following appropriate dilution with PBS (pH 7.4), the concentration of mesalamine hydrochloride was measured spectrophotometrically at a wavelength of 266 nm. The encapsulation efficiency (EE) and loading capacity (LC) of the microspheres for mesalamine hydrochloride were calculated using equations (1) and (2), respectively

$$\% EE = (X-Y)/X \times 100\% \quad (2)$$

$$\% LC = (X-Y)/Z \times 100\% \quad (3)$$

where X is the total amount of the drug added, Y was the free amount of the drug in the supernatant, and Z is the weight of the microspheres.

The *in vitro* liberation study of the GGM and E-SGGM formulations was carried out using a palette type solution apparatus as described in USP XXIII. For this study, 500 mg of microspheres, which is equivalent to 200 mg of mesalamine hydrochloride, were weighed accurately and struck carefully through the 900 ml surface of the medium of dissolution. The palette turned at a speed of 100 rpm inside a container with controlled temperature maintained at 37±2 ° C. The optimal conditions of the sink were maintained throughout the drug dissolution experiment. The release of the drug was examined in gastrointestinal fluids simulated to variable pH levels in the following order to replicate the transit from mouth to colon: (a) in simulated gastric fluid (pH 1.2) during the first 2 hours; (b) in a mixture of simulated gastric and intestinal fluid (pH 4.5) from the third to the fourth hour; (c) in the simulated intestinal fluid (pH 6.8) during the 5th hours; and (d) in the simulated colonic fluid (pH 7.6) with a rating cecal content of 4% v/v from 7 ° to the tenth hour.

The medium was passed through Whitman's filter paper after 2, 4 and 6 hours, and the residue collected in the filter paper was added to the posterior medium immediately to continue the dissolution study. Samples of the solution vessel at intervals of 1 hour were taken and

spectrophotometrically were analyzed (Shimadzu 1800, Japan) at a wavelength of 266 nm.

Statistical Analysis: Statistical analysis was performed with Graph Pad Instate software (Version 5.00 Graph pad Software, San Diego California USA) using one-way ANOVA followed by Tukey-Kramer multiple comparison test. Difference with $p< 0.05$ was considered statistically significant.

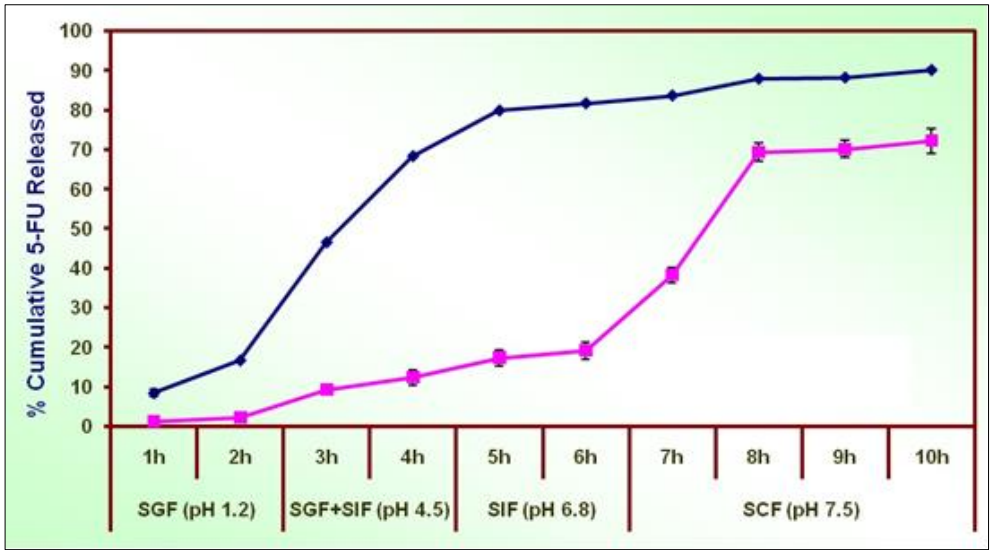


Fig 2: % Cumulative 5-FU released from Guar Gum and Eudragit S-100 coated guar gum microspheres in different pH of simulated GIT fluids.

Degree of Swelling

The guar gum expands in water and the aqueous fluids of the gastrointestinal tract (git) in the upper portion, which could lead to the premature release of the drug before the colon reaches. To mitigate this problem, starch microspheres were covered with Eudragit S-100 to inhibit the dissolution of the starch and, therefore, prevent the release of the drug in the upper git; therefore, the influence of Eudragit S-100 was examined in the behavior of swelling of starch microspheres. For this purpose, 1 gram of starch microspheres and microspheres coated with Eudragit S-100 was with precision and then submerged separately in 5 ml of distilled water at room temperature for a predetermined duration. The formula used to calculate the degree of swelling is provided below

$$\alpha = [\omega_g - \omega_0]/\omega_0$$

Where α = degree of swelling, ω_0 = initial weight of microspheres, ω_g = final weight of microspheres.

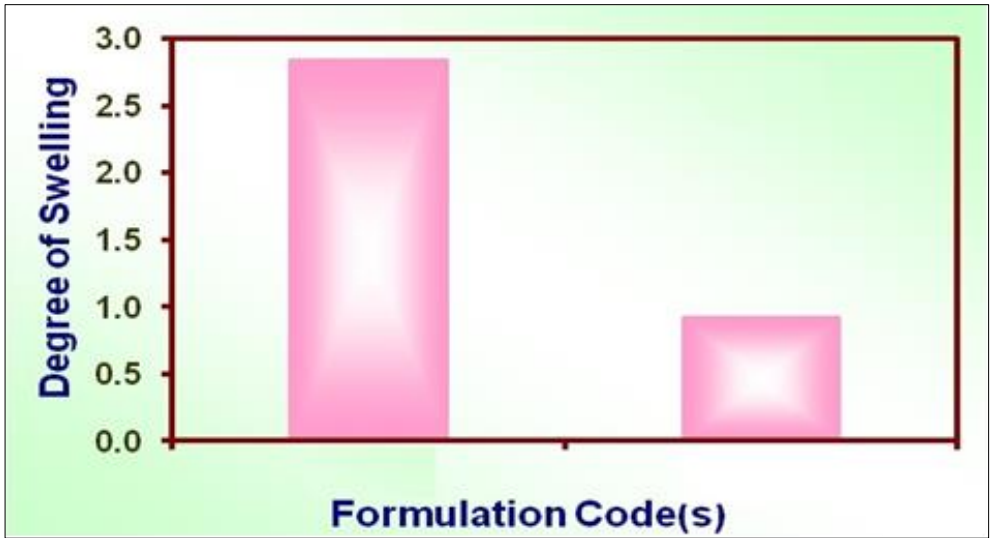


Fig 3: Degree of swelling of guar gum microspheres and Eudragit S-100 coated guar gum microspheres.

Stability studies.

Effect of storage temperature on particles size

Alterations in structural integrity and particle size of the optimized guide microspheres and the starch microspheres coated with Eudragit S100 were evaluated individually using optical microscopy (ERMA, Japan) after stored at temperatures of 35 ± 1 ° C, 50 ± 1 ° C, and 65 ± 1 ° C for specified durations of 15, 30, 45 and 60 days.

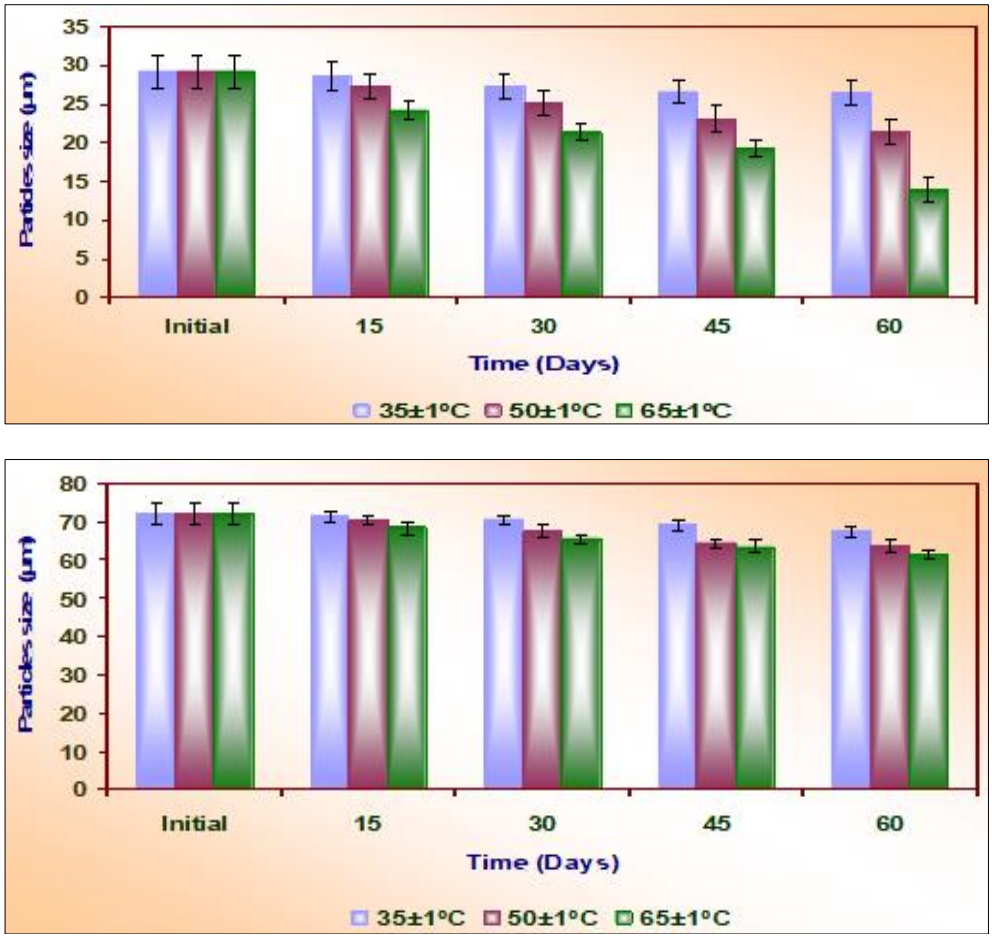


Fig 4: Effect of storage temperature on particles size of (A) Guar gum microspheres and (B) Eudragit S-100 coated guar gum microspheres.

Effect of storage temperature on % residual drug content

The percentage of the residual drug content in the optimized guide microosphere formulation stored after several storage durations of 15, 30, 45 and 60 days was evaluated by dissolving the microspheres in 5 ml of a solution of distilled water (5000 units) and allowing that settles for 1 hour. The resulting digested mixture underwent centrifugation at 3000 rpm for 5 minutes and then leaked using a 0.2 µm filter (Millipore, USA.). After the appropriate dilution with PBS (pH 7.4), 5-FU was measured spectrophotometrically to a wavelength of 266 nm. The percentage of the residual drug content for each sample was evaluated in triplicate, and the results are presented in Fig 5.

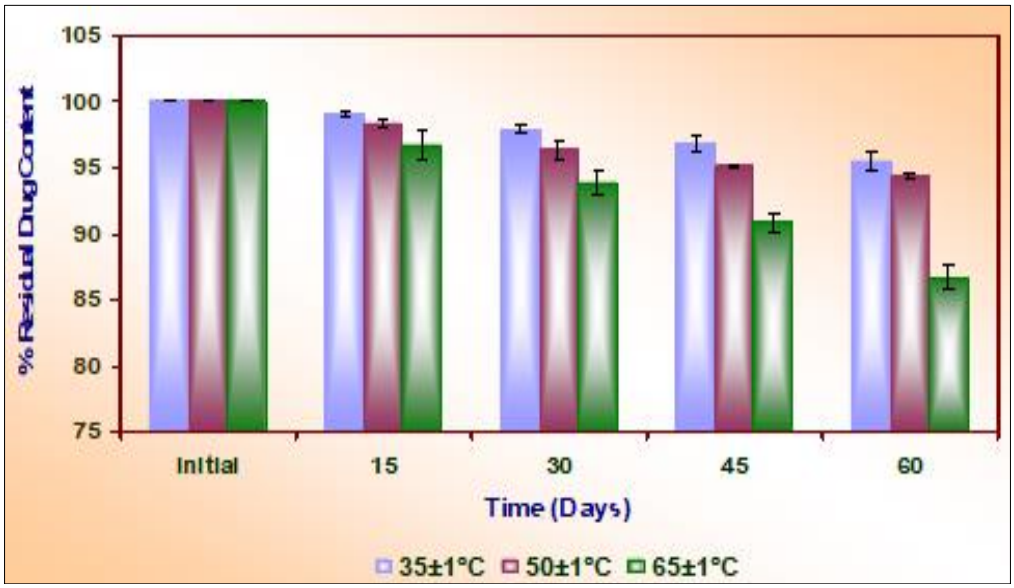
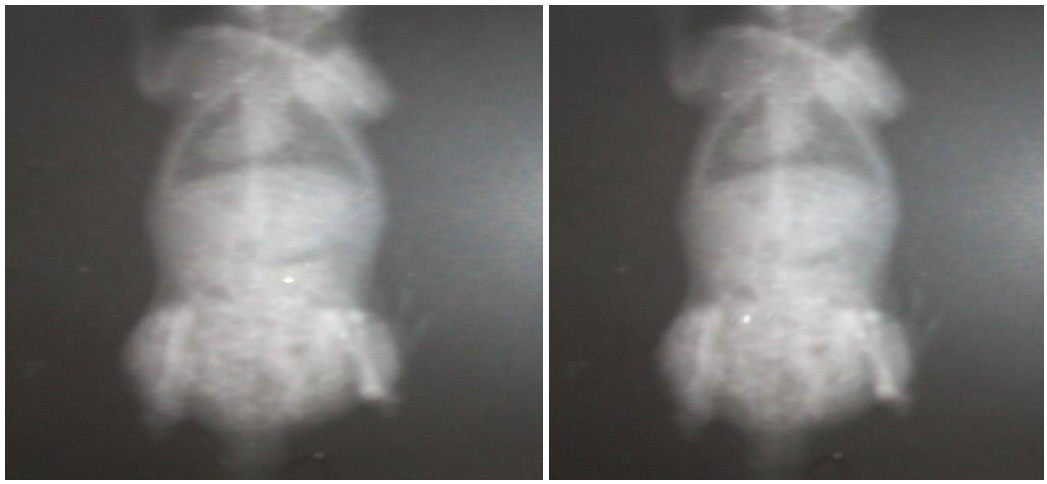


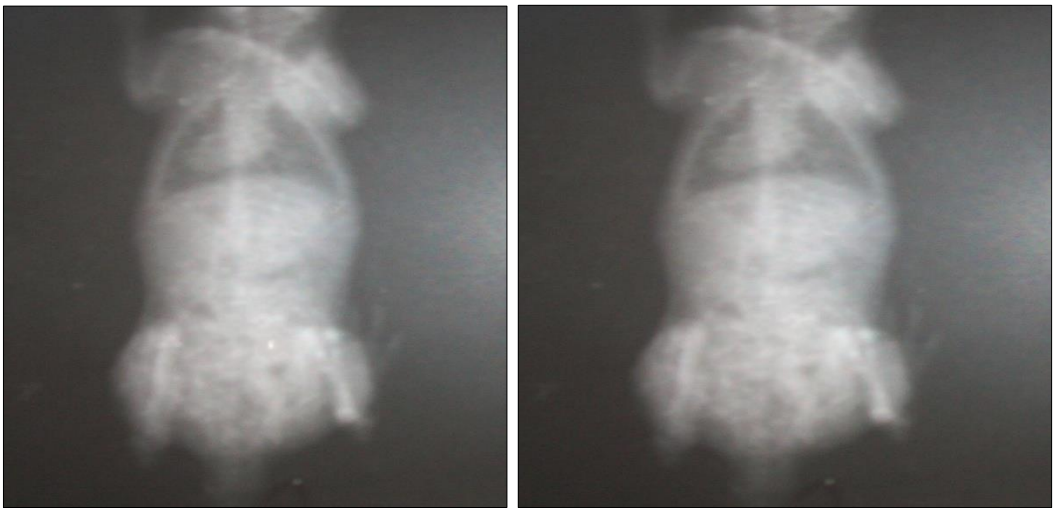
Fig 5: Effect of storage temperature on % residual drug content in (A) Guar gum microspheres (B) Eudragit S-100 coated guar gum microspheres.

Intragastric behavior of Eudragit S-100 coated Guar gum microspheres by X-ray study

The study investigated the in vivo yield of Guar rubber microspheres coated with Eudragit S100 to evaluate its disintegration in different regions of the gastrointestinal tract for several periods of time. This was achieved by encapsulating the 60% uografine (sodium diatrhizoate: meglumine diatrhizoate; 10:66 iodine, 292 mg/ml) instead of a medication. A 500 mg dose of the formulation was dissolved in 3 ml of water and administered orally to a rat using a cannula. The behavior of the formulation within the stomach was monitored by capturing a series of X -ray images at appropriate time intervals, as shown in Figure 6.



(A) After 1 hr. **(B) After 3 hr.**



(C) After 5 hr. **(D) After 15-20 hr.**

Fig 6: X-ray photographs of rat at different time interval showing intragastric behavior of Eudragit S-100 coated guar gum microspheres

Organs level drug distribution study

The adult albino rats of both sexes were used for research at drug organs. The rats remained with a standard commercial diet and had access to water. Healthy rats were selected with consistent body weight (approximately 100 ± 20 g) and no prior exposure to medications for this study were not selected. The albino rats were divided into four groups, each containing six rats. Rats in group I served as a control group. Animals in group II received 10 ml of a simple drug solution (equivalent to 40 mg/kg of mesalamine hydrochloride) depending on their body weight. Animals in Group III received 10 ml of Guar Rubber microspheres (equivalent to 40 mg/kg of mesalamine hydrochloride) depending on their body weight. Rats in group IV received 10 ml of starch microspheres coated with Eudragit S100 optimized (equivalent to 40 mg/kg of mesalamine hydrochloride) depending on their body weight using a cannula. After 2, 4, 6 and 8 hours, the animals were sacrificed, and the stomach, the small intestine and the colon were extracted. These organs were homogenized with a small volume of PBS (pH 7.4), followed by the addition of 1 ml of acetonitrile to the homogenized, which was left for 30 minutes. The mixture was centrifuged and the supernatant was picked up. After an adequate dilution of the supernatants, the concentration of the drug was quantified by measuring the absorbance at 266 nm against the respective blank. Drug levels in several segments of the gastrointestinal tract in different time points are represented graphically in Figure 7.

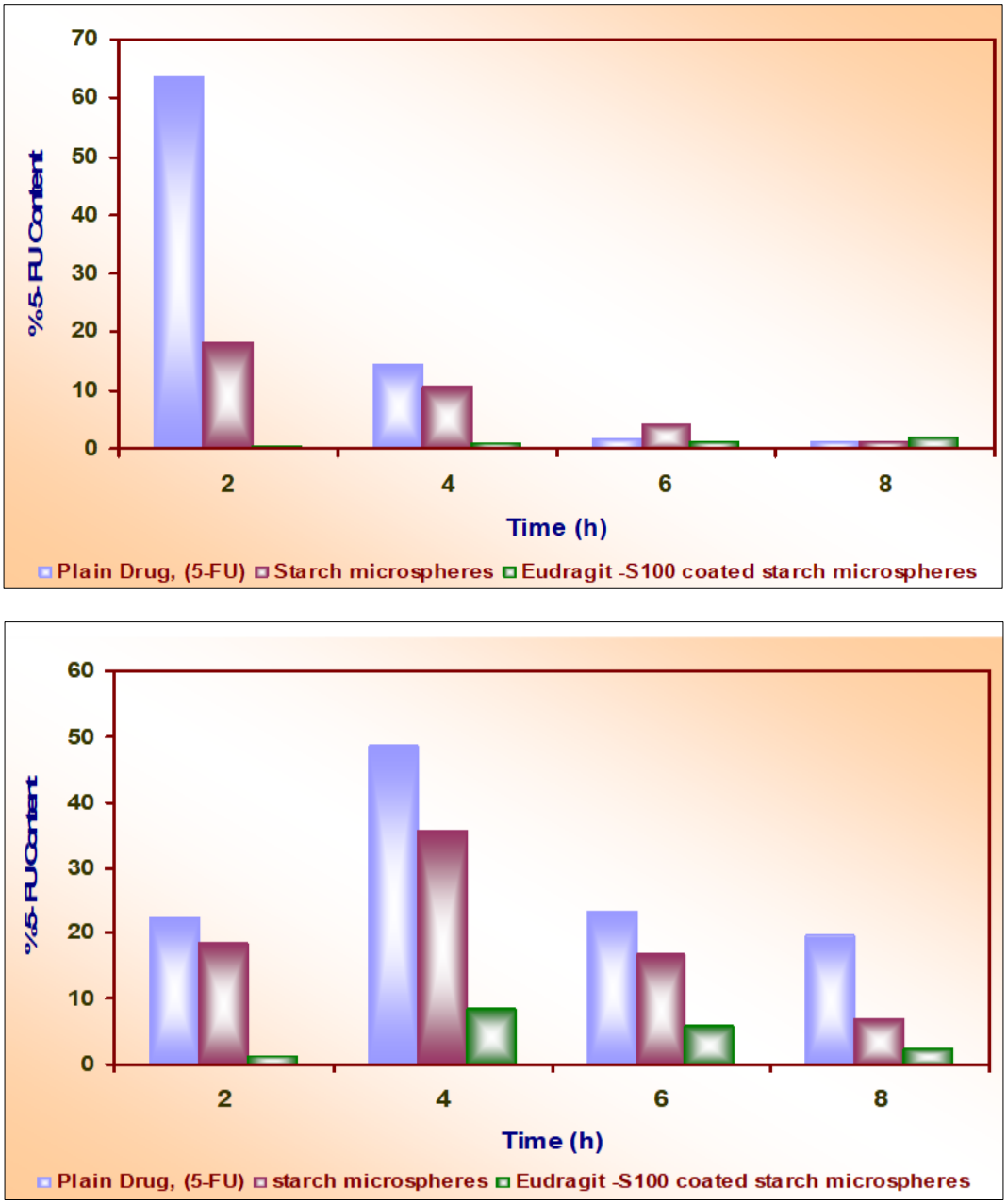


Fig 7: % Drug content in isolated (A) stomach (B) small intestine and (C) colon of albino rat after oral administration different formulation.

Results and Discussion

Mesalamine hydrochloride microspheres were created using guide gum through a modified method of emulsion reticulation, and various formulations and process factors, including polymers concentration, drug concentration, the amount of reticulation agent, concentration of emulsifying agent, the speed of agitation and the duration of agitation were optimized to achieve specular particles. With the greatest entrapment efficiency. Guar rubber concentrations of 0.5%, 1.0%, 1.5% and 2.0% w/v were used in the preparation of microspheres. It was found that the average particle size increased as the guar gum concentration rose; however, the particles became irregular, ellipsoidal and deformed when the concentration exceeded 1.5% w/v.

To optimize drug concentration, Guar rubber microspheres were prepared with different amounts of mesalamine hydrochloride, specifically 20, 40, 60 and 80 mg per 100 mg of Guar rubber. It was observed that the increase in the concentration of the drug resulted in a better entrapment efficiency of up to 40/100 mg, but the additional increases in the concentration of the drug led to a decrease in the efficiency of entrapment, probably due to the saturation of the Guer guar with the medication, without significant changes. In the particle size. In addition, the particle size decreased when the span 80 concentration in the oil phase was raised, which can be attributed to the increase in surface tension of the aqueous phase, facilitating the formation of microsized particles. The optimal particle size was 36.4 ± 2.6 µm with a 90.6 ± 1.6% drug trapping level to a tension concentration of 1.5% v/v. However, with an additional increase in the concentration of surfactant, while particle size decreased due to micelle formation, the trapping efficiency decreased due to drug leaching. The volume of gluteraldehyde, the chemical reticulation agent, used in the preparation of Guar gum microspheres, revealing that the average particle size increased with an increase in the volume of gluteraldehyde. The formulation with 0.8 mL exhibited a particle size of 36.2 ± 2.4 µm with a 91.5 ± 1.9%entrap efficiency, attributed to a higher reticulation density. Beyond 0.8 ml of gluteraldehyde, drug trapping

efficiency decreased due to the creation of a gummous dispersion similar to a gel.

The agitation speed of the process variable was optimized with respect to the average particle size and the maximum efficiency of drug trapping. The results of this experiment indicated that as the agitation speed increased, the average particle size of starch microspheres decreased. At 600 rpm, the formulation achieved the narrower size distribution of 31.2 ± 1.8 µm, while exhibiting a spherical shape and an efficiency of drug trapping of 92.1 ± 1.4%. The average particle size of starch microspheres decreased with an increase in agitation time. After 4 hours, a narrow size distribution of 28.5 ± 1.6 µm was recorded, together with a drug trapping efficiency of 90.6 ± 2.1%. However, agitation for more than 4 hours led to the separation of the aqueous phase due to the agglomeration of the Guar rubber.

Guar gum microspheres were covered using the immersion coating technique with Eudragit S-100. To optimize the final formulation, several proportions of nucleus / cars of 1: 5 and 1:10 were used. The E-SGGM formulation exhibited an average particle size of 72 ± 2.6 µm, showed a spherical shape and showed a uniform coating after drying at room temperature for 24 hours.

The photomicrography of sweeping electrons (SEM) of optimized GGM microspheres and those coated with Eudragit S-100 reveals that microspheres maintain a spherical shape; however, the surface of the GGM microspheres exhibits some roughness, probably resulting from the contraction of starch microspheres during the drying process as water evaporates. Photomicrographs are shown in Figure 1 (b).

An in vitro study was conducted to evaluate the release of optimized guide microspheres USP XXIII in several simulated in several simulated gastrointestinal fluid media at different pH levels. The cumulative percentage of mesalamine hydrochloride released from starch microspheres in SGF (pH 1.2) and SIF (pH 6.8) varied from 8.52 to 81.72% after 6 hours. On the contrary, Guar rubber microspheres covered with Eudragit S-100 exhibited a release that varies from 1.26 ± 0.46 to 19.12 ± 2.13% after 6 hours, which can be attributed to the influence of enteric coating of starch microspheres with Eudragit S-100 coating. Additional drug release evaluations were performed in simulated colonic liquid (SCF, pH 7.6) combined with a medium of dissolution of CECAL content of rat of 4% v/v. Guar gum microspheres covered by Eudragit S-100 demonstrated a greater drug release in several time intervals, which shows a release of 72.22 ± 3.18% after 10 hours. It is likely that this improvement is due to the various bacteria found in the CECUM, which facilitate the digestion or decomposition of the starch in the middle and, consequently, releases the drug from microspheres. These findings are illustrated in (Figure 2). The results of the dissolution speed study indicated that the starch microspheres coated with Eudragit S-100 supply the drug sustained on the colon site.

The range of swelling for optimized microspheres Guar was measured to 2.84, while Eudragit S -00 coated rubber microspheres showed a degree of swelling of 0.18. The decrease in swelling observed in the coated Eudragit-S100 formulation suggests that the Eudragit S-100 coating acted as an obstruction to water permeation. These results are illustrated in (Figure 3).

Stability investigations were carried out, storing GGM and E-GGM formulations in dust-shaped at 35 ± 1°C, 50 ± 1°C and 65 ± 1°C dust for a duration of 45 days. The particle size of the formulations was evaluated using optical microscopy with a calibrated ocular micrometer. It was observed that the particle size of the microspheres decreased slightly to 65 ± 1°C, probably due to the evaporation of the residual organic solvent of the starch microspheres and the guar gum microspheres coated with Eudragit S100 at high temperatures. At 65 ± 1°C, microspheres began to lose their spherical shape, indicating instability at this highest temperature. After a month, microspheres agglomerates were formed, which can be attributed to the merger of the polymer. These findings are illustrated in (Figure 4 A and B).

The levels of residual drugs of the optimized microspheres of starch and the coated rubber microspheres of Eudragit-S100 were evaluated by storing the formulations at 35 ± 1 ° C, 50 ± 1 ° C and 65 ± 1 ° C for durations of 15, 30, 45, 45, 45, 45, 45, and 60 days, with the initial content of the drug of both formulations established 100%. The results indicate that 94.4 ± 1.6% of the mesalamine hydrochloride remained in guar gum microspheres to 35 ± 1°C, 92.2 ± 2.2% at 50 ± 1°C, while only 81.4 ± 2.3% persisted at 65 ± 1°C After 60 days after 60 days. This loss can be attributed to the contraction and escape of the drug formulation of the microsphere at high temperatures, as illustrated in (Figure 5 A). On the contrary, Eudragit-S100 (E-SGGM) starch microspheres showed that 95.46 ± 0.8% of the mesalamine hydrochloride was removed at 35 ± 1°C, 94.38 ± 0.2% to 50 ± 1°C and 86.69 ± 0.9% at 65 ± 1°C after 60 days. This decrease could be due to the interruption of the coating, dehydration and the subsequent drug leakage of the guar-coated microspheres formulation of Eudragit-S100 rubber at higher temperatures, as shown in (Figure 5 B).

In vivo research of Guar rubber microspheres and guar-covered rubber microspheres covered with Eudragit-S100 Oral administration points (2, 4, 6 and 8 hours). The purpose was to measure the concentration of mesalamine hydrochloride in these specific GIT regions to identify where the highest drug release occurred. The findings revealed that the highest concentration of mesalamine hydrochloride, with 63.59%, was detected in the stomach after 2 hours of administering simple mesalamine hydrochloride. In the hours that followed, a significantly lower amount of the drug was found in the small intestine, and there was only a small amount present in the colon. With the conventional dosage form, simply 11.40% of the total medicine reached the colon after 8 hours. The amount of mesalamine hydrochloride released from the Guar Rubber microspheres in the colon was significantly better at 35.89% compared to the simple drug, while the small intestine contained the highest drug concentration in 51.41% after 8 hours. Guar-coated rubber microspheres coated with Eudragit-S100 remained largely intact in the upper GIT, with approximately 8.61% of the total drug content observed in this region after 5 hours see (Figure 6 C). However, the concentration of mesalamine hydrochloride in the colon increased to 76.53% after 8 hours. This improvement is likely to be attributed to the protective characteristics of drug release in the upper GIT due to enteric coating. When exposed to a higher pH, the Eudragit-S100 coating was dissolved, which led to the swelling and improved the muroadhesive properties of Guar rubber microspheres, which allowed a greater amount of drug to reach the colon site. The results are illustrated graphically in (Figure 7 A, B & C).

Conclusion

The findings of all experiments indicated that colorectal cancer can be treated effectively by administering the correct dose of the drug directly to the colon by using guar gum microspheres covered with the Eudragit S100 enteric polymer. This directed delivery of mesalamine hydrochloride can minimize the side effects associated with its absorption in the upper gastrointestinal tract when it occurs in traditional forms such as tablets and capsules. Consequently, the specific drug administration system of the proposed site would offer a reliable method for the effective treatment of colorectal cancer.

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Declaration of Interest

The authors do not report that there are no conflicts of interest. Only authors are responsible for the content and writing of this article.

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