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Formulation Optimization & Evaluation of Fexofenadine Hydrochloride Melt in Mouth Pellets

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Abstract: The oral route is the most popular and ideal method of administering medication. The purpose of novel oral drug delivery systems is to improve patient compliance and medication safety and efficacy by developing a convenient dose form that is easy to administer. One of these systems is Melt in Mouth Pellets (MMP). Because superdisintegrants are included in the formulation, the idea behind MMP is to disperse the pellets in the mouth in the presence of saliva in a matter of seconds, without the need for water, and without causing swallowing difficulties.Melt in Mouth Pellets prepare by using fexofenadine hydrochloride, MCC PH 101, Sucralose, Mannitol, crosspovidone use as a superdisintegrant and Eudragit E 100 used as a taste masking agent. The all purpose equipment
(Pelletizer Assembly) used to prepare Melt in Mouth Pellets.The formulation was optimized based on Design expert software and
Central Composite Design was used for study. Drug and polymers were studied for compatibility and interaction study, carried out by FTIR and DSC and found to be compatible to each other. The % Drug Content, Friability, Disintegration time, dissolution study of formulated batches was evaluated.. From the result, FFH 8 batch was observed optimized formulation because up to 10 min 97.89% drug was released and disintegrate within 15 Sec.

Index Terms **– Melt in Mouth Pellets , Orally Disintegrating , Superdisintegrant**

I. INTRODUCTION:

Oral dose forms, such as tablets and capsules, are commonly used for patients who have difficulty swallowing, particularly those who are bedridden, nauseated, or noncompliant. These patients include pediatric and geriatric populations. Orally dissolving pill forms must be inserted into the mouth and allowed to dissolve in saliva on their own, without the need for water. Orally disintegrating pellets are also called as ordispersible, mouth dissolving, rapidly disintegrating, fast melt, Melt in Mouth and quick dissolve system.[1]

Oral dosage form can be broadly classified into two categories: Single-unit and Multiple-unit dosage forms. The single-unit dosage forms include matrix tablet or coated/uncoated tablet or capsules. The multiple-unit dosage forms consist of pellets or microencapsulated drug filled in a capsule, sachet or compressed into a tablet.[3,11]

Multiparticulate drug delivery systems include pellets, granules, micro particles (like microspheres, microcapsules, nano particles, mini tablets, mini depots, multiparticulate pulsatile drug delivery systems. These forms play a major role in the design of solid dosage form processes because of their unique properties and the flexibility found in their manufacture.[2,3]

The pellets were prepared directly from powder by using all purpose equipment (Pelletizer Assembly) Centrifugal force is applied to the powder bed after it has been combined and wet with a binder or solvent. Agglomerates, which flatten out into homogeneous, dense pellets, are formed during this process by the impact and acceleration forces. The density and size of the pellets are directly impacted by the speed of rotation. Drying follows the wet pellets.[4]

Fexofenadine hydrochloride, the major active metabolite of terfenadine, is an antihistamine with selective peripheral H1-receptor antagonist activity. Fexofenadine hydrochloride is indicated for the relief of symptoms associated with seasonal allergic rhinitis in adults or persons aged 6 years and older[5] It is also used in treatment of uncomplicated skin manifestations of chronic idiopathic urticaria.[15] Its bitter taste makes it poor candidate for mouth dissolving dosage form. Crospovidone use as a superdisintegrant and Eudragit E 100 used for masked the bitter taste of drug with orange flavor to improve mouth feel and patient compliance.[4,6]

II. MATERIALS & METHOD

Materials

Fexofenadine hydrochloride was obtained from Yarrow Pharma Chem. Pvt Ltd. MCC PH 101, Mannitol, Crospovidone, Eudragit E 100 Orange flavor were obtained from Medley Pharma LTD., Andheri, Sucralose, Citric acid, PVP K 30 were obtained from Jinendra Scientific, Jalgaon, Acetone, Isopropyl Alcohol were obtained from Pure Chem, Mumbai.

Method

To prepare the taste-masked pellets of Fexofenadine HCl, begin by accurately weighing all the ingredients. Next, dissolve Eudragit E 100 in a mixture of IPA and Acetone. This solution will be used to mask the taste of Fexofenadine HCl, which is done manually in the next step. The resulting material is then air-dried. Meanwhile, sift the other ingredients through a #60 mesh without a binder and dry mix them. Prepare a binder solution by dissolving PVP K 30 in IPA. Combine the air-dried material from step 4 with the dry-mixed material from step 5 and mix well. Transfer this mixture to an all-purpose instrument with a pelletizer type assembly. Slowly add the binder solution using a ladling method to obtain spherical-shaped, taste-masked pellets. Once the pellets have achieved the desired size, shape, and taste masking, air dry them for a few minutes. Finally, weigh the pellets, fill them into aluminum sachets, and label the sachets.[5]

Doe Software Used For Study:

Design expert software was used for optimization of formulation in that Central composite design (CCD) was used for experimental design containing two independent variables Crospovidone (X1) and PVP K30 (X2) were investigated at three levels as low, medium and high given in table 1. While putting the values nine baches were generated by using central composite design. In that dependent variables were investigated in the response i.e %DR (Y1) and DT (Y2). The statistical experimental design was evaluated through the analysis of variance (ANOVA) test using the Design Expert software (Version 13)[8]

Table 1. Factor Combination as per the Experimental Design

Experiment No.	Crosspovidone (%)		PVP K30 (%)	
FFH 1	+1	5	-1	0.5
FFH 2	+α	5.62132	0	2.75
FFH 3	+1	5	+1	5
FFH 4	0	3.5	+α	5.93198
FFH 5	-α	1.37868	0	2.75
FFH 6	0	3.5	0	2.75
FFH 7	0	3.5	-α	-0.431981
FFH 8	-1	2	-1	0.5
FFH 9	-1	2	+1	5

Table 2: Formulation and Optimized Batches of Fexofenadine Hydrochloride Melt in Mouth Pellets

Ingredient (mg/Sachet)	**Batches**								
	FFH1	**FFH2**	**FFH3**	**FFH4**	**FFH5**	**FFH6**	**FFH7**	**FFH8**	**FFH9**
Fexofenadine HCl	30	30	30	30	30	30	30	**30**	30
MCC PH 101	171.1	179.75	176.75	167.96	175.25	185.7	166.25	**177.5**	191.75
Sucralose	10	10	10	10	10	10	10	**10**	10
Mannitol	50	50	50	50	50	50	50	**50**	50
Crosspovidone	16.86	15	6	10.50	6	10.50	15	**10.50**	6.85
Eudragit E 100	8	8	8	8	8	8	8	**8**	8
Citric acid	0.75	0.75	0.75	0.75	0.75	0.75	0.75	**0.75**	0.75
Orange flavor	5	5	5	5	5	5	5	**5**	5
PVP K 30	8.25	1.50	1.50	17.79	15	1.29	15	**8.25**	8.25
Acetone (40%)	q.s	q.s	q.s	q.s	q.s	q.s	q.s	**q.s**	q.s
Isopropyl Alcohol (60%)	q.s	q.s	q.s	q.s	q.s	q.s	q.s	**q.s**	q.s
Average wt. (mg)	300	300	300	300	300	300	300	**300**	300

*All ingredients are in mg

III. EVALUATION PARAMETERS MELT IN MOUTH PELLETS:

Appearance:

The pellet were visually observed for colour and taste.

Friability: [13]

Accurately weighed quantity of pellets (3 g) taken from final batch of pellets and placed in a friabilator and tumbled for 100 revolutions at 25 RPM. The pellets were collected from the friabilator and again placed on the sieve. The pellets having a smaller diameter than the aperture of sieve pass through the sieve. The pellets remained on the sieve were reweighed. The friability was determined as the percentage loss of mass of pellets after the test was recorded.

Percent Friability % F = Initial weight - Final weight/ Initial weight x 100

Drug Content: [11]

The one sachet from each batch were precisely weighed and powdered. The powdered equivalent to 300 mg Fexofenadine HCl was weighed and shaken in 100ml of Phosphate Buffer in a volumetric flask, and 1ml was pipetted out and diluted up to 10 ml. The resulting solution was filtered and measured at 220 nm, and the Fexofenadine HCl content was calculated.

It was calculated by using formula,

Drug Content = Test absorbance/Standard absorbance X 100

In Vitro Disintegration Time: [13 ,14]

The in vitro disintegration time was determined for the pellets. This test was performed to ensure disintegration of pellets in the water. In vitro disintegration time was measured by dropping a little quantity of the pellets in a measuring cylinder containing 6 mL of water. The disintegration time was defined as the time necessary for the melt in mouth Pellets to completely disintegrate until no solid residue remains or only a trace amount of soft residue remains on the screen. A digital stopwatch was used to record the disintegration time to the nearest second. Only one melt in mouth pellets was analyzed at a time in order to ensure maximum accuracy.

In-Vitro Dissolution Studies: [2,4,]

The USP dissolution test apparatus (apparatus II paddle type) was used to study the drug release from the pellets. The dissolution medium was 900ml of Phosphate buffer pH 6.8. The release was performed at 37±0.5°C, with rotation speed 50 rpm. 5ml of sample was withdrawn at predetermined time intervals and replaced with fresh medium. The samples were analysed after appropriate dilution by UV spectrophotometer schimadzu 1800 at 220 nm and drug release was determined by following formula,

%Drug Release = (Test abs. / Std. abs.) x Std. Dilution x Test Dilution x Purity/ label claim

Taste / Mouth Sensation:[12]

Mouth feel of bitter drug is critical and patients should receive a product that feels pleasant. One tablet from each batch is tested for sensation by placing the pellets on the tongue. The healthy human volunteers are used for evaluation of mouth feel. Taste evaluation was done by a panel of 5 members using time intensity method. Sample of MMP was put in mouth for 30 seconds without swallowing (the pellets or saliva), and then spitting it out then record taste instantly and then after 10 sec, 1, 2, 4 & 6 min. Volunteers opinion for the taste was rated by giving different score values as follows:

Table 3: Taste Evaluation of Taste Masked Fexofenadine HCI MMP

Numerical Value	Score
0	Tasteless
1	Slightly Bitter
2	Moderately Bitter
3	Bitter

IV. RESULT AND DISCUSSION:

Result of Taste Masking of Fexofenadine Hydrochloride

Table 4: Taste Masking of Fexofenadine Hydrochloride

Batches	**Volunteers**					**Bitter Index**
	1	**2**	**3**	**4**	**5**	
FFH 1	0	0	0	0	0	0
FFH 2	0	0	0	0	0	0
FFH 3	0	0	0	0	0	0
FFH 4	0	0	1	0	0	0
FFH 5	0	0	0	0	0	0
FFH 6	0	0	0	0	0	0
FFH 7	0	0	0	0	0	0
FFH 8	**0**	**0**	**0**	**0**	**0**	**0**
FFH 9	0	0	0	0	0	0

Table 5: Quality Control Parameters of the Developed Formulation (FFH 8)

Parameter	**Result**
Appearance	Off-white coloured
Taste	Tasteless
Mouthfeel	Good
Flavour	Orange
Friability (%)	0.41 ± 0.01
Deug Content (%)	89.37%

In-Vitro Diaintegration Time (Sec.)	15 Sec.
In-Vitro Drug Release (%)	97.89 %

V. CONCLUSION

The main objective to carry out this research work was to formulate, optimized & evaluate melt in mouth pellets of fexofenadine hydrochloride. Melt in Mouth Pellets offer the advantages of solving the problems encountered in administration of drugs mainly to paediatrics and geriatric patients. MMP of Fexofenadine HCl were prepared using superdisintegrant by palletization technique in which Eudragit E100 was used as a taste masking agent. The batch FFH8 was given as the best batch by the Design Expert Software. The formulation FFH8 showed the maximum drug release 97.89 for 10 min % and DT in 15 Sec. Thus on the basis of results obtained we can concluded that the objective of taste masking of fexofenadine HCl by using Eudragit E100 and formulation into MMP by pelletization technique was successfully achieved with improved dissolution rate and DT within time limit.

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