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Formulation and In vitro Evaluation of Microbially Triggered Colon Specific drug delivery of Satranidazole using Sesbania gum

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ABSTRACT

The colon drug delivery system has gained recent importance in delivery of the drug to the colon. These system facilitate the delivery of the drug to the colon and mainly releases the drug in the colonic environment and thereby reduces various side effects of conventional dosage forms like lower dose is required and hence lowering the side effects caused by higher doses. In the present study natural polysaccharide approach is employed and sesbania gum powder was used as a carrier for delivery of the drug to the colon . Satranidazole was selected as a drug of choice because it is most potent nitroimidazole derivative and clinically useful against common protozoa, it is twice as effective as other nitroimidazoles against amoebiasis. Colon targeted tablet of satranidazole can maintain minimum inhibitory concentration for desired duration in fewer doses with fewer side effects. The aim of the present research work is to develop core tablets of satranidazole and compression coated with different ratios of sesbania gum powder. All the formulations were then subjected for evaluation and were tested for hardness, drug content uniformity an in vitro drug release studies. The compression coated formulation CCS 2 released less than 5% of satranidazole drug in the physiological environment of stomach and intestine, when the dissolution studies was further continued in simulated colonic fluids the compression coated tablets with 150mg of sesbania gum powder released another 70% of satranidazole in the colon after degradation by colonic bacteria at the end of 12 hrs.

Keywords: Satranidazole, compression coated, Microbially triggered, polysaccharides, colon targeted tablets.

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INTRODUCTION

Colon specific drug delivery has gained recent increased importance in the delivery of drugs for the treatment of local disease associated with the colon such as crohn's disease, ulcerative colitis, colorectal cancer, irritable bowel syndrome, inflammatory bowel disease and amoebiasis and for systemic absorption of protein and peptide drugs due to following reasons-

1. Less diversity and intensity of digestive enzymes.
2. Comparative proteolytic activity of colon mucosa is much less than that observed in small intestine due to which hydrolysis and enzymatic degradation of protein and peptide drug are prevented in duodenum and jejunum.
3. Colon drug delivery system releases the drug into ileum or colon which leads to greater systemic bioavailability.
4. Colon has a long residence time (upto 5 days).

Colon drug delivery systems (CDDS) has been developing as one of the site specific drug delivery systems which by means of combining of one or more controlled release mechanism controls release of the drug in the upper part of the gastrointestinal tract (GI) but rapidly releases the drug in the colon after oral administration and the bioactive agent should not be degraded in either of the dissolution sites but only release and absorbed once the system reaches the colon[1].

The necessity and advantages of CDDS have been well recognised and reviewed recently. CDDS are specifically delivering drug to the colon, a lot of benefits would be acquired in terms of improving safety and reducing toxicity when treating local or systemic diseases. CDDS would be advantageous when a delay in absorption is desirable from a therapeutic point of view as for treatments of diseases that have peak symptoms in the early morning and that exhibit circadian rhythms such as nocturnal asthma, angina pectoris and rheumatoid arthritis[2].

Advantages of colon drug delivery systems [2,13] -

1. Reducing dosing frequency, thus lowering cost of expensive drugs.
2. Reduce incidence of side effects and drug interactions.
3. Extended daytime or night time activity.
4. Longer retention time thus enhances the absorption of poorly absorbed drugs.
5. Improve patient compliance.
6. By pass initial first pass metabolism.
7. Reduce gastric irritation.
8. Low hostile environment, less peptidase activity thus peptides, oral vaccines, insulin, growth hormones can be given through this delivery system.

Limitations of colon drug delivery systems-

1. Multiple manufacturing steps.
2. Incomplete release rates.
3. The resident micro flora could also affect colonic performance by metabolic degradation of the drug.
4. Less availability of appropriate dissolution testing methods to check in vitro drug release study.
5. Bioavailability of drug may be lower due to potentially binding of drug in a non specific way to dietary residues, mucus or faecal matter.

Various approaches have been proposed for delivery of drugs to colon namely pH and time dependent systems, pressure controlled systems, osmotic systems, pro-drugs and polysaccharide based delivery system [6,16].

The pH approach has been shown to lack site specificity because of inter or intra subject variation and the similarity of the pH between small intestine and the colon. Time released system depend on the relative consistency of the small intestinal transit time, but the high variability in gastric retention times makes prediction of the accurate location of drug release difficult [6,16].

Pro-drugs and polysaccharide based drug delivery system depends on the enzymatic degradation carried out by the inherent bacterial micro flora present in the colon, thereby resulting drug release. The enzyme trigger mechanism in such delivery systems make them highly site specific [6,17].

Since biodegradable enzymes are present in the colon the use of biodegradable polymers for colon specific drug delivery seems to be most site specific, these polymers shield the drug from the environment of stomach and intestine and are able to deliver drugs to the colon [3,10].

Among the different systems available for targeting drugs to the colon the best alternative approach for colon specific drug delivery is the use of carriers that are degraded by colonic bacteria. The micro flora of the colon is in the range of 10^{11}-10^{12}CFU/ml consisting mainly of anaerobic bacteria e.g. Bacteriocides, Bifidobacteria, Eubacteria, Clostridia, Enterococci, Enterobacteria and Ruminococcus etc [6,8,13].

An attempt has been made to formulate a dosage form that –

1. Retards drug release in upper GI tract.
2. Consisting of polysaccharide as a carrier.
3. Is degradable by colonic micro flora.

4. Shows a rapid release of drug in the colon.

5. Could be formulated using tablet techniques.

As natural polysaccharide are now widely used for the development of dosage form for the delivery of the drug to the colon. A large number of polysaccharide have been studied as a carrier for colon drug delivery of drugs namely chitosan, pectin, cyclodextrins, dextrans, guar gum, locust bean gum, insulin and amylase.

Sesbania gum a natural polysaccharide which is derived from the endosperm of seeds of plant *sesbania grandiflora linn* belonging to family Leguminosae [3,18] . It contains high molecular weight hydro colloidal polysaccharides composed of galactan and mannan units combined through glycosidic linkages [3, 19, 20]. The good swelling characteristics of sesbania gum powder can be valuable in the formulation of sustained release tablets because of controlled drug release due to swelling of polymer and it has a pH dependent swelling this characteristic is valuable in delivery of drugs to colon and sesbania gum has the characteristic of degradation by the the microbial and the enzymatic flora present in the colon.

Satranidazole was selected as the drug of choice because it is the most potent nitroimidazole derivative and clinically useful against common protozoa, it is twice as active as other nitroimidazoles against giardiasis and amoebiasis and have longer t1/2(14hrs) and claimed that has better tolerability no nausea, vomiting, metallic taste, absence of neurological and disulfiram like reactions and it does not produce the acetamide metabolites which is a precarcinogen. It is also significantly more active against anaerobes than other nitroimidazole. Duration of action is 12 hrs [12,13]. Colon specific drug delivery of satranidazole will not only increase the availability of the drug at the target site but may reduce the dose requirement and side effects.

MATERIALS AND METHODS-

Satranidazole was obtained as a gift sample from alkem laboratories Mumbai. PVP K-30 , Talc and magnesium stearate was obtained from S.D Fine Ltd. Mumbai. Sodium starch glycolate was obtained from Merck Ltd Mumbai. All ingredients were of pharmaceutical grade.

Preformulation Studies-

Preformulation studies are done for investigation of physical and chemical properties of a drug substance alone and when combined with excipients. It is the first step in the rational development of dosage forms. Preformulation commences when a newly synthesized drug shows sufficient pharmacologic promise in animal models to warrant evaluation in human. These studies should focus on those physicochemical properties of the new compound that could affect

drug performance and development of an efficacious dosage form. A thorough understanding of these properties may ultimately provide a rationale for formulation design, or support the need for molecular modification. The overall objective of preformulation testing is to generate information useful to the formulation in developing a stable and bioavailable dosage forms. The use of preformulation parameters maximizes the chances in formulating to an acceptable, safe, efficacious and stable product.

IDENTIFICATION OF DRUG-

U.V absorption Maxima:

Selection of solvent:

Methanol was selected as a better solvent for satranidazole, as it is UV transparent and a good solvent for polar and non polar drugs and it causes no degradation and no interference in the peak of satranidazole.

Determination of λmax:

10 mg of satranidazole was transferred to 100ml of volumetric flask, sufficient quantity of methanol was added to dissolve it. The volume was made upto 100ml to make stock solution, then this solution was scanned between 200-400nm in double beam UV/Visible double beam spectrophotometer to obtain UV spectra.

The λmax of satranidazole was found to be 318nm and it was also found as per various official literatures.

IR spectroscopy:

Dried sample of pure drug was scanned with FTIR and peaks obtained was compared with reported spectra. The IR value of obtained spectra were similar to that reported by other authors. Sample and reported IR spectra match with each other this concludes that obtained satranidazole sample is pure.

Melting point measurement:

The Thiels's tube method of melting point determination in liquid paraffin is used for melting point measurement. Drug was finely powdered and then filled in a capillary tube and melting point was measured. Since satranidazole is not in any official pharmacopoeia so the melting point obtained was compared with compared with melting point in different journals.

The melting point of satranidazole was found to be 186-189^{0}C which was compared to reported value(184-189^{0}C).

Solubility:

The study was carried out in glass vials of 10ml capacity. Each vial was filled with 5ml of

distilled water and different dissolution media and excess quantity of satranidazole. The vials were closed with rubber closures and kept for equilibrium at $25^0C \pm 2^0C$ for a period of 24 hrs with continuous shaking the solution were then filtered and analysed for drug content at 318nm.

PREPARATION OF DISSOLUTION MEDIUM-

Preparation of 0.1 N HCl(Simulated gastric fluid, SGF)[26]:

0.1 N HCl was prepared by diluting 8.5 ml of concentrated hydrochloric acid to 1000ml with distilled water.

Preparation of pH 7.4 phosphate buffer (Simulated intestinal fluid, SIF)[26]:

50 ml of 0.2 M potassium dihydrogen phosphate was placed in a 200 ml volumetric flask, add 39.1 ml of 0.2 m sodium hydroxide and then add distilled water to make volume to 200 ml.

Preparation of pH 6.8 phosphate buffer(Simulated colonic fluid, SCF)[26]:

50 ml of 0.2 M potassium dihydrogen phosphate was placed in a 200 ml volumetric flask, add 22.4 ml of 0.2 m sodium hydroxide and then add distilled water to make volume to 200 ml.

Table 1.Solubility of satranidazole in different media

S.No	Medium	Solubility(mg/ml)
1	Water	0.509
2	Simulated gastric fluid	0.612
3	Simulated intestinal fluid	0.493
4	Simulated colonic fluid	0.517

Calibration curve of drug in different dissolution medium:

The calibration curve of estimation was prepared in three different dissolution medium i.e 0.1N HCl (pH 1.2 simulated gastric fluid), pH 7.4 phosphate buffer (simulated intestinal fluid) and pH 6.8 phosphate buffer (simulated colonic fluid).

10mg of satranidazole was weighed and transferred to 100ml volumetric flask. The drug was dissolved in 0.1 N HCl and then the volume was made to 100ml to obtain the final concentration of 100µg/ml.This stock solution was scanned for the maximum absorbance using U.V visible double beam spectrophotometer.

From this stock solution 2.5, 5, 7.5, 10, 12.5, 15, 17.5 and 20µg/ml concentration satranidazole solution were prepared. Similarly calibration curve was carried out in pH 7.4 phosphate buffer and pH 6.8 phosphate buffer solution.

Drug excipient interaction-

Drug and various excipients were mixed in ratio 1:1 and were stored at room temperature and at 50^0C in closed vials. 10% W/W water was added in the samples which were kept at 50^0C to study effect of moisture. After three weeks samples were scanned with FTIR before and after

storage .The spectra of pure drug and drug with excipients were compared to check incompatibility. No incompatibility was found.

Method-

Pre-compression studies of granules-

Angle of repose [24]:

The angle of repose of granules was determined by funnel method. The accurately weight granules were taken in the funnel. The granules were allowed to flow through the funnel freely on to the surface. The diameter of the granules cone was measured and the height of the granule blend was measured and the angle of repose was calculated using the following equation-

$$\text{Tan } \Theta = h/r$$

Where, h=height of the powder cone, r=radius of the powder cone

Bulk density [24]:

Both loose bulk density (LBD) and tapped bulk density (TBD) was determined. A quantity of 2gm of granules from each formula previously shaken to break any agglomerates formed and was introduced into 10ml measuring cylinder .After that the initial volume was noted and the cylinder was allowed to fall under its own weight on to a hard surface from the height of 2.5 cm at second intervals. Tapping was continued until no further change in volume was noted. LBD and TBD were calculated using the following equations-

LBD = weight of the granules / untapped volume of the packing

TBD = weight of the granules / tapped volume of the packing

Compressibility index [24]:

The compressibility index of the granules was determined by carr's (compressibility index). It is a simple test to evaluate the LBD and TBD of a granules and the rate at which it packed down. The formula of Carr's index is as below-

Carr's index (%) = (TBD-LBD)*100/TBD

Preparation of satranidazole core tablet-

Satranidazole, di-calcium phosphate, sodium starch glycolate were weighed, grinded in mortar pestle to reduce the size and passed through 100 mesh sieve and blended manually in polyethylene bags so to ensure proper mixing. The blended powder was granulated by adding sufficient quantity of 10% PVP K-30 in isopropyl alcohol as 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}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 talc in polyethylene bag. Then the granules

were compressed into tablets with hand operated single punch tablet machine.

Preparation of sesbania gum coat formulation-

The compression coat formulations were prepared with varying concentration of sesbania gum powder. Sesbania gum powder, di-calcium phosphate was weighed and grinded in mortar pestle to reduce size and passed through 100 mesh sieve and blended manually in polyethylene bag to ensure proper mixing. The blended powder was granulated by adding sufficient quantity of 10% PVP K30 in isopropyl alcohol as a binder to obtain a mass of proper wetness and the mass was passed through sieve no.12 to obtain granules and dried at 40^0C for 30 minutes. Dried granules was passed through 20 mesh sieve to obtain uniform sized granules and mixed with 1% of magnesium stearate and 2% of talc in polyethylene bag. The blend was now ready for compression.

Compression coating of satranidazole core tablets-

Satranidazole core tablets were compression coated with different ratio of sesbania gum coat formulation. Initially 50% of coat material was placed in die cavity of tablet compression machine followed by entering the core tablet and addition of remainder coat material. The coating material was compressed around the core tablet with high compression force in tablet punching machine.

EVALUATION OF THE CORE AND COATED TABLETS:

Tablet hardness[21]:

The hardness of the tablets was determined by using Monsanto hardness tester. It is expressed in terms of Kg/cm^2. The tablets were randomly selected from batches of each formulation and the mean and standard deviation value were calculated.

Weight variation[21]:

Twenty tablets were randomly selected from each formulation and average weight was measured. Then individual weight of tablet were measured and compared with average weight. It is the variation under limit within the Indian Pharmacopoeia (I.P), then tablets pass the weight variation test.

Table 2. Weight Variation Specification as per I.P

Average Weight of Tablet	% Deviation
80 mg or less	±10
More than 80 mg but less than 250 mg	±7.5
250 mg or more	±5

Friability[21]:

The friability of tablets was determined by Rouche Friabilator. It is expressed in the terms of

percentage. Ten tablets was initially weight ($W_{initial}$) and transferred into the Rouche Fribilator. The friabilitor was operated and rotated at 25 rpm for 4 minutes i.e. 100 rotations. The tablets were dusted off and weight again (W_{final}). The percentage friability was then calculated by the fallowing formula:

$$F = \frac{W_{initial} - W_{final}}{W_{initial}} \times 100$$

Percentage friability of tablet less than 1% is considered as acceptable.

Drug Content[24]:

Five tablets were individually weighed and powdered. The powder equivalent to average weight of tablet was weighed and drug was extracted in phosphate buffer pH 6.8.The drug content was determined by measuring the absorbance at 318nm after suitable dilution using a UV-Visible double beam spectrophotometer.

In-vitro drug release studies-

Drug release studies were carried out using a dissolution rate test apparatus (Apparatus 1, 100 rpm, 37 °C) for 2 hr in simulated gastric fluid (0.1 M HCl (900 ml)) as the average gastric emptying time is about 2 hr. Then the dissolution medium was replaced with simulated intestinal fluid pH-7.4 (900 ml) and tested for drug release for 3 hr as the average small intestinal transit time is about 3 hr. After 5 hr the dissolution medium was replaced with simulated colonic fluid pH 6.8 (900 ml) and tested for drug release up to 12 hr. At the end of the time period 10 ml of the samples were taken and analyzed for satranidazole content. A 10 ml volume of fresh and filtered dissolution medium was added to make the volume after each sample withdrawal.

In vitro drug release studies in the presence of 4 %w/v rat cecal media-

The drug release studies were carried out in dissolution rate test apparatus (apparatus 1, 100 rpm, 37°C) with slight modification. A beaker (capacity 150 ml) containing 100 ml of dissolution medium was immersed in the water contained in the 1000 ml vessel, which in turn, was the water bath of the apparatus. The swollen formulations after completing the dissolution study in simulated gastric fluid 0.1 M HCl (2 hr) and simulated intestinal fluid pH-7.4 (3 hr) were placed in the baskets of the apparatus and immersed in the dissolution medium containing rat caecal content medium. The experiment was carried out with continuous CO_2 supply into the beakers to simulate anaerobic environment of the cecum. The drug release studies were carried out up to 12 hr and 1 ml samples were withdrawn at specified time intervals without a pre- filter and replaced with 1 ml of fresh PBS bubbled with CO_2. 1 ml of methanol was added in sample and was analyzed for satranidazole content.

Statistical analysis [22, 23]-

The cumulative percent of satranidazole released from the compression coated tablets in the dissolution medium up to 12 hr with and without rat cecal contents was compared using USP dissolution specification, *f2* value, a similarity factor. A value less than 50 was considered significant value indicating dissimilarity in dissolution profiles.

This similarity factor is calculated by following formula-

$$f2 = 50 \text{ x } \log \{[1 + (1/n) \sum_{j=1}^{n} | Rj - Tj |^2]^{-0.5} \text{ x } 100 \}$$

When n is the number of dissolution time and Rj and Tj are the reference and test

RESULTS AND DISCUSSION

Three formulation of satranidazole drug was prepared with varying concentration of sesbania gum powder. The core tablets of satranidazole were compression coated with a coat formulation consisting of various strength of sesbania gum powder.

The calibration curve of the drug in simulated gastric fluid, simulated intestinal fluid, and simulated colonic fluid shows straight line in range of 2.5 – 20 µg/ml concentration with respective R^2 values of 0.9995, 0.9991, 0.9997 which follows beers-lambert law.

Three batches of formulation was prepared namely CCS1, CCS2, CCS3 there composition and formula are shown in table no. 6 and table no. 7.

Pre-compression studies-

The granules of the tablet preparation were prepared according to formula given in table no.6 and 7. The granules of different formulation were evaluated for angle of repose, LBD and TBD and compressibility index the results of angle of repose ranges from 23.90 ± 0.11 to 29.85 ± 0.01 indicate good flow properties and this was supported by lower compressibility index which ranges from 9.2 ± 0.005 to 10.5 ± 1.387, generally compressibility index values from 8.7 ± 1.039 to 12% result in good flow properties. All these results indicate that the granules possessed satisfactory flow properties and compressibility.

Post-compression studies-

Tablets of different formulations were subjected to various evaluations test like uniformity of weight, drug content, hardness and friability. The percentage drug content of all batches was more than 99%. The hardness of tablets was found to be in the range 4.1 ± 0.5 to 5.3 ± 0.6 indicate to have better binding properties of granules. The percentage friability of all the formulations was below 1% indicating that friability is within prescribed limits. The hardness of

core tablet was found to be 4.1 ± 0.5 and the hardness of compression coated tablets was found in range 5.2 ± 0.3 to 5.3 ± 0.6. All the formulation showed acceptable pharmacopoeial limits for weight variation, drug content, friability and hardness.

In vitro drug release study-

The cumulative amount of drug release from compression coated formulations CCS1,CCS2,CCS3 containing 100, 150, 200 mg sesbania gum powder respectively was found to 76.37%, 3.96% and 3.13% respectively after 5hr of the dissolution study in simulated gastric, intestinal and colonic fluids. It shows that formulation CCS1 gives fast drug release in simulated gastric and intestinal fluids which may be due to lower amount of sesbania gum i.e sesbania gum as 100mg coat was not able to retard the drug release in simulated gastric and intestinal fluids and the formulation CCS2 and CCS3 were capable of protecting release in the physiological environment of stomach and intestine.

For further drug release studies dissolution test was carried out without and without addition of rat cecal medium to pH 6.8 phosphate buffer solution. At the end of 12 hrs the percent drug release was 99.84, 39.26 and 22.63 without the addition of rat cecal medium. And when the dissolution study was carried out in rat cecal medium the percent drug release were 99.97, 75.61 and 28.36 at the end of 12 hrs. For the formulation CCS3 no significant difference was observed in drug release with and without rat cecal medium which might be due to presence of higher amount of sesbania gum which not degrade completely during time of testing.

Table 3. Calibration curve in simulated gastric fluid-

Sr.No	Conc(µg/ml)	Absorbance
1.	0	0
2.	2.5	0.123
3.	5	0.245
4.	7.5	0.366
5.	10	0.506
6.	12.5	0.625
7.	15	0.751
8.	17.5	0.886
9.	20	0.990

Table 4. Calibration curve in simulated intestinal fluid-

Sr.No	Conc(µg/ml)	Absorbance
1.	0	0
2.	2.5	0.102
3.	5	0.186
4.	7.5	0.277
5.	10	0.356
6.	12.5	0.462

7.	15	0.543
8.	17.5	0.623
9.	20	0.706

Table 5. Calibration curve in simulated colonic fluid-

Sr.No	Conc(µg/ml)	Absorbance
1.	0	0
2.	2.5	0.108
3.	5	0.209
4.	7.5	0.308
5.	10	0.410
6.	12.5	0.517
7.	15	0.617
8.	17.5	0.705
9.	20	0.812

Table 6. Composition of fast disintegrating core tablets of satranidazole -

Ingredients	Quantity(mg)
Satranidazole	200
Dicalcium phosphate(anhydrous)	22.5
Sodium starch glycolate	10
PVP-K30	10
Talc	5
Magnesium stearate	2.5

Table 7. Composition of sesbania gum coat formulation

Ingredients	Quantity(mg) present in the coat formulation		
	CC1	CC2	CC3
Sesbania gum	100	150	200
Dicalcium phosphate(anhydrous)	115	65	15
PVP-K30	10	10	10
Talc	4	4	4
Magnesium stearate	2	2	2

Table 8. Results of pre-compression studies of granules of core tablet of satranidazole-

Formulation	Bulk Density(gm/cm^3)	Tapped Density(gm/cm^3)	Car's index(%)	Angle of repose
Core granules	0.412±.0045	0.462±.0052	9.5±.115	27.39±.04

Table 9. Results of pre-compression studies of granules of sesbania gum powder coat formulation-

Formulation	Bulk Density(gm/cm^3)	Tapped Density(gm/cm^3)	Car's index(%)	Angle of repose
CC1	0.418±.0022	0.464±.0057	10.5±1.387	26.89±.07
CC2	0.411±.0044	0.46±.0051	9.6±.114	29.85±.01
CC3	0.407±.0020	0.447±.0035	9.2±.005	23.90±.11

Table 10. Results of post-compression studies of satranidazole core and compression coated tablets

Tablets	Hardness(kg/cm^2)	Friability(%)	Weight variation(mg)	Drug content(%)
Core tablet	4.1±0.5	0.65±0.02	249±3.14	99.42±0.31
CC1	5.2±0.3	0.55±0.07	481±5.63	99.30±0.25
CC2	5.5±0.5	0.59±0.05	478±4.50	98.61±0.63
CC3	5.3±0.6	0.45±0.06	482±2.14	101.20±0.31

Table 11. In vitro dissolution data of formulation CCS1 with and without rat caecal medium-

Sr No.	Time (Hours)	% Release(without rat caecal media)	% Release(with rat caecal media)
1.	1	25.47	23.67
2.	2	48.85	47.95
3.	3	67.11	64.41
4.	4	76.37	74.87
5.	5	80.53	79.33
6.	6	87.08	87.08
7.	7	93.34	94.84
8.	8	97.8	99.30
9.	9	99.55	99.55
10.	10	99.80	99.87
11.	11	99.82	99.91
12.	12	99.94	99.97

Table 12. In vitro dissolution data of formulation CCS2 with and without rat caecal medium-

Sr No.	Time (Hours)	% Release(without rat caecal media)	% Release(with rat caecal media)
1.	1	2.13	2.44
2.	2	2.74	3.06
3.	3	3.76	3.35
4.	4	3.96	4.28
5.	5	4.58	4.89
6.	6	7.72	8.35
7.	7	10.55	15.62
8.	8	16.87	21.61
9.	9	23.81	33.31
10.	10	27.59	48.49
11.	11	33.27	67.15
12.	12	39.26	75.61

Table 13. In vitro dissolution data of formulation CCS3 with and without rat caecal medium-

Sr No.	Time (Hours)	% Release(without rat caecal media)	% Release(with rat caecal media)
1.	1	1.29	0.05
2.	2	1.90	0.13
3.	3	2.63	1.19

4.	4	3.13	2.52
5.	5	4.05	2.82
6.	6	5.28	5.28
7.	7	5.90	7.44
8.	8	7.44	10.82
9.	9	8.05	13.28
10.	10	16.05	18.81
11.	11	19.72	22.61
12.	12	22.63	28.35

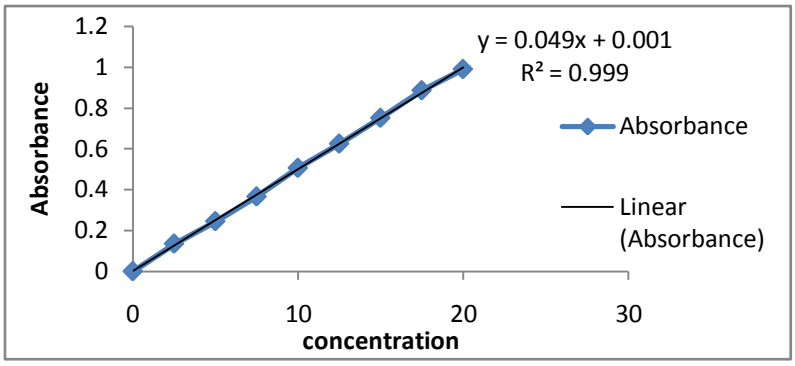

Figure 1.Calibration curve in simulated gastric fluid

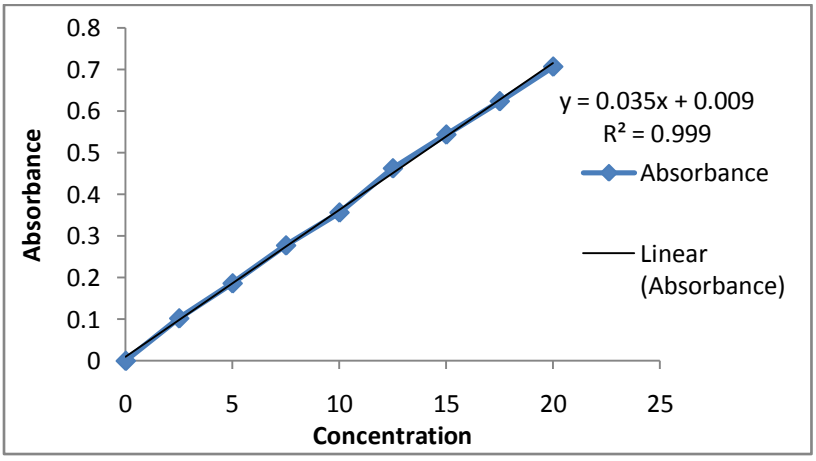

Figure 2.Calibration curve in simulated intestinal fluid.

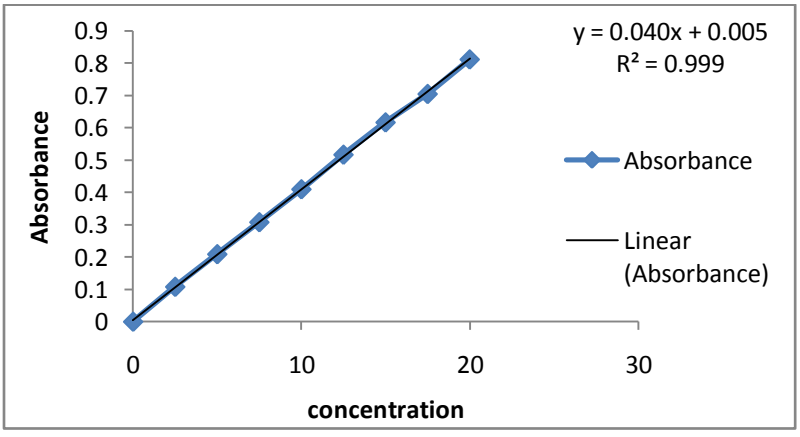

Figure 3.Calibration curve in simulated colonic fluid.

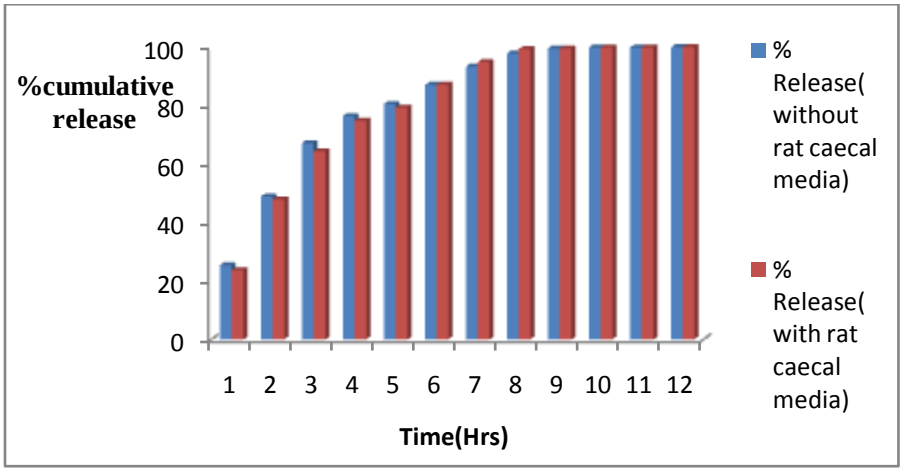

Figure.4:In-vitro drug release profile of formulation CCS1 with and without rat caecal media.

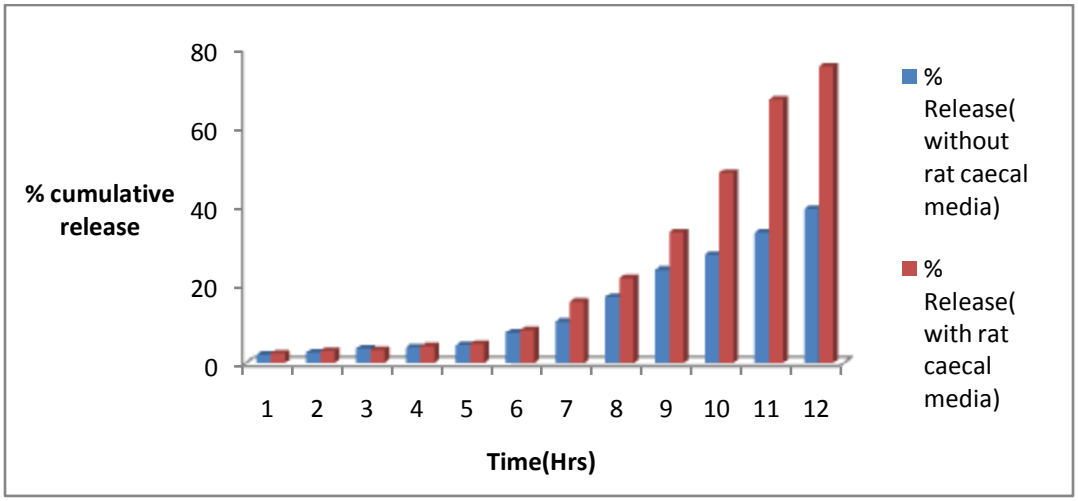

Figure.5: In-vitro drug release profile of formulation CCS2 with and without rat caecal media.

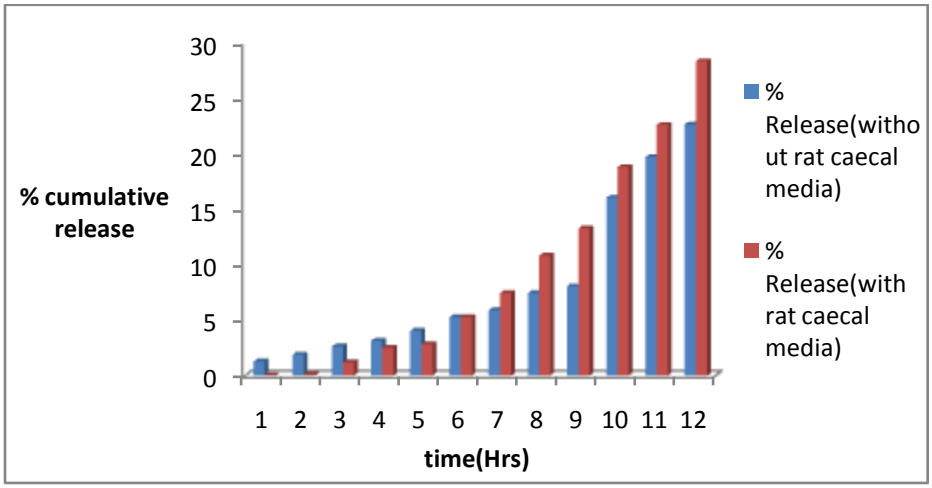

Figure.6: In-vitro drug release profile of formulation CCS3 with and without rat caecal media.

CONCLUSION-

From the above results it can be concluded that the sesbania gum as 100mg coat weight was found insufficient to protect satranidazole release till 5hrs of dissolution studies. The compression coated satranidazole tablets coated with sesbania gum as 150mg provided best control the drug release till colon since it provides best degradation in simulated colonic fluids and it appears that compression coated satranidazole tablets with 150mg sesbania gum coat formulation is most likely to provide targeted delivery of satranidazole to the colon.

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