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Research Article

Formulation and Evaluation of Olopatidine Hydrochloride Immediate Release Tablet

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ABSTRACT:

The objective of present work is to formulate immediate release tablet of Olopatidine hydrochloride. To achieve this goal various formulations of Olopatadine hydrochloride were prepared by direct compression method to achieve maximum drug content with reference to innovator. Varying proportion of superdisintegrants such as sodium starch glycolate, Kyron T-134 used to compare drug release profile with innovator. Different formulations were prepared and evaluated with respect to various pre compression and post compression parameters. The results indicate that the superdisintegrants used have influenced on the disintegration time. The final selection of the formulation F6 containing 4 % Kyron T-134 was showed better drug release with reference to marketed product

Keywords: Olopatadine hydrochloride, direct compression, superdisintegrants, Kyron T-134, drug release.

INTRODUCTION

Since time immemorial, oral drug administration is one of the most convenient and widely accepted routes of delivery for most therapeutic agents. 90 % of all drugs used to produce systemic effects are administered by oral route [1-2]. In oral drug delivery system, there are many types of dosage form are available to deliver the drug such as tablet, capsule, liquid. Tablet dosage form is most preferred because of their accurate dose, good physical and chemical stability, competitive unit production cost and an elegant distinctive appearance results in high level of patient acceptability [3].

Immediate release solid oral dosage forms are divided in either having rapid or slow dissolution rates. Immediate release dosage forms are those for which ≥85% of labeled amount dissolves within 30 min. For immediate release tablets, the only barrier to drug release is simple disintegration or erosion stage, which is generally done in less than one hour [4].

Olopatadine is a selective histamine H1 antagonist that binds to the histamine H1 receptor. These blocks the action of endogenous histamine, which subsequently leads to temporary relief of the negative symptoms brought on by histamine. Olopatadine is devoid of effects on alpha-adrenergic, dopamine and muscarinic type 1 and 2 receptors having half life 3 hours.

The objective of the present investigation was to prepare immediate release tablet of Olopatidine hydrochloride and to evaluate the effect of concentration of superdisintegrants on their disintegration time and drug release.

MATERIALS AND METHODS

Materials

Olopatidine hydrochloride was gift sample from Ajanta pharmaceuticals, Mumbai, India. Sodium starch glycolate and Kyron T-134 were gift samples from Corel pharmachem, Ahmadabad. Microcrystalline cellulose (MCC) pH-102 was purchased from Balaji drug, Ahmadabad. All other chemicals and reagents used were either analytical or pharmaceutical grades.

Methods

Preparation of immediate release tablets of Olopatidine hydrochloride

Immediate release tablets of Olopatidine hydrochloride were prepared by direct compression. Olopatidine hydrochloride, microcrystalline cellulose, sodium starch glycolate, Kyron T-134 and PVP K-30 were passed through 80 mesh and dry mixed. The dry mixing was carried at a slow speed for 10 min by geometric order and ensured uniform mixing. Then accurately weighed magnesium stearate, talc was sifted through 80 # sieve and added

to above blend and mixed properly for 2 min. Then it was subjected for compression into tablets of 100 mg using 6 mm round convex punches on 10 station rotary tablet punching machine (Rimek mini press, model RSB-4, M/S: Karnavathi engineering, Ahmadabad).

Table- 1: Composition of Olopatidine hydrochloride immediate release tablet

Ingredients (mg)	F1	F2	F3	F4	F5	F6
Olopatidine hydrochloride	5	5	5	5	5	5
Microcrystalline cellulose	90	87	84	91	89.5	88
Sodium starch glycolate	2	5	8	--	--	--
Kyron T-134	--	--	--	1	2.5	4
PVP K-30	1	1	1	1	1	1
Talc	1	1	1	1	1	1
Magnesium stearate	1	1	1	1	1	1
Total	100	100	100	100	100	100

Evaluation of tablet

Angle of repose (θ)

Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and horizontal plane. The frictional force in a loose powder or granules can be calculated by angle of repose [5].

$\theta = \tan^{-1}(h/r)$

Where, θ = angle of repose

h = height of pile

r = radius of the base of the pile.

Bulk density

Accurately weighed 5 gm of blend, which was previously passed through 80 # sieve, was transferred in 50 ml graduated cylinder. The powder in the cylinder was leveled without compacting, and the unsettled apparent volume was noted. The apparent bulk density (gm/ml) was calculated by the following formula [6].

$$\text{Bulk Density} = \frac{\text{weight of the bend}}{\text{untapped volume of the packing}}$$

Tapped density

Weighed accurately 5 gm of blend, which was previously passed through 80 # sieve, was transferred in 50 ml graduated cylinder. Then mechanically tap the cylinder containing the sample by raising the cylinder and tapped the cylinder for 100 times and calculate the tapped bulk density in gm/ml by the following formula [7].

$$\text{Tapped Density} = \frac{\text{weight of the blend}}{\text{Tapped volume of the packing}}$$

Compressibility index

The compressibility Index and Hausner's ratio are measures of the propensity of powder to be compressed. Calculate the compressibility index and Hausner's ratio by following formula [2].

$$\text{Compresibility index (\%)} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \text{ X } 100$$

$$\text{Hausner's ratio (\%)} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

PHYSICAL PARAMETERS

Thickness

Thickness of tablets was measured in mm by using Vernier caliper.

Hardness

Hardness of the tablet, which is the force applied across the diameter of the tablet to break a tablet into halves. The hardness of five tablets was measured using Pfizer hardness tester [8].

Friability

The tablets were subjected to the test of friability with initial weight (Wi) almost equivalent to 6.5 gm of the tablets. The tablets were allowed to fall on it from a height of 6 inches while the friabilator drum was rotated at 25 RPM for 4 minutes. The final weight (Wf) of the tablets after subjecting to friability was noted and the friability was calculated according to the formula [9].

Friability = (Wi-Wf/Wi)*100

Weight variation

Randomly selected twenty tablets were weighed accurately and together in a single pan balance. The

average weight was noted and standard deviation was calculated. The tablet passes the test if not more than two tablets fall outside the percentage limit and none of the tablet differ by more than double percentage limit [9].

Table- 2: Standards of uniformity of weight as per USP

Sr. No	Average weight of tablet	% of deviation
1	130 or less	10
2	From 130-324	7.5
3	More than 324	5

Drug Content:

Five tablets weighted and crushed in a mortar then weighed powder contained equivalent to one tablet (100 mg) of theoretical drug content was weighted and dispersed in 100 ml of pH 1.2 buffer. The UV Absorbance after suitable dilution and filtration was measured at wavelength 220 nm against blank reagent. The test was performed in triplicate [10-12].

Disintegration test

The disintegration of the immediate release tablets were determined using disintegration test apparatus as per Indian pharmacopoeia 2007 specifications. One tablet in each of the six tubes of the basket was placed. Add the disc to each tube and run the apparatus using 900 ml of pH 1.2 buffer as the immersion liquid. The assembly should be raised and lowered between 30 cycles per minute in pH 1.2 buffer maintained at 37º C. The time in seconds for complete disintegration of the tablets with no palable mass remaining in the apparatus was measured and recorded [10-11].

Dissolution test

The dissolution studies of the prepared tablets were carried out using USP XXIII apparatus II. Dissolution was performed in 900 ml of pH 1.2 buffer medium at 37±0.5°C and at 50 rpm. Aliquots samples were withdrawn at 5, 10, 15, 30, 45 and 60 minutes and analyzed by UV spectrophotometer at 220nm. Sink condition was maintained throughout experiment by replacing with pH 1.2 buffer medium [12].

RESULT AND DISCUSION

Olopatidine hydrochloride immediate release tablets were formulated by direct compression method using varying concentrations of superdisintegrants like sodium starch glycolate and Kyron T-314. Methyl carboxy cellulose (MCC), Magnesium stearate and Talc were employed for their disintegration, lubricant and glidant property respectively.

The powder blend of six formulations were evaluated for angle of repose, bulk density, tapped density, Carr's index, and Hausner ratio. Table 3 showed the pre compressed blend has good flow property. The angle of repose of all batches was found to be below 30^0, which indicated the blend having good flow property. The bulk density was found in the range 0.4735 - 0.5198 g/ml. The tapped density was observed in the range of 0.5623 - 0.5987 gm/ml. The compressibility and Hausner's ratio of various blends was calculated by using bulk density and tapped density data. The compressibility index was found in the range 12.04 – 17.30 % the compressibility index between 5-15 % indicates excellent flow. Hausner's ratio was found in the range 1.14 - 1.16. Hausner's ratio less than 1.15 indicates good flow.

The formulated tablets were evaluated for thickness, hardness, weight variation, % friability, and disintegration time and % drug content. The table 4 represents all the tablet parameters evaluated. The thickness of prepared tablet was found to be in the range of 2.85 ± 0.020 to 2.91 ± 0.0.207. Tablet hardness reflects differences in tablet density and porosity, which are supposed to result in different release patterns of the drug by affecting the rate of penetration of the dissolution fluid at the surface of the tablet. In the present study, the hardness of formulation was found to be in the range of 3.16 ± 0.11 to 3.76 ± 0.114. The friability of formulated tablets found to be in the range of 0.39 to 0.60 %. Tablets that loose less than 1 % of their weight are generally considered acceptable. Percent friability of the formulations was below 1 % limit as shown in the pharmacopoeia indicating that the friability is within the standard limit. The tablets showed no evidence of capping, cracking, cleavage or breaking after tumbling in the Roche friabilator. It ensures that the tablets were mechanically stable. The weight of all batches of tablet was found to be in the range of 98.29 ± 7.44 to 99.98 ± 1.10. The weight of all batches of tablet was found to be uniform with low standard deviation values indicating efficient mixing of drug and excipient. The uniformity in content could be related to the low weight variation of the core tablet which could be due to the narrow size distribution and free flowing nature of the pre-compressed blend. The tablets showed no signs of sticking or binding during compression. All batches of tablet passed the test for uniformity of weight. The percentage drug content was found to be in the range of 98.38 ± 0.64 to 99.35 ± 0.32. The percentage drug content for tablet indicating good content uniformity in all the batches that indicates drug was uniformly

distributed throughout the tablets. The disintegration time was found to be in the range of 15.26 ± 0.72 to 58.77 ± 0.45 sec. The immediate-release tablets passed the disintegration test for uncoated tablets as they were found to quick disintegrated. The quick disintegrating time of the tablets can be attributed due to the presence of the super disintegrant Kyron T-314 in optimum concentration in the formulae.

Table - 3: Pre compression parameter

Formulation code	Angle of repose (θ)	Bulk density	Tapped density	Hausner's Ratio	Carr's index
F1	22.97 ± 0.39	0.4735±0.002	0.5623±0.0012	1.14±0.01	12.04±0.75
F2	24.1 ± 0.03	0.4933±0.006	0.5714±0.0096	1.14±0.015	13.25±0.12
F3	25.16±0.064	0.5057±0.0057	0.5821±0.0041	1.16±0.015	13.81±0.56
F4	23.16±0.036	0.4864 ± 0.053	0.5516±0.003	1.15±0.011	14.36±0.200
F5	25.15±0.040	0.483±0.0072	0.553±10.0024	1.16±0.005	15.69±0.1352
F6	24.19±0.030	0.5198±0.0027	0.5987±0.002	1.16±0.051	17.30±0.2150

(n=3 ± standard deviation)

Table- 4: Post compression parameter

Formulation code	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Weight variation (mg)	Disintegration time (sec)	% drug content
F1	2.88 ±0.024	3.54 ±0.11	0.39 ±0.35	98.29 ±7.44	58.77 ±0.45	98.91 ±0.67
F2	2.88 ±0.030	3.34 ±0.19	0.43 ±0.02	99.84 ±1.11	41.37 ±0.90	99.24 ±0.65
F3	2.89 ±0.020	3.16 ±0.114	0.513 ±0.020	99.98 ±1.10	25.60 ±0.62	98.43 ±0.52
F4	2.91 ±0.017	3.58 ±0.13	0.603 ±0.025	99.86 ±1.04	49.28 ±0.60	98.57 ±0.62
F5	2.85 ±0.020	3.70 ±0.07	0.47 ±0.015	99.59 ±1.10	33.48 ±0.80	98.38 ±0.64
F6	2.91 ±0.022	3.76 ±0.11	0.34 ±0.018	99.83 ±0.79	15.26 ±0.72	99.35 ±0.32

(n=3 ± standard deviation)

In vitro Dissolution study

The in vitro dissolution studies of all formulation were carried for 1 hr and cumulative drug release calculated at every 5 min up to 45 min and lastly at 60 min. (Table 5 and Fig.I)

The formulation F1, F2, and F3 contain 2 %, 5 %, 8 % Sodium starch glycolate respectively. Formulation F1 showed 88.67 % drug release in 60 minutes, Formulation F2 showed 90.98 % drug release in 60 minutes, formulation F3 showed 94.38 % drug release in 60 minutes. The formulation F4, F5, F6 contains 1 %, 2.5 %, 4 % Kyron T-134 respectively. Formulation F4 showed 89.96 % drug release in 60 minutes, formulation F5 showed 93.73 % drug release in 60 minutes while the formulation F6 showed 98.73 % drug release in 30 minutes.

Table- 5: Comparative % drug release

Time (min)	Innovator	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0	0
5	64.3	45.13	50.18	57.13	48.17	52.14	65.33
10	74.9	57.44	58.67	59.64	57.38	59.63	78.54
15	86.1	64.18	68.43	70.58	66.36	68.74	87.56
30	94.7	75.67	77.18	79.32	77.13	79.39	98.73
45	97.3	84.90	86.13	88.15	85.58	89.56	--
60	100	88.67	90.98	94.38	89.96	93.73	--

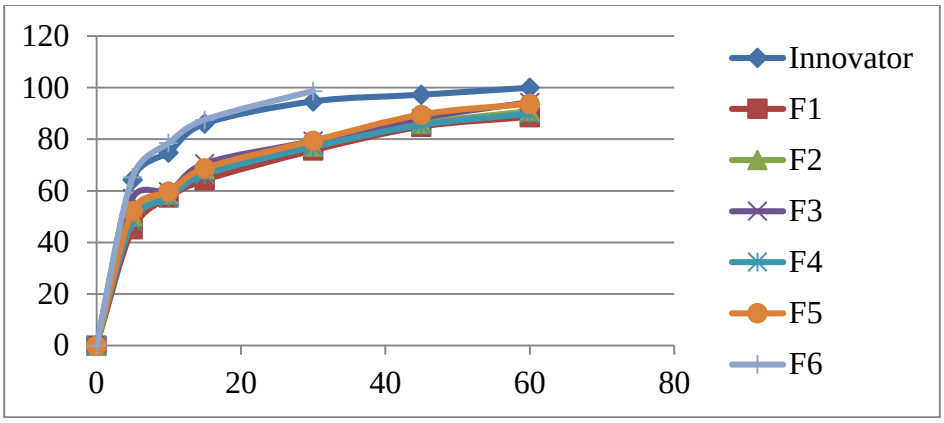

Fig. I. % drug release study

CONCLUSION

From the results it was concluded that formulation F6 containing 4 % Kyron T-134 shows better drug release in comparison with the formulation F1, F2, F3, F4 and F5. The percentage drug content was found to be in the range of 98.38 ± 0.64 to 99.35 ± 0.32 which shows uniformity in all batches. The study indicates that Kyron T–314 is suitable super disintegrant to formulate immediate release tablet of Olopatidine hydrochloride.

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