ORIGINAL ARTICLE

Formulation and Evaluation of Colon Targeted Compression Coated Tablet of Mesalamine and Prednisolone for Ulcerative Colitis

Grace Rathnam, Rasika Bhadane

Department of Pharmaceutics, C.L. Baid Metha College of Pharmacy, Thoraipakkam, Chennai, Tamil Nadu, India

Abstract

Introduction: The purpose of this study was to formulate compression coated tablets of mesalamine and prednisolone for colon specific delivery and evaluate their *in vitro* and *in vivo* performances. **Materials and Methods:** Mesalamine is 5-amino salicylic acid used as a topical anti-inflammatory agent and prednisolone is a synthetic glucocorticoid used for the treatment of various types of inflammatory and autoimmune conditions. Pectin was used as an enzyme dependent polymer. Eudragit S 100 was used to enteric coat the compression coated tablets to avoid prerelease of the drug into the upper gastrointestinal tract. *In vitro* release study was carried out at various pH (1.2, 6.8 and 7.4) and in the presence of the pectinolytic enzyme. Therapeutic efficacy of the prepared tablets was evaluated in trinitrobenzene sulfonic acid-induced rabbit colitis model. **Results:** Formulation CF3c which was compression coated with of 150% of pectin and enteric coated with 7.5% Eudragit S 100 released 35.86% of mesalamine and 45.49% of prednisolone at the end of 7 h. The release increased significantly to 73.53% of mesalamine and 87.53% of prednisolone on addition of pectinolytic enzyme to the dissolution medium at the end of 10 h. Formula CF3c significantly reduced the inflammation of the treated group and the myeloperoxidase activity to 3.91 U/g. **Conclusion:** Studies demonstrated that orally administered compression coated tablets could be used effectively for the delivery of the drug to the colon.

Key words: Compression coated tablet, enzyme dependent release, Eudragit S 100, mesalamine, pectin, prednisolone

INTRODUCTION

Ulcerative colitis is an idiopathic inflammatory bowel disease that affects the colonic mucosa and is clinically characterized by diarrhea, abdominal pain, and hematochezia.[1] Colon targeted drug delivery is used for local treatment of several colonic diseases, mainly irritable bowel syndrome, inflammatory bowel disease (Crohn's disease and ulcerative colitis), and colon cancer. Most of the conventional drug delivery systems for treating the colon disorders such as inflammatory bowel diseases (e.g., irritable bowel syndrome, ulcerative colitis, and Crohn's disease), infectious diseases (e.g., amebiasis), and colon cancer are failing as the drugs do not reach the site of action in appropriate concentrations. Thus, an effective and safe therapy of these colonic disorders, using site-specific drug delivery systems is a challenging task to the pharmaceutical technologists.[2]

A combination therapy of oral glucocorticoid and high dose of 5-amino salicylic acid is recommended as an initial therapy for the treatment of ulcerative colitis.[3] Prednisolone, a synthetic glucocorticoid was combined with high dose of mesalamine; a 5-aminosalicylic acid into a single dosage unit to improve the patient compliance. Pectin is a natural polysaccharide which is degraded by the microflora in the colon and hence ensures site specificity to target the drug into colon.[4,5] The formulation was further enteric coated to avoid prerelease of the drug in the upper gastrointestinal (GIT) region.

The aim of this study was to formulate a delayed release colon targeted compression coated tablet of mesalamine[6]

Address for correspondence:
Grace Rathnam, Department of Pharmaceutics, C.L. Baid Metha College of Pharmacy, Thoraipakkam, Chennai, Tamil Nadu, India. E-mail: gracerathnam@gmail.com

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and prednisolone[7] for ulcerative colitis and to evaluate the *in vitro* characteristics and therapeutic efficacy of the prepared formulation.

MATERIALS AND METHODS

Mesalamine and prednisolone were gifted by Dr. Reddy's Laboratory, Hyderabad and Madras Pharmaceuticals, Chennai, respectively. Pectin and hexadecyltrimethylammonium bromide (HTAB) buffer were obtained from Hi Media. Eudragit S 100 was supplied by Vikrant Suppliers, Ahmedabad. Pectinase (from *Aspergillus Niger*) and trinitrobenzene sulfonic (TNBS) acid were obtained from Sigma-Aldrich. Dimethylformamide was gifted by Steril-Gene, Pondicherry. All other chemicals and reagents used were of laboratory grade.

Preformulation study

The organoleptic characters, solubility study, flow properties, and compressibility of the drug and excipients were determined.

Compatibility study

Compatibility of the two drugs (mesalamine and prednisolone) was established using Fourier transform-infrared (FTIR) analysis and between drugs and polymer using differential scanning calorimetry (DSC) analysis.

FTIR analysis

The compatibility of mesalamine and prednisolone was studied using (FTIR - 8400, Shimadzu Co., Japan) spectroscopy. The pelletization was done using KBr press. The FTIR spectra were recorded in the wavelength region between 4000 and 400 cm^{-1}.[8] The spectra obtained for pure drug, i.e., mesalamine and prednisolone were compared for compatibility.

DSC study

About 3 mg of sample was weighed and crimped into an aluminum pan and analyzed at a scan range 35-400°C at a heating rate 10°C/min. Nitrogen gas was purged at a rate of 10 ml/min for maintaining inert atmosphere.[9] It was measured using DSC Q20 V 24.10 Build 122, Universal V450 TA instruments.

Calibration curve

Stock solutions (1000 µg/ml) of mesalamine and prednisolone were prepared by dissolving separately 100 mg of drug in minimum quantity of dimethylformamide and finally diluted with 0.1 N hydrochloric acid, phosphate buffer (pH 6.8) and phosphate buffer (pH 7.4) to make up the volume to 100 ml. The maximum absorbance (λ_{max}) of mesalamine and prednisolone were obtained at 332 nm and 246 nm, respectively, for simultaneous estimation of mesalamine and prednisolone. A series of standard drug solutions in concentration range of 2-10 µg/ml were prepared by diluting appropriate volumes of the standard stock solutions. The ultraviolet (UV) scanning for solution of mesalamine and prednisolone were carried out in the range of 200-400 nm against 0.1 M hydrochloric acid, phosphate buffer (pH 6.8) and phosphate buffer (pH 7.4) solution as blank for obtaining the overlain spectra that were used in the analysis.[10] The absorbance of series of standard solutions was recorded at selected wavelengths using Shimadzu A11 6352023 54CD UV spectrometer, Japan.

Preformulation studies

Bulk density

Apparent bulk density (g/ml) was determined by pouring presieved (40-mesh) bulk blend into a graduated cylinder via a large funnel and measuring the volume and weight "as is."[11]

Tapped density

Tapped density was determined by placing a known mass of powder blend in a graduated cylinder placed on a mechanical tapper apparatus until the powder bed has reached a minimum.[11]

Compressibility index

The compressibility index is a measure of the propensity of a powder to be compressed.[11] The compressibility index was calculated using measured values for bulk density (ρ_0) and tapped density (ρ_t).

Hausner ratio: Hausner ratio was calculated by following equation.[11]

Hausner ratio = bulk density/tapped density.

Angle of repose

Angle of repose was determined using funnel method. Accurately weighed blend was poured from funnel which was raised vertically until a maximum cone height (h) was obtained and diameter heap (d) was measured.[11]

Preparation of compression coated tablet

Preparation of fast disintegrating core tablet

Core tablets were prepared by wet granulation method. The composition of core tablets is as shown in Table 1. Accurately

weighed quantities of drug (mesalamine and prednisolone), disintegrant (Avicel®) and diluent (lactose) were mixed in a mortar. Starch mucilage (binder) was added to the above blend to form a wet mass. Granules were prepared by passing the wet dough mass through sieve No. 16 and dried at 50°C for 15 min. The dried granules were passed through sieve No. 18. Required quantity of lubricant (magnesium stearate) and glidant (talc) sieved using 60 mesh sieve were added to the granules and mixed well. The lubricated granules were compressed to form core tablet (8 mm) using Minipress tablet compression machine with flat round punches and dies at optimum pressure. Average weight of core tablet was found to be 251 mg.

Compression coating of fast disintegrating core tablet

Based on disintegration time, formulation three was chosen for the further investigation. The fast disintegrating core tablet was compression coated with pectin as enzyme dependent polymer. Pectin is a polysaccharide which is degraded by colonic microflora which ensures site specificity. The composition of compression coating granules is as shown in Table 2. Pectin was accurately weighed and placed in a mortar. The binder (ethyl cellulose) was dissolved in isopropyl alcohol along with the colorant. Polymer granules were prepared by passing the wet dough through sieve No. 16 and air dried. 40% of the required quantity of polymer granules was placed in the die cavity following the fast disintegrating core tablet and later remaining 60% of the remaining polymer granules were poured over it. Then, it was compressed to form a compression coated tablet. CF1 was compression coated with polymer granules weighing 187.5 mg, i.e., 75% weight of the core tablet, CF2 was compression coated with polymer granules weighing 250 mg, i.e., 100% weight of the core tablet, CF3 was compression coated with polymer granules weighing 375 mg, i.e,. 150% weight of the core tablet and CF4 was compression coated with polymer granules weighing 500 mg i.e., 200% weight of the core tablet.

Enteric coating of compression coated tablet

The compression coated tablet, i.e., CF3 was chosen for enteric coating using Eudragit S 100. Accurately weighed quantity of Eudragit S 100 (2.5, 5 or 7.5% as shown in Table 3) was added to the coating solvent (isopropyl alcohol: acetone;1:1) and stirred using a mechanical stirrer. Dibutyl phthalate was added as a plasticizer. The compression coated tablet was enteric coated using dip coating method. In this method, the tablet was dipped into the coating solution. Excess amount of coating solution was drained and the tablet was dried. The procedure was repeated until the required increase in weight was obtained. The composition of the enteric coating solution is as shown in Table 3.

Table 1: Composition of fast disintegrating core tablet

Ingredients	Quantity (mg/tablet)		
	1	2	3
Mesalamine	200	200	200
Prednisolone	10	10	10
Avicel®	12.5	18.7	25
Starch mucilage (5% w/v)	q.s	q.s	q.s
Lactose	16.5	10.2	4
Magnesium stearate	1	1	1
Talc	10	10	10

Table 2: Composition of compression coated tablet

Ingredients	Quantity
Pectin	20 g
Ethyl cellulose	0.6 g
Isopropyl alcohol	10 ml
Quinine yellow	q.s

Table 3: Composition of enteric coating solution

Ingredients	a	b	c
Eudragit S 100 (g)	2.5	5	7.5
Dibutyl phthalate (ml)	1	1	1
Isopropyl alcohol (ml)	50	50	50
Acetone (ml)	50	50	50

Evaluation of fast disintegrating core tablet

Hardness test

The crushing strength (kg/cm^2) of prepared tablets was determined by using hardness tester (Monsanto type.) A tablet was placed between the anvils and the crushing strength, which caused the tablet to break, was recorded. Average of three readings were taken and noted.[12]

Friability testing

About 10 tablets were taken and weighed. The initial weight was noted. The tablets were then placed into the Roche friabilator (Electrolab EF-2) and test was performed for 4 min at 25 rpm. The tablets were dedusted and weighed again. Percent weight loss was determined using following formula.[12]

Thickness of tablet

Tablet thickness is an important characteristic in reproducing appearance; average thickness of the tablets were calculated and presented with deviation using Vernier Caliper (Mitutoyo, Japan).[12]

Uniformity of weight

Individual tablets were weighed and average weight was calculated, NMT 2 tablets from this average weight should not deviate. The test was performed according to the Indian Pharmacopoeia 2010. Briefly, 20 tablets were weighed together, and the average weight was calculated. The same tablets were weighed individually, and percent deviation was calculated. Not more than two of the individual weights deviate from the average weight by more than the percentage of acceptance criteria, and none deviates by more than twice that percentage.

Disintegration test of core tablet

Disintegration test of core tablet was performed using phosphate buffer pH 7.4. The tablets were taken and placed in 6 respective tubes of USP disintegration apparatus and disintegration time of the tablet was noted.[12]

Evaluation of coated tablet

Hardness, friability, thickness of coated tablet, and weight variation were measured as mentioned above.

Drug content

The tablets were tested for their drug content. Randomly 20 tablets were weighed and powered. The powder equivalent to 100 mg was weighed accurately and transferred to 100 ml of volumetric flask and dissolved with 5 ml of dimethylformamide. The flask was sonicated for 5 min. The volume was then made up to 100 ml with phosphate buffer pH 7.4. The above solution was filtered through Whatman paper and absorbance was measured in Shimadzu A11 6352023 54CD UV spectrometer, Japan, at 332 nm and 246 nm.[10]

In vitro dissolution study of coated tablet

Drug release from the compression-coated tablets was assessed by USP Dissolution Tester, (Electrolab TDT 08 L) Apparatus I (rotating basket) at a rotation speed of 50 rpm maintained at 37.0 ± 0.5°C. The release study was performed in 250 ml 0.1 N hydrochloric acid for 2 h, followed by 250 ml phosphate buffer (pH 6.8) for another 3 h and finally, 250 ml phosphate buffer (pH 7.4) till the end of 10 h. 5 ml of dissolution medium was withdrawn after every hour and replaced with an equal volume of media. The collected sample was filtered. 1 ml of sample was diluted up to 10 ml, and concentration of dissolved drug was measured using Shimadzu A11 6352023 54CD UV - spectrometer, Japan at 332 nm and 246 nm for mesalamine and prednisolone respectively.

To evaluate enzyme-triggered drug release of pectin, 1 ml of pectinolytic enzyme was added after 7 h to phosphate buffer (pH 7.4) to simulate the degradation of polymer by microflora.[13] The *in vitro* dissolution profile of mesalamine and prednisolone was as shown in Figure 1a and b.

Kinetic studies

To determine the suitable drug release kinetic model describing the dissolution profile, the nonlinear regression module of Statistica 5.0 was used. The model dependent approaches included zero order, first order, Higuchi, Korsmeyer-Peppas models.[14]

Acid uptake studies

Six coated tablets were weighed individually and place in the disintegration tubes. The disintegration basket was filled with 0.1 N hydrochloric acid, and the test was performed up to 2 h in acidic medium. The tablets were removed from the disintegration basket then dehydrated with tissue paper and weighed again. The percentage of weight gain was reported as percentage acid uptake.[15] If the value is <0.5%, it suggests that the tablets would readily pass the acid phase of the delayed release dissolution testing.

Rupture test

The rupture test on coated tablets was carried out using USP Type II apparatus. Here, all other parameters were same as *in vitro* dissolution method. The rupture time was determined in pH 1.2, 6.8 and 7.4.[16] The time at which the outer coating layer starts to rupture is called as lag time.

Swelling studies

The percentage swelling capacity of tablets was determined in containers filled with 10 ml of pH 1.2 and pH 7.4 phosphate buffers. Tablets were removed from containers at predetermined regular intervals, blotted with tissue paper,

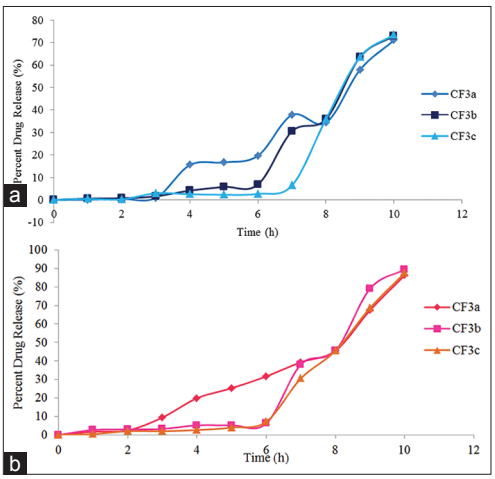

Figure 1: (a) Percent drug release of mesalamine, (b) percent drug release of prednisolone

weighed, and again placed in medium till the outer coating of tablet started to rupture.[17]

Accelerated stability studies

Accelerated stability studies were performed as per the ICH guidelines (Q1C). Selected formulations of compressed coated tablet were sealed in aluminum foil cover and stored at (40 ± 2°C/75 ± 5% R.H) for 3 months and evaluated for physical appearance, hardness, drug content, and percentage drug release.[18]

In vivo study

Induction of experimental colitis

The TNBS-induced experimental rabbit colitis model was selected because the pharmacological response of rabbit colonic smooth muscle to inflammatory mediators closely resembles to those of the human colon. 18 adult male rabbits weighing 2.5-3 kg were used throughout the study. The animals were randomly divided into three groups, each consisted of six animals: Group I, normal control group; Group II, induced colitis group; Group III, animals treated with CF3c. Briefly, rabbits were fasted for 24 h with free access to water before experimentation. Colitis was induced in all rabbits except the control group. A rubber catheter was inserted approximately 15 cm into the colon and inflated with 3 cm of air. Gentle withdrawal of the catheter caused fecal pellets in the distal colon and rectum to be expelled by muscle action. Colitis was induced by slow intrarectal administration of 2 ml containing 75 mg/kg TNBS in water. The rabbits were housed for 3 days without treatment to maintain the development of a full inflammatory bowel disease model. The animal of Group III received one tablet (containing 36.5 mg/kg of mesalamine and 1.8 mg/kg of prednisolone) once daily for five continuous days *via* gastric intubation and animals were sacrificed 24 h after the last drug administration.[19]

Histopathological evaluation

Two tissue samples were excised from each colon and maintained in 10% (v/v) formalin in saline for histopathological evaluation. Sections of 5 µm were stained with hematoxylin and eosin.[13] The histologic damage was evaluated. The study protocol was reviewed and approved by IAEC vide No. IAEC/XLIX/01/CLBMCP/2016.

Myeloperoxidase (MPO) activity

The distal colon specimen (200 mg) was minced in a beaker containing ten times its amount of water for injection in ice, transferred to a test tube, and homogenized three times for 30 s each. The homogenate (0.5 ml) was mixed with 0.5 ml of HTAB buffer (0.5% HTAB in 50 ml phosphate buffer, pH 6.0) and the mixture was sonicated for 10 s and centrifuged at 10,000 rpm for 15 min. The supernatant was assayed for MPO activity. MPO activity was measured spectrophotometrically. 0.1 ml of supernatant was combined with 2.9 ml containing 0.167 mg/ml O-diansidine hydrochloride and 0.0005% hydrogen peroxide. The change in absorbance at 460 nm was measured every minute for 4 min. One unit of MPO activity is defined as the amount which degrades 1 mmol of the peroxide per minute at 25°C (13). The results are expressed as the mean±standard deviation of the mean.

RESULTS AND DISCUSSION

Preformulation studies

The organoleptic characteristics observed were as shown in Table 4.

Solubility studies

Solubility studies were studied with distilled water, pH 1.2, 6.8 and 7.4. The pure drugs show partial solubility in distilled water and shows highest amount of solubility in pH 7.4. The result is shown in Table 5.

Compatibility study

DSC analysis was performed using (DSC Q20 V 24.10 Universal V450 TA instruments) for pure drug and polymer are shown in Figure 2. The DSC thermogram of mesalamine and prednisolone presented a single characteristic peak at 288.58°C and 246.35°C, respectively, signifying that mesalamine and prednisolone used were in a pure crystalline state. The endothermic peak of physical mixture of mesalamine and prednisolone was at obtained at 277.06°C and 219.00°C, respectively, and for physical

Table 4: Organoleptic characteristics

Characteristic	Mesalamine	Prednisolone
Appearance	Light pink crystalline powder	White crystalline powder
Odor	Odorless	Odorless

Table 5: Solubility analysis

Solvent	Solubility (mg/ml)	
	Mesalamine	Prednisolone
Distilled water	51	89
pH 1.2	69	93
pH 6.8	85	138
pH 7.4	98	145

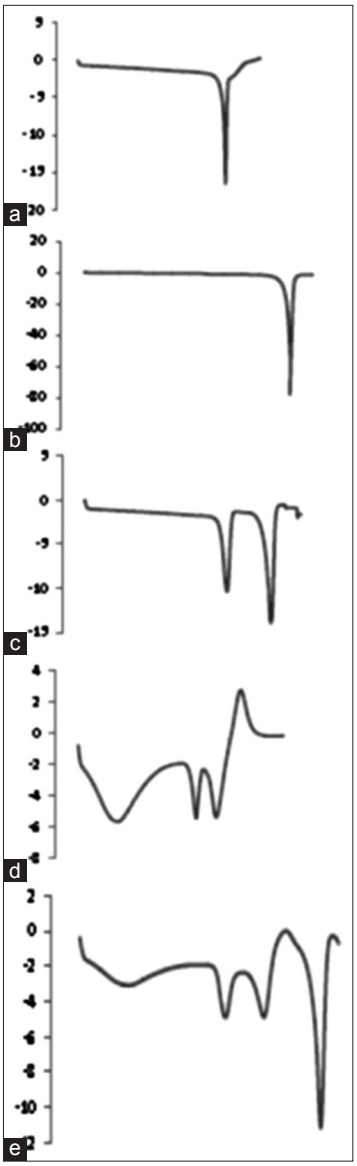

Figure 2: Differential scanning calorimetry thermograms of (a) mesalamine, (b) prednisolone, (c) physical mixture of mesalamine and prednisolone, (d) pectin, (e) physical mixture of mesalamine, prednisolone and pectin

mixture with pectin was obtained at 179.89°C, 220.00°C and 278.29°C, respectively. The peaks for the physical mixtures have shorted but did not disappeared completely indicating that there was no interaction between the drugs and polymer.

The IR spectra of the two pure drugs are shown in Figure 3. Results obtained from the spectra showed that stressed conditions do not influence any interaction between the two drugs. All the functional groups assigned in the wave numbers exhibited maxima which are around the same wavelength and had similar intensities to that of the reference spectrum. Hence, it was concluded that there was no interaction between mesalamine and prednisolone.

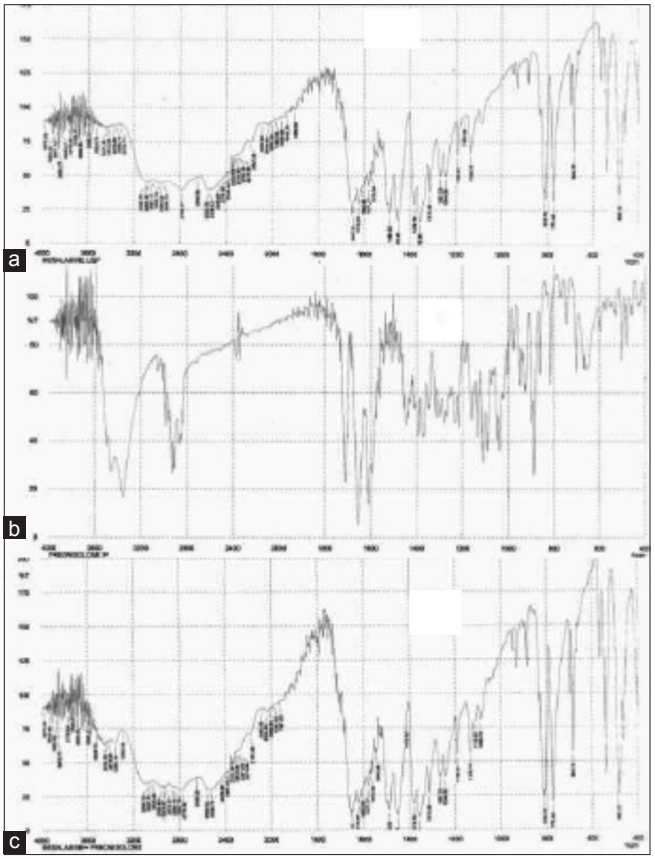

Figure 3: Fourier transform-infrared spectrum of (a) mesalamine, (b) prednisolone, (c) physical mixture of mesalamine and prednisolone

Precompression evaluation

The bulk density of the powdered blend was measured by graduated cylinder. The bulk density was found in the range of 0.317-0.348 g/cm^2. The tapped density was found in the range of 0.412-0.441 g/cm^2.

The compressibility index and Hausner's ratio was determined using bulk density and tapped density data. It was found in the range 30.17-21.08% and 1.30-1.26, respectively, indicating the compressibility was fair.

The angle of repose was found to be in the range from 30.6-33.4° indicating that all the powder blends exhibit good flow characteristics.

Post compression evaluation of fast disintegrating core tablet

The core tablet was prepared by wet granulation method and evaluated for thickness, hardness, friability, disintegration, and weight variation as per Pharmacopoeial specifications. The thickness of the tablet was found to be in the range 5.21-5.24 mm. Hardness was evaluated using Monsanto Hardness Tester and was found in the range of 4.0-4.1 kg/cm.

Table 6: Postcompression evaluation

Formulation	Thickness (mm)	Hardness (kg/cm²)	Weight variation (mg)	Drug content (%)
CF1	3.81±0.7	2.41±1.6	488±1.4	99.7±1.5
CF2	4.09±1.2	3.43±1.1	625±1.1	99.4±2.1
CF3a	5.08±1.6	6.06±1.7	705±1.9	99.6±1.6
CF3b	5.10±2.1	6.67±1.3	721±1.5	101.5±1.7
CF3c	5.11±1.3	6.98±1.2	740±1.3	100.6±0.9
CF4a	5.10±1.7	6.50±0.9	717±1.5	98.3±0.7
CF4b	5.13±1.5	6.80±0.8	736±1.8	99.7±1.4
CF4c	5.14±1.3	7.10±1.2	750±1.1	100.7±1.1

The friability was found in the range of 0.95-0.97%. The disintegration time was found in the range of 7-9 min. The weight of all the tablets was found to be within limit.

Evaluation of compression coated tablets

The compression coated tablets were prepared by wet granulation method and evaluated for thickness, hardness, friability, weight variation as per pharmacopoeial specification.

The results were shown in Table 6. The thickness of the tablet was found to be in the range 3.81-5.14 mm. Hardness was evaluated using Monsanto Hardness Tester and was found in the range of 3.41-7.10 kg/cm^2. The weight of all the tablets was found to be within limit. The drug content was found in the range 98.3-100.7%.

In vitro dissolution studies

The *in vitro* drug release study was performed for formulations CF3 using dissolution Type I (rotating basket), at 100 rpm. The media used was of varying pH range from pH 1.2 to 7.4. The dissolution was carried out in pH 1.2 for first 2 h followed by pH 6.8 for next 3 h and in pH 7.4 for next 2 h. 1 ml pectinase was added at the end of 8th hour to simulate the microbial degradation of pectin. The result shows that the percent drug release of mesalamine and prednisolone from CF3a, CF3b, CF3c at the end of 2 h was found to be 0.474±1.4%, 0747±2.6%, 0.269±2.6% and 2.40±2.6%, 2.93±5.4%, 1.99±3.1%, respectively. The percentage drug release of mesalamine and prednisolone from CF3a, CF3b, and CF3c at the end of 5 h was found to be 16.72±2.6%, 5.80±1.6%, 2.29±0.8% and 25.23±4.4%, 5.19±1.6%, 3.98±2.3%, respectively. The percentage drug release of mesalamine and prednisolone released from CF3a, CF3b and CF3c at the end of 7 h was found to be 37.80±1.6%, 30.50± 5.4%, 36.45±4.7% and 39.31.51±5.4%, 38.04±0.5%, 30.50±3.9%, respectively. The percentage drug release of mesalamine and prednisolone released after addition of pectinase from CF3a, CF3b and CF3c at the end of 10 h was found to be 71.03±3.7%, 73.07±4.2%, 73.53±0.5% and 86.28±0.7%, 73.53±0.5%, 87.53±1.5%, respectively. The drug release was observed after a lag time of 4 h, 6 h and 7 h.

Table 7: Myeloperoxidase activity

Group	Myeloperoxidase activity (U/g)
I	1.12±1.02
II	8.75±0.98
III	3.91±0.21

Kinetic analysis of the dissolution data

Drug release data of formulation CF3c (mesalamine) were best explained by zero order equation as the plot showed the highest linearity (r^2 = 0.8583). As the drug release was best fitted in zero order equation indicated that the release is independent of concentration. Further, the mechanism of drug release was found by Korsmeyer-Peppas equation; the diffusion exponent "n" was found to be 3.23, which indicated super Case-II, i.e., combined mechanism (diffusion through the matrix and partially through water-filled pores).

Drug release data of formulation CF3c (prednisolone) were best explained by zero order equation, as the plot shows the highest linearity (r^2 = 0.8658). As the drug release was best fitted in zero order equation indicated that the release is independent of concentration.

Further, the mechanism of drug release was found by Korsmeyer-Peppas equation; the diffusion exponent "n" was found to be 2.28 which indicated super Case-II, i.e., combined mechanism (diffusion through the matrix and partially through water-filled pores).

Acid uptake test

The percent acid uptake was found to be 0.004% indicating that the formulation CF3c provided enteric protection to surpass the gastric region.

Rupture test

The time required for the rupture of the outer coat was found to be 7 h [Figure 1].

Swelling study

The percent swelling in pH 7.4 was found to be 10.87% while that in pH 1.2 was found to be 5.20%.

In vivo studies

Histopathological evaluation

Figure 4 indicates photomicrographs of the colon tissue. The normal colon is formed of mucosa, submucosa, musculosa, and serosa. The mucosa is differentiated into glands, connective tissue core around the glands, and muscularis mucosa as shown in Group I. In case of Group II, a marked hyperplasia was observed along with disturbed mucosal architecture. Group III showed mucosal and submucosal inflammation infiltrates. Hence, a marked reduction in inflammation was observed in the CF3c treated group.

MPO activity

The activity of MPO, which is found in neutrophils, was used for evaluating the degree of inflammation in the intestine MPO activity, which is an important quantitative index for colonic inflammation, was determined in terms of units per gram tissue weight. MPO activity for normal control group was 1.12 ± 0.26 U/g tissue weight. However, MPO activity of the induced colitis group was found to be 8.7 ± 1.52 U/g tissue weight. This MPO was significantly decreased to 3.91 ± 0.37 U/g tissue weight in the case of CF3c treated group indicating a significant reduction of inflammation [Table 7].

CONCLUSION

From this study, it can be concluded that the prepared novel tablet formulation can be used for colon-specific drug delivery.

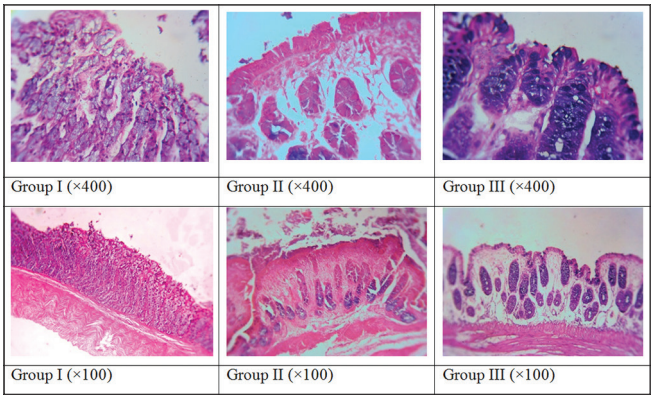

Figure 4: Histopathological evaluation

The prepared tablets met the compendia limits in terms of physical parameters and dissolution studies. As a result, colon delivery of mesalamine and prednisolone appeared to be a promising alternative to traditional drug administration routes. Today, the stress is on patient compliance and to achieve this objective there is a spurt in the development of NDDS. Biodegradable polysaccharides exhibit favorable properties for fabrication of colonic delivery system. The colon is rich in harboring excellent microflora, which can be used for targeting of drug release to colon. Formulation containing enteric coated microbial degradable polymers passes intact from the upper GIT and release the drug in the colon. Thus, polysaccharides appear to be promising agents for obtaining colon-specific drug delivery systems.

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