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Evaluation of guar gum as a compression coat for drug targeting to colon

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Abstract

Colon-specific drug delivery systems based on a polysaccharide, guar gum, were evaluated using in vitro and in vivo methods. In vitro drug release studies have shown that guar gum in the form of compression coat applied over indomethacin core tablets protects the drug from being released under conditions mimicking mouth to colon transit. Studies in pH 6.8 phosphate buffered saline (PBS) containing 4% w/v rat caecal contents have demonstrated the susceptibility of guar gum to the colonic bacterial enzyme action with consequent drug release. gamma-scintigraphic studies in human volunteers with technetium-99m-DTPA as a tracer in sodium chloride core tablets compression coated with guar gum have shown that the gum coat protect the drug (tracer in the present study) from being released in the stomach and small intestine. On entering the ascending colon, the tablets commenced to release the tracer indicating the breakdown of the gum coat by the enzymatic action of colonic bacteria. The tablets disintegrated in the ascending colon of all the volunteers, except one, resulting in the distribution of released tracer across the entire colon. The study clearly established that guar gum, in the form of compression coat, is a potential carrier for drug targeting to colon.

Keywords: Guar gum; Polysaccharide; Colonic drug delivery; Rat caecal contents; Gamma-scintigraphy

1. Introduction

Drug targeting to colon is highly desirable in a variety of colonic disorders such as inflammatory bowel diseases (IBD), infectious diseases and colon cancer. Colon is also found to be a promising site for systemic absorption of peptide and protein drugs because of less hostile environment prevailing in the colon compared with stomach and small intestine (Antonin et al., 1996; Tozaki et al., 1997). The different approaches for targeting orally administered drugs to the colon include coating with pH-dependent polymers, design of timed-release dosage forms and the utilisation of

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carriers that are degraded exclusively by colonic bacteria (Van den Mooter et al., 1995; Rama Prasad et al., 1996). The poor site-specificity of pH-dependent systems, because of large variations in the pH of the gastrointestinal tract, was very well established (Evans et al., 1988; Ashford et al., 1993a). The site-specificity of timed-release dosage forms is considered poor because of large variations in gastric emptying times (Davis et al., 1984) and passage across the ileo-caecal junction (Marvola et al., 1987).

A variety of metabolic reactions like hydrolysis, reduction, decarboxylation, dealkylation etc. are carried out by the anaerobic bacteria residing in the colon. Colon-specific drug delivery systems developed on the basis of these metabolic reactions include prodrugs (Chan et al., 1983; Friend et al., 1991; McLeod et al., 1994; Leopold and Friend, 1995) which are cleaved by colonic bacterial enzymes thereby releasing the actual drug in the colon. Different azo polymers (Kopecek et al., 1992; Van den Mooter et al., 1993, 1994; Kalala et al., 1996) are under investigation as coating materials for the delivery of drugs to the colon which are reduced by azoreductase enzymes present specifically in the colon.

Some studies are also under way on the basis of the activity of colonic bacteria on polysaccharide based carrier systems. The different polysaccharides that are under evaluation as carriers for colonic drug delivery include pectin and its salts (Ashford et al., 1993b, 1994; Rubinstein et al., 1993; Wakerly et al., 1996a,b), chondroitin sulfate (Rubinstein et al., 1992a,b), amylose (Milojevic et al., 1995) and inulinHP (Vervoort and Kinget, 1996). In another study, a suspension of natural polygalactomannans in polymethacrylate solution was used to form a degradable coating which delayed the drug release in the small intestine by forming a swellable layer around the drug core and is degraded by colonic bacterial enzymes thereby releasing the drug in the colon (Lehmann and Dreher, 1991). This formed the basis to investigate the usefulness of guar gum, which also contains polygalactomannans, as a carrier for drug targeting to colon. Further, dexamethasone matrix tablets containing guar gum were studied for colon-specific drug delivery (Kenyon et al., 1997).

Guar gum is a high molecular weight (220000) hydrocolloidal polysaccharide derived from the seeds of *Cyamopsis tetragonolobus*, family Leguminosae. The plant is grown in India, Pakistan and South-western region of USA. The gum consists of linear chains of $(1\rightarrow4)$-β-D-mannopyranosyl units with α-D-galactopyranosyl units attached by $(1\rightarrow6)$ linkages (Goldstein et al., 1973). The pH of 1% w/v aqueous dispersion varies from 5 to 7 and is stable over a wide pH range. The viscosity of guar gum dispersion is same in both acidic and alkaline media. In pharmaceutical formulations, guar gum is used as a binder, disintegrant, suspending agent, thickening agent and stabilising agent.

In the present investigation, guar gum, in the form of compression coat applied over core tablets, was evaluated as a carrier for colon-specific drug delivery. In vitro drug release studies were carried out on indomethacin core tablets compression coated with different quantities of guar gum in simulated gastrointestinal (GI) fluids in the presence and absence of rat caecal contents. Further, gamma-scintigraphic studies were carried out in healthy male volunteers with technetium-99m-DTPA (^{99m}Tc-DTPA) as a tracer in sodium chloride core tablets compression coated with guar gum to find their in vivo behaviour.

2. Materials and methods

2.1. Materials

Guar gum (viscosity of 1% w/v aqueous dispersion 2300 cps at 25°C), magnesium stearate and talc were obtained from Dabur, India and were of pharmacopoeia quality. Indomethacin (BP) was obtained from Recon, Bangalore, India. Molybdenum-99 (source of Tc-99m) and diethylene triamine pentaacetic acid (DTPA) were obtained from Board of Radiation and Isotope Technology, Mumbai, India. Other materials used were microcrystalline cellulose (Avicel, FMC Type pH-105), sodium starch glycollate, sodium lauryl sulphate, sodium chloride and methanol, and were used as received.

Table 1
Composition and thickness of guar gum coats used to cover indomethacin core tablets

Coat formulation	Coat weight (mg)	Composition (mg)				Coat thickness (mm)
		Guar gum	MCC	Magnesium stearate	Talc	
F1	230	200	25	2	3	1.96
F2	175	150	20	2	3	1.33
F3	175	125	45	2	3	1.18
F4	175	100	70	2	3	1.09

2.2. Preparation of compression coated tablets

Indomethacin, a poor water soluble drug, was chosen as a model drug to evaluate guar gum for its colon-specific drug delivery and to differentiate the drug release by the disintegration of coat and not by simple diffusion. Each core tablet (average weight 80 mg) for in vitro drug release studies consisted of indomethacin (40 mg), microcrystalline cellulose (MCC, 29 mg), dried sodium starch glycollate (5 mg), sodium lauryl sulphate (4 mg), talc (1.5 mg) and magnesium stearate (0.5 mg). Sodium starch glycollate and sodium lauryl sulphate were added to obtain fast disintegration tablets (disintegration time < 1 min) of indomethacin. The materials were weighed, mixed and passed through a mesh (250 μm) to ensure complete mixing. The tablets were prepared by compressing the thoroughly mixed materials using 6 mm round, flat and plain punches on a single station tablet machine (Cadmach, India). The thickness of the core tablets was 2.00 ± 0.005 mm and their crushing strength was 3 kg/cm^2. These core tablets were compression coated with different quantities (Table 1) of coating material containing 200, 150, 125 and 100 mg of guar gum. Since guar gum alone gave very soft coats, microcrystalline cellulose was included in the coat formulations to impart enough hardness. Half the quantity of the coating material was placed in the die cavity, the core tablet was carefully positioned in the centre of the die cavity and was filled with the other half of the coating material. The coating material was compressed around the core at an applied force of 5000 kg using 9 mm round, flat and plain punches. The crushing strength of the compression coated tablets was 5 kg/cm^2.

Each core tablet (average weight 100 mg) for in vivo studies consisted of sodium chloride (80 mg), microcrystalline cellulose (18 mg), talc (1 mg) and magnesium stearate (1 mg). Sodium chloride was used as a bulking agent and 74 MBq of ^{99m}Tc-DTPA, a soluble radiolabelled compound, was adsorbed on to it. ^{99m}Tc-DTPA was prepared by radiolabelling a standard DTPA test kit with sodium pertechnetate solution which was obtained by the elution of Molybdenum-99 in a work station. Sodium chloride was dissolved in the resultant ^{99m}Tc-DTPA solution, evaporated to dryness, mixed with other excipients and compressed into tablets using 6 mm round, flat and plain punches. The crushing strength of the tablets was 3 kg/cm^2 and their thickness was 2.00 ± 0.005 mm. These core tablets were compression coated with 175 mg of coating material containing 125 mg of guar gum (coat formulation F3) at an applied force of 5000 kg using 9 mm round, flat and plain punches as described above.

2.3. In vitro drug release studies

The compression coated tablets of indomethacin were evaluated for their integrity in the physiological environment of stomach and small intestine under conditions mimicking mouth to colon transit. These studies were carried out using a USP XXIII dissolution rate test apparatus (apparatus 1, 100 rpm, 37°C). The tablets were tested for drug release for 2 h in 0.1 N HCl (900 ml) as the average gastric emptying time is about 2 h. Then the dissolution medium was replaced with pH 7.4 Sorensen's phosphate buffer (900 ml) and tested for drug release for 3 h as the average small intestinal transit time is about 3 h. At the

end of the time periods, two samples each of 1 ml were taken, suitably diluted and analysed for indomethacin content at 318 nm using a double beam UV spectrophotometer (Shimadzu, UV-150-02).

The susceptibility of guar gum coats to the enzymatic action of colonic bacteria was assessed by continuing the drug release studies in 100 ml of pH 6.8 phosphate buffered saline (PBS) containing 4%w/v of rat caecal contents. The caecal contents were obtained from male albino rats (supplied by Ghosh, Calcutta, India, weighing 150–200 g) after pre-treatment for 7 days with guar gum dispersion. Our earlier studies (Rama Prasad et al., 1998) have shown that the presence of 4% w/v rat caecal contents in pH 6.8 PBS obtained after 7 days of pre-treatment of rats with 1 ml of 2% w/v aqueous dispersion of guar gum provide the best conditions for in vitro evaluation of guar gum. 30 min before the commencement of drug release studies, five rats were killed by spinal traction. The abdomen were opened, the caecai were isolated, ligated at both ends, dissected and immediately transferred into pH 6.8 PBS, previously bubbled with CO_2. The caecal bags were opened, their contents were individually weighed, pooled and then suspended in PBS to give a final caecal dilution of 4% w/v. As the caecum is naturally anaerobic, all these operations were carried out under CO_2.

The drug release studies were carried out in USP dissolution rate test apparatus (apparatus 1, 100 rpm, 37°C) with slight modification. A beaker (capacity 150 ml, internal diameter 55 mm) containing 100 ml of dissolution medium was immersed in the water contained in the 1000 ml vessel, which was, in turn, in the water bath of the apparatus. The tablets were placed in the baskets of the apparatus and immersed in the dissolution medium containing rat caecal contents. The experiment was carried out with continuous CO_2 supply into the beakers to simulate anaerobic environment of the caecum. The drug release studies were carried out for 21 h (usual colonic transit time is 20–30 h) and 1 ml samples were taken at different time intervals without a prefilter and replaced with 1 ml of fresh PBS bubbled with CO_2. To the samples, 1 ml of methanol was added to ensure solubility of finely suspended drug particles released due to break down of the coat by the caecal enzymes. The volume was made up to 10 ml with PBS, centrifuged and the supernatant was filtered through a bacteria-proof filter and the filtrate was analysed for indomethacin content at 318 nm as described above. The above study was carried out on all the indomethacin tablets coated with different coat compositions (F1, F2 and F3) and also without caecal matter in pH 6.8 PBS (control).

2.4. In vivo γ-scintigraphic studies

Six healthy male subjects of 20–23 years of age and 55–70 kg weight participated in the study as volunteers. They were non-alcoholics, non-smokers and were not on any drugs. The purpose of the study was fully explained and each volunteer had given his written consent. After overnight fasting, each volunteer orally ingested technetium-^{99m}-DTPA-containing sodium chloride core tablets compression coated with coat formulation F3 with 200 ml of water. The tablets were visualised using a γ-camera (EGC 1400, Electronic Corporation of India) with a 36 cm field of view and fitted with a low energy parallel hole collimator. An external marker was used to allow correct alignment of subjects during successive imaging. The subjects were served with breakfast, lunch and dinner after 2, 4 and 10 h of tablet administration respectively. Anterior images of 60 s duration were taken with subjects in supine position immediately after tablet administration and after 0.5, 1, 1.5, 2, 3, 4, 5, 6, 8, 10 and 12 h. A follow up image was taken next day morning at 24 h in those volunteers in whom the tracer still remained in the colon.

3. Results

3.1. In vitro drug release studies

The percent drug released at different time periods from indomethacin tablets compression coated with coat formulations F1, F2 and F3 in 0.1 N HCl (2 h), pH 7.4 Sorensen's phosphate

buffer (3 h) and pH 6.8 PBS (21 h) are shown in Fig. 1. At the end of the experiment, all these three formulations were found to be intact retaining their coats and slight swelling of coats due to water sorption was observed. However, tablets coated with coat formulation F4 were found broken within 10 min in 0.1 N HCl and hence were not studied further. The results of the drug release studies carried out in the presence of 4% w/v of rat caecal contents in pH 6.8 PBS are shown in Fig. 2. At the end of 26 h of testing, indomethacin tablets coated with coat formulation F1 were found to be intact. The tablets coated with coat formulation F2 were found broken at one point indicating commencement of the disintegration of the coat whereas the coat formulation F3 was completely disintegrated.

3.2. In vivo γ-scintigraphic studies

From the scintigraphs taken at regular time intervals, the gastric emptying time was found to be 30–60 min and the small intestinal transit time was 2–3 h. The colonic arrival time of the tablets

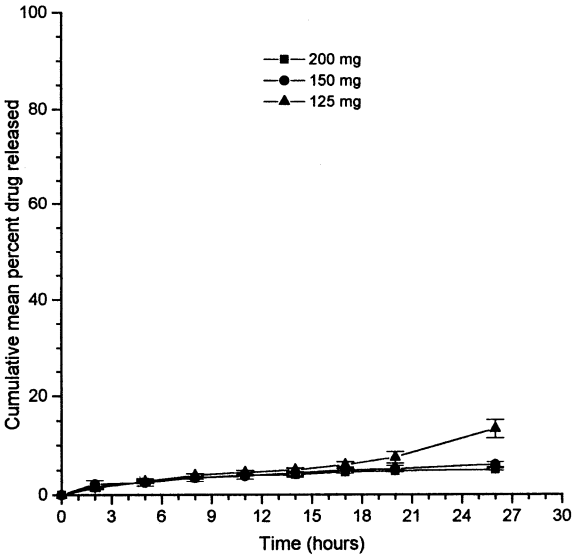

Fig. 1. Cumulative mean (±S.E.M.) percent drug released from indomethacin tablets ($n=3$) compression coated with different quantities of coating material containing 200, 150 and 125 mg of guar gum in 0.1 N HCl (2 h), pH 7.4 buffer (3 h) and pH 6.8 PBS (21 h).

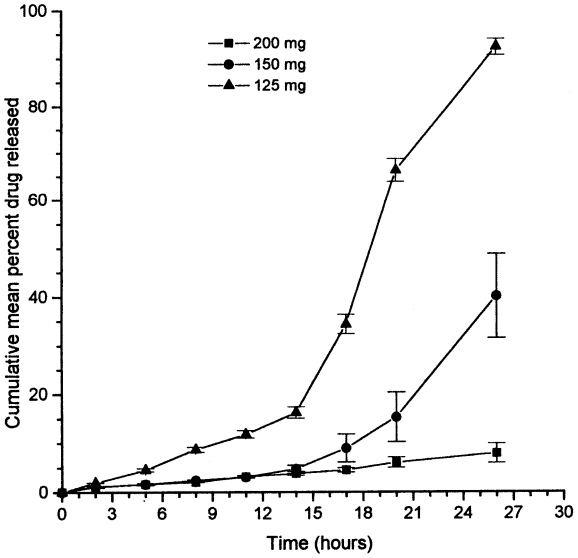

Fig. 2. Cumulative mean (±S.E.M.) percent drug released from indomethacin tablets ($n=3$) compression coated with different quantities of coating material containing 200, 150 and 125 mg of guar gum in 0.1 N HCl (2 h), pH 7.4 buffer (3 h) and pH 6.8 PBS containing 4% w/v of rat caecal contents (21 h).

was 3–4 h in all the volunteers. The tracer was not released either in stomach or in small intestine of the volunteers. On entering the caecum/ascending colon only, the tablets began to release the tracer indicating the degradation of the gum coats.

Scintigraphs showing intact tablet in small intestine (2 h), the commencement of disintegration of the coat (4 h), distribution of broken pieces of the tablet in ascending colon, hepatic flexure, transverse colon and splenic flexure (8 h) and uniform distribution of the released tracer across the entire colon (12 h) in volunteer 3 are shown in Fig. 3. The position of the released tracer in the colon at different time intervals in the volunteers is given in Table 2. At the end of 12 h, the released tracer was found distributed in different segments of the colon in four out of the six volunteers. In volunteer 2, the released tracer was concentrated in ascending colon after 12 h of tablet administration. The colonic transit time was short in volunteer 4 and hence the tablet mass reached the sigmoid colon within 4 h of entering the colon. In the present study, only anterior

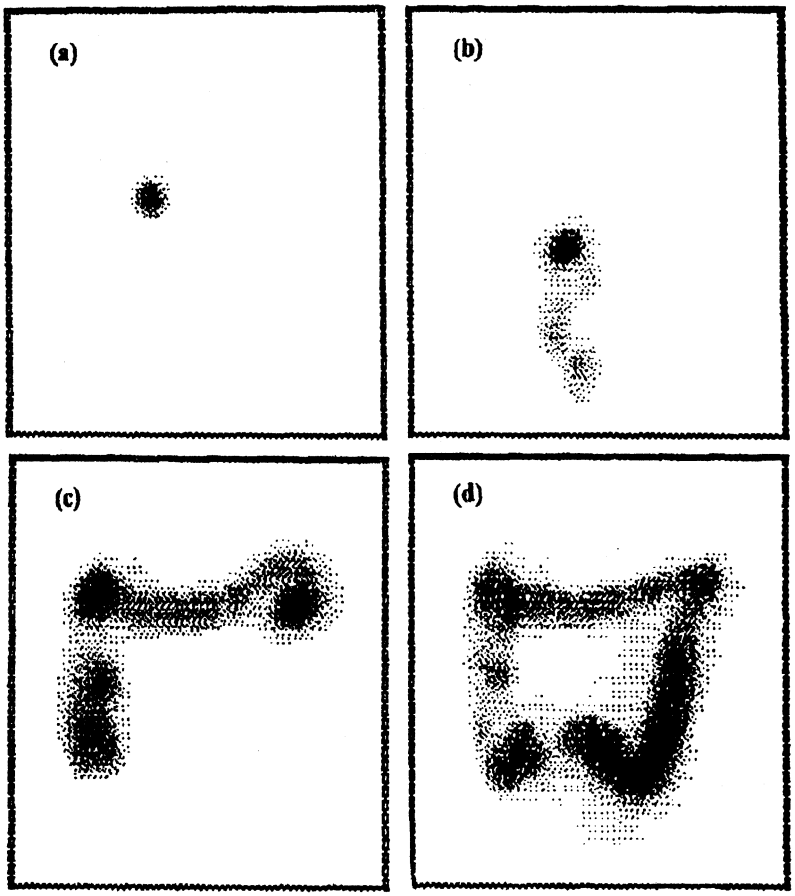

Fig. 3. Γ-Scintigraphs showing (a) guar gum coated tablet remaining intact in small intestine at 2 h (b) commencement of disintegration in ascending colon at 4 h (c) disintegration and distribution of broken pieces of tablet in ascending colon, hepatic flexure, transverse colon and splenic flexure at 8 h and (d) complete disintegration of the tablet and distribution of the tracer throughout the colon at 12 h (volunteer 3).

images of 60 s duration were taken by placing the volunteers in supine position using a γ-camera. Hence, no data with respect to percent tracer released in different segments of colon were available with this type of imaging. This is because of variations in the distance from the γ-camera to the biological location of the tablet or the released tracer.

4. Discussion

Successful delivery of drugs specifically to the colon requires the protection of drug from being released in stomach and small intestine. In the present investigation, guar gum in the form of compression coat was applied over indomethacin core tablets and drug release studies were carried out under conditions mimicking mouth to colon transit. Different types of dissolution apparatus such as rotating sealed glass vials/fermenter (Rubinstein et al., 1993), flow through dissolution apparatus (Ashford et al., 1994; Wakerly et al., 1996b), USP apparatus 1 (Ashford et al., 1993b), USP apparatus 2 (Wakerly et al., 1996a; Munjeri et al., 1997) and USP apparatus 3 (Wong et al., 1997) were used for in vitro evaluation of colon-specific drug delivery systems. Though all the

Table 2
Position of the released tracer in colon at different time periods in the volunteers

Volunteer	Position of the released tracer at		
	4 h	8 h	12 h
1	Ascending colon	Ascending colon, transverse colon and splenic flexure	Hepatic flexure, transverse colon, splenic flexure and descending colon
2	Ascending colon	Ascending colon	Ascending colon
3	Ascending colon	Ascending colon, hepatic flexure, transverse colon and splenic flexure	Ascending colon, hepatic flexure, transverse colon, splenic flexure and descending colon
4	Ascending colon	Hepatic flexure, descending colon and sigmoid colon	Sigmoid colon
5	Ascending colon	Ascending colon, hepatic flexure, transverse colon, splenic flexure and descending colon	Ascending colon, hepatic flexure, transverse colon, splenic flexure, descending colon and sigmoid colon
6	Ascending colon	Ascending colon	Hepatic flexure, spreading towards transverse colon

above gave satisfactory results, none of them is established as standard apparatus for the evaluation of colonic drug delivery systems. In the present in vitro study, the volume of dissolution fluid, containing rat caecal contents, was only 100 ml in order to simulate the fluid volume of the colon. Apparatus 2 is not suitable since the wider paddle blade (diameter 75 mm) can not be dipped in the dissolution fluid contained in the beaker (diameter 55 mm).

USP apparatus 3 was used for the evaluation of guar gum formulations meant for colonic drug delivery (Wong et al., 1997). In this study the authors used water soluble enzyme, galactomannase, at a concentration of 0.01 mg/ml. The level of polysaccharidases in 4 g of rat caecal contents used in the present study, though not estimated, may be far less than what was used by Wong et al. (1997). Hence, it is necessary that the guar gum formulations be continuously in contact with the dissolution fluid for better access to the caecal enzymes. This could be achieved by the use of USP apparatus 1. Moreover, the use of USP apparatus 3 also results in settling of the rat caecal contents in the bottom of the vessel. The maintenance of an anaerobic environment in USP apparatus 3 may also be problematic. Because of these reasons, USP apparatus 1 with slight modifications was used in the present study to evaluate guar gum as a carrier in the form of compression coat for colon-specific drug delivery. Further, earlier workers (Ashford et al., 1993b) also used apparatus 1 for the evaluation of colonic delivery systems.

Indomethacin was used as a model drug to assess the ability of guar gum to deliver the drugs selectively to the colon by conducting in vitro drug release studies. The cumulative mean percent indomethacin released from tablets coated with coat formulations containing 200, 150 and 125 mg of guar gum (F1, F2 and F3) was found to vary from 2.45 to 2.65 after 5 h of testing in simulated gastric and intestinal fluids (Fig. 1). On exposure to the dissolution fluids, the gum gets hydrated and forms a viscous gel layer that slows down further seeping-in of dissolution fluids towards the core tablets. The hydration of guar gum seems not to be affected by the pH of the dissolution medium. Thus, guar gum in the form of coat is capable of protecting the drug from being released completely in the physiological environment of stomach and small intestine. However, the tablets with coat formulation F4 were found disintegrated within 10 min in 0.1 N HCl and this may be due to lesser gum content (100 mg) of the coat which was unable to remain intact and failed to protect the drug core from being released. To assess the integrity of the coats, the drug release studies were further continued for 21 h by replacing the dissolution medium with pH 6.8 PBS. At

the end of the experiment, the cumulative mean percent drug released from coat formulations F1, F2 and F3 was between 5 and 13.5 and the coats were intact. This indicates that the gum will not permit the release of the bulk of the drug core until the coat is broken.

The drug delivery systems targeted to the colon should not only protect the drug from being released in the physiological environment of stomach and small intestine, but also release the drug in colon after enzymatic degradation by colonic bacteria. Hence, in vitro drug release studies were carried out in pH 6.8 PBS containing 4% w/v of rat caecal contents. At the end of 26 h of testing which includes testing in simulated gastric and intestinal fluids, the percent drug released from indomethacin tablets coated with coat formulation F1 was found to be only 7.87 ± 1.97 (Fig. 2) and the coat remained intact. The presence of higher amount of guar gum (200 mg) in the coat with resultant thicker coat (1.96 mm) might not have allowed the disintegration of the coat during the time period of testing. This also indicates that the drug will not be released unless the coat is broken.

The percent drug released from tablets coated with coat formulation F2 was found to increase from 17 h onwards indicating the commencement of breaking of gum coats. The percent drug released after 26 h of testing was 40.23 ± 8.69 and the tablet coat was found to be broken at one point making way for the release of the drug. In case of tablets coated with coat formulation F3, a significant increase in percent drug released was observed from 14 h onwards and at the end of the experiment $92.49 \pm 1.71\%$ of indomethacin was released. The coat was completely degraded by the rat caecal enzymes thereby releasing the drug into the dissolution medium. Since the guar gum content and thickness of coat formulation F3 were lesser (125 mg, 1.18 mm) compared to coat formulations F1 (200 mg, 1.96 mm) and F2 (150 mg, 1.33 mm), the coat might have been completely hydrated and subsequently degraded by the caecal enzymes at a faster rate resulting in the release of about 92% of indomethacin. It is evident from the results of the drug release studies in the presence and absence of rat caecal contents that the drug release occurred by the degradation of guar gum coats by the enzymes present in the caecal matter.

The in vitro drug release studies in the presence of rat caecal contents showed that coat formulation F3 containing 125 mg of guar gum was optimal for selective delivery of drugs to colon. However, the evaluation of the dosage forms in humans is the ultimate requirement to establish their credibility. Hence, γ-scintigraphic studies were carried out in six healthy male volunteers to assess the in vivo performance of the coat formulation F3. The studies were carried out using Tc-99m-DTPA, adsorbed onto sodium chloride, as a tracer since indomethacin can not be visualised by the γ-camera. However, Tc-99m-DTPA could have been adsorbed onto indomethacin for visualising the compression coated tablets. But, the hydrophobic nature of indomethacin did not permit uniform adsorption of the tracer onto it. Hence, the salt core (NaCl) was used because of the ease of adsorption with Tc-99m-DTPA and its use in the evaluation of pectin-based colonic delivery systems was established by earlier workers (Ashford et al., 1993b).

The tablets coated with coat formulation F3 did not release any amount of tracer either in stomach or small intestine in all the six volunteers indicating that guar gum coat, in the amount used, could successfully prevent the release of drug in stomach and small intestine. The gastric emptying times were found to vary in between 30 and 60 min which is almost similar to those reported for healthy subjects under fasting conditions (Khosla and Davis, 1989). The small intestinal transit time was found to vary from 2.5 to 3 h. Hence, the colonic arrival time in all the volunteers was between 3 and 4 h. Stasis at ileocaecal junction for about 1 h was observed in volunteers 3 and 5 and this might be the reason for taking about 4 h for the tablets to enter the colon in these volunteers.

On entering the ascending colon, the coatings of the tablets began to disintegrate because of bacterial enzymatic action, which was evident from the released tracer visible in the ascending colon (Fig. 3b). After 12 h of tablet administration, the tracer was uniformly distributed

throughout the colon (Fig. 3d) indicating enzymatic degradation of guar gum coats by human colonic bacteria. The absence of release of the tracer either in the stomach or small intestine (Fig. 3a), the release of tracer only on entering the colon (Fig. 3b) and the subsequent breaking of the tablet into pieces in the colon (Fig. 3c) clearly indicate that the release of tracer was the result of the breakdown of the guar gum coat. Since the core consisted of water soluble material (NaCl), it is possible that the release of the tracer was a combined effect of enzymatic action and diffusion of sodium chloride. It appears that guar gum, when applied as a compression coat, could successfully prevent the release of even soluble drugs in stomach and small intestine. This is evident from the absence of release of the tracer either in stomach or in small intestine (Fig. 3a).

After 12 h of tablet administration, the tablets were completely disintegrated and the tracer was distributed in different segments of the colon in volunteers 1, 3, 5 and 6 (Table 2) In volunteer 4, the colonic transit of the tablet mass was fast and it reached sigmoid colon within 4 h after entering the colon. Though some amount of tracer was released in ascending, transverse and descending colon, most of the tracer was retained in the tablet mass. The short period of residence of the tablet in proximal colon might not have permitted complete degradation of the gum coat by the colonic bacterial enzymes. But, in volunteer 2, the released tracer remained in the ascending colon itself even after 12 h of tablet administration. For this particular volunteer, a follow up image was also obtained after 24 h which was not possible with other volunteers. The difference may be because of inter-subject variation in colonic transit times. Thus, the study established the transit times and disintegration sites of the tablets across the different regions of the GI tract.

In vitro drug release studies using indomethacin as a model drug and in vivo γ-scintigraphic studies using Tc-99m-DTPA as a tracer indicate that guar gum coat applied over a core tablet is capable of protecting the drug from being released in the physiological environment of stomach and small intestine and is susceptible to colonic bacterial enzymatic action with resultant drug release in the colon. Thus, the study clearly demonstrated that guar gum is a potential colon-specific drug delivery carrier.

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