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FORMULATION AND EVALUATION OF ORODISPERSIBLE TABLETS OF OFLOXACIN BY USING DIFFERENT NATURAL SUPER DISINTEGRATING AGENTS

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Keywords:

Orodispersible tablet, Taste masked microspheres, Solvent evaporation method, Ofloxacin, Natural superdisintegrants

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ABSTRACT: Fast disintegrating tablets have received ever-increasing demand during the last decade, particularly the fast disintegrating tablet drug delivery systems formulated with natural polymers have more demand because natural materials are easily available, easy to administer, non-toxic and non-irritant nature etc. The main aim of the present study was to formulate the fast dissolving tablet of Ofloxacin using Hibiscus leaves and Okra fruit dried mucilage. The results obtained from the natural polymer were compared with the synthetic super disintegrants sodium starch glycolate. Ofloxacin in an antibacterial drug used to treat various infections and having bitter taste. Its bitter taste is first masked by entrapping it into microspheres using Eudragit RL 100 polymer. The microspheres were evaluated for particle size, entrapment efficiency, *in-vitro* release and bitterness threshold. The selected microspheres were directly compressed into the tablets. The orodispersible tablets using different super disintegrants with varying concentrations were evaluated for weight variation, hardness, friability, wetting time, water absorption ratio, drug content, disintegration time and drug release. FTIR and DSC study of drug and polymer were done to check drug-polymer interaction. The orodispersible tablet made from natural disintegrants was found superior over an orodispersible tablet made from a synthetic polymer.

INTRODUCTION: For the past two decades, there has been an enhanced demand for more patient compliance dosage forms. As a result, the demand for their technologies has been increasing three-fold annually. Since the development cost of a new chemical entity is very high, the pharmaceutical companies are now focusing on the development of new drug delivery systems for an existing drug with improved efficacy and bioavailability together with reduced dosing frequency to minimize side effects [1-2].

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Ofloxacin is a broad-spectrum, synthetic fluoroquinolone antibacterial drug for oral administration having extremely bitter taste [3]. The oral route of drug administration is perhaps the most appealing route for the delivery of drugs. Difficulty in swallowing (dysphasia) is a common problem due to the non-availability of water, physiological changes associated with elderly and pediatrics age groups, mentally ill patients, and patients suffering from nausea, motion sickness, sudden episodes of allergic attack or coughing [4].

To overcome these problems orodispersible tablet is a novel drug delivery approach that disintegrates rapidly in saliva without the need for drinking water [5]. Superdisintegrants are the newer substances that are added to tablet formulations to promote the breakup of the tablet into smaller fragments in an aqueous environment thereby

increasing the available surface area and promoting a more rapid release of the drug substance at lower concentrations with greater disintegrating efficiency and mechanical strength [6]. Natural super disintegrating agents are natural in origin and are preferred over synthetic substances because they are comparatively cheaper, abundantly available, non-irritating and non-toxic in nature. There are several gums and mucilage are available which have super disintegrating activity [7].

The bitter taste of Ofloxacin makes it unsuitable for an orodispersible tablet. The coating of the drug moiety can make it palatable. Microencapsulation is a good approach to mask the taste by entrapping the molecule. Eudragit RL 100 is a biocompatible copolymer synthesized from acrylic and methacrylic acid ester. This polymer is well tolerated by the skin and has been used in the microencapsulation of the drug. Eudragit RL 100 is insoluble in, but permeable to water and digestive juices, releasing drug by diffusion [8].

MATERIALS AND METHODS:

Materials: Ofloxacin 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 of SPS, IFTM University. Okra fruits were taken from the local market. Albino Rats used in the study were also taken from the Animal House of Faculty of Pharmacy, IFTM University.

Methodology:

Extraction of Hibiscus Leaves Mucilage: The fresh leaves of Hibiscus were 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 aside 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].

Extraction of Okra Fruit Mucilage: 1 kg of unripe and tender okra fruits (pods) was purchased from the local market. The seeds were removed as they don't contain any mucilage. The fruits were washed and sliced thinly with a knife. The sliced mass was soaked in distilled water overnight to extract out the mucilage. After soaking, a white muslin cloth was used to filter out the viscous gum mucilage (mucilage). Acetone was added to precipitate the gum at a ratio of 3 parts of acetone to one part of the gum extract. Then, the precipitated gum was dried in an oven at a temperature < 50 °C. Size reduction and screening of the dried gum were carried out using a stainless steel grinder and no. 40 stainless steel mesh sieve. Airtight powder bottles were used to store the undersized fractions. Subsequently, the physico-chemical characterization of okra gum powder was conducted [10].

Characterization of Dried Mucilage: Characterization of dried mucilage was done for organoleptic evaluation, flow properties by an angle of repose, Carr's index and Hausner ratio and physiochemical evaluation (solubility, % loss on drying, pH, ash value, viscosity and swelling index) [9-10].

Toxicity Study of Dried Mucilage: Twelve rats were divided into three groups, with each group containing four animals per sex having similar weights (200 ± 30 g). Group, I was the control untreated, Group II has treated with Hibiscus dried mucilage and Group III was treated with Okra dried mucilage at 300 mg/kg respectively. The dose was selected from the previous studies. The dried mucilage was suspended into the distilled water (10 ml/kg body weight). All the animals were weighed and orally administered using an oral feeding tube. The control untreated group received an equivalent quantity of water orally. All the animals were observed for the mortality, clinical and behavioural signs for the first 10, 30, 60, 120, 240 and 360 min post-dose, and after that 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 fasted overnight and blood samples were collected from the orbital sinus for analyzing the hematological parameters, the 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 Ofloxacin were prepared by the 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 into the vessel of 250 ml containing 30 ml of liquid paraffin while stirring at the rate minimum 1000 rpm. Stirring was continued for about 2 h 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 infrared spectrophotometer (Shimadzu, Mumbai, India). DSC was performed on the differential scanning calorimeter (exstar 6300) and scanning electron 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} specific nm.

The experiment was done in the triplicate. The drug entrapment efficiency was calculated using the following formula:

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

***In-vitro* Drug Release Studies:** The dissolution studies of microspheres were performed in pH 1.2 HCl for 2 h, then in pH 6.8 phosphate buffer for 4 h and then 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 sample was analyzed λ_{max} 284 nm [12].

***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). The animal was housed in standard conditions of temperature (25 ± 2 °C), relative humidity (60 ± 5%) and light (12 h of the light-dark cycle). Rats were administered standard feed from SPS, IFTM University. Rats were deprived of 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 F3 formulation, ODTs and 10mg/ml drug solution. Number of times the rats licks the formulations were counted and % licking frequency was calculated from the following formula [13].

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

Preparation of Orodispersible Tablet from Taste Masked Microspheres: The optimized drug-loaded microspheres (F3) were compressed to form a tablet by using Hibiscus, Okra and Sodium Starch Glycolate as Superdisintegrants, micro-crystalline cellulose as diluents, while magnesium

stearate as a lubricant. A tablet of 250 mg was prepared by direct compression method. The amount of microspheres equivalent to 100 mg drug was 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. The hardness of the tablet was tested using the Monsanto 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].

TABLE 2: PREPARATION OF ORODISPERSIBLE TABLET USING NATURAL SUPERDISINTEGRANTS

Ingredients (mg/tab)	T_1	T_2	T_3	T_4	T_5	T_6
Ofloxacin (microspheres equivalent to 100 mg drug)	122	122	122	122	122	122
Hibuscus	6	10	-	-	-	-
Okra	-	-	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

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 the complete wetting of the tablet was then recorded [14].

***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 the temperature at 37 ± 2 ℃. 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 was analyzed λ_{max} 284 nm (UV-Visible Double Beam Spectrophotometer, Systronics 2101) [14].

Statistical Analysis: Statistical analysis of the results was 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 the mean.

RESULTS AND DISCUSSION: 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 the temperature is applied. The polymers have good solubility at pH 6.8 by visual observation this may be due to the nature of polymer is slightly acidic as the pH of the polymer was found in the acid range. The solubility of polymer is good for the disintegration of the tablet into saliva. Ash values used to determine the quality and purity of the crude drug. It indicates the presence of various impurities like carbonate, oxalate and silicate present in the extracted polymer.

The acid insoluble ash consists mainly of silica and indicates contamination with earthy material. The water-soluble ash is used to estimate the amount of inorganic elements present in drugs. The ash value present 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.

TABLE 3: CHARACTERIZATION OF HIBUSCUS AND OKRA DRIED MUCILAGE

Parameters	Observation	
	Hibiscus leaves dried mucilage	**Okra fruit dried mucilage**
State	Amorphous powder	Amorphous powder
Color	Greenish	Off white or cream
Odour	Characteristic	Odourless
Taste	Mucilaginous	Mucilaginous
% yield	23.4	27
Bulk density	0.614 g/cm^3	0.635g/cm^3
Tapped density	0.568 g/cm^3	0.639 g/cm^3
Angle of repose	22^0	21.4^0
Carr's Index	12%	13%
Hausner's ratio	1.13	1.05
pH	3.75	4.49
% LOD	8.5	8.91
Solubility	Slightly soluble in water, insoluble in acetone, chloroform and ethanol, soluble at pH 6.8	Sparingly soluble in water, insoluble in acetone, chloroform and ethanol, soluble at pH 6.8
Total Ash Value	2%	3.5%
Acid insoluble Ash	0.38%	0.75%
Sulphated Ash value	0.7%	0.78%
Water soluble Ash	0.43%	0.52%
Viscosity (0.5%W/V)	74.6cp	62.3cp
Viscosity (1% W/V)	200.34 cp	228.64 cp
Swelling index	22%	86.91%

TABLE 4: TOXICITY STUDY OF HIBUSCUS AND OKRA DRIED MUCILAGE

Parameters	Control	Hibiscus	Okra
Body weight (g)			
1st	203.7 ± 0.1	204 ± 0.04	203.3 ± 0.01
14th	210.3 ± 0.04	211.3 ± 0.07	213 ± 0.09
28th	225.33 ± 0.2	227.66 ± 0.05	225.66 ± 0.03
Food consumption (g/animal/day)			
1st	1.47 ± 0.8	1.5 ± 0.06	1.4 ± 0.06
14th	1.37 ± 0.05	1.33 ± 0.78	1.43 ± 0.07
28th	1.5 ± 0.25	1.67 ± 0.9	1.5 ± 0.87
Haematological profile			
Hb (g/dl)	12.2 ± 0.05	12.3 ± 0.01	11.9 ± 0.08
Platelets 10^3 cells/µl	274 ± 0.053	320 ± 0.02	339 ± 0.04
RBC (million/cumin)	4.5 ± 0.04	4.8 ± 0.017	3.5 ± 0.009
WBC (million/cumin)	4200 ± 0.04	4422 ± 0.06	4900 ± 0.1
Liver function Analysis			
S. Albumin (gm %)	3.9 ± 0.07	4.3 ± 0.02	4.5 ± 0.005
S. Alkaline phosphate (IU/L)	274 ± 0.053	320 ± 0.02	339 ± 0.04
S.Bilirubin (mg/dl)	0.4 ± 0.2	0.29 ± 0.021	0.3 ± 0.03
S. Protein (gm %)	5.9 ± 0.005	6.1 ± 0.09	7.4 ± 0.5
SGOT(AST) (IU/L)	52 ± 0.001	55 ± 0.02	45 ± 0.057
SGPT(ALT) (IU/L)	46.8 ± 0.004	50.2 ± 0 .053	45.9 ± 0.039
Renal Function Analysis			
Calcium (mmol/L)	8.9 ± 0.07	8.3 ± 0.017	10.2 ± 0.06
Chloride (mmol/L)	112.3 ± 0.06	111.9 ± 0.06	110.2 ± 0.14
Creatinine (mg/dl)	0.89 ± 0.07	0.92 ± 0.054	0.87 ± 0.06
Potassium (mmol/L)	4.9 ± 0.01	5.1 ± 0.007	4.8 ± 0.09
Sodium (mmol/L)	144.6 ± 0.03	145.6 ± 0.12	146.9 ± 0.05
Urea (mg/dl)	37.4 ± 0.024	29.8 ± 0.012	33.4 ± 0.04
Uric Acid (mg/dl)	1.2 ± 0.09	3.2 ± 0.002	2.3 ± 0.019
Serum biochemical parameters			
Cholesterol (mg/dl)	63.4 ± 0.03	81.2 ± 0.008	69.4 ± 0.01
HDL (mg/dl)	18.9 ± 0.07	19.4 ± 0.05	18.2 ± 0.01
LDL (mg/dl)	19.4 ± 0.05	17.3 ± 0.041	18.3 ± 0.051
Triglyceride (mg/dl)	99.4 ± 0.09	93.2 ± 0.042	90.8 ± 0.053

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

During 28 days toxicity study period, the body weight (g) of untreated control animals increased from 103.7 ± 0.1 to 125.33 ± 0.2 g with an average growth of 0.77 g ± 0.07 g/day, Hibiscus treated animals weight increases from 104 ± 0.04 to 127.66 ± 0.05 g with an average growth of 0.84 ± 0.3g/day, and Okra treated animals weight increases from 103.3 ± 0.01 to 125.66 ± 0.03 g with an average growth of 0.79 ± 0.05 g/day. Finding 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 the untreated control group was nearly 1.45 ± 0.02 g / animal/day, the food intake of Hibiscus treated animals were 1.49 ± 0.5 g / animal/day and the food intake of Okra treated animals was 1.44 ± 0.03 g / 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 the treated group of rats **Table 4**.

The histopathological examination of various organs of animals treated with 1000 mg/kg b. wt. of FHE showed normal cellular architecture when compared with those of the untreated groups of animals. The tissue sections of the 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 the tubular epithelium in both treated and untreated sections.

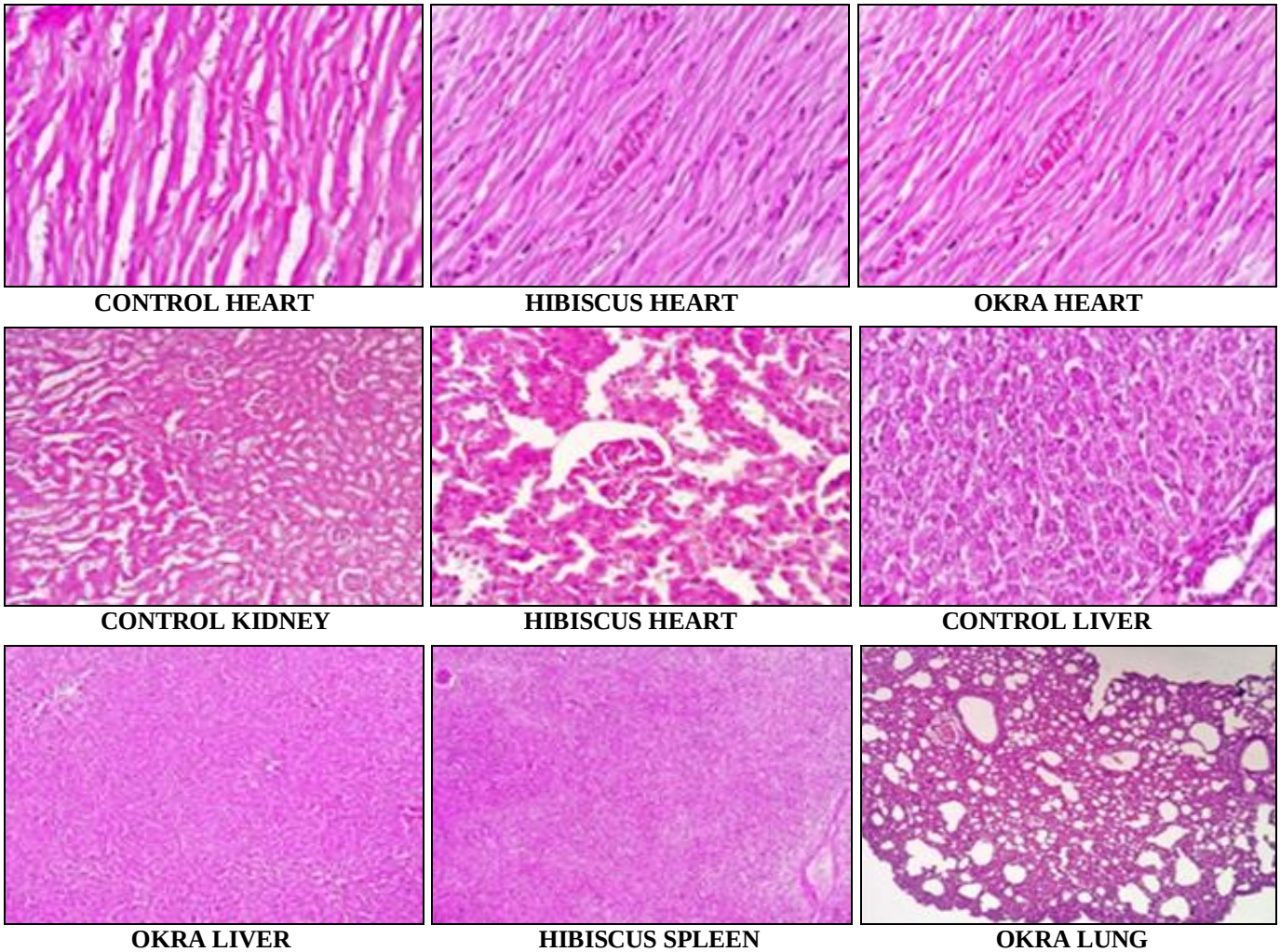

FIG. 1: HISTOPATHOLOGY OBSERVATION OF DIFFERENT ORGANS OF TREATED AND CONTROL RATS

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 the spleen, treated animals showed normal lymphoid follicles with areas prominent in germinal centers. The 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 appeared with no apparent abnormalities when compared with the tissues of an untreated group of animals **Fig. 1**. The Percentage yield of taste-masked microspheres ranges 62 to 93%. The highest yield was found in F3 formulation (1:3), it was 93.503% and the lowest was in F1 formulation (1:1) *i.e.* 62.56% **Table 5**.

The particle size analysis was performed on the 500 microspheres and the size range of microspheres was determined in **Table 5**. It is found that by increasing the drug-polymer ratio there is a shift towards the higher particles. A higher concentration of polymer produced a more viscous dispersion which formed larger droplets and consequently larger micro-spheres. The highest particle size was found in F3 formulation (1:3), it was 321.095 µm and the lowest was in F1 formulation (1:1) *i.e.* 36.774 µm. The drug entrapment efficiency of ofloxacin microspheres ranges from 52 to 96%. The highest %DEE was found in O3 formulation (1:3), it was 96.503% and the lowest was in O1 formulation (1:1) *i.e.* 52.56%.

TABLE 5: EVALUATION OF MICROSPHERES

Parameters	F_1	F_2	F_3	F_4	F_5
%Yield	62.566 ± 2.040	71.037 ± 0.230	93.503 ± 0.793	74.45 ± 0.506	73.64 ± 1.427
Particle size Range	23-59	81-155	267-392	108-148	81-243
%DEE	52.566 ± 2.040	71.378 ± 0.230	96.503 ± 0.793	74.45 ± 0.506	73.64 ± 1.427

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 the figure the surface of microspheres was found rough, spherical and exhibited pores on its surface. Such pores were also reported by Lamprecht *et al.,* 2004. These were due to the interconnectivity of internal phase droplets during the final stage of solvent evaporation [15].

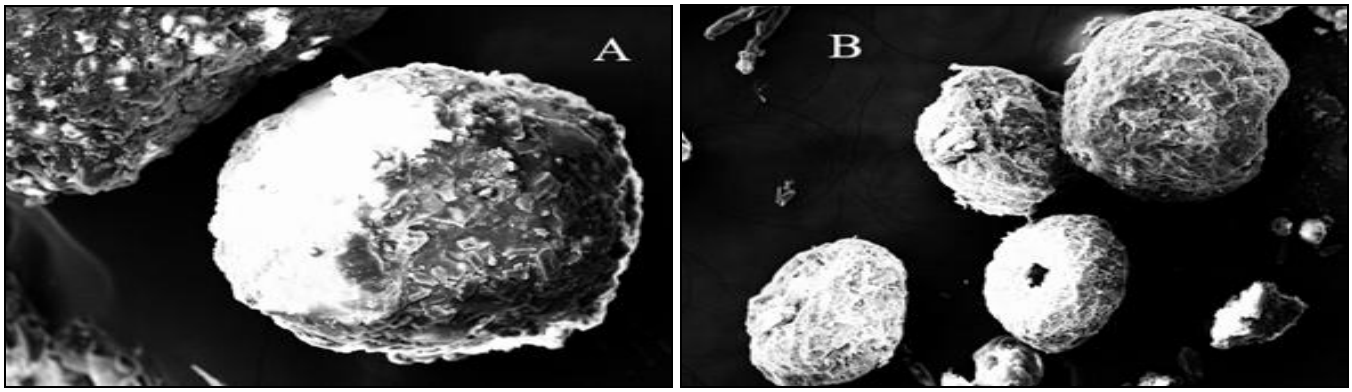

FIG. 2: SCANNING ELECTRON MICROSCOPY OF [A] MICROSPHERES, [B] TABLETTED MICROSPHERES

Eudragit RL 100 is pH-independent time-controlled polymer. *The in-vitro* release profile of micro-spheres 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 an increase in polymer concentration; the decreased rate of drug release from microspheres. Around, 40% 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**. Furthermore, there is no significant difference in the drug release characteristic of the Eudragit RL 100 microspheres irrespective of the polymer-drug concentration [16]. Licking the 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 10 mg/ml, which was considered as the highest bitter solution among the all.

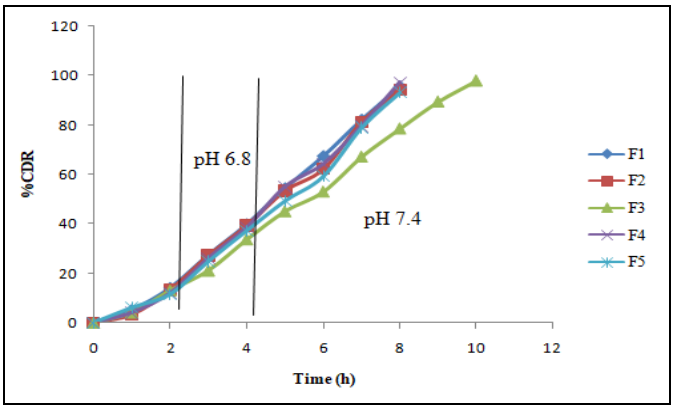

FIG. 3: *IN-VITRO* RELEASE STUDIES OF OFLOXACIN LOADED MICROSPHERES

TABLE 6: PERCENTAGE OF LICKING RESPONSE OF RATS

Rats	1	2	3	4	5	Mean ± SD
10 mg/ml	30	25	29	24	29	27.4 ± 0.02
Microspheres (10 mg/ml)	80	81	75	82	84	80.4 ± 0.03
ODTs (10 mg/ml)	74	80	83	85	81	80.6 ± 0.031
ODTs	79	78	81	82	84	80.8 ± 0.02

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

In the FTIR spectra of Ofloxacin, one prominent characteristic peak was found at 3043.4 cm^{-1}, which was assigned to stretching vibration of OH group and intramolecular hydrogen bonding **Fig. 4**. This band also suggests the NH stretching vibration of the imino-moiety of piperazinyl group which was less prominent due to intense OH stretching vibration. The peak at 2700 cm^{-1} was assigned to $-CH_3$ of the methyl group.

The band at 1713.7 cm^{-1} represented the acidic carbonyl C=O stretching vibration. The peak at 1622.0 cm^{-1} was assigned to NH bending vibration of quinolones. The 1524.3 cm^{-1} represented the CH_2 of the aromatic ring. The band at 1467.5 cm^{-1} was assigned to the stretching vibration of CH_2 confirming the presence of the methylene group of benzoxazine ring.

The peak at 1397.5 cm^{-1} represented the bending vibration of hydroxyl group of carboxylic acid. The band at 1242.0 cm^{-1} suggested the –O- (oxo) group. In addition, a strong absorption peak at 1055 was assigned to C-F group. The band 900-700 cm^{-1} represented the out of plane bending vibration of double bond enes or =CH group **Fig. 4**.

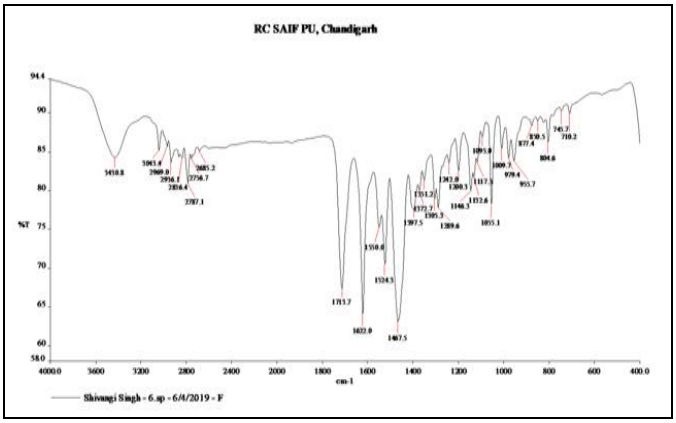

FIG. 4: FTIR SPECTRA OF OFLOXACIN

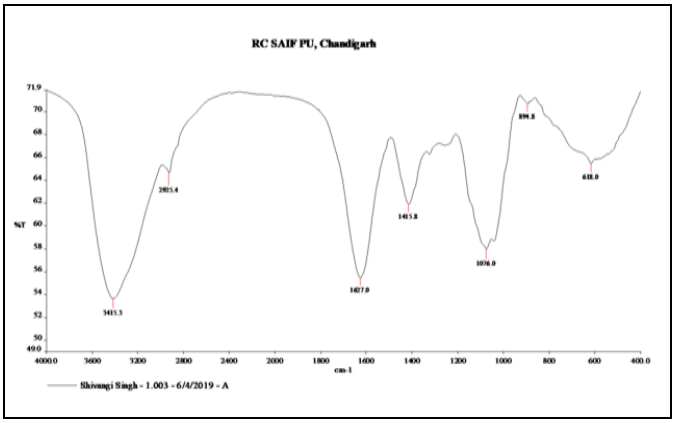

FIG. 5: FTIR SPECTRA OF HIBISCUS DRIED MUCILAGE

The FTIR spectra of dried mucilage of Hibiscus showed sharp and characteristic peaks at 3415.3, 2925.4, 1627.0, 1415.8, 1360, 1270, and 1076.0 cm^{-1}. The FTIR spectra of dried mucilage of Okra showed sharp and characteristic peaks at 3409.5, 2929.3, 1725.8, 1637.4, 1420.5, 1251.4, 1150.5, and 1043.0 cm^{-1}. The DSC of drug showed a sharp endothermic peak at 110 °C for a pure Dextromethorphan HBr as the melting point of drug **Fig. 6**. The reported valve of the melting point is 109 °C - 111 °C and the endothermic peak of Ofloxacin was found at 256 °C **Fig. 8**. The reported valve of the melting point of Ofloxacin is 250 °C - 257 °C. The average thickness of ODTs was found to be in range 3.278 ± 0.07 mm to 3.936 ± 0.08 mm **Table 7**. The hardness of ODTs was found to be in range 2.561 ± 0.57 kg/cm^2 to 3.983 ± 0.06 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 the 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 the rapid wetting and disintegration of the tablets. It was clear from the results that the increase of the drug ratio to super disintegrants led to a decrease in the ODTs hardness.

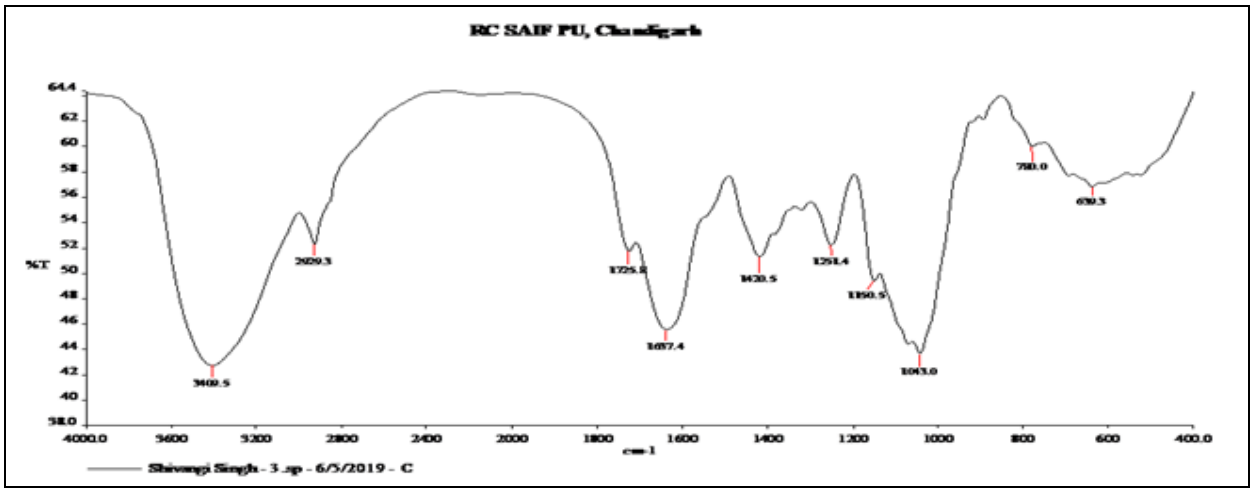

FIG. 6: FTIR SPECTRA OF OKRA DRIED MUCILAGE

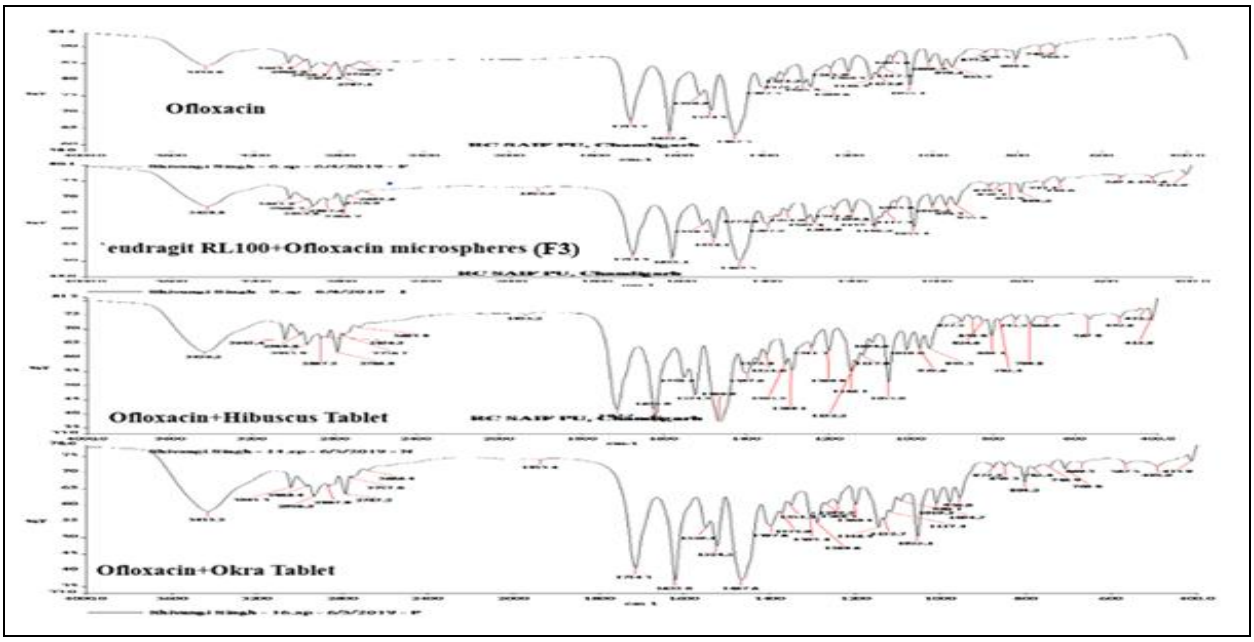

FIG 7: FTIR SPECTRA OF DRUG IN DIFFERENT FORMULATIONS

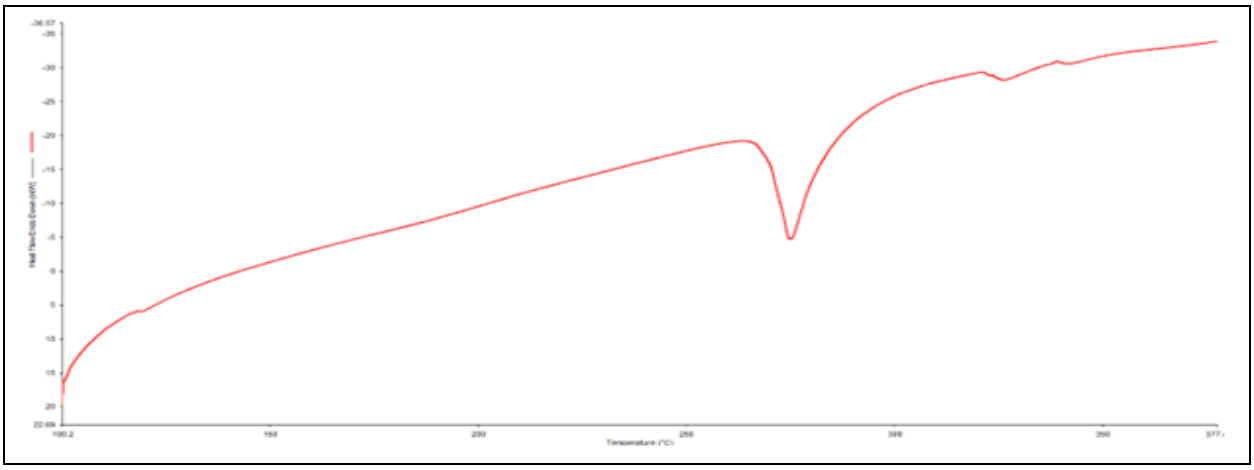

FIG. 8: DSC SPECTRA OF OFLOXACIN

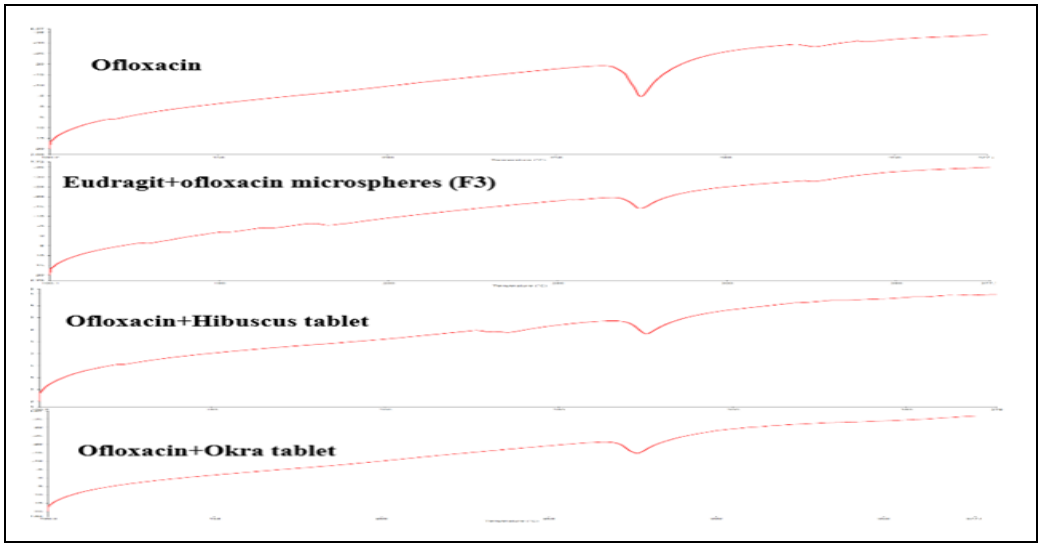

FIG. 9: DSC SPECTRA OF OFLOXACIN IN DIFFERENT FORMULATIONS

TABLE 8: EVALUATION PARAMETER OF TABLET

Parameters	Formulations					
	T_1	T_2	T_3	T_4	T_5	T_6
Thickness (mm)	3.679 ± 0.09	3.467 ± 0.18	3.598 ± 0.08	3.278 ± 0.07	3.478 ± 0.02	3.936 ± 0.08
Hardness (kg/ cm^2)	3.983 ± 0.06	2.561 ± 0.57	3.796 ± 0.05	3.382 ± 0.61	3.956 ± 0.35	3.459 ± 0.03
Weight variation (%)	247.33 ± 0.32	249.33 ± 0.18	250.33 ± 0.08	252.33 ± 0.09	249.33 ± 0.03	250.33 ±0.01
Friability (%)	0.198 ± 0.07	0.218 ± 0.05	0.123 ± 0.04	0.098 ± 0.02	0.245 ± 0.17	87.78 ± 0.46
Drug content (%)	94.09 ± 0.09	93.87 ± 0.06	92.45 ± 0.07	88.76 ± 0.18	0.235 ± 0.45	85.43 ± 0.51
Wetting time(s)	22.47 ± 0.07	18.76 ± 0.04	60.06 ± 0.51	58.89 ± 0.78	43.78 ± 0.09	42.45 ± 0.23
Disintegration time (s)	26.67 ± 0.43	21.52 ± 0.59	54.87 ± 0.05	53.38 ± 0.08	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 252.33 ± 0.09%. According to 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 0.098 ± 0.02% to 0.245 ± 0.17%. 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 the disintegration properties of the tablets. Wetting is closely related to the internal structure of the tablet and to the hydrophilicity of the excipients. From the results of wetting time shown in Tables 27 and 28, it was found that all formulations prepared from natural super disintegrants gave the acceptable result [18]. The wetting time of different ODTs ranged from 18.76 ± 0.04s to 60.06 ± 0.51s. 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 [18]. Disintegration time ranges from 21.52 ± 0.59 s to 54.87 ± 0.05 s.

The Okra dried mucilage tablet showed slower disintegration time than those containing Hibiscus because, in addition to the above reasons, Okra dried mucilage has a slow swelling rate, slow wetting than the Hibiscus 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.

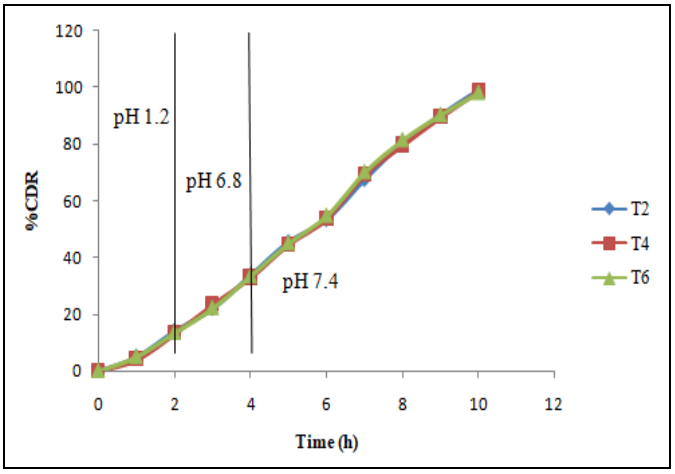

FIG. 10: *IN-VITRO* RELEASE STUDIES OF OFLOXACIN LOADED ODTS

Moreover, it is obvious from the figure the release rate of ODTs was slow compared to that from untabletted microspheres. This may be due to the 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 a particular method. Microencapsulation is a good technique to mask the bitter taste of the drug.

The formulation of the orodispersible tablet was made by using Ofloxacin and Eudragit RL 100 microspheres by direct compression. Hibiscus dried mucilage as a natural super disintegrant showed good results over the widely used synthetic super disintegrants; sodium starch glycolate.

Okra dried mucilage also showed results under the pharmacopeial limit. So, Hibiscus and Okra dried mucilage can also be used for further development of orodispersible tablets.

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