JPP Journal of Pharmacy and Pharmacology

JPP 2007, 59: 359–365

Received July 24, 2006
Accepted October 26, 2006
DOI 10.1211/jpp.59.3.0004
ISSN 0022-3573

Compression coated systems for colonic delivery of 5-fluorouracil

V. R. Sinha, Asmita Singh, Sanjay Singh and J. R. Bhinge

Abstract

Compression coating is one of the approaches for delaying the release of drugs. The aim of this study was to develop colon-specific compression coated systems of 5-fluorouracil (5-FU) for the treatment of colorectal cancer using xanthan gum, boswellia gum and hydroxypropyl methylcellulose (HPMC) as the coating materials. Core tablets containing 50 mg of 5-FU were prepared by direct compression. The coating of the core tablets was done using different coat weights (230, 250, 275 and 300 mg) and different ratios (1:2, 2:1, 1:3, 1:7 and 3:4) of boswellia gum and xanthan gum and different ratios (1:1, 1:2, 2:1, and 2:3) of boswellia gum and HPMC. In-vitro release studies were carried out using simulated gastric and intestinal fluids, with and without rat caecal contents. Among the different ratios used for coating with boswellia:xanthan gum combination, ratio 1:3 gave the best release profile with the lowest coating weights of 230 mg (7.47 ± 1.56% in initial 5 h). Further increase in the coat weights to 250, 275 and 300 mg led to drug release of 5.63 ± 0.53%, 5.09 ± 1.56% and 4.57 ± 0.88%, respectively, in the initial 5 h and 96.90 ± 0.66%, 85.05 ± 1.01% and 80.22 ± 0.35%, respectively, in 24 h. When coating was carried out using different ratios of the combination boswellia gum and HPMC, the ratio 2:3 gave the best results among the initial trial batches (7.80 ± 0.57% in 5 h). Increasing the coat weights to 250, 275 and 300 mg led to drug release of 6.5 ± 0.27%, 3.70 ± 2.3% and 2.99 ± 0.72%, respectively, in the initial 5 h and 96.90 ± 0.66%, 85.05 ± 1.01% and 80.22 ± 0.35%, respectively, in 24 h. In-vitro studies were further carried out in the presence of 2% w/v rat caecal contents, which led to complete release of the drug from the tablets. Therefore, this study lays a basis for use of compression coating of 5-FU as a tool for delaying the release of the drug, which ensures better clinical management of the disease.

Pharmaceutics Division, University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh 160014, India

V. R. Sinha, Asmita Singh, J. R. Bhinge

Department of Pharmaceutics, IT, BHU, Varanasi 221005, India

Sanjay Singh

Correspondence: V. R. Sinha, Pharmaceutics Division, University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh 160014, India. E-mail: vr_sinha@yahoo.com

Acknowledgements and Funding: The authors acknowledge the financial support received from All India council for technical education and University Grant Commission, New Delhi. The authors greatly acknowledge M/s Getwell Pharmaceuticals, Gurgaon, India and Dabur Research Foundation, Ghaziabad, India for gift samples of 5-fluorouracil and xanthan gum, respectively.

Introduction

Colorectal cancer is becoming increasingly common in Asian countries and still remains the second leading cause of cancer deaths in the USA (Wargovich 2001). The treatment options available for stage II or stage III colorectal cancer are surgery alone or surgery in combination with radiation therapy. However, such cases tend to exhibit recurrence on later stages and hence chemotherapy is advised after surgery to reduce risk. Among the various chemotherapeutic agents available, 5-fluorouracil (5-FU) is considered to be the standard first-line treatment, which exhibits clinical activity against colorectal carcinoma (Calabresi & Chabner 1992). 5-FU is usually administered intravenously, since its oral bioavailability is erratic. Intravenous administration, however, leads to severe haematological, neural, gastrointestinal and cardiac side effects (Diasio & Harris 1989). To minimize these side effects, to increase clinical efficacy and to provide a safe and effective therapy with 5-FU for colorectal cancer, vigorous research is underway for developing site-specific rate controlling/targeting systems (Zambito et al 2005). A great deal of research work has been devoted for developing site-specific delivery to the colon (Lamprecht et al 2003; Xu et al 2005; Rahman et al 2006). However, approaches for the colon-specific delivery of 5-FU are very few, and among them the most noteworthy are based on the use of compression coating (Krishnaiah et al 2002; Sinha & Kumria 2003, 2004, 2005; Odeku & Fell 2005).

Compression coated systems as a means for delaying and targeting drug moieties to the colon offer numerous benefits over the conventional coating methods, such as short processing times, reduction in the equipment and labour costs, decreased energy expenditure and

restriction of steps and solvents in the manufacturing process (Lin et al 2004). Moreover, compression coated systems are formulated making use of biodegradable polymers, which offer more benefits like ease of degradation by the colonic microflora and delayed, as well as site-specific, release in the colon.

Working on this rationale, this investigation was based on the utilization of naturally occurring, biodegradable and drug-release-retarding ingredients falling under the category of polysaccharides (i.e. xanthan gum (XG) and boswellia gum). Boswellia gum is obtained from various species of *Boswellia*. It has been used for its beneficial anti-proliferative and anti-carcinogenic potential in colorectal cancer (Liu et al 2002), besides its utility as a pharmaceutical excipient. The gum portion of *B. sacra* comprises two polysaccharides, one of equal proportions of galactose and arabinose, the other of galactose and galactouronic acid in the proportions 2:1 (Rees 1995). The polysaccharide portion might be susceptible to the wide variety of enzymes secreted by colonic microflora.

Xanthan gum has a high molecular weight. It contains D-glucose and D-mannose as dominant hexose units, along with D-glucuronic acid. It retards drug release considerably due to its swelling properties (Talukdar & Kinget 1995; Sujja-areevath et al 1998). Hydroxypropyl methylcellulose (HPMC) is another synthetic retardant that is widely used as an extended release agent in the pharmaceutical industry. It offers very good swelling and gel-forming properties (Kiil & Dam-Johansen 2003; Rinaki et al 2003; Kavanagh & Corrigan 2004).

The main aim of this study was to formulate a dosage form that could provide a delayed delivery of 5-FU to the colonic region for the treatment of colorectal cancer using inexpensive, naturally occurring and abundantly available polysaccharides by means of a compression coating technique.

Materials and Methods

Materials

5-Fluorouracil was a gift from Getwell Pharmaceuticals (Gurgaon, India). Boswellia gum was procured from Arya Vastu Bhandar (Uttaranchal, India). Xanthan gum USNF was a gift from Dabur Research Foundation (Ghaziabad, India). HPMC K-4M was procured from Ranbaxy laboratories Ltd (Gurgoan, India). Starch, talc and magnesium stearate used for the preparation of tablets were of pharmacopoeial grade.

Preparation of 5-FU core and compression coated tablets

Core tablets consisting of 5-FU (250 mg), microcrystalline cellulose and spray-dried lactose were prepared. A weighed quantity of 5-FU required for the batch was mixed thoroughly with the required amount of microcrystalline cellulose and spray-dried lactose. After thorough mixing the blend was lubricated. A 350-mg quantity was taken and compressed individually into tablets using 11.5-mm-deep concave punches on a single punch tableting machine (Modern Engg Works, New Delhi, India) using 4000 kg compression force.

Table 1 Composition of the compression coating mixture containing different ratios of boswellia gum and xanthan gum

Formulation code	Ratio		Total weight (mg)
	Boswellia gum	Xanthan gum	
BXC_1	1	2	230
BXC_2	2	1	230
BXC_3	1	3	230
BXC_4	1	7	230
BXC_5	3	4	230
BXC_6	1	3	250
BXC_7	1	3	275
BXC_8	1	3	300

Table 2 Composition of the compression coating mixture containing different ratios of boswellia gum and HPMC

Formulation code	Ratio		Total weight (mg)
	Boswellia gum	HPMC	
BHC_1	1	1	230
BHC_2	1	2	230
BHC_3	2	1	230
BHC_4	2	3	230
BHC_5	2	3	250
BHC_6	2	3	275
BHC_7	2	3	300

The compression coat was prepared using two different combinations of polymers, one comprising boswellia gum and xanthan gum and other comprising boswellia gum and HPMC. The core tablets were coated with different coat weights as well as with different ratios of polymers. Tables 1 and 2 outline the composition of coats. The polymers were sifted and mixed in different ratios before compression. An amount equivalent to 40% of coat weight was placed in the die cavity followed by carefully centering of the core tablet and addition of the remainder of coat weight. The coating material was compressed around the core tablet using a single-station tableting machine with 13-mm standard flat punches. Core tablets were compression coated with different coating mixtures. Initially, 230 mg of coat material was applied onto the core tablets. Further, in an attempt to reduce the drug release, coating weights were increased to 250, 275 and to a maximum of 300 mg, which was applied over the core tablets. Compression coated 5-FU tablets with different compositions were tested for thickness, hardness, drug content and drug release characteristics.

Determination of drug content

The core tablets, as well as compression coated tablets, of 5-FU were tested for their drug content. The tablets were finely powdered and a quantity of the powder equivalent to 250 mg of 5-FU was accurately weighed and transferred to a 100-mL volumetric flask containing pH 6.8 phosphate buffer. The flask was allowed to stand for 2 h with intermittent vortexing to ensure complete solubility of the drug. The solutions were made up to the volume and filtered. After a suitable dilution the

amount of 5-FU was analysed using a UV spectrophotometer. All the determinations were performed in triplicate.

Preparation of rat caecal content medium

Seven Wistar rats, 150–200 g, fed on a normal diet, were killed by spinal traction 1 h before the in-vitro studies. The abdomens were opened, the caecae were located, ligated at both the ends, dissected and the caecal contents were weighed and immediately transferred into pH 6.8 buffer previously bubbled with nitrogen. The suspension was filtered through a muslin cloth and added to the dissolution media to give a final caecal content concentration of 2% w/v. All the above procedures were carried out under nitrogen to maintain anaerobic conditions.

Drug release studies

The ability of the prepared tablets to retard drug release in the physiological environment of the stomach and the small intestine was assessed by conducting drug release studies in simulated stomach and small intestinal pH, respectively. The changing pH of the media, Method 1, USP 24, for delayed release tablets was used. The dissolution test was conducted in USP type II apparatus at 50 rev min^{-1} and a temperature of 37°C. Initial drug release studies were conducted in 750 mL of 0.1 N HCl for 2 h. Then, 250 mL of 0.2 M trisodium phosphate was added to the dissolution media and the pH adjusted to 6.8. Samples were withdrawn after regular intervals of time to evaluate drug release. These were analysed spectrophotometrically at a wavelength of 266 nm, as absorption maxima studies showed λ_{Max} at 266 nm in both the media (i.e. 0.1 N HCl (pH 1.2) and pH 6.8 phosphate buffer).

Drug release studies in the presence of caecal content were also carried out using USP dissolution test apparatus. However, a slight modification in the procedure was made. The experiments were carried out in a 250-mL beaker immersed in the jars of the dissolution test apparatus (type I). Initial studies were carried out in 187.5 mL of 0.1 N HCl (pH 1.2) for 2 h. After this, 62.5 mL of 0.2 M trisodium phosphate was added to the dissolution media and the pH adjusted to 6.8. The study at a pH of 6.8 was continued for 3 h, after which caecal content equivalent to 5 g was added to 250 mL of buffer (pH 6.8) to give a final caecal dilution of 2% w/v. Dissolution in the caecal content media was carried out until completion at 24 h. The experiments in caecal content media were carried out in the presence of a continuous supply of nitrogen. At different time intervals a 5-mL sample was withdrawn from the dissolution medium and replaced with fresh buffer containing caecal content. Samples were filtered thought a 0.45-μm membrane filter and were analysed spectrophotometrically at 266 nm after appropriate dilution against the suitable blank to avoid any interference due to caecal content.

Statistical analysis

Statistical analysis to compare the effect of coating composition and coat weights on the tablet dissolution performance was performed using Friedman's test, a nonparametric multiple comparison test. The individual differences between the different formulations were tested using Dunn's test. The cumulative percent of 5-FU released from the compression coated tablets (n = 3) in the dissolution medium at 24 h with and without rat caecal contents was compared and the statistical significance was tested by Mann–Whitney *U*-test, using the software Sigmastat 2.0 (Jandel Sigmastat, USA). $P < 0.05$ was considered statistically significant in all the tests.

Results and Discussion

Core tablets

The core tablets of 5-FU were prepared by direct compression of the blend prepared by mixing all the ingredients. The core tablets had a diameter of 11.50 ± 0.13 mm and thickness 3.82 ± 0.08 mm. Microcrystalline cellulose was added to the tablet core to make the core disintegrate rapidly. The hardness of the core tablets was found to be in the range of 3.0–4.0 kg cm^{-2}. These tablets were found to comply with the friability test since the weight loss was found to be less than 0.66%.

Compression coated tablets

The different coat materials used for the coating purpose are outlined in Table 1 and Table 2. The mixture was prepared by proper mixing of the respective materials. The hardness of the tablets was found to be in the range of 5–7.5 kg cm^{-2}. The compression coated tablets containing an outer shell of boswellia gum and xanthan gum mixture had a diameter of 13.02 ± 0.05 mm and thickness of 4.21 ± 0.09 mm. The compression coated tablets having boswellia gum and HPMC mixture in the outer shell had a diameter of 13.02 ± 0.04 mm and thickness of 4.21 ± 0.09 mm.

Drug content

The cores, as well as the coated tablets, were evaluated for their drug content. It was found that the core tablet contained 95.40–100% of 5-FU and the coated tablet contained 94.81–100% of 5-FU.

In-vitro drug release studies

Many factors, such as transit time, pH, microbial flora, etc., affect the design and development of a colonic dosage form and the release of the drug in a bioavailable fraction from the same. All these factors require due consideration to make the desired dosage form a success. A colon-targeted drug delivery system should not only prevent drug release in the initial 5 h (which mimics the transit from mouth to colon) but also needs to ensure the complete release of the drug from the dosage form at the desired site (Sinha & Kumria 2005). In this study, attempts were made to develop a new drug delivery system comprising a new degradable polysaccharide in combination with two release-retarding agents, xanthan gum and HPMC. For chemotherapeutic agents like 5-FU, the early release is required to be drastically minimized to avoid its

side effects. The compression coats were designed to undergo bacterial degradation in the colon, exposing the rapidly disintegrating drug core in the colon.

In-vitro release studies for batches prepared using boswellia gum and xanthan gum

The results of the drug release studies carried out on 5-FU tablets compression coated with a combination of xanthan gum and boswellia gum in different ratios and coating weights, in simulated gastric (pH 1.2) and small intestinal (pH 6.8) environment are shown in Figure 1. Five batches were initially prepared with varying ratios of boswellia gum (BL) and xanthan gum (XG) (BL:XG 1:2 (BXC_1); BL:XG 2:1 (BXC_2); BL:XG 1:3 (BXC_3); BL:XG 1:7 (BXC_4); and BL:XG 3:4 (BXC_5)) with a coating weight of 230 mg. Tablets in all the batches showed swelling properties that were higher as the proportion of xanthan gum was increased in the coat mixture. The tablets showed a burst effect after 12 h, leading to a sudden increase in the drug release. The physical appearance of the tablets after 12 h and 24 h of dissolution studies are shown in Figure 2. As is evident from the pictures, the tablets remains intact in a swollen state until 12 h, after which it shows marked increase in swelling leading to the burst effect and complete release of the drug. BL:XG 1:2 showed a drug release of $8.16 \pm 0.67\%$ in the initial 5 h and $98.58 \pm 1.56\%$ of drug was released in 24 h, indicating that compression coating could prove to be one of the most successful approaches in retarding drug release. On increasing the proportion of boswellia gum in the coat as in formulation BL:XG 2:1, the drug release in 5 h increased ($14.22 \pm 0.53\%$) and $98.33 \pm 0.89\%$ of the drug was released in 24 h. Hence in the next formulation, BL:XG 1:3, the proportion of xanthan gum was increased. BL:XG 1:3 showed a further decrease in drug release compared with BL:XG 1:2, showing that the major contributing agent towards retardation of drug release was xanthan gum. It showed a drug release of $7.47 \pm 1.56\%$ in the initial 5 h and $99.04 \pm 1.01\%$ of drug was released in 24 h. However, increasing the concentration of xanthan gum to 7 parts per 1 part of boswellia gum, BL:XG 1:7, gave results contradictory to expected. Instead of decreasing the drug release, it led to a rise in the drug release to $23.67 \pm 0.66\%$ in the initial 5 h and $99.77 \pm 0.34\%$ in 24 h. This may be because an increase in the proportion of xanthan gum in the gum mixture could not show the desired retardation due to poor interaction with boswellia gum, which led to increased pore formation at higher concentration and hence increased drug release. BL:XG 3:4 showed results as per the normal trend, giving a release of $20.31 \pm 0.88\%$ in the initial 5 h and $97.01 \pm 1.76\%$ in 24 h. Analysis using Friedman's test showed that there was a statistically significant difference ($P < 0.01$) in the percentage of drug released from the formulations with different coating compositions, which was further individually compared using Dunn's test. There was statistically significant difference ($P < 0.05$) among the formulations. From results of the dissolution test, it can be concluded that batch BL:XG 1:3 could best retard the drug release. To prevent drug release

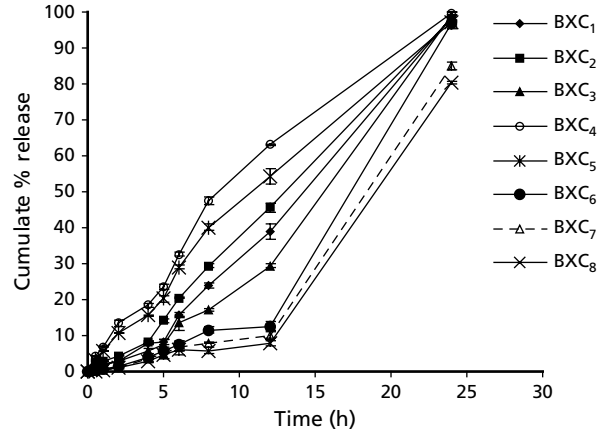

Figure 1 Cumulative percentage of drug released from 5-FU compression coated boswellia gum (BL)–xanthan gum (XG) tablets with different coating ratios: BXC_1 (BL:XG 1:2), BXC_2 (BL:XG 2:1), BXC_3 (BL:XG 1:3), BXC_4 (BL:XG 1:7) and BXC_5 (BL:XG 3:4) and different coat weights: BXC_6 (BL:XG 1:3, 250 mg), BXC_7 (275 mg) and BXC_8 (300 mg). Data are means ± s.d., n = 3.

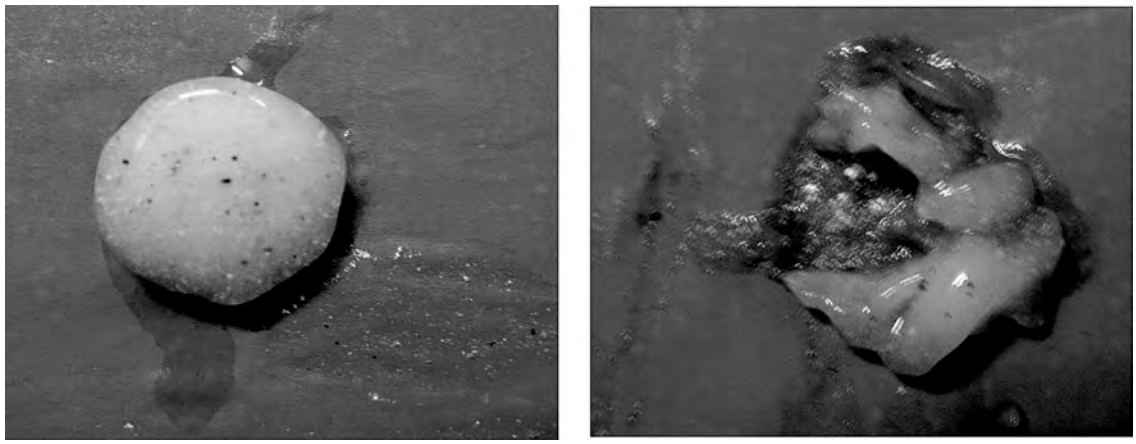

Figure 2 Physical appearance of the tablets after 12 h (left panel) and after 24 h (right panel) of dissolution.

in the upper gastrointestinal conditions, batches were prepared by increasing the coating weights. Samples BL:XG 1:3 (BXC_6, 250 mg), BL:XG 1:3 (BXC_7, 275 mg) and BL:XG 1:3 (BXC_8, 300 mg) showed a progressive decrease in the drug release with increase in coating weight (Figure 1). Whereas batch BL:XG 1:3 (250 mg) showed a release of 5.63 ± 0.53% in the initial 5 h and 96.90 ± 0.66% in 24 h, BL:XG 1:3 (275 mg) showed a further decrease to 5.09 ± 1.56% in the initial 5 h and 85.05 ± 1.01% in 24 h. Similarly, BL:XG 1:3 (300 mg) showed a drug release of 4.57 ± 0.88% in the initial 5 h and 80.22 ± 0.35% in 24 h. Analysis using Dunn's multiple comparison test showed that there was a statistically significant difference ($P < 0.05$) in the percentage drug release from the formulations BXC_6, BXC_7 and BXC_8. Thus, it can be concluded that increasing coat weight from 250 to 300 mg had a significant effect. So, by increasing the coat thickness, the drug release in the initial 5 h was retarded to the very low value of 4.5% but at the same time the final drug release was also affected. However, in the presence of rat caecal contents, complete drug release is expected due to degradation of boswellia gum. This was further tested in the presence of rat caecal contents.

In-vitro release studies in the presence of rat caecal contents for batches prepared using boswellia gum and xanthan gum

Studies were conducted on batches BXC_7 and BXC_8, to observe their performance in the presence of rat caecal contents. The two batches showed higher drug release in the later stage of dissolution, indicating their success as dosage forms to deliver maximum drug to the colon in a delayed fashion as well as ensuring the complete release of the drug in the colon in 24 h. Batch BXC_7 showed a release of 20.21 ± 0.85% in 6 h as compared with 6.71 ± 0.98% release in in-vitro conditions (Table 3). Similarly, BXC_8 showed a release of 20.21 ± 1.76% in the initial 6 h (Table 3). Both the batches showed complete dug release in 24 h (BXC_7 = 98.12 ± 0.67%; BXC_8 = 98.22 ± 0.44%). A significant difference ($P < 0.001$) was observed in the amount of 5-FU released at the end of 24 h of the dissolution study in both the batches with rat caecal content medium when compared with the dissolution study without rat caecal contents.

In-vitro release studies for batches prepared using boswellia gum and HPMC

Four batches of compression coated tablets were prepared using combination of boswellia gum and HPMC as the coating mixture (i.e. BHC_1 (BL:HPMC 1:1), BHC_2 (BL:HPMC 1:2), BHC_3 (BL:HPMC 2:1), BHC_4 (BL:HPMC 2:3)), with a coating weight of 230 mg. BHC_1 (BL:HPMC 1:1) showed a release of 11.56 ± 0.58% in the initial 5 h and 99.13 ± 0.54% in 24 h (Figure 3). BHC_2 (BL:HPMC 1:2) showed a retardation in release in the initial 5 h with increasing percentage of the HPMC (8.23 ± 0.45% in the initial 5 h and 99.33 ± 0.21% in 24 h). Similarly, BHC_3 (BL:HPMC 2:1) had a release of 9.01 ± 0.26% in the initial 5 h and 99.16 ± 0.23% in 24 h. However, batch BHC_4 (BL:HPMC 2:3) showed a further decrease in drug release on increasing HPMC concentration (7.80 ± 0.80% in the initial 5 h and 99.70 ± 0.37% in 24 h). Analysis using Friedman's test showed that there was a statistically significant difference ($P < 0.05$) in the percentage of drug released from the formulations with different coating compositions, which was further individually compared using Dunn's test. There was statistically significant difference ($P < 0.05$) among the formulations, but among all the above batches, BHC_4 (BL:HPMC 2:3) gave the most suitable results and further batches were taken with increased weights of this ratio.

Batches BHC_5, BHC_6 and BHC_7 were made with coating weights of 250, 275 and 300 mg, respectively. All these batches showed a progressive decrease in the drug release as the coating weight was increased (Figure 3). Whereas batch BHC_5 (BL:HPMC 2:3), showed a release of 6.5 ± 0.27% in the initial 5 h and 93.38 ± 0.25% in 24 h, BHC_6 (BL:HPMC 2:3) showed a further decrease to 3.7 ± 2.3% in the initial 5 h and 89.89 ± 0.77% in 24 h. Similarly, BHC_7 (BL:HPMC 2:3) showed a drug release of 2.99 ± 0.72% in the initial 5 h and 85.46 ± 0.28% in 24 h (Figure 3). Analysis using Dunn's multiple comparison test showed that there was a statistically significant difference ($P < 0.05$) in the percentage of drug released from the formulations, which indicated that increasing the coat weight from 250 to 300 mg affected the percentage of

Table 3 Percentage of 5-FU released from batches BXC_7 (BL:XG 1:3, 275 mg coat weight) and BXC_8 (BL:XG 1:3, 300 mg coat weight) with and without rat caecal contents

Time (h)	Cumulative % release from BXC_7		Cumulative % release from BXC_8	
	Without rat caecal contents	With rat caecal contents	Without rat caecal contents	With rat caecal contents
5	5.09 ± 0.23	5.77 ± 0.38	4.57 ± 0.98	5.77 ± 0.33
6	6.71 ± 0.98	20.21 ± 0.85	6.09 ± 0.77	20.21 ± 1.76
8	7.93 ± 0.23	63.22 ± 0.66	5.79 ± 0.01	63.22 ± 0.66
10	10.12 ± 0.10	83.22 ± 0.45	7.92 ± 0.45	83.22 ± 0.73
24	85.05 ± 2.08	98.12 ± 0.67	80.22 ± 2.56	98.22 ± 0.44

Data are means ± s.d., n = 3.

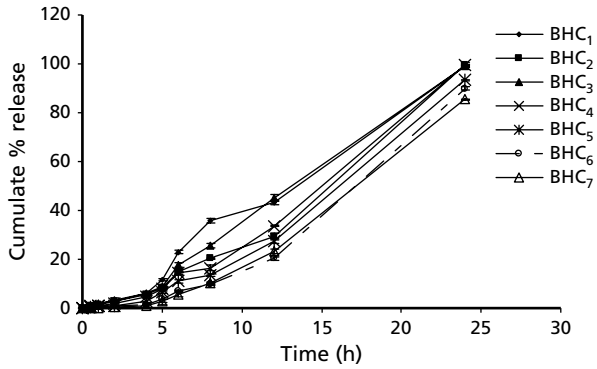

Figure 3 Cumulative percentage of drug released from 5-FU compression coated BL–HPMC tablets with different coating ratios: BHC_1 (BL:HPMC 1:1), BHC_2 (BL:HPMC 1:2), BHC_3 (BL:HPMC 2:1) and BHC_4 (BL:HPML 2:3) and different coat weights: BHC_5 (BL:HPMC 2:3, 250 mg), BHC_6 (275 mg) and BHC_7 (300 mg).

drug released. Thus, increasing the coating weight helped in minimizing the drug loss in the initial 5 h. Also, more than 80% of the drug was released after 24 h, which was expected to increase further in the presence of rat caecal contents due to the presence of polysaccharides in the outer coat.

In-vitro release studies in the presence of rat caecal contents for batches prepared using boswellia gum and HPMC

Similar studies were carried out in compression coated batches prepared using a combination of boswellia gum and HPMC (BHC_6 and BHC_7). BHC_6 showed a drug release of $27.22 \pm 0.78\%$ as against $6.22 \pm 0.33\%$ in the initial 6 h and $97.22 \pm 0.56\%$ release in 24 h (Table 4). BHC_7 showed a less pronounced effect with an increase in drug release of $16.45 \pm 1.2\%$ in 6 h and $96.11 \pm 0.34\%$ release in 24 h (Table 4). A significant difference ($P < 0.001$) was observed in the amount of 5-FU released at the end of 24 h of the dissolution study in both the batches with rat caecal content medium when compared with the dissolution study without rat caecal contents. These results demonstrate the biodegradability of the boswellia gum in the colonic contents. As the tablet swells with respect to time in the dissolution media, the gum gets exposed to colonic bacteria, which results in degradation of the gum by bacterial enzymes and thus results in complete release of the drug.

Conclusion

It is evident from the results that both the coating combinations were successful in retarding the initial drug release in the upper gastrointestinal tract. Moreover, since all the coating materials were biodegradable, there were no issues regarding complete release of the drug in the colon, since the colon harbours approximately 300–400 microbial species. So our study was mainly focused on minimizing the release of the drug in the hostile upper gastrointestinal environment and ensuring complete release of the drug once the dosage form reaches the colon. To achieve this target, a compression coating technique was used. Among the various batches containing boswellia gum and xanthan gum, the ratio 1:3 boswellia gum:xanthan gum gave the most suitable results initially and coating weight 300 mg achieved the best drug retardation. This batch was further validated for its release properties in the presence of rat caecal contents, which too showed that it could be one of the possible batches to give release profile close to the target.

Similar studies were carried for boswellia and HPMC coating mixture and it was found that the ratio 2:3 boswellia:HPMC showed the best retardation in the initial 5 h. An increased coating weight of 300 mg with the same ratio almost reduced the drug release to less than 5% in the initial 5 h. This release profile was further verified in the presence of rat caecal contents, which showed that in the presence of caecal contents there was a rapid and complete release of the drug in the colon, ensuring no loss of the drug. These studies indicate that compression coating of a sparingly soluble drug (USP 24) with boswellia gum along with drug retarding agents can be used as one promising approach to target the drug to the colon, thereby minimizing side effects and increasing the clinical efficacy of the drug molecule.

Table 4 Percentage of 5-FU released from batches BHC_6 (BL:HPMC 2:3, 275 mg coat weight) and BHC_7 (BL:HPMC 2:3, 300 mg coat weight) with and without rat caecal contents

Time (h)	Cumulative % release from BHC_6		Cumulative % release from BHC_7	
	Without rat caecal contents	With rat caecal contents	Without rat caecal contents	With rat caecal contents
5	3.70 ± 0.67	3.88 ± 0.18	2.99 ± 0.98	3.20 ± 0.33
6	6.22 ± 0.33	27.22 ± 0.78	5.80 ± 0.78	16.45 ± 1.2
8	9.90 ± 0.10	54.22 ± 0.33	10.22 ± 0.10	46.35 ± 0.11
10	20.27 ± 0.47	78.18 ± 0.27	23.35 ± 0.45	72.30 ± 0.33
24	89.89 ± 1.22	97.22 ± 0.56	85.46 ± 2.56	96.11 ± 0.34

Data are means ± s.d., n = 3.

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