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Research article

Preparation and drug release assessment of mesalazine matrix tablets

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ABSTRACT

The major objective is to develop colon targeted drug delivery system by using Chitosan, Eudragit S 100 and Ethylcellulose and to compare the results obtained by three different carrier systems. Results obtained were fitted to different mathematical models to estimate which model fits best to the drug release. Wet granulation technique was employed for the preparation of prolonged release matrix tablets. Tablets containing chitosan as carrier system were found to show prolonged release in the colon. Kinetic models were applied among which Higuchi model suits best.

1. Introduction

Ulcerative colitis is a form of inflammatory bowel disease in which leukotriene, prostaglandins, cyclooxygenase, lipoxygenase production increase which leads to increased mucosal secretion in the cells which line the colon. It leads to sores called ulcers. It is caused by environmental factors and genetic factors. Environmental factor includes air pollution, diet and hygiene. Western people have diet rich in carbohydrates and fats and more prone to develop ulcerative colitis. Environmental factors include air pollution. Children are being brought up in germ free environment but according to hygiene hypothesis exposure to germs is required to develop properly. Thus by colon specific drug targeting drug release do not occurs in upper part of the gastrointestinal tract rather it occurs in specific part that is colon[1].Thus by means of colon targeting drug delivery system safety and efficacy can be improved while toxicity can be reduced. Thus maximum amount of drug concentration reaches the colon. Colon is known to be the optimal absorption site for proteins and polypeptides because of the existence of relatively low proteolytic enzyme activity and long transit time in the colon[2].

Polysaccharides which can be used in colon drug targeting

- Chitosan
- Pectin
- Locust bean gum
- Dextrin
- Eudragit S 100
- Cyclodextrins
- Chondroitin sulphate
- Amylose
- Guar gum

Factors affecting drug release and absorption

Factors such as pH nature and volume of gastric secretions, and gastric mucosa play an important role in drug release and absorption.

I. pH in colon

The pH of the gastrointestinal tract is subject to both inter and intra subject variations. Diet, disease state and food intake influence the pH of the gastrointestinal fluid[3]. The change in pH along the gastrointestinal tract with value ranging from 1.2 in stomach through 6.6 in the proximal small intestine to a peak of about 7.5 in the distal small intestine. The pH difference between the stomach and small intestine has been exploited to deliver the drug to the small intestine by way of pH sensitive enteric coating. There is fall in pH on entry into the colon due to the presence of short chain fatty acids arising from bacterial fermentation of polysaccharides.

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For example, lactose is fermented by colonic bacteria to produce large amounts of lactic acid resulting in drop of pH to about 5.0[4]. The pH of various parts of colon is depicted in **table 1**.

Table 1: pH of parts of colon

S. No.	Location	pH
1	Rectum	7.0
2	Terminal ileum	7.5+0.5
3	First part of colon	6.4+0.6
4	Mid colon	6.6+0,8
5	Left colon	7.0+0,7
6	Right colon	6.4

II. Colonic micro flora and their enzymes

Intestinal enzymes are used to trigger drug release in various parts of the GIT. Usually these enzymes are derived from gut micro flora residing in high numbers in the colon. These enzymes are used to degrade coating/matrices as well as to break the bonds between an inert carrier and an active agent (i.e. release of drug from a prodrug). Over 400 distinct bacterial species have been found 20-30% which of the genus bacteriods. The upper region of the GIT has very small number of bacteria and predominately consists of gram positive facultative bacteria. The concentration of bacteria in the human colon is 10^{11} -10^{12} CFU/ml[5].

Transit of material in the colon

Gastric emptying of dosage forms is highly variable and depends primarily on whether the subject is fed or fasted and on the properties of dosage forms such as size and density. The arrival of an oral dosage form at the colon is determined by the rate of gastric emptying and the small intestinal transit time[6]. The transit times of dosage forms in the gastrointestinal tract are shown in **table 2**.

Table 2: Transit times of dosage forms in the gastrointestinal tract

Organ	Transit time(hr.)
Stomach	‹1(fasting) ›3(Fed)
Small intestine	3-4
Large intestine	20-30

The movement of materials through the colon is slow and tends to be highly variable and influenced by a number of factors such as diet, dietary fibre content, mobility, stress, disease and drugs.

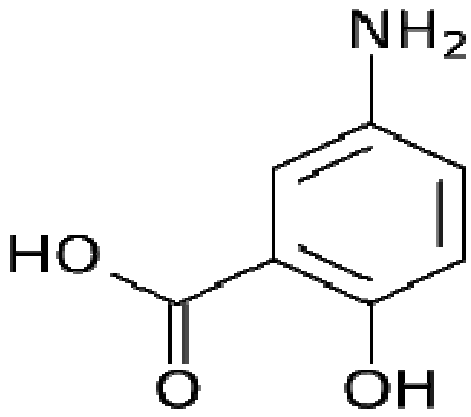
In healthy adult and young males, dosage forms such as tablets and capsules pass through the colon in approximately 20-30 hours although the transit time of a few hours to more than two days may occur. Diseases affecting colonic transit have important implications of drug delivery: diarrhoea increases colonic transit and constipation decreases it. However in most disease states, transit time appears to remain reasonably constant[7].

5-aminosalicyclic acid or mesalamine or mesalazine is a prescription drug used for the treatment of inflammatory bowel disease. It is an anti inflammatory category drug and belongs to class 1V according to biopharmaceutics classification system [8].

I. Chemical name: 5-Amino 2-hydroxybenzoic acid.

II. Synonym: m-amino salicylic acid.

III. Chemical structure:



IV. Description: 5-Aminosalicylic acid is white colored powder. It is slightly soluble in water. 20-30% absorbed when orally administered.

V. Molecular formula: $C_7H_7NO_3$

VI. Molecular weight: 153.14

VII. Melting point: 280˚C.

VIII. Therapeutic category: Anti-inflammatory drug.

IX. Partition coefficient: Log P (octanol/water) 1.2

X. pKa: 5.8

XI. Solubility: Soluble in dil HCl, dil solution of alkali hydroxide, slightly soluble in water.

XII. Half life: 5.0 hour[9]

XIII. Protein binding: 43%

2. Materials and methods

Materials

Mesalamine was obtained from IPCA Laboratories. Chitosan (Sigma Aldrich), Eudragit S 100(Alpha chemika), Sodium CMC, talc and magnesium stearate were of analytical grade. **Tables 3, 4** and **5** show the composition of matrix tablets**.**

Methods

Tablets were prepared by wet granulation technique.

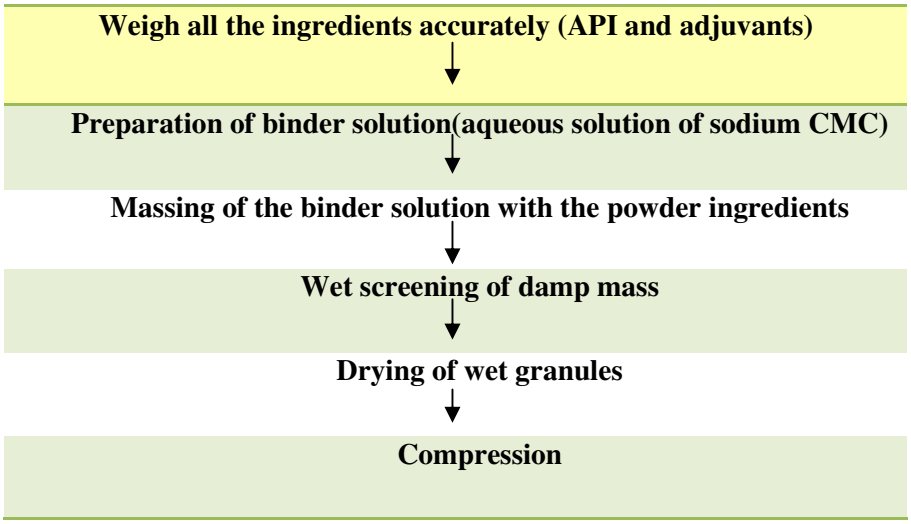


Table 3: Composition of matrix tablets using chitosan(F1)

Ingredients	Quantity(mg)
Mesalamine	100
Microcrystalline cellulose	280
Chitosan	100
Sodium CMC(aq. Sol)	15
Magnesium stearate	2
Talc	3

Table 4: Composition of matrix tablets using Eudragit S 100(F2)

Ingredients	Quantity(mg)
Mesalamine	100
Microcrystalline cellulose	340
Eudragit S 100	50
Sodium CMC(aq. Sol)	5
Magnesium stearate	2
Talc	3

Table 5: Composition of matrix tablets using Guar gum (F3)

Ingredients	Quantity(mg)
Mesalamine	100
Microcrystalline cellulose	310
Guar gum	75
Sodium CMC(aq. Sol)	10
Magnesium stearate	2
Talc	3

Evaluation parameters

I. Hardness

Force required to break the tablets into halves is the tablet crushing load. It was measured by Monsanto hardness tester. Hardness is expressed as tensile strength.

II. Weight variation

Twenty tablets were weighed together and then weighed individually to calculate the average weight and average weight was compared with the individual weight of the tablets.

III. Friability

Friability of tablets was done in a friabilator. It is done to estimate the effects of shocks which may cause chipping, capping effects.Friabilator consist of a plastic chamber which rotates at 25 rpm (100 revolutions). Six-Ten tablets were dropped at a distance of six inches. The weight loss in the tablets was calculated. Compressed tablets should not lose more than 1% of their weight.

IV. Thickness

It was measured by vernier caliper.

V. Content uniformity

Twenty tablets were weighed, powdered and crushed. Crushed powder equivalent to 150 mg was weighed and dissolved in phosphate buffer. Drug content was calculated at 230 nm.

VI. In vitro drug release

It was carried out in paddle type apparatus. 900 ml of the phosphate buffer pH 6.8 was used. Aliquots were taken at different time intervals and drug release was calculated.

VII. *In vitro* release kinetics

Raw data obtained was fitted into different mathematical equations and the model which suits the best was assessed[10-12].

3. Results

Table 6 shows the evaluation parameters and **Figure 1** and **2** represents the comparison of dissolution profiles of F1,F2 and F3,Higuchi plot respectively.

Table 6: Evaluation parameters for formulations F1,F2 and F3

Parameters	F1	F2	F3
Average weight of tablets(mg)	502	500	499
Average hardness(Kg/cm^2)	6.3	5.5	4.9
Friability	0.17	0.39	0.46
Thickness(mm)	3.1	3.0	3.0
%Entrapment efficiency	90.6	84.7	80.9
% Drug release	74.8	82.6	92.90
Kinetic model	Higuchi	Higuchi	Higuchi

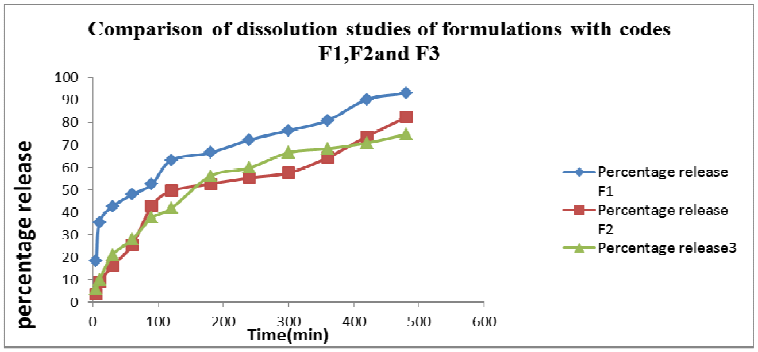


Figure 1: Percentage release of formulations F1,F2 and F3

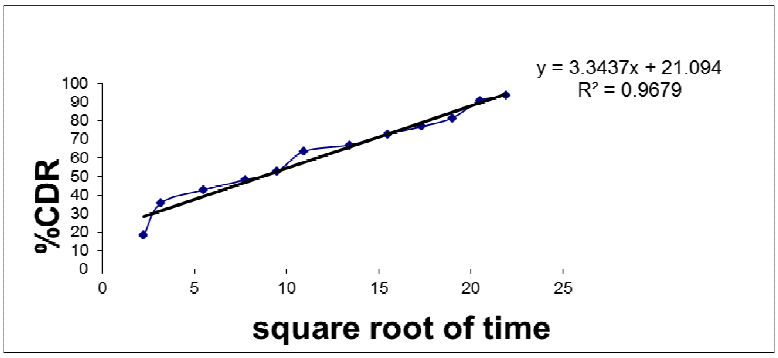


Figure 2: Higuchi plot

Matrix tablets formulated with chitosan was found to give the best release. It could be used for more prolonged release compared to the formulations F2 and F3[13].

9. Conclusion

The result obtained indicates that chitosan is more useful for controlled drug delivery as compared to Eudragit S 100 and Ethylcellulose. Dissolution thus can be prevented in upper part of the gastrointestinal tract and the drug can be reached to the targeted area that is colon. *In- vitro* release study was analyzed using various mathematical models. Cumulative percentage drug release with respect to time was found to be less for formulation F1. Based on regression coefficient values the best fit model was found to be higuchi model.

References

[1]. Kinget R., Kalala W.,Vervoort L.,Vanden Mooter G., Colonic drug targeting, J Drug target 1988;6:129-149.

[2]. Watts PJ., Iiium L., Colonic drug delivery, Drug Dev Ind Pharm.1997;23:893-913.

[3]. S. Avivi (Levi)., I Felner., I Novik., A Gedanken., The preparation of magnetic proteinaceous microspheres using the sonochemical method., Biochimica et Biophysica Acta, 2001;1527:123-129.

[4]. Jhunu Chatterjee., Yousef Haik., Ching-Jen Chen., Modication and characterization of polystyrene-based magnetic microspheres and comparison with albumin-based Magnetic Microspheres. Journal of Magnetism and Magnetic Materials, 2001; 225:21-29.

[5]. Denkbas EB.,Kilic ay EBRU., Birlikseven C.,Ozturk E., Magnetic chitosan microspheres: preparation and characterization, Reactive functional polymers. 2002; 50:225-232.

[6]. Chan y., Preparation and characterization of thermosensitive magnetic particles, Mater sci eng, 2002; 333:155-159.

[7]. Wada S., Tazawa K.,Furuta I., Nagae H., Antitumour effect of new local hyperthermia using dextran magnetite complex in hamster tongue carcinoma, Oral Dis 2003;9(4):218-223.

[8]. Altamash I Qureshi., Russel D Cohen., Mesalamine Delivery Systems: Do They Really Make Much Difference, Advanced Drug Delivery Reviews,2005;57:281-302.

[9]. Helieh S Oz., Jeffrey L., Ebersole., Application of prodrugs to inflammatory diseases of gut:a review, Molecules 2008;13:452-474.

[10]. Cohen DS and Erneux T., Free boundary problems in controlled release pharmaceuticals, I: diffusion in glassy polymers. SIAM. J. Appl. Math.1988; 48: 1451-1465.

[11]. Cohen DS and Erneux T., Free boundary problems in controlled release pharmaceuticals. II: swelling controlled release. SIAM. J. Appl. Math.1988; 48: 1466-1474.

[12]. Cox PJ., Khan KA., Munday DL and Sujja-areevath J., Development and evaluation of a multiple-unit oral sustained release dosage form for S(+)-ibuprofen: preparation and release kinetics. Int.J.Pharm., 1999;193: 73-84.

[13]. Alok Semwal., Singh Ramandeep., Preparation, characterization and biological evaluation of chitosan-moxifloxacin prodrugs for pharmaceuticals, Marmara PharmaceuticalJournal,2014;18:36-42.

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