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Design and Characterization of Dual Drug Loaded Microspheres for Colon Drug Targeting

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ABSTRACT

The present investigation was focus to prepared and characterized eudragit coated pectin microspheres for the delivery of mesalamine and prednisolone to the colon. The pectin microspheres were prepared using emulsion dehydration technique. A 3^3 full factorial design (three variables in three levels) was employed to evaluate the combined effect of the selected independent variables: drugs to polymer ratio, emulsifier concentrations and stirring speed on dependent variables such as particle size and size distribution, percentage yield, % drug entrapment and swelling ratio. Optimized formulation i.e. F18, F24, and F27 were coated with eudragit S100 by the solvent evaporation technique to prevent drug release in the stomach. Eudragit S100 coated pectin microspheres were further characterized for coating thickness and *in-vitro* release kinetics. The cumulative percent drug release of mesalamine and prednisolone from formulation in pH 7.4 phosphate buffer was found to be 97.01 ± 1.35% and 96.89 ± 0.67% for mesalamine and prednisolone, respectively. Optimized formulation (F24) was characterized for *in-vivo* studies. The eudragit-coated pectin microspheres may improve therapeutic efficacy by local action and reduce the side effects by minimizing the systemic absorption of mesalamine and prednisolone. Amalgamation of mesalamine and prednisolone in therapeutic regimen will show synergism action for treatment of Ulcerative Colitis (UC).

Keywords: Mesalamine, Prednisolone, pectin microspheres, Eudragit coating, colon targeting

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INTRODUCTION

Amongst the various routes of drug delivery, oral route is the most preferred route for patient and the clinician alike[1] although oral delivery has become a widely accepted route of administration of therapeutic drugs; the gastrointestinal tract presents several formidable barriers to drug delivery[2]. The site-specific delivery of drugs to lower parts of the GI tract is advantageous for localized treatment of several colonic diseases, mainly inflammatory bowel disease (IBD) like ulcerative colitis (UC) and crohn's disease (CD), irritable bowel syndrome, and colon cancer. Precise colon drug delivery requires that the triggering mechanism in the delivery system only respond to the physiological conditions particular to the colon. Incessant efforts have been made on manipulative colon targeted drug delivery systems with improved site specificity and versatile drug release kinetics to fulfil different therapeutic needs[3].

Ulcerative colitis (UC) is a chronic disorder that affects the mucosal lining of the large intestine (colon) and rectum. It is an intermittent disease, with periods of exacerbated symptoms, and periods that are relatively symptom-free. It is treated as an autoimmune disease. Treatment and management includes successful suppression of active inflammatory disease medically and attempt to conserve the small bowel. Therapeutic regimens are based upon the severity of UC and the extent of gastrointestinal tract involvement[4].

Mesalamine (MSM) also known as mesalazine or 5-aminosalicylic acid, is an anti-inflammatory drug used to treat inflammatory bowel disease, such as UC and mild-to-moderate CD. Therapeutic agents containing mesalamine are first-line therapy for patients with UC. Mesalamine diminishes inflammation by blocking cyclooxygenase and inhibiting prostaglandin production in the colon[5].

Prednisolone (PRD) is a synthetic glucocorticoid used as anti-inflammatory or immunosuppressive agent. It reduces inflammatory reaction by limiting the capillary dilatation and permeability of the vascular structures. It is the second line drug in the therapy of UC. Prednisolone can inhibit leukocyte infiltration at the site of inflammation, interfere with mediators of inflammatory response, and suppress humoral immune responses[6]. The combination may result in

synergistic action for the treatment of the UC and may cause significant lowering of treatment failure rate along with slower development of resistance.

Most of the colon-specific drug delivery systems developed so far is single-unit systems. On the contrary, multi-particulate systems can offer several advantages compared to single dosage forms, for example more reliable drug release profiles and less local irritation. In particular, multiple-unit systems based on such specifically biodegradable polymers showed to quickly spread out on their arrival to the colon, with a sharp increase of surface area exposed to bacterial breakdown that produces a rapid drug release and thereby improves drug absorption[7, 8].

Pectin is a predominately linear polymer of mainly α-(1-4)-linked D-galacturonic acid residues interrupted by 1, 2-linked L-rhamnase residues. Pectin is suitable for use as colon-specific drug delivery vehicle as it is selectively digested by colonic microflora to release drug with minimal degradation in upper gastrointestinal tract. Biodegradable pectin microspheres offer a novel approach for developing sustained release drug delivery systems that have potential for colonic drug delivery [9,10].

Eudragit S100 is an anionic copolymer based on methacrylic acid and methyl methacrylate. It is a polyacrylic resin that has been suggested to be used in microencapsulation for controlled-release applications due to its unique solubility profile. The free carboxylic acid groups make the polymer pH sensitive, being soluble at 7 or above pH 7 so suitable for targeting of drug into the colon[11].

Thus, in the present work, pectin and Eudragit S100 (pH-responsive enteric polymer) were chosen to fabricate microperticulate drug delivery systems for site-specific delivery of mesalamine and prednisolone for the effective treatment of Ulcerative colitis (UC). The proposed delivery system eudragit-coated pectin microspheres is premised to protect the drug loss in the upper GI tract because of the deterrent nature of Eudragit S100 (ES) to the milieu of the upper GI tract and to deliver drugs upon reaching the colon due to the amiable pH of the colonic fluid. Moreover the proposed microparticulate system will improve therapeutic efficacy by local action.

MATERIALS AND METHODS

Mesalamine (MSM) and Prednisolone (PRD) were supplied as a gift samples by Cipla Ltd., Ratlam (India) and Kwality Pharmaceuticals Pvt. Ltd., Amritsar (India) respectively. Pectin was purchased from Himedia Laboratories Limited, Mumbai. Eudragit S100 was obtained as a gift sample from Ranbaxy Laboratory Limited, India. All other chemicals and reagents used were of analytical grades.

Preparation of microspheres

The pectin microspheres were prepared by emulsion dehydration technique as reported by Esposito *et al.*[12]. Pectin and drugs were dissolved in 20 ml of distilled water and stirred overnight to solubilize completely. Drug-Polymer ratio (w/v) was used as 1:1, 1:2 and 1:3. The ratio of both the drug taken in equal amount and this drugs-polymer solution was dispersed in 50 ml iso-octane containing Span 85 and stirred continuously to obtain stable water/oil (w/o) emulsion. The solution was rapidly cooled to 15ºC and then 50 ml of acetone was added in order to dehydrate the pectin droplets. This system was maintained under mechanical agitation at 25ºC for 30 min. to allow the complete solvent evaporation. The microspheres were washed with acetone, collected and freeze dried overnight and kept in airtight container for further studies.

Table 1: Design of Experiment and Optimization of Variables

Formulation Code	Drugs Polymer Ratio (w/v)	Emulsifier Concentration (v/v)	Stirring Speed (rpm)
F1	1:1	0.5	500
F2	1:2	0.5	500
F3	1:3	0.5	500
F4	1:1	0.5	1000
F5	1:2	0.5	1000
F6	1:3	0.5	1000
F7	1:1	0.5	1500
F8	1:2	0.5	1500
F9	1:3	0.5	1500
F10	1:1	1.0	500
F11	1:2	1.0	500
F12	1:3	1.0	500
F13	1;1	1.0	1000
F14	1:2	1.0	1000
F15	1:3	1.0	1000
F16	1:1	1.0	1500
F17	1:2	1.0	1500
F18	1:3	1.0	1500
F19	1:1	1.5	500
F20	1:2	1.5	500
F21	1:3	1.5	500
F22	1:1	1.5	1000
F23	1:2	1.5	1000
F24	1:3	1.5	1000
F25	1:1	1.5	1500
F26	1:2	1.5	1500
F27	1:3	1.5	1500

A 3^3 full factorial design (three variables in three levels) was employed to evaluate the combined effect of the selected independent variables: drug to polymer ratio (A), emulsifier concentrations (B) and stirring speed (C) on dependent variables such as particle size and size distribution, percentage yield, % drug entrapment and swelling ratio.

The drug: polymer ratio (1:1, 1:2, 1:3) emulsifier concentrations (0.5, 1, 1.5 ml) and stirring speed (500, 1000, 1500) were varied in batches F1 – F27 as shown in table 1.

Characterization of microspheres

Size and size determination

It was carried out by using compound microscope. Dried pectin microspheres were firstly redispersed in distilled water. These were then placed on a glass slide. The number of divisions of the calibrated eyepiece was counted by a micrometer using the stage micrometer[13]. All formulations were characterized for their average particle size, results were shown in Fig.2.

Percentage yield

Total percentage yield of pectin microspheres calculated by weighing of prepared microspheres was divided by total amount of the non-volatile components used for the preparation of the microspheres[14].

$$\% \text{ yield of production} = \frac{\text{Practical yield}}{\text{Theoretical yield}} \text{x } 100$$

Results were shown in Fig.2.

% Drug entrapment

The microspheres obtained after two washings were digested in 10 ml of pectinase solution (4% w/w) for 1 hrs. The digested homogenate was analyzed for drugs content at 332nm for MSM and 246nm for PRD by UV/Visible Spectrophotometer (UV- 1800Shimadzu, Japan) [15].

$$\% \text{ Drug entrapment} = \frac{\text{Practical Entrapped Drug}}{\text{Total Drug Taken}} \text{x } 100$$

Results were shown in Fig.3.

Swelling ratio

100 mg of drugs-loaded pectin microspheres and eudragit-coated pectin microspheres were placed in enzyme-free simulated intestinal fluid (SIF, pH 7.4) and allowed to swell up to constant weight at 37ºC ± 0.5ºC. The microspheres were periodically removed and blotted with filter paper, and then their change in weight was measured until attainment of equilibrium[16].

$$SR = \omega_g - \omega_o / \omega_o$$

Where, SR indicates swelling ratio; ω_o, initial weight of microspheres; and ω_g, final weight of microspheres, results were shown in Table.2.

Coating of prepared pectin microspheres by eudragit S100

The coating of Eudragit S100 on pectin microspheres was done by oil-in-oil solvent evaporation method as reported by Lorenzo-Lomora *et al*[17].

50 mg of pectin microspheres were dispersed in 12% w/v acetone in which eudragit S100 was previously dissolved to give 1:10 core: coat ratio. This organic phase was then poured in light liquid paraffin containing 1% w/v Span 85. The system was maintained under agitation speed of 1000 rpm at room temperature for 3 hours to allow the evaporation of solvent. Finally, the coated microspheres were filtered, washed with n-Hexane and dried for 24 hrs. All prepared pectin microspheres were coated with eudragit S100 and weighed and the mean coating weight calculated by difference with respect to the initial microspheres weight.[18]

Coating thickness

The mean diameter of representative microspheres samples of each batch was estimated with a calibrated ocular eyepiece. The mean coating thickness was determined by difference between the mean diameter of microspheres after and before the coating[19], results were shown in Table.3.

***In-Vitro* drug release studies in simulated gastrointestinal fluids of different pH**

On the basis of particle size, percentage yield and entrapment efficiency three formulations (F18, F24, and F27) of eudragit coated pectin microspheres were evaluated for the *in-vitro* drug release study. The drug dissolution tests of microspheres were carried out by the paddle method specified in USP XXIII. 100 mg of microspheres were weighed accurately and gently spread over the surface of 900 ml of dissolution medium as specified in the IP 1996. The content were rotated at 100 rpm and thermostatically controlled at 37±0.5˚C. Sink condition was maintained during dissolution.

In-Vitro Drug release was studied in simulated gastrointestinal fluids of different pH in the following sequence, in order to mimic mouth-to-colon transit: In simulated gastric fluid (pH 1.2) 2nd hrs; In simulated intestinal fluid (pH 6.8) 3rd-4th hrs; In simulated colonic fluid (pH 7.4) 5th-24th hrs.

The medium was filtered through whatmann filter paper after 2nd and 5th hrs and the residue on filter paper was added to the next medium immediately. The dissolution study was continued further and samples were withdrawn at suitable time intervals from the dissolution vessel and analyzed for drugs content at 332nm for MSM and 246nm for PRD by UV/Visible Spectrophotometer (UV- 1800Shimadzu, Japan). [20] The % cumulative drug release profile of formulations F18, F24 and F27 are shown in Fig.4, 5 and 6.

Shape and surface morphology

In order to examine the surface morphology, the pectin microspheres and optimized formulations F24 was analysed through scanning electron microscope (LEO 435 VP, Eindhoven Netherlands). The sample for SEM was prepared by lightly sprinkling the microspheres powder on a double adhesive tape, which was stuck on an aluminum stub. The stubs were then coated with gold to thickness of about 300 Å using a sputter coater[21]. The photomicrographs were taken with the help of SEM analyzer, the micrograph depicted in Fig.7.

***In- Vivo* Studies [22, 23]:**

In colitis induced rats

The protocol of present study was duly approved by the Institutional Animal Ethics Committee of Smriti College of pharmaceutical sciences, Indore (M.P.) (Reference no. 12/DB/177 (1) and the studies were carried out in accordance with the Council for Purpose & Supervision of Experiment on Animals (CPCSEA), Ministry of Social Justice & Empowerment Govt. of India. Healthy male wistar rats (average weight 230 g) were fasted for 48 hrs before the induction of UC. Inflammatory lesions were induced by acetic acid. Each group of treated animals contained six rats. The colitis group was treated by the following procedure to

effectuate an inflammation: After light narcotizing with ether, the rats were catheterized 8 cm intrarectally, by the 4% acetic acid (2 ml/day) for 3 days for full induction of UC model.

Estimation of induction of ulcer colitis (UC)

Weight loss measurement

Animals were weighed on the weighing balance before and after administration of acetic acid and weight loss after acetic acid administration a parameter which indicates induction of UC. Body weight of each animal was taken for 14 days and result were shown in Fig.8.

Stool consistency

Stool consistency, 0 point was given for well formed pellets, 2 points for pasty and semi formed stools that did not stick to the anus, and 4 points was given for liquid stools that stick to the anus, result were shown in Table.4.

Rectal bleeding

Bleeding was scored as 0 point for no blood, 2 points for positive finding, and 4 points for gross bleeding. The mean of these scores was forming the clinical score ranging from 0 (healthy) to 4 (maximal activity of colitis), result were shown in Table.5.

Blood testing

Blood samples were collected and analyzed for blood glucose level, total white blood cell count, neutrophills count and monocytes count, result were shown in Fig.9-12.

Histopathology of colon

The animals were sacrificed 24 hrs after the last drug/particle administration and their colons were resected. Resected colon was stored in 10% formalin solution and samples were sending for histopathogical studies, the micrographs depicted in Fig.13.

Animals were divided into four groups where each group contained 6 animals.

Group A: Normal control group received normal saline

Group B: Colitis control group received normal saline

Group C: Colitis group received microspheres suspension

Group D: Colitis group received drugs solution

Colitis group was treated with MSM and PRD solution (dose: 100 mg/kg and 40 mg/kg) and microspheres suspension once a daily dose for 7 days. Dose of microspheres were calculated after the determination of entrapment efficiency.

Colitis control group was treated same as the colitis group was treated with normal saline. Normal control group contains healthy animals.

***In-Vivo* targetability[24]**

The eudragit coated pectin microspheres were prepared using the same amounts of composition except that the amount of drugs was replaced with fluorescent dye.

Fluorescent imaging

The Fluorescent imaging study was carried out using male wistar rats. In experiment, the animal was allowed to fast overnight with free access to water. The microspheres were administered and after 24 hrs. Animal was sacrificed and then colon part send for histopathological study, the micrograph depicted in Fig.14.

Statistical analyses

The Student t test was used to find the statistical significance. Quantitative data were expressed as the mean ± standard deviation. P values\0.05 were considered significant.

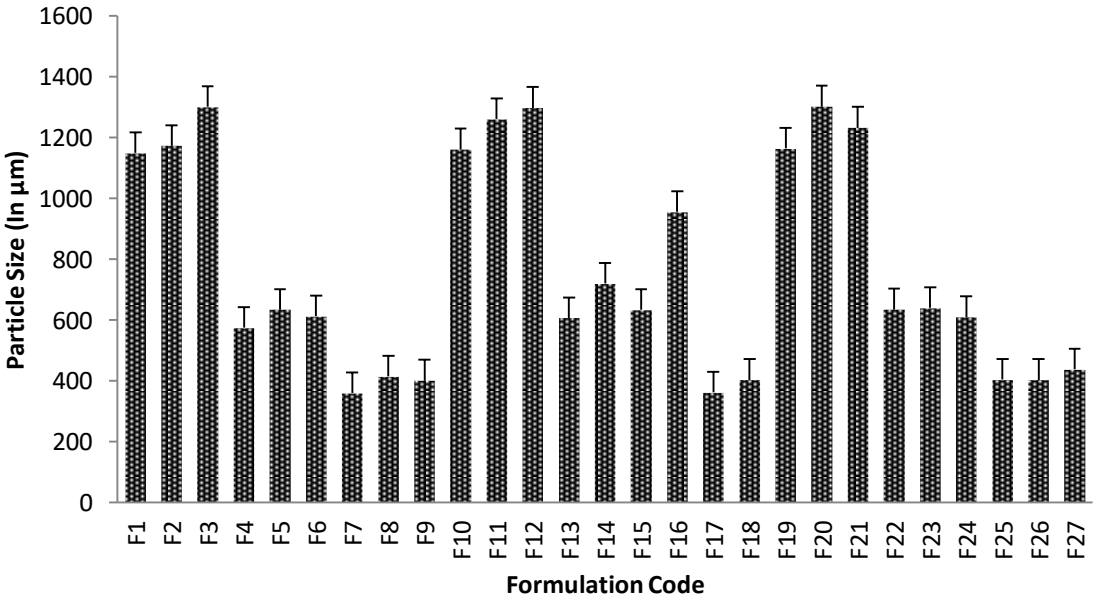


Figure 1: Particle size of all formulations of pectin microspheres

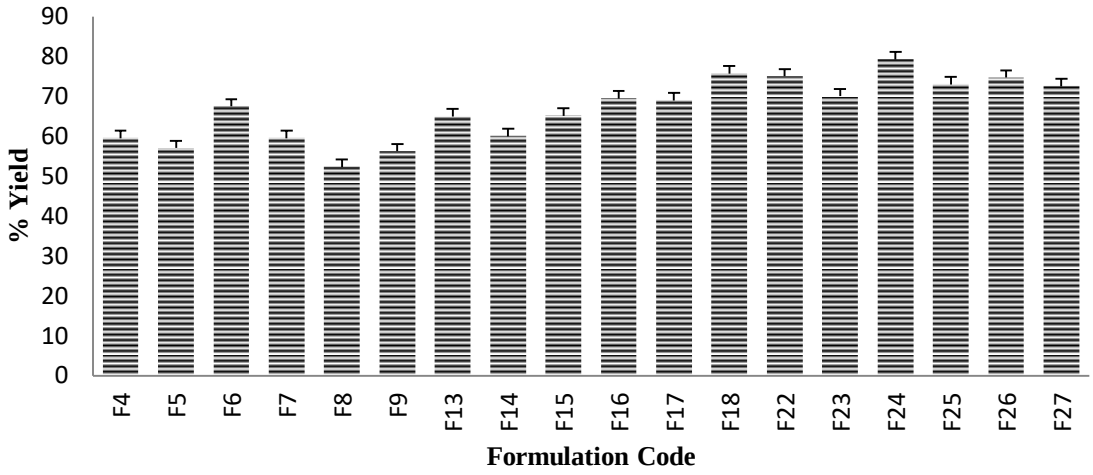


Figure 2: Percentage yield of optimized formulations of pectin microspheres

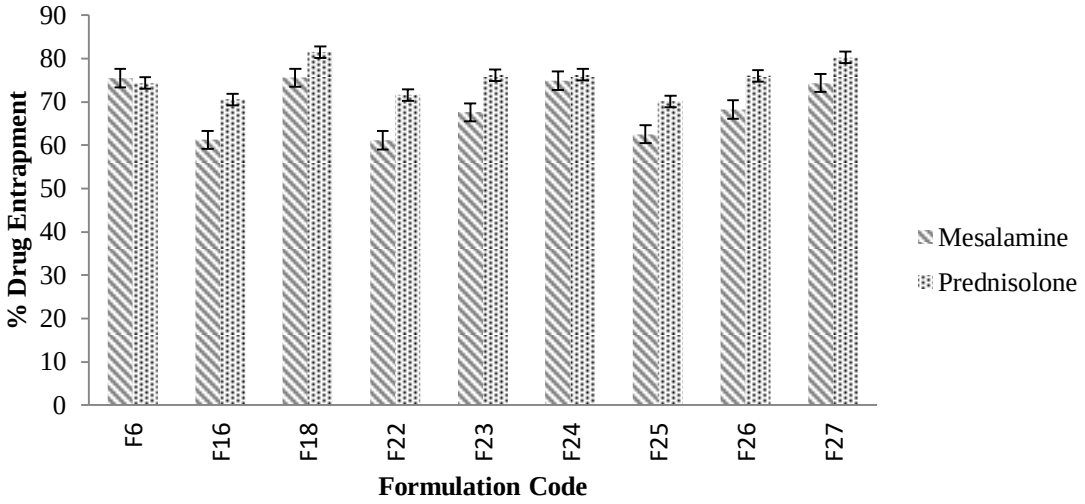


Figure 3: % Drugs entrapment of optimized formulations of pectin microspheres

Table 2: Swelling ratio of optimized formulations of pectin microspheres

S. No	Formulation Code	Swelling Ratio
1	F6	1.18
2	F16	0.94
3	F18	1.45
4	F22	0.96
5	F23	1.10
6	F24	1.44
7	F25	1.05
8	F26	1.13
9	F27	1.60

All the values are expressed as ± S.D, n=3

Table 3: Coating thickness of optimized formulations of pectin microspheres

S. N.	Selected formulation	Coating thickness (µm)
1	F18	111.06
2	F24	154.63
3	F27	118.52

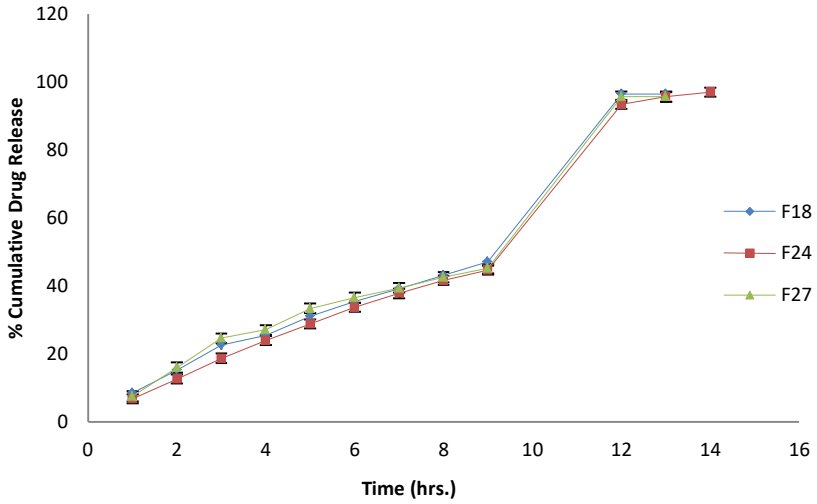


Figure 4: Percent cumulative release of mesalamine from optimized formulations of eudragit S100 coated pectin microspheres in PBS (pH 7.4)

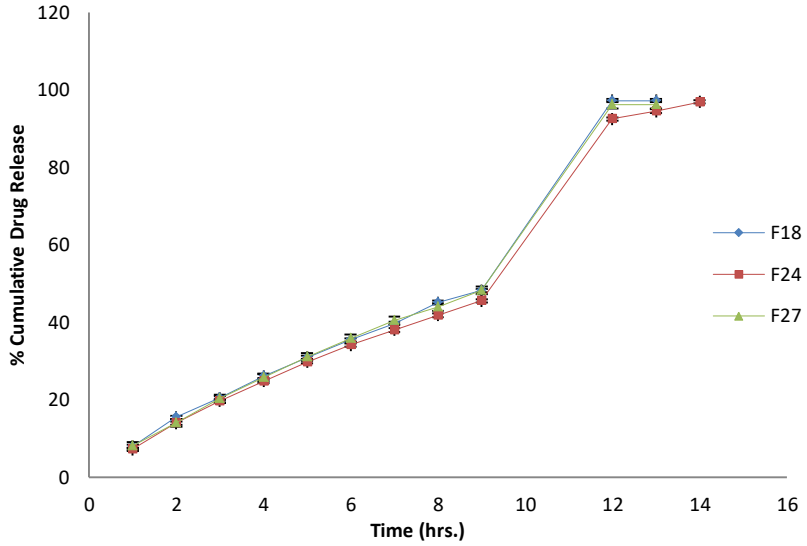


Figure 5: Percent cumulative release of prednisolone from optimized formulations of eudragit S100 coated pectin microspheres in PBS (pH 7.4)

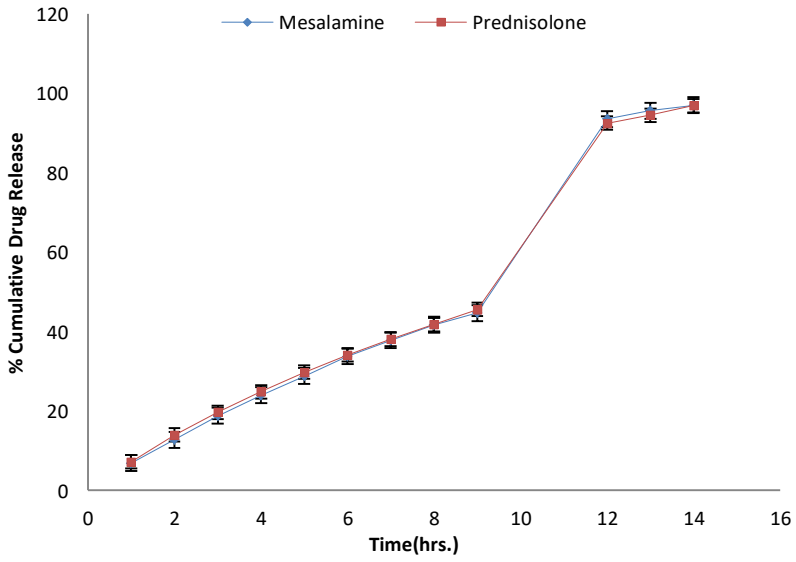
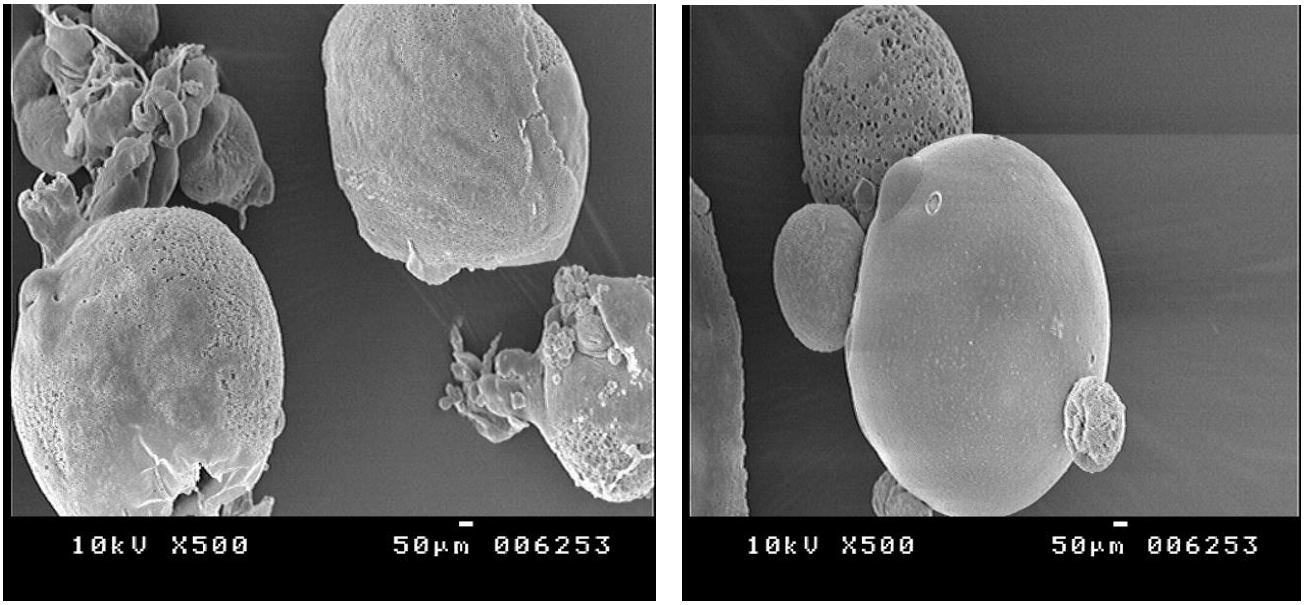
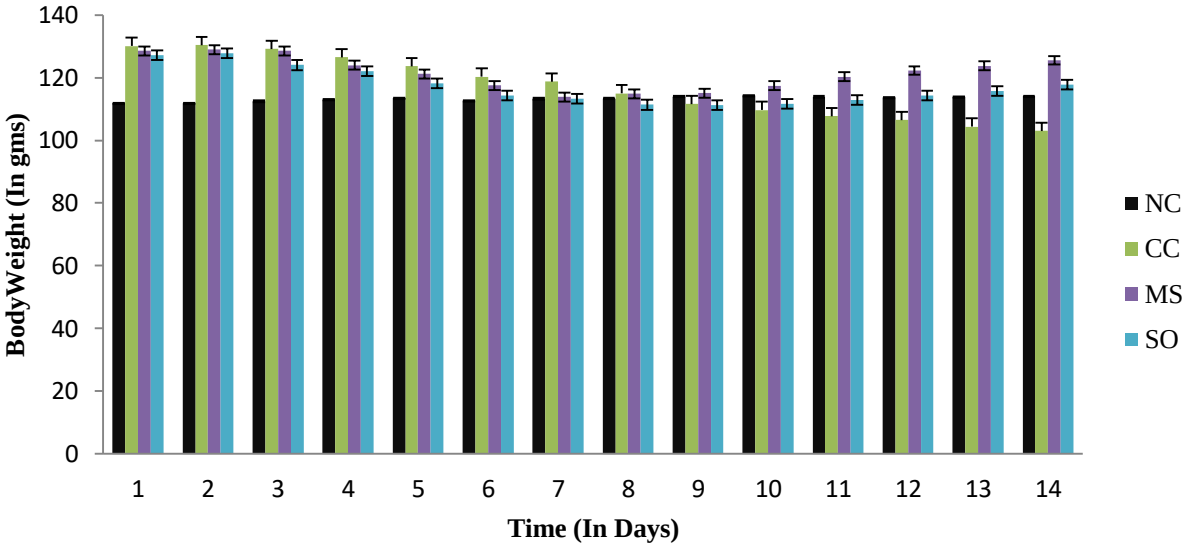


Figure 6: Percent cumulative drug release from optimized formulation of eudragit S100 coated pectin microspheres (F24) in PBS (pH 7.4)



(a) (b)

Figure 7: SEM photographs optimized formulations (F24) (a) Pectin microspheres (b) Eudragit S100 coated pectin microspheres



NC- Normal control group CC-Colitis control group MS- Microspheric group SO- Drugs solution group

Figure 8: Body weight comparison of different groups of animals

Table 4: Stool consistency of different groups of animals

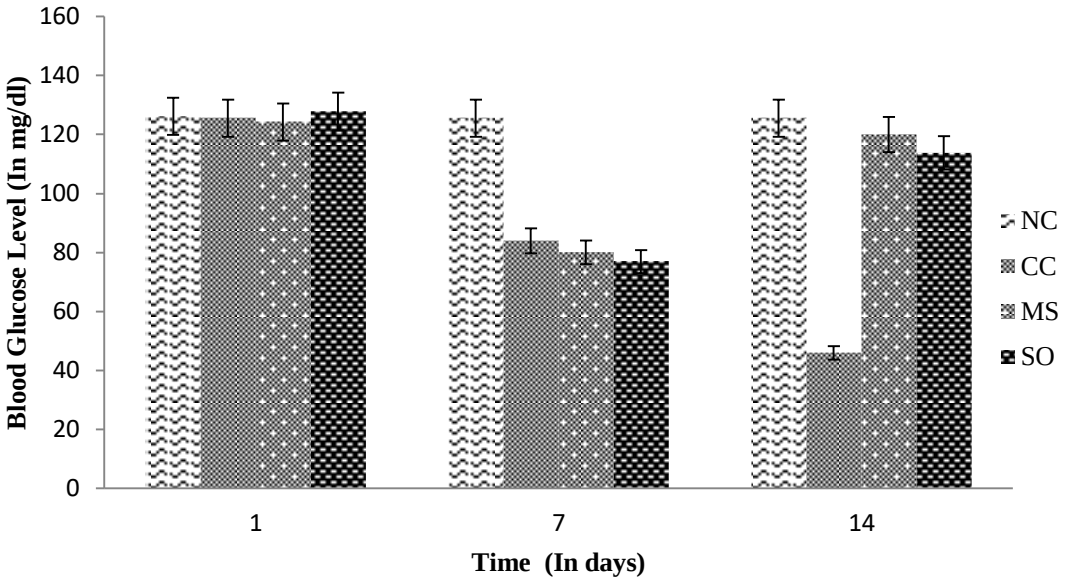
S. N.	Day	Normal Control group	Colitis Control group	Microspheric group	Drugs Solution group
1	1	Pellets	Pellets	Pellets	Pellets
2	7	Pellets	Pasty	Pasty	Pasty
3	14	Pellets	Liquid	Pellets	Pasty

Rectal Bleeding:

Table 5: Rectal Bleeding of Different Groups of Animals

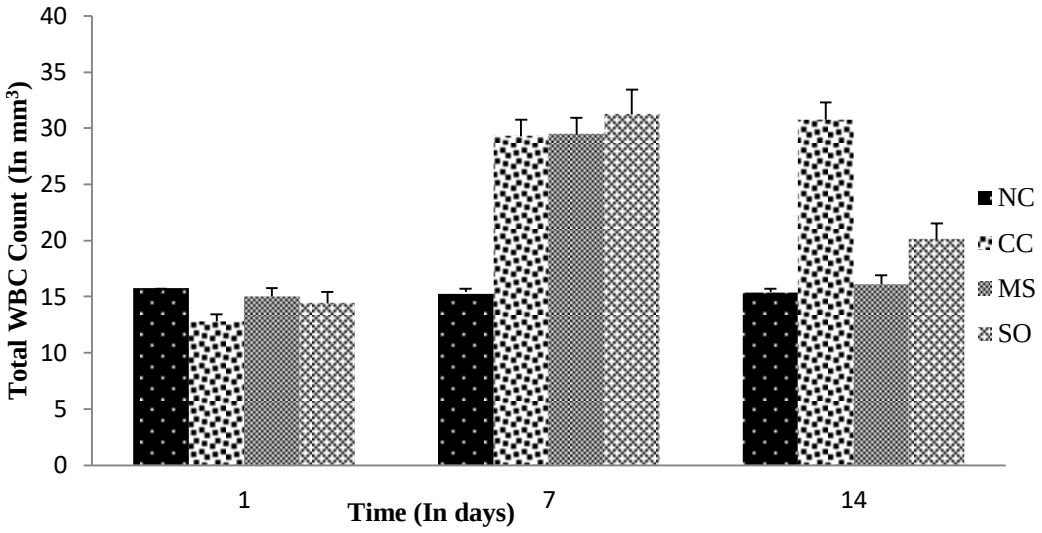
S. No	Day	Normal Control group	Colitis Control group	Microspheric group	Drugs Solution group
1	1	No Bleeding	No Bleeding	No Bleeding	No Bleeding
2	7	No Bleeding	Positive	Positive	Positive
3	14	No Bleeding	Gross	No Bleeding	No Bleeding

Blood Testing:



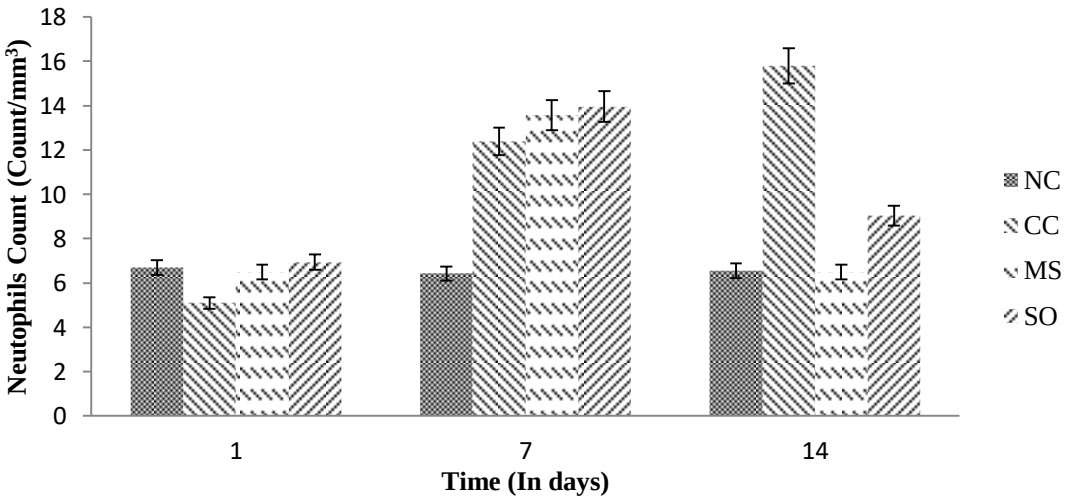
NC- Normal control group CC-Colitis control group MS- Microspheric group SO- Drugs solution group

Figure 9: Blood glucose level comparison of different groups of animals



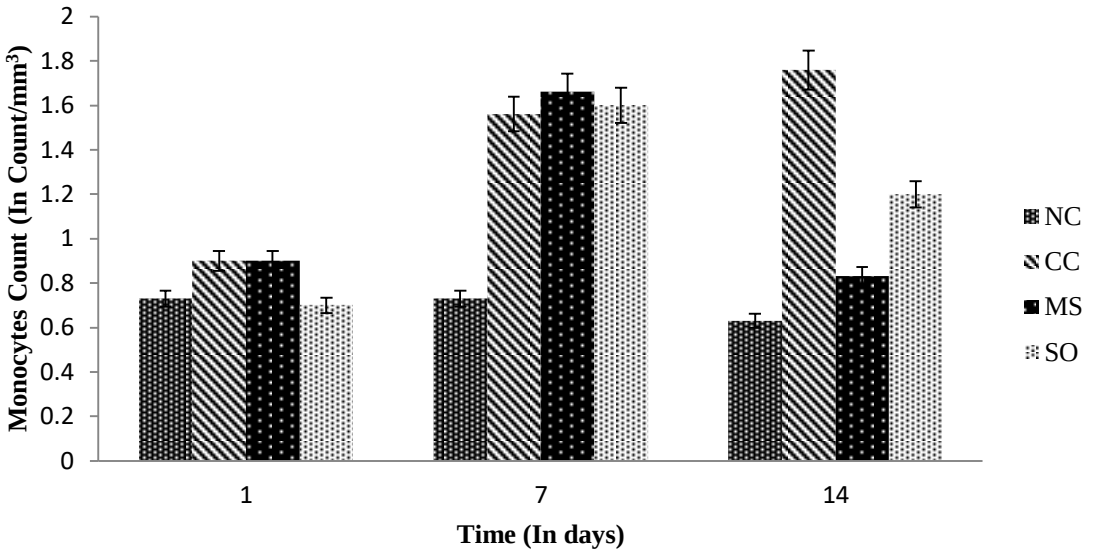
NC- Normal control group CC-Colitis control group MS- Microspheric group SO- Drugs solution group

Figure 10: Total WBC count comparison of different groups of animal



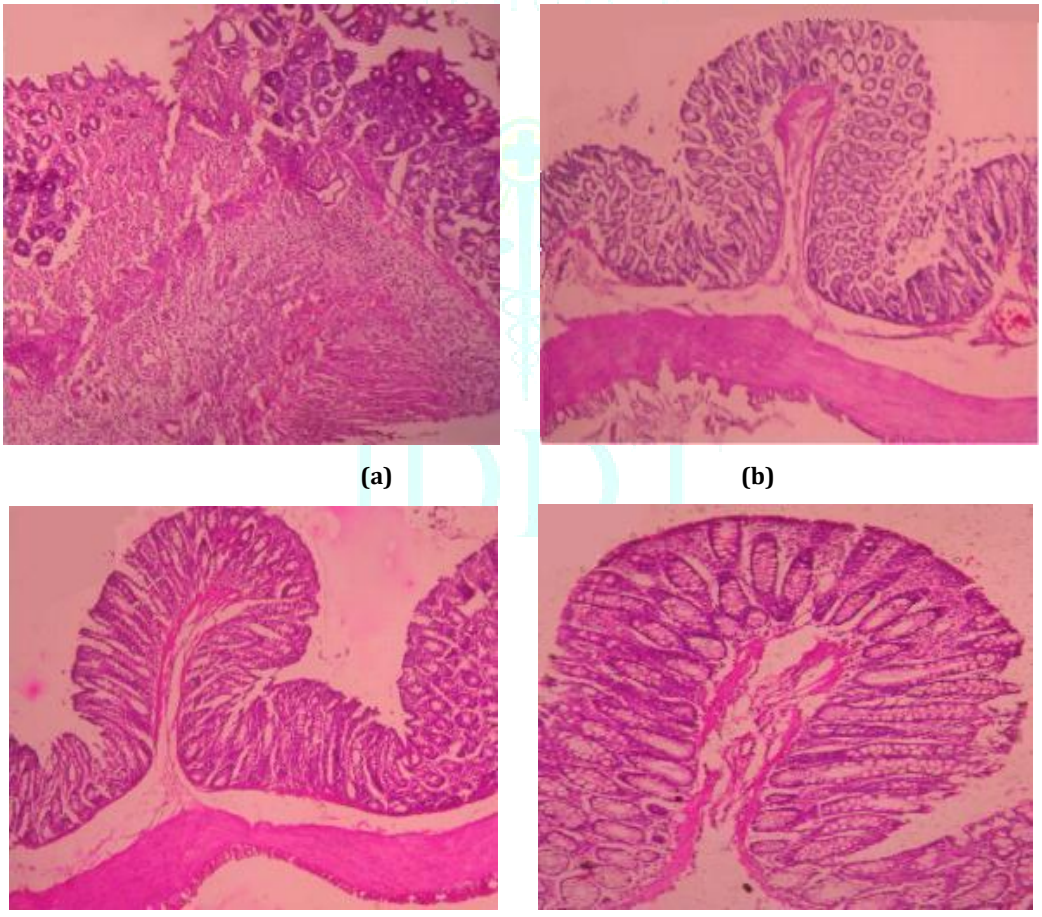
NC- Normal control group CC-Colitis control group MS- Microspheric group SO- Drugs solution group

Figure 11: Neutrophils count comparison of different groups of animals



NC- Normal control group CC-Colitis control group MS- Microspheric group SO- Drugs solution group

Figure12: Monocytes count comparison of different groups of animals



(a) (b)

(c) (d)

(a)- Normal control group (b)-Colitis control group (c)- Microspheric group (d) - Drugs solution group

Figure 13: Histological microscopic photographs of different groups of animals

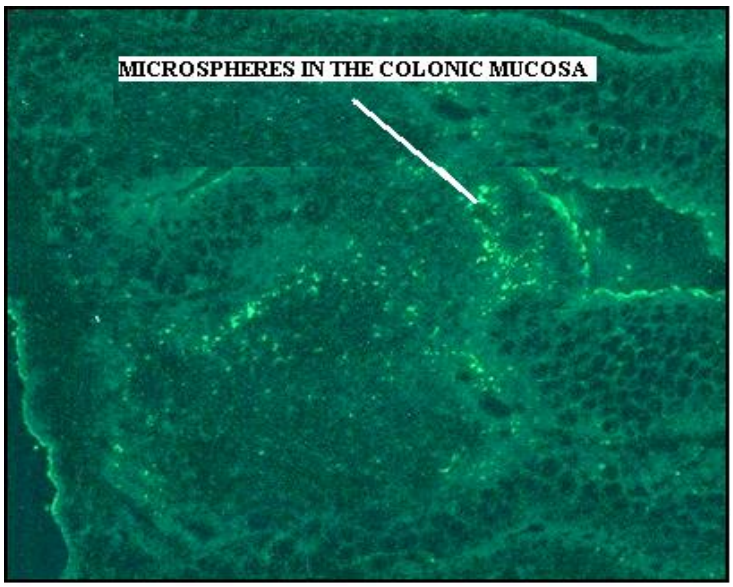


Figure 14: Fluorescent microscopic photograph of optimized formulation (F24) in colitis induced rat

RESULT AND DISCUSSION

Pectin microspheres containing mesalamine and prednisolone were prepared by emulsion-dehydration technique. A 3^3 full factorial design (three variables in three levels) was employed to evaluate the combined effect of the selected independent variables: drug to polymer ratio (A), emulsifier concentrations (B) and stirring speed (C) on dependent variables such as particle size and size distribution, percentage yield, % drug entrapment and swelling ratio. The drug: polymer ratio (1:1, 1:2, 1:3) emulsifier concentrations (0.5, 1, 1.5) and stirring speed (500, 1000, 1500) were varied in batches F1 – F27 as shown in table 1.

Twenty seven formulations were prepared which were characterized for their average particle size and on the basis of particle size selected batches optimized for percentage yield, % drug entrapment and swelling ratio, results depicted in Fig.1, 2 and 3 and Table 2 respectively.

Particle size of the pectin microspheres increased from 359.66 to 1300.40 µm with decreasing in stirring speed from 1500 to 500 rpm. The average particle size of microspheres increased with decreasing amount of emulsifier (span 85), which got dispersed into larger droplets. The particle size of pectin microspheres decreased with increasing amount of span 85 from 0.5 to 1.50%. Increased emulsifier concentration led to the formation of particles with a lower mean geometric diameter. Increasing concentration of span 85 from 0.5 to 1.50 % v/v led to stabilization of the emulsion droplets avoiding their coalescence, resulting in smaller microspheres. The particle size of pectin microspheres decreased with increasing stirring rate from 500 to 1500 rpm. Results showed that the particle size of microspheres was controlled by stirring rate. These results show that a high stirring speed produced smaller microspheres due to the smaller emulsion droplets produced by a higher stirring speed, which provided more energy to disperse the oil phase in water, but higher agitation speeds resulted in irregularly shaped microspheres. The particle size of pectin microspheres decreased from 359.66 to 1300.40 µm with increasing the amount of drugs. The drug entrapment efficiency varied from 61.14 $\pm$ 0.5% to 75.59 $\pm$ 0.96% for mesalamine and 70.16 $\pm$ 1.27% to 81.53 $\pm$ 0.73% for prednisolone. The highest entrapment efficiency and percentage yield were found with F18, F24, and F27 formulations, therefore these formulations were selected for further evaluation.

On the basis of particle size, Percentage yield, % drugs entrapment and swelling ratio optimized formulation i.e. F18, F24, and F27 were coated with eudragit S 100, therse frmulations were further characterized for coating thickness, and results were shown in table 4.

The *in vitro* drug release study of optimized formulation (F24) was carried out by buffer change method to mimic the GIT environment. The cumulative percentage drug release from Eudragit-coated pectin microspheres showed the desired rate, as there was no measurable drug release observed up to 2 hours in SGF (pH 1.2), and release as intended in the simulated distal ileum and colon. Cumulative percent drug release of mesalamine and prednisolone from formulation in pH 7.4 phosphate buffer was found to be 97.01 $\pm$ 1.35% and 96.89 $\pm$ 0.67% for mesalamine and prednisolone, respectively as shown in Fig. 4, 5 and 6.

Optimized Formulation (F24) and eudragit S100 coated pectin microspheres were spherical, non-aggregated with smooth surface, in scanning electron micrographs as shown in Fig. 7.

In-vivo study of optimized formulation (F24) was performed in colitis induced rats and compared with drugs solution to treat UC in male wistar rats. Study shows that optimized formulation effectively treat UC in rats. Male wistar rats (average weight 230 g) were fasted for 48 hrs before the induction of ulcerative colitis. Inflammatory lesions were induced by acetic acid. Each group of treated animals contained at least six rats. The colitis group was treated by the following procedure to effectuate an inflammation: After light narcotizing with ether, the rats were catheterized 8 cm intrarectally, by the 4% acetic acid (2 ml/day) for 3 days for full induction of UC model[46].

Animals were weighed on the weighing balance before and after administration of acetic acid and weight loss after acetic acid administration a parameter which indicates induction of UC[47]. Stool consistency, 0 point was given for well formed pellets, 2 points for pasty and semi formed stools that did not stick to the anus, and 4 points was given for liquid stools that stick to the anus[47]. Bleeding was scored as 0 point for no blood, 2 points for positive finding, and 4 points for gross bleeding. Results of body weight comparison of different groups of animals, stool consistency and rectal bleeding of

animals are shown in figure 8, table 4 and 5 respectively. The mean of these scores was forming the clinical score ranging from 0 (healthy) to 4 (maximal activity of colitis) [47].Blood samples were collected and analyzed for total white blood cell count, neutrophills count, and blood glucose level[47]. The results are shown in figure 9, 10 and 11.

The animals were sacrificed 24 hrs after the last drug/particle administration and their colons were resected. Resected colon was stored in formaline solution and samples were sending for histopathogical studies[48]. Histological microscopic photographs are shown in figure 13.

Four groups of animals were prepared each group contains 6 animals, Male wistar rats (average weight 230 gm) Two Colitis group, Colitis control group and Normal control group.

Colitis group was treated with Mesalamine and Prednisolone solution (dose: 100 mg/kg and 40 mg/kg) and microspheres suspension once a daily dose for 7 days. Dose of microspheres were calculated after the determination of entrapment efficiency.

Colitis control group was treated same as the colitis group was treated with normal saline. Normal control group contains healthy animals. The pectin microspheres were prepared using the same amounts of ingredients except that the amount of drugs was replaced with fluorescent dye.

The Fluorescent imaging study was carried out using male wistar rats. In experiment, the animal was allowed to fast overnight with free access to water. The microspheres were administered and after 24 hrs. animal was sacrificed and then colon part send for histopathological study.

Fluorescent microscopic photograph of colitis induced rat colon showed the microspheres reaches in the colonic mucosa of rat which proves the targeting of microspheres. The Fluorescent microscopic photograph of optimized formulation (F24) in colitis induced rat shown in figure 14.

The optimized microspheres (F 24) produced were generally spherical having size range 600-700 µm.. The designed site specific delivery of Mesalamine and Prednisolone from the system may reduced the side effect of drugs by targeting the drugs into colon. The experiment results demonstrated that eudragit S100 coated pectin microspheres have potential to be used in the treatment of ulcerative colitis.

Conclusion

Eudragit S100 coated pectin microspheres have the potential to be an efficient, viable, safe and cost-effective system for administration of mesalamine and prednisolone on account of their biodegradability, biocompatibility, and suitability for oral applications.

Conflicts of interest: The authors declare that there are no conflicts of interest.

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