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Formulation and evaluation of oro dispersible tablets of levocetrizine by melt granulation technology

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ABSTRACT

The purpose of the present research was to optimize the formulation of Orodispersible tablets of Levocetrizine. Orodispersible tablets of Levocetrizine were prepared by Melt Granulation Technology. The formulations were evaluated for Tablet weight variation, content uniformity, hardness, friability, wetting time, dispersion time, drug content and in vitro release also have been studied. All formulations showed satisfactory mechanical strength and tablets containing Crospovidone (10%) showed excellent in vitro dispersion time and drug release as compared to other formulations. The results revealed that the tablets containing 10% Crospovidone (F_8) showed short dispersion time (12 sec) with maximum drug release (100%) in 20 min. FTIR & DSC results showed no evidence of interaction between the drug and polymers. This study helps in revealing the effect of formulation processing variables on tablet properties. It can be concluded that the Orodispersible tablets of Levocetrizine tablets could be prepared by Melt Granulation Technology using Crospovidone as superdisintegrant.

Key Words: Lecocetrizine, Crospovidone, Orodispersible Tablets, Melt Granulation Technology.

INTRODUCTION

Recent advances in novel drug-delivery system aims to enhance the safety and efficacy of the drug molecule by formulating a dosage form being convenient for the administration. Difficulty in swallowing (i.e., dysphagia) is experienced by patients such as paediatrics, geriatric, bedridden, disabled, mentally ill, including motion sickness and sudden episodes of allergic attacks, hence resulting in higher incidence of noncompliance and ineffective therapy [1]. In order to solve this problem and improve patient acceptance and compliance, the development of solid dosage forms that disintegrate rapidly or dissolve even when taken orally without water is being undertaken. Oral fast-disintegrating dosage forms (tablet or a capsule) are a relatively novel dosage technology that involves the rapid disintegration or dissolution of the dosage form [2] into a solution or suspension in the mouth without the need for water [3]. The dosage form begins to disintegrate immediately after coming into contact with saliva, with complete disintegration normally occurring within 30–50 s after administration [4]. The solution containing the active ingredients is swallowed, and the active ingredients are then absorbed through the gastrointestinal epithelium to reach the target and produce the desired effect. Tablet is the most widely used dosage form because of its convenience in terms of self-administration, compactness, and ease in manufacturing [5]. Orally disintegrating tablets are also called as Orodispersible tablets, quick-disintegrating tablets, mouth-dissolving tablets, fast-disintegrating tablets, fast dissolving tablets, rapid-dissolving tablets, porous tablets, and rapid melts. However, of all the above terms, the United States Pharmacopoeia (USP) approved these dosage forms as Orodispersible tablets (ODTs). Recently, the European Pharmacopoeia has used the term Orodispersible tablets for tablets that disperse readily and within 3 min in the mouth before swallowing. The United States Food and Drug Administration define ODT as “a

solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue." The disintegration time for ODTs generally ranges from several seconds to about a minute [6]. Other advantages of ODTs that have been investigated are their potential to increase the bioavailability of poorly water soluble drug through enhancing the dissolution profile of the drug [7]. Moreover, pharmaceutical companies also have commercial reasons for formulating ODTs. As a drug reaches the end of its patent, the development and formulation of the drug into new dosage forms allow pharmaceutical companies to extend the patent life and "market exclusivity"[8]. The ODTs could be prepared using various techniques such as tablet moulding, spray drying, sublimation, lyophilization, solid dispersion, or addition of disintegrants [9–13]. The basic approach to the development of ODTs is the use of superdisintegrants such as Croscarmellose sodium and sodium starch glycolate. Another approach used in developing ODTs is maximizing the pore structure of the tablet matrix. Freeze drying and vacuum drying techniques have been tried by researchers to maximize the pore structure of the tablet matrix [14–16]. However, freeze drying is cumbersome and yields a fragile and hygroscopic product. Vacuum drying along with the sublimation of volatilizable ingredient has been employed to increase tablet porosity. While in designing dispersible tablets, it is possible to achieve effective taste masking as well as a pleasant feel in the mouth. The main criterion for ODTs is the ability to disintegrate or dissolve rapidly in saliva of the oral cavity in 15 to 60 s and have a pleasant mouth feel [17].To improve the quality of life and treatment compliance, great efforts have been made to develop fast-disintegrating tablets (FDTs) in the oral cavity, using jelly, water-absorbing, and swelling-gelated materials or water-soluble polymers [18].

MATERIALS AND METHODS

MATERIALS

Levocetrizine was chosen as an active ingredient and it was gift sample from Hetero Labs, India. Eudragit EPO, Precirol ATO5, Crospovidone, Xylitol, Acesulfame Potassium, and Magnesium stearate were purchased from colorcon, Mumbai, India. All other reagents were of analytical grade.

METHOD OF FORMULATION

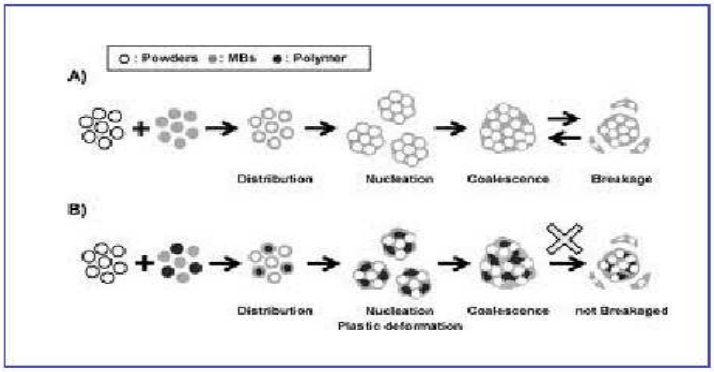
Levocetrizine Oro-dispersible tablets were formulated by using Melt Granulation Technology. Melt granulation is processes by which granules are obtained through the addition of either a molten binder or a solid binder which melts during the process. This process is also called melt agglomeration and thermoplastic granulation.

Principle involved in melt granulation: The process of granulation consists of a combination of three phases:
I. Wetting and nucleation,
II. Coalescence step,
III. Attrition and breakage.

Wetting and nucleation step: During the nucleation step the binder comes into contact with the powder bed and some liquid bridges are formed, leading to the formation of small agglomerates. Two nucleation mechanisms are proposed by Schafer and Mathiesen.

I. Immersion
II. Distribution

Immersion: Nucleation by immersion occurs when the size of the molten binder droplets is greater than that of the fine solid particles. Immersion proceeds by the deposition of fine solid particles onto the surfaces of molten binder droplets.



Distribution: In the distribution method a molten binding liquid is distributed onto the surfaces of fine solid particles. The nuclei are formed by the collision between the wetted particles. Generally, small binder droplet size, low binder viscosity, and high shearing forces are favorable conditions for nucleation by the distribution method.

Coalescence step: It involves nuclei that have residual surface liquid to promote successful fusion of nuclei. The surface liquid imparts plasticity to the nuclei and is essential for enabling the deformation of nuclei surface for coalescence as well as promoting the rounding of granulation.

Attrition-breakage step: Attrition and breakage refer to the phenomenon of granulation fragmentation in that are solidified by tray cooling to ambient temperature without the need for drying by a tumbling process. Consequently, breakage is known to have a more essential role in affecting the resultant properties of the melt granulation during the granulation phase. The granules were lubricated with magnesium stearate. The above lubricated blend was compressed using 6mm round punch at a tablet weight of 100mg.

CHARACTERIZATION OF ORODISPERSIBLE TABLETS

The prepared tablets were evaluated for different Pre-Compressional and Post Compressional properties like Micrometric Properties (Bulk Density and Tapped Density), Angle of Repose, Hausner's Ratio, Carr's Index, weight variation, friability, hardness, thickness, disintegration time, wetting time, Drug Content and In vitro dissolution studies.

MICROMERITIC PROPERTIES

The loose bulk density (LBD) and tapped bulk density (TBD) of plain Levocetrizine and its spherical crystals were determined using a bulk density test apparatus (Kumar Industries, India). Carr's index and Hausner's ratio were calculated using LBD and TBD values [20]. The angle of repose was assessed by the fixed funnel method. A known amount of agglomerates was allowed to flow through a funnel fixed at a constant height (*h*) and the height and diameter (2*r*) of the pile of powder were measured to calculate the angle of repose as $\tan \theta = h/r$.

WEIGHT VARIATION [21- 24]

20 tablets were selected at a random and then the average weight was determined. All the 20 tablets were weighed individually and compared with the average weight the tablets meet USP specifications if no more than 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit.

FRABILITY [21- 24]

The friability test was performed for all the formulated Oro-dispersible Levocetrizine tablets. Twenty tablets were taken and their weight was determined. Then they were placed in the Roche friabilator and allowed to make 100 revolutions. The tablets were then de-dusted and reweighed. The percentage weight loss was calculated. Percentage Friability was calculated as follows

Percentage Friability = $(W_1 - W_2) \times 100/W_1$

Where, W1 = Initial weight of the 20 tablets.
W_2 = Final weight of the 20 tablets after testing.

Friability values below 1% are generally acceptable.

HARDNESS [21- 24]

Monsanto hardness tester was used for measuring the hardness of the formulated Oro-dispersible Levocetrizine tablets. From each batch five tablets were taken and subjected to test. The mean of the five tablets were calculated. The breaking strength (in kg) of each tablet was tested using a Stokes-Monsanto hardness tester (DT Stokes, Bristol, PA). The formulated as well as the commercial tablets were circular and flat. After the dial on the tester was set to zero, a tablet was placed between the two jaws. The breaking point was determined by gradually increasing the force on the tester. Breaking strength is the force applied (in kg) to break the tablet radially into two halves.

WETTING TIME [25- 27]

The wetting time of the tablets was measured using a simple procedure. Five circular tissue papers of 10cm diameter were placed in a Petridish containing 10.0 ml 0f water containing Eosin blue. A tablet was carefully placed on the surface of tissue paper. The time required for develop blue color on the upper surface of the tablet was noted as the wetting time.

THICKNESS OF TABLETS [21- 24]

Thickness is measured by using instrument called digital "vernier calipers". Randomly 10 tablets were taken and thickness was measured for each tablet by placing between two anvils and rotating sliding knob until the tablet was tightly fitted and the reading was noted on the digital scale.

***IN- VITRO* DISPERSION TIME** [28]

In vitro dispersion time was measured by dropping a tablet in spoonful of water or in 20ml of water in a beaker. The time for the tablet to completely disintegrate into fine particles was noted. Three tablets from each batch were randomly selected and *in vitro* dispersion time was performed.

DRUG CONTENT

10 tablets were taken, powdered well and a quantity of powder equivalent to 100mg of Levocetrizine was accurately weighed and dissolved in 100ml of 0.1N HCl and filtered. The absorbance of the solution was measured at 230nm against blank (0.1N HCl). The concentration of the sample was calculated using standard graph.

TASTE AND MOUTH FEEL EVALUATION [29]

A panel of 6 volunteers was employed to assess the color, taste and mouth feeling of prepared Levocetrizine Orodispersible tablets. The human test was performed according to the guidelines of WMA Helsinki declaration [30]. The comments of the panel members were recorded.

FTIR

The FT-IR spectrums of pure drug and formulation were determined. A FT-IR (Thermo Nicolet 670 spectrometer) was used for the analysis in the frequency range between 4000 and 400 cm^{-1}, and 4 cm^{-1} resolution. The results were the means of 6 determinations. A quantity equivalent to 2 mg of pure drug was used for the study.

DSC

Thermal properties of pure drug and the formulation were evaluated by Differential scanning calorimetry (DSC) using a Diamond DSC (Mettler Star SW 8.10). The analysis was performed at a rate 50°C min-1 from 500°C to 2000°C temperature range under nitrogen flow of 25 ml min^{-1}.

ACCELERATED STABILITY STUDIES

Levocetrizine tablets were stored at 30 ± 2°C/65 ± 5% RH and 40 ± 2°C/75 ± 5% RH in a stability analysis chamber and in a refrigerator (2-8°C) for a period of 12 week[31]. At 1 month, 2 months, and 3 months interval; tablets were withdrawn for analysis of appearance, hardness, moisture content, *in-vitro* dissolution test, content of active ingredient and related substances; and results were compared with respect to preliminary result (analysis result of samples prior to stability charging) and result of respective samples kept at 2-8°C.

***IN-VITRO* DRUG RELEASE**

In vitro dissolution studies for all the formulated tablets was carried out using USP paddle method at 50 rpm in 900ml of 0.1N HCl as dissolution media, maintained at 37±0.5°C. 5 ml aliquot was withdrawn at the specified time intervals, filtered through wattmann filter paper and assayed spectrophotometrically at 230nm. An equal volume of fresh medium, which was pre-warmed at 37°C, was replaced into the dissolution media after each sampling to maintain the constant volume throughout the test. Dissolution study of conventional marketed tablet of Levocetrizine is also carried out using same method.

STATISTICAL ANALYSIS

The results were analyzed by two tailed Student's t-test using the Graph Pad Instat Software (GPIS; Version: 1.13)[20].

RESULTS AND DISCUSSION

Micromeritic Properties

Table - 2 shows the results of loose bulk density (LBD) and tapped bulk density (TBD). These parameters were used to assess the packability of the crystals. The pure drug powder was more bulky and fluffy, which was indicated by the lowest LBD value (0.27 ± 0.01 g mL–1, *n* = 3). The highest TBD value (0.98 ± 0.01 g mL–1, *n* = 3) of pure drug indicates a high intergranular space between particles. In contrast, the melt granules exhibited higher LBD (0.46 ± 0.01 to 0.59 ± 0.01 g mL–1, *n* = 3) and TBD (0. 53 ± 0.01 to 0.68 ± 0.01 g mL–1, *n* = 3) values [20]. These results indicate good packability of the prepared melt granules when compared with pure Levocetrizine. The results of Carr's index, Hausner's ratio and angle of repose of spherical crystals in comparison with pure drug are presented in Table - 2. These parameters were used to assess the flow and compressibility properties of the agglomerates. Carr's

index and Hausner's ratio of pure drug were 21.8 ± 0.01 % and 1.19 ± 0.01 (n = 3), respectively, indicating extremely poor flow properties. The powder could not pass through the funnel during the angle of repose experiment. The poor flow of Levocetrizine could be due to the irregular shape and high fineness of the powder, which posed hurdles in the uniform flow from the funnel. On the other hand, all the prepared crystals exhibited low Carr's index, Hausner's ratio and angle of repose values, indicating excellent flow properties and compressibility. The improved flowability and compressibility of granules may be due to the sphericity, regular and larger size of crystals [21-23]. Among all the prepared granules, the granules prepared with 10% Crospovidone exhibited good micromeritic properties.

Hardness

Table - 2 shows the hardness of all formulations, and the hardness was constantly maintained between 3-4 kg/cm^2 for all formulations during compression.

Friability

Table 2 shows the friability values all the formulations. The results indicated that the % friability was between 0.11 to 0.72%. The low values of friability indicate that tablets were mechanically hard enough.

Thickness

As shown in Table - 2, thickness of tablets ranged from 2mm to 3 mm.

Wetting Time

Table – 2 & Figure - 1 show the wetting time studies of all formulations. Wetting time is lesser in case of Crospovidone (10%) because of higher capillary action.

Fig - 1: Wetting time of Crospovidone (10%) at 5 (a), 25 (b) & 33 (c) Seconds.

Drug Content of Tablets

Table -2 shows the drug content of tablets ranged between 99 to 100%.

***In Vitro* Dispersion Time**

Figure – 2 shows *in vitro* dispersion time, by dropping a tablet in spoonful of water or in 20ml of water in a beaker. The time for the tablet to completely disintegrate into fine particles was noted. Three tablets from each batch were randomly selected and *in vitro* dispersion time was performed.

(c)

Figure – 2: A, B represents Invitro Dispersion time in spoonful of water and C represents invitro dispersion in 20ml of water in a beaker in 15 Seconds.

Taste and Mouth Feel Evaluation

Table – 5 shows the prepared tablets were evaluated for taste and mouths feel in 6 volunteers. The formulations with Eudragit EPO and Peppermint flavor scored various acceptability results. Among them formulation (F8) showed good acceptability.

Table – 5: Taste and Mouth Feel Evaluation

Formulation Code	Average Points by Volunteer	Acceptability
F_1	90	B
F_2	90	B
F_3	89	C
F_4	90	B
F_5	89	C
F_6	89	C
F_7	90	B
F_8	99	A
F_9	92	B

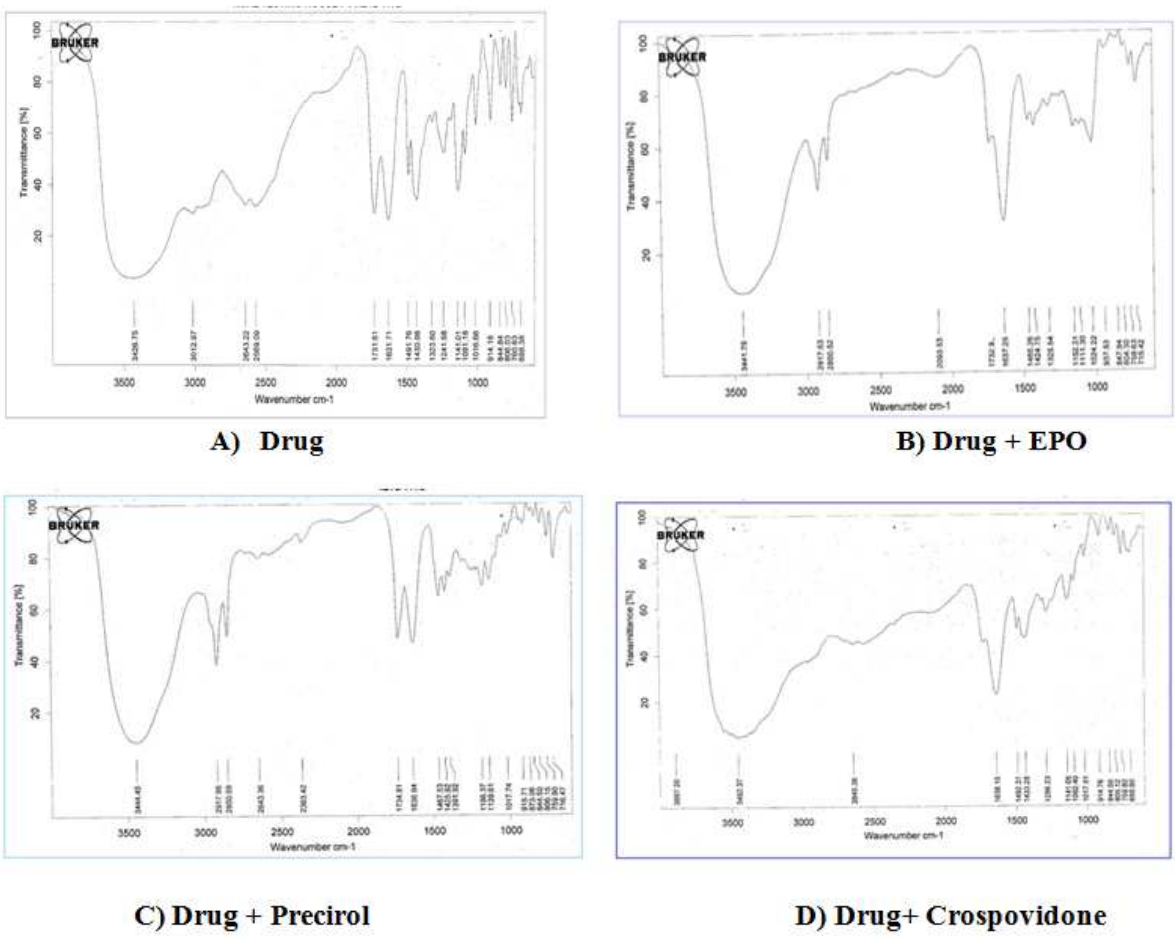
A: *Good,* ***B:*** *Average,* ***C:*** *Bitter*

Differential scanning calorimetric study (DSC)

DSC results with sharp endothermic peak for the pure Levocetrizine at 142.7^{0}C. Similar sharp endothermic peaks were observed in the formulations at almost similar temperatures. This clearly indicates that there is no drug excipient Interaction.

Fourier Transform Infrared Spectroscopy (FTIR)

The FTIR spectrum shows all the functional groups of pure drug Levocetrizine at 3289.12 cm^{-1}(N-H Streching), 2916.7 cm^{-1} (C-H Streching), 1650 cm^{-1} (the Carbonyl Group), 1458.4 cm^{-1}(ether Group). Similar spectrum peak points were observed in all the formulations. This clearly indicates that there is no drug excipient interaction.



Figs - 3: A – D Shows the FTIR Studies of Levocetrizine with Various Excipients Stability Studies

Table – 1: Formulation of Levocetrizine Tablets.

INGREDIENTS (mg)	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9
Levocetrizine Dihydrochloride	10	10	10	10	10	10	10	10	10
Eudragit EPO	5	7.5	10	15	-	-	-	7.5	-
Precirol ATO5	-	-	-	-	5	7.5	10	-	5
Crospovidone	7.5	7.5	7.5	7.5	7.5	7.5	7.5	10	10
Xylitol	71	68.5	66	61	71	68.5	66	66	68.5
Acesulfame Potasssium	5	5	5	5	5	5	5	5	5
Peppermint Flavor	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Mg.stearate	1	1	1	1	1	1	1	1	1
Total Weight	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**

**Each value represents mean ±S.D (n=3).*

Table - 3: Appearance, % Drug Content and Disintegration time of F_8.

Time in Days	Formulation F_8					
	Appearence		Disintegration Time		% Drug Content	
	40^0C/75% R.H	Room Temperature	40^0C/75% R.H	Room Temperature	40^0C/75% R.H	Room Temperature
0	White	White	20	20	99.89	99.89
30	White	White	21	20	99.87	99.89
60	White	White	20	21	99.99	99.99
90	White	White	21	21	99.99	99.89

Table - 4: Results - In vitro Dissolution Profile for Batch F_8

Time in minutes	% Drug Release			
	Initial	30 days	60 days	90 days
5	68.23	69.96	71.65	75.96
10	81.20	80.66	84.66	85.35
15	98.07	99.54	99.79	99.95
30	99.14	100.33	100.69	100.89

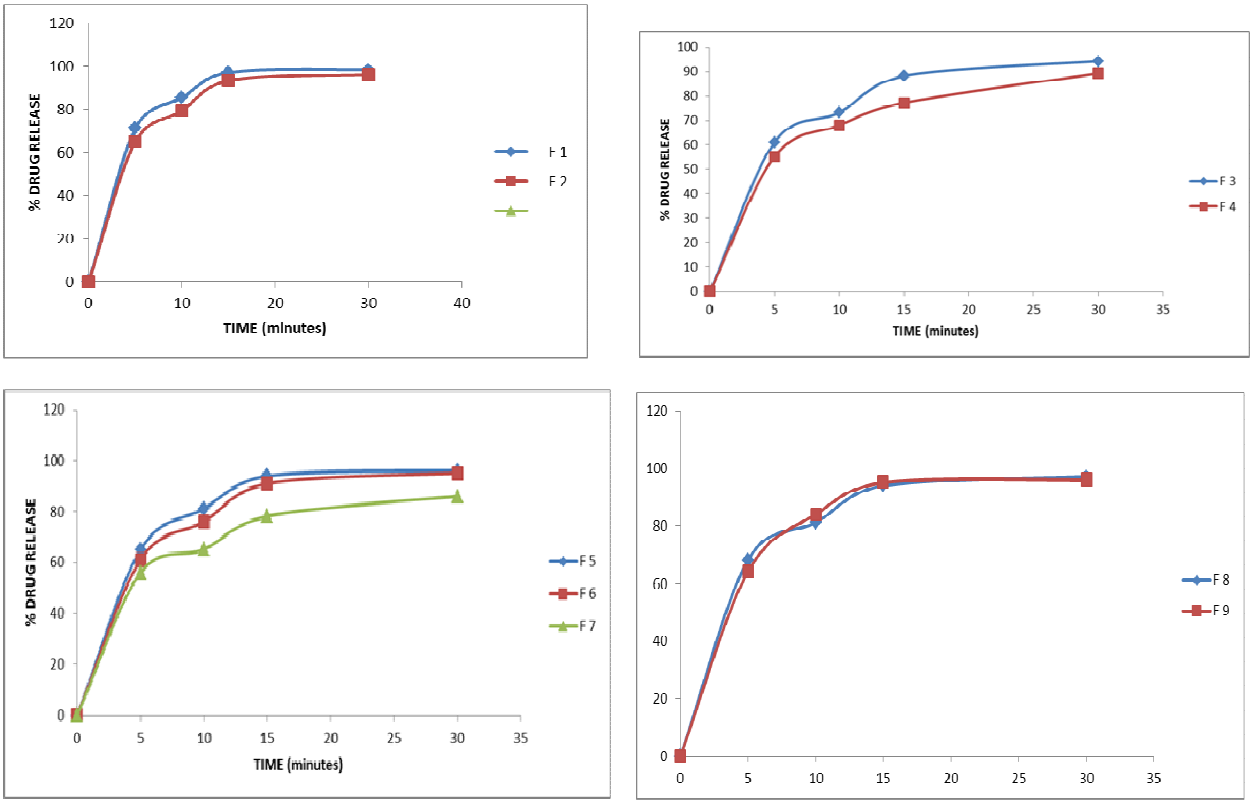


Figure - 4: Cumulative %Drug release vs Time profiles of Levocetrizine ODT

Disintegration Time

Table -1 show the disintegration time of the formulations. As the percentage of superdisintegrant increased (7.5% to 10%) the disintegration time decreased significantly ($p<0.05$). It is because Crospovidone (10%) containing tablets

rapidly exhibits high capillary activity and pronounced hydration with a little tendency to gel formation and disintegration the tablets rapidly.

The stabilized tablets are checked for their appearance, Drug Content and Disintegration Time parameters. Initially the tablets of all nine batches were white in color. The optimized tablets were subjected to disintegration time test to check for any changes in their disintegration times. The USP Disintegration Test Apparatus was used to carry out this test. The stability test was carried out on the optimized formulations only, which are those with the best evaluation parameters. Of the nine batches formulated F_8 had the least disintegration time and hence was selected to be subjected to stability studies. The stability studies are conducted on those formulations which stand out from the other formulations in their evaluation parameters and are promising for their efficacy. Drug Content can be done to check for the drug uniformity after the stability studies have been carried out. The Percentage drug release profile is carried out as a measure of check for stability.

Table – 2: Pre – Compressional & Post – Compressional Parameters, Disintegration times, Wetting time, Drug Content & Dissolution time of different Tablet formulations.

Parameters	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9
Loose Bulk Density (g mL^{-1})	0.46 ± 0.01	0.46 ± 0.01	0.46 ± 0.02	0.59 ± 0.01	0.48 ± 0.01	0.50 ± 0.01	0.49 ± 0.01	0.47± 0.01	0.46 ± 0.01
Tapped Bulk Density (g mL^{-1})	0.59 ± 0.02	0.56 ± 0.01	0.55 ± 0.01	0.68 ± 0.01	0.63 ± 0.01	0.58 ± 0.01	0.56 ± 0.01	0.54 ± 0.01	0.53 ± 0.01
Carr's Index (%)	21.8 ± 0.01	21.39 ± 0.01	16.36 ± 0.01	13.04 ± 0.01	24.5 ± 0.02	13.79 ± 0.01	12.50 ±0.02	12.96 ± 0.01	13.20 ± 0.01
Hausner's Ratio	1.25 ± 0.01	1.19 ± 0.02	1.19 ± 0.01	1.15 ± 0.02	1.25 ± 0.01	1.16 ± 0.02	1.14 ± 0.01	1.15 ± 0.01	1.15 ± 0.01
Angle of Repose (θ)	26.06 ± 0.01	25.42 ± 0.01	22.62 ± 0.01	19.19 ± 0.02	23.72 ± 0.01	24.02 ± 0.02	23.51 ±	22.68 ± 0.02	21.82 ± 0.02
Weight Variation* (mg)	102± 1.5	101± 1.8	102.3± 1.6	102± 1.8	101.1± 1.1	101.2± 1.6	102.2± 1.5	102.2± 1.5	102.1± 1.8
Friability (%)	0.12 ± 0.01	0.23 ± 0.02	0.54 ± 0.01	0.72 ± 0.03	0.18 ± 0.02	0.11 ± 0.01	0.18 ± 0.01	0.31 ± 0.01	0.52 ± 0.01
Hardness* (Kg/cm^2)	3.0 ± 0.5	3.1 ± 0.5	3.2 ± 0.5	3.2 ± 0.5	3.1 ± 0.5	3.0 ± 0.5	3.0 ± 0.5	3.1 ± 0.5	3.0 ± 0.5
Thickness (mm)	0.92 ± 0.03	0.91 ± 0.03	0.93 ± 0.09	0.94 ± 0.05	0.92 ± 0.02	0.95 ± 0.09	0.96 ± 0.09	0.93 ± 0.05	0.95 ± 0.03
Disintegration time*(Sec)	35 ± 0.1	30 ± 0.1	30 ± 0.1	35 ± 0.1	35 ± 0.1	40 ± 0.1	40 ± 0.1	20 ± 0.1	26 ± 0.1
Wetting time* (sec)	5.47 ± 1.6	9.56 ± 2.8	14.24 ± 2.2	16.61 ± 1.9	17.29 ± 2.5	13.25 ± 3.2	15.12 ± 1.7	7.15 ± 1.0	6.23 ± 1.5
Drug Content (%)	99.32 ± 0.01	99.32 ± 0.01	99.32 ± 0.01	99.32 ± 0.01	99.32 ± 0.01	99.32 ± 0.01	99.32 ± 0.01	99.32 ± 0.01	99.32 ± 0.01
	Time (Min)				**% Cumulative Drug Release**				
5	71.15 ± 0.01	65.04 ± 0.02	61.06 ± 0.01	55.22 ± 0.01	65.04 ± 0.01	61.06 ± 0.01	56.01 ± 0.01	68.23 ± 0.01	64.24 ± 0.01
10	85.21 ± 0.03	79.04 ± 0.01	73.15 ± 0.02	68.04 ± 0.03	81.16 ± 0.01	76.07 ± 0.01	65.13 ± 0.02	91.20 ± 0.01	84.07 ± 0.03
15	97.04 ± 0.02	9.25 ± 0.03	88.15 ± 0.01	77.20 ± 0.01	94.07 ± 0.02	91.10 ± 0.01	78.23 ± 0.01	99.39 ± 0.01	95.17 ± 0.02
30	98.23 ± 0.01	96.07 ± 0.01	94.15 ± 0.03	89.25 ± 0.01	96.07 ± 0.01	95.25 ± 0.01	86.08 ± 0.01	99.89 ± 0.01	96.09 ± 0.01

**Each value represents mean ± S.D (n=3).*
LBD – Loose bulk density, TBD – Tapped bulk density.
a Mean ± SEM, n = 3.
b Significantly different compared to pure Levocetrizine (p < 0.05).

DISCUSSION

Levocetrizine Orally dispersible tablets were developed with an aim to improve the patient's compliance. The formulations were developed with an objective to use by the pediatric and geriatric patients. The Levocetrizine ODT formulations were developed with Crospovidone as superdisintegrant 10% Concentration.

CONCLUSION

Oral disintegrating tablets of Levocetrizine were successfully prepared using Melt Granulation Technology. The present investigations were helped in understanding the effect of formulation process variables especially the concentration of super disintegrant on the dispersion time and drug release profile. The present study concluded that 10% Crospovidone is effective as super-distegrant for the preparation of Levocetrizine Orodispersible tablets. Taste masking and rapid disintegration of tablets formulated in this investigation may possibly help in administration of

Levocetrizine in a more palatable form without water. Thus, the "patient-friendly dosage form" of bitter drug Levocetrizine, especially for pediatric, geriatric, bedridden, and non-cooperative patients. By the availability of various technologies and manifold advantages of Orodispersible Tablets will surely enhance the patience compliance, low dosing and rapid onset of action, increased bioavailability, low side effects, and good stability.

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