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Research Article

EVALUATION OF POLYMERS FOR COMPRESSION COATING OF 5-AMINOSALICYLIC ACID MATRIX TABLETS FOR COLON TARGETING

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ABSTRACT

Objective: Colon targeted delivery systems require coating to avoid drug release in stomach and small intestine. Compression coating is a newer approach which eliminates the use of costly solvents and the coating is done in a simple single step. In this study, the effect of various polymers on drug release from compression coated tablets, have been studied, for possible targeted drug delivery and thereafter sustained drug release in the colon.

Methods: Matrix tablets have been prepared with Pectin and Hydroxypropylmethylcellulose (HPMC) K4M and have been compression coated with Eudragit S100, Shellac and HPMC K100M. The prepared tablets have been evaluated by compatibility studies, physical parameter testing and 8 hour in-vitro drug release studies in multiple media.

Results: The tablets passed the physical parameter tests. The in-vitro release studies revealed that the release pattern of the tablets was mainly influenced by the type of coating, the release being minimum for HPMC K100M coated tablets and maximum for Eudragit S100 coated tablets. Shellac coated tablets gave an average rate of release throughout the 8 hour study.

Conclusion: Among the various batches prepared, FBC1 (HPMC K4M tablets coated with HPMC K100M), FAC1(Pectin tablets coated with HPMC K100M) and FAC2 (Pectin tablets coated with Shellac) were found to avoid significant drug release in the first 5 hours of dissolution and released 35%, 10% and 54% drug throughout the 8 hour dissolution study.

Keywords: Colon targeting, Compression coating, Sustained release, HPMC, Shellac, Eudragit S100, Pectin, 5-Aminosalicylic acid.

INTRODUCTION

Colon targeting of drugs is a much researched topic. Drugs have been targeted to the human colon for various purposes, for local and systemic actions. Drugs are targeted to the colon for treating local colonic diseases like ulcerative colitis, chron's disease, amoebiasis and colon cancer. Colon is not a very suitable area for systemic absorption of drugs due to low amount of viscous colonic fluid, available in pockets. However, certain drugs can be degraded by enzymes present in small intestine and have to be targeted to colon, if intended for absorption in the gastrointestinal tract after oral administration, like proteins [1, 2]. Insulin entrapped colon targeted formulations are available in the market [3].

Colon targeting has been achieved through several strategies like pH dependent approaches [4, 5], time dependent systems [6, 7], microbial triggered systems [8, 9, 10], osmotically controlled [11] and pressure controlled systems [12], utilizing several kinds of delivery systems like matrix tablets [13], multiparticulate systems [14], microshperes [15], nanoparticles [16], liposomes [17], microcapsules [18] and nanocapsules [19] etc. Among the various colon targeted oral dosage forms, tablets are preferred due to simple production techniques, lesser scale up problems and low cost of production. Therefore, matrix tablets for colon targeting have been chosen as the delivery system in the present study.

The basic strategy for almost all of the delivery systems and targeting strategies is to prevent drug release in the stomach and small intestine and start release of drug in colon and thus, the delivery systems require coating. Compression coating is a newer approach to coat tablets in a simple operation, avoiding the use of costly solvents or complicated procedures [20, 21].

In the present study, compression coated matrix tablets have been prepared with the objective of targeted release in the colon and thereafter sustaining the release for effective therapy.

MATERIALS

5-Aminosalicylic acid was chosen for colonic delivery for therapeutic management of ulcerative colitis. Pectin and HPMC K4M were used as rate controlling agents to achieve sustained release in colon. Eudragit S100, HPMC K100M and Shellac were used as coating materials to protect the core tablets from premature drug release in the upper parts of the gastrointestinal tract. Besides, microcrystalline cellulose was used as diluent, PVP K-30 was used as binder, magnesium stearate and colloidal silica were used as lubricant and glidant respectively, purified water was used as granulating agent.

METHODS

Drug-excipient compatibility studies by FTIR

The infrared spectra of 5-Aminosalicylic acid, physical mixture of drug (5-Aminosalicylic acid) and excipients and placebo were recorded between 400 to 4000 cm^{-1} on FTIR spectrometer. The IR spectra for the test samples was obtained using KBr disk method using an FTIR spectrometer (Perkin Elmer BX-I system, USA).

Preparation of core tablets

Core tablets were prepared by wet granulation method. Drug, rate controlling polymer, microcrystalline cellulose as diluents were mixed, passed through #40 mesh and granulated with purified water. The wet mass was semi-dried on a petri dish in a tray drier and thereafter passed through #20 mesh sieve. The granules were collected and further dried at 60^0C for 30minutes. The dried granules were collected and weighed to find out the yield percentage. The granules were further mixed with required amounts of magnesium stearate and colloidal Silica, which were previously passed through #60mesh. Thereafter, accurately weighed amount of the granules were compressed with 9mm flat faced punches in a 10 station Cadmach compression machine to get the core tablets.

Preparation of compression-coated tablets

For compression coating of the core tablets, the coating materials were granulated. Coat I was prepared from HPMC K100M which was granulated with minimum amount of purified water as the granulating liquid. Coat II was prepared from Shellac which was granulated with the help of HPMC K100M as binder and purified water as the granulating liquid. Coat III was prepared from Eudragit

S100 which was granulated with help of Pectin and PVP K-30 as binding agent and purified water as the granulating liquid. Then, compression coating was done by first filling the die with 40% of coating material, placing the core tablet carefully at the center and then adding the remaining 60% of the coating granules in the die cavity and tablets were compressed with 11mm punches to get the compression coated tablets.

The formulation variables of the core tablets and the compression coated tablets are represented in Tables 1 and 2.

Table 1: Formulation variables of core tablets

Formulation batch	Amount of drug (mg)	Amount of Pectin (mg)	Amount of HPMC K4M (mg)	Amount of PVP-K30 (mg)	Amount of MCC (mg)
FA	100	120	-	60	100
FB	100	-	180	-	100

Table 2: Formulation variables of coated tablets

Formulation batch	Core tablet used	Amount of Coating Polymers used		
		HPMC K100M (mg)	Shellac (mg)	Eudragit S100 (mg)
FAC1	FA	200	-	-
FAC2	FA	-	200	-
FAC3	FA	-	-	200
FBC1	FB	200	-	-
FBC2	FB	-	200	-
FBC3	FB	-	-	200

Tablet Quality control tests

Tablet quality control tests such as weight variation, content uniformity, hardness, and dissolution rates in different media were performed with the compression coated tablets. Hardness of randomly selected tablets was tested using Monsanto hardness tester.

Determination of drug content in tablet formulations

Both the core tablets and compression-coated tablets were tested for their drug content. Ten tablets were finely powdered and quantities of the powder equivalent to 5mg of 5-Aminosalicylic acid were accurately weighed, transferred to 100 ml volumetric flasks containing 100ml of phosphate buffer pH 6.4 and were shaken vigorously and kept for 30 minutes with occasional shaking to ensure complete solubility of the drug. Thereafter, the mixture was made up to volume with phosphate buffer pH 6.4, filtered and the absorbance values were determined by UV-Visible spectrophotometer at 330 nm. The drug concentration was calculated from the calibration curve.

In-vitro drug release studies

The formulated compression coated tablets were tested for drug release by in-vitro dissolution test, by sequential pH change method. The release studies were conducted in 8-station dissolution apparatus at 100r.p.m and at 37±0.5^{0}C. The buffer media used in the study and the duration of time during which the tablets were kept in the buffers are highlighted in Table 3. This was chosen according to the pH environment and residence time of dosage forms in the various parts of the gastrointestinal tract (g.i.t).

Table 3: Various buffers used and the duration of time for drug dissolution studies by sequential pH change method

Buffer media used	Duration of time (hr.)
HCl buffer pH1.2	2
Phosphate buffer pH 6.6	2
Phosphate buffer pH 7.4	1
Phosphate buffer pH 6.4	3

RESULTS AND DISCUSSIONS

Drug-excipient compatibility studies by FTIR studies:

No drug-polymer interaction was observed in the FTIR spectra of the powder mixture of the formulations, since the absorption peaks of the drug still could be detected in the mixture.

Tablet quality control tests

The various physical properties of the core and compression coated tablets are enlisted in Table 4. The tablets passed the weight uniformity, content uniformity and hardness tests.

Table 4: Physical parameter tests of core and compression coated tablets

Formulation Code	Hardness (Kg/cm^2)	Deviation in weight (mg)	Drug Content (%)
FA (Core)	4.5	386±0.52	108.0
FB (Core)	5.0	383±0.26	102.0
FAC1	7.0	605±0.99	99.73
FAC2	7.5	594±0.83	98.65
FAC3	6.5	589±1.66	101.11
FBC1	7.0	581±3.0	103.5
FBC2	6.0	602±0.5	97.56
FBC3	6.5	597±0.33	100.03

In-vitro drug release studies

The drug release studies of the various formulation batches gave interesting results. The 8 hour drug release studies in multiple media were conducted with compression coated tablets. The release pattern of the tablets was mainly influenced by the type of coating, the release being minimum for HPMC K100M coated tablets and maximum for Eudragit S100 coated tablets. Shellac coated tablets gave an average rate of release throughout the 8 hour study. The drug release after first 5 hours of dissolution study was especially taken into account. This was because the total transit time through the stomach and small intestine is considered as approximately 5 hours. The gastric emptying time of insoluble drug formulation, under fasted condition is normally 1-2 hours [22] and the small intestinal transit time ranges from 1-2 hours [23]. Therefore, the average time of the delivery systems to reach the colon may be considered as 5 hours approximately. Therefore, in order to achieve colon targeted drug release, the formulations should not release significant amount of drug in the first 5 hours of dissolution.

The release behavior of the various batches of compression coated tablets is highlighted below.

- Eudragit S100 coated tablets:

The tablets failed to prevent drug release in the first 5 hours of dissolution study and thus were not found suitable for coating the

tablets by compression coating. This may be due to the low compressibility characteristics of the polymer. Among the Eudragit S100 coated tablets, both the batches gave about 95% drug release in 8 hours.

- Shellac coated tablets:

The Shellac coated tablets gave better performance as compared to the Eudragit S100 coated tablets. This may be due to the better compressibility of the polymer, compared to Eudragit. Among the two batches of Shellac coated tablets, the Pectin tablets gave better results than the HPMC K4M tablets. The Pectin tablets coated with Shellac released about 15% and 54% drug in first 5 hours and 8 hours of dissolution, respectively. The HPMC K4M tablets coated with Shellac released about 38% and 75% drug in first 5 hours and 8 hours of dissolution, respectively, and thus failed to avoid drug release in first 5 hours of dissolution or to sustain drug release in effective manner.

- HPMC K100M coated tablets:

HPMC K100M is a high viscosity polymer (10^5 mPa s) [24]. The polymer has been used for sustained drug delivery in various delivery systems. In the present study, HPMC K100M has been used for compression coating of tablets and the tablets coated with the polymer have been able to avoid drug release in the first 5 hours of dissolution and thereafter, was able to sustain the release. The pectin tablets coated with HPMC K100M gave minimum drug release of 2% in first 5 hours and 10% drug release in 8 hours of dissolution. The HPMC K4M tablets coated with HPMC K100M gave 6 % drug release in 5 hours and 35% drug release in 8 hours. Therefore, the tablets were able to avoid significant drug release in the first 5 hours of dissolution and thereafter were able to prolong the release of drug further. However, the pectin tablets releasing only 10% drug in 8 hours may not be found suitable, because it may result in ineffective therapy.

Among the various batches of compression coated tablets, the formulations which were able to deliver favorable release profiles were FBC1, FAC2 and FAC1. They released insignificant amount of drug in the first 5hours of dissolution (2hours in pH1.2 buffer, 2hours in phosphate buffer pH6.6 and 1hour in phosphate buffer pH7.4) and sustained drug release till 8 hours. The percentage release of the various batches at different time points is represented in Table 5 and Figure1.

Table 5: Percentage release of drug through 8 hours of dissolution study

	Percentage release of drug (%)					
TIME (HR)	**FAC1**	**FAC2**	**FAC3**	**FBC1**	**FBC2**	**FBC3**
2	1.1864	5.2227	37.3091	2.2841	20.9659	25.4114
4	2.1613	11.2224	73.4135	6.7262	30.3836	67.0118
5	2.1613	15.8936	83.8201	6.7262	38.4015	83.8283
6	5.6522	28.4662	97.127	13.7652	56.6093	94.2454
8	9.7578	54.5881	98.9554	35.341	75.606	96.5917

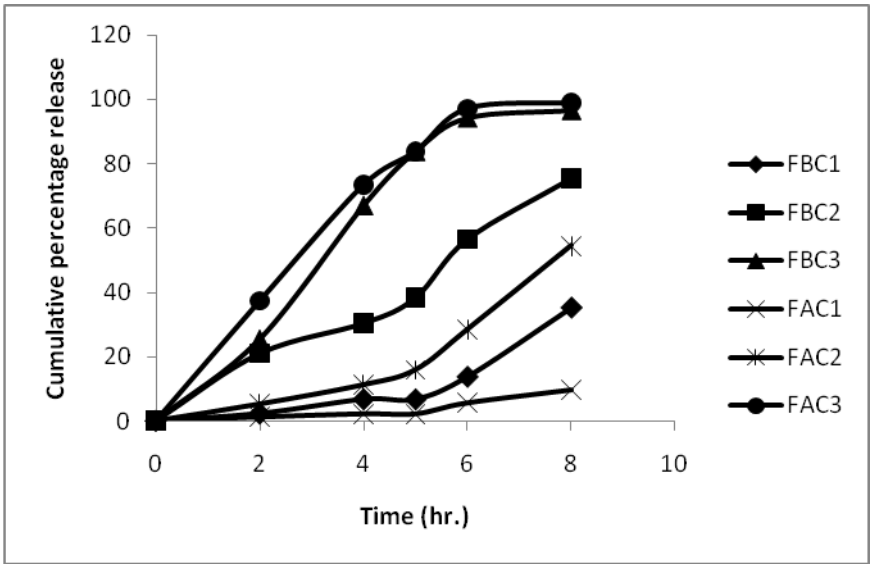

Fig. 1: Percentage drug release vs. time profile for various formulation batches

(FAC1: Pectin tablets coated with HPMC K100M, FAC2: Pectin tablets coated with Shellac, FAC3: Pectin tablets coated with Eudragit S100, FBC1: HPMC K4M tablets coated with HPMC K100M, FBC2: HPMC K4M tablets coated with Shellac, FBC3: HPMC K4M tablets coated with Eudragit S100.)

CONCLUSION

Among the various batches prepared, FBC1 (HPMC K4M tablets coated with HPMC K100M), FAC1(Pectin tablets coated with HPMC K100M) and FAC2 (Pectin tablets coated with Shellac) were found to deliver favorable release profiles. They were able to avoid drug release in the frist 5 hours of dissolution and were able to sustain release till 8 hours. Therefore, they may be successfully employed to achieve colon targeted drug release and sustained drug release thereafter, to achieve maximum therapeutic efficacy.

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