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Research Article

Formulation and Development of Polysaccharide Based Mesalamine Nanoparticles

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ABSTRACT
In the present research work mesalamine loaded nanoparticles were developed by hot homogenization method by using different concentration of sodium alginate as polysaccharide and ratio of triglycerides monostearate and stearic acid, for site specific delivery to colon. 5-Amino salicylic acid (5-ASA or mesalamine) was selected as a model drug. The developed nanoparticulate formulations were characterized for with respect to shape and surface morphology, particle size, encapsulation efficiency, zeta potential, *in-vitro* drug release and release kinetics. The particle size and zeta potential of formulations were determined by Malvern zetasizer. Shape and surface morphology was confirmed by scanning electron microscope (SEM). The average particle size and zeta potential of the F5 formulation (containing 5:5 ratio of triglyceryl monostearate and stearic acid and 0.4%w/v sodium alginate) were found to be 217±6 and -30.7±5 mV respectively. The maximum percentage entrapment efficiency was reported with F5 formulation i.e. 72.71%. The *in vitro* drug release from advanced formulations was examined using a USP dissolution type-1apparatus in different media for different periods of time. 90±3.7% drug release was recorded with uncoated mesalamine nanoparticles in phosphate buffer solution pH 6.8, whereas coated nanoparticles displayed 87±4.0% and 76±4.2% release after 24 hours in rat cecal media and in human cecal media, respectively. The developed polysaccharide based nanoparticles would be a potential candidate for colon specific drug delivery of wide variety of drugs in various disease conditions.

Keywords: Nanoparticles, Mesalamine, Colon Targeting

INTRODUCTION

Ongoing study in the area of oral delivery of drugs, a regimen which has basked in the bright beam light of pharmaceutical sciences for the prior 70 years, has led to enhanced and profound intuition into the physiology, anatomy and physical chemistry (pharmacokinetics, partitioning phenomenon) of organs, compartments, cells, membranes, cellular organelles and working proteins (e.g. transporters) correlated with absorption development of drugs in the gastrointestinal tract (GIT). Most of the research has concentrated on distribution of drug to the small intestine. The large intestine, still, on account of its remoteness and comparably different physiology captured the status of fugitive. From last two decades, interest in area of advancement of oral colon targeted drug delivery systems (CTDDS) expanded, for medication of local colonic disorders[1]. Colon offers assorted potential therapeutic benefits as a site for drug delivery such as-

The colon has a great retention time and appears well responsive to agents that embellish the absorption of poorly absorbed drugs. The colon is captivating interest as a site where poorly absorbed drug molecule may have an enhanced bioavailability. The colon is affluent in lymphoid tissue, uptake of antigens into the mast cells of the colonic mucosa outcomes rapid local production of antibodies and this helps in effective vaccine delivery. Diminished proteolytic action in the colon may be beneficial in achieving reasonable absorption of convinced drugs that are enzymatically labile in small intestine. Decreased fluid mobility and motility in the colon when distinguished with small intestine is favourable formulation consists of

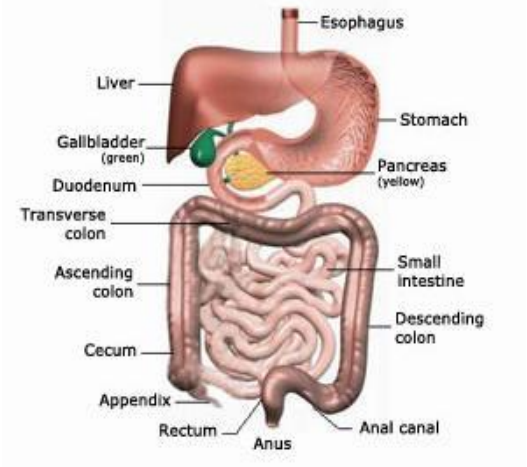

Figure 1: Anatomy of Gastrointestinal tract.

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Table 1: Composition of Various nanoparticle formulations.

Excipients	F1	F2	F3	F4	F5	F6
Mesalamine (mg)	10	10	10	10	10	10
Triglyceride monostearate (mg)	30	50	70	50	50	50
Stearic acid (mg)	70	50	30	50	50	50
Polysorbate 80 (µl)	20	20	20	20	20	20
Milli-QWater (µl)	1980	1980	1980	---	---	---
Sodium Alginate (0.2%w/v) (µl)	---	---	---	1980	---	---
Sodium Alginate (0.4%w/v) (µl)	---	---	---	---	1980	---
Sodium Alginate (0.6%w/v) (µl)	---	---	---	---	---	1980

Table 2: Average particle size, Encapsulation efficiency and polydispersity of Nanoparticles.

Formulation codes	Avg. Particle size (nm)	Encapsulation efficiency	Polydispersity Index	Loading efficiency
F1	135±0.7	61.26±0.5%	0.423±4	1.10±0.5%.
F2	127±0.4	65.38±1.2%	0.382±2	1.17±0.1%.
F3	131±0.8	63.24±1.1%	0.451±1	1.12±0.6%.
F4	210±0.3	62.38±0.4%	0.512±2	1.15±0.7%.
F5	217±0.6	72.71±4.2%	0.340±4	1.27±0.4%.
F6	341±0.2	56.38±3.1%	0.623±7	1.09±0.2%.

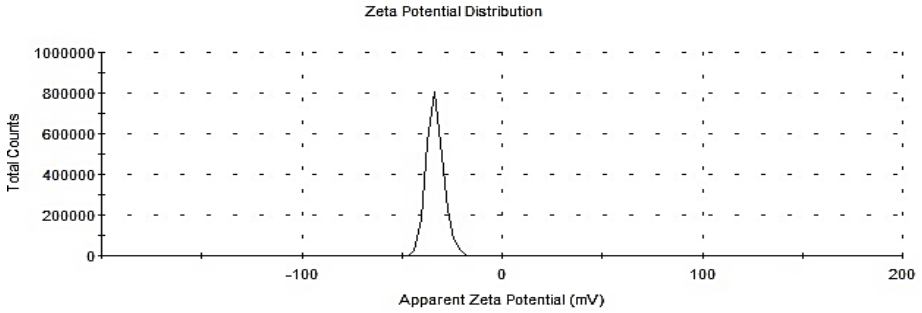


Figure 2: Surface charge distribution of mesalamine nanoparticles.

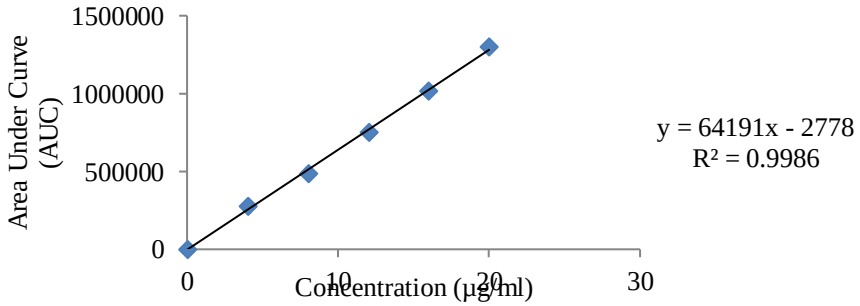


Figure 3: Calibration plot for Mesalamine in 1% HCl solution using HPLC.

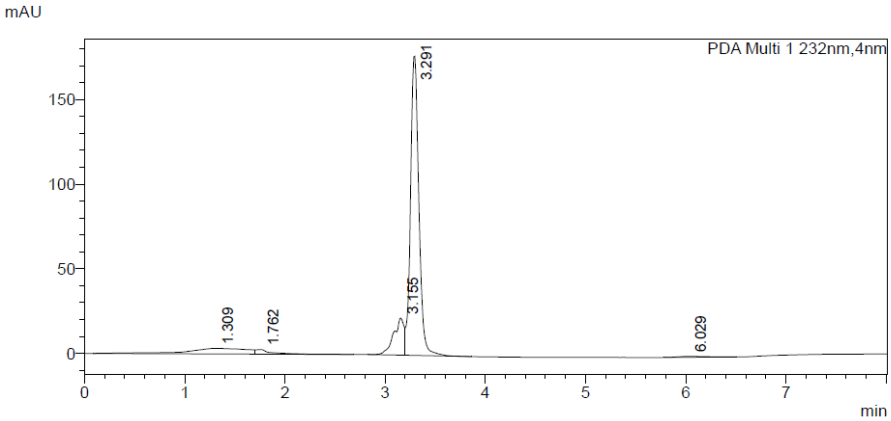
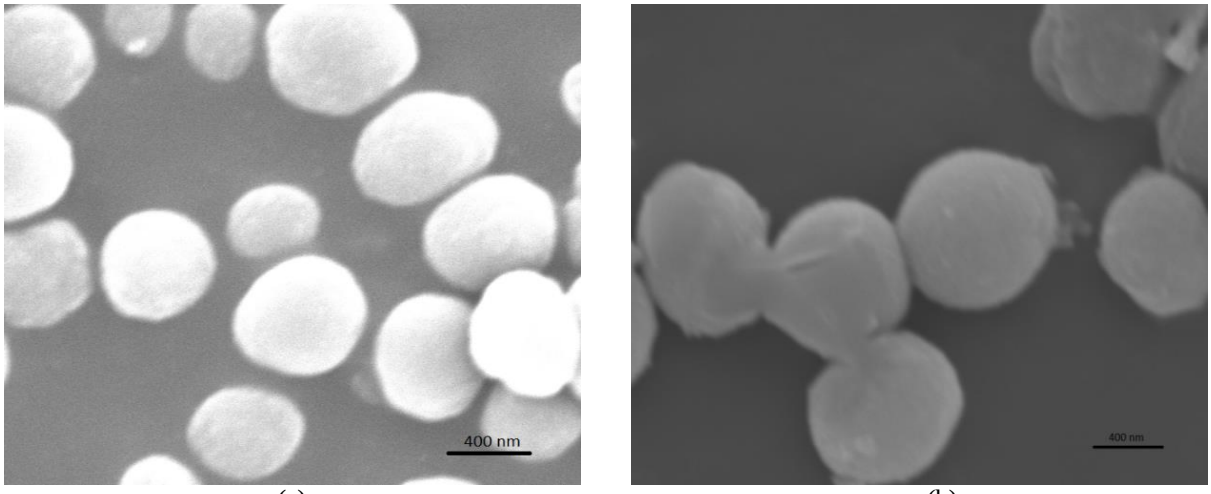


Figure 4: Chromatogram for 5-ASA showing AUC at 3.291 min for 16 µg/ml concentration solution.



(a) (b)

Figure 5: SEM Photomicrographs of a) uncoated nanoparticles (F2) b) Coated nanoparticles (F5).

multiple elements such as permeation enhancers that must extent epithelial layer to accomplish close spatial proximity with each other. The colonic region has considerably less hostile environment with less variety and less intensity of action as correlated to stomach and small intestine[2-4]. Targeting of drugs to colon is of expanding importance for local treatment of inflammatory bowel diseases (IBD) of the colon specific as ulcerative colitis and crohn's disease (CD)[5].

Anatomy and physiology of colon

Most digestion and absorption arise in the small intestine. The small intestine contains 3 parts: the duodenum, the jejunum and the ileum as presented in fig 1. Enzymes and other entity made by intestinal cells, pancreas and liver, are secreted into the small intestine and breakdown starches, sugars, fats and proteins[6]. Absorption of nutrients develops over the millions of tiny finger like projections called villi and the even microscopic projections on the villi called microvilli.

The large intestine has 3 parts: the cecum, the colon, and the rectum. The main activity of the large intestine is to remove water and salts (electrolytes) from the undigested component and to form solid waste (feces) that can be excreted. The staying contents of the large intestine move to the rectum. Nanotechnology is now traditionally used for various applications in fiber and textiles, agriculture, electronics, forensic science, space and medical therapeutics[7]. However, biodegradable nanoparticles are commonly used to improve the therapeutic value of assorted water soluble/insoluble medicinal drugs and bioactive molecules by developing bioavailability, solubility and retention time[8]. These nanoparticle drug formulation decrease the patient expenses, and risks of toxicity[9]. Nanoencapsulation of medicinal drugs (nanomedicines) increases drug efficacy, specificity, tolerability and therapeutic index of corresponding drugs[10]. These nanomedicines have many benefits in the protection of premature degradation and interplay with the biological environment, improvement of absorption into a preferred tissue, bioavailability, retention time and enhancement of intra-cellular penetration[11]. Assorted disease accompanying drugs/bioactive molecules are successfully encapsulated into nanocarriers to improve bioavailability, bioactivity and control delivery[12]. Nanomedicines of the alarming diseases like cancer, AIDS, diabetes, malaria, prion disease and tuberculosis are in different trial phase for the testing and some of them are commercialized[13]. Nanomedicine formulation depends on the choice of suitable polymeric system having utmost encapsulation (maximum encapsulation efficiency), advancement of bioavailability and retention time. The craved nanomedicines are traditionally achieved by hit and trial system (no specific rule) still, the encapsulation process with polymeric nanoparticles is in more forward condition in correlation to other nanoparticle systems. These drug nanoformulations (nanodrug) are exceptional to traditional medicine with respect to control release, targeted delivery and therapeutic impact. This targeting efficiency of nanomedicines was affected by particle size, surface charge, surface modification, and hydrophobicity. Amid these, the size and size distributions of nanoparticles are substantial to determine their interplay with the cell membrane and their infiltration across the physiological drug barriers. The size of nanoparticles for bridging different biological barriers is reliant on the tissue, target site and circulation. For the biological internalization of the nanoparticles, surface charge is substantial in determining whether the nanoparticles would array in blood flow or would comply to, or interact with oppositely charged cellsmembrane[14]. Mesalamine is an anti-inflammatory agent which is used to cure inflammatory bowel disease, crohn's disease and ulcerative colitis. The mechanism of activity of Mesalamine is not fully understood, but arrives to have a topical anti-inflammatory activity on the colonic epithelial cells. Mucosal management of arachidonic acid metabolites, both over the cyclooxygenase and lipoxygenase pathways, is expanded in patients with chronic inflammatory bowel disease, and it is attainable that Mesalamine curtails inflammation by obstructing cyclooxygenase and constraining prostaglandin production in the colon. Mesalamine has the probable to restrict the activation of nuclear factor kappa

Table 3: *In vitro* drug release of uncoated nanoparticle formulations.

Time (hr)	F1 formulation	F2 formulation	F3 formulation
0	0	0	0
2	61±0.2	45±0.3	65.4±0.6
3	66±0.6	49±0.8	70.1±1.5
5	70±1.2	56±1.5	73.4±1.6
6	74±1.4	64±1.8	79.5±1.2
9	77±0.5	74±0.5	85.2±1.4
12	78.1±0.3	78±1.9	88.7±0.3
15	79±0.2	86±0.5	89.4±0.1
18	80±0.6	89.6±0.2	89.8±0.2
21	82±0.2	90±0.1	90.4±0.2
24	85±0.7	90.3±0.1	90.8±0.1

Table 4: *In vitro* drug release of F4 formulation.

Time (hr)	Buffer media	Fecal media	Rat caecal media
0	0	0	0
2	0.5±0.2	0.6±0.2	0.6±0.4
3	9.4±1.2	10.6±0.5	11.8±1.4
5	17.6±2.2	23.2±1.3	25.2±2.0
6	21.8±0.4	26.3±1.2	29.1±1.4
9	23.6±1.2	29.4±1.6	34.6±1.1
12	30.3±1.3	40±1.2	49.6±2.0
15	35.4±0.2	45.6±1.4	62.1±2.6
18	36.2±0.4	54±2.6	78.4±1.2
21	37.8±0.1	75±1.2	86±1.2
24	39±0.6	79±1.1	89±0.6

Table 5: *In vitro* drug release of F5 formulation.

Time (hr)	Buffer media	Fecal media	Rat caecal media
0	0	0	0
2	0.5±0.2	0.6±0.2	0.5±0.2
3	2.7±0.3	2.3±0.5	2.5±0.6
5	8.4±2.0	7.7±1.5	7.8±2.0
6	19.5±1.1	17.5±1.4	21±2.1
9	22±1.2	28±2.1	33±2.3
12	30±1.3	39±2.2	48±3.0
15	35±1.8	44.8±3.0	60±2.8
18	36±0.1	52±2.8	76±1.8
21	36.6±0.2	72±1.1	84±2.8
24	37±0.7	76±1.2	87±1.0

B (NFκB) and as a consequence the management of key pro-inflammatory cytokines. It has been expected that declined expression of PPARγ nuclear receptors (γ-form of peroxisome proliferator-activated receptors) may be involved in ulcerative colitis. There is a proof that mesalamine produces pharmaco-dynamic belongings through blunt activation of PPARγ receptors in the colonic /rectal epithelium[15]. In the present research, polysaccharide based nanoparticles of mesalamine were advanced and evaluated for particle size, shape, surface morphology, entrapment efficiency, *in-vitro* studies and drug release kinetics.

MATERIALS AND METHODS

Table 6: *In vitro* drug release of F6 formulation.

Time (hr)	Buffer media	Fecal media	Rat caecal media
0	0	0	0
2	0.5±0.2	0.6±0.2	0.5±0.2
3	2.0±1.4	2.1±1.5	2.2±1.4
5	6.4±2.1	6.7±2.1	7.2±1.8
6	15.2±0.6	14.7±1.8	16.4±2.4
9	17.4±1.4	23.5±2.4	25.5±1.3
12	23.6±2.6	28.6±2.6	32.4±1.6
15	29.6±1.4	34.9±1.8	38.2±1.4
18	33.2±1.2	40.1±2.1	44.1±2.2
21	34.5±0.5	46.4±0.4	50.4±1.3
24	35.4±0.4	52.8±1.5	59.2±1.1

The active material (Mesalamine), Sodium alginate was purchased from Sigma-Aldrich, India. Triglyceride monostearate, Stearic acid, Polysorbate 80 were obtained from Molychem Manufacturers (P) Ltd, Mumbai, India.

Preparation of drug loaded mesalamine nanoparticles

Mesalamine loaded nanoparticles were prepared at different ratio of TGM and stearic acid and sodium alginate (table 1) by using hot homogenization followed by the probe sonication method as reported earlier with slight modification[16]. Firstly, weighted amount of stearic acid and triglyceride were melted by heating to 5℃ above the melting point of the lipid followed by addition of mesalamine into the obtained hot melt. Polysorbate 80 as emulsifier was added drop wise into above hot phase with simultaneous homogenization at 2500 rpm and 70℃ using a mechanical stirrer for 30 minutes to produced coarse oil in water emulsion. Emulsion was sonicated for 25 minutes by utilizing probe soincator. Sodium alginate was combined to above solution with sonication and then the hot nanoemulsion homogenised was allow cooling at room temperature and stored at 4℃ in the refrigerator.

Characterization of the Mesalamine Nanoparticles

Particle size

Particles sizes of the formulations were determined using photon correlation spectroscopy (PCS) (Malvern S4700 PCS System, Malvern Instruments, Ltd, Malvern, UK). The analysis was performed at a scattering angle of 90 ° and at a temperature of 25 ℃ using samples appropriately diluted with filtered water.

Zeta Potential

The zeta potential of the particles was determined by laser Doppler anemometry (Malvern Zetasizer IV, Malvern Instruments Ltd, Malvern, UK). All analyses were accomplished on samples appropriately diluted with 1mM HEPES buffer (adjusted to pH 7.4 with 1 M HCl) in order to continue a constant ionic strength.

Encapsulation Efficiency

The entrapment efficiency of the formulation was determined by dialysis bag method as reported earlier with slight modification[17].The nanoparticles were loaded in dialysis bags of cellophane membrane with molecular cut off of 3.5 kDa. The stock solution (containing 1 mg of drug) was transferred to the dialysis bags. Milli-Q water was chosen as release medium. The dialysis bags were then kept in medium in falcon tubes of 50ml capacity and were

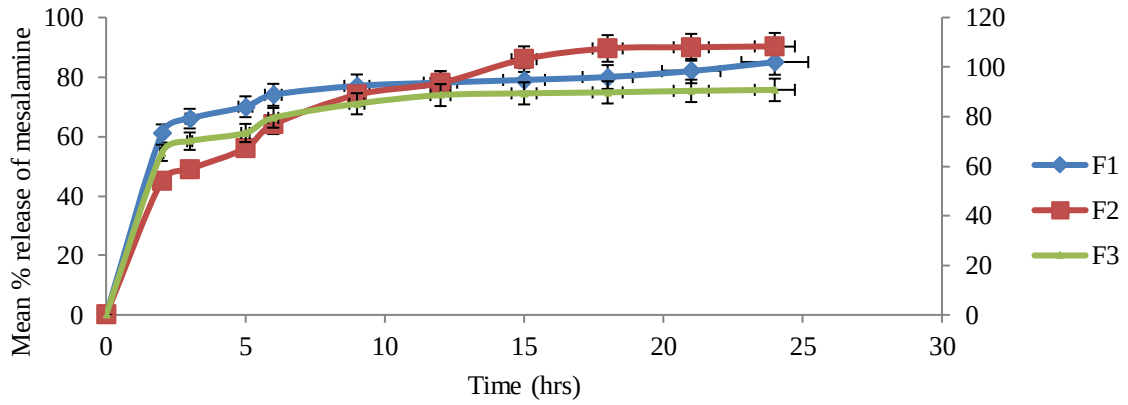


Figure 6: Mesalamine release studies of F1, F2 and F3 formulations in 6.8 pH Buffer.

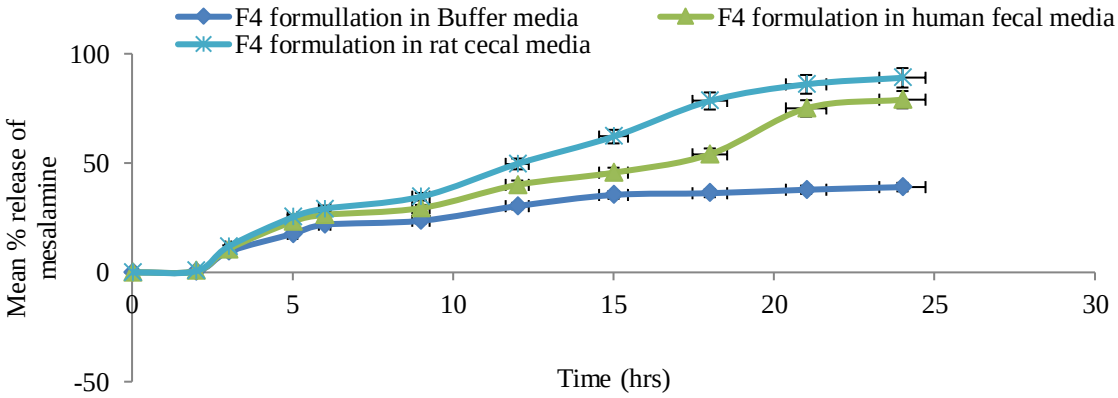


Figure 7: Mesalamine release studies in simulated gastric fluids of F4.

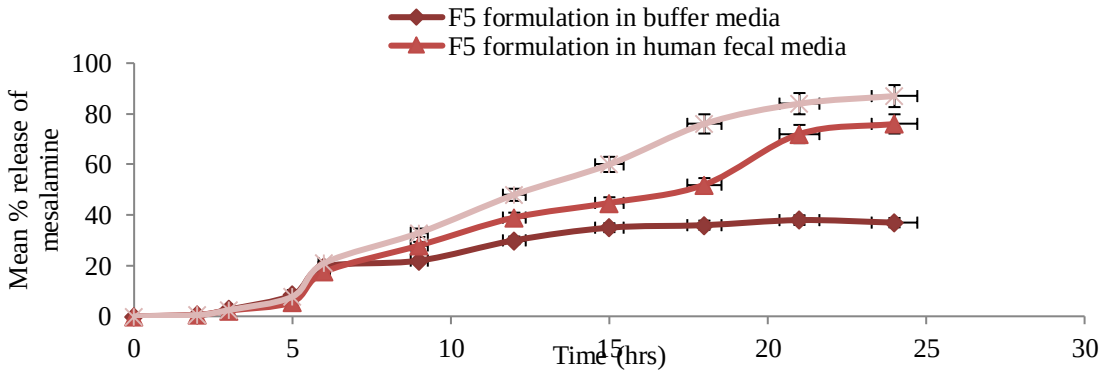


Figure 8: Mesalamine release studies in simulated gastric fluids of F5.

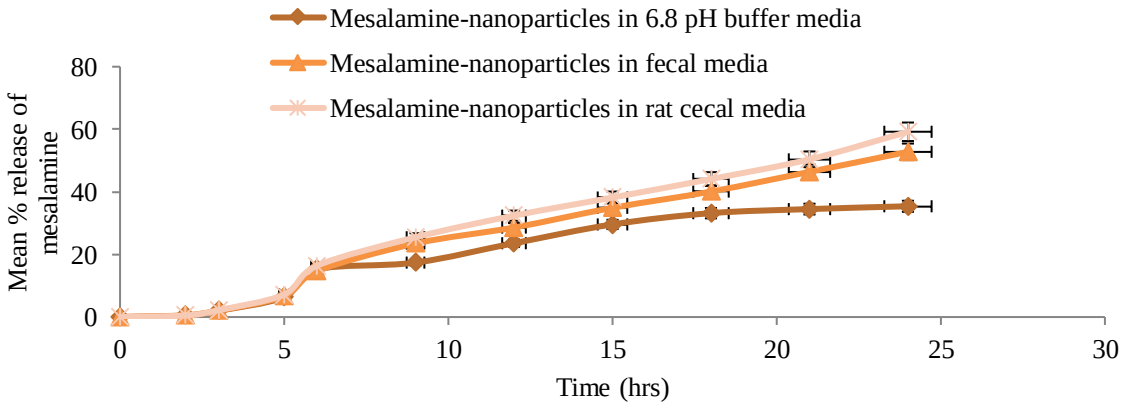


Figure 9: Mesalamine release studies in simulated gastric fluids of F6.

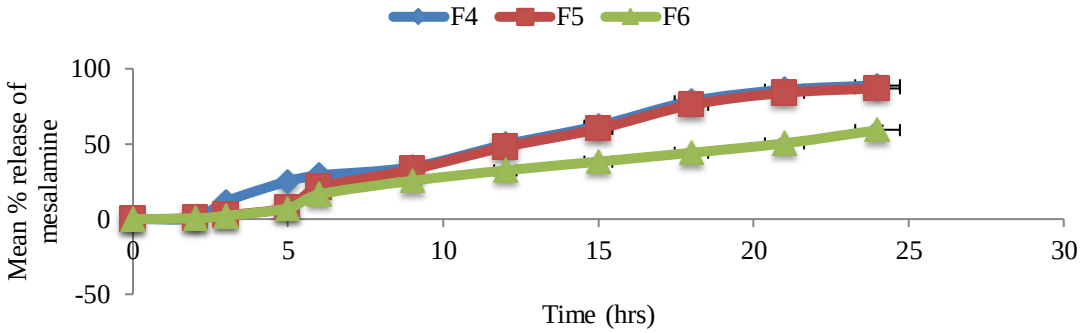


Figure 10: Mesalamine release studies in rat cecal media of F4, F5 and F6 formulations.

shaken continuously in a mechanical shaker at 130 rpm. After 24 hours, nanoparticle solutions was withdrawn from the dialysis bags and lyophilized. The lyophilized powder from each bag was then dissolved in 1% HCl and concentrations of drug were determined by RP-HPLC method at λ_{max} 230nm.

HPLC method for mesalamine

Mesalamine was estimated using RP-HPLC method (Shimadzu LC-20 AD liquid chromatography, SIL-20AC HT auto sampler, CTO-10 AS VP column oven and SPD-M20A with photo diode array detector at λ_{max} 230nm as reported earlier[18]. The C18 MG II S5 of size 4.6mm I. D.× 250mm and pore size 5 µm columns was used. The mobile phase consisted of 60% methanol and 40% milli-Q water. The flow rate was set as 1 ml/min for gradient flow with injection rate of 15 µl. Dimethyl sulfoxide (DMSO) was used as a solvent for dissolution of 5-ASA. The retention time was found to be 2.7 min.

Shape and surface morphology

Shape and surface morphology of the Mesalamine loaded nanoparticles was determined by scanning electron microscope (SEM- Jeol, JSM-6100). Sample drop was loaded on adhesive tape, which was stuck on an aluminium stub, further it is coated with gold utilizing a sputter coater and photographs of the cases were taken for shape and surface morphology[19].

Preparation of Dissolution Medias

Preparation of Phosphate buffer saline media (pH 6.8)

Phosphate buffer saline media of pH 6.8 was prepared by dissolving of 28.80g of disodium hydrogen phosphate and 11.45g of potassium hydrogen phosphate in water and final volume was made up to 1000ml[20]. Finally the pH of the buffer solution was adjusted to 6.8.

Preparation of fresh human fecal content medium

The slurry was developed by homogenising fresh feces (5% w/v with respect to 200ml volume of dissolution) retrieved from healthy human volunteers in anaerobic 0.1 M sodium phosphate buffer (pH 6.8) beneath anaerobic surroundings. This slurry was incorporate into the dissolution media to give a final fecal dilution of 5%. All the above procedure was carried out down the carbon dioxide in order to preserve anaerobic conditions[21].

Preparation of rat caecal medium

Rat's caecal matter was collected from animal house and contents were exclusively weighed, pooled, and pensile in the pH 6.8 buffer continuously bubbled with carbon dioxide. These were finally supplemented to the dissolution media to give a final cecal dilution of 4% w/v all the above process were carried out under carbon dioxide in order to preserve anaerobic conditions[22].

In vitro drug release studies

Invitro drug release studies were carried out by using dialysis bag technique in phosphate buffer saline pH 6.8 using basket type dissolution test apparatus. Nanoparticles formulations were placed in the dialysis bag and immersed in phosphate buffered saline (PBS). The entire system was kept on continuous mechanical shaker. Samples were withdrawn from the receptor compartment at predetermined intervals at 2, 3, 5, 6, 9, 12, 15, 18, 21 and 24h and replaced by fresh medium. Samples were analysed by HPLC at λmax 230nm to determine the concentration of drug. For the first 2 hours the dissolution study of mesalamine nanoparticles was carried out in 0.1N HCl having pH 1.2 with 100rpm at 37 ± 0.5°c. Afterwards the pH of the dissolution media was adjusted to pH 6.8 phosphate buffers and the study is continued for upto 24h. Similar method as mentioned for PBS pH 6.8 was applied for *in vitro* drug release studies of the drug loaded nanoparticles in Human fecal media and Rat cecal media. At the end of the fourth hour, the media was degassed using carbon dioxide gas to remove undissolved oxygen and to maintain anaerobic conditions inside the medium for 15 min. Then the 5% w/v of freshly prepared fecal slurry and 4% w/v of rat caecal content were added to the dissolution media and the study was continued upto 24h under the continuous purging of CO_2 throughout the study. The samples were withdrawn at 2, 3, 5, 6, 9, 12, 15, 18, 21 and 24h respectively from the dissolution medium and it was replaced by the fresh medium which was maintained under anaerobic condition. The volume of the sample was filtered by using 0.22micron membrane filters and concentration of drug was estimated by HPLC.

In-vitro drug release kinetics

Different kinetic models specific as zero order, first order, Higuchi model and Korsmeyer-peppas (log time vs. log % drug release) models were applied to interpret the drug release kinetics from the formulations. Based on the topmost regression values for correlation coefficients for formulations, the best-fit model was decided. The release rate and mechanism of drug release from prepared

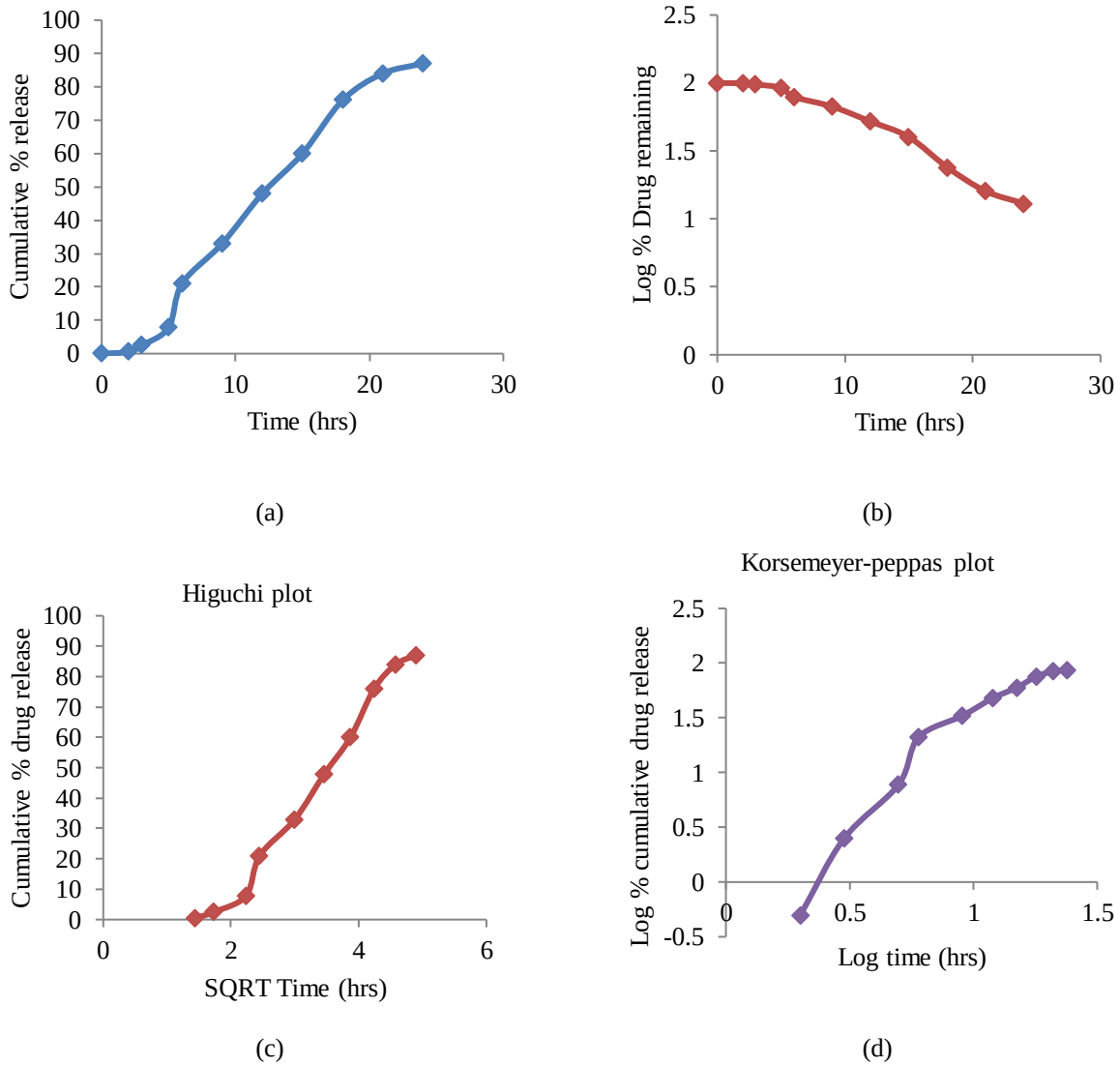


Figure 11: Drug Relaes kinetics of F5 formulation (A) Zero order, (B) First order, (C) Higuchi and (D) Korsemeyer-peppas.

nanoparticles were analysed by fitting release data into

Zero-order equation,

$Q = K_0 t$, Where, Q is the amount of drug release at time, t and K_0 is the release rate constant.

First order equation

$\text{Log } Q = K_1 t$, Where Q is the % of drug delivery at time, t and K_1 is the release rate constant.

Higuchi's equation

$Q = K_2 t^{½}$, Where, Q is the percentage of drug delivery at time t and K_2 is the diffusion rate constant.

Peppa's equation

$Mt/M\infty = Ktn$, Where $Mt/M\infty$ is the fractional release of the drug, t is the release time, K is a constant including structural and geometric distinctive of the release device, 'n' is the release exponent exhibitive of mechanism of delivery. For non-Fickian (anomalous/zero order) release, n value is middle among two points 0.5-1.0; for Fickian diffusion, $n < 0.5$; for zero order release, $n = 1$; n is predicted from linear regression of log ($Mt/M\infty$) Vs log t.

RESULTS AND DISCUSSION

Particle size

The particle size of the nanoparticle was determined by Malvern zetasizer and results were displayed in table 2. Average particle size of the mesalamine loaded nanoparticles (F1-F3) was recorded within the range of 127-135 nm whereas the average particle size of the sodium alginate coated nanoparticles was obtained in the range of 210-341nm. Polydispersity index of the mesalamine loaded nanoparticles (F1-F3) was recorded within the range of 0.382-0.451 nm whereas the particle size of the sodium alginate coated nanoparticles was obtained in the range of 0.340-0.623nm

Zeta (ζ) potential

The zeta potential of nanoparticles was determined by Malvern zeta seizer and was found to be -8.6 and -30.7±5 mV for without coated and with coated nanoparticles respectively as displayed in fig. 2. This indicates that sodium alginate has substantial negative surface charge which aids in attachment of nanoparticles to the targeted colonic region.

Table 9: Release kinetics.

Release Model		Formulation Code F4	F5	F6
Zero order	R^2	0.9787	0.9891	0.9740
First order	R^2	0.8857	0.9842	0.9283
Higuchi	R^2	0.9231	0.9013	0.9314
	^2R	0.9646	0.9559	0.9632
Peppas	n	1.4582	1.4552	1.4028
Best Fit Model		Zero order	Zero order	Zero order

Table 10: Results of formulation F5.

S. No.	Parameter	Results
1.	Average Particle Size	217±6 nm in diameter
2.	Zeta Potential	-30.7±5 mV
3.	Polydispersity Index	0.340±4
4.	% entrapment efficiency	72.71±4.2%
5.	*In-vitro* studies	87±4.0 in 24 hours
6.	*In-vitro* release kinetic studies	Proved that the formulation F2 follows mixed order Kinetics and best-fitted in Zero order kinetics.

Calibration curve for mesalamine using HPLC method

The calibration curve of mesalamine was prepared by RP-HPLC method at λmax 230nm. The results as shown in fig.3 displayed that linearity was obtained with in the concentration range of ---and a regression value was found to be 0.9986.

Encapsulation Efficiency and Loading Efficiency

Entrapment efficiency of mesalamine nanoparticles were determined by dialysis bag method and results were shown in Table 2. Drug expulsion in nanoparticles can arise when the lipid matrix transforms from great energy modifications, distinguished by the existence of many imperfections, to the β-modification produce a perfect crystal with no room for guest molecules. This phenomenon was even more pronounced when high purity lipids are used. Encapsulation efficiency of the formulations was released within the range of 56.3-72.7%. The highest drug entrapment was recorded with F5 formulation where F6 formulation displayed lower encapsulation efficiency. Loading efficiency was found within the range of 1.09-1.27%. The highest drug loading was recorded with F5 formulation where F6 formulation displayed lower loading efficiency.

Shape and surface morphology

Morphology of the nanoparticles including the shape and size were measured by scanning electron microscope (SEM). The result was shown in Fig 5 a & b indicated that the particles had nanometre-size spherical shapes and no drug crystal (variable crystallization with the ample majority of needle or rod crystal) was visible. The average particle size of F5 mesalamine loaded nanoparticles was found to be 127-341 nm respectively. *In vitro drug release studies*

Dissolution studies were developed by using conventional basket method (Type I USP) was conducted in different media and transit time. The pH was adjusted to 6.8 using phosphate buffer to mimic intestinal conditions and temperature was kept 37± 5^0C at 75± 4 rpm. The samples were withdrawn at predetermined time intervals and the absorbance was consistent at 230 nm for pH 6.8 phosphate buffer and different media In order to evaluate the controlled release potential of the developed formulations, the release of mesalamine from the nanoparticles was investigated upto 24h. Cumulative percentage of drug release from various nanoparticle formulations F1 to F6 displayed drug release of 61%, 45%, 65.4%, 0.6%, 0.5% and 0.5% in 0.1N HCl whereas 85%, 90.3%, 90.8%, 89%, 87% and 59.2% of drug release was achieved it in phosphate buffer pH 6.8. These findings imply that F2 formulation displayed good release among uncoated as displayed in table 3 and fig. 6whereas F5 formulation showed best release among coated formulations as displayed in table 4, 5 & 6 and fig. 7, 8, 9 & 10.

In-vitro drug release kinetics

The release kinetics of mesalamine loaded nanoparticles were evaluated by fitting the data into various kinetic models like first order, zero order, Higuchi, Peppas equations. The drug release kinetic data of mesalamine loaded nanoparticles was Shown in table 9 respectively and shown in fig. 11. It was found that all the formulation follows mixed order kinetics models i.e., initially the release pattern follows first order kinetic followed by zero order kinetics so it was concluded that all the formulations follows Mixed order kinetics, which release the drug at different rate and time of drug release to achieve pharmacological prolong action. Based on the results, the release of mesalamine from nanoparticles was best-fitted in Zero order fitting kinetics. The various in vitro characterization parameters of F5 formulation () like Average particle size, Zeta potential, Polydispersity index, percentage Entrapment efficiency, *invitro* studies and *invitro* release kinetics were displayed in table 10.

CONCLUSION

The developed nanoparticles demonstrate the possibilities in innovative drug delivery for the treatment of ulcerative colitis by targeted delivery based on factors directly related to the location and intensity of inflammation. Additionally these nanoparticles might selectively enhanced drug penetration into the inflamed tissue compared with free drug. In the present research work, mesalamine, used for the treatment of inflammatory bowel diseases such as ulcerative colitis, was loaded in nanocarriers for targeting the colonic region. The overall results obtained from studies revealed that nanoparticles might be a good candidate for colon specific delivery of mesalamine in case of ulcerative colitis.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this paper.

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