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FORMULATION AND DEVELOPMENT OF TASTE-MASKED MEDICATED ORAL JELLY FOR PEDIATRICS

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Abstract:

The aim of present research work was to develop taste masked confectionery form of Montelukast sodium designed especially for oral delivery to pediatric patients. Effective taste masking of Montelukast sodium was achieved with selected 2- Hydroxypropyl beta cyclodextrin (CavasolW7HP). Inclusion Complex prepared by kneading method i.e. batch KM4 (1:4) showing taste score 1 (tasteless) was selected and further subjected to in-vitro taste assessment study. Based on human panel studies, tasteless MS-2HPBCD complex KM4 was selected as optimized batch. Oral jellies were prepared by incorporating MS-2HPBCD inclusion complex equivalent to 4mg of MS with varying concentrations of gelling agents and with different flavors like orange, strawberry, lemon, etc. Formulation batch F4 containing agar-agar powder and gelatin with orange flavor was more acceptable to human volunteers and showed desired consistency and appearance as soft gummies. Medicated chocolates were also formulated by incorporating taste-masked inclusion complex in chocolate base. Results conclusively demonstrated that successful taste masking of MS was accomplished and suggest that it could be formulated in confectionery form with more acceptability to pediatrics.

Keywords: *Montelukast Sodium; 2- Hydroxypropyl beta cyclodextrin; Oral jelly; Medicated chocolate; Inclusion complex; Taste-masking; Confectionery.*

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INTRODUCTION:

A 'patient-friendly dosage form' improves patient acceptance and compliance. Major challenge to this is the bitter tasting formulations. Montelukast sodium is intense metallic, leukotriene receptor antagonist used for the maintenance therapy of asthma and to relieve symptoms of seasonal allergies. Long-term treatment with montelukast sodium is beneficial to asthma patients since it decreases IgE levels. It has been observed that doctors generally prescribe montelukast treatment for 3 or 6 months in paediatric patients suffering from asthma orallergic rhinitis. The drug is prone to photolytic and oxidative degradation under stressed conditions. Montelukast has been demonstrated to be safe and effective for children ages 2–5 years old and 6–12 years old in treatment of asthma and seasonal allergic rhinitis. Currently formulations that are available in market include oral suspensions, chewable tablets and oral granules. Paediatric patients find it difficult to swallow tablets and also sometimes they resist taking liquid medication.

The taste masking of drug was carried out by forming drug-cyclodextrin inclusion complexes. Cyclodextrin (CD) is crystalline, cyclic oligosaccharides derived from starch. The most commonly used forms are α-, β-, and γcyclodextrin, which have respectively 6, 7, and 8 glucose units. β -Cyclodextrin is widely used in taste masking purpose; in which β-Cyclodextrin make an inclusion complex with drug (guest) molecules & act as a hydrophobic host cavity so drugs make a complex in inert carrier matrix. This characteristic of the polymer enables encapsulation of the drug in the cavity resulting in the improvement in the solubility, drug release as well as taste masking. [1-5]

This would not only improve taste of drug but it would also enhance drug stability. By masking the unpleasant taste of drug, patient acceptance and compliance can be improved. The confectionery form will be more acceptable among the paediatric population.

MATERIALS:

Montelukast Sodium was a gift sample from Zeon Drugs Pvt. Ltd., Navi Mumbai. Cyclodextrin was gifted from Ashland, Mumbai. Sucralose was obtained as a gift sample from Alkem Labs, Mumbai. All other chemicals used were of analytical grade.

METHODS:

1.Pre-formulation study-

a) Organoleptic properties and description

The sample of Montelukast Sodium was studied for organoleptic characters and description.

b) Melting point determination

Melting point of drug was determined by capillary method. The capillary filled with drug powder was placed in Thiele's tube filled with liquid paraffin. The tube was heated and the melting point of drug powder was noted.

c) Drug-excipient compatibility:

The FTIR spectrum of drug and a physical mixture of drug and excipient were obtained using KBr press pellet method. The discs were prepared using manually operated KBr press model M-15. The scanning range was 4000-400cm^{-1}. The FTIR spectrum of the sample drug was compared with the standard FTIR spectrum of the pure drug to ascertain any significant changes in the sample drug.

d) Solubility Study of drug in different solvents

The aim of the solubility study was to decide or select solvent for drug extraction during percent drug content determination. Solubility of drug was determined in distilled water, methanol, and Phosphate buffer pH 6.8, 0.1N NaOH and 0.1 N HCl.

2. Analytical method development of MS

a. Determination of analytical wavelength

Stock solution of Montelukast Sodium was prepared by accurately weighing 10 mg of drug and dissolved in 10 ml of methanol to get concentration of 1000 µg/ml. From the above stock solution, 10 µg/ml solution with a concentration of 10 µg/ml was prepared in methanol, distilled water and phosphate buffer pH 6.8. Each of these solutions were subjected to UV scan from 200-800 nm using the double beam UV spectrophotometer to determine the wavelength of maximum absorbance.

b. Preparation of calibration curve of MS in methanol

Stock solution of Montelukast Sodium was prepared by accurately weighing 10 mg of drug and dissolved in 10 ml of methanol to get concentration of 1000 µg/ml. From the above stock solution, different solutions in the concentration range of 5-30 µg/ml were prepared in methanol. The absorbance of each solution was recorded at λmax 283.4 nm using UV spectroscopy. The graph of absorbance versus concentration was plotted.

c. Preparation of calibration curve of MS in distilled water

Stock solution of Montelukast Sodium was prepared by accurately weighing 10 mg of drug and dissolved in 10 ml of distilled water to get concentration of 1000 µg/ml. From the above stock solution, different solutions in the concentration range of 5-30 µg/ml were prepared in distilled water. The absorbance of each solution was

recorded at λmax 283.4 nm using UV spectroscopy. The graph of absorbance versus concentration was plotted.

d. Preparation of calibration curve of MS in phosphate buffer pH 6.8

Stock solution of Montelukast Sodium was prepared by accurately weighing 100 mg of drug and dissolved in 10 ml of methanol and the volume was then made to 100 ml with phosphate buffer pH 6.8 to get concentration of 1000 µg/ml. From the above stock solution, different solutions in the concentration range of 5-30 µg/ml were prepared in phosphate buffer pH 6.8. The absorbance of each solution was recorded at λmax 283.4 nm using UV spectroscopy. The graph of absorbance versus concentration was plotted.

2. Estimation of Threshold concentration for Montelukast Sodium

The threshold concentration of bitter taste of drug was checked by a sensory test on human volunteers. Aqueous solution of (10,20,30,40,50, 60, 70, 80, 90µg/ml) were prepared. 1ml of each solution was placed on the center of the tongue of human volunteers for 10 second. The volunteers were then told to spit out after 10 second and told to rinse mouth thoroughly with distilled water. The volunteers were asked to comment on the taste of each solution. A gap of 5 min was maintained in between testing two different solutions. Threshold value was selected on the basis of bitterness scale value. Bitterness level was recorded using numerical scale and scored from 0-4 (0=good, 1= tasteless, 2= slightly bitter, 3= bitter and 4 = very bitter).

3. Preparation of taste masked drug inclusion complex

Complexation of drug was carried out using Cavasol W7HP (2-hydroxypropyl-beta cyclodextrin) derivative by two different methods like Physical Mixtureand kneading method in different molar ratios, i.e. 1:1,1:2,1:3,1:4 and 1:53

3.1.1 Physical Mixture

Drug and2-Hydroxypropyl-beta cyclodextrin were weighed accurately and mixed in above said ratios by geometric dilution method. The mixture was triturated for 10 min to obtain a homogenous powder blend and it was further passed through sieve no. 80.

3.1.2Kneading Method

Drug and 2-Hydroxypropyl-beta cyclodextrin in above said ratios were mixed in a mortar for 1 hour with aid of water and kneaded thoroughly with pestle to get slurry-like consistency. Then slurry was dried in hot air oven at temperature not exceeding 40°C for 24 hr. Dried complex was sifted with sieve #80 and stored in desiccator for further use.

Table 1: Drug – 2HPBCD inclusion complex ratio

Method	Drug to carrier	Drug to carrier ratio	Batches with Cavosol W7HP
Physical mixing	MS:HPBCD	1:1 1:2 1:3 1:4 1:5	PM 1 PM 2 PM 3 PM 4 PM 5
Kneading	MS:HPBCD	1:1 1:2 1:3 1:4 1:5	KM 1 KM 2 KM 3 KM 4 KM 5

4. Characterization of Inclusion Complex

a) Human panel studies-

The prepared inclusion complexes of different batches were given to healthy human volunteers for taste perception. Sample equivalent to 4mg of drug dose was held in mouth for 10 sec. Time interval between different samples was 5 min. Bitterness level was recorded using numerical scale and scored from 0-4 (0=good, 1= tasteless, 2= slightly bitter, 3= bitter and 4 = very bitter). Based on evaluation study, tasteless complex was selected as optimized complex. Optimized complex was further evaluated for DSC analysis, drug content, etc.

b) Drug content of inclusion complexes-

For determination of drug content, 10mg of complex was weighed and diluted with 10ml of methanol and sonicated for 15 min till dissolved. 1 ml of this solution was transferred into volumetric flask and volume was made up to 10ml with water. This solution was subjected to UV visible spectrophotometry analysis and the percent drug content was calculated.

c) *In-vitro* taste evaluation-

Taste of drug inclusion complex was studied in vitro by determining drug release in simulated

salivary fluid (SSF) (pH 6.8) to predict release in the human saliva. Drug inclusion complex equivalent to dose of API was placed in 10mL of SSF and shaken for 60 seconds. 1 ml of this solution was transferred into volumetric flask and volume was made up to 10ml with water. The amount of drug released was analyzed using UV visible spectrophotometry.

d) Differential Scanning Calorimetric Analysis-
The thermal analysis of MS, 2HPBCD and MS-2HPBCD inclusion complex was carried out by employing DSC (Mettler Toledo DSC). Sample equivalent to 5 mg weight was heated in aluminum pans over a temperature range of 30°C to 300°C at a constant rate 10°C/min under nitrogen purge (40ml/min).

e) Powder characterization-
Powder was characterized for angle of repose, Bulk density, tapped density, Hauser's ratio and Carr's index.

5. Formulation of oral jelly-
Oral jelly was developed and optimized by mixing MS-2HPBCD inclusion complex equivalent to 4mg of MS with varying concentrations of gelling agents and with different flavors like orange, lemon, andstrawberry, etc.

5.1Procedure-
Selected composition of gelling agent was dissolved in distilled water at temperature 80°C-100°C. As temperature falls down to 40°C, MS-2HPBCD inclusion complex was then transferred to beaker containing mixture of gelling agents; followed by addition of sucralose, flavors, colors and preservatives etc. The mixture was then transferred to moulds and allowed to set in refrigerator. The compositions of different batches of oral jelly of MS are shown in table no. 2.

Table 2: Composition of different batches of oral jelly of MS

Formulation Ingredient	F1	F2	F3	**F4**	F5	F6	F7	F8
Complex Equivalent to 4mg of drug	45.87	45.87	45.87	**45.87**	45.87	45.87	45.87	45.87
Agar agar powder (%)	-	-	1	**2**	-	-	1	1
Gelatin (%)	1	1	-	**0.5**	-	2	1	-
Pectin (%)	-	-	-	-	1	1	-	1
Instant Jellymix (%)	-	1	-	-	-	-	-	-
Sucralose (%)	0.5	0.5	0.5	**0.5**	0.5	0.5	0.5	0.5
Strawberry flavor (%)	0.5	-	-	-	0.5	-	0.5	-
Orange flavor (%)	-	0.5	-	**0.5**	-	-	-	0.5
Lemon flavor (%)	-	-	0.5	-	-	0.5	-	-
Sodium Citrate (%)	0.2	0.2	0.2	**0.2**	0.2	0.2	0.2	0.2
Methyl paraben (%)	0.05	0.05	0.05	**0.05**	0.05	0.05	0.05	0.05
Water (ml)	1.5	1.5	1.5	**1**	1	1	2	2
Total (mg)	1000	1000	1000	**1000**	1000	1000	1000	1000

6. Evaluation of oral jelly
a) Physical appearance:
The prepared jellies were observed visually for clarity, odor, texture and presence of any particles. The texture was evaluated in terms of stickiness and grittiness by mild rubbing the jellies between two fingers.
b) Weight variation:
The average weight of ten jellies was taken to determine weight variation. The jellies were taken out of the moulds in a beaker and weighed individually.

c) pH:
The pH of prepared jellies was measured using a digital pH meter at room temperature (25°C ± 5°C). For this purpose, 0.5 g of jelly was dispersed in 50 mL of distilled water, and the pH was noted.

d) Gustatory sensation test (Taste evaluation):
Taste masking ability of developed formulation was evaluated using taste panel of six healthy human volunteers. One oral jelly of each batch F1 to F8 was given to the healthy human volunteers. The volunteers were asked to taste samples kept in the mouth for 60seconds and then they spit out and asked to give score. The numerical scale with following values 0= Good, 1= Tasteless, 2=

Slightly bitter, 3=Moderately bitter and 4= Extremely bitter.

Based on evaluation study more acceptable formulation was selected as a optimized batch. The optimized batch was further evaluated for drug content, syneresis etc.

e) Drug content:
For determination of drug content, the jellies were taken out of moulds and weighed individually, pooled and mixed. The gel equivalent to 4 mg of MS was taken in 100 ml volumetric flask and diluted with 100 ml of methanol. It was then sonicated for 15-20 min for dissolving. This solution was then filtered and subjected to UV analysis and the percent drug content was calculated.

f) Syneresis:
For determination of drug content 10mg of oral flavored powder was diluted with 10ml of methanol and sonicated for 15 mins to dissolve. 1 ml of this solution was transferred into volumetric flask and volume made upto 10ml with mobile phase. This solution was subjected to HPLC analysis and the percent drug content was calculated.

***g) In-vitro* evaluation:**
In Vitro Drug release studies the release rate of taste masked oral jelly of MS was determined using USP dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml of phosphate buffer pH 6.8, at 37 ±0.5°C and 75rpm. Sampling was done at 5, 10, 15, 20, 25, 30, 45, 50 minutes. For each sample five ml of the dissolution medium was withdrawn and the same amount of dissolution medium at 37±0.5 ºC was replenished to the dissolution medium. The sample withdrawn was filtered using a 0.2-µm nylon disc filter. The filtered samples were suitably diluted if necessary and analysed for the MS content using UV spectrophotometer.

e) *In-vivo* evaluation
Six male Wistar rats (200–250g) were employed for the study as per the animal protocol approved by the Institutional Animal Ethics Committee (IAEC), protocol no. 879/PO/Ere/S/05/CPCSEA. Animals were housed in standard conditions of temperature), relative humidity (605%) and light (12h of light–dark cycles).
The Rat Behavioral Avoidance Taste Model is based on the principle that presentation of a bitter solution to water-deprived rats reduces the drinking frequency. Six male wistar rats weight ranging from 200-250g were used for the study.

Procedure:
On first Day rat were deprived of water for overnight to motivate licking behavior but have access to food. On second day after the water deprivation period 50 ml of water in graduated siphon drinking bottles was subjected to the rats for a period of 30 min, followed by removal of the bottles and recording of the volume consumed. After that on third- and fourth-day rats were allowed for free access to water. At the end of fourth day again rats were subjected overnight to water deprivation cycle. On fifth day after the water deprivation period 50mL of (0.1mg/ml) of drug solution was subjected to rats for a period of 30 min and the volume consumed was recorded. Then again for sixth- and seventh-day rats were allowed for free access to water. At the end of seventh day again rats were subjected overnight to water deprivation cycle. On eighth day 50mL of 0.1mg/ml of Taste-masked formulation was subjected to rats for a period of 30min, followed by removal of the bottles and recording of the volume consumed. Throughout the experiment temperature was kept constant. Other behavioural responses of rats were also observed.

Statistical Analysis
The differences between the groups were analyzed by one-way analysis of variance (ANOVA) followed by Dunnett's t test or Tukey's multiple comparison test. A difference of $P<0.05$ was considered statistically significant as compared to the groups defined in the Figure legends.

f. Stability studies
The optimised batch was subjected for stability study as per international council on harmonization (ICH). Formulation was packed in laminated aluminum packs and stored at different temperature for stability.

Table 3: Stability studies condition and evaluation parameters

Condition	Long Term Storage 25ºc±2ºc/60±5%RH 3 Months	Long Term Storage 0±2-8°C 3 Months	Accelerated Conditions 40°C±2°C/75±5% RH 3 Months
Evaluation	Physical Appearance, Drug Content and*In-Vitro* Dissolution Study.	Physical Appearance, Drug Content and*In-Vitro* Dissolution Study.	Physical Appearance, Drug Content and*In-Vitro* Dissolution Study.

7. Results and Discussion:

7.1.1 Preliminary study on MS

Table 4: Preliminary study data of MS

Sr. No.	Parameter	Drug (MS)
1	Color	White to off-white powder
2	Odor	Odorless
3	Taste	Intense metallic
4	Melting point	112-114°C

7.1.2 FTIR spectrum of Montelukast Sodium

The IR spectrum of pure drug was found to be similar to the reference standard IR spectrum of Montelukast Sodium. Compatibility of MS and selected excipient to produce oral jelly was assessed by placing mixture of MS and each excipient in caped glass vials at room temperature for 30 days. Visual observation of each mixture suggested that there was no change in color and appearance even after 30 days of the study. These results suggest that there is no chemical interaction between drug and excipient used for formulations.

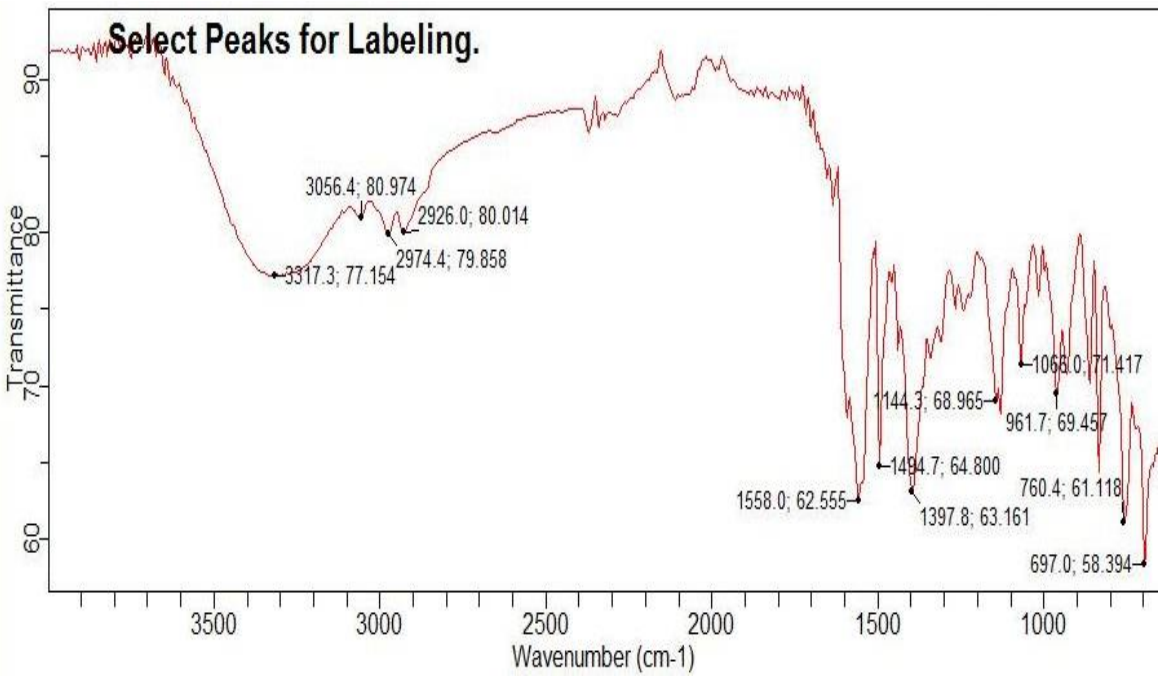

Fig. 1: FTIR spectrum of Montelukast Sodium

Table 5: Interpretation of IR spectrum of MS

Wave number cm^{-1}	Assignment
3317.3	O-H stretching
3056.4	C-H stretching
2974-2926	N-H stretching
1558	Aromatic C-C stretching
760.4-697	C-Cl stretch alkyl halide
1066	C-O stretch alcohol, Caboxylic acid

7.1.3 Solubility Study of drug in different solvents-

Table 6: Solubility of MS in various solvents

Vehicles	Solubility (mg/ml)
Methanol	30
Distilled Water	4
Phosphate buffer pH 6.8	8
0.1NNaOH	10
0.1N HCL	6

From the above results it was concluded that drug shows good solubility in methanol, 0.1N NaOH, soluble in Phosphate buffer pH 6.8.

7.1.4 Analytical method development for estimation of MS

Wavelength scan from 800-200 nm was performed to find absorption maxima. Maximum absorption was found at 283.40 nm in methanol and distilled water, 285.80 nm in phosphate buffer pH 6.8.

7.1.5 Calibration curve of MS in methanol

The concentration range of 5 to 30 µg/ml of drug was used for preparation of standard curve in methanol. The value of R^2 was found to be 0.9996 indicating that the relation of drug concentration and absorbance was linear.

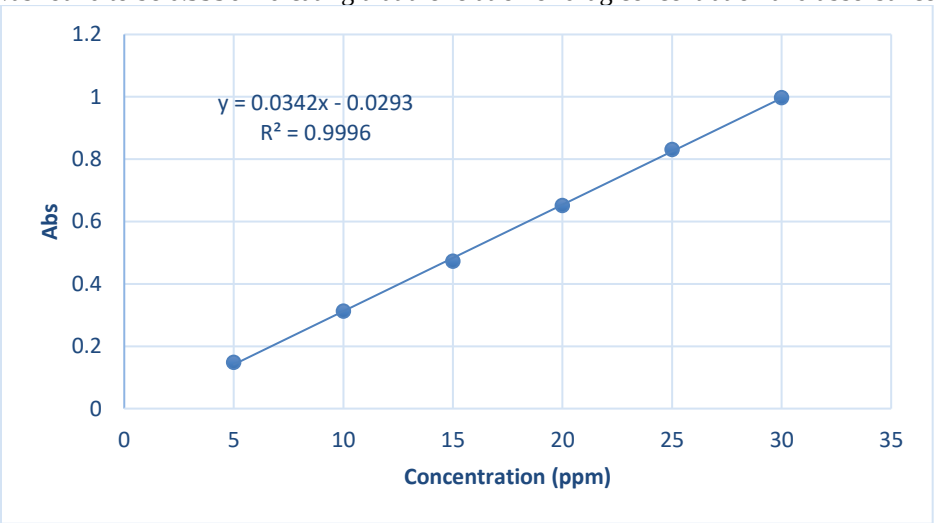

Fig. 2: Calibration curve in methanol

7.1.6 Calibration curve of MS in phosphate buffer pH 6.8

The concentration range of 5 to 30µg/ml of drug was used for preparation of standard curve in phosphate buffer pH 6.8. The value of R^2 was found to be 0.9991 indicating that the relation of drug concentration and absorbance was linear.

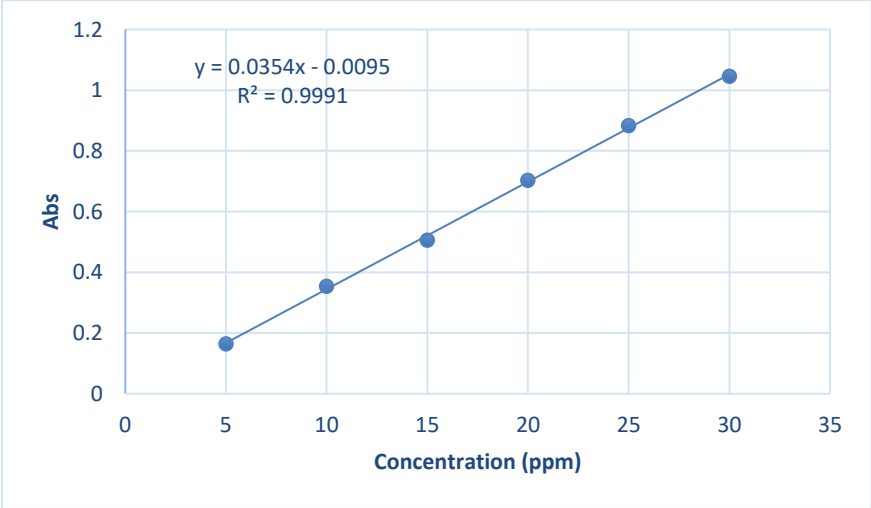

Fig. 3: Calibration curve in phosphate buffer pH 6.8

7.1.7 Calibration curve of drug in distilled water

The concentration range of 5 to 30 µg/ml of drug was selected for development of standard curve in methanol. The value of R^2 was found to be 0.9968 indicating that the relation of drug concentration and absorbance was linear.

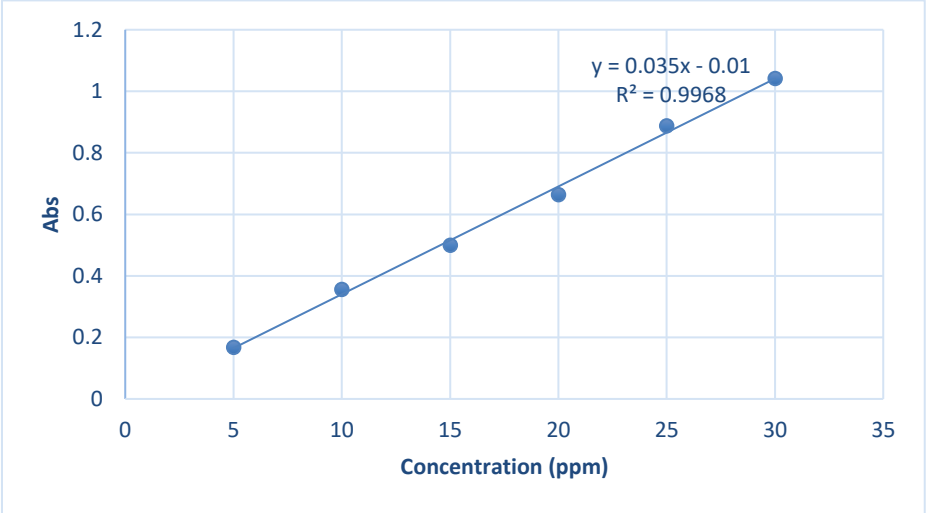

Fig. 4: Calibration curve of drug in distilled water

7.1.8 Estimation of Threshold concentration for Montelukast Sodium

The bitterness threshold was reported approximately to be 80µg/ml. No bitter taste was observed till a concentration less than 80 µg/ml by any of the six human volunteers.

Table 7: Determination of Bitterness Threshold Concentration of MS

Drug solution (ppm)	Human volunteers					
	1	2	3	4	5	6
10	1	1	1	1	1	1
20	1	1	1	1	1	1
30	1	1	1	1	1	1
40	1	1	1	1	1	1
50	1	1	1	1	1	1
60	1	1	1	1	1	1
70	1	1	1	1	1	1
80	**2**	**2**	**2**	**2**	**2**	**2**
90	3	3	3	3	3	3

7.1.9 Characterization of taste masked drug inclusion complex

a. Human panel study-

The results of taste evaluation of MS-2HPBCD complex by human volunteers for Cavasol W7HP are depicted in table no 8. The batch KM4 showed taste score 1 which confirmed that bitter taste of MS was successfully masked by using Cavasol W7HP.

Table 8: Taste evaluation of MS-2HPBCD complex by volunteers for Cavasol W7HP

BATCH NO	HUMAN VOUNTEERS					
	1	2	3	4	5	6
PM1	4	4	4	4	4	4
PM2	4	4	4	4	4	4
PM3	4	4	4	4	4	4
PM4	3	3	3	3	3	3
PM5	3	3	3	3	3	3
KM1	4	4	4	4	4	4
KM2	3	3	3	3	3	3
KM3	2	2	2	1	1	1
KM4	**0**	**0**	**0**	**0**	**0**	**0**
KM5	0	0	0	0	0	0

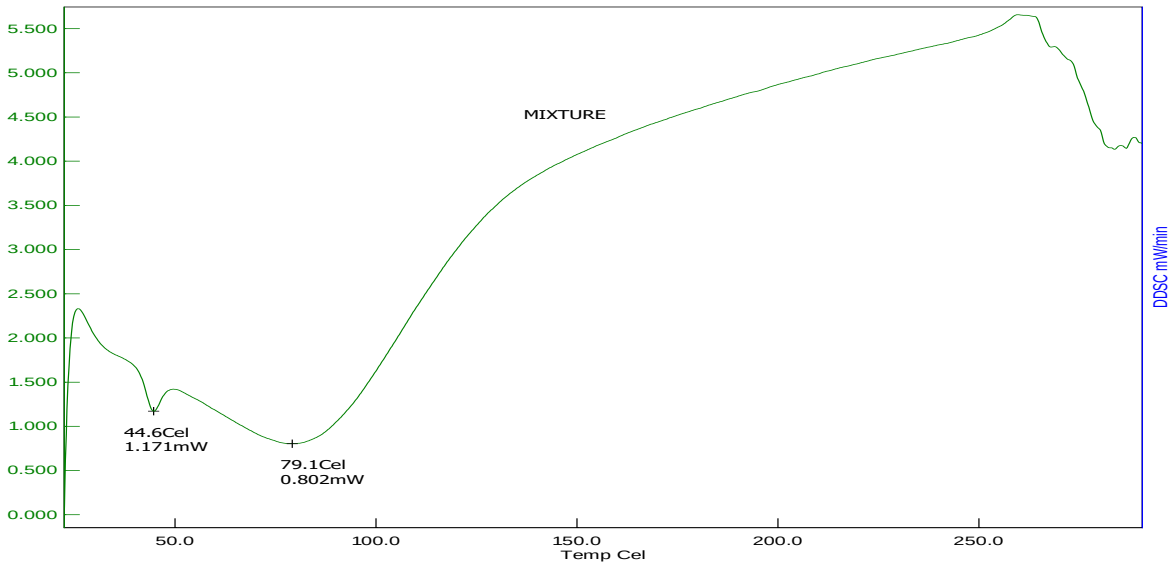

Fig. 5: DSC thermogram of MS

c. Drug content assay

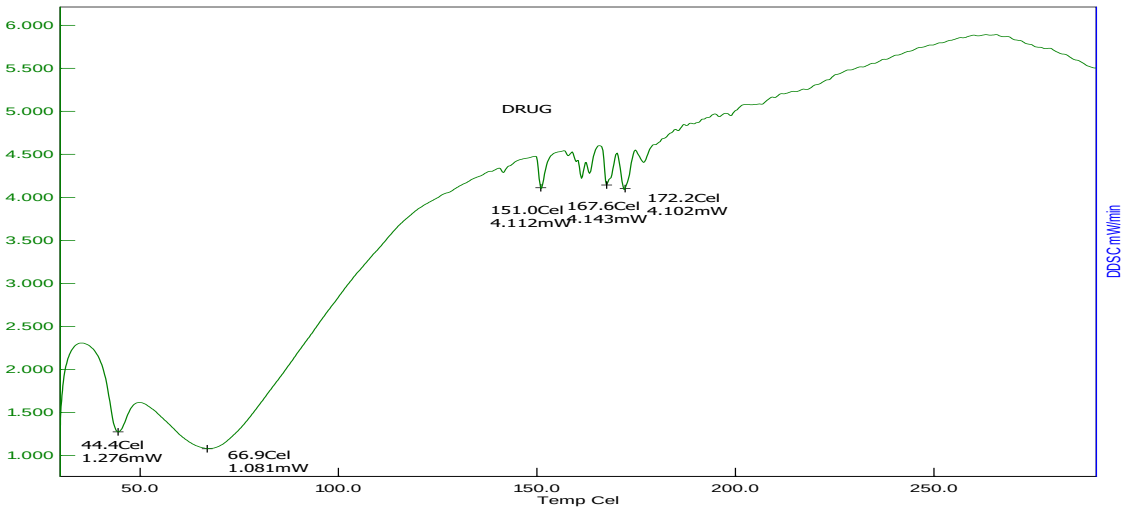

Fig. 6: DSC thermogram of MS-2HPBCD

d. *In vitro* taste evaluation

The amount of drug released at salivary pH was found to be 0.08628mg/10ml i.e. 8.628 ppm in 60 seconds. The results of threshold response study showed that threshold concentration of MS is 80 ppm which is significantly lower than that obtained from *in-vitro* taste evaluation.

e. Differential Scanning Calorimetric analysis

When DSC thermogram of MS and 2HPBCD are compared with that of MS-2HPBCD inclusion complex, it was observed that in thermogram of MS-2HPBCD inclusion complex the endothermic peak at 134.4°C corresponding to 2HPBCD is slightly shifted to 127°C and the endothermic peak at 204°C corresponding to MS was not visible indicating complete encapsulation of drug in 2HPBCD.

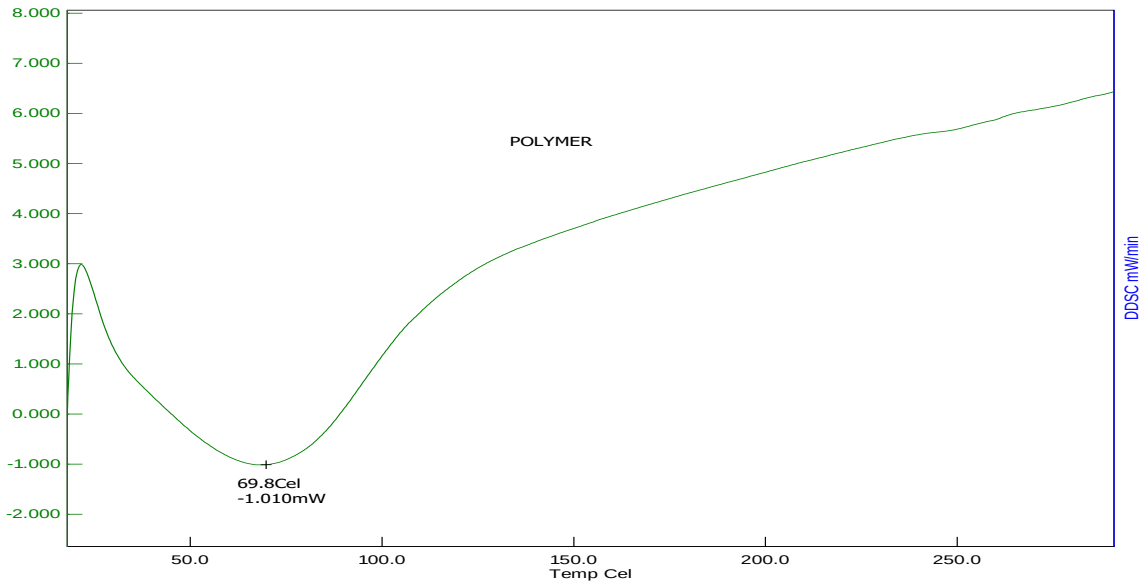

Fig. 7: DSC thermogram of 2-HPBCD

f. Powder characterization

The results for evaluation of flow properties of optimized inclusion complex are shown in the following table no. 10.

Table 10: Flow properties of inclusion complex

Batch	KM4- 1:4 (kneading method)
Angle of repose	32.95°±0.12
Bulk density	0.60±0.12gm/cm^3
Tapped density	0.70±0.14gm/cm^3
Carr's index	14%
Hausner's ratio	1.17

7.2 Evaluation of oral jelly

7.2.1 Physical observation

On physical observation of jellies from batch KM4, it was observed that the jellies were smooth, shiny and non-sticky in texture.

Fig 8: Shows the image of the optimized formulation F4

7.2.2 Gustatory sensation test:

All the developed formulations (F1-F8) showed acceptable palatability, but the batch F4 formulated using orange flavor was more acceptable to volunteer's, so batch F4 was selected as an optimized batch.

Table 11: Taste evaluation of formulations by volunteer

Batch no	**Human volunteers**					
	1	2	3	4	5	6
F1	0	0	0	0	0	0
F2	0	0	0	0	0	0
F3	0	0	0	0	0	0
F4	**0**	**0**	**0**	**0**	**0**	**0**
F5	0	0	0	0	0	0
F6	0	0	0	0	0	0
F7	0	0	0	0	0	0
F8	0	0	0	0	0	0

W

7.2.3 pH and weight variation

The result of the pH and weight variation of the oral jellies from optimized batch F4 are given in table no. 12 respectively.

Table 12: Results of pH and weight variation

Batch	Weight variation (%)	pH
F4	2.45%±0.58%	6.5

7.2.4 Drug content

Drug content of oral jelly of optimized batch F4 was found to be 95±0.14 %

7.2.5 *In-vitro* release study

The results of the dissolution study profile of optimized batch F4 in phosphate buffer pH 6.8 are shown in the table no. 13 and figure 9. It is evident from the observation that MS oral jelly showed a dramatic improvement in the release profile within 60 minutes. The percent cumulative release was found to be 98±0.10% in 60 minutes.

Table 13: In-vitro drug release data of MS from optimized batch F4

Sr. no	Sampling time (minutes)	% Cumulative drug release
1.	5	6.75
2.	10	13.94
3.	15	31.85
4.	20	46.32
5	25	68
6.	30	83.3
7.	40	91.18
8.	50	95.55
9.	60	98

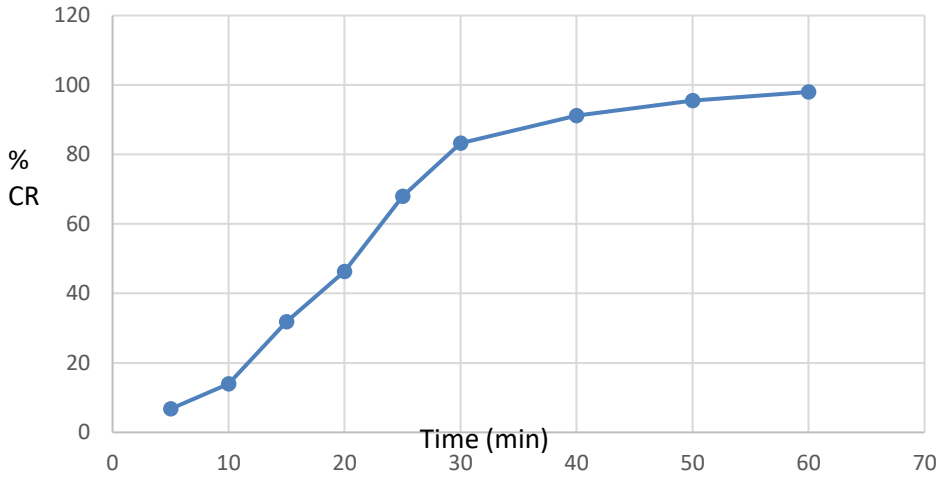

Fig. 9: *In-vitro* drug release profile of batch F4

7.2.6 *In-vivo* evaluation

The observations for the volume consumed and the rat's behavior indicated that the bitter taste of MS was effectively masked. The observation was further supported in this study by the higher consumption of the test solutions over that of pure drug solution by the rats, which indicated that the rats liked the taste of the test solutions.

The following figures 10, 11 and 12 demonstrate the results of the observations recorded in the in-vivo study.

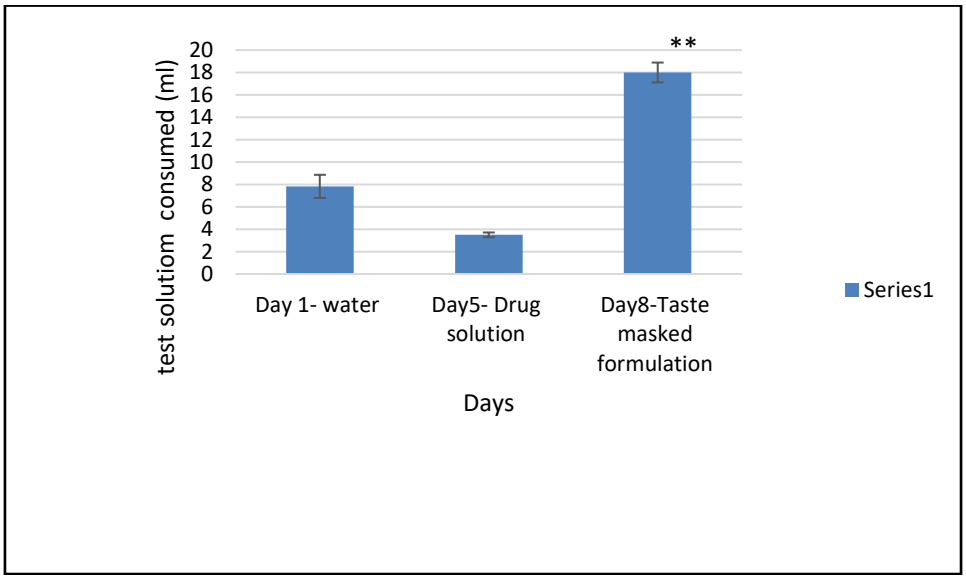

Fig. 10: In vivo taste assessment. *P<0.05

During the in-vivo evaluation study, the rats were also observed for some behavioral responses towards taste assessment. Figures 11 and 12 depict their observed behavioral responses in favor of likeliness towards the taste of the test solution.

Fig.11: Paw licking

Fig.12: Frequent sipping of test solution

7.2.7 Stability study

Table no. 14 shows the parameters evaluated during stability study. It was observed that the parameters evaluated were within the acceptable limits indicating that the formulation was stable over the period of 3 months.

Table 14: Results of the parameters studied during Stability study of oral jelly

Parameters assessed	Physical appearance	Drug content %	% cumulative drug release
25^0C ±2.0^0C/ 60% RH% ±5.0%			
0 days	Shiny Orange	95	98
30 days	Shiny Orange	95	98
60 days	Shiny Orange	-	-
90 days	Shiny Orange	-	-
5^0C±3.0^0C			
0 days	Shiny Orange	95	98
30 days	Shiny Orange	95	98
60 days	Shiny Orange	95	97
90 days	Shiny Orange	95	96
40^0C±2.0^0C/ 75% RH% ±5.0%			
0 days	Shiny orange	95	98
30 days	Syneresis seen	-	-
60 days	Syneresis seen	-	-
90 days	Syneresis seen	-	-

8. CONCLUSION:

Formulation was subjected to stability study for three months at different temperature conditions and was found to be stable.

Results conclusively demonstrated that successful taste masking of MS was accomplished and suggest that it could be formulated in confectionery form as oral jelly for paediatrics with more acceptability so as to ensure pediatric compliance with the therapy.

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