IJPSR (2022), Volume 13, Issue 3 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 15 January 2021; received in revised form, 29 January 2022; accepted, 22 February 2022; published 01 March 2022

DESIGN AND CHARACTERIZATION OF TASTE MASKED DEXTROMETHORPHAN HBR ORAL DISINTEGRATING TABLET BY USING NATURAL SUPERDISINTEGRANTS

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Keywords:

Eudragit RL 100, Fenugreek, Hibiscus, Microspheres, Taste masked

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ABSTRACT: Objective: Our work was to develop an ordispersible tablet of Dextromethorphan HBr with acceptable palatability to help patients of all age groups. **Methods:** The bitter taste of the drug was masked by entrapping the drug into Eudragit RL 100. The microspheres were prepared from solvent evaporation method. The effect of particle size, drug entrapment efficiency, % yield and % drug release of the microspheres was studied. Drug loading increased significantly with increasing the drug polymer ratio. Dextromethorphan was than further transformed into orodispersible tablet by using Hibuscus and Fenugreek as a superdisintegrants by using direct compression method. Physiochemical parameters and animal toxicity study of dried mucilage obtained from Hibiscus and Fenugreek were performed. *In-vitro* disintegration and *in-vitro* dissolution was carried out to observe the disintegration time and sustain release of drug. **Results:** *In-vivo* taste masked study was performed on albino rats. SEM, DSC and FTIR were done for identification, compatibility study and surface morphology. The or dispersible tablet made from sustained release microspheres showed release up to 10 h. **Conclusion:** All the results of ODTs prepared from natural super disintegrants were compared over synthetic. ODTs of natural superdisintegrants showed good results over the synthetic superdisintegrants.

INTRODUCTION: The aim and objective of the present study is to develop and evaluate orodispersible tablets of Dextromethorphan HBr to enhance the patient acceptance, palatability by Direct compression method. These formulations are beneficial for children, elderly and schizophrenic patients who have difficulty in swallowing conventional solid dosage form [1].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.13(3).1291-03

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.13(3).1291-03

Direct compression technique was used because of its ease of access and contains limited number of unit operations. The main problem of ODTS is to mask the bitter taste of active pharmaceutical ingredients, since most drugs have bitter taste [2]. The distasteful sensation of a drug can be masked by the addition of flavors, sweeteners and effervescent agents or by reducing direct contact with the patient's taste buds through coating and granulation [3].

Microencapsulation is a good approach to mask the taste by entrapping the molecule. Eudragit RL 100 is a biocompatible copolymers synthesized from acrylic and methacrylic acid ester. This polymer is well tolerated in the GIT and has been used in the

microencapsulation of drug. Eudragit RL 100 is insoluble in, but permeable to water and digestive juices, releasing drug by diffusion [4]. This polymer is also useful for sustained release of the drug having short half life.

In this study the basic approach is the use of natural superdisintegrants over synthetic super-disintegrants. Natural superdisinegrating agents are natural in origin and are preferred over synthetic substances because they are comparatively cheaper, abundantly available, non-irritating and nontoxic in nature. There are several gums and mucilage are available which have super disintegrating activity [5]. Dextromethorphan hydrobromide, a centrally acting non opioid antitussive drug is an effective for the control of cough and asthma in patients. It is readily absorbed from the upper GIT. Its dose is 10-30 mg daily in divided dose. It is having 11% oral bioavailability and belongs to class II of biopharmaceutics classification system [6]. Due to its short biological half life (1.4 to 3.9 h), it requires multiple dosing (2 to 3 times a day). Multiple dosing leads to fluctuation in the drug blood level and often dose related adverse effects. Multiple dosing also often results in poor compliance and inefficient therapy. To increase therapeutic efficacy, reduce frequency of administration and for better patient compliance, the sustained release microspheres of drug is important [7].

MATERIAL AND METHODS

Materials: Dextromethorphan HBr was gifted from Akums Pvt. Ltd. Haridwar. Eudragit RL 100 and Sodium starch glycolate were provided from CDH Delhi. Hibiscus leaves were taken from the medicinal garden. Fenugrek seeds were taken from local market. Albino Rats used in the study were also taken from the Animal House of Faculty of Pharmacy, IFTM University.

Extraction of Fenugreek Leaves Mucilage: Fenugreek seeds were grounded by using stainless steel grinder. The fine powder was extracted with boiling hexane in Soxhlet apparatus for 80 min. The obtained extract was treated with 85% ethanol for 130 min in a conical flask to remove the unwanted saponin. Further the enzyme deactivation was initiated by refluxing the extract with 70% ethanol for 180 min. If necessary, than resulting mixture was repeatedly treated with ethanol to remove undissolved traces. The residue was filtered by using sintered glass funnel at room temperature. The filtered residue was subjected to mechanical stirring at 700 rpm with addition of water for 8 h. The obtained mixture was centrifuged at 5000 rpm for 12 min at 10 °C. The supernatant contained crude fenugreek gum which was decanted and precipitated by adding 70% ethanol. Then the gum precipitate was washed with acetone, diethyl ether and water. The pure fenugreek gum was oven dried at a temperature < 50 °C. Now the powder was passed through a stainless steel sieve (mesh no# 80) and stored in an airtight bottle for further use [8].

Extraction of Hibiscus Leaves Mucilage The fresh leaves of Hibuscus was collected locally and washed with water to remove the dirt and debris. The leaves were dried in shadow for one week and powdered manually. Then, the powdered leaves were soaked in water in a beaker for 5-6 h and boiled for 30 min on a hot plate. After boiling it was kept a side at least 1 h for complete release of mucilage into the water. The material was squeezed from an eight fold muslin cloth to remove marc from the solution. Acetone was added to the filtrate to precipitate the gum mucilage in a quantity of three times the volume of total filtrate. The mucilage was separated and dried in an oven at a temperature < 50 °C. Now the powder was passed through a stainless steel sieve (mesh no# 80) and stored in an airtight bottle for further use [9].

Characterization of Dried Mucilage: Characterization of dried mucilage was done for organoleptic evaluation, flow properties by angle of repose, Carr's index and Hausner ratio and physiochemical evaluation (solubility, % loss on drying, pH, ash value, viscosity and swelling index [10].

Toxicity Study of Dried Mucilage: Twelve rats were divided into three groups, with each group containing four animals per sex having similar weights (200±30g). Group I was the control untreated, Group II was treated with Hibuscus dried mucilage and Group III was treated with Fenugreek dried mucilage at 300 mg/kg respectively. The dose was selected from the previous studies. The dried mucilage was suspended into the distilled water (10ml/kg body weight).

All the animals were weighed and orally administered using an oral feeding tube. The control untreated group received equivalent quantity of water orally. All the animals were observed for the mortality, clinical and behavioral signs for the first 10, 30, 60, 120, 240 and 360 min post dose, and thereafter twice daily for mortality, and once daily for clinical signs during the study period of 28 days. The animals were examined particularly for changes in the skin, fur and occurrence of secretions, excretions and autonomic activity.

Followed by daily observation, individual animal body weights and food intake were recorded at the one day before dosing (day 0) and every day until 28 days. At the end of 28 day period, the animals were fasted overnight and blood samples were collected from the orbital sinus for analyzing the hematological parameters, biochemistry of serum and urine and lipid profile. Then the animals were sacrificed by cervical dislocation under anesthesia and necropsy was performed. Organs like liver, Heart, Kidney and spleen were isolated and histopathology was done [11].

TABLE 1: TASTE MASKED MICROSPHERES FORMULATION

Formulation code	F_1	F_2	F_3	F_4	F_5
Drug (mg)	100	100	100	100	100
Eudragit RL 100 (mg)	100	200	300	400	500
Liquid Paraffin (ml)	30	30	30	30	30
Acetone (ml)	10	10	10	10	10
Stirring speed (rpm)	800	800	800	800	800
% of surfactant (%W/V)	0.3	0.3	0.3	0.3	0.3

Preparation of Taste Masked Microspheres: The microspheres of Dextromethorphan HBr were prepared by solvent evaporation method. The ingredients used to prepare the microspheres are given in **Table 1**. The polymer solution was prepared by dissolving it in 10 ml of acetone using a magnetic stirrer. The powdered drug was then dissolved in the polymer solution. The resultant solution was then poured in to the a vessel of 250 ml containing 30 ml of liquid paraffin while stirring at the rate minimum 1000 rpm. Stirring was continued for about 2 hours until acetone evaporated completely. After evaporation of acetone the microspheres formed were filtered and washed 4-5 times with n-hexane. Finally the washed microspheres were dried at room temperature and collected **Table 1** [12].

Evaluation of Taste Masked Microspheres: The microspheres were characterized for FTIR, DSC, SEM, %Percentage yield, Particle size, Drug entrapment efficiency and % Drug release. FTIR of the formulations was done Fourier transform infra red spectrophotometer (shimadzu, mumbai, india). DSC was performed on the differential scanning calorimeter (exstar 6300) and scanning electrom microscopy was done on zessis (ego 40).

Drug Entrapment Efficiency: A weighed amount of drug loaded microspheres (equivalent to 100 mg of drug) was extracted using 10 ml of ethanol. The solution was suitably diluted and the absorbance was taken at λ_{max} 274 nm. The experiment was done in the triplicate. The drug entrapment efficiency was calculated using the following formula:

D.E.E = Actual drug content / Theoretical drug content × 100

***In-vitro* Drug Release Studies:** The dissolution studies of microspheres were performed in pH 1.2 HCl for 2 h, than in pH 6.8 phosphate buffer for 4 h and than in pH 7.4 phosphate buffer for 10 h using USP type II paddle method at 50 rpm until the drug completely released from the tablet under sink condition at 37±0.5°C. At specific time intervals aliquots were withdrawn and replaced by an equal volume of fresh dissolution medium to maintain sink condition. After suitable dilution the samples were analyzed λ_{max} 274 nm.

***In-vivo* Evaluation of Taste Masking Using Rats:** Five albino rats of both sexes were employed for the study as per the animal protocol approved by IAEC (2015/837ac/PhD/12). Animal were housed in standard conditions of temperature (25±2°C), relative humidity (60±5%) and light (12 h of light-dark cycle). Rats were administered standard feed from SPS, IFTM University. Rats were deprived to water, then made of lick petridish containing water and licking activity observed in 5 min for water was taken as standard. Rats were then allowed to

lick the F_3 formulation, ODTs and 10mg/ml drug solution. Number of times the rats licks the formulations was counted and % licking frequency was calculated from the following formula [13].

% Licking frequency = Mean number of licks stimulus / Mean number of licks to water × 100

Preparation of Orodispersible Tablet from Taste Masked Microspheres: The optimized drug loaded microspheres (F_3) were compressed to form tablet by using Fenugreek, Hibuscus and Sodium Starch Glycolate as Superdisintegrants, microcrystalline cellulose as diluents, while magnesium stearate as lubricant. A tablet of 250 mg was prepared by direct compression method. The amount of microspheres equivalent to 100 mg drug were used to prepare 250 mg **Table 2** [14].

Evaluation of Orodispersible Tablet: The prepared orodispersible tablets were evaluated for hardness, thickness, weight variation, % friability, drug content, wetting time, *In vitro* disintegration time and *In vitro* drug release. Hardness of the tablet was tested using Monsento Hardness tester. The thickness of the tablets was measured by Vernier caliper. %Friability was determined in Roche friabilator. Weight variation test was performed according to the official method [14].

Wetting Time: A piece of tissue paper folded twice was placed in a small Petri dish (10 cm diameter) containing 10 ml of water. A tablet was put on the tissue paper and allowed to wet completely. The time required for complete wetting of the tablet was then recorded [14].

TABLE 2: PREPARATION OF ORODISPERSIBLE TABLET USING NATURAL SUPERDISINTEGRANTS

Ingredients (mg/tab)	T_1	T_2	T_3	T_4	T_5	T_6
Dextromethorphan (microspheres equivalent to 15 mg drug)	142	142	142	142	142	142
Fenugreek	6	10	-	-	-	-
Hibuscus	-	-	6	10	-	-
Sodium Starch Glycolate	-	-	-	-	6	10
Magnesium stearate	3	3	3	3	3	3
Talc	3	3	3	3	3	3
Microcrystalline cellulose	120	116	112	120	116	112

***In-vitro* Disintegration Test:** The tablet disintegration was carried out by placing one tablet in each tube (6 tablets) of the basket and the assembly was suspended in a beaker containing pH 6.8 phosphate buffer (SSF; simulated saliva fluid) by maintaining temperature at 37±2°C. The experiment was carried out in triplicate using disintegration tester (Elactrolab ED: 2AL) [14].

***In-vitro* Drug Release Studies:** The dissolution studies of ODTs were performed in pH 1.2, 6.8 and 7.4 phosphate buffer using USP type II paddle method at 50 rpm (Dissolution Tester (USP), Electrolab 1301014) until the drug completely released from the tablet under sink condition at 37±0.5°C. At specific time intervals aliquots were withdrawn and replaced by an equal volume of fresh dissolution medium to maintain sink volume. After suitable dilution the sample were analyzed λ_{max} 284 nm (UV-Visible Double Beam Spectrophotometer, Systronics 2101) [14].

Statistical Analysis: Statistical analysis of the results were done by using paired *t-test* (SPSS software) to compare the mean of two groups of observations or the same related subject over time or in differing circumstances. All the results were given in mean and standard deviation from mean.

RESULT AND DISCUSSSION: The physio-chemical characterizations which have been performed are given in **Table 3**. Loss on drying was found in the reasonable limit. The polymer is slightly soluble in water and insoluble in acetone, chloroform and ethanol. It was found that an increase in solubility when temperature is applied. The polymers have good solubility at pH 6.8 by visually observation this may be due to the nature of polymer is slightly acidic as pH of the polymer was found in the acid range. The solubility of polymer is good for the disintegration of tablet into saliva.

Ash values used to determine quality and purity of crude drug. It indicates the presence of various impurities like carbonate, oxalate and silicate present in the extracted polymer. The acid insoluble ash consist mainly silica and indicate contamination with earthy material. The water soluble ash is used to estimate the amount of

inorganic elements present in drugs. The ash value presence in the polymer sample is negligible or very less which indicates that there is no contamination of powder sample with silica, earthy material or with other inorganic materials present in the crude drug. Swelling index and viscosity extracted polymer is also found within the limit, a good swelling behavior helps in the dispersion as the more water will get absorb from the saliva to dissolve the dosage form. During 28 days toxicity study period, the body weight (g) of untreated control animals increased from 203.7±0.1 to 225.33±0.2 g with an average growth of 0.77g±0.07 g/day, Hibiscus treated animals weight increases from 204±0.04 to 227.66±0.05 g with an average growth of 0.84± 0.3g/day, and Fenugreek treated animals weight increases from 202.66±0.03 to 226±0.05 g with an average growth of 0.83±0.02 g/day. Finding of these results indicates there is no significant difference between weight gain and growth rate among the treated and untreated animals. The average food intake of untreated control group was nearly 1.45±0.02g/animal/day, the food intake of Hibuscus treated animals was 1.49±0.5 g/animal/day and the food intake of Fenugreek treated animals was 1.40±0.01g/ animal/day. The result shows no significant differences among the food intake of treated and untreated animals. Water consumption was also unchanged when treated animals compared to untreated animals. The Hematological parameter, Liver analysis, serum analysis and urine analysis parameters were found in the normal range in control as well as treated group of rats **Table 4**.

TABLE 3: CHARACTERIZATION OF FENUGREEK AND HIBUSCUS DRIED MUCILAGE

Parameters	Observation	
	Fenugreek seed gum	**Hibuscus leaves dried mucilage**
State	Amorphous powder	Amorphous powder
Color	Brownish	Greenish
Odour	Characteristic	Characteristic
Taste	Mucilaginous	Mucilaginous
% yield	39	23.4
Bulk density	0.538 g/cm^3	0.614 g/cm^3
Tapped density	0.553 g/cm^3	0.568 g/cm^3
Angle of repose	20.4^0	22^0
Carr's Index	10.5%	12%
Hausner's ratio	1.09	1.13
pH	3.3	3.75
% LOD	7.54	8.5
Solubility	Slightly soluble in water, sparingly in warm water, insoluble in acetone, chloroform and ethanol, soluble at pH 6.8	Slightly soluble in water, insoluble in acetone, chloroform and ethanol, soluble at pH 6.8
Total Ash Value	0.79%	2%
Acid insoluble Ash	0.25%	0.38%
Sulphated Ash value	0.68%	0.7%
Water soluble Ash	0.40%	0.43%
Viscosity (0.5%W/V)	70.5cp	74.6cp
Viscosity (1% W/V)	122.76cp	200.34cp
Swelling index	48%	22%

The histopathological examination of various organs of animals treated with 1000 mg/kg b. wt. of polymer showed normal cellular architecture when compared with those of the untreated groups of animals.

The tissue sections of heart showed normal tissue in treated as well as untreated sections. The histopathology of kidney tissues, treated animals showed mild glomerular atrophy with degenerative changes in tubular epithelium in both treated and untreated sections. The liver section of treated animals, showed normal portal triads and central venous system; normal hepatocytes were arranged in cords with Kupffer cells and showed normal sinusoidal spaces, which were identical with those from the untreated animals.

The tissue sections of spleen, treated animals showed normal lymphoid follicles with areas prominent in germinal centers. Medullary region showed mild depletion of lymphocytes with normal

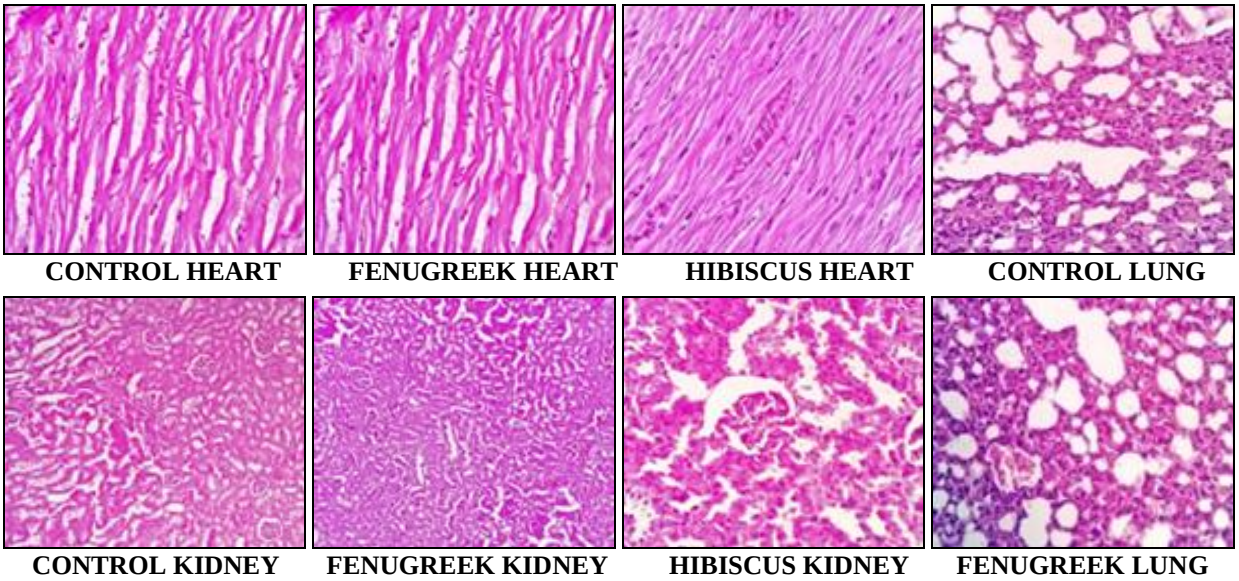
red and white pulp, cellular architecture and morphology similar to that of untreated control animals.

The interstitial tissues of lungs were appeared with no apparent abnormalities when compared with the tissues of untreated group of animals **Fig. 1**.

TABLE 4: TOXICITY STUDY OF FENUGREEK AND HIBUSCUS DRIED MUCILAGE

Parameteres	Control	Fenugreek	Hibuscus
Body weight (g)			
1st	203.7±0.1	202.66±0.03	204±0.04
14th	210.3±0.04	213.67±0.02	211.3±0.07
28th	225.33±0.2	226±0.05	227.66±0.05
Food consumption (g/animal/day)			
1st	1.47±0.8	1.1±0.04	1.5±0.06
14th	1.37±0.05	1.7±0.57	1.33±0.78
28th	1.5±0.25	1.4±0.06	1.67±0.9
Haematological profile			
Hb (g/dl)	12.2±0.05	11.8±0.002	12.3±0.01
Platelets 10^3cells/µl	274±0.053	319±0.041	320±0.02
RBC (million/cumin)	4.5±0.04	3.7±0.006	4.8±0.017
WBC (million/cumin)	4200±0.04	4370±0.02	4422±0.06
Liver function Analysis			
S. Albumin (gm %)	3.9±0.07	4.±20.06	4.3±0.02
S. Alkaline phosphate (IU/L)	274±0.053	319±0.041	320±0.02
S. Bilirubin (mg/dl)	0.4±0.2	0.39±0.003	0.29±0.021
S. Protein (gm %)	5.9±0.005	6.2±0.2	6.1±0.09
SGOT(AST) (IU/L)	52±0.001	53±0.01	55±0.02
SGPT(ALT) (IU/L)	46.8±0.004	50.1±0.06	50.2±0.053
Renal Function Analysis			
Calcium (mmol/L)	8.9±0.07	8.4±0.008	8.3±0.017
Chloride (mmol/L)	112.3±0.06	109.2±0.06	111.9±0.06
Creatinine (mg/dl)	0.89±0.07	0.9±0.037	0.92±0.054
Potassium (mmol/L)	4.9±0.01	4.6±0.022	5.1±0.007
Sodium (mmol/L)	144.6±0.03	143.6±0.041	145.6±0.12
Urea (mg/dl)	37.4±0.024	41.2±0.20	29.8±0.012
Uric Acid (mg/dl)	1.2±0.09	1.3±0.08	3.2±0.002
Serum biochemical parameters			
Cholesterol (mg/dl)	63.4±0.03	73.2±0.009	81.2±0.008
HDL (mg/dl)	18.9±0.07	20.1±0.019	19.4±0.05
LDL (mg/dl)	19.4±0.05	18.7±0.067	17.3±0.041
Triglyceride (mg/dl)	99.4±0.09	96.1±0.028	93.2±0.042

Mean ± SD, p=0.001 (paired t-test p<0.05)



CONTROL HEART **FENUGREEK HEART** **HIBISCUS HEART** **CONTROL LUNG**

CONTROL KIDNEY **FENUGREEK KIDNEY** **HIBISCUS KIDNEY** **FENUGREEK LUNG**

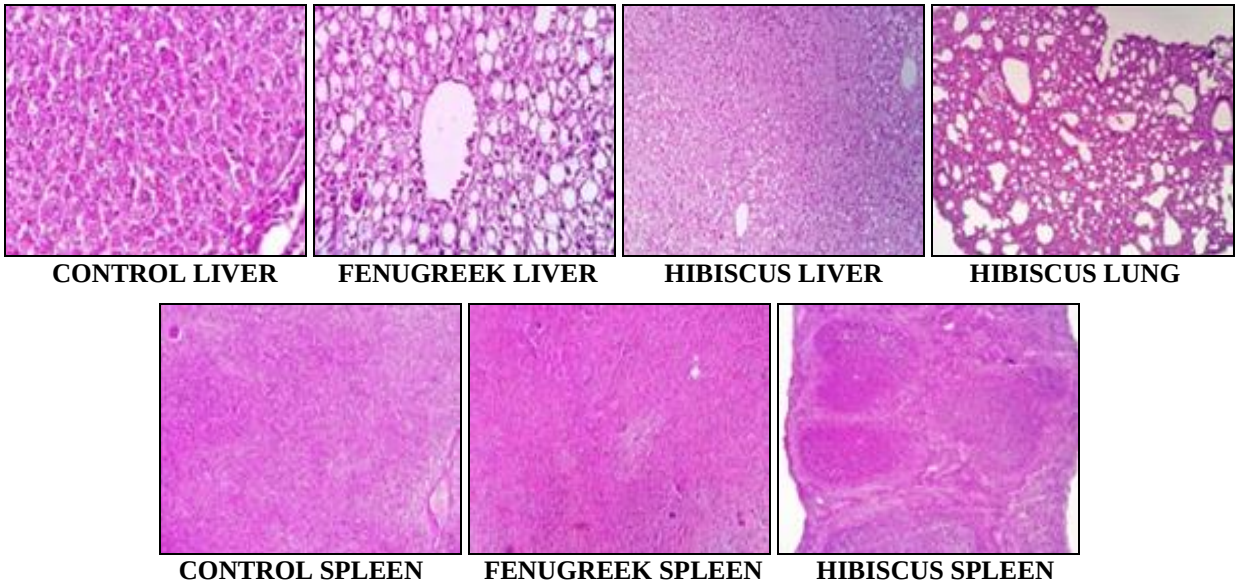


FIG. 1: HISTOPATHOLOGY OBSERVATION OF DIFFERENT ORGANS OF TREATED AND CONTROL RATS

The Percentage yield of taste masked microspheres ranges 64 to 95%. The highest yield was found in F_4 formulation (1:4), it was 95.298% and the lowest was in F_1 formulation (1:1) *i.e.* 64.766% **Table 5**. The particle size analysis was performed on the 500 microspheres and size range of microspheres was determined **Table 5**. It is found that by increasing the drug-polymer ratio there is a shift towards the higher particles. Higher concentration of polymer produced a more viscous dispersion which formed larger droplets and consequently larger microspheres. The highest particle size was found in F_4 formulation (1:4), it was 432.571 µm and the lowest was in F_1 formulation (1:1) *i.e.* 65.772 µm.

The drug entrapment efficiency of Dextromethorphan microspheres ranges from 52 to 96%. The highest %DEE was found in F_4 formulation (1:4), it was 94.729% and the lowest was in F_1 formulation (1:1) *i.e*. 49.178%.

TABLE 5: EVALUATION OF MICROSPHERES

Parameters	F_1	F_2	F_3	F_4	F_5
%Yield	64.766±0.152	79.334±1.616	78.718±1.634	95.298±1.024	85.676±0.585
Particle size Range	27-108	81-162	165-298	243-431	270-375
%DEE	49.178±4.234	76.576±8.555	89.761±3.605	94.729±5.411	87.053±0.205

Mean ±SD, p=0.001 (paired t-test p<0.05)

The surface morphology and structure of microspheres were investigated using SEM **Fig. 2**. As seen in figure the surface of microspheres were found rough, spherical and exhibited pores on its surface. Such pores were also reported by Lamprecht *et al* 2004. These were due to interconnectivity of internal phase droplets during final stage of solvent evaporation [15].

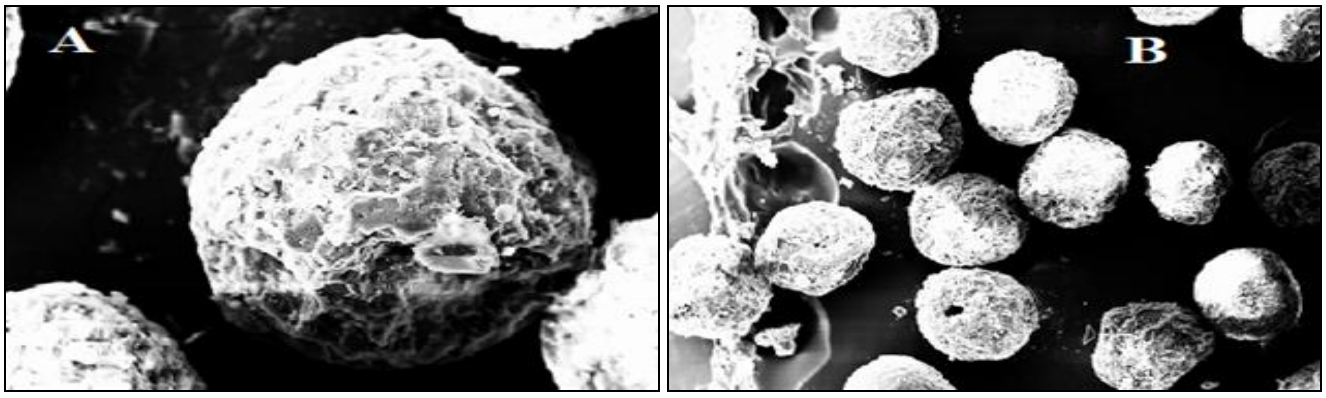


FIG. 2: SCANNING ELECTRON MICROSCOPY OF [A] MICROSPHERES, [B] TABLETTED MICROSPHERES

Eudragit RL 100 is pH independent time controlled polymer. In vitro release profile of microspheres from the preparation was examined in pH 1.2 (0.1 N HCl) for 0-2 h, pH 6.8 phosphate buffer for 3-4 h and pH 7.4 phosphate buffer 4-10 h. Dissolution test results showed that increase in polymer concentration; decreased rate of drug release from microspheres. Around, 14% drug was found to be released at pH 1.2 from microspheres, at pH 6.8 more than 40% drug released within 4 h and more than 90 % drug released up to 10 h at pH 7.4 **Fig. 3**. Futhermore, there is no significant difference in the drug release characteristic of the Eudragit RL 100 microspheres irrespective of the polymer drug concentration.

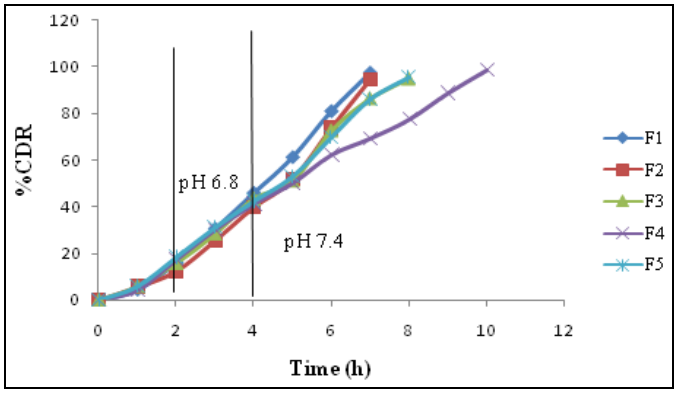


FIG. 3: *IN-VITRO* RELEASE STUDIES OF DEXTROMETHORPHAN HBR LOADED MICROSPHERES

Licking response of the rats is given in table 6. According to the experimental procedure, rats were first permitted to drink water and then had access to test substances at fixed time points and the licking frequency was counted compared to water. The licking frequency of water was taken as 100%.

A higher licking frequency was found up to 80.8% was obtained from the ODTs, whereas there is no more difference between the microspheres and ODTs solution. The licking frequency was found to be less in pure drug solution of 10mg/ml, which was considered as the highest bitter solution among the all.

In FTIR spectra of Dextromethorphan, one prominent characteristic peak was found at 3298.8 cm^{-1}, which was assigned to stretching vibration of NH group of imino-moiety of piperazinyl group. The peak at 2930 cm^{-1} was assigned to $–CH_3$ of methyl group.

The band at 1615.5 cm^{-1} represented the NH bending vibration of quinolones. The peak at 1576.4 cm^{-1} was assigned to –C=C- bending vibration of cyclic alkenes. The band at 1460.9 cm-1 was assigned to stretching vibration of CH_2 confirming the presence of methylene group of benzoxazine ring.

TABLE 6: PERCENTAGE OF LICKING RESPONSE OF RATS

Rats	1	2	3	4	5	Mean ± SD
10 mg/ml	35	28	25	28	29	29±0.04
Microspheres (10mg/ml)	80	84	78	81	83	81.2±0.02
ODTs (10mg/ml)	75	81	82	82	83	80.6±0.01
ODTs	79	77	83	84	86	81.8±0.03

Mean ± SD, p=0.001 (paired t-test p<0.05)

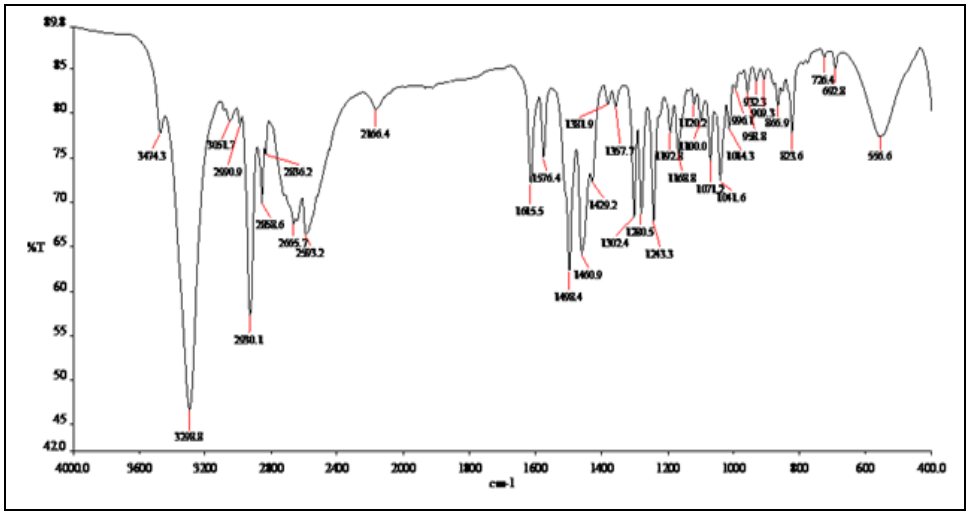


FIG. 4: FTIR SPECTRA OF DEXTROMETHRPHAN HBR

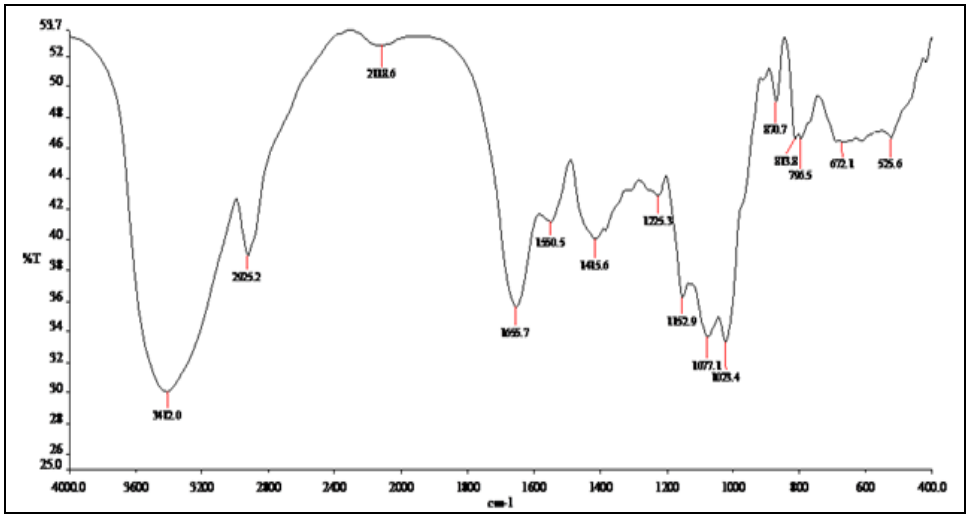


FIG. 5: FTIR SPECTRA OF FENUGREEK DRIED MUCILAGE

The peak at 1243.3 cm^{-1} represented the –O- (oxo) group. The band 900-700 cm-1 represented the out of plane bending vibration of double bond enes or =CH group.

In addition, a strong absorption peak at 556.6 was assigned to HBr **Fig. 4.** The FTIR spectra of dried mucilage of Fenugreek showed sharp and characteristic peaks at 3412, 2925.2, 2118.6, 1655.7, 1550.5, 1415.6, 1225.3, 1152.9, 1077.1, and 1023.4 cm-1 presented in **Fig. 5.**

The FTIR spectra of dried mucilage of Hibuscus showed sharp and characteristic peaks at 3415.3, 2925.4, 1627.0, 1415.8, 1360, 1270, and 1076.0 cm^{-1} presented in **Fig. 6.**

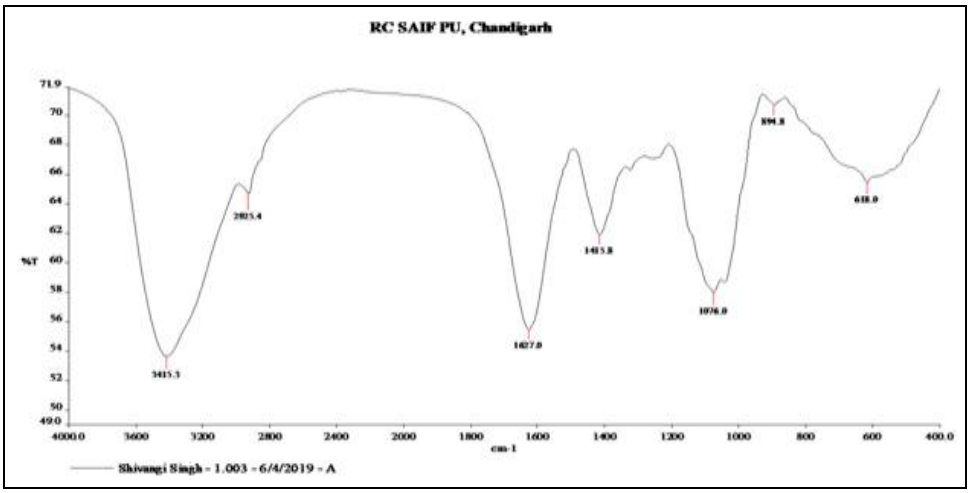
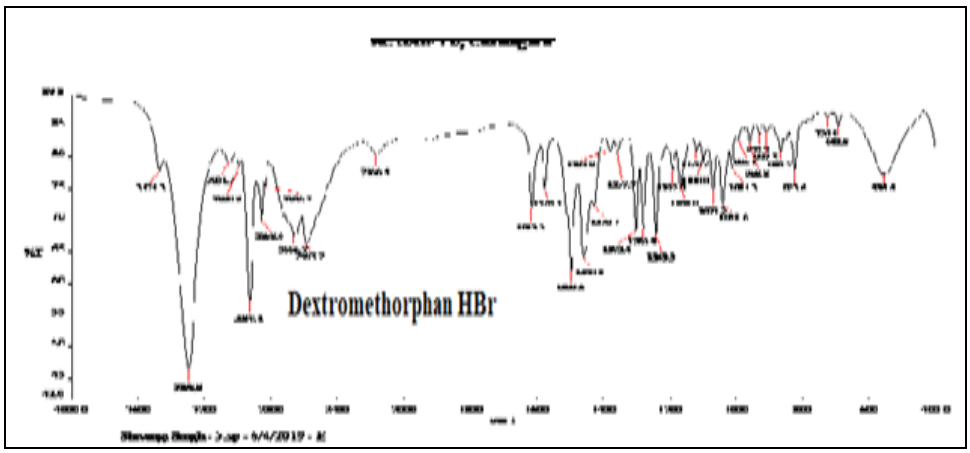


FIG. 6: FTIR SPECTRA OF HIBUSCUS DRIED MUCILAGE



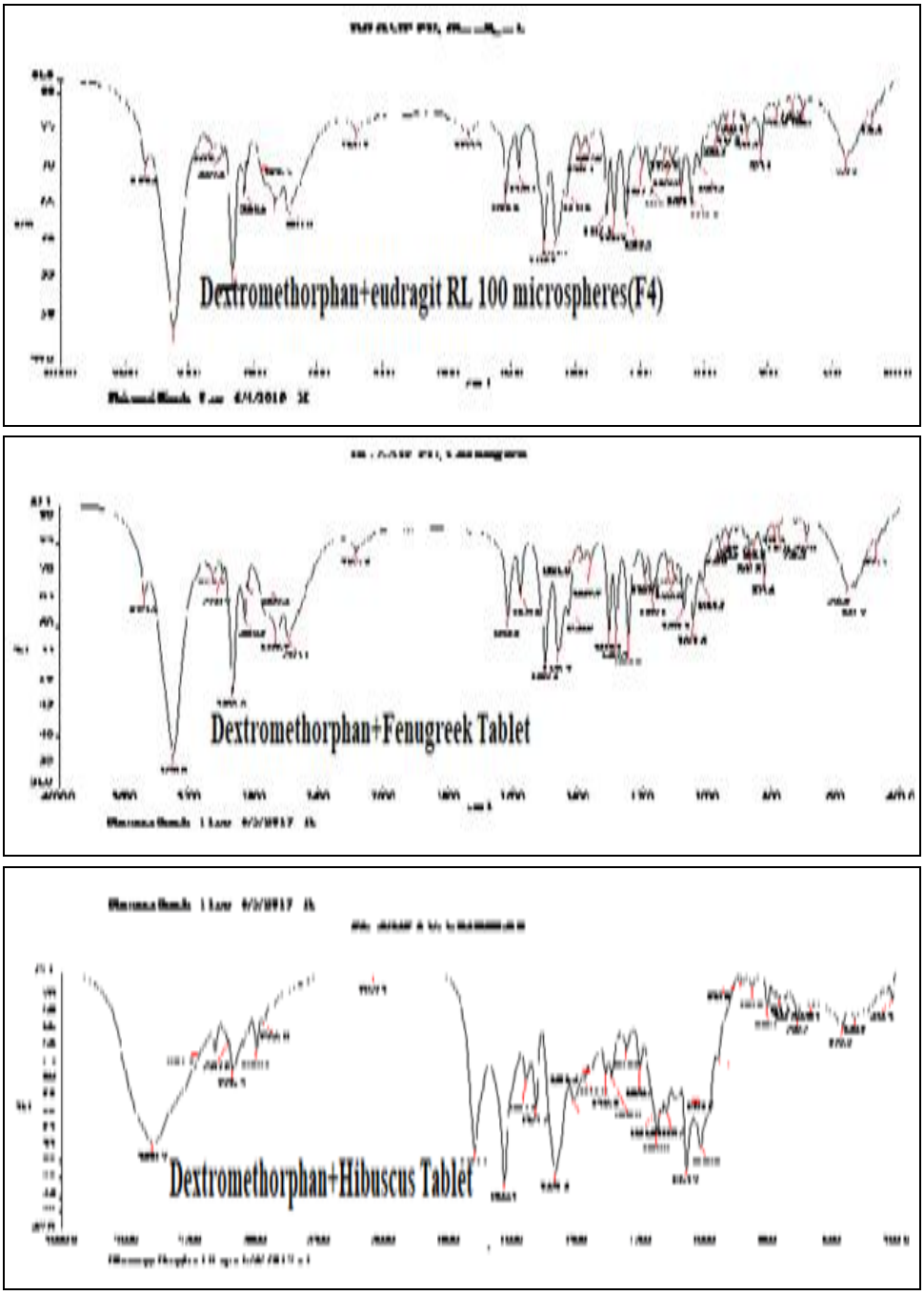


FIG.7: FTIR SPECTRA OF DRUG IN DIFFERENT FORMULATIONS

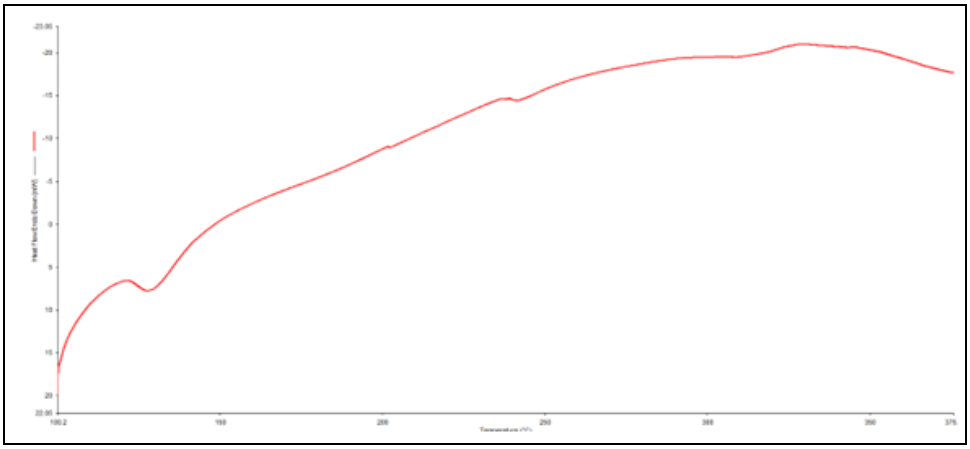


FIG. 8: DSC SPECTRA OF DEXTROMETHORPHAN HBR

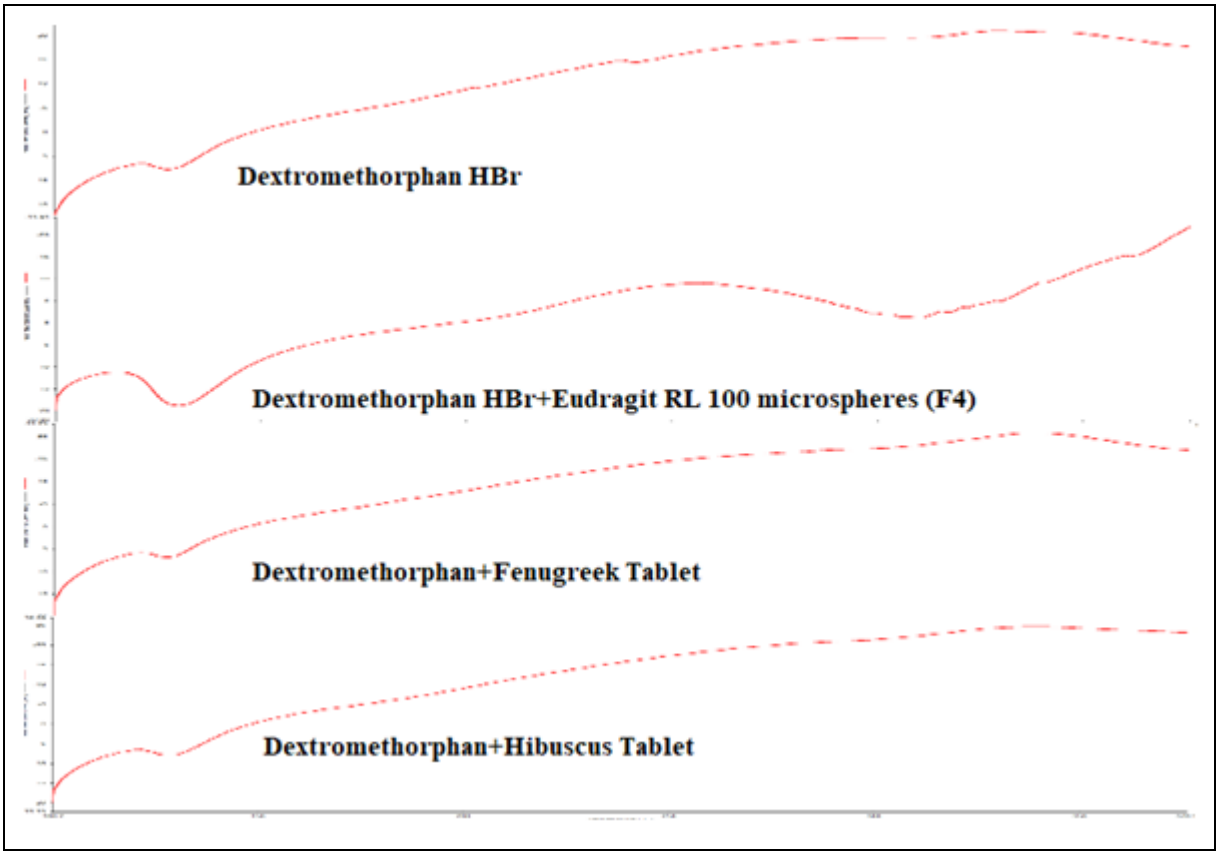


FIG. 9: DSC SPECTRA OF DEXTROMETHORPHAN IN DIFFERENT FORMULATIONS

The DSC of drug showed a sharp endothermic peak at 110°C for a pure Dextromethorphan HBr as the melting point of drug **Fig. 8.** The reported valve of melting point is 109°C-111°C.

The average thickness of ODTs was found to be in range 3.467±0.18 mm to 3.936±0.08 mm **Table 7**. The hardness of ODTs was found to be in range 2.561±0.57 kg/cm2 to 3.984±0.03 kg/cm^2.

The hardness of tablets depends upon the compression force and the amount and type of binding agent present. The compression force for all the formulations was same; therefore the change in all the formulations was minor or very minimum.

So, this relatively low hardness provided enough strength and porosity to ensure rapid wetting and disintegration of the tablets.

It was clear from the results that the increase of the drug ratio to superdisintegrants led to a decrease in the ODTs hardness.

TABLE 7: EVALUATION PARAMETER OF TABLET

Parameters	Formulations					
	T_1	T_2	T_3	T_4	T_5	T_6
Thickness (mm)	3.546±012	3.675±0.34	3.679±0.09	3.467±0.18	3.478±0.02	3.936±0.08
Hardness (kg/ cm^2)	3.984±0.03	2.873±0.05	3.983±0.06	2.561±0.57	3.956±0.35	3.459±0.03
Weight variation (%)	248.33±0.05	251.33±0.07	247.33±0.32	249.33±0.18	249.33±0.03	250.33±0.01
Friability (%)	0.431±0.08	0.435±0.21	0.198±0.07	0.218±0.05	0.245±0.17	87.78±0.46
Drug content (%)	93.78±0.04	90.56±0.13	94.09±0.09	93.87±0.06	0.235±0.45	85.43±0.51
Wetting time(s)	29.45±0.34	26.56±0.09	22.47±0.07	18.76±0.04	43.78±0.09	42.45±0.23
Disintegration time (s)	33.75±0.89	29.87±0.29	26.67±0.43	21.52±0.59	37.94±0.39	37.59±0.20

Mean ± SD, p=0.001 (paired t-test p<0.05)

The weight variation of different ODTs ranged from 247.33±0.32 % to 251.33±0.07%. According IP % weight variation limit is ±5% for 250 mg.

All ODTs did not break or show any capping during the test. All tablets showed acceptable friability according to IP **Table 7**.

The friability of different ODTs ranged from 0.198±0.07 % to 0.435±0.21%. Results in **Table 7** showed that the average drug content of the tablets from each formula was found above 90 % of the label claim. Thus, all formulations complied with the pharmacopeial limits (IP 2010) [17]. Wetting time is an important parameter for disintegration properties of the tablets. Wetting is closely related to the internal structure of tablet and to the hydrophilicity of the excipients. From the results of wetting time shown in **Table 7**, it was found that all formulations prepared from natural super disintegrants gave the acceptable result.

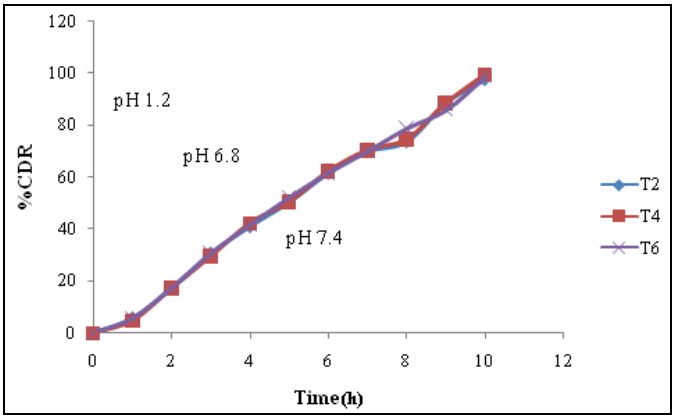


FIG. 10: *IN-VITRO* RELEASE STUDIES OF DEXTROMETHORPHAN HBR LOADED ODTS

The wetting time of different ODTs ranged from 18.76±0.04s to 43.78±0.09s. Slow and incomplete disintegration of tablets leads to low bioavailability of the drug from it. Although the compendial standards state that disintegration time for the fast dissolving tablets should be within 3 min, many critics find that a maximum disintegration time of 3 min for any tablet is too long and that the presence of a gritty tablet in the patient's mouth for 3 min would be unpleasant and uncomfortable. According to the literature, the oral disintegration time of mouth dissolved tablet is 1 min or less, preferably about 30 s or less. Disintegration depends upon the effect of disintegrants and water soluble excipients in the formula. Disintegration time ranges from 21.52±0.59 s to 37.94±0.39 s. The Okra dried mucilage tablet showed slower disintegration time than those containing Hibuscus because, in addition to the above reasons, Okra dried mucilage have slow swelling rate, slow wetting than the Hibuscus that delayed the disintegration time. From these results it was observed that all the formulations showed a gradient and sustained increase in the drug release. Moreover, it is obvious from the fig the release rate of ODTs was slow compared to that from untabletted microspheres. This may be due to formation of a hydrophobic tortuous matrix during compression of the microspheres.

CONCLUSION: Assessment of successful taste masking comes along with challenges depending on the choice of particular method. Microencapsulation is a good technique to mask the bitter taste of drug. The formulation of orodispersible tablet was made by using Dextromethorphan HBr and Eudragit RL 100 microspheres by direct compression. Fenugreek and Hibuscus dried mucilage as a natural superdisintegrants showed good results over the widely used synthetic superdisintegrants; sodium starch glycolate. So, Fenugreek and Hibuscus dried mucilage can also be used for further development of orodispersible tablet.

ACKNOWLEDGEMENT: Author is thankful to Dr Mahendra Prasad Pandey, Vice Chancellor, IFTM University for providing laboratory facilities to conduct the research work.

CONFLICT OF INTEREST: There is no conflict of interest during this study.

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How to cite this article:
Singh S, Malik A and Verma N: Design and characterization of taste masked dextromethorphan HBR oral disintegrating tablet by using natural superdisintegrants. Int J Pharm Sci & Res 2022; 13(3): 1291-03. doi: 10.13040/IJPSR.0975-8232.13(3).1291-03.