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FORMULATION AND *IN-VITRO* EVALUATION OF MESALAZINE COLON TARGETED DRUG DELIVERY SYSTEM

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ABSTRACT

The objective of this work is to formulate Mesalazine tablet in capsule system for targeting colon and evaluate the formulation for various parameters. Release the active ingredient after predetermined time in a predetermined location with better pharmaceutical and therapeutic properties. To protected from upper GIT tract. To increase bioavailability by first pass effect and protein binding minimize the side effects by preventing unwanted absorption at unwanted site. To develop and formulate Mesalazine mini tablets by direct compression method. The prepared mini tablets will be evaluated for various parameters such as thickness test, hardness test, weight variation test, drug content, disintegration test, friability test and *invitro* drug release studies. To optimize minitablet in capsule system evaluated for *in-vitro* drug release studies. From the dissolution studies it was found that formulation (F8) containing 75mg of Ethyl cellulose, 75mg of HPMC K100M shows 5 hour drug release minimum in upper GIT and maximum drug release in colon being kept in the system,it has shown maximum drug release for7 hour. The drug release kinetics for the optimized formulation F8 followed the zero order kinetics and follows super case II transport mechanism.

Keywords: Mesalazine, Sodium starch glycolate, Croscarmellose sodium, HPMC K100 M.

INTRODUCTION

Oral medication conveyance framework is the best course for medication conveyance due to its ease of administration, better patient compliance and patient liability in design and formulation development[1-4].However, the oral course of medication administration using conventional tablets cannot be used for targeting the drug to lower gastro intestinal parts due to their almost complete release at upper gastro intestinal tract (GIT), which leads to their limited availability at the lower GIT.

Colon targeted drug delivery system (CTDDS) used to focus conveyance of medications into the lower gastro intestinal tract, which happens principally in the large intestine[5-8].Directed medication conveyance into colon is highly desirable approach for local treatment for variety of colonal bowel diseases like Ulcerative colitis, Crohn's disease, amebiosis, colonic cancer, local treatment of colonic pathologies and system delivery of protein and peptide drugs, anti-asthmatic drugs, anti- diabetic agents, anti-hypertensive drugs.

For effective and safe therapy of colonal disorders, CTDDS is necessary i.e. drug release and absorption should not occur in the stomach as well as small intestine, and neither the bioactive specialist should be corrupted in both of the disintegration destination show ever just discharged and consumed once the framework comes to the colon[9-12].

MATERIALS AND METHODS

Mesalazine were procured from BMR Chemicals, Hyderabad. Sodium starch glycolate, Croscarmellose sodium, HPMC K100 M, Magnesium stearate and Talc were procured from Vijay Enterprises, Hyderabad.

Preparation of Mesalazine immediate release tablets

Mesalazine immediate release tablets were prepared by direct compression technique. Tablet ingredients were accurately weighed as mentioned in the table. All powders were then passed through #20 mesh sieve. After screening, the powdered ingredients were blended in a large size poly bag by tumbling action. Finally, magnesium stearate was added and again mixed for 5 minutes so that particle surface was coated by lubricant evenly. The blend was then compressed into tablets weighing about 250 mg using 10 mm shallow biconcave punches in rotary tablet punching machine to a hardness of 3-4 kg/cm^2. The prepared mini tablets were used for further evaluation studies. Thecomposition was shown in Table-1.

Formaldehyde treatment

- In this treatment,'0' size 100 Hard gelatin capsules were taken. Their bodies were separated from the caps and deposit on a wire mesh, spread as a solitary layer.
- 25 ml of 15% v/v of formaldehyde solution was prepared and placedin a desiccator and add 5 grams of potassium permanganate to the above solution.
- The wire mesh containing the bodies of the capsules was placed on the top of desiccator containing formaldehyde liquid at the base and instantly the desiccator tightly closed and sealed.
- The bodies of capsules were made to react with formaldehyde vapors by exposing various time periods i.e., 2, 4, 6, 8 and12hours.
- Then they are removed and deposit on a filter paper and dried for 24 hours to ensure a polythene bag completion of reaction between hard gelatin capsule and formaldehyde mist, afterwards the capsules deposit in an open climate, to removal of residual formaldehyde and stored in

Hydrogel plug

- HPMC K100 M, ethyl cellulose are used for developing hydrogel plug.
- Hydrogel plug is prepared as a compressed mini tablets, deposit at the opening of capsule body at that point capsule body shut by utilizing cap
- A tight joint between container shell and plug fitting is important to control water penetration into the case material and the medication discharge introductory to finish swelling of attachment. Hydrogel plug expulsion finished by disintegration, pushing out by inside pressure, enzyme degradation, swelling on contact with aqueous fluids. The composition was shown in Table-2.

Flow properties

Angle of repose

Angle of repose is determined as the maximum angle possible between the surface of the pile of the powder and horizontal plane. Fixed funnel method was used to determine the angle of repose of powder or granules.

Bulk density

Weighed amount of the powder blend was taken and transferred to a measuring cylinder. Bulk volume of the blend is noted as per the reading on the measuring cylinder.

Tapped density

Tapped density is determined by the weighed quantity of powder blend is poured into the graduated cylinder, which is then tapped for 100 taps.

Compressibility index

Compressibility index is important to measure the tendency of powder formulation. It indicates the flow properties of the blend. Low percentage of compressibility index indicates free flowing powder, whereas high compressibility index indicates poor flowing powder. Compressibility index was calculated from the readings of bulk density and tapped density. The results were shown in Table 3.

***InVitro* Dissolution Studies**

Invitro dissolution studies were carried out using USP dissolution type 1 (basket) apparatus. Mini tablets containing capsules placed in the basket and immersed completely in dissolution media. In order to stimulate the pH changes along with gastrointestinal tract three different dissolution media with pH 1.2, 6.8 and 7.4 buffers were used. The dissolution media were maintained at a 37±0.5^{0}C temperature throughout the experiment and ration speed of basket maintained at 50 rpm, 900 ml of dissolution medium was used at each time. Mesalazine mini tablets in capsule system was placed basket to prevent floating. When performing experiments, the 0.1NHCL was used for first two hours because the average gastric emptying time is two hours, then dissolution medium was removed and add fresh dissolution medium at pH 6.8 phosphate buffer for three hours, then removed the pH 6.8 buffer and add fresh dissolution medium at pH 7.4 phosphate buffer for remaining rest of

time (24hours). A 5 ml of dissolution media was withdrawn at predetermined time intervals and fresh dissolution media was replaced. The withdrawn samples were analyzed by using UV-Visible spectrophotometer and calculate the cumulative amount of drug release over the sampling times. The *invitro* release profiles were shown in Figure 1.

FT-IR STUDIES

The IR spectrum of pure drug was found to be similar to the standard spectrum of Mesalazine From the spectra of Mesalazine, combination of Mesalazine with polymers, it was observed that all characteristic peaks of Mesalazine were not altered and present without alteration in the combination spectrum, thus indicating compatibility of the drug and polymers. FT-IR spectra of Mesalazine and optimized formulation are shown in Figure 2and 3 respectively.

RESULTS AND DISCUSSION

Formulation and *in vitro* evaluation of tablet in capsule system for targeting colon was prepared and evaluated with various evaluation parameters. Calibration Curve of Mesalazine was evaluated in various pH Medias (pH 1.2, pH 6.8 phosphate buffer and pH 7.4 phosphate buffers). In 0.1 N HCl and small intestine buffer and large intestine buffer. Calibration curve of Mesalazine concentration is 5-30µg/mL and correlation coefficient found be 0.9996, 0.9995 and 0.9997respectively.In drug excipient compatibility studies, Mesalazine with various polymers mixture and pure drug of Mesalazine was estimated. Immediate release mini tablets developed by direct compression method. The immediate release mini tablets entire formulations are analyzed for different post compression evaluation parameters.

The weight variation limits of immediate release mini tablets are<80mg,10% deviation may occurs and immediate release mini tablets all formulations was found 1.05-2.14, this results indicates acceptable range. The hardness test limits of immediate release mini tablets is 3-4 kg/cm^3 and all formulations of immediate release mini tablets was found within the range of 3.2-4.6 kg/cm^3, this outcomes shown within acceptable range. The thickness test specifications of immediate release mini tablets is 3-4 mm and all formulations of immediate release mini tablets was and found within the range of 3.82 to 3.96 mm, this results shows that within acceptable range. The disintegration of immediate release mini tablets is 3 minutes and all formulations of immediate release mini tablets was found within the range of 14-38 sec, this out comes shown with in satisfactory points of confinement. The friability of immediate release mini tablets is less than 1% and all formulations of immediate release mini tablets was found within 0.17-0.87. These results showed that all formulations passed the friability. The drug content of all formulations of immediate release mini tablets was found within the range of 92.73-98.62 %which shows good content uniformity range. From post compression parameters results of mini tablets, based upon the disintegration studies and percentage drug content F6 formulation containing croscramellose sodium was optimized and further placed in formaldehyde treated for colon targeting system. Based on hard gelatin capsule disintegration time in pH 1.2, pH 6.8 and pH 7.4 phosphate buffer, it indicates that 6 hours (M3) formaldehyde treated capsule was optimized capsule as the lag time of 5 hour maintained by 6 hour formaldehyde treatment is enough to carry the formulation to colon. The desired lag time for colon targeting is 5 hour and it's achieved in 6 hour treatment. Accordingly 5 immediate release mini tablets are set in hard gelatin capsule, 6 hour formaldehyde treated capsules are chosen as optimized treated capsules and 150 mg hydro gel plug was put at the opening of capsule body and closed with cap. In view of all above parameters, to design colon targeting system on frame work which has a maintain lag time of 5 hour. From the dissolution studies it was found that formulation (F8) containing 75mg of Ethyl cellulose 75mg of HPMC K100M shows 5 hour drug release minimum in upper GIT and maximum drug release in colon, in colon being kept in the system, it has shown maximum drug release for7 hour. The drug release kinetics for the optimized formulation F8 followed the zero order kinetics and follows super case II transport mechanism.

CONCLUSION

In conclusion, super disintegrates such as cross carmellose sodium and rate controlling polymer such as HPMC K 100 M and hydrophobic polymers such as ethyl cellulose can be successfully employed in utilized in the preparation of Mesalazine tablet in capsule system for targeting colon. In this better results are employed when use of combination of polymers. The research study explained more use full information for the formulation scientists on formulation, Characterization was done during development of CTDDS of Mesalazine using above polymers.

Table 1: Formulation of immediate release tablets

Ingredients	F1	F2	F3	F4	F5	F6
Drug	50	50	50	50	50	50
SSG	5	10	15	-	-	-
CCS	-	-	-	5	10	15
MCC	191	186	181	191	186	181
Mg. stearate	2	2	2	2	2	2
Talc	2	2	2	2	2	2
Total	250	250	250	250	250	250

Table 2: Formulation of hydrogel plug

Content of formulations	F7 (mg)	F8 (mg)	F9 (mg)	F10 (mg)
Ethyl cellulose	100	75	50	75
HPMC K100M	50	75	100	100

Table 3: Flow properties of powder blend

Formulation Code	Angle of Repose	Bulk density(g/ml)	Tapped Density (g/ml)	Carr's Index(%)	Hausner's ratio
F1	29.33	0.632	0.727	14.48	1.18
F2	25.45	0.646	0.716	12.56	1.15
F3	26.37	0.625	0.712	11.31	1.16
F4	30.26	0.624	0.725	15.44	1.17
F5	28.34	0.639	0.756	16.84	1.29
F6	27.71	0.643	0.734	13.83	1.18

Table 4: Post compression evaluations for immediate release mini tablets

F.C.	Weight variation (%)	Hardness (kg/cm3)	Thickness (mm)	Disintegration (Sec)	Friability (%)	Drug content (%)
F1	1.05	3.3	3.96	38	0.26	95.16
F2	1.34	3.3	3.87	29	0.41	96.43
F3	1.95	3.1	3.82	24	0.85	95.04
F4	2.14	3.4	3.86	35	0.17	98.13
F5	1.46	3.0	3.94	26	0.36	92.73
F6	1.18	3.1	3.89	14	0.21	98.62

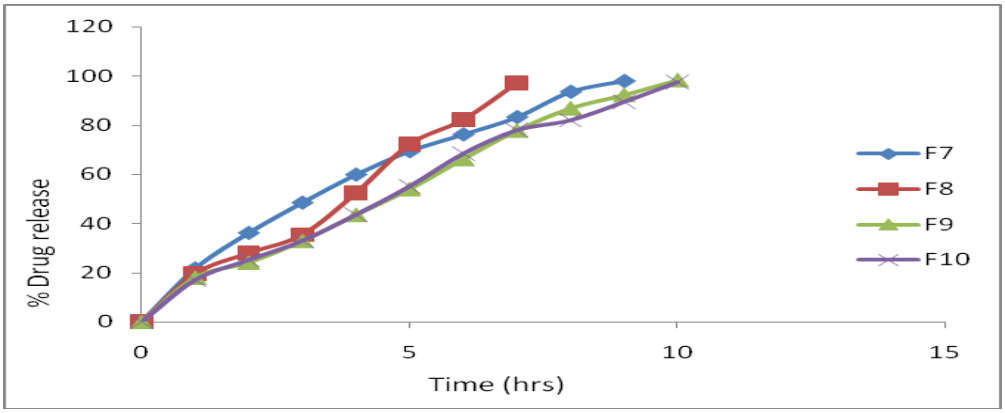

Fig. 1: *Invitro* dissolution data of formulations F7 to F10

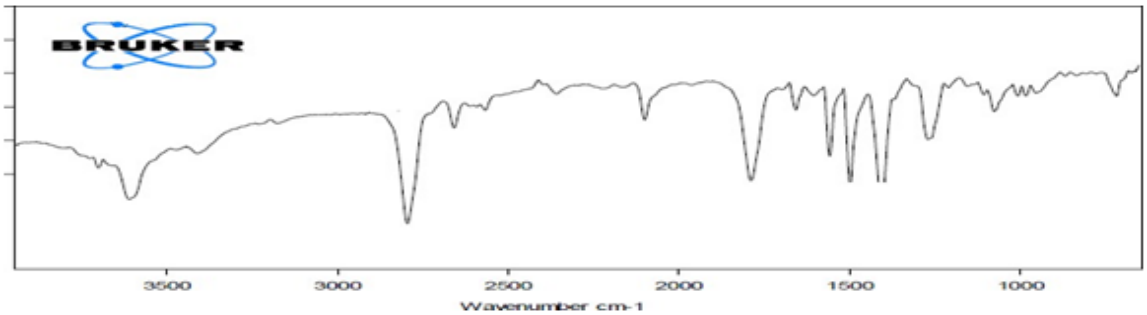

Fig. 2: FT-IR spectrum of Mesalazine

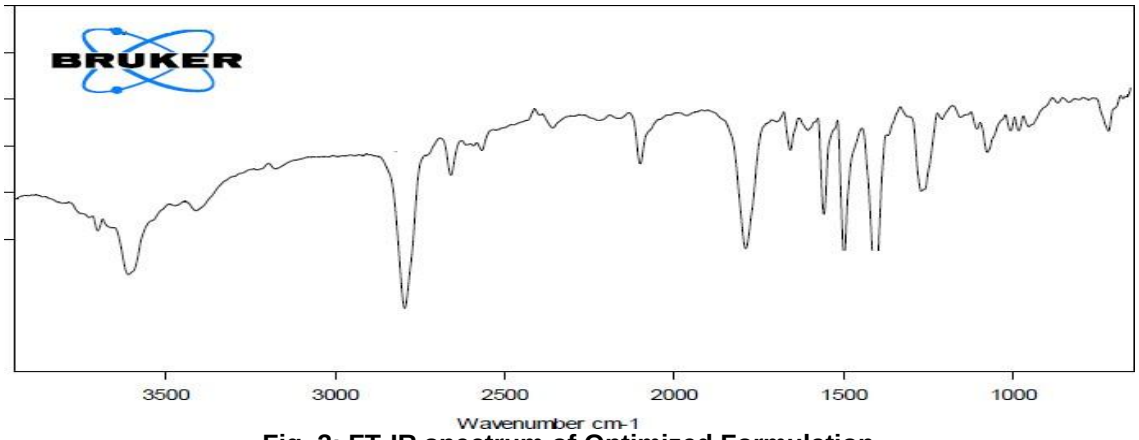

Fig. 3: FT-IR spectrum of Optimized Formulation

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