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Formulation and Evaluation of Gastro Resistant-Colon Targeted Drug Delivery System Containing Mesalazine Tablets

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Abstract: ***The formulation and evaluation of a gastro-resistant colon-targeted drug delivery system containing mesalazine tablets are explored in this study. Mesalazine, a medication used to treat inflammatory bowel diseases, requires targeted delivery to the colon to maximize therapeutic efficacy and minimizing the systemic side effects. To achieve this, a novel drug delivery system was developed to bypass the gastric degradation and a PH controlled drug release in the colon. The formulation involved the following steps such as formulation of mesalazine tablets by direct compression method, encapsulation of mesalazine with gastro-resistant coating using enteric coating agents Eudragit S-100 and Hydroxypropyl methylcellulose (HPMC) in various proportions thereby preventing tablets from stomach acid and enzyme degradation. The tablets were designed to release the drug in the colon, where it is needed most. The evaluation of this delivery system encompassed various parameters such as in vitro drug release studies, physicochemical characterization, and stability testing. The drug release kinetics was investigated under simulated physiological conditions to assess the targeted release profiles. Physicochemical properties of the tablets were analyzed to ensure the integrity of the formulation. Additionally, stability testing was conducted to assess the shelf-life and viability of the formulated tablets over time. The results demonstrated the successful formulation of mesalazine tablets with gastro-resistant colon-targeted drug delivery capabilities. The developed system exhibited controlled drug release patterns, ensuring sustained therapeutic levels of mesalazine in the colon. This approach has the potential to enhance treatment outcomes and minimize unwanted systemic effects associated with conventional delivery methods.***

Keywords: Colon targeted drug delivery system, mesalazine gastro resistant tablets, novel drug delivery systems, direct compression tablets

1. Introduction

The treatment of inflammatory bowel diseases (IBD), such as Crohn's disease and ulcerative colitis, often involves the use of drugs like mesalazine (5-aminosalicylic acid) to alleviate symptoms and induce remission. However, the effective drug delivery of mesalazine to the target site, the colon, while minimizing systemic exposure and associated side effects, remains a big challenge. Conventional oral drug formulations often result in premature drug release in the stomach or small intestine, undergoing degradation by gastric enzymes thereby leading to suboptimal therapeutic outcomes and potential adverse effects. To address these limitations, the formulation and evaluation of a novel gastro-resistant colon-targeted drug delivery system containing mesalazine tablets were explored in this research. The primary objective of this research work was to design a novel drug delivery system that could ensure the controlled and targeted release of mesalazine specifically within the colon, where its therapeutic action is most required, while bypassing the gastric acidic and enzymatic environment of the stomach. To achieve this, two coating agents, namely Eudragit S-100 and Hydroxy Propyl Methyl Cellulose (HPMC), were used in various proportions in the formulations. Eudragit S-100 is known for its pH-dependent solubility, while HPMC is recognized for its mucoadhesive properties and controlled drug release characteristics. By utilizing these coating agents in various propositions, it was hypothesized that the mesalazine tablets could remain intact in the stomach and releases the drug specifically in the colon. This research aims to contribute to the development of a novel targeted drug delivery system that enhances the therapeutic efficacy of mesalazine tablets while minimizing its potential side effects. The use of Eudragit S-100 and HPMC as coating agents in the formulations holds promise for achieving gastro-resistance and colon-specific targeted drug delivery. The study's objectives encompass the pre formulation studies, formulation process, physicochemical characterization, in vitro drug release studies under simulated physiological conditions, and stability studies of the various formulated tablets. The findings of this research could provide valuable insights into the design, development and optimization of gastro-resistant colon-targeted drug delivery systems, not only for mesalazine but also for other medications used in the treatment of gastrointestinal disorders. Ultimately, this research may pave the way for more effective and patient-friendly treatment approaches for individuals suffering from inflammatory bowel diseases.

2. Literature Survey

Neha Singh Raghuvanshi et al. (2014)23 Formulated and evaluated matrix tablets of Prednisolone by wet granulation method using different proportions of Sterculia gum with Carbopol 934P and Sterculia gum with ethyl cellulose in 1:1, 1:5 and 1:2 ratio and coated with Eudragit S100. All preparations were tested for their properties before and after compression and for their in vitro dissolution in different pH buffers (0.1N HCL, pH 7.4 and pH 6.8) to simulate the conditions of GIT. All parameters were within the limits. Formulation F4 had 85.46 % after 12 hours and proved to be the best formulation.

Sumit Kumar et al (2012)24 developed naproxen tablets with targeted matrix for colon to prolong release for sustained effect. Different formulations (MT1 TO MT3) were prepared using different polymers and their varying proportions (guar gum, Xanthan gum) using wet granulation techniques. The matrix tablets prepared were evaluated for their pre-compression parameters, physical properties such as hardness, friability, uniformity of weight, uniformity of drug content and in vitro drug release. All parameters were within the limits. From this study, batch MT3 released 77.99% more active ingredient than the other batches. Batch MT3 showed maximum extended release up to 12 hours and was found to be the best formulation.

Sharma Madhu et al., (2012)25 Formulated and evaluated the sustained delayed release tablets of Mesalazine. The time and pH dependent drug delivery system, reduce the frequency of dose administration, to prevent ulcerative colitis by developing sustained delayed release tablets of Mesalazine using combination of Eudragit S-100 as colon target enteric coating. The core tablets of Mesalazine were prepared using wet granulation containing a super disintegrant. The aim of study was to develop colon specific drug delivery of Mesalazine sustained release matrix tablets for ulcerative colitis using HPMC as a semi synthetic polymer. Effect of polymer concentration and super disintegrant level was also investigated. The matrix tablets of Mesalazine are subjected to an in-vitro drug release study using simulated gastric fluid (0.1N HCl) for 2 hours, simulated intestinal fluid (pH 7.4) for 3 hours and simulated colonic fluid (pH 6.8) for 7 hours as dissolution fluid. The study showed that, lag time prior to drug release was highly affected by the coating. Colon drug delivery is advantageous in treatment of colonic disease and oral delivery of drugs that are unstable and susceptible to enzymatic degradation in upper GI tract. The disintegration data obtained from tablets demonstrated that disintegration data rate of studied tablets is dependent on: (i) The polymer used to coat the tablets (ii) pH of disintegration media. Results also demonstrated that combination of Eudragit S-100 and L-100 can be successfully used to coat tablets for colon targeted delivery of drug. Tablets were evaluated in terms of their pre-compression parameters, physical characteristics like hardness, friability, uniformity of weight, uniformity of drug content and in-vitro drug release. All the parameters were found to be within the limits. Formulation F4 showed 90.25% at the end of 12 hrs and emerged as best formulation.

R. Prashanthi et al., (2014)26 Developed the controlled release matrix tablets of Flurbiprofen by selecting different polymers like HPMC K100, Sodium Carboxy Methyl Cellulose, Xanthan gum and Guar gum. All the formulations were prepared by direct compression method using 12mm punch on 8 station rotary tablet punching machine. The blend of all the formulations showed good flow properties such as angle of repose, bulk density, tapped density. The prepared tablets were showed good post compression parameters and they passed all the quality control evaluation parameters as per I.P limits. Among all the formulations F12 formulation that is with Guar Gum showed maximum percentage drug release 99.18 % in 12 hours

Lone Krishnakumar Devrao et al., (2012)27 Formulated and Evaluated the Matrix Tablet of Mesalazine with Hydroxypropylmethylcellulose Phthalate. In this study slow released matrix tablets of Mesalazine were prepared using pH sensitive polymer HPMC-P with six concentrations by wet granulation method. The granules were evaluated for angle of repose, bulk density, tapped density, compressibility index and Hausner's ratio. The tablets were subjected to weight variation, hardness, friability and drug content test. Invitro release studies revealed that only one formulation, P3 qualified the first stage of release while all the formulations qualified the second stage of drug release except P4 which deviated slightly. The release profiles were affected by variable concentration of matrix forming polymer and hence, the release of Mesalazine retarded with increase in proportion of HPMC-P. As HPMC-P is a pH sensitive polymer with threshold value 5.8 because of this effectively prevented the escape of drug at acid stage but allowed considerable amounts to be released in buffer stage I. The prepared tablets were evaluated in terms of their pre-compression parameters, physical characteristics like hardness, friability, uniformity of weight, uniformity of drug content and in-vitro drug release. All the parameters were found to be within the limits. Formulation P6 showed 99.32% at the end of 12 hrs and emerged as best formulation.

Rajeswari P. et al., (2016)28 Developed colon targeted drug delivery system by using Chitosan as a carrier for Mesalazine. Matrix tablets containing various excipients and Chitosan were prepared by wet granulation technique using different binder systems. The prepared tablets were evaluated for Hardness, Weight variation, Drug uniformity, Friability and In-vitro Drug release study. All the parameters were found to be within the limits. The final product is expected to have the advantage of being biodegradable and pH dependant. The matrix tablet containing Chitosan as a carrier and xanthum gum as binder was found to be suitable for targeting mesalazine for local action in the colon as compare to other matrix tablets containing different binders. Matrix tablets containing Chitosan released 99.99% of mesalazine in simulated colonic fluid. The stability study for prepared tablets at 40°C/75% relative humidity for three months showed no significant change in In-vitro drug release pattern. The results of in-vitro study indicate that matrix tablets containing Chitosan as carrier and xanthum gum as binder are most suitable to deliver the drug specifically in colonic region. The final formulation of mesalazine for colon-specific drug delivery gives pH, time

and enzyme controlled release. Formulation F6 showed 99.29% at the end of 24 hrs and emerged as best formulation.

Prasanta kumar Choudhury' et al., (2012)29 Developed the matrix tablets of Ornidazole were prepared by wet granulation method using matrix forming natural polymers like Guar gum and Xanthan gum in combination with different proportions. The further effect of enteric coat on the matrix tablets for colon specific drug release was investigated. The Ornidazole optimized matrix formulation OM1 showed drug release around 32.37±0.33% in 2 hrs. So it was further enteric coated with 5% Eudragit S100 and coded as OME1 which showed 44.09±0.16% of drug release after 12 hrs. All formulations were subjected to Hardness test, Friability test, determination of uniform diameter and thickness, drug content for optimization and further evaluation. In-vitro dissolution studies indicated that the drug release in upper part of GIT from matrix tablets of Ornidazole can be prevented by enteric coating with pH sensitive polymer (Eudragit®S100), which releases the drug specifically in colonic region to achieve target delivery. All the parameters were found to be within the limits. Formulation OME1 showed 44.09% of drug release at the end of 12 hrs and emerged as best formulation.

Basavaraja et al., (2015)30 Formulated and evaluated the sustained release matrix tablets of Flurbiprofen. By using the natural and synthetic polymers. Flurbiprofen is NSAID drug used extensively in the treatment of rheumatoid arthritis, degenerative joint disease, osteoarthritis, Ankylosing Spondylitis, acute musculoskeletal disorders, low back pain and allied conditions. The natural polymers are Xanthan gum, Karaya gum, and synthetic polymers like HPMC K-100, Ethyl cellulose were utilized in the formulation of matrix tablets containing Flurbiprofen by wet granulation technique and evaluated for its in-vitro drug release. All the formulations showed compliance with Pharmacopeia standards. Among all the formulation, F12 showed 97.23% of drug which was better controlled release at the end of 12 hrs. It has been found that the optimized formulation F-12 containing 500 mg of ethyl cellulose better sustained effect for 12 hrs and emerged as best formulation.

B. Manjula et al., (2016) 31 Formulated and evaluated the colon specific tablets of Ornidazole tablets were successfully prepared using enteric coated polymers Eudragit, guar gum and HPMC k15m study of the pre-formulation characteristics and FTIR studies indicates that there was no interaction between Ornidazole and excipients used in the formulation. In-vitro release profiles of optimized form of F7 were found to show delayed release pattern in a much customized manner which was very much required for the colon specific drug delivery. In-vitro release profiles of optimized formulation of Ornidazole controlled release tablets (F-7) were found to be improvised and followed zero-order kinetics, hence the release of the drug from the dosage form was independent of concentration and followed Higuchi model, and hence release of drug from press coated tablet was by diffusion mechanism. The drug delivery system was designed to deliver the drug at such a time when it was needed nocturnal time. Formulation F7 showed 75.98% of drug release at the end of 10 hrs and emerged as best formulation.

L. Matsyagiri et al., (2014)32 Formulated and evaluated the colon specific drug release of Albendazole with the purpose of developing a release of drug at colon region for local action, which is very convenient for administration, without the problem of enzymatic degradation and effect of pH of upper part of GIT like stomach and small intestine. Colon specific matrix tablets of Albendazole were prepared using guar gum, xanthenes gum and HPMC polymers as matrix. FTIR showed that there is no interaction between drug and excipients. In-vitro dissolution of prepared matrix tablets of Albendazole performed by using USP type II apparatus in pH 0.1N first 2 hrs and remaining three hours in phosphate buffer pH 7.4 phosphate buffer solutions. It is concluded that colon specific drug release of Albendazole give all satisfactory results for formulation F1-F9. Formulation F7 showed 87.02% of drug release at the end of 12 hrs and emerged as best formulation.

Patel Jayvadan K et al., (2009)33 Developed the colon targeted drug delivery system by using Chitosan as a carrier for Mesalazine. Matrix tablets containing various excipients and Chitosan were prepared by wet granulation technique using different binder systems. The surface of the device of best formulation was coated with Eudragit S100 to ensure that the device was more pH dependent and trigger the drug release only at higher pH. Matrix tablets containing Chitosan released 97- 99% of mesalazine in simulated colonic fluid. The stability study for prepared tablets at 40oC/75% relative humidity for three months showed no significant change in In-vitro drug release pattern. The final formulation of mesalazine for colon specific drug delivery gives pH, time and enzyme controlled release. All the parameters were found to be within the limits. Formulation F9 showed 90.25% at the end of 12 hrs and emerged as best formulation.

Sam T Mathew et al., (2016)34 Formulated and evaluated the matrix tablets of Albendazole containing various proportions (20%, 25%, 30% and 35%) of guar gum, Xanthan gum and dextrin were prepared by direct compression technique using 10 mm concave punch. The prepared tablets were evaluated for hardness, friability, weight variation, drug content uniformity and were subjected to in-vitro drug release with and without rat caecal content (4% w / v). All formulations (F1 - F12) which shows restricted drug release in stomach and small intestine and which shows more release in colonic environment. The drug release was independent of its concentration and the mechanism of drug release followed by super case-II transport. The accelerated stability studies revealed that there was no significant change in the colour, shape and drug content. The formulation (F9) is most suitable to target colon without being released significantly in the stomach and small intestine, and also it may avoid systemic side effects in the gastrointestinal tract. All the parameters were found to be within the limits. Formulation F9 showed 94.25% at the end of 12 hrs and emerged as best formulation.

Dr. T. Satyanarayana et al., (2017)35 Formulated and Evaluated the Mesalazine colon targeted matrix tablets was

done by using various polymers. To achieve pH independent drug release of Mesalazine, pH modifying agents (buffering agents) were used. Colon targeted tablets were prepared in two steps. Initially core tablets were prepared and then the tablets were coated by using different pH dependent polymers. Ethyl cellulose and Eudragit S100 were used as enteric coating polymers. The tablets were passed all the tests. Among all the formulations F7 formulation was found to be optimized as it was retarded the drug release up to 12 hours and showed maximum of 97.87% drug release. It followed first order kinetics mechanism. Stability studies was Performed no chemical changes was occurred.

Chourey N et al 202236 manufactured the matrix tablets using the direct compression process, which is now considered a cost-effective and simple manufacturing process. The tablets were coated with different concentrations of the polymer Eudragit S100 using an immersion process. All formulations were subjected to stability tests according to the recommendations of ICH. The tablets coated with Eudragit S100 (20 per cent w/v) had a sustained release of 78.39 per cent over 12 hours, while the uncoated tablets released the drug after 9 hours. Stability testing of the tablets showed that there was less degradation with accelerated storage and storage at room temperature over a 6-month period. In the colon, the mesalazine matrix tablets coated with Eudragit S100 showed promising site-specific drug release.

Sanaz Mehdi-alamdarlou et al 202237 formulated a system for the controlled release of mesalazine, an anti-inflammatory agent, by fluidized bed coating. The formulation was prepared using hydroxyl propyl methyl cellulose (HPMC) for sustained release and cellulose acetate phthalate for enteric coating. The prepared granules were evaluated for particle size, moisture content, friability and dissolution test. The granules prepared by wet granulation had suitable size and free flowability with Carr's Index less than 20. It was concluded that the prepared granules could be successfully formulated using release retarding polymers. The formulation showed adequate release retardation of the drug, indicating the potential of a delivery system. For a better evaluation of the formulation, further studies such as the preparation of the capsules and the study of the bacterial count are required.

3. Materials and Methodology

3.1 Materials

The following are the materials used in this research; Mesalazine: Active pharmaceutical ingredient (API) used in the formulation, Microcrystalline Cellulose (MCC): Binder and filler for tablet formulation, Lactose: Diluent and filler for tablet formulation, Eudragit S-100: pH-dependent polymer for gastro-resistant coating, Hydroxypropyl Methylcellulose (HPMC): Polymer with controlled release and mucoadhesive properties, Talc: Lubricant for tablet compression, Magnesium Stearate: Lubricant for tablet compression. Isopropyl Alcohol: Solvent for coating solution preparation, Purified Water: Solvent for coating solution preparation, Simulated Gastric Fluid (SGF): Medium for in vitro dissolution studies, Simulated Intestinal Fluid (SIF): Medium for in vitro dissolution studies, Phosphate Buffer Solution (PBS): Medium for in vitro dissolution studies, Disintegration Tester: Equipment to test tablet disintegration time, Dissolution Apparatus: Equipment for in vitro dissolution studies, UV-Vis Spectrophotometer: Instrument for drug content analysis.

3.2 Methodology

The methodology is to develop six (6) experimental formulations F1, F2, F3, F4, F5 and F6 of mesalazine tablets containing various proportions of enteric coating agents Eudragit S 100 and HPMC and evaluate the various formulations for pre and post formulation studies evaluating the various physical properties, efficacy, and stability of mesalazine Tablets. The following are the stages of development of formulations

a) Formulation of Mesalazine Tablets: MCC, lactose, and mesalazine were mixed in a dry state. The blend was granulated using a suitable binder. The granules were dried and sieved to obtain a uniform particle size. Lubricants were added to the blend, and tablets were compressed using a tablet press.
b) Preparation of Coating Solutions: Eudragit S-100 and HPMC were separately dissolved in isopropyl alcohol in varying proportions and purified water, respectively. The resulting solutions were mixed to achieve the desired coating properties.
c) Coating of Tablets: The mesalazine tablets were coated with Eudragit S-100, followed by a coat of HPMC.

Table 1: Quantity of Ingredients in various mesalazine tablet formulations

S. No.	Ingredients	Quantity of Ingredients (mg/tab)					
		F1	F2	F3	F4	F5	F6
1	Mesalazine	200	200	200	200	200	200
2	Eudragit S-100	80	60	50	35	20	10
3	Hydroxypropyl methylcellulose (HPMC)	60	55	40	25	15	14
4	Lactose	50	75	100	130	154	165
5	Talc	5	5	5	5	5	5
6	Magnesium stearate	5	5	5	5	6	6
Total weight (mg)		**400**	**400**	**400**	**400**	**400**	**400**

d) Characterization Studies: Tablets were evaluated for physical parameters like hardness, thickness, weight variation, and disintegration time. Drug content analysis was performed using a UV-Vis spectrophotometer. In vitro dissolution studies were conducted using dissolution apparatus in SGF, SIF, and PBS.
e) Stability Testing: Coated tablets were subjected to stability testing under controlled conditions of

temperature and humidity. Drug content and dissolution profiles were monitored over time.

f) Data Analysis: Physical parameters, drug content, and dissolution data were analyzed statistically to assess the formulation's performance.

The experimental setup and methods were designed to evaluate the effectiveness of the gastro-resistant colon-targeted drug delivery system containing mesalazine tablets. The chosen materials and techniques aimed to achieve controlled drug release in the colon while maintaining gastro-resistance, with the ultimate goal of enhancing therapeutic outcomes and patient compliance in the treatment of inflammatory bowel diseases.

4. Results and Discussion

4.1 Pre-formulation Studies:

Before proceeding with tablet formulation, a series of pre-formulation studies were conducted to assess the compatibility of mesalazine (Evaluation of API) with excipients, establish optimal drug-excipient ratios, and evaluate the physicochemical properties of the drug substance. Preformulation studies includes the following evaluations

a) Background – Compound chemical name, chemical structure, solvent of recrystallization, purity, therapeutic category.
b) Organoleptic properties – Appearance, colour and odour.
c) Microscopic examination – Crystal habit, crystal shape and size.
d) Physical properties – Density, particle size, surface area, flow properties, hygroscopicity.
e) Solvent properties – pH of solution, solubility and dissolution rate, drug excipient compatibility study.
f) Other properties – Melting point, Loss on drying, Powder compressibility, Chemical compatibility studies by FT-IR

Table 2: Evaluation of mesalazine (API) - physical characteristics of API

S. No	Tests	Results
1	Colour	Pink powder
2	Solubility	Complies
3	Melting point	76.4°C
4	Moisture content	0.3% w/w

Discussion: The colour, solubility, melting point and moisture content of the API were evaluated. It was found to be within the range of the monograph.

Table 3: Angle of repose of mesalazine

S. No	Raw material (API)	Angle of repose (Degree)	Average
1	Mesalazine	$32^0.14'$	$32^0.52' \pm 0.69$
2	Mesalazine	$32^0.32'$	
3	Mesalazine	$33^0.12'$	

Discussion: The angle of repose of mesalazine API was found to be $38^0.56' \pm 0.69$. Hence the drug belongs to fair flow and requires glidants to improve the flow property.

Table 4: Bulk density and tapped density of mesalazine

S. No	Raw Material (API)	Bulk density (g/ml)	Average bulk density (g/ml)	Tapped density (g/ml)	Average tapped density (g/ml)
1	Mesalazine	0.428	0.438 ± 0.01	0.516	0.516± 0.003
2	Mesalazine	0.442		0.514	
3	Mesalazine	0.445		0.518	

Discussion: The average bulk density and tapped density was found to be 0.453 ± 0.01 and 0.614± 0.003 g/ml respectively.

Table 5: Powder compressibility and Hausner's ratio compressibility index and Hausner's ratio

Raw material (API)	Compressibility index (%)	Hausner's ratio
MESALAZINE	15.116	1.17

Discussion: Based on Compressibility index and Hausner's ratio, it indicates the mesalazine (API) belongs to poor flow property.

Table 6: Particle size distribution of mesalazine

Sieve no	Empty weight of sieve	Quantity retained (gm)	Mass retained (gm)	Cumulative mass retained (gm)	Cumulative % retained	Percentage passing %
#20	367.8	368.55	0.75	0.75	4.34	95.66
#30	417.65	417.85	0.2	0.95	5.5	94.5
#40	358.05	365.65	7.6	8.55	49.56	50.44
#60	343.45	343.65	0.2	8.75	50.72	49.28
#80	340.75	340.9	0.15	8.9	51.59	48.41
#100	332.5	332.85	0.35	9.25	53.62	46.38
Base	540.45	548.45	8	17.25	100	0

Discussion: From the particle size analysis it was concluded that the particles size of the mesalazine API was found to be moderately coarse powder.

Table 7: Drug - excipients compatibility studies:

S. No	Composition	Initial	After 15days	After 30days	Conclusion
1	MESALAZINE	Pink	NCC	NCC	Complies
2	MESALAZINE + Excipients	Pink	NCC	NCC	Complies

NCC - No Characteristic Change

Discussion:

From the drug excipients compatibility study, it was observed that there was no characteristic change or interaction between drug and excipients. Thus it was concluded that the excipients selected for the formulation were compatible with Mesalazine.

IR Spectral Analysis

The FTIR studies of Mesalazine and MESALAZINE with Excipients. The results are shown in Table No: 8 and Figure No: 1 and 2.

Table 8: FT-IR spectral values of pure mesalazine

S. No.	Functional Group	Peaks observed
1	C=C stretch of the aromatic group N-H bond Scissoring	1621.24
2	C-H stretch of the aromatic group	2976.52
3	C-C stretching mode	1487.79
4	O-H deformation of the hydroxyl group	1582, 1487, 1450
5	C-O stretching mode	1194.91
6	In plane bending mode	1192.24 - 1265.96
7	C-H bond out of plane bending mode: Ring deformation of the aromatic group	685.01

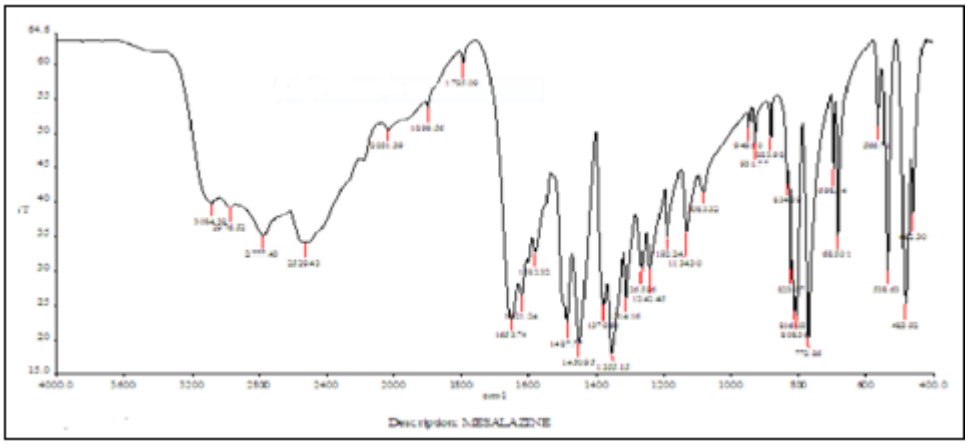

Figure 1: FT-IR Spectra of Pure Mesalazine

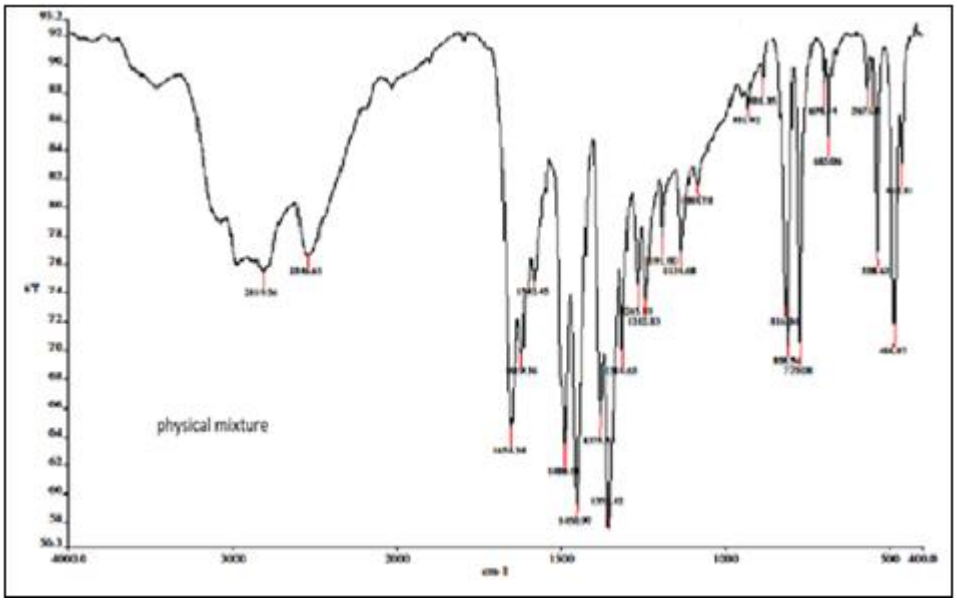

Figure 2: FT-IR Spectra of Mesalazine with Excipients

4.2 Post-formulation Studies

a) Physical Characteristics of Tablets:
The physical parameters of the formulated tablets using direct compression method such as hardness, thickness, weight variation, and disintegration time, were evaluated. The matrix tablets formulated exhibited consistent and acceptable physical characteristics across all formulations. The disintegration time was notably extended compared to uncoated tablets, indicating the effectiveness of the coating layers in preventing premature drug release.

b) Drug Content Analysis:
The drug content analysis revealed that all formulations had drug content within the acceptable range, demonstrating uniform drug distribution during tablet manufacturing.

c) In vitro Dissolution Studies:
The in vitro dissolution profiles of the coated mesalazine tablets were investigated using simulated gastric fluid (SGF), simulated intestinal fluid (SIF), and phosphate buffer solution (PBS) to mimic different gastrointestinal conditions. The formulation containing a combination of Eudragit S-100 and HPMC at varying proportions demonstrated a controlled and pH-dependent drug release pattern. In SGF, the tablets exhibited minimal drug release, confirming the gastro-resistant nature of the coating. As the tablets moved into the simulated intestinal environment (SIF and PBS), the drug release increased gradually due to the pH-dependent solubility of Eudragit S-100. The presence of HPMC further contributed to sustained drug release, possibly through its mucoadhesive properties.

d) Influence of Coating Composition:
The proportion of Eudragit S-100 and HPMC in the coating composition significantly affected the drug release profiles. Increasing the proportion of Eudragit S-100 led to a more pronounced pH-dependent drug release, while higher proportions of HPMC contributed to sustained and controlled release kinetics. This suggests that a fine-tuned balance between the two polymers could yield the desired colon-targeted drug release behavior.

e) Stability Studies:
Stability studies over a defined period showed that the coated tablets maintained their physical integrity, drug content, and controlled release profiles. This indicates that the formulated gastro-resistant colon-targeted drug delivery system could withstand storage conditions without compromising its functionality.

5. Conclusion

The formulation and evaluation of gastro-resistant colon-targeted drug delivery systems containing mesalazine tablets were successful. The combined use of Eudragit S-100 and HPMC as coating agents allowed for pH-dependent and controlled drug release in the colon. The varying proportions of these polymers, along with the addition of HPMC, enabled customization of drug release kinetics. The developed system holds promise for optimizing mesalazine therapy in inflammatory bowel diseases by enhancing drug efficacy and minimizing systemic side effects. From among the entire batches, formulation F6 showed 97.21% drug release at 24 hrs. Since it provide greater protection to the core under acidic condition while at the same time show the fastest drug release under intestinal pH. So the formulation F6 was considered as best formulation. From the results obtained, it can be concluded that formulation F6 containing coated matrix tablet of Mesalazine would be a promising formulation to achieve the purpose which treat inflammatory bowel diseases (ulcerative colitis) without any gastric irritation or ulcers, which is useful for patients having pre history of ulcerative colitis. Further studies could delve into the in vivo performance of these formulations to validate their clinical potential.

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