

Colon Targeting Guar Gum Microspheres of 5-Aminosalicylic Acid: Evaluation of Various Process Variables, Characterization and *In-vitro* Drug Release

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ABSTRACT

Background and objectives: 5-Amino salicylic acid (5-ASA), a drug of choice for the treatment of crohn's disease and ulcerative colitis, rapidly absorbs from the small intestine and there is little localization of 5-ASA in the colon. Thus, we have developed a colon-specific delivery cargo of 5-ASA to release the maximum drug in colon. **Methods and Results:** 5-ASA loaded guar gum microspheres were prepared by emulsion polymerization technique and optimized for particle size, entrapment efficiency and *in-vitro* drug release in colonic environment. FTIR, PXRD and DSC were used as the techniques to characterize the drug-polymer interaction. 5-ASA-loaded microspheres offer high entrapment efficiency of $82.39 \pm 1.06\%$ with a mean particle size of $150.32 \pm 11.8 \mu\text{m}$. *In-vitro* release of optimized formulation indicated $9.32 \pm 0.63\%$ release of drug in SGF (pH 1.2; without pepsin); $13.93 \pm 0.90\%$ in SIF (pH 7.5), $32.11 \pm 2.80\%$ in SCF (pH 7.0; without rat caecal contents) while a significant increase in drug release ($94.62 \pm 4.50\%$) was observed in SCF (pH 7.0) medium containing 4% rat caecal content after 6 days of enzyme induction. **Conclusion:** 5-ASA loaded guar gum microspheres can be used as therapeutic agent for the treatment of ulcerative colitis.

Key words: 5-ASA, 5-aminosalicylic acids, Colon, Guar gum, *In vitro* drug release.

INTRODUCTION

5-Amino salicylic acid (5-ASA) (Figure 1), a typical anti-inflammatory agent is the drug of choice for the treatment of crohn's disease and ulcerative colitis.¹ The oral administration of 5-ASA significantly improves mucosal permeation and protects the intestinal mucosa against injury in ulcerative colitis.² However, 5-ASA rapidly absorbs from the small intestine and there is little localization of 5-ASA in the colon relative to small intestine.³ Thus, it is necessary to develop a colon-specific delivery system for 5-ASA in the treatment of ulcerative colitis. Colonic drug delivery has gained increased attention not just for the delivery of the drugs for the treatment of local diseases associated with the colon but also for its potential for the delivery of proteins and therapeutic peptides. In colonic delivery, a drug needs to be protected from absorption and/or the environment of the upper

gastrointestinal tract (GIT) and then be abruptly released into the proximal colon, which is considered the optimum site for colon-targeted delivery of drugs. Colon targeting is naturally of value for the topical treatment of diseases of colon such as Chron's diseases, ulcerative colitis, colorectal cancer and amebiasis.⁴

Recently, we have customized 5-Fluorouracil loaded chitosan and guar gum microspheres (GGM) for colon targeting.⁵ Earlier, chitosan was selected as a polymer for synthesis of colon-specific delivery system. Chitosan rapidly dissolves in the gastric cavity. As, amino groups of chitosan can undergo protonation and the polymer swells, hence, chitosan-based drug delivery devices release most of the active ingredients in the stomach. Moreover, initial burst release phenomenon is associated with chitosan-based delivery systems; hence

Submission Date : 04-07-15

Revised Date : 18-08-15

Accepted Date : 13-02-16

DOI: 10.5530/ijper.50.2.25

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their utility for the controlled delivery of drugs in gastrointestinal tract is questionable.¹ On the other hand, guar gum is a natural polysaccharide obtained from the ground endosperms of *Cyamopsis tetragonolobus* (Fam. Leguminosae).⁶ It consists chiefly of high molecular-weight hydrocolloidal polysaccharide, consists of linear chains of (1→4) β-D-manopyranosyl units with α-D-galactopyranosyl units attached by (1→6) linkages, which may be described chemically as a galactomannan.⁷ Guar gum occurs as an odorless or nearly odorless, white to yellowish-white powder with a bland taste and degraded by Bacteroids species (*B. fragilis*, *B. ovatus*, *B. variabilis*, *B. uniformis*, *B. distasonis* and *B. thetaiotaomicron*) and Ruminococcus.⁸ The gelling property of guar gum retards the release of the drug from the dosage form as well as it is susceptible to degradation in the colonic environment.⁹ The most favorable property of guar gum is their approval as pharmaceutical excipients.^{10,11} In present investigation, we have customized 5-ASA loaded GGM and evaluated various process variables to optimize the formulation (5-ASA GGM) in terms of particle size and entrapment efficiency. We have also examined the initial release profile in different physiological solution to prove the potential of 5-ASA GGM as colon specific drug delivery system.

MATERIALS AND METHODS

Materials

5-ASA was purchased from Himedia Laboratories, Mumbai, India. Guar gum was purchased from Central Drug House, New Delhi, India. Span 80 were procured from Loba Chemie, India. Glutaraldehyde (25% aqueous solution) was procured from S.D. Fine Chemicals, Mumbai, India. All other solvents and reagents were of analytical grade.

Preparation of cross-linked guar gum microspheres

5-ASA bearing guar gum microspheres (5-ASA GGM) were prepared by emulsion polymerization method.⁵ An aqueous dispersion containing 2-8% w/v of guar gum (an accurately weighed amount of guar gum was dispersed in a specified volume of cold water containing the 5-ASA and allowed to swell for 2 h) was dispersed in 100 g of castor oil containing 3 g of span 80 using a mechanical stirrer (Eltek, India) at 4000 rpm. After complete mixing, 0.2 ml of concentrated sulfuric acid and 1.5 ml of glutaraldehyde (GLA) were added to the dispersion, followed by stirring at a constant speed for 4 h at 50 ± 1°C. The microspheres formed were collected by sedimentation followed by decantation of oil, then

washed several times with isopropyl alcohol to remove traces of oil

The final preparation was a free-flowing powder consisting of spherical micron-sized particles. The physical mixture of 5-ASA and GGM was prepared by mixing the individual component in 1:1 ratio to form a uniform powder.

Characterization of microspheres

Determination of particle size

Particle size was measured by optical microscopy (INKO, Ambala, India) using a compound microscope. An ethereal suspension of GGM was allowed to dry on a clean glass slide to form a thin film. The slide containing the dry film of GGM was mounted on the stage of the microscope and a size of at least 500 particles was measured using a calibrated ocular micrometer. This process was repeated thrice for each batch prepared. The mean particle size was determined for each batch prepared. The 2-tailed paired 't' test was used to show the level of significance at p<0.05. The arithmetic mean diameter (ADM) was calculated using the formula (2):

$$ADM = \frac{(n_1d_1 + n_2d_2 + \dots + n_md_m)}{(n_1 + n_2 + \dots + n_m)} \quad (2)$$

Where n_1, n_2, \dots, n_m are the number of particles and d_1, d_2, \dots, d_m are diameter of particles.

Shape and surface morphology

The shape and surface morphology of the microspheres were investigated using scanning electron microscopy (SEM) (LEO-430, Cambridge, U.K.). The GGM were fixed on supports with carbon-glue, and coated with gold using a gold sputter module in a high-vacuum evaporator. Samples were then observed with the SEM at 15 kV.

Determination of encapsulation efficiency

50 mg of GGM were digested in 10 ml of phosphate buffer saline (PBS, pH 7.4) and heated for 10 min and kept aside for 72 h. Subsequently the solution containing GGM was centrifuged at 6000 rpm and a pellet was formed. The supernatant solution was withdrawn and filtered through 0.22 μm membrane filter (MDI, India) and an aliquot of the filtrate was diluted appropriately with PBS (pH 7.4) and absorbance was read at 330 nm¹ using UV-Visible spectrophotometer (Shimadzu, Kyoto, Japan). The percent encapsulation efficiency was calculated from the following formula:

$$\text{Encapsulation efficiency} = \frac{\text{Amount of drug recovered}}{\text{Amount of drug added}} \times 100$$

Fourier-transform infrared (FT-IR) spectroscopy

Fourier-transform infrared spectrum (FTIR) were recorded for 5-ASA, blank GGM, physical mixture of 5-ASA and blank GGM and 5-ASA GGM using Spectrum BX (Perkin Elmer) infrared spectrophotometer. Samples were prepared in KBr disk (2 mg sample/200 mg KBr) with a hydrostatic press at a force of 40 psi for 4 min. The scanning range employed was 450-4000 cm^{-1} .

Differential scanning calorimetry (DSC)

Thermal behavior of 5-ASA, blank GGM, physical mixture of 5-ASA and blank GGM and 5-ASA GGM was examined using a differential scanning calorimetry (DSC) Q 10V 8.1 Build 261 (Universal V 3.9 A TA Instruments) thermal analyzer. Argon was used as carrier gas and the DSC analysis was carried out at a heating rate of 10°C/min with argon flow rate of 35 cc/min. The sample size was 5 mg and the observations were recorded at the temperature range of 0 to 300°C.

Powder X-Ray diffraction pattern (PXRD)

Powder X-ray diffraction pattern (PXRD) was performed using a RIGAKU, Rotaflex, RV 200 (Rigaku Corporation, Japan) with Ni-filtered, Cu K α -radiation, at voltage of 45 Kv and current of 40 mA. The scanning rate employed was 1°C/min over at 25°C diffraction angle (2 θ) range. The PXRD patterns of 5-ASA, blank GGM, physical mixture of blank GGM and 5-ASA and 5-ASA GGM were recorded.

In-vitro release pattern

The *in-vitro* drug release studies were performed using USP dissolution rate test apparatus (paddle apparatus, 100 rpm, 37 \pm 0.1°C). 500 mg 5-ASA GGM were suspended in 900 ml of simulated gastric fluid (SGF, pH 1.2; without pepsin) for 2 h. The dissolution media was then replaced with simulated intestinal fluid (SIF, pH 7.5) and the release study was carried out for further 3 h, which corresponds to the average small intestinal transit time. Samples were withdrawn at different time intervals and the amount of 5-ASA was quantified using UV-Visible spectrophotometer (Shimadzu, kyoto, Japan) at 330 nm.¹ Sink condition were adjusted with the addition of an equal volume of fresh medium at the same temperature.

In-vitro release in presence of rat caecal contents

An *in-vitro* digestion study of 5-ASA GGM was also performed in the presence of rat caecal contents to ensure complete delivery of loaded drug in the colon. The animal experimentation protocols were conducted as per the guidelines of CPCSEA (Committee for the

Purpose of Control and Supervision of Experimental Animals), Ministry of culture, Government of India, New Delhi. The Institution Animal Ethics Committee approved the study. Albino rats weighing (150 \pm 50) g were kept on standard normal diet and water ad libitum. 1 ml of 1% w/v solution of guar gum in distilled water was administered orally in order to induce the enzymes, which are specified for the biodegradation of the guar gum during its passage through the colon. This treatment was continued for 2, 4 and 6 days in different sets of animals for enzyme induction. Rats were anaesthetized with diethyl ether, dissected and caecal contents were removed. The caecal contents were then transferred into simulated colonic fluid (SCF, pH 7.0), to produce 2% and 4% w/v caecal dilution. The formulation, which was previously subjected to *in vitro* drug release studies in SGF (pH 1.2) and SIF (pH 7.5) were kept in an empty gelatin capsule and immersed in the dissolution media. Samples were withdrawn at different time intervals and compensated with the same amount of fresh SCF (pH 7.0). The sample was filtered through a 0.22 μm (MDI, India) membrane filter and the amount of 5-ASA was quantified UV-Visible spectrophotometer (Shimadzu, Kyoto, Japan) at 330 nm¹.

RESULTS AND DISCUSSION

Evaluation of various process variables

In the present investigation, cross-linked microspheres of guar gum were prepared for colon-specific drug delivery of 5-ASA. Guar gum microspheres bearing 5-ASA (5-ASA GGM) were successfully prepared by the emulsion polymerization technique⁵ using castor oil in the external phase. The effect of various process variables such as stirring speed, stirring time, glutaraldehyde (GLA) content and temperature was analyzed in order to optimize the formulation (Table 1). It was observed that these variables considerably influence the shape, size as well as the entrapment efficiency of microspheres. Rigidity of the microspheres was imparted by chemical cross-linking method utilizing GLA as cross-linker. The acidic medium required for the process of cross-linking was imparted by the addition of concentrated sulfuric acid. The optimum concentration of GLA was found to be 1.5 ml. Particle size as well as entrapment efficiency was found to be decreasing with increasing the concentration of GLA. Below the optimized concentration the GGM were not formed. Span 80 was used to facilitate the stable dispersion of the polymer in oil. With affixed rotational speed, the stability of the dispersion of a particular polymer system depends on the concentration of emulsifier. An optimal concentration of

Table 1. Results of Evaluation of Various Process Variables

Code	5-ASA (mg)	GG (%)	GLA (ml)	Stirring Speed (rpm)	Temp. (°C)	Span80 (gm)	Particle size (µm)	Entrapment Efficiency (%)
F ₁	2%	1.5	4000	50	3	103.45 ± 10.32	-	-
F ₂	200	2%	1.5	4000	50	3	128.32 ± 4.95	65.12 ± 0.85
F ₃	400	2%	1.5	4000	50	3	129.42 ± 4.75	68.32 ± 0.59
F ₄	600	2%	1.5	4000	50	3	130.13 ± 5.86	76.31 ± 2.89
F ₅	800	2%	1.5	4000	50	3	131.89 ± 8.22	72.69 ± 1.47
F ₆	600	4%	1.5	4000	50	3	135.92 ± 10.08	77.37 ± 0.91
F ₇	600	6%	1.5	4000	50	3	140.87 ± 13.75	80.17 ± 1.04
F ₈ *	600	8%	1.5	4000	50	3	150.32 ± 11.8	82.39 ± 1.06
F ₉	600	8%	2	4000	50	3	137.14 ± 10.96	78.14 ± 1.10
F ₁₀	600	8%	4	4000	50	3	135.16 ± 10.41	76.41 ± 1.76
F ₁₁	600	8%	1.5	5000	50	3	145.45 ± 9.35	75.46 ± 5.48
F ₁₂	600	8%	1.5	4000	60	3	160.32 ± 8.45	83.38 ± 4.89
F ₁₃	600	8%	1.5	4000	70	3	162.45 ± 7.13	81.41 ± 2.13
F ₁₄	600	8%	1.5	4000	50	4	145.10 ± 11.92	78.31 ± 6.85
F ₁₅	600	8%	1.5	4000	50	5	141.33 ± 9.03	75.38 ± 1.04

5-ASA: 5-Amino salicylic acid (drug); GG: guar gum; GLA: Glutaraldehyde; F: Formulation; Temp: Temperature; Conc: Concentration.

emulsifier is required to produce the finest stable dispersion. Below this concentration the dispersion globules/droplets tends to fused and produced larger globules because a high amount of emulsifying agent increases the viscosity of the dispersion medium and by increasing the concentration of span 80, the irregular shaped GGM were formed with low entrapment efficiency. The optimal concentration of span 80 was found to be 3 gm. Excellent GGM were produced when the process was carried out with 8% guar gum. Particle size and entrapment efficiency was found to be increasing with the increasing guar gum concentration. The size of the GGM can be controlled by the size of the dispersed droplets of guar gum in castor oil. When the concentration of the guar gum in the formulation was increased, there was increase in the size of dispersed droplets that resulted in the formulation of GGM having bigger particle size. There was a profound influence of the speed of the stirrer on the size of the GGM. A significant reduction in the size of the GGM was observed but results also suggest that there was a mixing rate limit for a particular polymer concentration. A higher mixing rate did not further reduce the mean diameter. The mixing speed of 4000 rpm was found to be optimum for GGM. Mean particle size was found to be 130.13 ± 5.86 µm in case of GGM having 2% guar gum of formulation F₄ while it was significantly increased to 150.32 ± 11.8 µm with 8% guar gum concentration of formulation F₈* at stirring rate 4000 rpm by using 1.5 ml GLA and 3 gm span 80. Stirring time at a particular rotational speed

also influences the shape as well as the size distribution of GGM. A mixing time of 4 h was found to be optimal. The temperature of system plays a vital role in the process of formulation of GGM. GGM with relatively hard surfaces and cracks were produced when the process was performed at 70 ± 1°C and below 50 ± 1°C, GGM were not formed. Cracks were produced due to rapid evaporation of water from the dispersed solution of guar gum in castor oil. Entrapment efficiency also increases when the process was performed at 70 ± 1°C but produced GGM was unstable.

Surface morphology

Smooth surface microspheres were produced when the process was carried at 50 ± 1°C using 3 gm span 80 and 1.5 mL glutaraldehyde with stirring speed 4000 for 4 h (Figure 2). The mean particle size was found to be 130.13 ± 5.86 µm in case of GGM having 2% guar gum of formulation F₄ while it was significantly increased to 150.32 ± 11.8 µm with 8% guar gum concentration of formulation F₈* (Figure 2a and c). Microspheres with relatively hard surfaces and cracks were produced when the process was performed at 70 ± 1°C (Figure 2d).

FT-IR

We characterized GGM by various spectroscopy techniques. The FTIR spectrum peaks of 5-ASA, blank GGM, physical mixture of 5-ASA and blank GGM and 5-ASA GGM shown in Table 2. The FTIR spectrum of

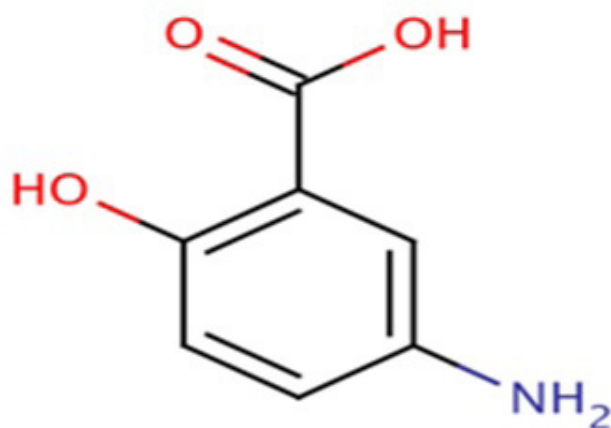


Figure 1: Schematic representation of chemical structure of 5-Amino salicylic acid

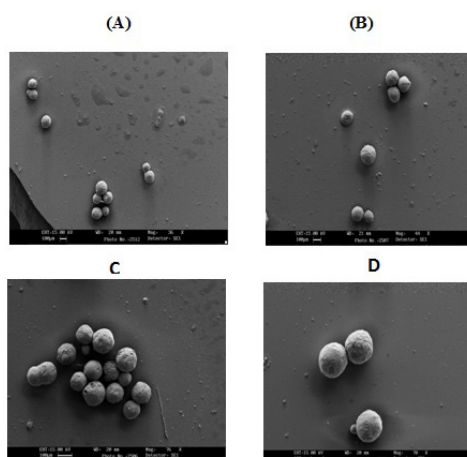


Figure 2: Scanning electron microscopy of (A), F₁ (Blank GGM prepared with 2% guar gum using 1.5 ml of GLA at 50 ± 1°C temperature) (B), F₄ (5-ASA GGM prepared with 2% guar gum using 1.5 ml of GLA at 50 ± 1°C temperature) (C), F₈ (5-ASA GGM prepared with 8% guar gum using 1.5 ml of GLA at 50 ± 1°C temperature); (D), F₁₃ (5-ASA GGM prepared with 8% guar gum using 1.5 ml of GLA at 70 ± 1°C temperature)

pure 5-ASA shows characteristic peaks at 1266.2 cm⁻¹ for C-N stretching vibration, 1620.3 cm⁻¹ indicates for N-H in plane bending and at 1794.7 cm⁻¹ and 1487.9 cm⁻¹ indicating the presence of benzene ring. Other peaks are observed at 2982.8 cm⁻¹ for aryl C-H stretching and 1651.0 cm⁻¹ for C=O stretching vibration of carboxylic acid. The FTIR spectrum of blank GGM shows characteristic peaks at 810.4 cm⁻¹ and 1158.8 cm⁻¹ indicating the C-(CH₂)-C in plane bending and C-O-C symmetric stretching respectively. Other peaks are observed at 1377.9 for C-H bending vibration, 2926.9 cm⁻¹ for C-H stretching, 874.2 for C-O-C stretching, 1024.5 for O-H in plane bending vibration, 1742.4 for C=O stretching and 3384.6 for polymeric O-H stretching. In physical mixture of 5-ASA and blank GGM peaks observed at

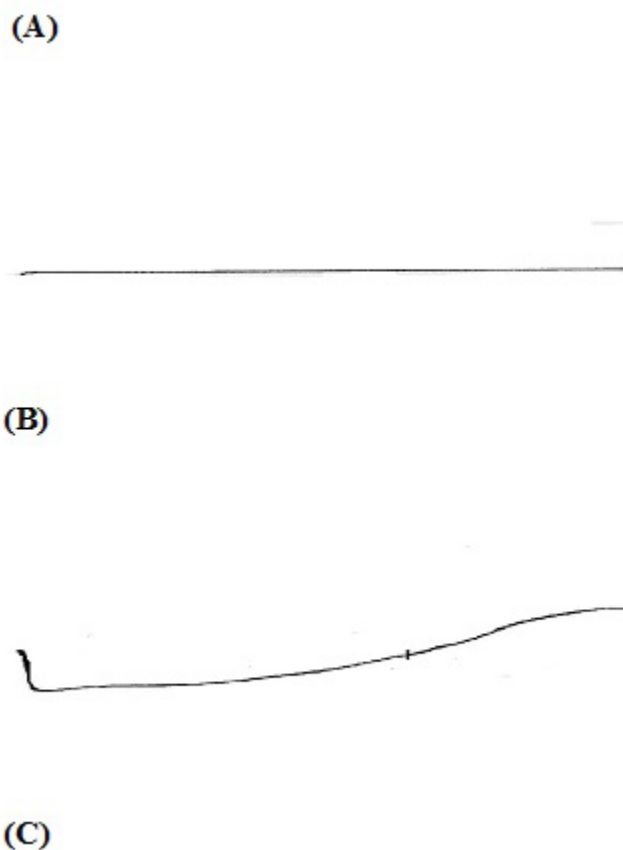


Figure 3: Differential scanning calorimetry of (A), 5-ASA; (B), Blank GGM (C), Physical mixture of 5-ASA and blank GGM (D), 5-ASA GGM

811.8 cm⁻¹, 1265.4 cm⁻¹ which indicating the C-(CH₂)-C in plane bending and C-N stretching vibration. Other peaks are observed at 884.1 cm⁻¹ for O-H out of plane bending, 3447.2 cm⁻¹ for Polymeric O-H stretching, 683.8 cm⁻¹ for C-C out plane bending in benzene ring and 1650.5 cm⁻¹ for C=O stretching vibration of carboxylic acid. The 5-ASA GMM shows characteristic peaks at 3400.3 cm⁻¹ for Polymeric O-H stretching, 2931.4 cm⁻¹ for C-H stretching, 1623.4 cm⁻¹ for N-H in plane bending, 879.8 cm⁻¹ for C-O-C stretching, 681.7 cm⁻¹ for C-C out plane bending in benzene ring and 1679.3 cm⁻¹ for C=O stretching vibration of carboxylic acid. FTIR spectra were recorded to analyze the GGM, it was observed that no new chemical bond was formed when the drug was encapsulated in the guar gum microspheres and compared with the spectra of individual components as shown in Table 2.

DSC

The DSC was carried out to examine the thermal behavior of 5-ASA GGM whether the drug was encapsulated in microspheres or not. The characteristic endothermic

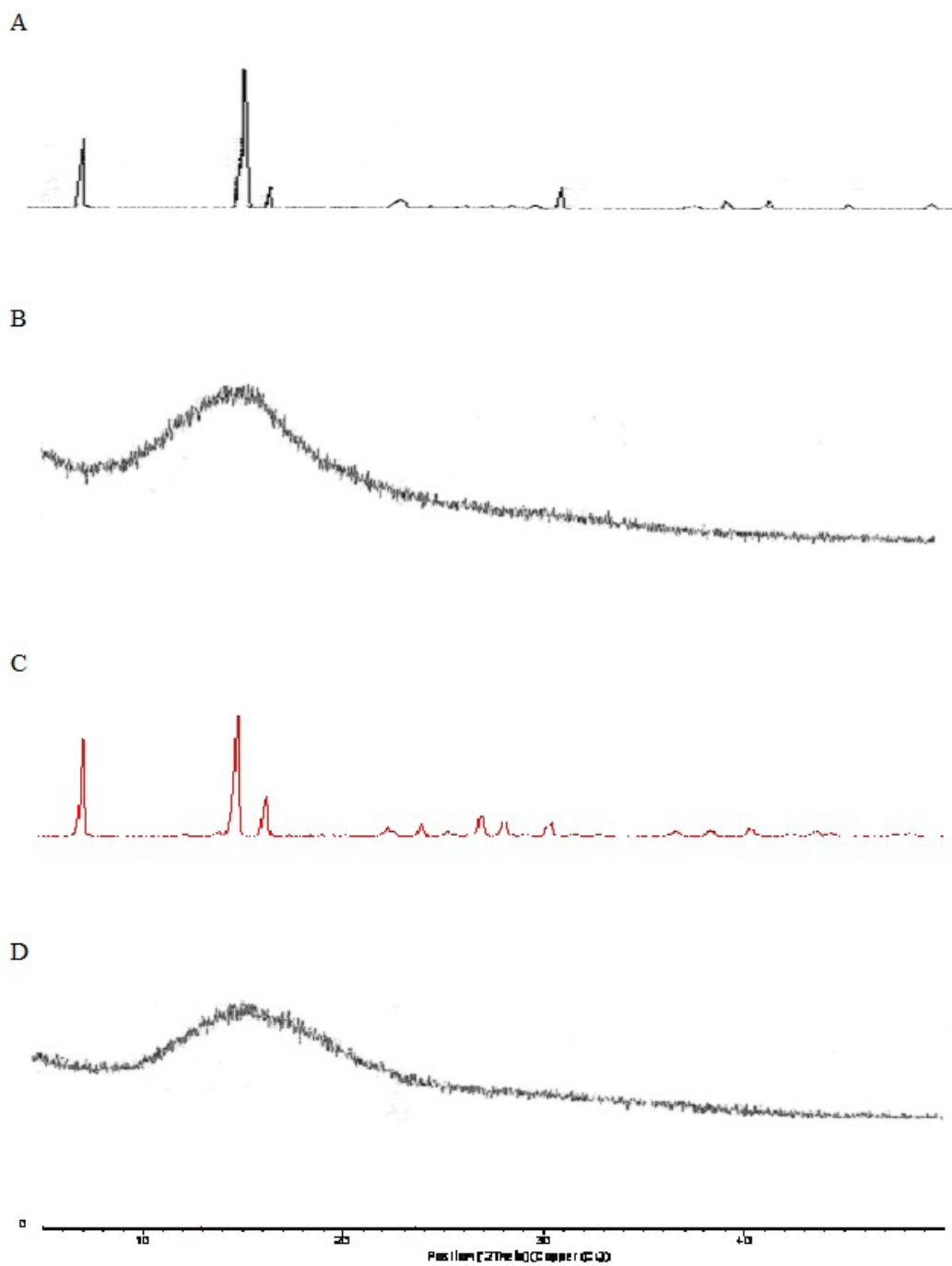


Figure 4

Figure 4: Powder X-ray diffraction pattern of (A), 5-ASA; (B), Blank GGM (C), Physical mixture of 5-ASA and blank GGM (D), 5-ASA GGM

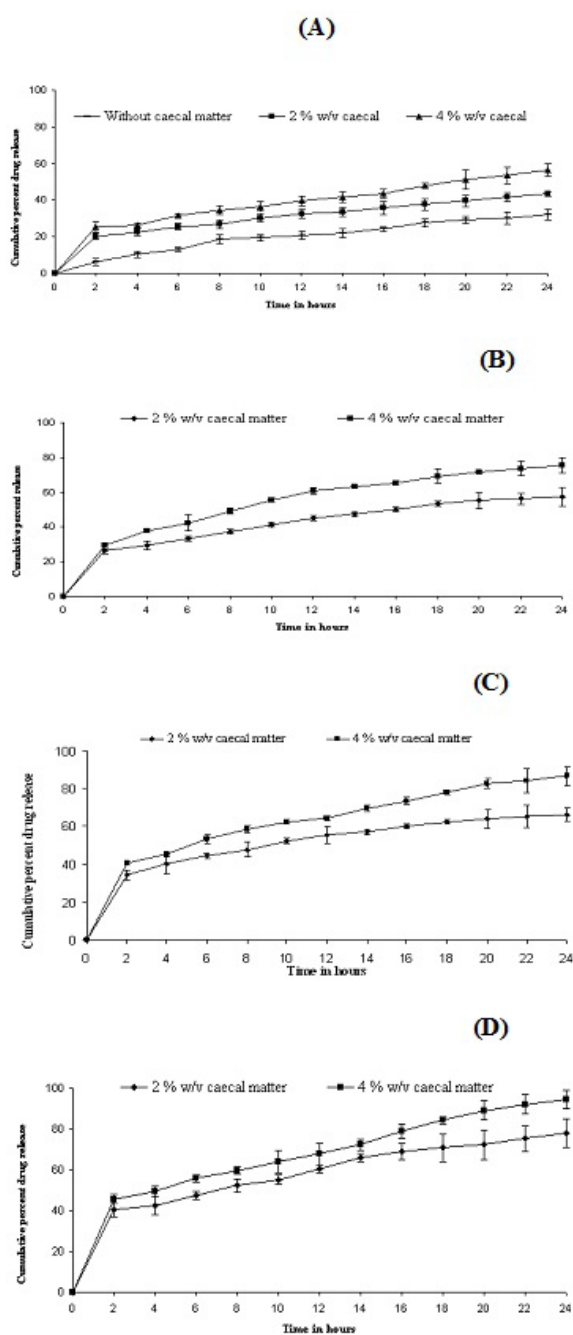


Figure 5

Figure 5: In vitro drug release of (A) 5-ASA from formulation F_8 in SCF (pH 7.0) without caecal contents, 2% and 4% rat caecal content (B) 5-ASA in SCF (pH 7.0) with 2% and 4% rat caecal matter from formulation F_8 after 2 days enzyme induction (C) 5-ASA in SCF (pH 7.0) with 2% and 4% rat caecal matter from formulation F_8 after 4 days enzyme induction (D) 5-ASA in SCF (pH 7.0) with 2% and 4% rat caecal matter from formulation F_8 after 6 days enzyme induction

peak appeared at 298.38°C and 163.50°C for 5-ASA and blank guar gum microspheres, respectively, disappeared in 5-ASA loaded guar gum microspheres curve, in which a new characteristic peak at 207.78°C appeared (Figure 3

a-d). The DSC curve of the physical mixture also differed from that of 5-ASA GGM and shows endothermic peak at 295.57 of 155.08 of 5-ASA and blank GGM, respectively. This demonstrated the molecular encapsulation of 5-ASA in polymeric matrix of GGM and hence; indicating the single broad peak of 5-ASA-GGM. This is consistent to the results published previously.¹²

PXRD

PXRD technique was used to define the crystalline structure of 5-ASA in GGM. The X-ray diffraction pattern of 5-ASA, blank GGM, and physical mixture of 5-ASA and blank GGM as well as 5-ASA GGM are shown in (Figure 4). The XRD pattern of 5-ASA showed peaks that was intense and sharp, indicating its crystalline structure. However, 5-ASA GGM presented the peak of diminished intensity, which suggested the amorphous structure of 5-ASA in the GGM.

In-vitro drug release

The optimized formulation F_8 was subjected to *in-vitro* drug release rate studies in SGF (pH 1.2) for 2 h and SIF (pH 7.5) for further 3 h in order to investigate the capability of the formulation to withstand the physiologic environment of the stomach and small intestine. The amount of the 5-ASA released during 5 h studies was found to be $(13.93 \pm 0.62) \%$, which attests the ability of guar gum to remain intact in the physiological environment of stomach and small intestine. It is a well-established fact that the gelling property retards release of the 5-ASA from the GGM. The little amount of drug, which is released during 5 h release rate studies, is due to the presence to un-entrapped drug on the surface of the GGM. The initial release of drug present on the surface was higher during the 2 h study, which could be due to the fact that there was no viscous gel layer around it, which controls the release of the entrapped drug and it might have formed after 2 or 3 h which controlled the further release of drug. The *in-vitro* drug release studies were performed in SCF (pH 7.0) with and without using rat caecal content (Figure 5 a-d). The amount of drug released from formulation was found to be higher having 2% rat caecal content $(43.32 \pm 1.33) \%$ when compared to the study conducted without rat caecal content (32.11 ± 0.87) at the end of the 24 h from dissolution medium. In case of dissolution medium with 4% caecal content $(56.39 \pm 2.38) \%$, drug released from formulation was found to be higher in comparison to study involving 2% rat caecal content $(43.32 \pm 1.33) \%$. The study reveals that the release of drug in the physiologic environment of the colon is due to degradation of guar gum by colonic bacteria released

from rat caecal content. The release of drug from F_8 was supposed to take place after swelling which resulted in the formation of gel followed by the dissolution of 5-ASA and diffusion through the gel. The gel strength of the GGM swelled in the dissolution media may too high, preventing the release of drug from formulation. The colonic bacteria action of rat caecal content medium (2% and 4%) might not be sufficient to degrade the high strength gel barrier of the swollen microspheres. As a result, only $(43.32 \pm 1.33) \%$ and $(56.39 \pm 3.30) \%$ of drug were released after 24 h with 2% and 4% rat caecal content medium, respectively. Hence, different set of animals was administered with 1 ml of 1% (w/v) aqueous solution of guar gum for 2, 4 and 6 days to induce the enzymes that specifically act on guar gum during passage of formulation through the colon. The drug release in case of GGM with 2% and 4% rat caecal matter obtained after 4 days enzyme induction was found to be $(66.31 \pm 3.44) \%$ and $(86.41 \pm 5.01) \%$ respectively. The release of higher amount of drug in case of microspheres with 2% and 4% rat caecal matter obtained after 6 days enzyme induction was found to be $(78.12 \pm 7.06) \%$ and $(94.62 \pm 4.50) \%$ respectively. The amount of drug released from F_8 formulation was found to be higher after enzyme induction. The release of higher amount of drug in case of microspheres with 4% rat caecal matter obtained after 6 days enzyme induction may be attributed to enhancement in the concentration of degrading enzyme in dissolution medium that ultimately improved the release rate.

CONCLUSION

The emulsion polymerization method proposed for the guar gum microspheres was found to be a good technique to entrap 5-ASA and capable of providing protection to drug in the hostile environment of upper gastrointestinal tract and release of drug at target site. In the present investigation, we established that guar gum may be used as the biopolymer to target the anti-inflammatory drug (5-ASA) for the management of colitis. Various studied parameters including particle size, surface morphology and *in vitro* drug release indicating the utility of 5-ASA-GGM in the delivery of

therapeutic moiety to the colon. Therefore our targeting nanoformulation, 5-ASA-GGM warrants further *in vivo* investigations to scale up the technology for clinical translation.

ACKNOWLEDGEMENT

We are highly thankful to the management of Hindu College of Pharmacy, Sonapat (Haryana) for providing financial assistance to carry out this research work.

CONFLICT OF INTEREST

There is no conflict of interest.

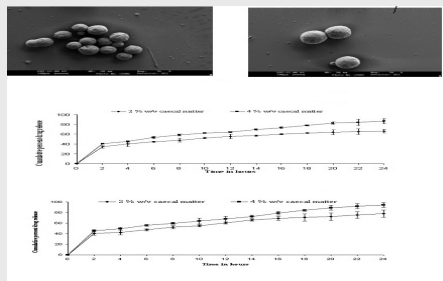
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SUMMARY

- 5-Amino salicylic acid (5-ASA), a drug of choice for the treatment of crohn's disease and ulcerative colitis.
- 5-ASA loaded guar gum microspheres can be used as therapeutic agent for the treatment of ulcerative colitis at specific site.

PICTORIAL ABSTRACT



ABBREVIATIONS USED

5-ASA: 5-AminoSalicylic Acid; **GGM:** Guar Gum Microspheres; **SGF:** Simulated Gastric Fluid; **SIF:** Simulated Intestinal Fluid; **SCF:** Simulated Colonic Fluid; **SEM:** Scanning electron microscopy; **DSC:** Differential Scanning Calorimetry; **PXRD:** Powder X-Ray Diffraction.

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