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Development, Optimization and Evaluation of Mesalamine and Curcumin Loaded Microparticles for the Treatment of Ulcerative Colitis

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ABSTRACT

The present study aimed to develop and optimize microparticles containing mesalamine and curcumin for targeted treatment of ulcerative colitis. Eudragit S100 and Eudragit RS100 were employed as dual polymers to achieve both pH-dependent and sustained drug release specifically in the colon. The formulation was designed to deliver a low dose of mesalamine along with curcumin as a complementary adjuvant to improve the formulation stability. Microparticles were prepared using the double emulsion solvent evaporation technique, and the formulation process was statistically optimized through a Box–Behnken design, considering polymer ratio, coating strength, and surfactant concentration as key independent variables. The optimized formulation demonstrated uniform particle size distribution, high entrapment efficiency, and optimum drug loading of mesalamine along with curcumin within the polymeric matrix. Differential Scanning Calorimetry (DSC) analysis confirmed the molecular dispersion of the drug in the polymer system, indicating successful encapsulation and partial amorphization. The *in vitro* drug release of mesalamine demonstrated a sustained and controlled release over 8 hours, ensuring colonic delivery while minimizing premature gastric release following Korsmeyer-peppas model, indicating diffusion controlled non-fickian release and polymeric erosion. Stability testing under accelerated conditions confirmed that MCMP 14 retained its physicochemical integrity and release characteristics. The optimized microparticles provided controlled, pH-dependent and localized drug delivery in the colon. The inclusion of curcumin offered antioxidant property, making the formulation more effective for ulcerative colitis.

KEY-WORDS: Mesalamine, Curcumin, Microparticles, Colon-specific drug delivery, Ulcerative colitis, Box–Behnken Design.

INTRODUCTION

Inflammatory bowel disease (IBD), primarily comprising Crohn's disease and ulcerative colitis (UC), is characterized by chronic and idiopathic inflammatory responses, predominantly affecting the ileum, rectum, and colon. The disease is marked by the recruitment and infiltration of immune cells, secretion of pro-inflammatory cytokines, and accumulation of reactive oxygen species (ROS), leading to tissue damage and ulceration that characterizes UC. Increasing evidence points to oxidative stress and inflammatory stimuli as pivotal in triggering UC[1]. Ulcerative colitis (UC), one of the two forms of IBD, is a chronic inflammatory condition that affects millions of people around the world. Therefore, UC persists throughout the patient's whole life, with the clinical course being characterized by alternating periods of exacerbation and remission. The affected regions are the mucosa and submucosa, mainly in the colon and rectum. The etiology and pathogenesis of IBD are not fully understood, however considerable progress is constantly being made in this direction[2].

Microparticles are referred to approximately spherical particle in the range of 1–1000 μm enclosing a bioactive substance inside a semi-permeable polymeric membrane. The size particle in a few millimeters is included. Terms as microbeads, microspheres, microcapsules and micropellets are used according size, form and distribution of bioactive agent[3].

Microparticles drug delivery system has been gaining an immense importance for local targeting of drug to colon at a controlled and sustained rate. Combined approaches such as pH dependent and time dependent system provide the maximum release of drug into colon via oral route[3].

Mesalamine (5-aminosalicylic acid) is the first line therapy of Inflammatory Bowel Disease, often accompanied by various adjunct therapies such as corticosteroids and anti-inflammatory drugs. The exact mechanism of mesalamine is unknown so far, however, it is acknowledged widely that mesalamine targets *cyclo*-oxygenase and lipo-oxygenase pathways to reduce the biosynthesis of prostaglandins and leukotrienes which are chief mediators of inflammation[4].

The medicine of choice for treating moderate to severe UC continues to be mesalamine (5-amino salicylic acid (5-ASA)). Both oral and rectal mesalamine seem to be more beneficial than either alone in treating severe or distal colitis. The active ingredient is mesalamine (5-aminosalicylic acid), and it is used to treat inflammatory bowel illnesses including Crohn's disease and ulcerative colitis. After a few minutes of oral administration, approximately all of the Mesalazine will have been absorbed in the small intestine. Hence, only a tiny fraction of the medicine from quick release dosage forms reaches the target areas of the lower GI tract: the ileac and colonic mucosa[5].

Turmeric (*Curcuma longa* Linn), a member of the Zingiberaceae family, is widely cultivated in tropical and subtropical regions, especially in India and Southeast Asia, where it has long been used as both a spice and traditional medicine. Its major bioactive constituents, known as curcuminoids primarily curcumin (CUR), demethoxycurcumin (DMC), and bisdemethoxycurcumin (BDMC) are responsible for its therapeutic potential. Among them, curcumin exhibits potent anti-inflammatory, antioxidant, anti-microbial, and anti-proliferative properties. It modulates multiple molecular targets, including NF-κB, COX-2, and TNF-α, thereby effectively reducing inflammation and oxidative stress. In UC, a chronic inflammatory bowel disease, functional excipient to provide antioxidant stabilization for mesalamine loaded microparticles[6, 37].

Based on the current literature and formulation challenges, this study aimed to develop a low-dose mesalamine oral solid dosage form with curcumin as a complementary adjuvant. Literature reports suggest that combining curcumin with mesalamine can give supporting benefits to stable the drug from oxidative effects in inflammatory bowel diseases like ulcerative colitis. Therefore, microparticles were designed to deliver a reduced dose of mesalamine along with utilization of complementary adjuvant directly to the colon. pH-sensitive polymers (Eudragit S100/RS100) were used to protect the drug from premature release in the stomach and ensure controlled, sustained release in the colon. The formulation was systematically optimized and characterized for particle size, surface morphology, drug entrapment, release behavior, and *in-vitro* dissolution under sequential gastrointestinal pH, and *in-vitro* cytotoxicity to improve local therapeutic effects.

MATERIALS AND METHOD

Materials

The pure drug Mesalamine and Curcumin was bought from Dhamtec Pharmaceuticals, Mumbai and Olive Lifesciences, Bangalore. Eudragit S 100 and Eudragit RS 100 were obtained from Yarrow Chemical Products Mumbai. Polyvinyl Alcohol (PVA) was supplied by Himedia Pharmaceutical Limited, Mumbai and Dichloromethane was purchased from Merck Specialities Pvt Ltd, India. Buffers and solutions were prepared with millipore water obtained from Direct-Q3® with Pump, Made in France and all the other chemicals/reagents were in analytical grade.

Method of Preparation

The mesalamine and curcumin-loaded microparticles were prepared by the double emulsion solvent evaporation method. Briefly, mesalamine was dissolved in distilled water (W1 phase), while curcumin was dispersed in a solution of Eudragit S100 and RS100 dissolved in dichloromethane (O phase). The W1 phase was then emulsified into the O phase using a high-speed homogenizer (10,000 rpm for 3–5 min) to form a primary emulsion. This emulsion was subsequently added dropwise into an external aqueous phase (W2) containing 1% w/v PVA under continuous magnetic stirring (1000 rpm) to form a double emulsion. The mixture was stirred at room temperature for 3–4 h to allow complete solvent evaporation. The formed microparticles were separated by centrifugation at 8000 rpm for 15 min, washed repeatedly with distilled water to remove excess PVA and unbound drug, and dried at room temperature to yield the final microparticles[7-8].

Optimization: Design of experiment

The optimization of the Mesalamine and curcumin loaded microparticles formulation was carried out

using a Design of Experiment (DOE) approach based on Box-Behnken Design[23] by using Design Expert software version. Box- Behnken Design was performed with 3 independent variables i.e. Polymer Ratio, Polymer coating strength and surfactant concentration. The ultimate goal of DOE was to optimize the critical process parameters to achieve Entrapment Efficiency (%), Drug release 0.1N HCl, Drug release 7.4 pH. A total of thirteen experimental runs were conducted to obtain an optimum formula. The collected data were analyzed by analysis of variance (ANOVA) to evaluate model significance and to identify the most influential parameters. Three-dimensional response surface plots and contour plots were constructed to visualize the effects of the formulation variables on the responses[23].

EVALUATION AND CHARACTERIZATION

Compatibility studies

FTIR analysis was employed to examine the compatibility of the drug and excipients in a physical mixture(1:1). The physical mixture in the ratio1:1 was divided into two samples, while one sample was subjected to FTIR analysis immediately the other sample was stored for one month in the hot air oven at 40ºC before subjecting to FTIR analysis. Before testing, the sample chamber was filled with nitrogen gas and dry desiccant to eliminate any moisture content presence. The sample pellets were made by using a dry KBr (IR grade) system of approximately 10-15 percent. Powder were ground in a small- sized mortar and pestle until the powder blend was fine and even for the background and correction of the baseline pure KBr powder was used. Samples were inserted in to the sample compartment. A spectrophotometer was used to scan samples in the 4000 – 400 cm^{-1} region[28].

pH Determination

The pH of microparticles was determined by dispersing an accurately weighed amount of microparticles in 10 mL of distilled water. The dispersion was kept stirring for at room temperature (25 ± 2 °C) . The pH of the dilution was measured using a Digital pH Meter (pre-calibrated with standard buffers)[9].

Production yield

The total amount of drug and polymer used for the preparation of microparticles was accurately weighed. After drying, the total weight of the obtained microparticles was recorded; percentage (w/w) was determined [34].

Entrapment efficiency

sample of microparticles were accurately weighed and dispersed in 10 mL of phosphate buffer (pH 7.4). The mixture was sonicated for 15 min and centrifuged at 2500 rpm for 10 min. The clear supernatant was collected and filtered through Whatman filter paper (No. 1).The absorbance of the filtrate was measured using a UV–Visible spectrophotometer (Shimadzu UV-1700)[34].

In vitro dissolution studies

The *in-vitro* dissolution study of microparticles was carried out using the USP Type II (Paddle) dissolution apparatus. 100mg of Microparticles(equivalent to 41.1mg) were weighed and dispersed in 900 mL of dissolution medium, maintained at 37 ± 0.5 °C with a paddle speed of 100 rpm. The study was performed in buffer 1.2 pH (simulate gastric pH) for 2 hours continuing with phosphate buffer pH 7.4 till 8 hours to simulate colonic pH. At predetermined intervals (0, 1, 2, 3, 4,5,7,6 and 8 h), 5 mL samples were withdrawn and replaced with an equal volume of fresh medium maintaining sink condition. The withdrawn samples were filtered through Whatman filter paper (0.45 µm), and the absorbance was measured at 331 nm using a UV–Visible spectrophotometer (Shimadzu UV-1700)[27].

Kinetics of drug release

Model dependent methods are useful for characterizing drug release profiles. In this study-Zero order, First order, Higuchi and Korsmeyer-Peppas models were employed to evaluate the drug release behaviour of mesalamine and curcumin loaded microparticles formulation.

Drug content

sample of microparticles were weighed and dissolved in 10mL phosphate buffer solution pH 7.4, after suitable dilution, the absorbance of the dilution was measured at 337 nm by using Shimadzu UV-1700 spectrophotomete[27].

In-vitro Cytotoxicity Studies

Maintenance of cell lines

The Raw 264.7 (Murine macrophage cell line) was purchased from NCCS, Pune, India. The cells were maintained in DMEM high glucose media supplemented with 10 % FBS along with the 1% antibiotic-antimycotic solution in the atmosphere of 5% CO_2, 18-20% O_2 at 37^0C temperature in the CO_2 incubator and sub-cultured for every 2 days. Passage number-45 was used for the current study[48].

Cell viability and proliferation studies: MTT assay

MTT assay is a colorimetric assay used for the determination of cell proliferation and cytotoxicity, based on reduction of the yellow colored water soluble tetrazolium dye MTT to formazan crystals. The cytotoxicity of the compound was evaluated on RAW 264.7 cells using the MTT assay, which measures reduction of MTT dye to formazan crystals as an indicator of cell viability. Cells (20,000/well) were seeded in 96-well plates and incubated for 24 h, followed by LPS stimulation (1 µg/ml, 2 h) to induce inflammation. Cells were then treated with varying concentrations of test agents, while untreated wells without LPS served as control. After 24 h incubation at 37 °C, 5% CO_2, the medium was replaced with MTT solution (0.5 mg/ml) and incubated for 3 h in the dark. Formazan crystals were dissolved with 100 µl DMSO and absorbance was read at 570 nm using an ELISA reader[21, 48].

Particle Size and Zeta potential

The average particle size of formulated microparticles was determined by using HORIBA SZ-100 particle analyzer[20]. Zeta potential controls charge interactions. It is measured by HORIBA SZ-100 zeta sizer[13].

Surface Morphology

A drop of microparticles was placed on the microscopic glass slide. Photographs of formulations were taken at 10x magnification using the digital camera [digicam 5 mega pixel] attached to the eyepiece of the Nikon projection microscope[19].

DSC Studies

Thermogram of the both, plain drug and optimized formulation was obtained by using DSC outfitted with an intercooler. Indium standard was used for calibrating DSC enthalpy and temperature scale. Samples were kept in aluminum pan hermetically and heated at constant heat of 10°C/min over temperature range of 25-300°C. By purging nitrogen with flow rate of 10ml/min inert atmosphere was maintained[8].

Stability studies

Stability studies were conducted to detect any changes in pH, Particle size, Transmittance, and Drug content. Accelerated stability studies of microparticles were carried out at a temperature of 40^0C±2^0C and relative humidity of 75% ± 5% .The samples were analyze data in interval of 15days for the period of 6 months for the changes in pH, % drug content, %drug release 7.4 pH of optimized formulation. Microparticles were evaluated for physicochemical properties[20].

RESULT AND DISCUSSION

The formulation was designed to deliver a low dose of mesalamine along with curcumin as a complementary adjuvant, providing local therapeutic effect within the colon. The microparticles provides effective approach for colon specific drug delivery that has been developed to protect mesalamine from premature degradation in the upper gastrointestinal tract while ensuring sustained release at the site.

Compatibility study by FTIR studies confirmed the absence of incompatibility between Drug and excipients, as supported by FTIR spectra showing the preservation of characteristic peaks of mesalamine (O–H at 3633 cm^{-1}, C=O at 1626 cm^{-1}) and curcumin (O–H at 3440 cm^{-1}, aromatic C=C at 1497 cm^{-1}) were retained in the drug–polymer blends with Eudragit S100 and RS100[28].

The surface pH of formulations ranges 7.16–7.56 was close to colonic physiological pH, minimizing mucosal irritation and enhancing patient compliance[9].

The production yield of formulations ranged between 67.5% and 88.1%. High yield in MCMP8

were associated with optimal polymer concentration, which demonstrate that the double emulsion solvent evaporation method produce high yield with good potential for scale up[34].

The entrapment efficiency ranged from 65.72% for mesalamine to 64.71% for curcumin confirming successful incorporation of drug and adjuvant with in the polymeric matrix. The optimized formulation MCMP 14 has 68.18% entrapment efficiency which closely matches with predicted value. The efficient co-encapsulation of curcumin as complementary adjuvant play crucial role for sustained release microparticle, facilitates stability of mesalamine loaded microparticles in treating ulcerative colitis[39,41,49].

Table 1: Composition of mesalamine and curcumin loaded microparticles

Formulation Code	Mesalamine (mg)	Curcumin (mg)	Eudragit S100:RS100	Total Polymer (mg)	PVA (%w/v)
MCMP 1	175	50	1:1.5 (100:150)	250	0.5
MCMP 2	175	50	1:1.5 (120:180)	300	1.5
MCMP 3	175	50	1:1.5 (100:150)	250	1.5
MCMP 4	175	50	1:1 (100:100)	200	1.5
MCMP 5	175	50	1:2 (100:200)	300	1.0
MCMP 6	175	50	1:2 (100:200)	300	1.0
MCMP 7	175	50	1:2 (100:200)	300	0.5
MCMP 8	175	50	1:1.5 (100:150)	250	1.0
MCMP 9	175	50	1:1.5 (100:150)	250	0.5
MCMP 10	175	50	1:1 (100:100)	200	1.0
MCMP 11	175	50	1:1 (150:150)	300	1.0
MCMP 12	175	50	1:2 (100:200)	300	1.5
MCMP 13	175	50	1:1 (100:100)	200	0.5

Table 2: Table of constraints in Optimisation in Mesalamine and Curcumin loaded Microparticles

Name	Goal	Lower Limit	Upper Limit	Lower Weight	Upper Weight	Importance
A:Polymer Ratio	is in range	1	2	1	1	3
B:Polymer Coating Strength	is in range	7.5	20	1	1	3
C:surfactant concentration	is in range	0.5	1.5	1	1	3
Entrapment Efficiency	is in range	67	72.59	1	1	3
Drug Release 0.1HCl	is in range	0	0.9	1	1	3
Drug Release 7.4pH	is in range	73.01	87.83	1	1	3

Table 3: Statistical data table for entrapment efficiency, drug content, drug release 1.2 pH and drug release 7.4 pH

	Model	p- value	Mean	C.V %	R^2	Adj. R^2	Pre. R^2	Adeq Precision	PRESS
Entrapment Efficiency	Quadratic	0.0026	69.12	0.4152	0.9951	0.9805		23.3513	
	Cubic	0.1000	69.12		1.00			0.000	
	2FI	0.0002	69.12	0.7170	0.9709	0.9419	0.9077	16.1604	4.68
	Linear	0.0003	69.12	1.27	0.8640	0.8187	0.7163	12.1072	14.38
	Quartic	0.1000	69.12		1.000			0.000	

	Model	p- value	Mean	C.V %	R2	Adj .R2	Pre. R2	Adeq Precision	PRESS
Drug release 0.1N HCl	Quadratic	0.0037	0.4875	10.18	0.9938	0.9752		22.3063	
	Cubic	0.100	0.4875		1.000			0.000	
	2FI	0.0001	0.4875	14.25	0.9757	0.9515	0.8665	19.0474	0.1593
	Linear	0.0001	0.4875	19.41	0.9324	0.9099	0.8513	18.4913	0.1774
	Quartic	0.100	0.4875		1.000			0.000	

	Model	p- value	Mean	C.V %	R^2	Adj .R^2	Pre. R^2	Adeq Precision	PRESS
Drug release 7.4 pH	Quadratic	0.0053	79.62	1.01	0.9922	0.9686		19.6601	
	Cubic	1.000	79.62		1.000			0.000	
	2FI	0.0004	79.62	1.49	0.9658	0.9316	0.8794	16.9452	29.79
	Linear	0.0001	79.62	1.88	0.9183	0.8910	0.8361	16.3046	40.49
	Quartic	1.000	79.62		1.000			0.000	

Table 4: Optimized Formulation MCMP 14 of Mesalamine and Curcumin loaded Microparticles

Formulation Code	Entrapment Efficiency (%)	Drug release 0.1N HCL	Drug release 7.4 pH
MCMP14T	69.620	0.530	79.963
MCMP14P	68.18	0.48	78.910

Table 5: Evaluation studies for Optimized Formulation MCMP14

Evaluation Parameters	Observed values
Production Yield (%)	88.1±0.0081
pH Determination	7.33±0.016
Drug content (%)	70.03±0.0168

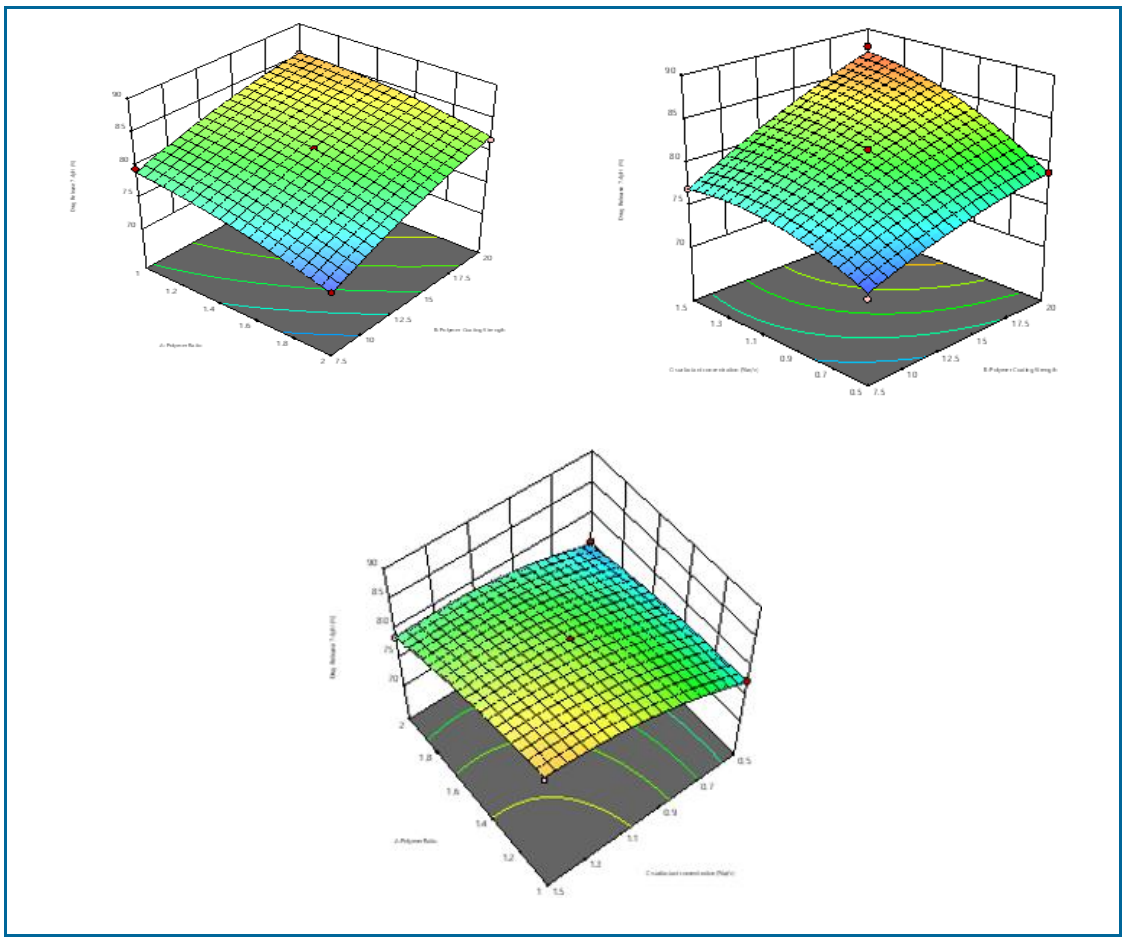


Figure 1: 3D graph plot of Drug release 7.4pH AB, BC, AC (Polymer ratio, coating strength, surfactant concentration)

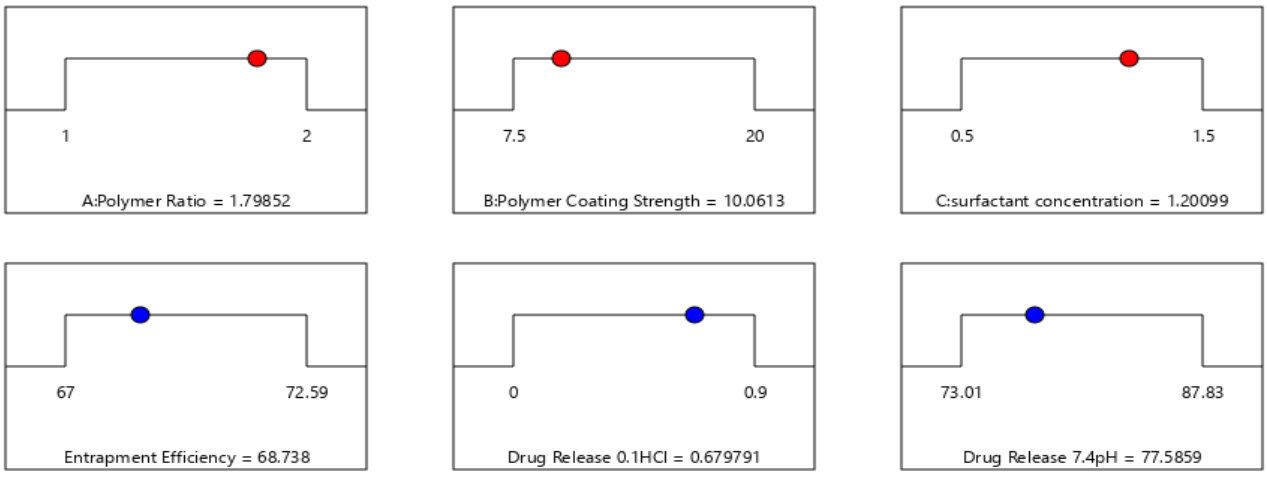


Figure 2: Numerical Optimized formulation RAMP profile graph of MCMP

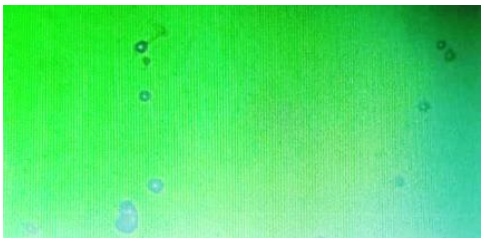


Figure 3: Optical microscopic image of optimized microparticles formulation MCMP 14

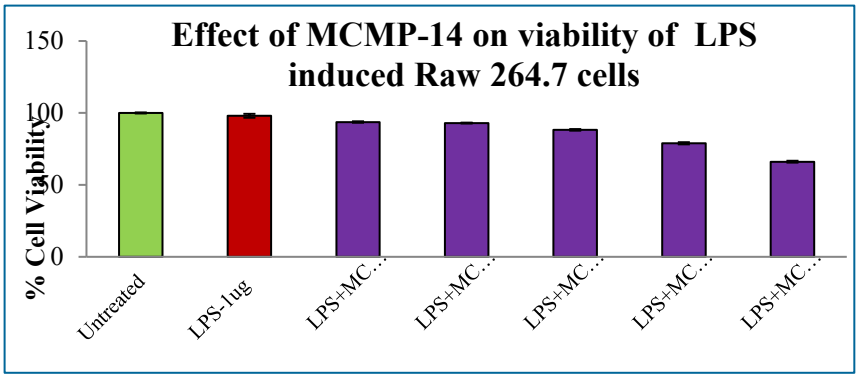


Figure 4: %cell viability of LPS induced Raw 264.7 cells treated with varying concentrations of MCMP-14 after 24 hours of incubation, as determined by the MTT assay.

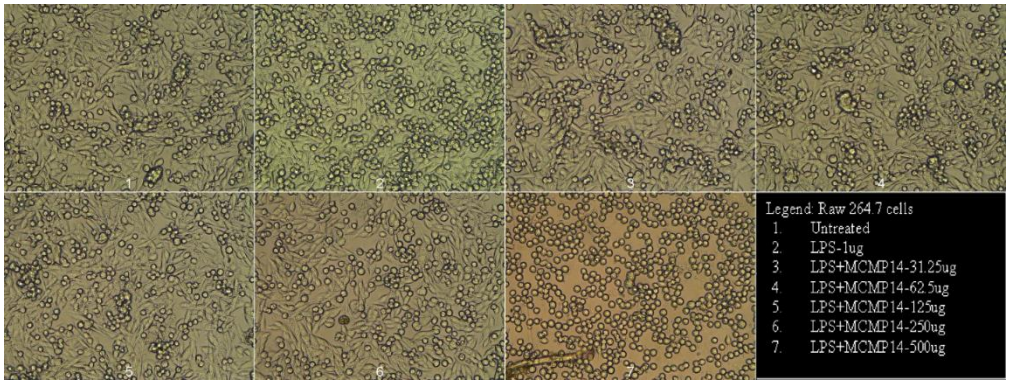


Figure 5: Overlaid montage image illustrating the morphological changes in LPS induced Raw 264.7 cells following treatment with varying concentrations of MCMP-14 for 24 hours. Images were captured using an inverted biological microscope at 20× magnification and recorded with a digital camera using MICAM software.

The *in-vitro* drug release studies of different formulation MCMP1-MCMP13 containing Eudragit S 100 and Eudragit RS 100 in the microparticles were carried out in different dissolution media (pH 1.2, 7.4). The formulated microparticles were coated with different ratio of Eudragit S 100 and Eudragit RS 100 (1:1, 1:2). The formulations MCMP2, MCMP4 and MCMP10 coated with different ratio of Eudragit S 100 and RS 100 showed negligible (<1%) drug release at gastric pH 1.2, justifies that the Eudragit coating remained intact under gastric pH, preventing premature release, and whereas 87.83 ± 0.011, 84.73 ± 0.031 and 85.39 ± 0.061 indicating maximum drug release at colonic pH 7.4 within 8h justifies the suitability of microparticles for colonic targeting [24].

In order to identify the drug dissolution mechanism through the polymer coated microparticles in each release medium, the Korsmeyers-Peppas model was tested. This model is developed to analyse non-Fickian release of drugs from polymeric delivery systems. The release data are fitted according to the selected model in the appropriate time intervals which are specified. In the model of Korsmeyer-Peppas, the exponent of time (n) is related to the drug release mechanism. So, n-values are indicative for non-

fickian diffusion and polymer erosion[24]. Therefore, release followed anomalous non-Fickian diffusion, confirming controlled, sustained delivery suitable for long-term therapeutic effect.

Drug content analysis revealed mesalamine loading in the range of 55–74% with the optimized formulation MCMP-14 achieving 70.03%. The high and uniform content reveals homogeneous drug distribution within the polymer matrix supporting the therapeutic efficacy at colon site[39,40].

In-vitro Cytotoxicity studies

The MTT assay confirmed that LPS induced inflammation in RAW 264.7 macrophages without significant cytotoxicity. Optimized formulation exhibited a dose-dependent effect, with lower concentrations (31.25–125 µg/mL) showing minimal toxicity and suitability for therapeutic use, while higher concentrations (250–500 µg/mL-) caused marked cytotoxicity[46,47]. These results promises anti-inflammatory candidate at lower doses, though further studies such as cytokine profiling and oxidative stress assays are needed to confirm its efficacy and define the safe therapeutic window[45,46,47].

Surface morphology revealed for optimized formulation, spherical microparticles with smooth surfaces, reducing aggregation and supporting uniform release. DSC thermograms showed amorphous drug dispersion within the polymer matrix, enhancing solubility and sustained release.

Optical microscopy was employed to evaluate the surface morphology and shape of the prepared microparticles. The micrograph reveals that the microparticles are spherical with smooth surfaces and exhibit a uniform dispersion with no visible cracks across the field. The absence of aggregation suggests that the formulation process and PVA concentration were adequate to maintain particle discreteness during solidification. The spherical morphology indicates efficient droplet formation during the emulsification stage and proper polymer precipitation during solvent evaporation, consistent with previously reported studies on polymeric microparticle fabrication[35,36].

The particle size shows that the optimized formulation possesses a uniform distribution with an average size of 432.8 µm, indicating uniform and reproducible particle formation. The sharp single peak confirms consistent particle size, crucial for optimizing drug release, entrapment efficiency. Particles within the 400–450 µm range are ideal for colon-targeted delivery, ensuring minimal upper GI absorption and localized drug release in the colon[3, 19].

The work successfully demonstrated that careful optimization of polymer ratio, coating strength, and surfactant concentration can yield microparticles with desirable properties for colon-targeted delivery by Box-Behnken Design. The ANOVA results and graphical analyses demonstrated that each of the three responses was governed by a combination of main effects, interactions, and non-linear behaviors. The contour plots and 3D surface graphs provided visual confirmation of these relationships, highlighting the existence of narrow optimal zones where the formulation meets all objectives simultaneously. The optimized formulation, consistently matched predicted values across all responses, validating the model and establishing the feasibility of using BBD for systematic pharmaceutical optimization[23,44].

Stability studies for the optimized mesalamine and curcumin-loaded microparticles were conducted under accelerated conditions at 40°C ± 2°C and 75% relative humidity (RH) ± 5% RH, in accordance with ICH guidelines. After 6 months of storage, the microparticles exhibited negligible changes in drug content (70.58% to 70.16%) and drug release at pH 7.4 (79.96% to 77.46%), indicating no influence on the physical and chemical stability. No visible cracks or surface deformities were observed, suggesting that the polymeric coating remained intact during storage[42,43].

CONCLUSION

The present study was able to develop and optimize mesalamine microparticles with inclusion of curcumin as a complementary adjuvant to support the formulation stability using Eudragit S100 and RS100 polymers for targeted

colon delivery in ulcerative colitis. The Box–Behnken Design enabled systematic optimization of polymer ratios, coating strength, and surfactant concentration, producing microparticles with uniform size, high yield, optimum drug loading, and efficient entrapment. Stability studies confirmed the physical and chemical integrity of the microparticles, with no surface cracks and negligible changes in drug release under both acidic and colonic pH conditions over 6 months. *In vitro* release studies demonstrated sustained, pH-dependent release following Korsmeyer–Peppas kinetics, ensuring targeted colonic delivery. The MTT assay confirmed that MCMP-14 is non-toxic to RAW 264.7 macrophages at lower concentrations, maintaining high cell viability. Collectively, this developed formulation shows considerable strategy to enhance the colon availability in the inflamed colon while preventing premature release at gastric pH with capability of overcoming the drawbacks of conventional mesalamine. Future research should focus on testing this formulation in cell lines to study their anti-inflammatory effects. Animal studies can follow to evaluate its therapeutic efficiency, biocompatibility and providing a platform for safe treatment for ulcerative colitis.

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Abbreviations: Abs, Absorbance; **BCS,** Bio pharmaceutics classification system; ºC, Degree Celsius; **cm**, centimetre; **cm²**, Centimetre square; **Cmax,** Peak plasma concentration; **Conc.,** Concentration; **CDR**, Cumulative Drug Release; **CDDS**, Controlled drug delivery system; **CR**, Controlled release; **CU**, Curcumin; **DOE,** Design of experiment; **DDS**, Drug Delivery System; **DMSO**, Di-methyl sulfoxide; **e.g.**, For Example; **FTIR**, Fourier transform Infra-red Spectrophotometer; **g**, Grams; **g/mol,** Gram per mol; **h**, Hours; **HCL,** Hydrochloric acid; **ICH**, International Conference on Harmonization; **IP,** Indian Pharmacopoeia; **mg,** Milligram; **min**, Minutes; **ml,** Millilitre; **µg,** Micro gram; **µg/ml**, Micro gram per milliliter; **µm,** Micro meter; **MSZ,** Mesalamine; **MCMP,** Mesalamine and curcumin loaded microparticles; **PB,** Phosphate buffer; **PK,** Pharmacokinetic; **PBS,** Phosphate buffer solution; **pH,** Hydrogen ion concentration; **RH,** Relative humidity; **%,** percentage; **rpm,** Rotation Per Minute; **DSC,** Differential Scanning Calorimetric; **w/v,** Weight by volume; **w/w,** Weight by weight; **DCM,** Dichloromethane.