Development and evaluation of taste-masked satranidazole granules by the polymer-coating technique

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Background and objective
The objective of the present study was to mask the bitter taste of satranidazole and develop a formulation that is easy to swallow and provides quick relief in amoebiasis.
Materials and methods
Taste-masked granules were formulated by the wet granulation method and further coated by spraying a coating solution of Eudragit E100. Various batches of granules were prepared by coating with different concentrations of the coating solution. The formulated granules were evaluated for taste masking by *in-vivo* and *in-vitro* methods. The granules were tested for their flow property, *in-vitro* drug release, drug content, granular friability, and size distribution. Scanning electron microscopy of coated and uncoated granules was performed. The optimized batch was subjected to a stability study. The *in-vitro* release of the drug from granules was compared with that of the marketed tablet formulation.
Results and conclusion
The formulated granules were found to possess good flow property. Differential scanning calorimetry and Fourier-transform infrared studies confirmed no interaction between the drug and the excipients. The taste-masked granules of the optimized batch showed 99.21% release of the drug within 15 min. The *in-vitro* release of the drug from granules was found to be better than that of the marketed tablet formulation. The optimized granular formulation was found to be palatable and to provide quick relief in amoebiasis.

Keywords:
Eudragit E100, satranidazole, taste-masked granules, wet granulation

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Introduction

The bitter taste of drugs is a major problem in pediatric and geriatric formulations. It is a challenge to mask the bitter taste of drugs in the development of all oral formulations. It is also necessary to ensure better patient compliance and product value, wherein the process and formulation should be economic, rapid and easy, involve the least number of equipments, and processing steps and the minimum number of excipients, without adverse effects on the drug's bioavailability [1]. There are numerous methods for effective taste masking — for example, the use of flavors and sweeteners, microencapsulation, complexing with an ion-exchange resin, the use of an insoluble prodrug, the formation of inclusion complexes, gelation, liposome, multiple emulsions, granulation, etc.

Satranidazole (STZ) is a new nitroimidazole derivative with potent antiamoebic action. It is a highly potent, well-tolerated, and clinically useful agent against common protozoa such as *Entamoeba histolytica*, *Trichomonas vaginalis*, *and Giardia* spp. [2]. Its dosage is 300 mg twice daily for 3–5 days in the treatment of amoebiasis and 600 mg as a single dose in the treatment of giardiasis and trichomoniasis. Also, it has been found to be more active than metronidazole against aerobic, microaerophilic, and anaerobic bacteria [3]. It is reported that STZ exhibits significantly higher plasma concentrations than metronidazole and has a plasma elimination half-life of 1.01 h, which is significantly shorter than the corresponding metronidazole half-life of 3.62 h [4]. Also, STZ has better tolerability, an absence of neurological and disulfiram-like reactions and it may be preferred for patients with susceptible neurological symptoms [5]. STZ is available in the market in the form of film-coated tablets.

The present study involves the development of an STZ taste-masked granular formulation by wet granulation followed by its coating with Eudragit E100 and its evaluation. The marketed tablet of STZ is film coated and releases the drug completely in the stomach in 1 h. In case of amoebiasis, immediate action is required to achieve quick relief. Hence, an immediate-release granular formulation of the drug was developed, which releases almost the complete drug within 15 min in the stomach.

Materials and methods

Materials

STZ was obtained as a gift sample from Alkem Laboratories (Mumbai, India). Eudragit E100 was

obtained from Evonik Degussa (Mumbai, India). Satrogyl tablets (Strength 300 mg) were purchased from the market. All the chemicals and reagents used were of analytical grade.

Preformulation studies

Ultraviolet (UV) and Fourier-transform infrared (FTIR) spectra of STZ were taken to confirm the identity of the drug. A compatibility study between the drug and the excipients was conducted using FTIR and differential scanning calorimetry (DSC). Infrared spectra were recorded using a FTIR spectrophotometer (Shimadzu Corporation, Japan) with Potassium bromide pellets. DSC thermogram of the drug and the optimized formulation were performed by scanning 10 mg of the sample in SEIKO SII EXSTAR DSC 6220 software, USA. Samples were heated in an open aluminum pan at a rate of 10°C/min in a 30–300°C range under a nitrogen flow of 10 ml/min. Alumina was used as the reference material.

Preparation of core granules

The drug and pulverized sugar were sieved through a 40# sieve and were mixed geometrically. All the ingredients were passed through 40# sieve and were mixed with the drug and pulverized sugar mixture. The dough was prepared using polyvinylpyrrolidone K30 in water as a binder. The wet mass was passed through 16# sieve, and granules were dried in an oven below 60°C till the moisture content was less than 5% w/w. Dried granules were then passed through a 20# sieve and were used for coating. The composition of the granules is described in Table 1.

Preparation of the coating solution

Eudragit E100 was dissolved in isopropyl alcohol with the help of a vortex mixer (Eltek vortex mixer VM301, Elektrocraft, India). Macrogol 6000 (Molychem, Mumbai, India) was added to a small amount of water and was dissolved by warming. Talc and aerosil were added to water and were mixed thoroughly. Both the solutions were then mixed together.

Coating of granules/the coating process

A laboratory-scale coating pan was used to coat the granules. The pan was rotated at 10–15 rpm with slow air speed. The inlet temperature was 35–40°C to evaporate isopropyl alcohol and the exhaust temperature was 25–30°C. Granules were coated manually using a spray gun in a conventional manner and were dried simultaneously after coating by blowing hot air.

The initial weight of the STZ granules was noted, and then the weights of the coated granules were determined at various intervals in between the coating process. The coating rate or the %weight gain of the granules was calculated using the following formula [6]:

$$\text{Coating rate} = \frac{W2 - W1}{W1} \times 100,$$

where W1 is the weight of granules before coating and W2 is the weight of granules after coating.

Initially, the granules were coated with three different concentrations (low, medium, and high) of Eudragit E100 containing the coating solution to achieve sufficient taste masking. The overall concentration of all the three coating solutions was kept constant at 8% w/v by considering the ease of spraying. The coating of granules was performed on a laboratory scale in the conventional manner by spraying the coating solution and simultaneously blowing hot air through the granule bed in a conventional coating pan. The composition of different coating solutions is shown in Table 2. The granules were withdrawn at different stages of coating and tested for taste masking using the *in-vitro* UV spectroscopic method. The % weight gain was determined at the stage when the taste was sufficiently masked.

Table 1 The formulation composition of uncoated satranidazole granules

Ingredients	Quantity/dose (mg)
STZ	300
Avicel pH 101	140.5
Pulverized sugar	900
Aerosil	5
Starch 1500	22
Hydroxypropyl cellulose (low substituted)	7.5
PVP K30 (dry mix)	5
PVP K30 (binder)	4
Purified water	q.s.

STZ, satranidazole.

Table 2 The composition of different coating solutions

Ingredients	Low (C1)	Medium (C2)	High (C3)
Eudragit E100 (mg)	300	450	600
Macrogol 6000 (mg)	30	30	30
Talc (mg)	129.304	129.304	129.304
Aerosil (mg)	2.496	2.496	2.496
Isopropyl alcohol (parts)	90	90	90
Water (parts)	10	10	10
Approximate % weight gain of granules	20.02–23.35	16.71–17.68	17.61–18.71
Approximate % of coating solution required	60–70	38–40	32–34
Drug-to-polymer ratio	1 : 1	01 : 1.5	1 : 2

Note: All the batches (C1, C2 and C3) showed less than the threshold value during *in-vitro* taste evaluation by ultraviolet spectroscoy. It means that all batches were taste masked.

A higher concentration of the coating solution (C3) was selected for further study to reduce the process time. To optimize the spraying rate, the granules were coated by spraying the higher concentration (C3) of the coating solution in different amounts (batch K1–K5). The coating rate was determined in terms of the %weight gain for all the batches. The percentage of the total coating solution required was calculated, and the approximate drug-to-polymer ratio was determined for each batch (Table 3).

Table 3 Optimization of the spraying rate (batches K1–K5)

Parameters	K1	K2	K3	K4	K5
% Weight gain of granules	11.01	13.76	16.53	19.26	22.01
Amount of coating solution sprayed (%)	20	25	30	35	40
Drug-to-polymer ratio	1.0 : 0.4	1.0 : 0.5	1.0 : 0.6	1.0 : 0.7	1.0 : 0.8

Evaluation of granules

The prepared batches were evaluated for the following parameters:

Flow properties

All the batches of granules were evaluated for various parameters such as the angle of repose, the bulk density and the tapped density, Hausner's ratio, and Carr's index [7,8].

Angle of repose: The fixed funnel method was used to determine the angle of repose and was calculated using the following equation:

$$\text{Tan } \theta = \frac{h}{r},$$

where h is the height of the pile in cm and r is the radius of the base of the pile in cm, and θ is the angle of repose.

Bulk density and tapped density: To measure the density, the granules were filled in a 100-ml-capacity measuring cylinder up to at least three-fourth the height. Bulk density is the quotient of the weight to the volume of the sample. Tapped density is the quotient of the weight of the sample to the volume after taping a measuring cylinder 500 times from a height of ~1.5 inch.

Hausner's ratio and Carr's index: Hausner's ratio was calculated using the following formula:

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}.$$

The percentage compressibility (Carr's index) was calculated as 100 times the ratio of the difference between the tapped density and the bulk density to the tapped density:

$$\text{Carr's index} = \frac{\text{Tapped density} - \text{bulk density}}{\text{Tapped density}} \times 100.$$

Granular friability

Ten grams of uncoated granules were subjected to friabilator at 25 rpm. After 4 min, the granules were sieved on a 200 mesh. The amount of granules passed through the 200 mesh was calculated as the percentage granular friability [7].

Particle size distribution

Particle size distribution was determined on the optimized batch using a nest of standard sieves (20#, 40#, 60#, 100#, and 120#). The sieves were agitated mechanically for 10 min on a sieve shaker, and the weight of the granules retained on each smaller sieve was noted. The mean granule size was calculated from the % weight retained on each sieve [8].

Taste-masking evaluation

Determination of the bitter taste recognition threshold of satranidazole: The threshold value of STZ was determined on the basis of the bitter taste recognized by eight volunteers in the age group of 21–28 years. Aqueous solutions of STZ with different concentrations (10, 20, 30, and 40 μg/ml) were prepared. One milliliter of the solution was placed on the center of the tongue of a volunteer for 30 s. The solution was spat out after 30 s, and the mouth was thoroughly rinsed with distilled water. The same procedure was repeated for all solutions and volunteers. A gap of 30 min was maintained in between tasting two different solutions. The same procedure was repeated for STZ solutions with concentrations of 24, 26, 28, 32, and 35 μg/ml. The threshold value was selected on the basis of the lowest concentration that had a bitter taste [9,10].

In-vitro evaluation of the bitter taste of granules: Granules equivalent to 25 mg of STZ were placed in a volumetric flask with 50 ml of phosphate buffer, pH 6.8, and stirred for 5 min. The mixture was filtered, and the filtrate was analyzed for the STZ concentration at 320 nm by a UV–visible spectrophotometer and this value was compared with the threshold value [11].

In-vivo taste evaluation: Two procedures were used for *in-vivo* taste evaluation:

(1) *A gustatory sensation taste*: Informed consent was obtained from 10 healthy volunteers before the taste evaluation study was carried out. The whole dose was added to 100 ml of water for 15 s. STZ was

used as the control. After 15 s, 1 ml of the dispersion was held in the mouth of each volunteer for 30 s and then spat out. The bitterness level was recorded using the numerical scale shown in Table 5 [9].

(2) Granules equivalent to 50 mg of STZ were held in the mouth of each volunteer for 30 s. After expectoration, the bitterness level was recorded using the numerical scale shown in Table 4.

Determination of drug content (% assay) using high-performance liquid chromatography

The assay of different batches of granules of STZ with Eudragit E100 was carried out using a previously developed and validated high-performance liquid chromatography (HPLC) method. Isocratic elution at a flow rate of 1.0 ml/min was used on a BDS Hypersil C18 (250 mm´4.6 mm, 5 μm) column (Thermo Scientific) at 25°C temperature. A mobile phase consisting of 0.16% v/v orthophosphoric acid solution, pH 3, and acetonitrile at a ratio of 60 : 40 v/v was used. The UV detection wavelength was 320 nm, and 20 μl sample was injected. The standard stock solution was prepared by dissolving 50 mg of STZ in 50 ml methanol and was further diluted with the mobile phase to obtain a standard solution of 40 μg/ml concentration. The sample solution was prepared by adding granules equivalent to 20 mg of STZ in methanol. The dispersion was sonicated for 30 min and was then filtered. The resultant solution was further diluted with mobile phase to obtain 40 μg/ml of test solution. The solutions were filtered through a 0.45-μm nylon filter. Equal volumes of sample preparation and standard preparation were injected separately into the HPLC (an Agilent HPLC equipped with quaternary pump; Agilent, Wilmington, Delaware, USA), and the chromatograms were recorded.

In-vitro dissolution studies in 0.1 N hydrochloric acid

In-vitro dissolution studies were carried out using the USP II apparatus, Electrolab, Mumbai, India (Paddle method) rotating at 75 rpm in 900 ml of 0.1 N hydrochloric acid (HCl) as the dissolution media maintained at 37 ± 0.5°C. Taste-masked granules equivalent to 300 mg of STZ were subjected to dissolution. Sampling was performed at different time intervals of 0, 5, 10, 15, 30, 45, and 60 min by withdrawing 5 ml of the dissolution medium and replacing with the same amount of the dissolution medium to maintain sink conditions. The withdrawn samples were filtered and the contents of samples were determined spectrophotometrically at 320 nm. The dissolution of the marketed formulation was also carried out under the same conditions. The cumulative release of drug was calculated using the standard calibration curve of STZ prepared in 0.1 N HCl.

Table 4 The numerical scale for the bitterness level

Scores	Inference
0	Pleasant
1	Tasteless
2	Slightly bitter
3	Moderately bitter
4	Extremely bitter

Scanning electron microscopy

The surface morphology of uncoated and coated granules was examined using a scanning electron microscope (Zeiss Ultraplus FESEM; Zeiss, Germany). The samples of granules were previously sputter-coated with gold.

Stability studies

Samples of taste-masked coated granules were packed in an aluminum pouch. These samples were then subjected to a stability study according to the ICH guidelines [12]. Tests were conducted at room temperature (RT) and under accelerated stability conditions. The samples were designated as time 0, 1, 2, and 3 months for RT and 0, 1, and 3 months for accelerated studies. Samples designed for RT storage were kept at 25 ± 2°C and 60 ± 5% relative humidity (RH). The samples in the accelerated stability study were kept at 40 ± 2°C and 75 ± 5% RH in a humidity chamber. Samples were tested for their appearance, dissolution, assay, taste masking, and flow properties using the previously described procedure to evaluate the stability of coated granules.

Results

The λ_{max} of STZ in methanol was found to be 320 nm, which was same as the value reported in

Table 5 Evaluation data of batches K1–K5

Parameters	K1	K2	K3	K4	K5
Bulk density (g/cm^3)	0.47 ± 0.015	0.45 ± 0.005	0.43 ± 0.020	0.44 ± 0.010	0.41 ± 0.015
Tapped density (g/cm^3)	0.55 ± 0.010	0.52 ± 0.020	0.5 ± 0.01	0.51 ± 0.025	0.48 ± 0.030
Carr's compressibility index (%)	14.54 ± 0.072	13.46 ± 0.080	14.25 ± 0.180	13.71 ± 0.157	14.5 ± 0.102
Angle of repose (deg.)	24.65 ± 0.132	24.98 ± 0.142	23.78 ± 0.110	23.07 ± 0.126	23.89 ± 0.100
Hausner's ratio	1.17 ± 0.005	1.15 ± 0.01	1.18 ± 0.015	1.16 ± 0.01	1.17 ± 0.01

the literature. STZ exhibited characteristic peaks at 1687, 1743, 1066, 1537, and 1215 cm^{-1} attributed to C = N stretching, C = O stretching, S = O stretching, C–NO_2 stretching and C–N vibrations. FTIR spectra showed all the important peaks of the drug in the spectra of the drug-excipient mixture and the formulation. FTIR of STZ, STZ–Eudragit E100, and the optimized formulation are represented in Fig. 1, Fig. 2, and Fig. 3, respectively.

DSC thermograms of the drug and the optimized formulation also showed that there were no significant changes in the endotherm of the drug in pure form and the formulation as seen in Figs 4 and 5. The pure drug shows a sharp endothermic peak at 192.7°C, which is also seen in the thermogram of the formulation with reduced intensity.

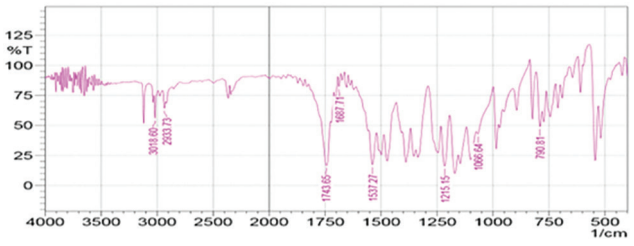
The results of bulk density, tapped density, Carr's index, Hausner's ratio, and the angle of repose are summarized in Table 5. The results indicated that the prepared granules possess good flow property [13].

The taste recognition threshold of STZ was determined on the basis of Table 6.

The threshold was found to be 28 μg/ml.

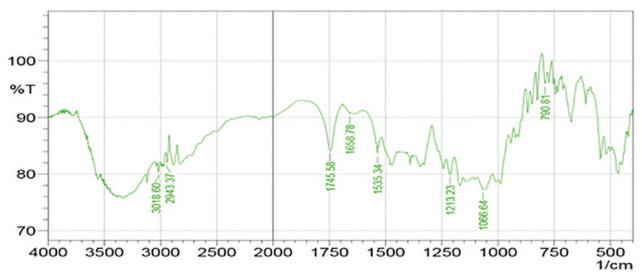
Taste-masking evaluation was performed by *in-vitro* and *in-vivo* methods. Table 7 indicates the *in-vivo* and the *in-vitro* taste-masking evaluation results of the granules.

Figure 1



Fourier-transform infrared of satranidazole.

Figure 3



Fourier-transform infrared of the optimized formulation.

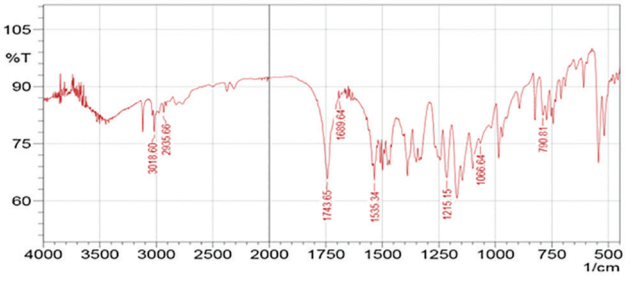
In the *in-vitro* taste-masking evaluation study, the drug release in pH 6.8 PBS was studied. Results of drug release from granules of batches K1 and K2 were found to be more than the threshold value (i.e. 28 μg/ml), which may be due to the incomplete coat formation of Eudragit E100 on the granules. The drug release from granules of batches K3, K4, and K5 was found to be less than the threshold value, which indicated taste masking of granules. Gustatory sensation test results obtained from eight healthy volunteers indicated that the granules of batches K3, K4, and K5 were found to be tasteless.

Table 6 Taste recognition threshold determination

Concentration (μg/ml)	Volunteers							
	1	2	3	4	5	6	7	8
10	N	N	N	N	N	N	N	N
20	N	N	N	N	N	N	N	N
22	N	N	N	N	N	N	N	N
24	N	N	N	N	N	N	N	N
26	N	N	N	N	N	N	N	N
28	N	N	N	Y	N	Y	N	N
30	Y	N	Y	N	Y	Y	Y	Y
32	Y	Y	Y	Y	Y	Y	Y	Y
35	Y	Y	Y	Y	Y	Y	Y	Y
40	Y	Y	Y	Y	Y	Y	Y	Y

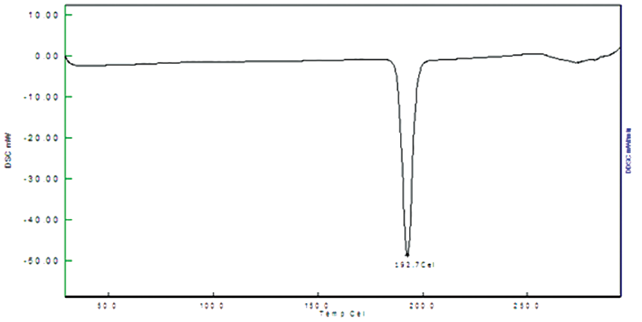
Y, recognition of bitter taste; N, no perception of bitter taste.

Figure 2



Fourier-transform infrared of the physical mixture of satranidazole–Eudragit E100.

Figure 4



Differential scanning calorimetry (DSC) of satranidazole.

The results of *in-vitro* dissolution studies and the drug content (assay) of different batches (K1–K5) are summarized in Table 8. A typical HPLC chromatogram of the test solution is represented in Fig. 6. The STZ peak was eluted at the retention time of about 4.31 min. The percentage of drug content for different batches was found to be in the range of 98–102%.

In-vitro dissolution studies in 0.1 N HCl of coated granules of the optimized batch showed almost 100% release of the drug in 15 min. The coated granules with a drug-to-polymer ratio of 1 : 0.6 showed better release in 0.1 N HCl with appropriate taste masking.

Table 7 *In-vivo* and *in-vitro* taste evaluation results

Batches	Drug : polymer ratio	Taste-masking score by the gustatory sensation test	*In-vitro* release of STZ by UV in 5 min (μg/ml)
K1	01 : 0.4	3	32.21
K2	01 : 0.5	2	28.3
K3	01 : 0.6	1	25.01
K4	01 : 0.7	1	24.8
K5	01 : 0.8	1	23.91

STZ, satranidazole; UV, ultraviolet.

The drug release of the marketed tablet and the optimized formulation is shown in Fig. 7.

The granular friability of uncoated drug granules of the optimized batch (K3) was found to be 0.41%. Results of the sieve analysis of the optimized batch K3 is shown in Table 9. The mean granular size of the granule was found to be 341.93 μm.

Scanning electron microscope photographs of uncoated and coated granules are as shown in Fig. 8 and Fig. 9, respectively. It was found that the surface of uncoated granules was rough, whereas the surface of coated granules was smooth and uniform.

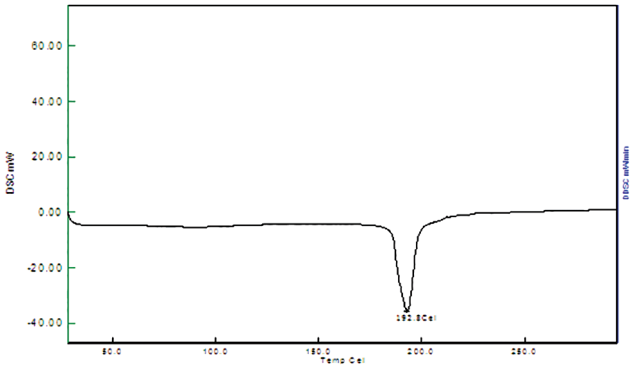
The stability study results indicated that there was no change in the physical appearance of the granules and the taste at RT as well as under accelerated conditions. The results of percent dissolution, assay, and flow properties of the coated granules at 25 ± 2°C and 60 ± 5% RH and at 40 ± 2°C and 75 ± 5% RH are as shown in Table 10 and Table 11, respectively. The optimized formulation was found to be stable.

Table 8 The dissolution study and assay (drug content) results of different batches in 0.1 N hydrochloric acid

		% Cumulative release[a]				
Time points (min)	Marketed tablet	Batches				
		K1	K2	K3	K4	K5
0	0	0	0	0	0	0
5	9.34 ± 0.432	86.85 ± 0.445	86.10 ± 0.501	85.21 ± 0.478	84.79 ± 0.499	83.87 ± 0.434
10	28.87 ± 0.471	99.33 ± 0.425	98.9 ± 0.414	98.17 ± 0.503	96.06 ± 0.675	96.14 ± 0.695
15	39.1 ± 0.572	99.23 ± 0.427	99.13 ± 0.443	99.21 ± 0.578	97.21 ± 0.578	97.67 ± 1.43
30	65.43 ± 0.503	101.06 ± 0.618	100.88 ± 0.405	100.57 ± 0.474	98.19 ± 0.493	97.84 ± 0.756
45	83.66 ± 0.66	100.7 ± 0.631	100.99 ± 0.728	101.08 ± 0.556	99.99 ± 0.461	98.17 ± 0.724
60	88.1 ± 0.55	100.93 ± 0.60	99.85 ± 0.698	100.82 ± 0.246	100.08 ± 0.447	98.25 ± 0.434
Assay (%)[b]	97.89 ± 0.464	101.98 ± 0.457	101.08 ± 0.447	98.18 ± 0.373	97.09 ± 0.453	98.23 ± 0.633

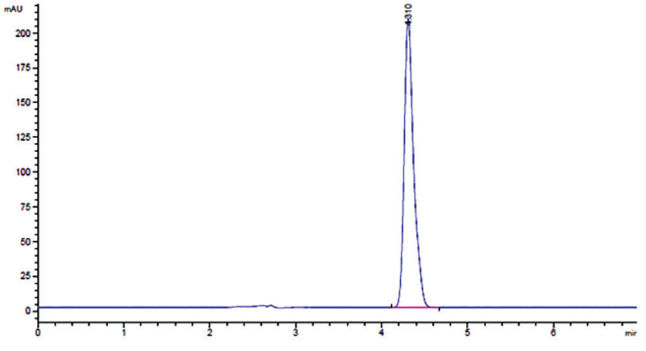
[a]All readings are given as average ± SD; $n = 6$; [b]$n = 3$.

Figure 5



Differential scanning calorimetry (DSC) of the optimized formulation.

Figure 6



Typical high-performance liquid chromatography chromatogram of the test solution.

Discussion

Taste masking of bitter drugs with a higher dose is challenging. STZ is given at a dose of 300 mg twice daily in amoebiasis and is available in the market in the form of film-coated tablets, which takes more than 1 h for 100% *in-vitro* release of the drug. Difficulty in swallowing tablets is a major problem, especially in case of geriatric and pediatric patients as well as in patients who are not able to swallow tablets. Taste-masked granules formed by coating with Eudragit E100 showed immediate release of STZ within 15 min. The optimized granular formulation was found to be palatable and to provide quick relief in amoebiasis.

All the excipients were selected on the basis of preformulation study results. Avicel pH 101 grade (FMC Biopolymer, India) was used as a diluent. PVP K30 was used in solution as well as dry forms as a binder. Hydroxypropyl cellulose was used as a binder when added intragranularly in a dry mix and as a disintegrant along with starch, for coated granules as they are exposed to aqueous fluid. PVP K30 yields porous granules, and hence, it causes difficulty in sizing. However, when used in combination with hydroxypropyl cellulose, it yielded granules that can be sized easily. Aerosil was used to prevent core granules from adhering to each other and to impart good flow properties to granulated cores. It also imparts viscosity to the coating suspension to avoid talc sedimentation during the coating process. Talc was used as an antiadherent and a lubricant/glidant.

As the dose of the drug was very high and it is intensely bitter, pulverized sugar was used as a diluent for the prepared granules. It also imparts sweetness and to some extent masks the bitter taste of STZ. Eudragit E100 was used to coat the granules and to prevent the release of the drug in mouth – that is, at salivary pH 6.8. Eudragit E100 was selected due to its property of being insoluble at and above pH 5.

In preliminary trials, it was found that when a low polymer concentration (C1) coating solution was used, taste masking was achieved after applying almost 60–70% of the total coating solution and the time required for the coating process was more. When a coating

Table 9 Sieve analysis of the optimized batch

Sieve numbers	Arithmetic mean of the size of opening (μm)	Weight retained on the sieve (g)	% Retained on the sieve	Mean granular size (μm)
20#	637.5	0.1517	1.517	341.93
40#	337.5	9.841	98.41	
60#	200	0.063	0.063	
100#	137.5	0	0	
120#	125	0	0	

Table 10 Stability data at 25 ± 2°C and 60 ± 5% relative humidity

Parameters	Periods			
	0 month	1 month	2 month	3 month
Assay (%)	98.17	98.13	98.08	98.02
% Dissolution of the drug in 0.1 N HCl	99.97	99.90	100.01	99.89
Flow property	Good	Good	Good	Good

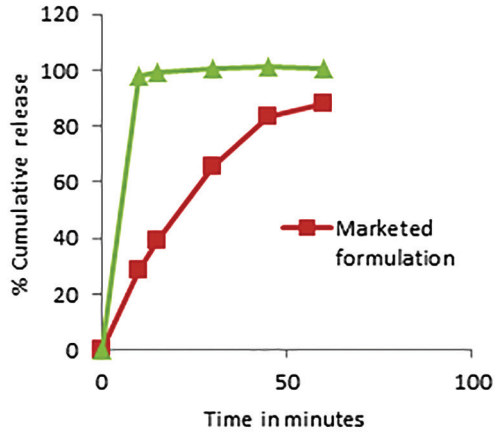
HCl, hydrochloric acid.

Table 11 Stability data at 40 ± 2°C and 75 ± 5% relative humidity

Parameters	Periods			
	0 month	1 month	2 month	3 month
Assay (%)	98.06	98.12	98.03	98.15
% Dissolution of the drug in 0.1 N HCl	99.98	100.10	99.67	99.90
Flow property	Good	Good	Good	Good

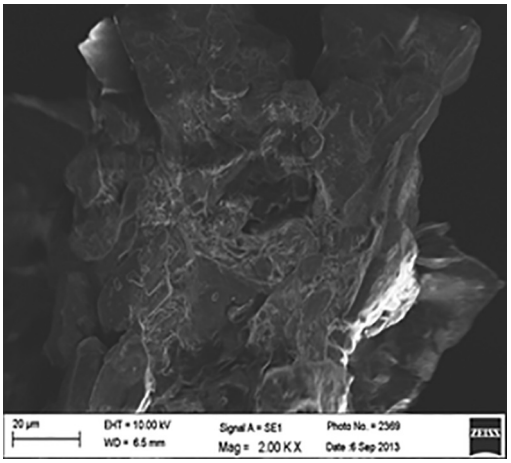
HCl, hydrochloric acid.

Figure 7



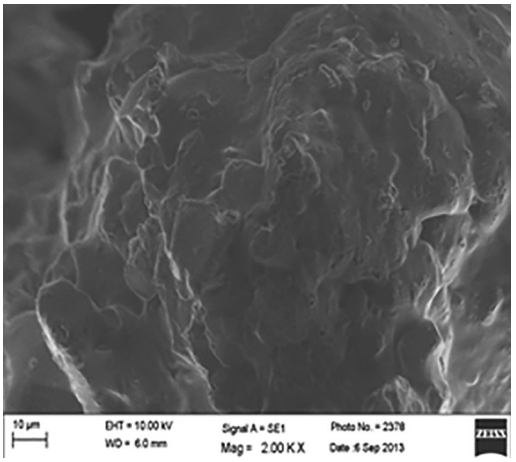
Comparison of the *in-vitro* dissolution study of the optimized formulation and the marketed tablet in 0.1 N hydrochloric acid.

Figure 8



Scanning electron microscope image of the uncoated granule.

Figure 9



Scanning electron microscope image of the coated granule.

solution with medium polymer concentration (C2) was sprayed, taste-masked granules were formed after applying 38–40% of the total coating solution, whereas 32–34% of the total coating solution of higher polymer concentration (C3) was required for taste masking of granules with less processing time. Hence, to decrease the process time and facilitate the coating process, a coating solution with a higher polymer concentration (C3) was selected. Various batches (K1–K5) of granules were prepared by coating the granules at different rates using a higher polymer concentration coating solution (C3), and they were evaluated for taste masking and other parameters such as flow property, drug content (assay) and *in-vitro* drug release.

There was no significant difference in the %cumulative release of K3 and K4 batches. The batch coated with a drug-to-polymer ratio of 1 : 0.6 (K3) was considered as the optimized batch to avoid unnecessary increase in the process time by further coating of the granules. The optimized batch was found to be stable throughout the stability study.

It was observed that as the concentration of the polymer increases, the release of drug in 0.1 N HCl gets retarded, with improved taste masking. The marketed tablets showed a release of less than 40% in 15 min in the same dissolution medium.

Conclusion

Taste masking of bitter drugs with higher doses is challenging. STZ is given at a dose of 300 mg twice daily in amoebiasis and is available in the market in the form of film-coated tablets, which takes more than 1 h for 100% *in-vitro* release of the drug. Difficulty in swallowing tablets is a major problem, especially in case of geriatric and pediatric patients as well as in patients who are not able to swallow tablets. Taste-masked granules formed by coating with Eudragit E100 showed immediate release of STZ within 15 min. The optimized granular formulation was found to be palatable and to provide quick relief in amoebiasis.

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Conflicts of interest

There are no conflicts of interest.

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