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An Investigation on Colon Drug Delivery System for Satranidazole Tablet

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ABSTRACT

The colon targeted matrix tablet of satranidazole which is composed of polysaccharides which are susceptible to enzymatic degradation i.e. Guar gum, Xanthan gum, Guar : Xanthan gum in combination at 2 ratios (1:1) and (2:1) and Pectin coated with enteric polymer Eudragit L, Eudragit S and Eudragit RS. The SF7 formulation was found to be able, to release up to 92% of drug into colon. PVP K 30 was used as binder to fabricate a tablet having desired release characteristics. MCC was used as diluent in formulation. Coating materials used were Eudragit L, Eudragit S and Eudragit RS. As the requirement of formulation to bypass the release in stomach and small intestine Eudragit L, Eudragit S and Eudragit RS was suitable polymer in combination. Tablets coated with Eudragit L, Eudragit S and Eudragit RS in ratio of 4:16:5 with less quantity of plasticizer PEG 400 showed excellent film properties and were able to release most of the drug into colon. 10% of coating was found to be optimum. Formulation SF7 was considered as optimum batch as it delivered 96 % of drug into colon. The formulation SF7 can be employed as a promising colon specific drug delivery system of satranidazole.

KEYWORDS: Polysaccharides; Colon Targeted; Xanthan gum; Plasticizer PEG 400.

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INTRODUCTION

Targeted drug delivery into the colon is highly desirable for local treatment of a variety of bowel diseases such as ulcerative colitis, Crohn's disease, amebiosis, colonic cancer, local treatment of colonic pathologies, and systemic delivery of protein and peptide drugs.[1,2] The colon specific drug delivery system (CDDS) should be capable of protecting the drug en route to the colon i.e. drug release and absorption should not occur in the stomach as well as the small intestine, and neither the bioactive agent should be degraded in either of the dissolution sites but only released and absorbed once the system reaches the colon.[3] The colon is believed to be a suitable absorption site for peptides and protein drugs for the following reasons; (i) less diversity, and intensity of digestive enzymes, (ii) comparative proteolytic activity of colon mucosa is much less than that observed in the small intestine, thus CDDS protects peptide drugs from hydrolysis, and enzymatic degradation in duodenum and jejunum, and eventually releases the drug into ileum or colon which leads to greater systemic bioavailability.[4] And finally, because the colon has a long residence time which is up to 5 days and is highly responsive to absorption enhancers.[5]Oral route is the most convenient and preferred route but other routes for CDDS may be used. Rectal administration offers the shortest route for targeting drugs to the colon. However, reaching the proximal part of colon via rectal administration is difficult. Rectal administration can also be uncomfortable for patients and compliance may be less than optimal.[6]

Advantages of CDDS over Conventional Drug Delivery

Chronic colitis, namely ulcerative colitis, and Crohn's disease are currently treated with glucocorticoids, and other anti-inflammatory agents.[7]Administration of glucocorticoids namely dexamethasone and methyl prednisolone by oral and intravenous routes produce systemic side effects including adenosuppression, immunosuppression, cushinoid symptoms, and bone resorption.[8] Thus selective delivery of drugs to the colon could not only lower the required dose but also reduce the systemic side effects caused by high doses.[9]

Criteria for Selection of Drug for CDDS

The best Candidates for CDDS are drugs which show poor absorption from the stomach or intestine including peptides. The drugs used in the treatment of IBD, ulcerative colitis, diarrhea, and colon cancer are ideal candidates for local colon delivery.[10]

Approaches used for Site Specific Drug Delivery to Colon (CDDS)

Several approaches are used for site-specific drug delivery. Among the primary approaches for CDDS, These include:

1) Primary Approaches for CDDS

a. pH Sensitive Polymer Coated Drug Delivery to the Colon

In the stomach, pH ranges between 1 and 2 during fasting but increases after eating.[11]The pH is about 6.5 in the proximal small intestine, and about 7.5 in the distal small intestine.[12] From the ileum to the colon, pH declines significantly. It is about 6.4 in the cecum. However, pH values as low as 5.7 have been measured in the ascending colon in healthy volunteers.[13]The pH in the transverse colon is 6.6 and 7.0 in the descending colon. Use of pH dependent polymers is based on these differences in pH levels. The polymers described as pH dependent in colon specific drug delivery are insoluble at low pH levels but become increasingly soluble as pH rises.[14]Although a pH dependent polymer can protect a formulation in the stomach, and proximal small intestine, it may start to dissolve in the lower small intestine, and the site-specificity of formulations can be poor.[15] The decline in pH from the end of the small intestine to the colon can also result in problems, lengthy lag times at the ileo-cecal junction or rapid transit through the ascending colon which can also result in poor site-specificity of enteric-coated single-unit formulations.[16]

b. Delayed (Time Controlled Release System) Release Drug Delivery to Colon

Time controlled release system (TCRS) such as sustained or delayed release dosage forms are also very promising drug release systems. However, due to potentially large variations of gastric emptying time of dosage forms in humans, in these approaches, colon arrival time of dosage forms cannot be accurately predicted, resulting in poor colonical availability.[17] The dosage forms may also be applicable as colon targeting dosage forms by prolonging the lag time of about 5 to 6 h. However, the disadvantages of this system are:

i. Gastric emptying time varies markedly between subjects or in a manner dependent on type and amount of food intake.

ii. Gastrointestinal movement, especially peristalsis or contraction in the stomach would result in change in gastrointestinal transit of the drug. Accelerated transit through different regions of the colon has been observed in patients with the IBD, the carcinoid syndrome and diarrhea, and the ulcerative colitis.

iii. Therefore, time dependent systems are not ideal to deliver drugs to the colon specifically for the treatment of colon related diseases. Appropriate integration of pH sensitive and time release functions into a single dosage form may improve the site specificity of drug delivery to the colon. Since the transit time of dosage forms in the small intestine is less variable i.e. about 3±1 hr.27 The time-release function (or timer function) should work more efficiently in the small intestine as compared the stomach. In the small intestine drug carrier will be delivered to the target side, and drug release will begin at a predetermined time point after gastric emptying. On the other hand, in the stomach, the drug release should be suppressed by a pH sensing function (acid resistance) in the dosage form, which would reduce variation in gastric residence time.[18] Enteric coated time-release press coated (ETP) tablets, are composed of three components, a drug containing core tablet (rapid release function), the press coated swellable hydrophobic polymer layer (Hydroxy propyl cellulose layer (HPC), time release function) and an enteric coating layer (acid resistance function).[19,20] The tablet does not release the drug in the stomach due to the acid resistance of the outer enteric coating layer. After gastric emptying, the enteric coating layer rapidly dissolves and the intestinal fluid begins to slowly erode the press coated polymer (HPC) layer. When the erosion front reaches the core tablet, rapid drug release occurs since the erosion process takes a long time as there is no drug release period (lag phase) after gastric emptying. The duration of lag phase is controlled either by the weight or composition of the polymer (HPC) laye[r21].

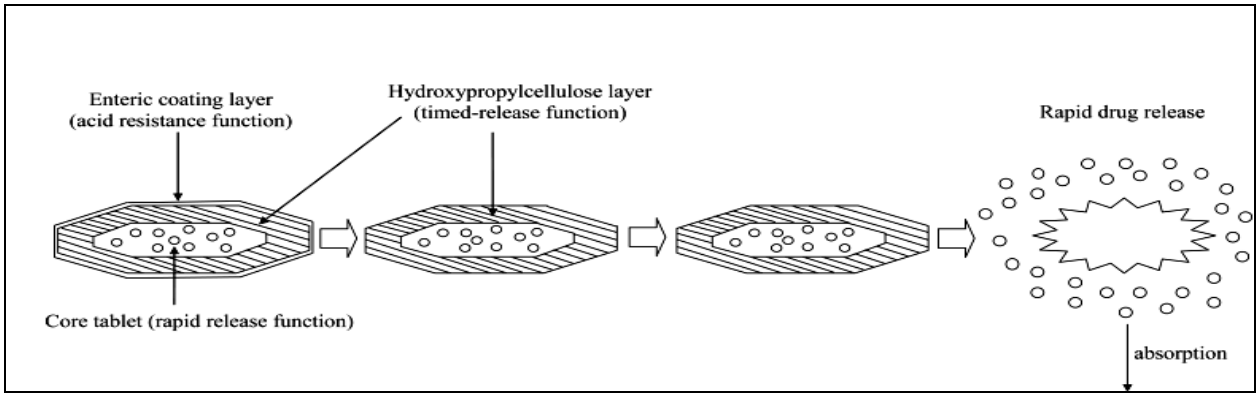

Figure No:1 Design of enteric coated timed-release press coated tablet (ETP Tablet)

Newly Developed Approaches for CDDS

a. Pressure Controlled Drug-Delivery Systems

As a result of peristalsis, higher pressures are encountered in the colon than in the small intestine. Takaya et al. developed pressure controlled colon-delivery capsules prepared using ethylcellulose, which is insoluble in water.[22] In such systems, drug release occurs following the disintegration of a water-insoluble polymer capsule because of pressure in the lumen of the colon. The thickness of the ethylcellulose membrane is the most important factor for the disintegration of the formulation.[23,24]The system also appeared to depend on capsule size and density. Because of reabsorption of water from the colon, the viscosity of luminal content is higher in the colon than in the small intestine. It has therefore been concluded that drug dissolution in the colon could present a problem in relation to colon-specific oral drug delivery systems. In pressure controlled ethylcellulose single unit capsules the drug is in a liquid.[25] Lag times of three to five hours in relation to drug absorption were noted when pressure-controlled capsules were administered to humans.

b. Novel Colon Targeted Delivery System (CODESTM)

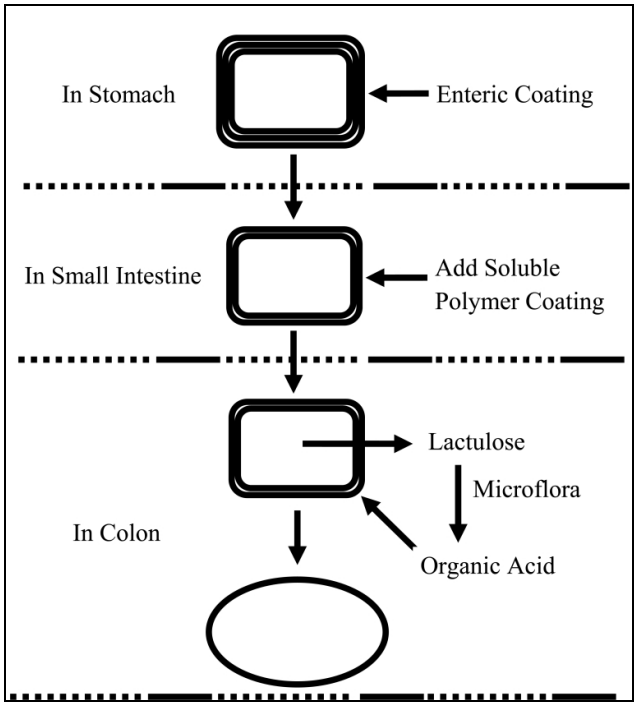

Figure No 2: Schematics of the conceptual design of CODES

CODESTM is an unique CDDS technology that was designed to avoid the inherent problems associated with pH or time dependent systems. CODESTM is a combined approach of pH dependent

and microbially triggered CDDS. It has been developed by utilizing a unique mechanism involving lactulose, which acts as a trigger for site specific drug release in the colon, The system consists of a traditional tablet core containing lactulose, which is over coated with and acid soluble material, Eudragit E, and then subsequently overcoated with an enteric material, Eudragit L. The premise of the technology is that the enteric coating protects the tablet while it is located in the stomach and then dissolves quickly following gastric emptying. The acid soluble material coating then protects the preparation as it passes through the alkaline pH of the small intestine. Once the tablet arrives in the colon, the bacteria enzymetically degrade the polysaccharide (lactulose) into organic acid. This lowers the pH surrounding the system sufficient to effect the dissolution of the acid soluble coating and subsequent drug release.[26,27,28,29]

MATERIAL AND METHODS

Table 1. List of Chemicals

S. No.	Chemical	Grade	Supplier
1	Satranidazole	Pharmaceutical grade	Gift sample- Alkem Laboratories Mumbai
2	Avicel pH 102	-	Signet Corporation, Mumbai
3	Lactose	AR	SD Fine Ltd., Mumbai
4	Guar gum	AR	Himedia laboratories
5	Eudragit L,Eudragit S, and Eudragit RS	AR	Gift sample-Degussa Rohm Pharma polymer.
6	Talc	AR	SD Fine Ltd., Mumbai
7	Magnesium stearate	AR	SD Fine Ltd., Mumbai
8	Pectin	AR	Himedia laboratories
19	Dichloromethane	AR	SD Fine Ltd., Mumbai
10	PEG 400	AR	SD Fine Ltd., Mumbai
11	Disodium hydrogen phosphate	AR	Merck Ltd., Mumbai
12	Dihydrogen potassium phosphate	AR	SD Fine Ltd., Mumbai
13	Polyvinyl pyrrolidone	AR	SD Fine Ltd., Mumbai
14	Acetone	AR	SD Fine Ltd., Mumbai
15	IPA	AR	SD Fine Ltd., Mumbai
16	Sodium chloride	AR	Merck Ltd., Mumbai

PREFORMULATION STUDIES OF SATRANIDAZOLE

Identification of drug

UV absorption maxima

Selection of solvent : As per the literature survey methanol was selected as a better solvent for satranidazole, as it is UV transparent and a good solvent for both polar and non-polar drugs, it causes no degradation and no interference in the peak of satranidazole. So methanol was selected for λmax study.

Determination of λmax: Ten mg of satranidazole was accurately weighed and transferred to 100 ml volumetric flask, sufficient quantity of methanol was added to dissolve it. The volume was made upto 100 ml with the methanol to obtain a stock solution. This solution was scanned between 200 nm to 400 nm in a double beam UV/ Visible spectrophotometer to get UV spectra[30].

IR Spectroscopy: For the further confirmation of satranidazole, dried sample of pure drug was scanned with FTIR (Thermo Nicolet corporation, USA, IR 200) and peaks obtained were compared with reference spectra.

Melting point measurement: For the measurement of melting point, satranidazole was crushed first and then filled it in a capillary and melting point was determined. Study was performed in triplicate for conformance.

Determination of solubility of drug: The study was carried out in glass vials of 10 ml capacity. Each vial charged with 5 ml of distilled water and different dissolution media and excess quantity of satranidazole. The vials were closed with rubber closures and kept for equilibrium at 25˚C±2˚C for a period of 24 hrs with continuous shaking, the solutions were then filtered and analyzed for the drug content spectrophotometrically at 318 nm.

Calibration curve of drug by UV absorption : In present studies Simulated gastric fluid, intestinal fluid, and colonic fluid without enzyme were used as a medium for drug release studies and hence estimation of satranidazole in these media was done by UV spectrophotometric method.

Preparation of simulated gastric fluid: Two grams of sodium chloride was accurately weighed and dissolved in sufficient quantity of DM water. 7.0 ml of 0.1 N hydrochloric acid was added to the above solution and the volume was made upto 1000ml using DM water. The pH was finally adjusted to 1.2 using 0.1 N HCl / 0.1 N NaOH.

Preparation of simulated intestinal fluid: 6.8 gms of monobasic potassium phosphate was dissolved in 250 ml. distilled water. In this solution 72 ml. of 0.2 M NaOH was added and volume was made up to 1000ml. with distilled water. The pH of the solution was adjusted to 6.8±0.1 using 0.1 N HCl/0.1M NaOH[31].

Preparation of simulated colonic fluid: 250-ml. of 0.2 M di potassium hydrogen phosphate solution was mixed with 28.5 ml. of 0.2 M NaOH solution and volume made up to 1000 ml. with distilled water. The pH of the solution was adjusted to 7.2±0.1 using 0.1 N HCl/0.1M NaOH.

Analysis of satranidazole in simulated gastric, intestinal and colonic fluid: Estimation of small amount of satranidazole was necessary for studying the release properties and determining percent active ingredients (a.i.) in matrix tablet formulation. This was achieved by using an UV spectroscopic method. Different aliquots of satranidazole were prepared in Simulated gastric fluid, intestinal fluid, and colonic fluid and calibration curve were obtained. The stock solution of satranidazole containing (1000mcg/ml) in different dissolution media was prepared and 318 λ_{max} was selected on the basis of maximum absorption found in UV spectrophotometer (Shimadzu 1601)[32].

FORMULATION OF SATRANIDAZOLE TABLETS

Preparation of tablets

Different formulation having the composition as shown in table 7 (SF1 TO SF8) were prepared. All ingredients were weighed, grinded in mortar pestle to reduce the size and passed through 100 mesh sieve. All ingredients were sieved through 100 mesh twice, mixed and blended manually in polyethylene bags so as to ensure proper mixing. The blended powder was granulated by adding sufficient quantity of 10% PVP K 30 in isopropyl alcohols a binder to obtain a mass of proper wetness and the mass was passed through sieve no.12 to obtain granules and dried at 40˚C for 30 minutes. Dried granules were passed through 30 mesh sieve to obtain uniform sized granules and mixed with 1% of Magnesium stearate and 2% of in polyethylene bag. This blend was now ready for compression. The granule mix was compressed into tablets of the target weight 450 ± 5 mg in a hand operated single punch tablet machine fitted with 11 mm biconcave punches. The compression pressure level was kept constant for all the batches by adjusting the pressure control knobs to the same setting.

Table 2. Tablet formulas and the corresponding different percentages

S.No	Ingredients	SF1	SF2	SF3	SF4	SF5	SF6	SF7	SF8	SF9
1	Drug	22.2	22.2	22.2	22.2	22.2	22.22	22.22	22.2	22.2
2	Guar gum	20	30	40	-	-	-	-	-	-
3	Xanthan gum	-	-	-	20	30	-	-	-	-
4	Guar:Xanthan	-	-	-	-	-	20(1:1)	20(2:1)	-	-
5	Pectin	-	-	-	-	-	-	-	20	30
6	Ethylcellulose	-	-	-	-	-	-	-	5	5
7	MCC	44.8	34.8	24.8	44.8	34.8	44.78	44.78	39.8	29.8
8	PVP K30 inIPA	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
9	Talc	2	2	2	2	2	2	2	2	2
9	Mg. stearate	1	1	1	1	1	1	1	1	1

All the quantaties expressed in percentage.

Coating of tablets

In order to protect the core tablets from the gastric environment. The prepared tablets were coated with three grades of Eudragit.

Composition and preparation of coating solution

Table 3. Composition of coating solution

S. No.	Ingredients	SC1	SC2
1.	Eudragit L100	4 g	3g
2.	Eudragit S100	16 g	12g
3.	Eudragit RS100	5 g	10 g
4	PEG 400	2 g	2 g
5.	Acetone	350 ml	350 ml
6.	Isopropyl alcohol	150 ml	150 ml

From the above coating solution compositions used for coating of tablets SC1 was most optimum and was used to coat the final formulation batches.

Coating of prepared tablets

The prepared concave tablets were loaded to a coating pan and heated for 20 min with the help of hair dryer. The tablets were coated by spray coating using spray gun. The pan speed was kept at 15 rpm and temperature of hot air at temperature of 40˚C was blown over the tablets using hair dryer to dry the coated tablets. The tablets were coated till it attains predetermined weight. Finally coated tablets were dried at 40˚C for 30 minutes[33].

Evaluation of coated tablets of satranidazole

All the batches (SF-1 to SF-8) were evaluated for following parameters.

- **Hardness.**
- **Weight variation.**
- **Friability.**
- **Thickness.**
- **Swelling studies**
- **Assay**

Hardness :Tablets require a certain amount of strength or hardness to withstand mechanical shocks of handling in manufacture, packaging and shipping. The monitoring of tablet hardness is especially important for drug products that possess real or potential bioavailability problems or that are sensitive to altered dissolution release profiles as a function of the compressive force employed. Hardness is also termed as "crushing strength ". Hardness tester (Monsanto

Weight Variation:With a tabled designed to contain a specific amount of drug in a specific amount of tablet formula, the weight of the tablet being made was routinely measured to help ensure that it contains the proper amount of drug. Samples of tablet (20) were taken and weighed throughout the compression process. The composite weight divided by 20, however provides an average weight. The maximum percentage allowed was 7.5 percent. The whole experiment was performed in triplicates.

Friability:Tablets require certain resistance to friability to with stand mechanical shocks of handling in manufacture, packaging and shipping. Adequate resistance to powdering and friability are necessary requisites for consumer acceptance. Friability tester (Veego Friabilator) was used, which subjects a number of tablets to the combined effects of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm, dropping the tablets a distance of six inches with each revolution. Pre weighed tablet sample was placed in the friabilitor, which was then operated for 100 revolutions. The tablets were the dusted and reweighed. The tablets that loose less than 0.5 to 1.0% of the weight were generally considered acceptable. The whole experiment was performed in triplicates.

Thickness:The thickness of a tablet from batch to batch needs to be controlled. Thickness may vary with no change in weight because of difference in the density of granulation and the pressure applied to the tablets, as well as the speed of the tablet compression. Not only is the tablet thickness important in reproducing tablets identical in appearance but also to ensure that every batch will be usable with selected packaging components. Thickness was calculated using vernier caliper.

Swelling studies:Prepared tablets, were subjected to swelling studies at a temperature of 37 ˚C , using the same medias that was used for dissolution studies. Swelling studies were conducted in triplicate for each binder concentration. Radial swelling of tablet width was noted, manually from time to time.

Assay:20 tablets were weighed and powdered. Quantity of powder equivalent to 100 mg of satranidazole was weighed accurately into a 500 ml volumetric flask and dissolved with the aid of water. The solution was diluted to volume with water, mixed and filtered. 20 ml of filtrate was diluted up to 100 ml water, mixed and analysed by UV spectroscopy at 318 nm.

IN VITRO DRUG RELEASE

For targeted drug delivery systems in vitro dissolution studies are important for determining drug availability. Data generated by in vitro dissolution studies can be used by the formulator in the development stages of product and batch to batch uniformity can be ensured. The percentage release of satranidazole (100 mg) from the coated matrix tablet was determined using USP dissolution paddle type apparatus, (model TDT-08I. Electrolab) using 900 ml of specific fluids as dissolution medium. The stirring rate of paddle was 75 rpm and the temperature of medium was maintained at 37˚C±0.5˚C. During the release studies 10 ml samples of dissolution fluid was withdrawn at an interval of 0.5, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 16, 18, 20, 22, and 24 hr and were replaced with fresh dissolution medium subsequently. The samples were analyzed using double beam UV spectrophotometer (Shimadzu) at 318 nm The mean of 3 determinations were used to calculate the drug released from samples.

The drug release studies were conducted in SGF, SIF and SCF in order to mimic the conditions similar to the gastro intestinal tract of human body. The media have been used in the past to evaluate colon specific drug delivery, e.g., like rat cecal content, human stool suspension, and media using one or more enzymes capable of degrading polymers present in the dosage form. Sacrificing the rats is the major disadvantage associated with rat cecal content as dissolution media. The induction of enzyme production in the rat is also a tedious process. Whereas, evaluating drug release using human stool creates problems like viscosity of suspension, incomplete recovery of drug during extraction, drug instability, and variability in the enzyme content[34,35,36].

RESULTS

Preformulation studies of satranidazole

Identification of drug

a) FTIR Spectra of pure Satranidazole.

Table 4. Requirements for FTIR Spectra

Instrument detail		Other details	
Make	Thermo Nicolet Corporation, USA	Temperature	30 °c
Model	IR 200	% RH	27.90%
Laser	Class II IR Diode Laser	No. of scans	24
Accessory	Attenuated Total Reflectance	Resolution	4
Software	EZ OMNIC (S/W), Package,Version 6.2	Correction	ATR

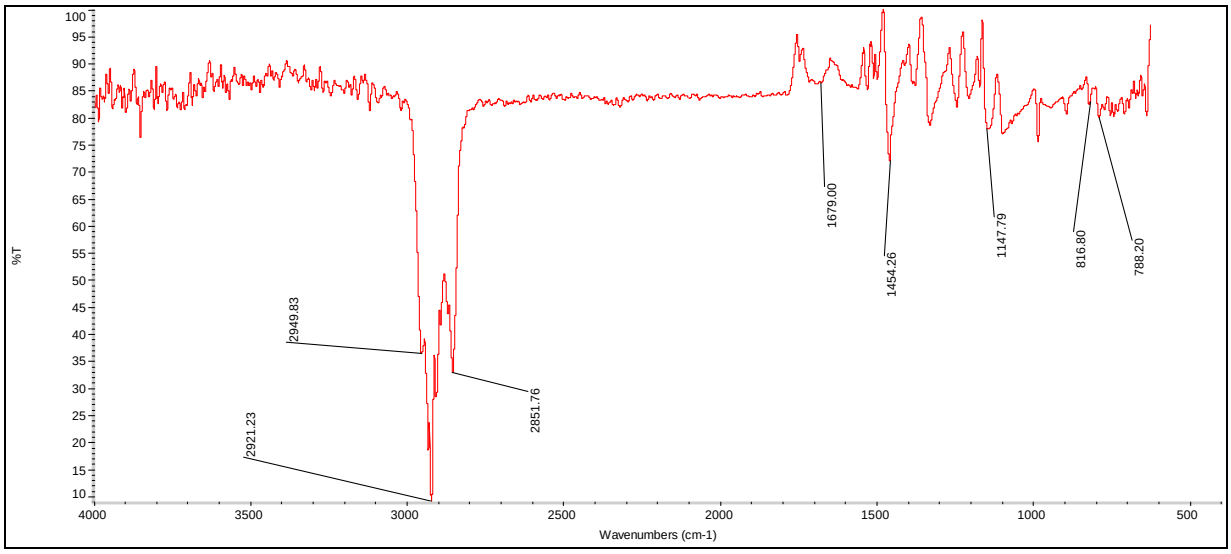

Figure No:3 FTIR spectra of satranidazole

b) UV absorption maxima The λmax was found to be 318 nm and it was as per official literature.

Table 5. Solubility of satranidazole in different media

S No	Medium	Solubility (mg/ml)
1	Water	0.506
2	Simulated gastric fluid	0.612
3	Simulated intestinal fluid	0.493
4	Simulated colonic fluid	0.517

CALIBRATION CURVE OF DRUG BY UV ABSORPTION IN SIMULATED GASTRIC FLUID

Table 6. Calibration Curve in (SGF)**.**

S.No	Conc.(mcg/ml)	Abs.
1	2	0.052
2	4	0.122
3	6	0.19
4	8	0.258
5	10	0.308
6	12	0.395
7	14	0.471
8	16	0.549
9	18	0.582
10	20	0.644

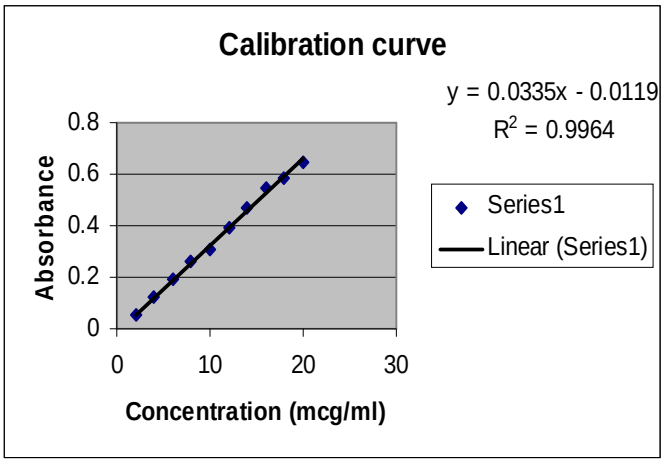

Figure No: 4 Calibration Curve in (SGF).

a) **Simulated Intestinal fluid**

Table 7. Calibration Curve in (SIF).

S.No	Conc.(mcg/ml)	Abs.
1	2	0.023
2	4	0.071
3	6	0.134
4	8	0.179
5	10	0.227
6	12	0.269
7	14	0.334
8	16	0.387
9	18	0.425
10	20	0.472

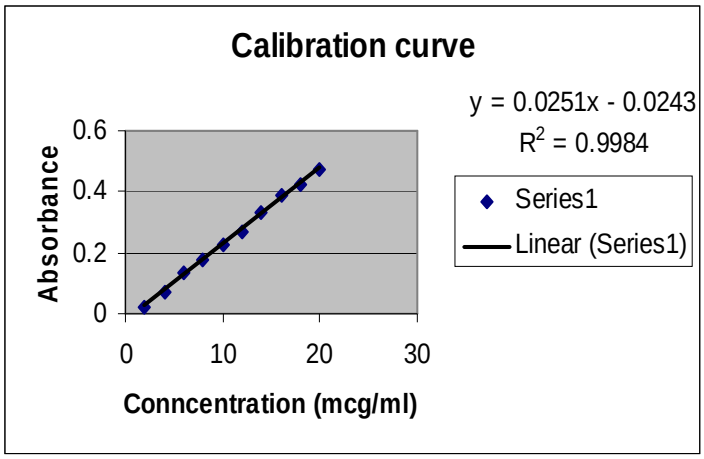

Figure No: 5 Calibration Curve in (SIF).

b) **Simulated Colonic fluid**

Table 8. Calibration Curve in (SCF).

S.No	Conc.(mcg/ml)	Abs.
1	2	0.04
2	4	0.105
3	6	0.172
4	8	0.225
5	10	0.312
6	12	0.351
7	14	0.401
8	16	0.479
9	18	0.519
10	20	0.58

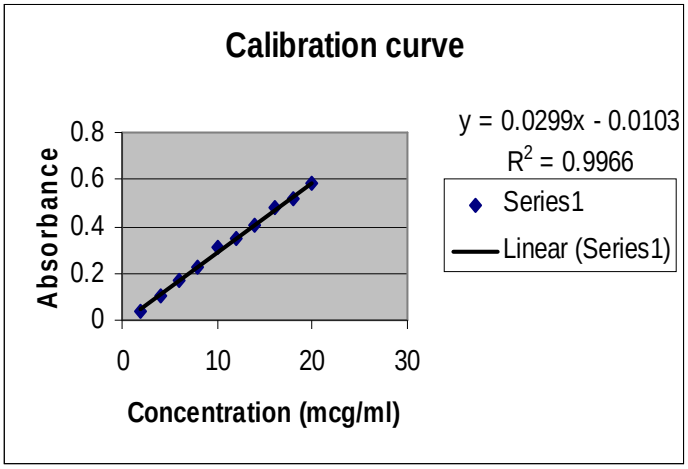

Figure No: 6 Calibration Curve in (SCF).

DRUG – EXCIPIENT INTERACTION

- Physical change

Table 9. Observation of drug mixture with excepients in solid state

S. No.	Excepients	Observation at 50˚C
1	Lactose	No change
2	MCC	No change
3	Guar gum	No change
4	Xanthan gum	No change
5	pectin	No change
6	Guar: Xanthan gum	No change
7	Eudrgit L100	No change
8	Eudrgit S100	No change
9	Talc	No change
10	Magnesium stearate	No change
11	PVP K30	No change
12	Ethylcellulose	No change
13	All Excipients	No change

After three weeks of drug interaction study, from the FTIR spectra of drug plus excipients, it was concluded that there was no interaction between any excipient and drug.

Evaluation of prepared tablet of satranidazole

Table 10. Evaluation of uncoated tablet.

Formulation	Hardness (Kg/sq.cm2± SD)	Friability (%± SD)	Weight variation (mg)	Average Weight (mg)	Drug content (mg)
SF1	7.5± 0.15	0.6±0.023	0.2±0.06	450-455	101.123
SF2	7.4 ± 0.15	0.6±0.012	0.4±0.10	450-455	100.654
SF3	7.4 ± 0.15	0.7±0.056	0.3±0.24	450-455	101.354
SF4	7.6 ± 0.15	0.7±0.034	0.2±0.07	450-455	100.712
SF5	7.4±0.15	0.7±0.021	0.6±0.05	450-455	102.245
SF6	7.5±0.15	0.6±0.041	0.2±0.08	450-455	100.219
SF7	7.4±0.15	0.8±0.052	0.4±0.01	450-455	101.356
SF8	5.7±0.15	0.7±0.039	0.5±0.06	450-455	100.458

Table 11. Evaluation of coated tablets.

S. No.	Parameters	Value obtained
1	Hardness (Kg/cm^2)	12.0-14.0
2	Thickness (mm)	4.25-4.35
3	Percentage weight gain on tablets after coating	9-10 %
4	Appearance of coating	Smooth, transparent without any coating defects

Swelling studies

Table No 12. Swelling studies of Batch SF1 to SF8

Time (hr.)	SF1	SF2	SF3	SF4	SF5	SF6	SF7	SF8
2	0.39	0.33	0.39	0.41	0.42	0.34	0.29	0.36
5	5.89	6.15	6.05	8.05	8.23	6.93	6.14	6.71
10	23.03	23.11	25.19	35.31	37.53	32.44	28.02	35.42
16	44.11	44.26	45.21	71.09	75.31	54.17	50.21	60.09
24	45.59	46.31	48.54	74.35	78.24	56.25	51.32	64.25

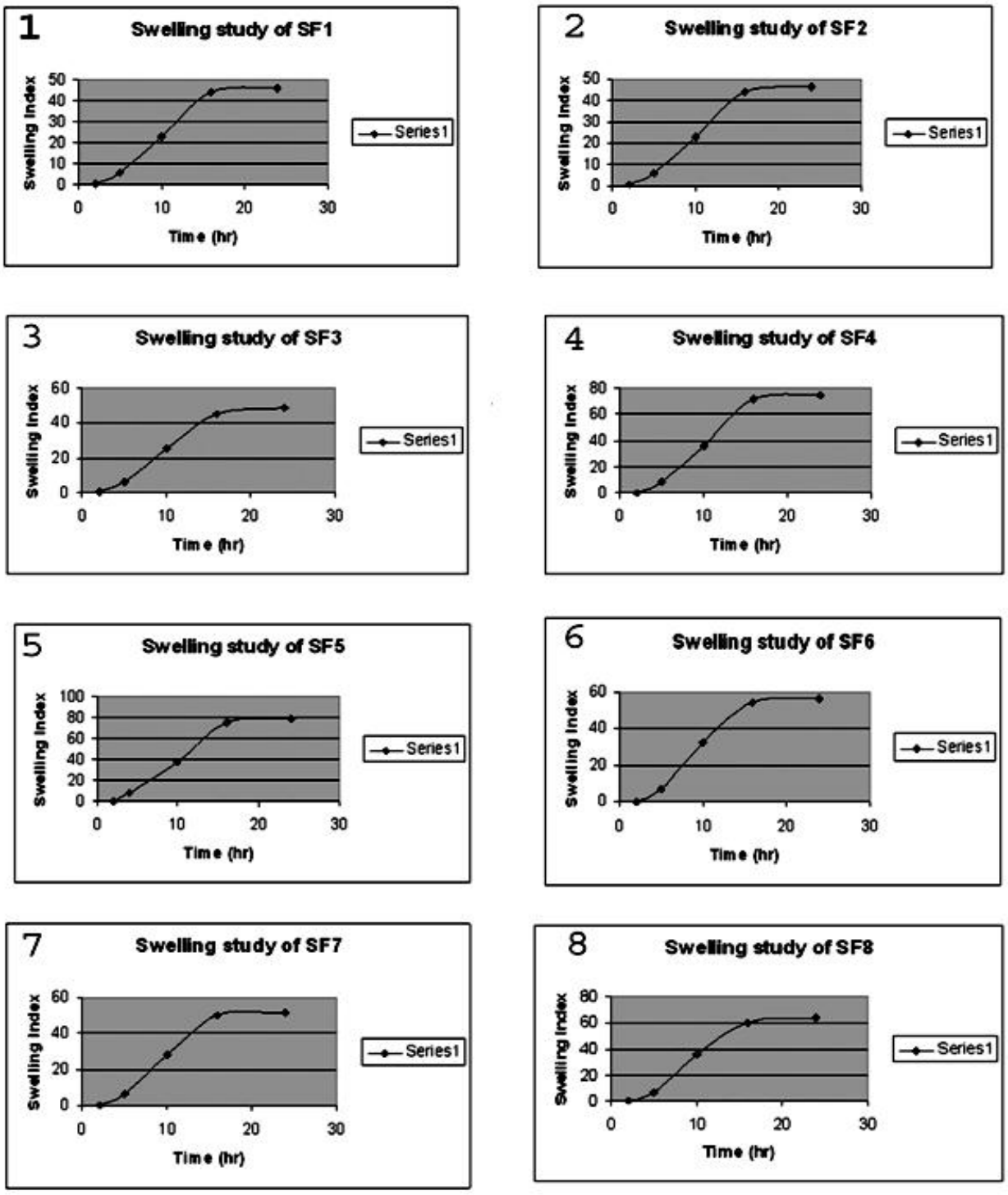

Figure No: 7 Swelling studies of Batch SF1 to SF8

IN VITRO DRUG

Table 13. Cumulative Percentage Drug Release of Batch SF1 to SF8

S. No.	Time (hr)	SF1	SF2	SF3	SF4	SF5	SF6	SF7	SF8
1	1	0.03	0.03	0.03	0.02	0.09	0.02	0.01	0.021
2	2	0.03	0.05	0.04	0.04	0.12	0.03	0.02	0.034
3	3	1.39	1.32	1.27	1.31	1.28	1.22	1.09	1.4
4	4	2.48	2.41	1.93	2.05	2.04	1.34	1.25	2.14
5	5	3.71	3.21	2.85	3.22	3.25	3.05	2.93	6.59
6	6	4.12	3.97	3.21	5.75	5.73	3.53	3.41	8.42
7	8	8.2	7.78	6.64	8.99	9.84	7.12	6.58	24.21
8	10	12.4	11.3	10.1	14.1	14.7	10.9	13.3	32.63
9	12	20.3	18.2	14	21	21.6	19.6	19	59.37
10	14	32.5	31.2	21.2	29.5	29.8	28.3	29.2	83.25
11	16	56.2	54	38.5	39.7	38.4	45.6	54.6	102.2
12	20	77.5	70.4	49.9	58.3	51.8	68.7	72.3	
13	24	85.7	78.5	61.3	72.2	62.2	77.3	80.2	

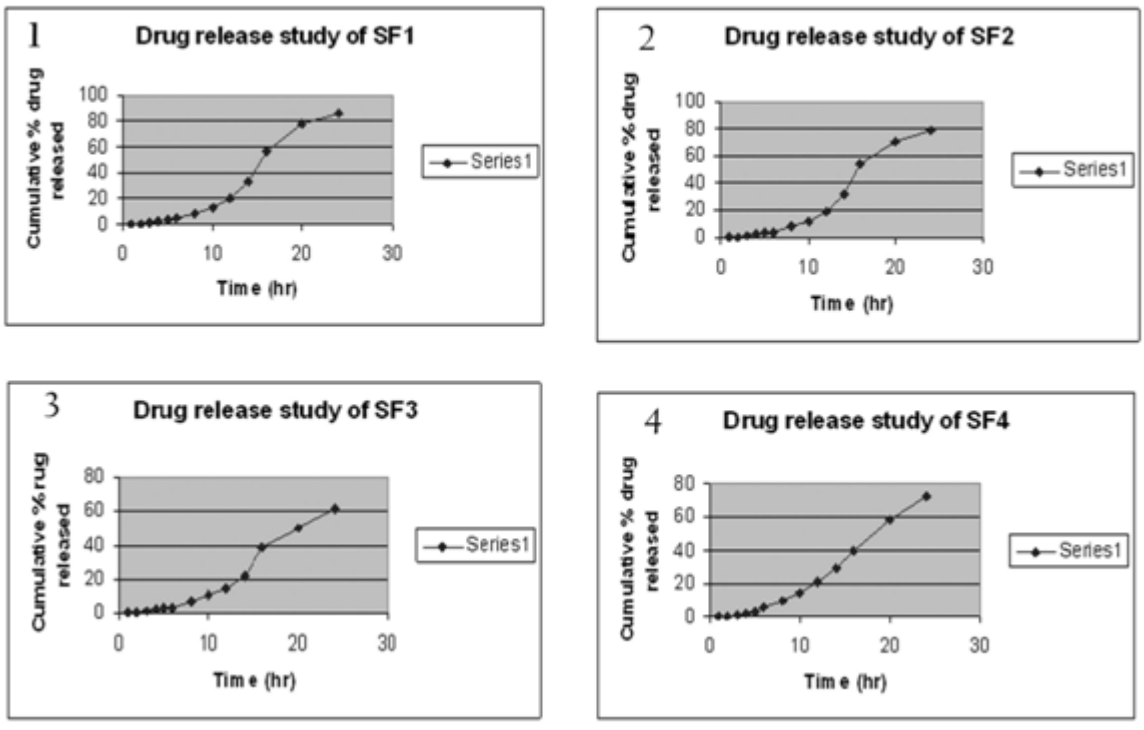

Figure No: 8. Drug release studies of Batch SF1 to SF4

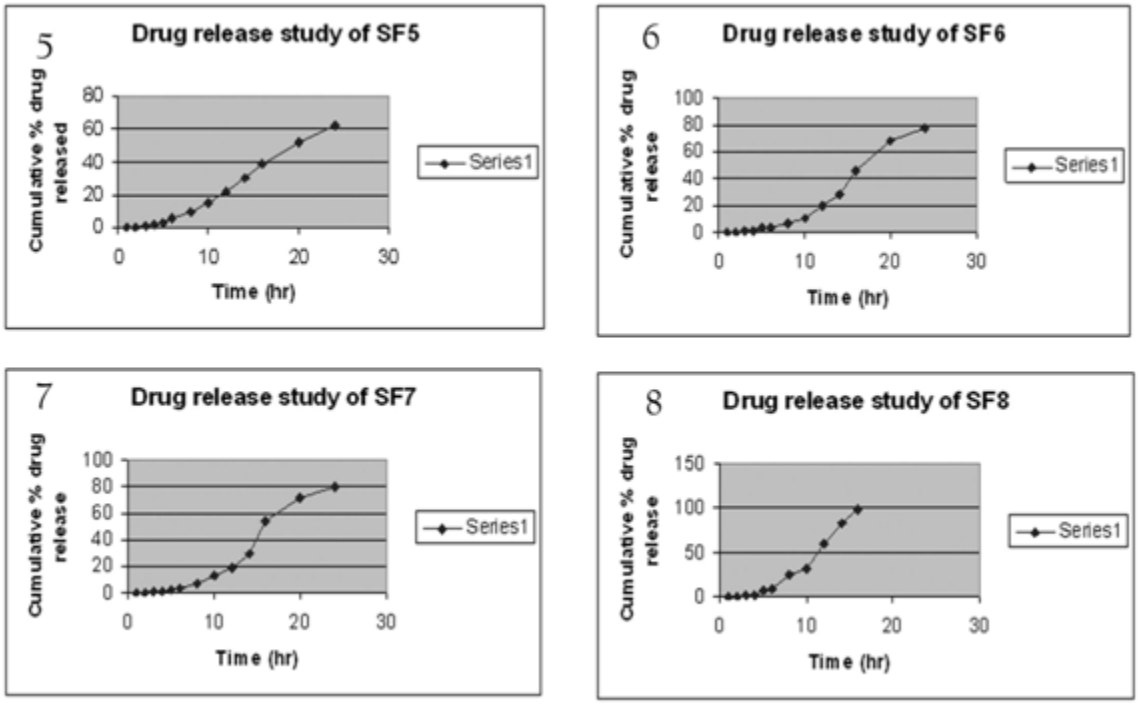

Figure No: 9. Drug release studies of Batch SF5 to SF8

DISCUSSION

UV spectra of satranidazole (50µg/ml) solution in DM water shows peak at wavelength 318 nm. This wavelength was considered as λ_{max} and all the observations by UV spectrophotometer to calculate the amount of drug were taken at this wavelength. Calibrartion curve of satranidazole in Simulated Gastric Fluid, Simulated Intestinsal Fluid and Simulated Colonic Fluid shows straight line in range of 2 to 20 µg/ml with respective R^2 value of 0.9964, 0.9984, and 0.9966 which follows Beer-Lambert law. Swelling study shows that xanthan gum had greater swelling index comparative to other polysaccharides. Studies carried out on swellable matrices have shown that as the concentration of the swellable polymer is increased in the formulation, the gel thickness increases upon swelling. This increases the diffusion path length, which in turn decreases the drug release from the tablet The dissolution studies were performed for all the batches and the release profile of drug was calculated. Maximum percent of drug release was attained in colon in all the batches, After 24 hr. from administration of dose was calculated. Guar gum, xanthan gum, guar xanthan combination and pectin were used as enzyme dependent polymer to reduce the drug release in stomach and small intestine and release the maximum amount of drug into colon. Guar gum was used in three concentrations viz. 20%,

30% and 40% in SF1, SF2 and SF3. Xanthan gum in 20% and 30%, Guar xanthan gum in combination at 20% with ratio (1:1) and (2:1) and pectin 20% and 30%. In all batches control drug release was observed up to small intestine. Batch with guar and xanthan gum in combination in a ratio with (2:1) was found to be most optimum as it releases 80.21% after 24 hour. Presence of xanthan gum in presence of guar gum would allow formation of a thicker viscous gel layer (as compared to while using guar gum alone) on being exposed to the fluids of the GIT. This viscous layer retards seeping of the fluids. Desirable results were found with Guar gum, at 30% concentration which releases 78.51% of drug after 24 hour. But the presence of xanthan gum in the matrix will help form more thicker gels (at a lower gum content) which, in turn, will reduce the gum content of the matrix (making processing easier). Thicker gels will reduce the diffusion of drug to negligible levels. Additionally, xanthan gum being a higher swelling gum and thereby giving greater surface area for the action of hydrolytic enzymes in the colon. Though the percent results showed by SF7 only 80.21% of drug release from the matrix tablet of satranidazole it is possible that the formulation may release majority of the drug in the physiological environment of human colon. This assertion was based on the fact that the human caecal contents would be much higher. PVP K 30 was found to be better as binder as compared to starch paste. Ethyl cellulose were found to better in controlling the drug release in SF8 as pectin is hydrophilic polymer and allow the entry of fluid but with the use of ethyl cellulose it was retarded as it is hydrophobic polymer, even though the drug release was not controlled up to 24 hrs. Formulation SF7 containing 20% guar xanthan combination (2:1) of was able to control 96% of drug of drug release in colon. SF3 also was able to control the 96% of drug of drug release in colon but the results show that SF3 guar gum at 40% concentration formulation was degrading slowly in simulated colonic fluids indicating that 40% of guar gum in the matrix formulation is high enough for the colonic enzymes to act upon the formulation and degrade it. Thus it can be said that combination of guar gum and xanthan gum in 2:1 ratio was most promising for colonic delivery of drug.

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