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Research Article

PREPARATION AND EVALUATION OF FAST DISSOLVING DRUG DELIVERY SYSTEM CONTAINING LEVOCETRIZINE HCl

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ABSTRACT

The objectives of this investigation were to prepare fast dissolving tablets of the H1-receptor antagonist drug, levocetirizine. This work investigated the possibility of developing fast dissolving disintegrating tablets of levocetrizine, which allowing fast, reproducible, and complete drug dissolution, by using. Solubility studies were performed to investigate the drug-carrier interactions in solution, Levocetrizine the tablets were prepared by direct compression technique. The prepared tablets were evaluated for thickness, uniformity of weight, content uniformity, hardness, friability, wetting time, in-vitro disintegration time, and in vitro drug release. The tablets are fulfilling all official and other specifications, the levocetrizine dissolution profile from the newly developed tablets was clearly better than those from various conventional tablets at the same drug dosage.

Keywords: levocetrizine HCl, Fast dissolving tablets, Thickness, Content uniformity

INTRODUCTION

The concept of Fast Dissolving Drug Delivery System emerged from the desire to provide patient with conventional mean of taking their medication. Difficulty in swallowing (Dysphagia) is a common problem of all age groups, especially elderly and pediatrics, because of physiological changes associated with these groups of patients. Solid dosage forms that can be disintegrated, dissolved, or suspended by saliva in the mouth resulting in easy swallowing can provide significant benefits to the pediatric and geriatric population, as well as other patients who prefer the convenience of easily swallowable dosage forms. This tablet disintegrates instantaneously when placed on tongue, releasing the drug that dissolves or disperses in the saliva[1].

MATERIALS AND METHODS

Materials

Levocetrizine HCl was obtained from Sun Pharma (Silvasa), Sorbitol were obtained as gift samples from Signet Chemicals (Mumbai).

Methods

Preparation Tablets: Tablets were made from blends by direct compression method. All the ingredients (shown in Table 01) were passed through mesh no. 60. All the ingredients were co ground in a pestle motor. Finally talc and magnesium stereate were added and mixed for 5 minutes. The quality of tablet, once formulated by rule, is generally dictated by the quality of physicochemical properties of blends. The mixed blend of excipients was compressed using a single punch machine to produce convex faced tablets weighing 400 mg each with 2.85 mm thickness and 7.8 mm in diameter. The tablets were evaluated for General Appearance, Size and Shape, Uniformity of weight, Tablet hardness, Friability, Disintegration time, Wetting time, In vitro dispersion time, Content Uniformity.

PREFORMULATION STUDIES [9,10]

Mannitol , Citric acid , Sod. Bicarbonate etc. were passed through a 100 # screen prior to mixing.

Bulk density [(9)]

Apparent bulk density (g/ml)was determined by placing pre-sieved bulk powder blend into a graduated cylinder via a large cylinder and measuring the volume and weight " as it is ".

LBD = weight of powder/volume of the packing

Tapped density[9]

It was determined by placing known mass of powder in a graduated cylinder & tapping it for fixed number of taps (around 250) until the powder volume reached a minimum. Using the weight of the powder in the cylinder and this volume, the tapped density was computed.

Angle of repose [9]

For the measurement of angle of repose, a glass funnel was secured with its tip at a given weight (H) above a piece of graph paper placed on a horizontal surface. Powder was poured through the funnel until the apex of conical pile touched the tip of the funnel. The angle of repose was calculated with the formula tan a =H/R, where a is the angle of repose and R is the radius of the conical pile.

Compressibility index[10]:

The compressibility index of the granules was determined by Carr's compressibility index.

Evaluation of formulated tablet [10, 11]:

Uniformity of weight (weight variation) [10]

Twenty tablets were selected at a random and average weight was determined. Then individual tablets were weighed and the individual weight was compared with an average weight.

Hardness[10]

The tablet crushing load, which is the force required to break a tablet by compression in the radial direction, was determined using a Monsanto hardness tester.

Friability [10]

Friability of tablets was measured by using roche friabilator. Friability was evaluated from the percentage weight loss of 20 tablets tumbled in a friabilator at 25 rpm for 4 minutes. The tablets were dedusted, and the loss in weight caused by fracture was recorded as the percentage weight loss. Friability below 1% was considered acceptable.

% Friability=100(1-W1/W2)

Where W1=Total weight of six tablets before friability

W2=Total weight of six tablets after friability

Drug Content

Five tablets were weighed individually mix together, take amount of one tablet (Avg. weight) was dissolved in small volume of 6.8 ph phosphate buffer, after complete dissolution, make the volume up to 100 ml and the solution was filtered through simple filter paper. The absorbance was measured at 231 nm after suitable dilution.

Disintegration Time[5]

The disintegration time of tablet was measured in water (37^{0}C) according to USP disintegration test apparatus. Three trials for each were performed

Wetting Time[6]

The method reported by Yunixia et.al.was followed to measure tablet-wetting time. A piece of tissue paper folded twice was placed in a small petry dish (ID6.5cm) containing 6ml of pH6.8 (simulated saliva fluid). A tablet was put on the paper and the time for complete wetting was measured. Three trials for each were performed. Data revealed in table no. 2

***In vitro* dissolution studies[10,11]**

In vitro dissolution studies of fast-dissolving tablets were performed by using type I apparatus as specified in Indian Pharmacopoeia at 50 rpm; and Sorenson's buffer (pH,6.8), 900 ml, was used as dissolution medium , temperature of dissolution medium was maintained at 370C±0.50C.

Aliquots of dissolution medium was withdrawn at a specific time interval and was filtered. Absorption of filtered solution was checked by UV spectroscopy (Shimadzu, Japan), and drug contant was determined from standard calibration curve. Dissolution rate was studied for all designed formulations.

Table 1: Composition of FDTs Levocetrizine HCl (400 mg tablets)

Ingredients	Batches (mg/tablets)							
	F1	F2	F3	F4	F5	F6	F7	F8
$NaHCO_3$:Mannitol	1:0	1:1	1:2	1:3	1:4	1:5	5:1	4:1
Levocetirizine HCl	15	15	15	15	15	15	15	15
$NaHCO_3$	355	177.5	118.32	88.75	71	59.16	295.84	284
Mannitol	0	177.5	236.68	266.25	284	295.84	59.16	71
Citric acid	6	6	6	6	6	6	6	6
PVP	20	20	20	20	20	20	20	20
Sod. Saccharine	2	2	2	2	2	2	2	2
Mg. Stearate	2	2	2	2	2	2	2	2

RESULTS AND DISCUSSION

All the tablets were exhibit in white color, odorless, smooth surface with zero defects. Formulated powder were evaluated for angle of repose, LBD, TBD, compressibility index, and drug content (Table 3). The results of angle of repose indicate good flow properties of the granules. This was further supported by lower compressibility index values (Table 2). Generally, compressibility index values up to 15% result in good to excellent flow properties. In addition, Bulk density may influence compressibility, dissolution, and other properties.

The average weight of the prepared tablet was found 402.54 to 406.89 mg. A tablet requires certain amount of hardness to withstand the mechanical shocks in handling, packaging and at the time of application. The hardness of the prepared tablet varied from 2.3 to 4.2 Kg/cm2 which have satisfactory strength to withstand the mechanical shocks. The friability of all the formulation was found to be less than 1.0 %. The results shows resistance to loss of weight indicates the tablet's ability to withstand abrasion in handling, packaging and shipment. The disintegration time of the tablets was varied form 19 to 29 seconds. The tablets with Ac-Di-Sol may disintegrate faster then the tablets with the crosspovidone. The in vitro swelling time of all the formulations were varied between 09 to 18 seconds. The drug content of all the formulations was varied from 14.9 to 16.4 mg per tablet The release found to be at the end of thirty minutes 95.58 – 99.83 % . The formulations F4 with 66.56% mannitol shows more release than the tablets with only sodium bicarbonate. All the formulations showed no significant variation in all the parameters under the test period.

Table 3: Evaluation Parameters

Parameters	Formulation						
	FDT1	FDT2	FDT3	FDT4	FDT5	FDT6	FDT7
Bulk Density (gm/cm3)	0.960	0.69	0.562	0.497	0.432	0.417	0.821
Tapped Density (gm/cm3)	1.09	0.79	0.631	0.573	0.495	0.481	0.919
Compressibilty Index (%)	11.92	12.65	10.93	13.26	12.72	13.30	10.66
Angle of Repose (^{0})	25.34	24.42	26.34	24.24	25.66	25.47	24.98
Wt. variation(mg)	403.61± 0.39	403.10± 0.12	405.48± 0.19	406.89± 0.41	415.38± 0.87	402.54± 0.28	404.21± 0.18
Hardness (kg/cm2)	2.3±0.1	2.8±0.3	3.2±0.1	3.8±0.4	4.1±0.1	4.2±0.2	2.5±0.3
Friability (%)	0.51± 0.2	0.43± 0.5	0.41±0	0.42±0	0.43±0.13	0.42±0.29	0.43±.11
Disintegration Time (sec)	19±2	21±4	24±2	18±5	19±4	23±6	19±3
Swelling Time (Sec)	9±2	12±3	15±2	14±4	13±2	15±1	11±3
Drug content (mg/tablet)	16.1	15.5	14.9	16.4	16.3	16.3	15.6
% Cumulative Release(30 min)	99.13	97.92	95.58	99.91	98.97	98.81	97.03

Table 4: *In vitro* % cumulative release of all formulations

TIME (min)	% Cumulative release							
	FDT1	FDT2	FDT3	FDT4	FDT5	FDT6	FDT7	FDT8
0	0	0	0	0	0	0	0	0
5	50.93	61.69	82.97	65.74	63.46	70.18	48.64	63.86
10	87.47	92.65	95.58	76.86	79.81	84.51	97.03	67.82
15	88.68	97.55	92	99.91	97.54	97.07	93.65	87.8
20	99.13	97.92	92.35	98.21	98.97	98.47	92.93	99.68
25	98.01	90.4	82.34	94.41	96.48	98.81	93.58	91.1
30	95.31	83.53	85.19	92.23	92.47	97.81	93.27	89.3

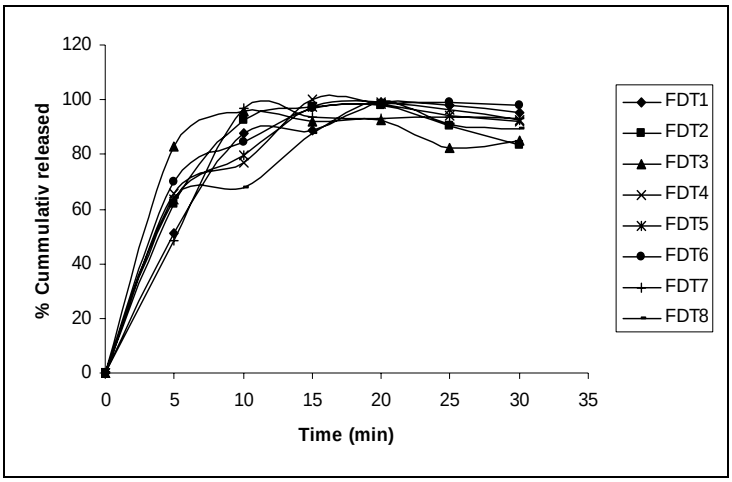

Fig. 1: Time Vs % Cummumlative released

CONCLUSION

The FDTs have potential advantages over conventional dosage forms, with their improved patient compliance; convenience bioavailability and rapid onset of action had drawn the attention of many manufacturers over a decade. FDT formulations obtained by some of these technologies have sufficient mechanical strength, quick disintegration/dissolution in the mouth without water. In conclusion , overall results suggests that the FDTs containing sodium bicarbonate and mannitol in the ratio of 1:3 (F4) shows best results in terms of percent drug release, compressibility index, hardness and disintegration time. Thus FDTs may be developed for levocetrizine HCl, for quick onset of action without need of water for swallowing or administration, however further studies are required for the development of FDT of levocetrizine HCl.

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