- Short communication

Formulation and Evaluation of Fexofenadine Mouth Dissolving Tablet

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Rapidly disintegrating tablets are appreciated by a significant segment of the population, particularly pediatric, geriatric, unconscious and bedridden patients, who have difficulty in swallowing conventional tablet or capsules.[1-2] Conventional fexofenadine tablet available in the market are not suitable for acute allergic conditions where quick onset of action of drug is required. This is because poor patient compliance particularly by the geriatric and pediatric patients who experience difficulty in swallowing or who are traveling and don't have an easy access to water.

To provide the patient with the most convenient mode of administration, there is need to develop fast disintegrating dosage form, particularly one that disintegrates and dissolve /disperse in saliva and can be administered without water, anywhere, any time. Such tablets are also called as "melt in mouth tablet". Several techniques were used to prepare fast dissolving tablets like lyophilisation,[3] tablet moulding,[4] spray drying[5] and sublimation[6]. Fexofenadine has been shown to have potent antiallergic or antihistaminic activities, similar to levocetrizine and desloratadine and due to its preferential H_1 blockade it has better safety than conventional antihistamines with respect to adverse effects on brain, gastrointestinal and cardiovascular system. Hence, an attempt was made to improve the dissolution of fexofenadine through the formulation of mouth dissolving tablets with appropriate mechanical strength, which would disintegrate in oral cavity, less than 30 s, and would provide an immediate relief from allergic reactions due to its faster dissolution/absorption in oral cavity.

Crosspovidone, sodium starch glycolate, magnesium stearate, talcum, sodium lauryl sulphate and aspartame were purchased from CDH (P) Ltd., New Delhi. Fexofenadine was obtained as gift sample from Ranbaxy Pharmaceutical Pvt. Ltd., avicel PH 102, ac-di-sol were obtained as a gift sample from Alembic Pharmaceutical Pvt Ltd, Barodara. All other materials used were of pharmaceutical grade.

Direct compression techniques were selected for developing a novel mouth dissolving formulation. In direct compression all material were passed through a 40 mesh. 15 batches were prepared by using different concentration (4, 6, 8, 10 and 12%) of superdisintegrants. Batches A1-A5, B1-B5 and C1-C5 contained Ac-Di-Sol, crospovidone and sodium starch glycolate as superdisintegrant respectively. Fexofenadine, superdisinteragrant, avicel PH 102, mannitol, sodium lauryl sulphate, talc and magnesium stearate were mixed properly. The resulting mass was then compressed into tablet using single punch tablet machine.

Compressed tablets were then evaluated for hardness, wetting time, disintegration, weight variation, friability, and drug content at 257 nm. Hardness was measured by Monsanto hardness

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tester.[7-8] For disintegration, a petridish (10 cm diameter) was filled with 10 ml of water. The tablet was carefully put in the centre of petridish and time for the tablet to completely disintegrate into fine particles was noted.[9]

Dissolution study of tablet was conducted using USP dissolution apparatus II, in 900 ml of PBS pH 7.4 maintained at 37±0.5° at a speed of 50 rpm. 1ml of sample was withdrawn at time intervals of 2.5, 5, 10, 15, 20, 25 and 30min. filtered through a 0.45 micron membrane filter, diluted, and assayed at 257 nm, using a UV/Vis spectrophotometer. The volume of dissolution fluid was adjusted to 900 ml, by replacing each one ml aliquot withdrawn with 1 ml of PBS pH 7.4. The cumulative % release of fexofenadine in tablet sample was determined by using standard curve.[10]

Fifteen tablet formulations were developed (batches A1 to A5, B1 to B5, and C1 to C5) and optimized using direct compression method by varying the disintegrants and their concentration (Table 1). In the present study, three disintegrants were used such as. Ac-Di-Sol, crosspovidone, and sodium starch glycolate (Table 1). The precompression parameters were studied. The Carr's index value ranged from 14.63 to 33.74 % that showed fair to good flow properties of all formulations. The angle of repose values ranged from 29.26 ^{o} to 39.79 ^{o}.

Table 1. Design layout of different formulations prepared with avicel PH 102 by direct compression

Formula	A1	A2	A3	A4	A5	B1	B2	B3	B4	B5	C1	C2	C3	C4	C5
Fexofenadine	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60
Avicel PH 102	142	138	134	130	126	142	138	134	130	126	142	138	134	130	126
Mannitol	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20
Ac-Di-Sol	12	16	20	24	28	-	-	-	-	-	-	-	-	-	-
Crospovidone	-	-	-	-	-	12	16	20	24	28	-	-	-	-	-
Sodium Starch glycolate	-	-	-	-	-	-	-	-	-	-	12	16	20	24	28
Aspartame	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Talc	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9
Magnesium stearate	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Sodium lauryl sulphate	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2

Table 2. Physical evaluation of formulations (A1-C5).

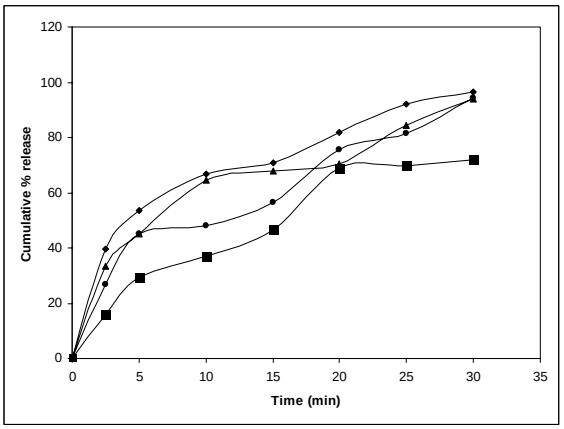
Formula	Crushing strength (kg/cm^2)	Weight variation	% Friability	Wetting time (sec.)	Disintegration time (sec.)	% Dissolution
A1	3.6	249.8 ± 3.5	0.56	17	42	88.87
A2	4.1	247.6 ± 2.1	0.42	17	35	93.53
A3	3.4	248.5 ± 5.6	0.54	16	31	96.35
A4	3.2	248.9 ± 1.8	0.63	14	29	90.61
A5	2.3	245.2 ±2.4	1.6	16	32	88.26
B1	3.4	248.3 ± 3.5	0.43	20	49	87.58
B2	3.7	247.7± 2.1	0.32	18	45	92.21
B3	3.1	248.5 ± 6.4	0.39	17	41	92.54
B4	3.2	246.7± 4.8	0.58	15	37	94.32
B5	4.2	247.7± 8.1	0.29	17	40	93.09
C1	4.1	246.3 ± 3.5	0.42	20	66	86.46
C2	3.2	249.1± 2.1	0.63	18	58	91.86
C3	3.5	247.8 ± 6.4	0.59	17	51	93.89
C4	3.3	247.3± 2.9	0.53	15	65	89.16
C5	3.9	248.1± 8.1	0.67	18	69	86.35

All the fifteen formulations prepared exhibited low weight variation 245.2 ± 2.4 and acceptable friability. Hardness of all the prepared tablets was found to be satisfactory. Other parameters like disintegration time and drug content were determined and were found to be within the limit for uncoated tablets. Hardness of the tablets were ranging from 2.3 to 4.2 kg/cm^2. Percent friability of all the formulations were ranging from 0.29 to 0.67, except formulation A5 which showed friability more than the limit. Wetting time of the tablets were ranged 14 to 20 sec and disintegration time were 29 to 69 sec which indicated fast wetting and disintegration of tablet formulations in mouth. All the tablets passed weight variation test, as the weight variation was within Pharmacopoeial limit of ± 7.5% and found to be from 245.2 to 249.8 mg (Table 2). All formulations had the drug content ranging from 93 to 98%.

The cumulative percentage of the drug released determined by dissolution was ranging from 88 to 96%. Superdisintegrants at different concentration level (4, 6, 8, 10 and 12% w/w) were used to assist disintegration. All formulations had disintegration time of less than 66 second. Among the three superdisintegrants we have used, Ac-Di-Sol showed maximum efficiency. Formulation A4 containing 10% w/w Ac-Di-Sol showed the least disintegration time of 29 sec. This result was compared with crospovidone and sodium starch glycolate and observed that crospovidone has more efficiency than sodium starch glycolate at higher concentration (6-10% w/w). For crospovidone, the minimum disintegration time was found to be 37 second at 10% w/w concentration whereas sodium starch glycolate is more efficient at lower concentration (8% w/w). For sodium starch glycolate minimum disintegration time was found to be 51 sec at 8% w/w concentration.

Different concentrations of superdisintegrant in all formulations may influence the dissolution rates. Formulationd containing Ac-Di-Sol and sodium starch glycolate, upto 8% w/w increase in dissolution rate however at higher concentration both the formulations showed decrease in dissolution rates. In the formulation containing crosspovidone up to 10% w/w showed increase in dissolution rate. Here we concluded that 8%w/w concentration is optimum for Ac-Di-Sol and Sodium starch glycolate, where as 10% w/w concentration is optimum for crosspovidone. Decrease in dissolution rate with increase in concentration of disintegrant may be due to the blockade of pores resulting in interior of tablets inaccessible to water.

In vitro dissolution studies of the best formulations A3, B4, C3 at different time intervals were performed. Ac-Di-Sol containing formulation showed maximum dissolution rates with 96.35% drug release in 30 min. Crospovidone containing formulation showed 94.32 % drug release in 30 min and sodium starch glycolate containing formulation showed 93.89 % drug release in 30 min. Accordingly the effectiveness of superdisintegrant was found to be in the order of Ac-Di-Sol > Crospovidone > Sodium starch glycolate. The formulation that contained 8% w/w Ac-Di-Sol was compared with marketed preparation in term of dissolution profiles and it showed better dissolution than marketed preparation (Figure 1). From the present study, it is concluded that mouth dissolving tablet of fexofenadine can be prepared by direct compression method using superdisintegrants. Ac-Di-Sol was found to be the best among the three superdisintegrants. At optimum concentration it showed least disintegration time of



---♦----A3, ---▲---B4, ---●---C3, ---■---Marketed Preparation

Figure 1. Comparative *in vitro* dissolution profiles of formulations of A3, B4, C3 with marketed preparation.

29 second and the highest (96.35 %) amount of drug release.

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