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RESEARCH

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Satranidazole-loaded chitosan/locust bean gum/xanthan gum polysaccharide composite multiunit pellets for colon targeting: in vitro–in vivo investigation

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Abstract

Background: The colon has a significant site to deliver numerous active materials for colonic diseases. Highly biodegradable polymers hold significant promise among the several techniques available to deliver the drug to the colon. This research aimed to prepare chitosan, locust bean gum and xanthan gum polysaccharide composite satranidazole multiunit pellets for colonic release and assesses the bioavailability with pharmacokinetic parameters after administration of satranidazole raw drug compared to multiunit pellets. Satranidazole multiple unit pellets were prepared based on chitosan, locust bean gum and xanthan gum, which were inexpensive and harmless. The bioavailability study was done by crossover design in which satranidazole raw drug and test formulation was administered to six healthy white albino rats.

Results: The pharmacokinetic analyses were estimated using the deconvolution of the plasma profile. Compared to the satranidazole drug used as a reference, for the pellets, the maximum plasma concentration was lower (35.02 ± 3.91 ng/ml vs. 51.07 ± 1.21 ng/ml for the satranidazole drug), and the time to attain maximum concentration was 2.50 ± 0.55 h for both drugs and test formulation. Colonic drug content was significantly higher than that of free administered drug.

Conclusion: The results indicate the acquired pharmacokinetic studies and colonic analysis established the reliability of the pharmaceutical technique and the ability to release satranidazole at the colonic site.

Keywords: Satranidazole, Colon targeting, Polysaccharide, Multiunit pellets, In vitro–in vivo investigation

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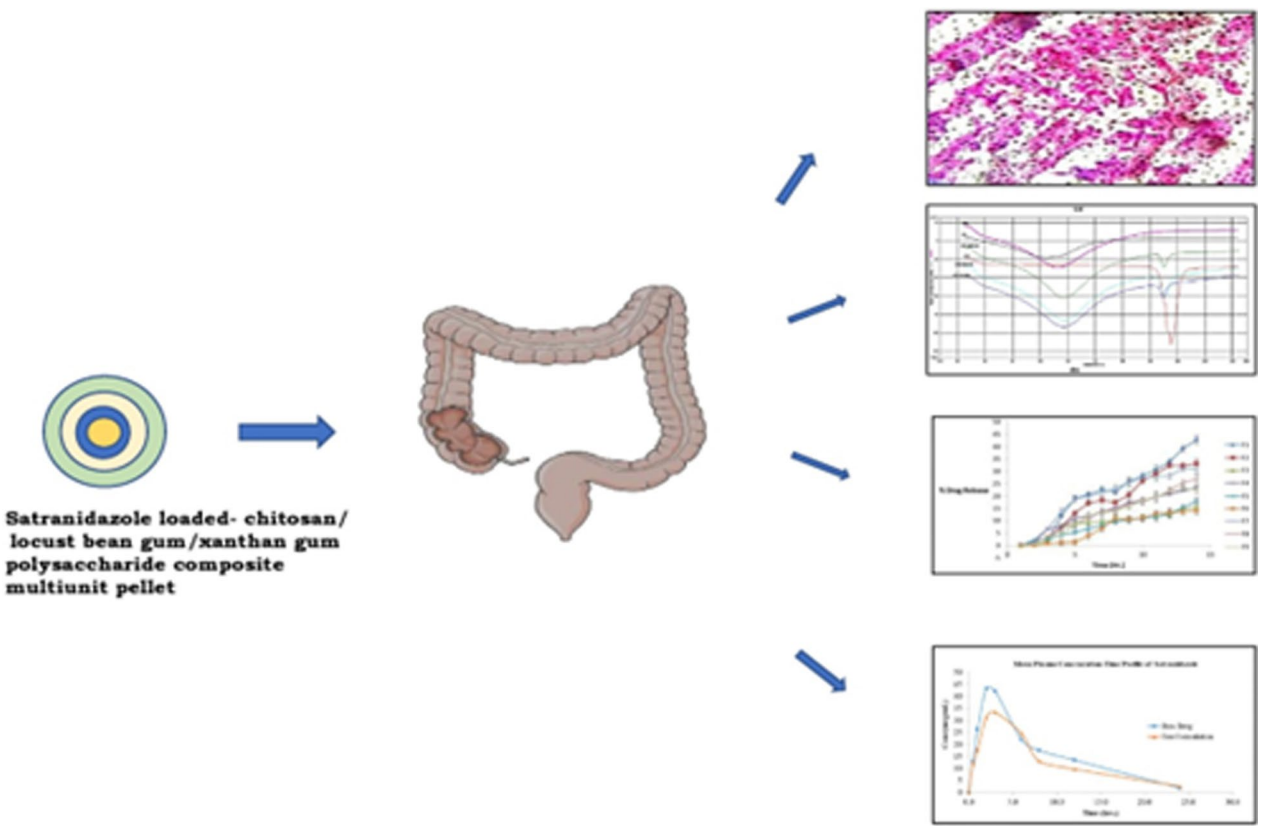
Graphical Abstract



1 Background

The colon is a major site that can deliver bioactive materials to the colon for colonic diseases and transport peptides or proteins into the colonic area for systemic absorption [1]. Highly biodegradable polymers hold significant promise among the several techniques available to deliver the drug to the colon. Locust bean gum has sparked interest in the biopharmaceutical area, particularly in oral administration, which delivers a precise dose to a specific biological site. Its solubility, molecular weight and chemical structure suggest that it could be utilized for in vivo biodegradation with specialized biopharmaceutical applications [2]. Chitosan has a cationic character that delivers drugs to the colon through mucosal attachment. Drugs are controlled by a multiparticulate system containing chitosan due to their biodegradability in the colon [3]. Xanthan gum has a high molecular weight with a side chain attached to glucose residue, enhancing the fabrication of matrices and retards drug release while maintaining time-dependent properties [4]. Polysaccharides have been studied to deliver specific drugs from the colon [5]. The acceptance of these materials as pharmaceutical excipients is their most advantageous feature.

Multiunit pellet dosage forms are more important in the pharmaceutical field and have several advantages over single-unit dosage forms. Pellets that can be encapsulated or compressed into tablets are widely accepted by the patient due to reduced transport difficulties from the esophageal area, lower cost, higher production rate, higher bioavailability, reduced systemic toxicity and predictable gastric emptying [6]. The pellets, as colonic release systems are coated with natural polysaccharides, capable of controlling the release of a drug by erosion or matrix dissolution mechanism through its enzymatic degradation by the colonic microflora and allow the drug to reach quickly and be reserved in the ascending part of the colon over a longer time with its smaller particles size compared to single-unit form. Therefore, the current

study focused on satranidazole powder layered colon-specific multiunit pellets [7, 8] based on the mixture of various natural polysaccharides.

Satranidazole is a 5-nitroimidazole group covered at the second position, named 1- methylsulfonyl-3-(1-methyl-5nitro-2-imidazolyl)-2-imidazolidinone and contains potential anti-disease activity protozoa and bacteria for the treatment of amoeba disease [9].

This research, based on using satranidazole drug for the colonic drug delivery system, is essential because the drug reached the colon quickly and was retained in the ascending colon for a longer time. The smaller size of the pellets made of satranidazole pellets allowed for easier drug passage through the GI tract. Satranidazole has a higher absorption rate than metronidazole [10, 11] and is more effective against protozoal infections. Satranidazole is also very patient-friendly and does not cause neurological reactions. This is helpful for patients with neurological side effects [12]. The research work aimed to develop multiunit layered satranidazole pellets based on coated polysaccharides that provided enzymatic and microbial degradation to release the drug into the colon and compare pharmacokinetic parameters after raw satranidazole drug administration to pellets. The pellets were coated with chitosan, locust bean gum and xanthan gum that were cheap and non-toxic and were organized efficiently by a multiunit system that ensured consistent medication distribution and release throughout the GIT with low variability. The requirement for in vivo investigations, particularly of pharmacokinetic characteristics with colonic analysis, revealed the pharmaceutical system's reliability and prevented satranidazole's release in the GIT, which was intended for the colonic region.

2 Methods

2.1 Materials

Alkem Laboratories Ltd., Sikkim, India, provided satranidazole. Xanthan gum, locust bean gum and chitosan gum were procured from Merck Specialities Pvt. Ltd., Mumbai, India. Anthem Biosciences, Bangalore, India, provided nonpareil sugar seeds. Loba Chemie Ltd., Mumbai, provides HPMC-K10 and PVP-K30. The solvents and chemicals that remained were of analytical grade.

2.2 Method of satranidazolemultiunit pellets

Satranidazole layered multiunit pellets were made by powder layer technology [13] using pan coating equipment that maintained all instrument parameters. Main core loading, powder application rate, type, plate speed, atomizing pressure, atomizer position, air cap type and bed temperature were taken to determine the best grades of pellets. The nonpareil sugar beads were coated with a binder polyvinyl pyrrolidone with isopropyl alcohol and purified water in a 70:30 ratio stirred at 200 rpm [14]. It was applied with spray guns and with a dispersed powder layer satranidazole drug delivered by a specially designed powder feed unit. Satranidazole layered pellets have been carried out using xanthan gum and locust bean gum blend (2:1) and locust bean gum and chitosan mixture (1:2) as film coating materials. Seal coating was used before film coating to prevent migration of the drug layer in the formulation [15] HPMC was used as the seal coating material in concentrations ranging from 5 to 15%. Eighteen batches were formed, as given in Table 1.

2.3 Drug polymer interaction studies

2.3.1 Fourier transform infrared spectroscopy study

An FTIR spectrophotometer was used to record infrared (IR) spectra between 4000 and 400 cm^{-1} utilizing the KBr pellet technique (PerkinElmer) [16] STZ, and a physical combination of STZ with polymers was tested to establish drug compatibility with polymers.

2.3.2 Differential scanning calorimeter study

Thermograms were achieved by a PerkinElmer differential scanning calorimeter (Pyris 6 DSC, Switzerland). Samples of 3 mg were weighed into aluminum pans and then sealed with aluminum caps [17]. Thermograms were obtained at 10 °C/min and a temperature of 50–350 °C. All of the trials were carried out twice.

2.4 In vitro drug release technique

The drug release study was selected using a USP paddle-type dissolution device with 900 ml of dissolving fluid at 37 °C ± 0.5 °C, maintaining a 50 rpm speed. The dissolution technique was performed by altering the pH of the dissolution medium at different period intervals with maintaining proper sink conditions. Here, 300 mg of pellets was weighed accurately and dissolved into 900 ml of medium. It was achieved using pH 1.2 in simulated gastric juice for 2 h, pH 4.5 in mixed simulated gastric and intestinal juice for 3 to 4 h, pH 7.4 in simulated intestinal liquid for 5–6 h and pH 7 in simulated colonic medium from 7 h onwards [18]. The process was done by withdrawing 1 ml of each sample and replacing it with the same amount of medium in the basket. The volume was increased to 10 ml and centrifuged properly. The solution was filtered using Whatman paper, and drug contents were measured at 320 nm in the UV (Shimadzu) spectrophotometer.

Table 1 Formulation of satranidazole multiunit pellets

Batch no	Batch code[a]	Ratio of coating mixture (locust bean gum:xanthane gum and locust bean gum:chitosan gum) (%)	Coating level (%)
1(F1)	LX	50	20
2(F2)	LX	50	10
3(F3)	LX	33.3	30
4(F4)	LX	33.3	10
5(F5)	LX	66.7	10
6(F6)	LX	66.7	30
7(F7)	LX	50	30
8(F8)	LX	33.3	20
9(F9)	LX	66.7	20
10(F10)	LC	50	20
11(F11)	LC	33.3	20
12(F12)	LC	66.7	20
13(F13)	LC	50	10
14(F14)	LC	50	30
15(F15)	LC	33.3	10
16(F16)	LC	33.3	30
17(F17)	LC	66.7	10
18(F18)	LC	66.7	30

[a] Batch no 1 to 9 (LX) = Locust bean gum:xanthan gum as a coating blend with 10 to 30% coating level and batch no 10 to 18 (LC) = locust bean gum:xanthan gum as a coating mixture with 10 to 30% coating level

2.5 In vivo study

2.5.1 In vivo drug availability study

This current study evaluated the in vivo pharmacokinetic parameters [19] and compared the satranidazole from multiunit pellets with raw drugs in a randomized, two-way crossover design. The result obtained was to target the satranidazole drug in the colonic region.

2.5.1.1 Experimental animals This study used six healthy male rats having 200 and 250 g weights. It was conducted according to animal ethics and ethical standards [20].

2.5.1.2 In vivo pharmacokinetics method design The investigation was created with a two-way crossover design [21], a randomized study with at least a 10-day washout time between the two dosing sessions. At each dosing session, the rats acquired either the satranidazole pellet test preparation or the satranidazole raw drug reference preparation at a specified time. Each animal was further marked for identification and assigned to separate cages. Animals were orally administered both the pellet formulation and the raw drugs at a 50 mg/kg dose using an oral feeding syringe [22].

2.5.1.3 HPLC analysis of plasma samples The HPLC method (Shimadzu Corp. HPLC) contained two VP pumps, LC 20AD, a C18 column (250 × 46 mm diameter, 5 µm particle size) and a 20 µL sample loop with a valve [23]. The mobile phase remained in phosphate buffer (pH3): Methanol (30:70), supplied at a 1 ml/min flow rate. Satranidazole and fluconazole (IS) were identified at a wavelength of 312 nm. The plasma calibration graph for satranidazole was linear at 0.5–64 mcg/ml. This study collected 0.5 ml of blood through retro-orbital puncture before dosing (0 h) and at 0.5, 1, 2, 3, 4, 6, 8, 12 and 24 h by heparinized centrifuge tubes centrifuged at 5000 rpm speed for 10 min. Blood plasma was gathered and stored at 200C [24]. 0.1 ml of blood sample mixed for 10 min by adding 0.5 ml of acetonitrile to extract the drug. 150 µl of subject plasma and 50 µl of IS were transferred to 1.5 ml polypropylene centrifuge microtubes. Deproteinization was executed by adding 300 µl of acetonitrile to the samples, shaking for 5 min and then centrifuging at 6000 rpm for 5 min. The supernatant solution was collected with a micropipette and filtered through a 0.45-micron filter, and 20 µl of the pure top layer was introduced directly into the HPLC chromatography system.

2.5.1.4 Pharmacokinetic analysis The pharmacokinetics analysis was done using the plot between drug concentration and time to determine the pharmacokinetic parameters, such as C_{max}, t_{max}, $AUC_{0\text{-}t}$, $AUC_{0\text{-}inf}$, $t_{1/2}$ and K_{el} [25]. Various pharmacokinetics constraints calculated the relative bioavailability of satranidazole, and statistical studies were presented as the mean ± SD computed using SPSS 13 software. The significance limit was set at 0.05.

2.5.2 Colonic drug content and histopathological study of the colon

Two sets of animals ($n=3$) were treated with satranidazole pellets and satranidazole drug, at 50 mg/kg rat bodyweight. These rats were killed after 12 h. The colon was then removed by cervical dislocation. The colon was ligated on both ends before being dissected longitudinally and preserved in a standard formalin solution to remove the colonic contents. The histopathological slide was prepared by using a microtome. The slide was analyzed under a microscope. At 4 °C, the colonic contents were weighed, and 20 ml buffer (pH 7.4) was added. The blend was shaken to achieve excellent homogenization, and 0.5 mL was mixed with 0.5 mL methanol under continual stirring [26]. The supernatant was maintained in a 0.05-mL container, and HPLC measured satranidazole. The colon was collected and kept in a typical formalin solution. The histopathological slides were prepared using a microtome and analyzed under a microscope.

3 Results

3.1 Method of satranidazole multiunit pellets

Multiunit pellets were prepared by the powder layer technique [27], as presented in Table 1. Here, 18 formulation batches were arranged according to formulation components.

3.2 Drug polymer interaction studies

3.2.1 Fourier transform infrared spectroscopy study

The STZ and the polymer mixtures show that there was no significant interaction between polymers and drugs, as shown in Fig. 1a.

3.2.2 Differential scanning calorimeter study

The current study shows thermograms of pure drug, LBG, XG and CG and polymer mixtures [28] used in Fig. 1b. Major melting endotherms of pure STZ and polymer were found at 194.99 °C and 112.95 °C (LBG), 104.28 °C (CG) and 115.34 °C (XG), respectively.

3.3 In vitro drug release technique

Drug release was described using USP paddle-type dissolution device [29]. The release was 0–2% at 2 h and below 20% at 6 h, and the maximum release was at 12 h for optimized formulation. The release study of pellets [30] (Batch 1–9) is shown in Fig. 2 in a simulated gastric medium (Fig. 2a) and simulated colonic fluid (Fig. 2b) using various combinations of polysaccharides with 10–30% coating levels. In vitro release of pellets (Batch 10–18) is presented in Fig. 3 in a simulated gastric liquid (Fig. 3a) and colonic medium (Fig. 3b) [31] with maintaining a 10–30% coating level using various polysaccharides as coating material.

3.4 In vivo study

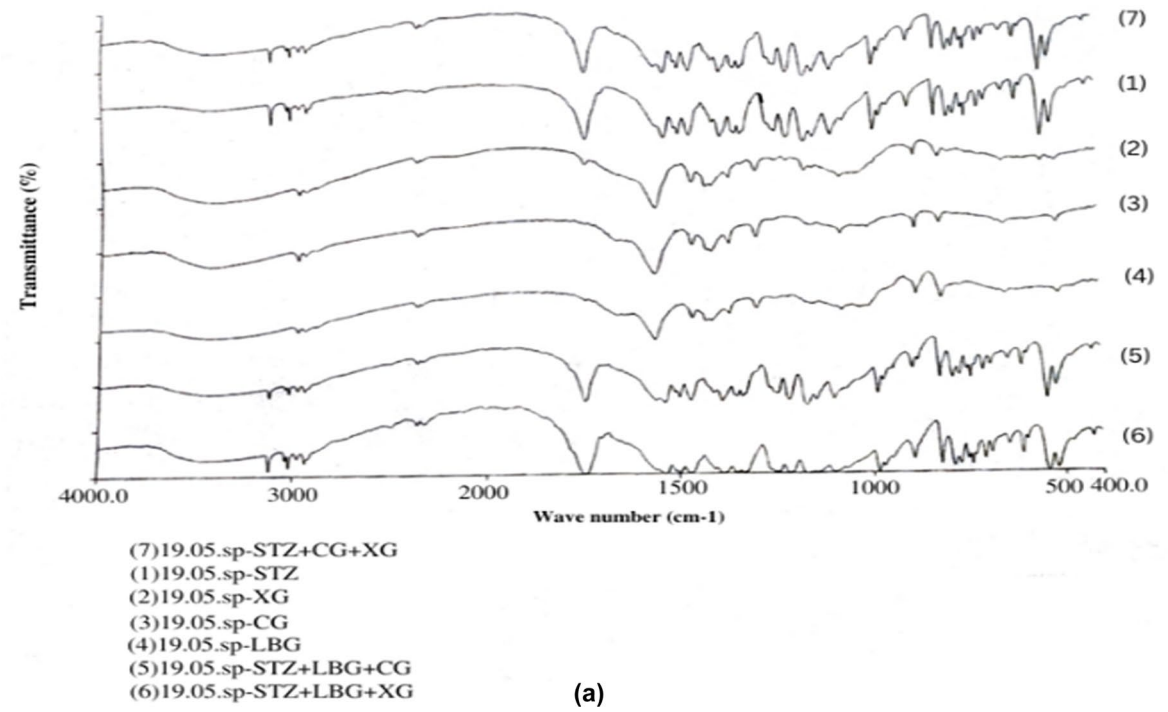
3.4.1 In vivo drug bioavailability study

3.4.1.1 Pharmacokinetic analysis The plasma calibration curve of satranidazole was drawn between peak area versus concentration with its representative chromatogram of satranidazole for calibration curve [32] as shown in Fig. 4a. The representative chromatogram of the rat plasma sample administered satranidazole with the reference drug ketoconazole (IS) is revealed in Fig. 4b, and the plasma concentration–time plots of free administered satranidazole drug and the test formulation are presented in Fig. 5. The pharmacokinetic characteristics of satranidazole acquired after administration of the drug and test formulation of satranidazole and the statistical analysis results are presented [33] in Tables 2 and 3, respectively.

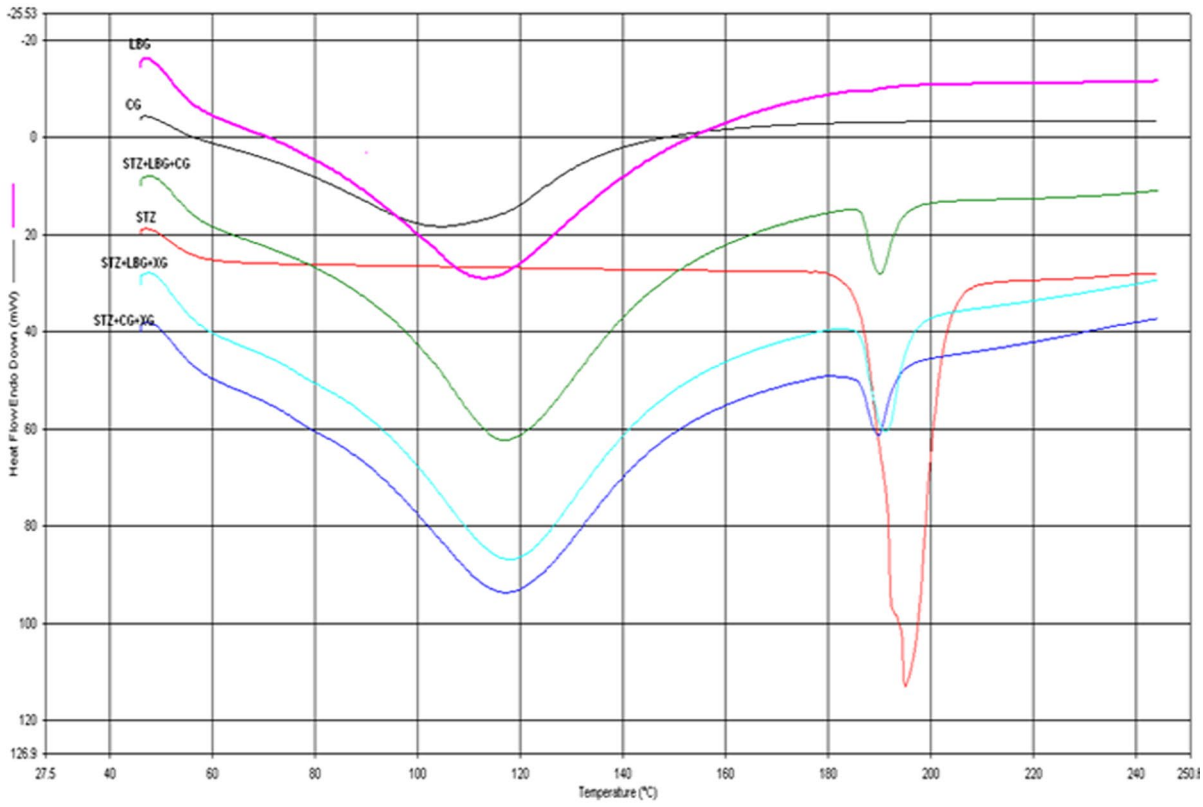
Cmax obtained for oral administration of 100 mg satranidazole and test formulation (pellets) [34] indicated considerable dissimilarities between the mean values acquired for the free administered drug and the pellet formulation as given in Table 3. t_{max} obtained for orally used 100 mg satranidazole and pellets showed no differences between the mean values acquired [35] for the raw drug and the pellet formulation (Table 3). The $AUC_{0\text{-}t}$ obtained after administration of satranidazole as a reference preparation was 381.95 ± 18.61 ng h/ml and 312.0 ± 31.66 ng h/ml for the test formulation (Table 3). The plasma elimination rate constant (Kel) of satranidazole as a drug was shown as 0.143 ± 0.006 h-1 for the reference preparation and 0.121 ± 0.004 h-1 for the test formulation (Table 3). The free administered drug and test formulation's plasma elimination half-life (t1/2) were 4.68 ± 0.19 h and 5.75 ± 0.19 h (Table 3).

3.4.2 Colonic drug content analysis and histopathological study of the colon

The colonic content of satranidazole-free administered drug and test formulation is shown by histogram plot in Fig. 6, and a statistical summary of colonic content is given in Table 4. Colonic histopathology was shown by



(a)



(b)

Fig. 1 Drug and polymers interaction studies **a** FTIR curve of drug &polymer mixture **b** DSC study of drug and polymer mixture

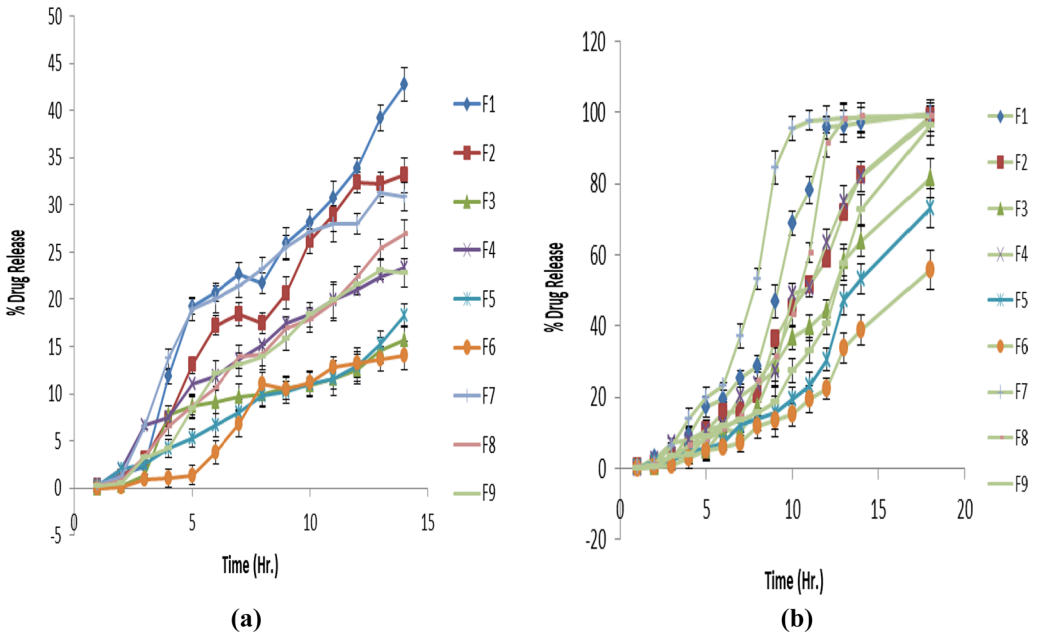


Fig. 2 In vitro drug release profiles of satranidazole pellets (Batch F1-F9) at **a** simulated gastrointestinal fluid (pH 1.2, pH 4.5 and pH 7.4) and **b** simulated colonic fluid (pH 7)

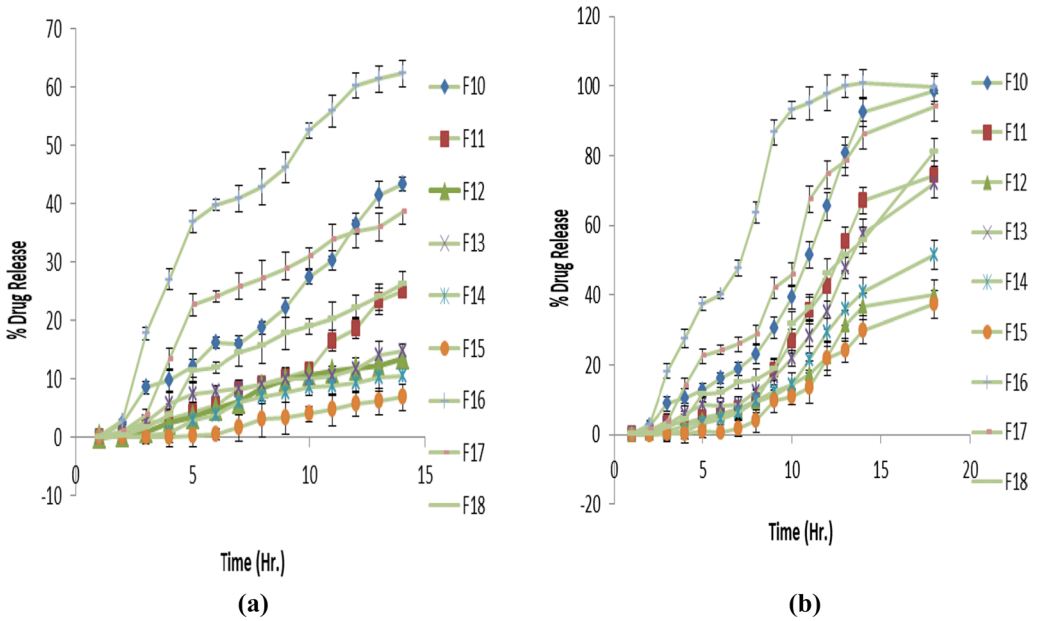
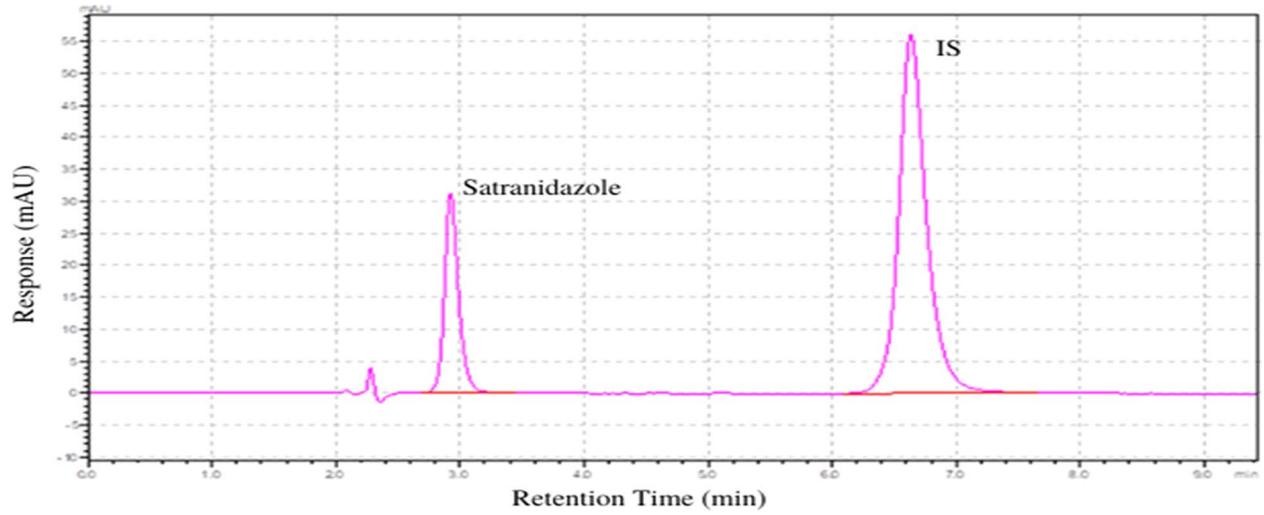
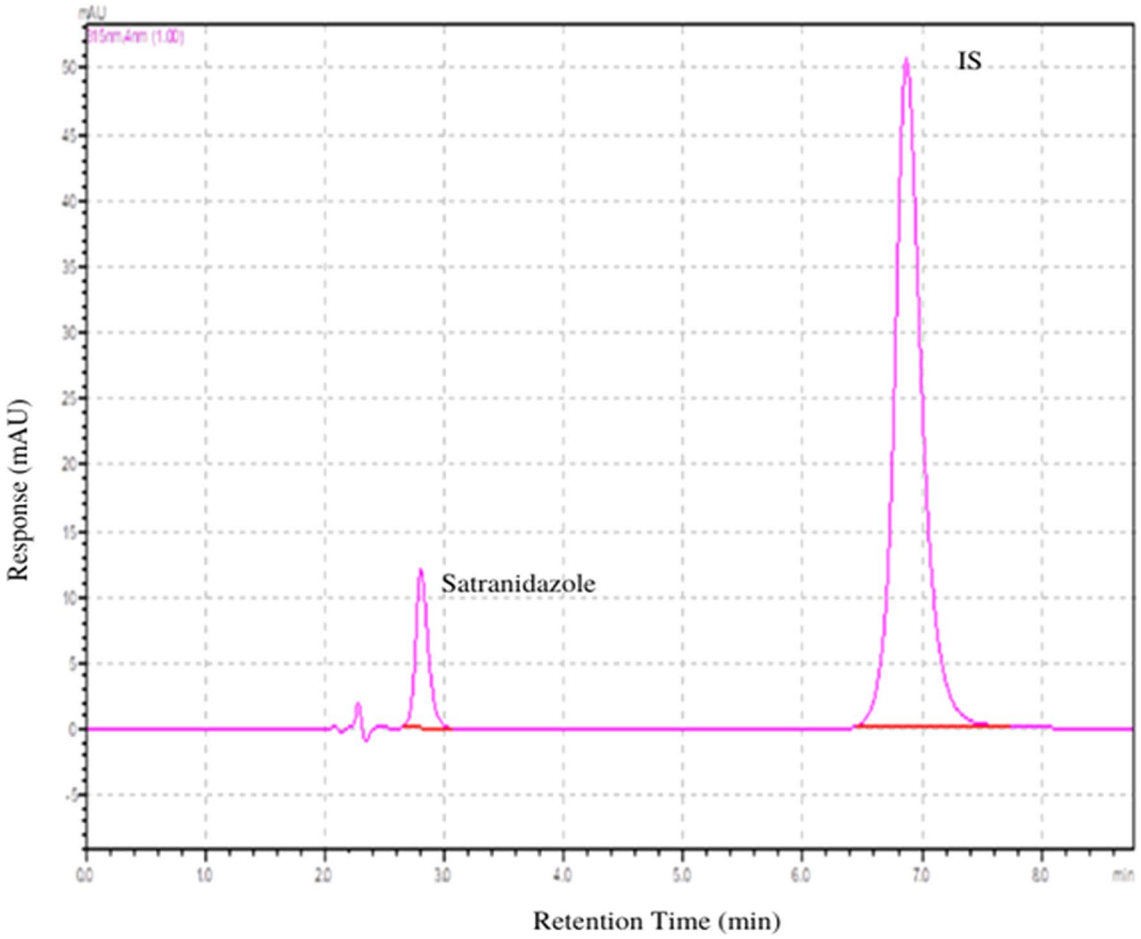


Fig. 3 In vitro drug release profiles of satranidazole pellets (Batch F10-F18) at **a** simulated gastrointestinal fluid (pH 1.2, pH 4.5 and pH 7.4) and **b** simulated colonic fluid (pH 7)



(a)



(b)

Fig. 4 HPLC studies **a** representative chromatogram of satranidazole for calibration curve and **b** representative chromatogram of plasma sample of rat administered with satranidazole. **IS* International standard (ketoconazole)

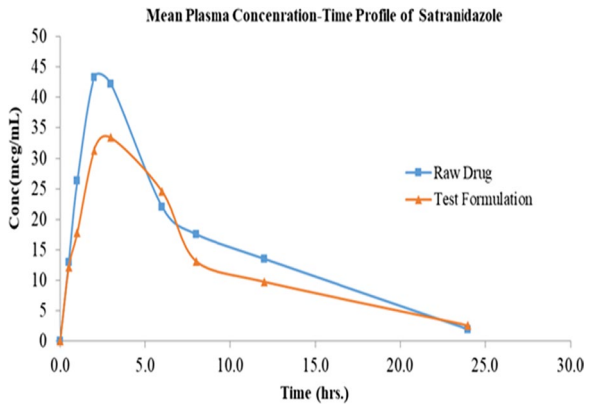


Fig. 5 Mean plasma concentration–time curves of free administered satranidazole drug and test formulation

experimental animals treated with satranidazole-free administered drug and test formulation [36] in Fig. 7a, b

4 Discussion

The formulations were designed using two independent variables the ratio of coating mixture and the percentage of coating level [37, 38]. The formulations were optimized using satranidazole layered powder with various amounts of chitosan, xanthan gum and locust bean gum combination, giving relevant results compared to the conventional product.

The FTIR peak of pure drug and polymer mixtures, containing their entire characteristic peck at their position, i.e., at 1465–1470 (C–H bending), 3414–3471(O–H stretching), 1244(O–H bending by STZ and polymer blends), 815–824 (C–H rocking, C–C stretching and C–H bending) and 1076–1100 (C–C and C–O stretching) cm^{-1} [39]. Hence, no chemical interchange between STZ and other polymers in combination is found in the FTIR studies.

Drug mixed biopolymers showed a small broad peak at 191.16 °C and 189.93 °C for LBG + XG + STZ and LBG + CG + STZ, respectively, indicating the existence of a drug in crystalline form. The decrease in height and sensitivity of the endotherm peak is due to polymers in the mixture. An increase in the endothermic property also indicates a thermodynamically favorable interaction between polymers, indicating physical cross-linking. It is clear from the thermogram that LBG is more miscible with XG than CG. In practice, during experiments, it is found so. Previous workers have shown that LBG undergoes highly extensive H-bonding with LBG but forms a Polyelectrolyte complex with CG [40]. The charge neutralization is not so effective with LBG because LBG is a poorly ionizable biopolymer because of little no of the polarizable group compared to XG and CG, so interaction between LBG and CG is not as extensive XG and CG.

The minimum drug was discharged in the gastric fluid, the maximum drug was discharged in the colonic part, and xanthan gum with locust bean gum [41] blend was the most effective polymer mixture for targeting the drug to the colonic site.

The linearity was evaluated by linear regression with correlation coefficient, $R^2 = 0.9997$. This method was linear in 0.5–64 ng/ml. The highest concentration was obtained from the satranidazole-free administered drug as a single dose in the provided condition at 51.07 ± 1.21 ng/ml and 35.02 ± 3.91 ng/ml for test formulation. The time to attain maximum concentration (tmax) was 2.50 ± 0.55 h for both free administered drug and test formulation. When administered as a single quantity in the fed state of free administered satranidazole drug as reference preparation, AUC0-α was 395.64 ± 18.20 ng h/ml and 312.0 ± 31.66 mcg h/ml for the pellets [42] (Table 3). There were no critical dissimilarities in the statistical analysis. Based on the pharmacokinetics parameter studied, the relative bioavailability of satranidazole pellets [43] as a test formulation was 81.69%, and log-transformed relative bioavailability was 96.60% with reference preparation of the satranidazole-free administered drug. The results show that a higher percentage of the drug was released in the colonic region with less bioavailable than the free administered drug that targets satranidazole drug in the colonic site.

The results revealed that the free administered drug colonic content was less than the formulation. The colonic drug content was significantly higher than free administered drugs [44]. The formulation was designed to release a high percentage of drugs in the colon region, and pellets could deliver high drug content into the colon. There was no necrosis and congestion below the superficial epithelium. At the submucosal level, no inflammatory cells were found. Colonic mucosa with barely visible lamina propria and rare inflammatory cells. Normal colonic mucosa with linear crypts and regular glandular arrangement. There was no space between the bottom of the colonic crypts and the muscular mucosa without any signs of epithelial damage. Colonic mucosa without any chronic inflammatory infiltrate indicates that the sediment did not induce any toxicity in the colon.

5 Conclusions

A multiunit pellets system for colonic release was developed in this study, and it was successful in achieving the goals of colon-specific satranidazole release. The pellets were designed with an HPMC-K10 as seal coating and

Table 2 Statistical summary of pharmacokinetic parameters for satranidazole drug and test formulation

Pharmacokinetic parameters	Treatments										Result details							*p*-value
C_{max}	Raw drug					Test formulation					Source							.00001(S)
	N	$\sum X$	Mean	$\sum X^2$	SD	*N*	$\sum X$	Mean	$\sum X^2$	SD	Between treatments			Within treatments				
											SS	df	MS	SS	df	MS	*F*	
	6	306.4	51.06	15,654.2	1.21	6	210.1	35.01	7433.53	3.91	772.80	1	7772.80	83.90	10	8.39	92.10	
t_{max}	6	15	2.5	39	0.54	6	15	2.5	39	0.54	0	1	0	3	10	0.3	0	1(NS)
AUC $_{0\text{-}t}$	6	2291.72	381.95	877,062.63	18.61	6	1872.02	312	589,088.95	31.66	14,679	1	14,679	6745.01	10	674.50	21.76	.00088(S)
AUC $_{0\text{-}\alpha}$	6	2373.87	395.64	940,865.51	18.19	6	2000.77	333.46	673,059.51	34.29	11,600.300	1	11,600.300	7535.13	10	753.51	15.39	.00089(S)
k_{el}	6	0.856	0.1427	0.1223	0.005	6	0.724	0.120	0.087	0.003	0.0015	1	0.0015	0.0002	10	0	63.49	.000012(S)
$t_{1/2}$	6	29.18	4.8633	142.08	0.185	6	34.49	5.74	198.40	0.168	2.349	1	2.349	0.314	10	0.031	74.63	.00001(S)

*C_{max} Maximum plasma concentration, t_{max} Time to maximum plasma concentration, $AUC_{0\text{-}t}$ The area under plasma concentration time curve, $AUC_{0\text{-}inf}$ The area under plasma concentration time curve 0 to infinity, $t_{1/2}$ Elimination half-life, K_{el} Elimination rate constant

**N* No of sample, $\sum X$ Sum of sample, $\sum X^2$ Sum of sample square, *SD* Standard deviation, *SS* Sum of square, df Degree of freedom, *MS* Mean square, *F* Test in one-way ANOVA

*Significant and nonsignificant value indicates by S and NS

Table 3 Comparative pharmacokinetic study of satranidazole drug and test formulation

Pharmacokinetic parameters	Raw drug		Test formulation		*p*-value
C_{max} (mcg. /ml.)	Mean	51.07	Mean	35.02	0.00001(S)
	±S.D	1.21	±S.D	3.91	
t_{max} (h)	Mean	2.50	Mean	2.50	1(NS)
	±S.D	0.55	±S.D	0.55	
$AUC_{0\text{-}t}$ (mcg. h/ml.)	Mean	381.95	Mean	312.00	0.00088(S)
	±S.D	18.61	±S.D	31.66	
$AUC_{0\text{-}\infty}$ (mcg. h/ml.)	Mean	395.64	Mean	333.46	0.00089(S)
	±S.D	18.20	±S.D	34.29	
k_{el} (h^{-1})	Mean	0.143	Mean	0.121	0.000012(S)
	±S.D	0.006	±S.D	0.004	
$t_{1/2}$ (h)	Mean	4.86	Mean	5.75	0.00001(S)
	±S.D	0.19	±S.D	0.17	
Relative bioavailability (%)	100%		81.69%		
Log-transformed (LN) relative bioavailability (%)	100%		96.60%		

*C_{max} Maximum plasma concentration, t_{max} Time to maximum plasma concentration, $AUC_{0\text{-}t}$ The area under plasma concentration time curve, $AUC_{0\text{-}inf}$ The area under plasma concentration time curve 0 to infinity, $t_{1/2}$ Elimination half-life, K_{el} Elimination rate constant

*Significant and nonsignificant value indicates by S and NS

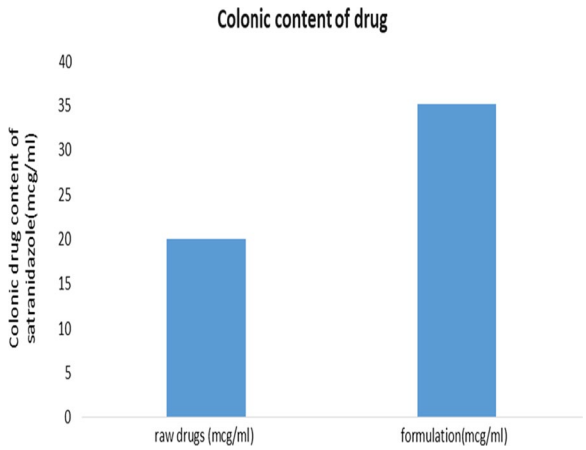


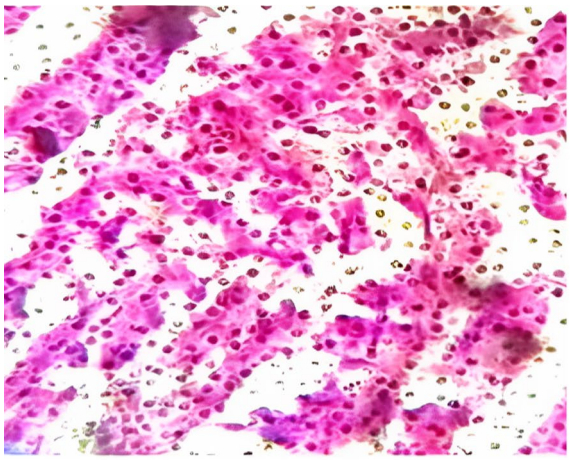
Fig. 6 Histogram diagram of mean concentration of colonic free administered drug and test formulation

film coating with various combinations of locust bean gum, xanthan gum and chitosan. In vitro release revealed that the pharmaceutical system was capable of preventing release in gastric medium (pH 1.2) for 2 h and also in a mixture of gastric and intestinal liquid (pH 4.5) for next 3 h, the drug release beginning after 6 h in simulated intestinal medium (pH 7.4) and a maximum drug release in 14 h approximately. The results acquired for the pharmacokinetic study, the relative bioavailability of satranidazole pellets was 81.69% which proved that a higher percentage of the drug was released in the colonic region with less bioavailable than the free administered drug to target in the colonic site. Colonic histopathology showed by treatment with test formulation that the pellet did not induce any toxicity in the colon. In conclusion, pharmacokinetic data with colonic content confirmed

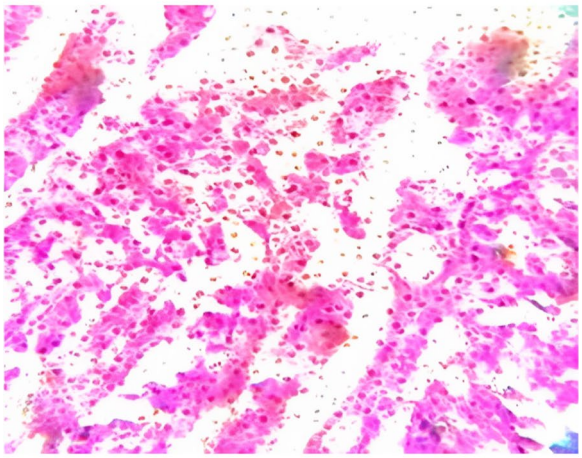
Table 4 Statistical summary of colonic content for satranidazole drug and test formulation

Statistical parameters	Treatments	
	Raw drug	Test formulation
N	6	6
∑X	120.54	211
Mean	20.09	35.16
$\sum X^2$	2437.89	7503
SD	1.80	4.07
	Result details	
	Source	
	Between treatments	**Within treatments**
SS	681.91	99.07
df	1	10
MS	681.91	9.90
F	68.82	
p-value	0.00001	

*N–No. of sample, ∑X sum of sample, $\sum X^2$ sum of sample square, *SD* standard deviation, *SS* sum of square, df degree of freedom, *MS* mean square, *F* test in one-way ANOVA



(a)



(b)

Fig. 7 Histopathological study of colon **a** experimental animal treated with satranidazole raw drugs **b** experimental animal treated with test formulation of satranidazole pellet

the reliability of the pharmaceutical technique in acquiring the colon-specific release of satranidazole.

Abbreviations

STZ: Satranidazole; HPMC: Hydroxypropyl methylcellulose; C_{max}: Maximum plasma concentration; PVP: Polyvinyl pyrrolidone; t_{max}: Time to attain maximum concentration; K_{el}: Plasma elimination rate constant; FTIR: Fourier transform infrared spectroscopy; DSC: Differential scanning colorimeter; HPLC: High performance liquid chromatography; LBG: Locust bean gum; XG: Xanthan gum; CG: Chitosan gum.

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Author contributions

We declare that this work was done by the authors named in this article: RM, BM and RP conceived and designed the study. RM and NP carried out the laboratory work, collected and analyzed the data, and SM drafted the manuscript. BM supervised the work, and RM assisted in the data analysis. All authors have read and approved the final manuscript.

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Availability of data and materials

All necessary data generated or analyzed during this study are included in this published article. Any additional data could be available from the corresponding author upon request.

Declarations

Ethics approval and consent to participate

The author's assert that all procedure contributing to this work comply with the ethical standards of the Institutional Animal Ethics Committee "TAAB Biostudy Services," 69 Ibrahimpur Road, Jadavpur, Kolkata–700032, and ethical approval number is 1938/PO/Rc/S/17/CPCSEA.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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