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FORMULATION AND EVALUATION OF PEDIATRIC TASTE MASKED ORAL SUSPENSION OF SATRANIDAZOLE

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ABSTRACT
Taste is an important factor in the development of dosage form. The problem of bitter and obnoxious taste of drug in pediatric and geriatric formulations is a challenge to the pharmacist in the present scenario. In order to ensure patient compliance taste masking becomes essential. The purpose of this research was to mask the intensely bitter taste of Satranidazole using ion exchange resin and to formulate oral suspension of the taste masked drug for pediatric patient. When suspension is swallowed bitter taste may not be felt because ion exchange resin complex does not release drug at salivary pH. When it comes in contact with acidic environment of stomach, the complex will be broken down releasing the drug which may then absorbed. Batch method was used for formation of drug resin complex. Various ion exchange resins such as Kyron T-134, Kyron T- 104 and Indion 234 were tried to obtain taste masked drug resin complex (DRC). Optimization of drug loading was carried out. With Indion 234, the drug-resin complex in the proportion of 1:1 achieved equilibrium in 8 hours. 93.74% w/w of drug loading was possible by this method. Complex formation was confirmed by DSC and IR studies. Oral taste masked suspension was prepared using xanthum gum and was evaluated with respect to parameters such as Colour, pH, Viscosity, Sedimentation volume, Redispersibility, Assay, Drug release. Taste masking was evaluated with the help of panel of human volunteers and Rat Behavioral Avoidance Taste Model. Taste masked suspension showed easy redispersibility and 87.93 % of the drug release within 60 minutes at pH 1.2. Thus, results conclusively demonstrated successful taste masking and formulation of suspension with taste masked drug especially for pediatric, geriatric, bedridden, and non cooperative patients.

KEY WORDS: Resin; Satranidazole; taste masking; pediatric.

INTRODUCTION
A wide variety of active pharmaceutical agents exhibit the undesirable characteristic of bitter taste either during or immediately after oral administration. Among these are included such diverse medicinal agents as acetaminophen, ampicillin, azithromycin, chlorpheniramine, cimetidine, dextromethorphan, nitroimidazole derivatives, diphenhydramine, erythromycin, ibuprofen, penicillin, phenylbutazone, psuedoephedrine, ranitidine, spironolactone and theophylline.[1-4]

Various techniques have been identified for taste masking which include polymer coating, inclusion complex formation with β-cyclodextrin, use of ion exchange resins, solubility limiting methods, etc. Conventional taste masking techniques such as the use of sweeteners and flavoring agents alone are often inadequate in masking the taste of highly bitter drugs. Coating is more efficient technology for aggressively bitter drugs even though coating imperfections, if present, reduce the efficiency of the technique.[5-7]

With respect to OTC preparations, such as cough and cold syrups, the bitterness of the preparation leads to lack of patient compliance.

Satranidazole is newer nitroimidazolederivative with broad spectrum bactericidal activity against protozoa and some anaerobic bacteria, selective toxicity to anaerobics with bitter taste.[8-9]

The present study is aimed to develop a pharmaceutically equivalent taste masked oral suspension formulation for paediatric population and to generate useful data to generalize the technique and to provide opportunities to the researchers for further improvement in the formulation perspectives related to oral formulations containing bitter drugs, for effective management of amoebiasis and amoebic dysentery in paediatric population.

Desired properties of pharmaceutical grade Ion Exchange Resins are

a) Fine, free flowing powders
b) Particle size of 25 - 150 microns
c) Contain functional group that capable of exchanging ions and/or ionic groups
d) Insoluble in all solvents & all pH conditions.
e) Not absorbed by body.

Ion exchange resins are water insoluble, cross-linked polymers containing salt forming groups in repeating position on the polymer chain. Drug can be bound to the ion exchange resin by either repeated exposure of the resin to the drug in a chromatographic column (column method) or by prolonged contact of resin with the drug solution (batch method). Drugs are attached to the oppositively charged resin substrates or resinates through weak ionic bonding so that dissociation of the drug-resin complex does not occur under salivary pH conditions. This suitably masks the unpleasant taste and odour of drugs.[10-13]

MATERIAL AND METHODS

Materials

Satranidazole was obtained as a gift sample from Alkem Laboratories Ltd., (Mumbai, India). Kyron T-104 and Kyron T-134 were obtained as gift sample from Corel Pharma Chem (Ahmedabad, India) whereas Indion-254 was obtained as gift sample from Ion Exchange India. (Mumbai, India). Sucrose, Sorbitol, Xanthum gum, Sucralose, Methyl paraben, Propyl paraben, Mango, Cherry and Pineapple flavour were purchased from S. D. Fine chemicals (Mumbai, India). All other chemicals/solvents of analytical grade were used.

Methodology

1) Development and validation of analytical method for Satranidazole

Satranidazole was analysed in hydroalcoholic solution, simulated salivary fluid (SSF) (pH 6.7), simulated gastric fluid (pH 1.2) by UV-spectrophotometer (Jasco V-530).

Scanning of Satranidazole in hydroalcoholic solution

The solution containing 10 µg/ml of satranidazole in hydroalcoholic solution was prepared and scanned over range of 200-400 nm against hydroalcoholic as blank using UV spectrophotometer. The λmax was found to be 317 nm.

A) Development of standard plot of Satranidazole in hydroalcoholic solution

The standard plot of Satranidazole in hydroalcoholic was developed as follows:

1. Satraniddazole, 25mg was accurately weighed on an electronic weighing balance.
2. The weighed amount of Satranidazole was dissolved in 25 ml hydroalcoholic solution in 25 ml volumetric flask to get a solution containing 1000µg/ml.
3. From above solution 2.5 ml was pipette out and transferred to 25 ml volumetric flask. Volume was made up with hydoalcoholic solution.
4. Different aliquots of above stock solution were suitably diluted with hydroalcoholic solution to give 30, 60, 90, 120, 150, 180 and 210 ppm concentration solution of Satranidazole.
5. The absorbance of above solutions was measured on UV spectrophotometer against hydroalcoholic solution as a blank at 317 nm.
6. The exercise was carried out in triplicate and mean of absorbance readings of each concentration were used to develop standard plot, equation and regression coefficient.

B) Development of standard plot of Satranidazole in simulated gastric fluid (SGF) pH 1.2 solution and simulated salivary fluid (SSF) pH 6.7

Development of standard plot of Satranidazole was carried out in SGF and SSF using same procedure used for development of standard curve of Satranidazole in hydroalcoholic solution.

VALIDATION OF ANALYTICAL METHOD

The methods were validated for linearity, intra and inter day precision.

1) Linearity

The linearity of analytical method was determined at concentration range of 30-210 ppm for hydroalcoholic solution, 10-30 ppm for SGF and 30-180 ppm for SSF.

2) Precision

The precision of analytical method was determined by repeatability (intraday) and intermediate precision (inter day) and reported as % RSD. The stock solution was diluted in triplicate to get three sets of solution containing 30-210 ppm (in hydroalcoholic solution), 10-30 ppm (in gastric fluid) and 30-180 ppm (in SSF) of Satranidazole and absorbencies were measured at respective λmax of drug in particular fluids thrice in a day and same was measured in next two consecutive days. % RSD was calculated and reported.

Formation of Drug Complex Using Suitable Ion Exchange Resin

Different ion exchange resins have found different application in pharmaceutical industry. One of their important applications is taste masking of unpleasant tasting Active Pharmaceutical Ingredients (APIs). Kyron T-104, Kyron T-134 and Indion 234 were selected for the study.

Preparation of drug resin complex (DRC)

There are two methods for preparation of resinate: column method and batch method. Drug-resin complex was prepared by batch process. Resins selected for the study were Kyron T-104, Kyron T-134 and Indion 234. Drug-resin complex was prepared with these resins in different ratios keeping drug amount constant and varying the resin concentration 1:1, 1:2, 1:3, 1:4.

Weighed amount of resin was taken in a beaker containing hydroalcoholic solution. It was stirred for half an hour at 800 rpm in order to allow polymer to swell uniformly. Drug was added slowly under stirring condition. The drug resin mixture was stirred for 8h, filtered and dried.

Drug to resin ratios were as shown in table No 1.

Table No 1 Quantities of drug and resins taken for different ratios.

Ratio of Drug:Resin	Amount of drug (gm)	Amount of resin (gm)	Volume of hydroalcoholic solution (ml)
1:1	1	1	100
1:2	1	2	100
1:3	1	3	100
1:4	1	4	100

Optimization of Process of Preparing Drug Resin Complex

The process of preparing drug-resinate was optimized with respect to:

- Time of adsorption.
- Drug resin proportion

Loading was carried out by batch method with weak cation exchange resins Indion 234, Kyron 104 and Kyron 134. The percentage of drug loading on the resin was calculated using UV-spectrophotometer.

Further, batches were prepared by keeping 1:1 ratio constant and varying stirring time from 4 to 8 hrs. Then next batches were prepared by keeping stirring time constant as 8h and varying ratio from 1:1 to 1:4.

Evaluation of drug loading by UV analytical method

The mixtures of drug resin complex to be evaluated were kept aside to allow the particles to sediment and then filtered. Absorbances of filtrates were noted at 317 nm, from which amount of uncomplexed drug was calculated. Drug

In *vitro* taste evaluation: In vitro taste masking study of resinate prepared with Kyron T- 104, Kyron T-134 and Indion-234 in different ratios:1:1, 1:2, 1:3, 1:4 was carried out in simulated salivary fluid (SSF) pH 6.8. Resinate was dispersed in 5 ml of SSF in conical flask. Samples of 1ml were withdrawn at time intervals of 30 sec. and filtered. The filtrates were analysed for Satranidazole at 319 nm using UV spectrophotometer.

Differential scanning calorimeter (DSC)

The formation of complex was confirmed by DSC. The endothermic peaks of drug, resin and resinate was characterised on Pyris 7 software (DSC8000).

Fourier Transmission Infrared Spectroscopy

The IR spectrum of drug, resin and resinate were recorded on FTIR (Jasco, FTIR-5300) spectrophotometer by using KBr disks within the scanning range of 4000-400 cm^{-1}.

Formulation of oral taste masked suspension

Specific quantity of water was boiled and sugar dissolved in it. It was cooled at room temperature. Glycerine and resinate were added to this mixture. Xanthan gum mucilage was added to the above mixture under stirring. Methyl paraben, propyl paraben were added as preservative. Flavouring agent was added and volume made up to required quantity using purified water. Formula is shown in table no 2.

Table No 2: Formula for taste masked suspension.

Resins	Kyron T-104				Kyron T-134				Indion 234			
Drug:Resin ratio	1:1	1:2	1:3	1:4	1:1	1:2	1:3	1:4	1:1	1:2	1:3	1:4
Sucrose	50	50	50	50	50	50	50	50	50	50	50	50
Glycerin	15	15	15	15	15	15	15	15	15	15	15	15
Methyl paraben	0.18	0.18	0.18	0.18	0.18	0.18	0.18	0.18	0.18	0.18	0.18	0.18
Propyl paraben	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
Xanthum gum	200	200	200	200	200	200	200	200	200	200	200	200
Distilled water q.s.ml	100	100	100	100	100	100	100	100	100	100	100	100
Mango emulsion	q. s.	q. s.	q. s.	q. s.	q. s.	q. s.	q. s.	q. s.	q. s.	q. s.	q. s.	q. s.

Evaluation of oral taste masked suspension
Colour and Odour
Developed suspension was evaluated for organoleptic properties like colour and odour.

pH
pH of developed suspension was determined by using pH meter (Universal Enterprises, Mumbai, India).

Viscosity
Viscosity of developed suspension was determined by using Brookfield viscometer. 15ml of suspension was taken into the beaker and was kept in such a way that the spindle was completely immersed into the suspension. Spindle no. Used was used to measure viscosity of developed suspension. Spindle no. used was 34.

Sedimentation Volume
Fifty ml of suspension was taken in 50 ml stopper graduated measuring cylinder. The suspension was dispersed thoroughly by moving upside down for three times. Later, the suspension was allowed to settle for three minutes and the volume of sediment was noted. This is the original volume of sediment (H0).The cylinder was kept undisturbed for 7 days. The volume of sediment read at 7 hr and every 24 hr for 7 days was considered as final volume of sediment (Hu).
Sedimentation Volume (F) = Hu/ Ho.

The ultimate height of the solid phase after settling depends on the concentration of solid and the Particle size. To obtain an acceptable suspension, should be at least 0.9 for 1 h but a longer period preferred for our purpose.

Redispersibility
Fixed volume of each suspension (50 ml) was kept in stoppered cylinder which was stored at room temperature for 7 days. At regular interval, one stoppered cylinder was removed and moved upside down until there was no sediment at the bottom of the cylinder.

ASSAY
5ml of suspension taken in 100ml volumetric flask, 0.1N HCl added to it and sonicated for 10 min. Volume made upto 100ml with 0.1N HCL. Filtered and filtrate was analysed by UV spectrophotometer.

In *vitro* drug release of oral taste masked suspension:
In vitro drug release of the suspension was carried out using USP – type II apparatus (paddle type). The dissolution medium, 500ml 0.1N HCl, was placed into dissolution flask maintaining temperature 37±5°C and 50 rpm. Suspension (10ml) was placed in flask. The apparatus was allowed to run 1hr.

Samples measuring 5ml were withdrawn after every 0, 10, 20, 30, 40, 50 and 60 min. The samples were filtered and analysed by UV spectrophotometer.

In vivo taste evaluation
Rat Behavioural Taste Avoidance Model
The Rat Behavioural Avoidance Taste Model is based on the principle that presentation of a bitter solution to water-deprived rats reduces the drinking frequency. Wistar rats (n=6) were used for the study. Rats were water deprived and trained to drink in a specialized testing chamber ("the Davis rig"; MS- 80; DiLog Instruments, Tallahassee, FL) that permitted brief access to water and test solutions and collection of lick activity data.

Training
Rats were water deprived for 22 h and on the first day, after which they were placed in the Davis rig and given access to water presented in front of a continuously open shutter for 30 min. Rats were returned to their cages and given access to water for an additional 15 min to allow them to rehydrate before water was removed again. On the second day, rats were returned to the Davis rig for additional training that consisted of opening the shutter for 5 min followed by closed shutter periods for 1 min. The 5 min/1 min cycles were continued for a total of 30 min of shutter open time. The rats were then allowed to rehydrate before water was removed overnight. On the third and final training day, rats were tested using a sequence of water presentations that mimicked the subsequent testing days. Up to 70 test cycles were presented each lasting 8 s (shutter open). These test periods were alternated with 2-s rinse periods (to mimic water rinse periods), before moving to the next test solution. Rats were considered successfully trained if they licked successfully for a minimum of 40 consecutive test periods. Rats were always allowed to rehydrate after testing and never fell below 80% of their pre-deprivation weights.

Testing
To test for the behavioural responses to the unknown compounds, two moderate concentrations of known bitter compounds (cycloheximide, denatonium) were prepared and included in the panel of test stimuli. The final two test chambers contained water, which served as the baseline for analysis of the other test compounds and served as the rinse between test stimuli. On the fourth day, each rat was placed in the Davis rig and run through a sequence of test solutions presented randomly. Each test solution was presented for 8 s twice during the experiment. All test trials were interspersed with 2-s water rinse trials. The animals were videotaped to document other behaviours associated with bitter tastants (jaw smacking, oral grooming, withdrawal). These behaviours were also analyzed in the present study.

Data collection
Data was obtained from a group of six rats per group. Data were averaged within each rat for the presentation of each stimulus. The average number of licks was then divided by the average number of licks during the water

presentation to generate the % inhibition of licking as follows:
%inhibition of licking = mean number of licks to stimulus/ mean number of licks to water × 100
The % inhibition of licking generated for each animal and each sample was then averaged across animals to generate the response functions.

Procedure
Rats were deprived of water for a period of 22 hrs. Rats were then made to lick bottles containing water and the licking activity obtained in 5 minutes for water was taken as baseline. Rats were then allowed to lick bottles containing suspension without drug, suspension without resin and developed final optimized suspension. The number of times the rat licks the bottle in 5 min. was counted and the concentration of drug solution causing 50% inhibition in licking frequency compared to water was calculated. Developed formulation and Marketed formulation were then presented to the rats and the licking activity obtained was counted. All test trials were interspersed with 2 min. water rinse trial. The average number of licks was then divided by average number of licks during the water presentation to generate the % of licking frequency as follows:

$$\% \text{ licking frequency} = \frac{\text{mean number of licks to stimulus}}{\text{mean number of licks to water}} \times 100$$

The other avoidance responses such as jaw smacking, withdrawal was also observed.

ii) Evaluation of Taste of developed suspension
Taste of developed suspension was checked by time intensity method. For this purpose 6 human volunteers were selected. In this method a sample equivalent to a normal dose 30 mg was held in mouth for 60 seconds and volunteers were asked to evaluate the developed suspension for taste. Bitterness levels were recorded at 2, 10 and 60 sec. The bitterness level was recorded against pure drug (30 mg) using a numerical scale (3-Strong Bitter, 2- Moderate Bitter, 1- Palatable, 0- No bitter). These volunteers were instructed not to swallow the suspensions, which were placed on the tongue. They were instructed to thoroughly gargle their mouth with water after the completion of test.

Accelerated Stability study
Developed suspension was packed in 60 ml bottles. The packed bottles were placed in stability chamber maintained at 25°C ± 2°C /60%±5% R. H. and 40°C ± 2°C /75% %±5% R. H. for 30 days. The analysis comprised of chemical testing of quantifiable parameters, which could possibly change during storage, such as viscosity, pH, drug content, sedimentation volume, redispersibility and any kind of microbial or fungal growth.

RESULTS AND DISCUSSIONS

Development of calibration curve
The calibration curve of Satranidazole developed at 319 using UV showed regression line equation y = 0.098x + 0.000 and R 2 = 0.999 for hydroalcoholic solution, y = 0.160x + 0.10 and R 2 = 0.998 for simulated salivary fluid and y = 0.115x + 0.172 and R = 0.999 for simulated gastric fluid.

Preparation and Evaluation of resinate
The resinate was prepared with different resins in different ratios by using batch method.

The process was optimised for time of stirring and drug-resin proportion. The process was optimised for 4, 6 and 8 h. This has been done by keeping drug:resin constant and varying stiring time from 4, 6 and 8 h. Further this has been optimised by keeping stirring time constant and varying drug:resin ratio. Maximum drug loading was observed with 8 h and there is no significant increase in drug loading after 8 h.

Drug-resin complex prepared using various resins in different ratios showed maximum drug loading (93.74%) with Indion 234 in 1:1 ratio therefore this complex was taken under consideration for further studies.

Table No 3 Drug loading of different resins in different proportions.

Drug:Resin ratio	Kyron T 104	Kyron T 134	Indion 234
1:1	84.17%	51.94%	93.74%
1:2	52%	82%	84%
1:3	49%	83%	78.92%
1:4	68%	71.97%	86%

From the results, as shown in the table no 3, resin Indion 234 in 1:1 ratio with drug had shown maximum drug loading. Indion 234 in 1:1 ratio had shown maximum drug loading i.e. 93.74% with stirring time 8 h.

In vitro taste evaluation
Resinates were prepared with different resins in different ratios with drug evaluated for in vitro taste evaluation in Simulated Salivary Fluid (SSF) at pH 6.7 for 240 second (4min) by using UV-spectrophotometer at 319 nm. The results for resinate prepared using indion 234 are shown below in the table 4.

Table no 4 % release of drug in SSF.

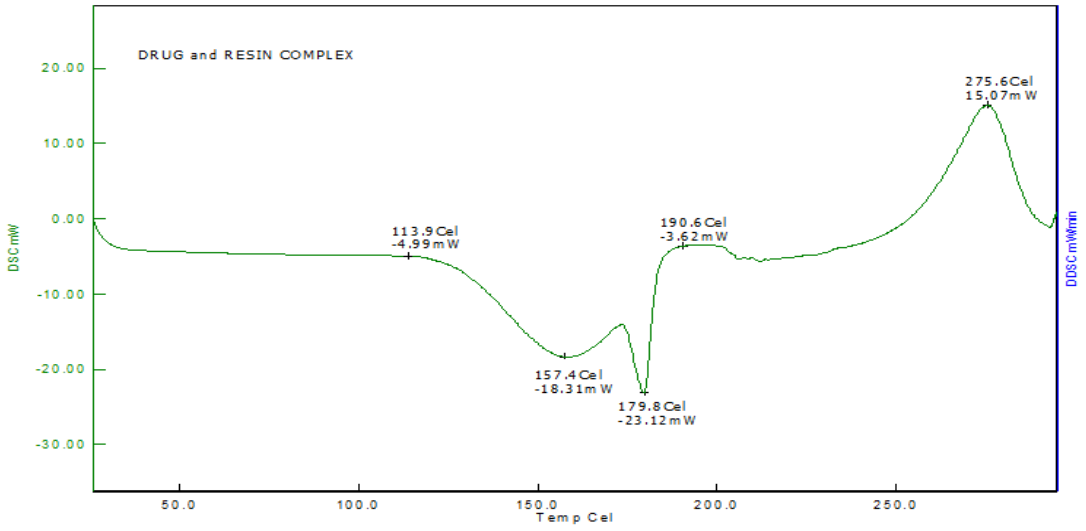
Time in second	% release of drug in SSF
30	3.06
60	4.89
90	8.65
120	12.09
150	13.43
180	13.10
210	12.86
240	13.24

Hence, this Indion 234 was finalised resin for the present study in 1:1 ratio. The resinate prepared with Indion 234 resin in the ratio of 1:1 was used for development of paediatric suspension. Oral taste masked paediatric suspension was developed with Indion 234 in 1:1 ratio. The drug –resin complex prepared with Indion 234 in 1:1 ratio was only considered for the further studies. Differential Scanning Calorimeter (DSC) and Fourier Transmission Infrared Spectroscopy (FTIR) were studied for this drug-resin complex to confirm the formation of complex.

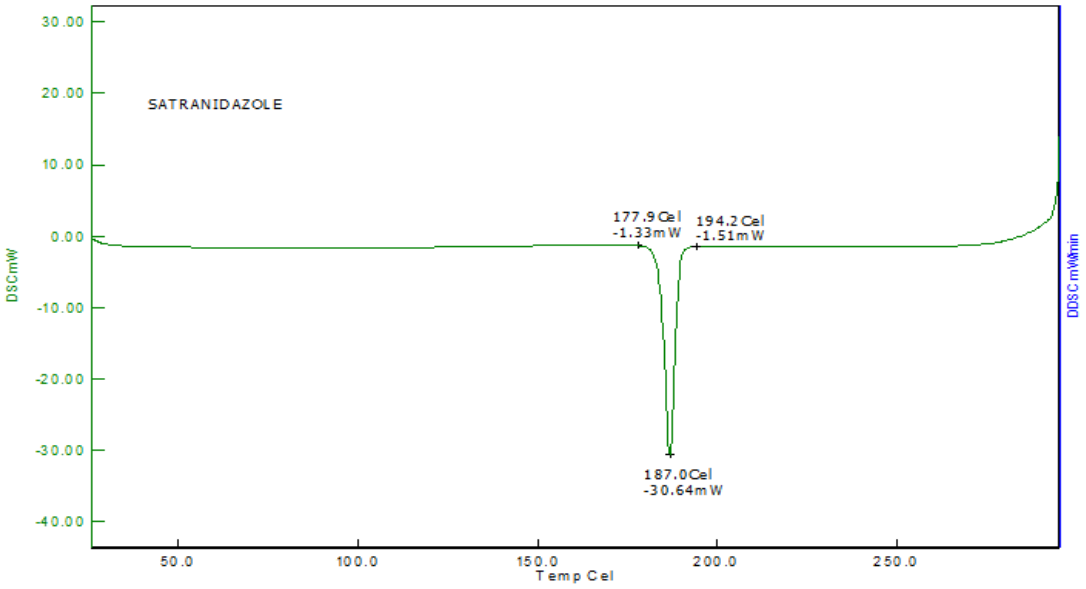
Differential Scanning Calorimeter (DSC) studies

The drug-resin complex prepared with Indion 234 in 1:1 ratio was evaluated for DSC studies. The formation of complex was confirmed by DSC analysis.

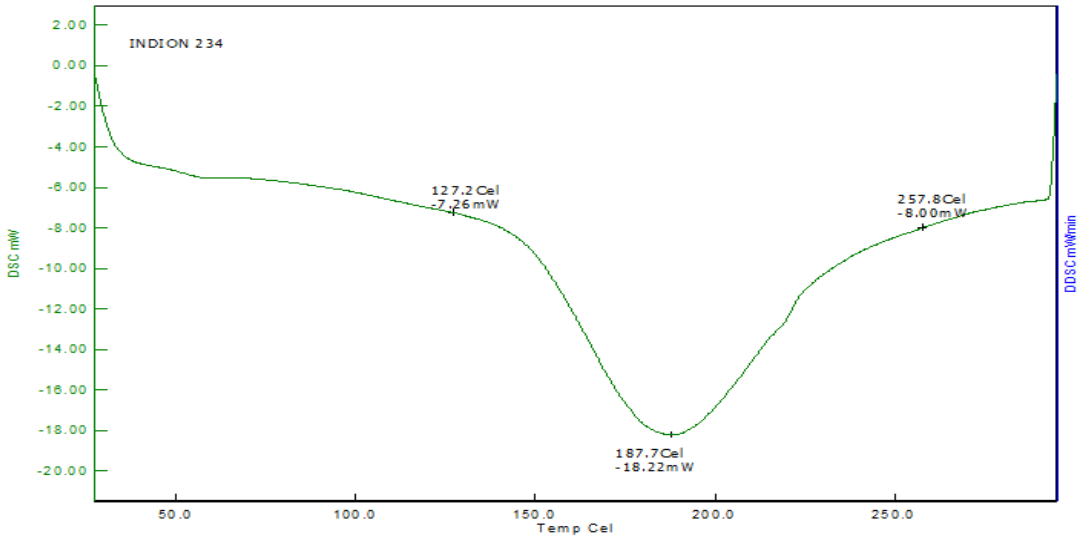
DSC study of Satranidazole



DSC study of Indion 234



DSC studies of drug-resin complex

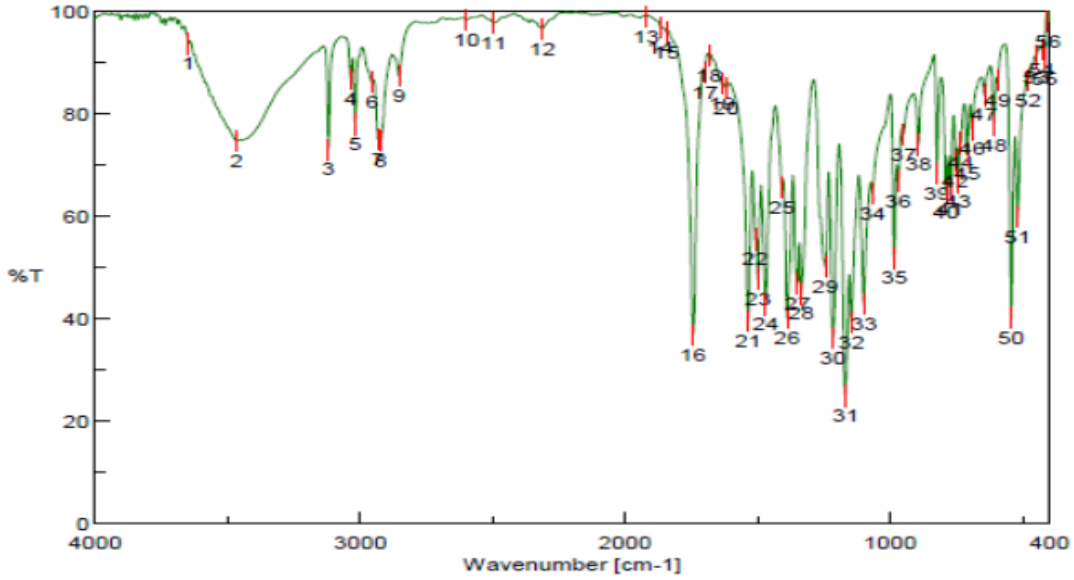


From DSC endothermic peaks, it was observed that pure drug was exhibiting sharp endothermic peak at 187°C. The endothermic peak for pure Indion 234 was observed at 187.7°C. The drug-resin complex had shown sharp endothermic peak at 179.8°C. Absence of sharp peak at 187°C in rug-resin complex indicates that change in physical form of the drug i.e. drug had gone under complete physical changes from crystalline to amorphous form. Further, the endothermic peak of drug-resin complex was observed at 179.8°C which is neither endothermic peak point of pure drug nor Indion 234. This confirms the formation of drug-resin complex.

Fourier Transmission Infrared Spectroscopy (FTIR) studies

FTIR studies of Satranidazole, Indion 234 and drug-resin complex were carried out to analyse the interaction between functional groups present in drug and resin.

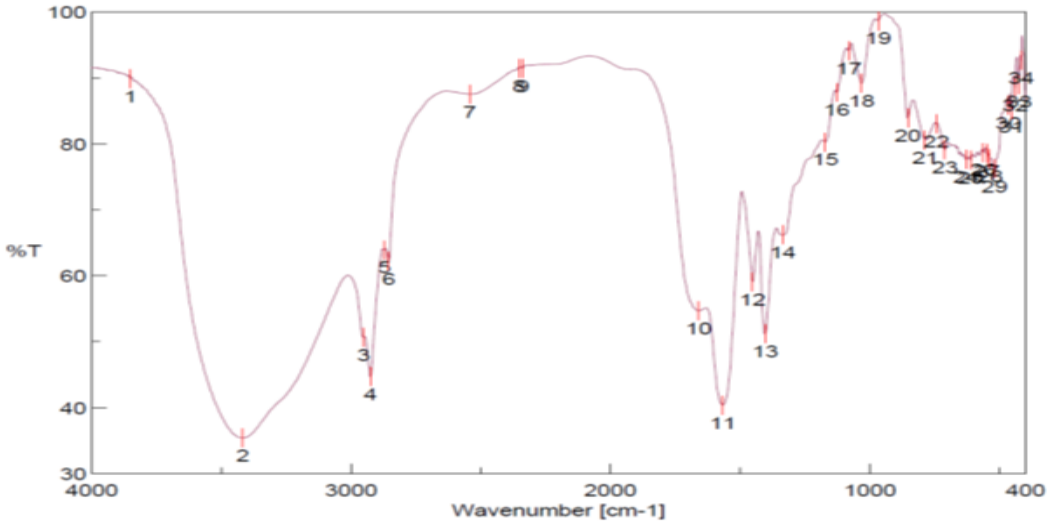
FTIR studies of Satranidazole



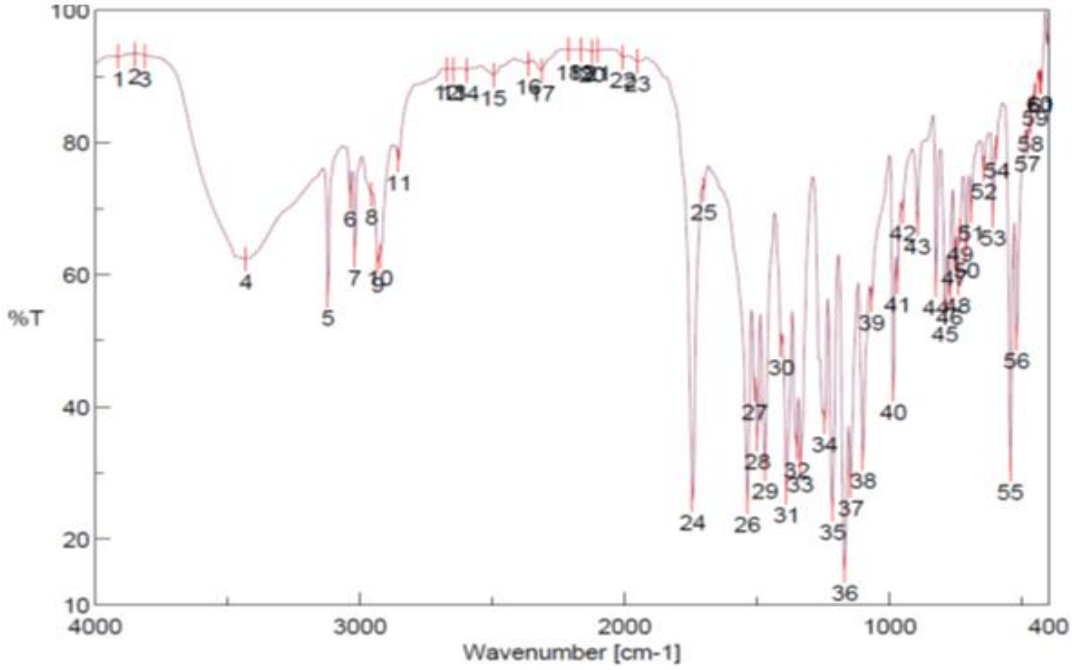
IR values of functional groups of Satranidazole

Functional Group	Peak No.	IR values
-C=N	18	1683.55
-C=O	16	1743.33
S=O	34	1076.41
C-NO_2	21	1536.99
C-N	1215.9	30

FTIR of Indion 234



FTIR studies of drug-resin complex



FTIR spectrum of drug-resin complex had showed formation of number of new peaks indicating formation of newer bonds. Complex formation was confirmed by absence of functional group intensities in the drug-resin complex spectrum when compared with the spectrum of pure drug.

Formulation of taste masked oral suspension

Paediatric taste masked suspension was developed with final optimised resinate. The sweetener used was sucrose and xanthum gum was used as suspending agent and viscosity building agent. Glycerin was used to enhance sweetness, i.e. sweetness enhancing agent in the formulation. It also provides viscosity and uniform appearance to the formulation. The preservatives used were methyl paraben and propyl paraben. These preservatives were used to prevent fungal growth and improve the stability of the suspension. The combination of both these preservatives is effective over a wide range of pH. The combination gives synergetic antimicrobial activity for a prolonged period of time. Hence, usually combination of these two always selected and in present formulation this combination was selected within their safer limits i.e. methyl paraben 0.18% and propyl paraben 0.02%. The colour and flavour selected were mango flavour. To impart flavour and colour mango emulsion was used. This had added both colour and flavour to the formulation. This is necessary to achieve aesthetic appeal of the formulation.

Evaluation of developed suspension
Developed suspension was evaluated for organoleptic properties like colour, odour. The colour was orange yellow with sweet mango fragrance as mango emulsion was used as a colorant and flavouring agent. pH of developed suspension was checked by using pH meter and was found to be 7.00-7.10.

Viscosity
Viscosoty was determined by Brookfield viscometer and was found to be 600 cps with speed 3 and spindle no.34.

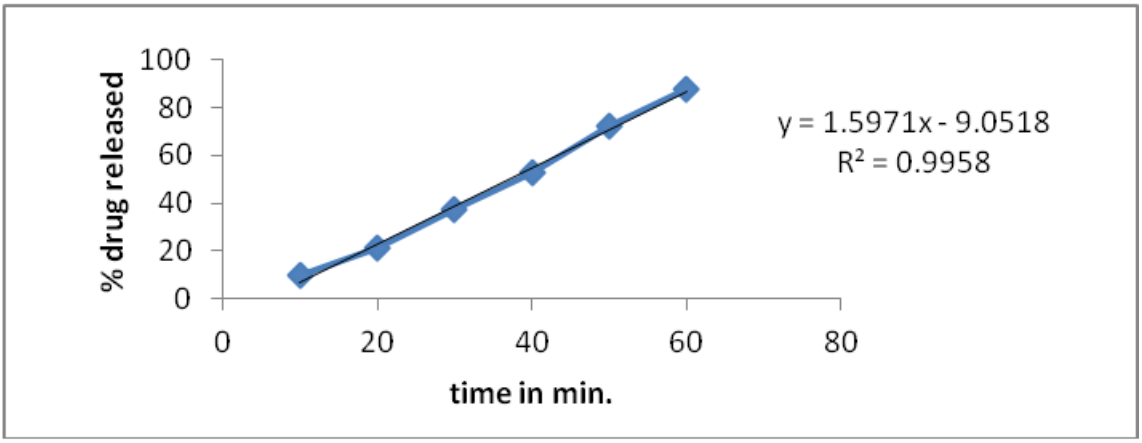
Redispersibility
Redispersibility of developed suspension was checked out and was found to be easy to re-disperse. The formulation was shaken for 3-4 min. to achieve redispesibility. The formulation was found to be easier to redisperse after gentle shaking for period of 3-4 min.

Assay
Assay of developed suspension was carried out using UV-spectrophotometer and was found to be 92.34%.

***In vitro* dissolution test**
The dissolution was studied in 0.1 N HCl and was found to be around 87.93% drug release in 1 hour as shown below in table.

Table No 5 *In vitro* dissolution test.

Absorbance	Conc.	Dilution factor	Conc. in diss	Cumulative release in µg	Cumulative release in mg	% Cumulative release	% Released
0.1178	0.4713043	4.71304348	4241.73913	4241.739	4.241739	424.1739	7.069565
0.2456	0.64	6.4	5760	5764.71304	5.76471304	576.471304	9.6078551
0.3368	1.4330435	14.3304348	12897.3913	12908.5043	12.9085043	1290.85043	21.514174
0.4563	2.4721739	24.7217391	22249.56522	22275.0087	22.2750087	2227.50087	37.125014
0.5765	3.5173913	35.173913	31656.52174	31706.687	31.706687	3170.6687	52.844478
0.72333	4.79391	47.9391	43145.19	43230.5291	43.2305291	4323.05291	72.050882
0.8445	5.84783	58.4783	52630.47	52763.7482	52.7637482	5276.37482	87.93958



different models were applied to check the release kinetics. R2 value was found to be maximum (R2 = 0.995) for zero order release as compared to the other models. Hence, the release of Satranidazole from resinate followed zero order kinetics.

In vivo taste evaluation
To evaluate taste of developed suspension, animal behavioural model was used. Total 6 animals were used for the study. Animals were presented suspension without drug, suspension without resin and developed suspension. Firstly water was presented to them as a baseline. Water deprivation is usual practice for such studies to motivate licking activity of the animal. It was found that animals were freely licking the suspension without drug. The volume consumed was compared with volume of water consumed. Each animal had consumed around 7-8 ml of water in 5 min. exposure period of time. The suspension without drug consumed by each animal was found to be almost same i.e.6-7 ml in 5 min. exposure period of time. The volume of developed suspension consumed by each animal in 5 min. exposure time was found to be equivalent to the volumes of water and suspension without drug i.e. around 5-6 ml.

Suspension without resin was presented for 5 min. and volume consumed was found that 2-3 ml by each animal. The number of licks made by each animal was counted and was averaged.

Average licks for water stimulus was found to be 8 and for suspension without drug and developed suspension were found to be 7 and 6 respectively.

% lick frequency for suspension without drug was found to be 87.5% and for developed suspension was found to be 75%.

% lick frequency for suspension without resin was found to be 25%.

The animal was freely licking the developed suspension like suspension without drug and volume consumed by each animal was equivalent to the consumed volume of suspension without drug.

Human volunteer study

Taste evaluation was performed on six healthy human volunteers and results are given in table no 6.

Table No 6 Results of Human Volunteer Study.

Form of suspension	Degree of bitterness at different time intervals		
	2sec	10sec	60sec
Suspension without resin	3	3	3
Suspension without drug	0	0	0
Developed suspension	0	0	1

*(numerical scale:3-strongly bitter, 2-moderately bitter, 1-palatable, 0-no bitter)

From these results it is clear that presence of drug in the formulation without resin caused around 70% inhibition in licking frequency of each animal whereas only 10-15% inhibition in licking frequency was observed with developed suspension when compared with suspension without drug. The presence of drug caused this inhibition of licking frequency but when drug was complexed with Indion 234 there was no significant inhibition in licking frequency observed. Also, results of human volunteer study showed that developed suspension was palatable when compared with the suspension without drug. Hence, the developed paediatric suspension was found to be palatable and would be acceptable by paediatric population.

Stability study results

Study revealed that prepared suspension can remain intact for longer period of time without any significant changes in assay, sedimentation volume, redispersibility, viscosity and dissolution studies.

Table No 7 Results of Accelerated Stability Study of Parameters for Initial 30 days.

Parameters	Stability condition		
	Initial	25°C± 2°C/60%±5% RH	40°C± 2°C/75%±5% RH
Colour	Orange yellow colour	No Change	No Change
Odour	Sweet mango fragrance	No Change	No Change
Viscosity cps	600	600	600
pH	7.10-7.20	7.10-7.20	7.12-7.23
Sedimentation volume ml	0.98	0.98	1
Assay	92.34%	92.45%	93.38%
Redispersibility	++	+++	+++
Dissolution studies	87.93%	88.12%	88.78%

SUMMARY AND CONCLUSION

Liquid formulations are widely prescribed for paediatric population. Palatability is critical issue in developing oral liquid formulations. This issue can be overcome by using ion-exchange resins for taste masking of APIs. Use of weak cation exchange resin offers good method for formulating taste-masked dosage forms of Satranidazole. Results obtained the present work showed that drugresin complexe effectively mask bitter taste of Satranidazole. Liquid formulations provide easier way to administer medications to children. Also to overcome the problem of non compliance with child especially around 8 years old for whom swallowing other dosage form can be challenging. Hence, the “patient friendly dosage form” of bitter drugs, especially for pediatric, geriatric, bedridden, and noncooperative patients, could be successfully formulated using this technology. Indion 234 resin was found to be effective in taste masking of Satranidazol in 1:1 ratio. The resinate was prepared by batch method. This method is easier, convenient and cheaper as compared to column method. The developed suspension was found to be stable. The oral taste masked paediatric suspension of Satranidazole could be successfully developed using Indion 234.

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