FORMULATION DEVELOPMENT AND CHARACTERIZATION OF EFFERVESCENT TABLETS ALONG WITH LEVOCETIRIZINE DIHYDROCHLORIDE

SEMIMUL AKHTAR[1]*, SOEB HUSSAIN[1], SUDIP KUMAR MANDAL[2]

[1]Department of Pharmaceutics, Shri Ram Murti Smarak College of Engineering and Technology (Pharmacy), Bareilly, Uttar Pradesh, India.
[2]Department of Phrmaceutical Chemistry, Dr. B C Roy College of Pharmacy and Allied Health Sciences, Dr. Meghnad Saha Sarani, Durgapur, West Bengal, India. Email: akhtar.mpharm@gmail.com

ABSTRACT

Objective: Levocetirizine dihydrochloride is also known as "Xyzol." Levocetirizine dihydrochloride is a second-generation piperazine derivative, potent H1 selective agent. Levocetirizine dihydrochloride is the active R (-) enantiomer of cetirizine dihydrochloride. In the case of an allergic or histaminic reaction, the medication must respond rapidly. Many older patients, infants, and dysphagia patients have trouble swallowing traditional tablets or capsules. Hence, a need exists for a relatively fast-acting effervescent tablet form.

Methods: The tablets were prepared by direct compression method using citric acid and sodium bicarbonate as effervescent agents. Then, they were tested for parameters of pre- and post-compression. Tablets were evaluated for studies of general appearance, uniformity of substance, hardness, friability, and *in vitro* dissolution.

Results: More than 90% of the drug was released from almost all the formulations within 1 min. More formulations underwent rapid 90-day stability trials.

Conclusion: No major changes in the taste, disintegration, and dissolution profiles were found in tablets.

Keywords: Levocetirizine dihydrochloride, Effervescent tablet, Direct compression method, citric acid, Sodium bicarbonate.

INTRODUCTION

Various first-generation antihistamine drugs can be used in the treatment of allergy but not used because they cause sedation although initial second-generation drugs-like terfenadine and astemizole were found effective in allergic rhinitis and idiopathic urticaria without any sedation but had cardiac associated interactions. Other second-generation medications such as loratadine and cetirizine show efficacious in the treatment of allergic rhinitis and chronic idiopathic urticaria [1]. Levocetirizine dihydrochloride is a drug that comes under the category of second-generation antihistamine, and it an enantiomer levorotatory (-) form of cetirizine which is pharmacologically active and most selectively inhibit H_1 histamine receptor [2]. Chemically levocetirizine dihydrochloride is (R)-[2-[4-[(4-chlorophenyl) phenylmethyl)-1-piperazinyl] ethoxy] acetic acid dihydrochloride. It is having the same pharmacological activity as cetirizine but produces less sedation as compared to cetirizine and thus more preferred nowadays [3]. Interestingly, levocetirizine has many other pharmacological consequences, partly linked to its H-1 antagonism. T lymphocytes, dendritic cells, and lung macrophages express the H-1 histamine receptor on their cell surface that induces activation molecules and cytokine and chemokine synthesis with proinflammatory effects when enabled [4]. It shows inhibitory action on keratinocytes, and also blocks the secretion of chemocytokine and granulocyte-macrophage colony-stimulating factor [5]. It is administered orally and achieves peak plasma concentration after 0.9 h of administration. On single and repeated 5 mg/day indicates the peak concentrations typically 270 ng/mL and 308 ng/mL, respectively, when levocetirizine dihydrochloride in the form of solution orally administered to an adult, the mean peak plasma concentration achieved in 0.5 h after administration. Protein binding *in-vivo* is about 91–92%. About <14% of levocetirizine dihydrochloride metabolized in the body by different metabolic reactions. In healthy adult, plasma half-life is 8–9 h of levocetirizine dihydrochloride after administration in the form of oral tablet and oral solution. Adverse effects include fatigue, dry mouth, somnolence, pharyngitis, cough, and pyrexia. On overdose sigh and symptoms include drowsiness, agitation, and restlessness, so symptomatic treatment can be done, no antidote therapy is available for the overdose of levocetirizine dihydrochloride [6].

The oral route of drug administration is the most important and convenient method of administering the drug. Probably at least 90% of all the drugs used to produce the systemic effects are administered by the oral route. When a new drug is discovered, the pharmaceutical company makes every effort to ensure that the drug can be so formulated that it is capable of being administered orally. However, most elderly patients, children, and patients with dysphagia have difficulty in swallowing conventional tablets and hard gelatin capsules, and therefore do not take medication as prescribed by physicians. It is estimated that 35% of the general population, 30–40% of elderly nursing home patients, and 25–50% of patients hospitalized for acute neuromuscular disorders and head injuries have dysphagia [7]. Hence, the efforts are being made by the researchers in the field of novel drug delivery systems to overcome these above problems and enhance the efficacy, safety, and stability of the drug molecule and also improved patient compliance [8]. Effervescence is defined as the evolution of bubbles of gas from a liquid as the result of a chemical reaction. Effervescent mixtures have been known for many years and are used medicinally. Effervescent powders utilized as saline cathartics were available in the 18th century and were then listed in the official compendium as compound effervescent powders. These were more commonly known commercially as "Seidlitz Powders." When tableting equipment was developed, these granular materials began to be compressed into tablets that offer some advantages over the powdered dosage forms. Effervescent tablets are effective, simple to use, and premeditated ways of dosage. The powdered preparations cannot leak out as they can.

These can be individually packed to prevent moisture and thereby avoid the issue of product instability during storage of the unused products. Throughout the years, a large range of effervescent tablets has been developed. These include formulations containing antioxidants, contact lens cleaners, washing powder formulations, beverage sweetening pills, chewable dentifrices, denture cleaners, surgical instrument sterilizers, analgesics, effervescent candy, and other prescription medication preparations such as antibiotics, ergotamine, digoxin, methadone, and L-dopa. Preparations have also been established for veterinary use. Effervescent tablets are not meant to be ingested or used without prior dissolution, usually in water, which leads to rapid absorption and onset of action [9]. The overall use of the tablet solution plays a major role in product formulation, especially in choosing the raw materials to be used. Some substances have useful properties in tablet formulation, the solutions of which are not ingestible while at the same time possessing additional properties which make them useless if the solution is to be ingested (i.e., boric acid as a tablet lubricant, sodium bisulfite as an acid source, or sodium bicarbonate as a source of carbon dioxide in a sodium-free potassium supplement) [10]. Effervescent tablet having certain advantages on other types of tablets, which includes having pleasant taste due to which improved patients acceptance, a large amount of drug can be administered, ease of use, accurate dosing, also having good stomach and intestinal tolerance. An effervescent tablet can easily administer to the child, adults, and older age patients [11].

The objective of this study was that to increase the efficacy, safety, and stability of dosage form, and to overcome the problems with the conventional solid dosage form means tablet. In this study, the effervescent tablet of levocetirizine dihydrochloride had been developed and evaluated before compression (and after the compression). In this technique had been used direct compression of evaluated granules. Effervescent tablets of levocetirizine dihydrochloride are not available [12].

MATERIALS AND METHODS

Methods

Preformulation studies

The objectives of preformulation studies are to select the correct form of the drug substance, assess its physical and chemical properties, and generate a thorough understanding of the stability of the material under the conditions that will lead to the development of a particular Data Distribution Service.

The goals of the preformulation study are:
- To determine the physicochemical characteristics required for a new drug product
- To assess the rate of its kinetic release
- To assess compatibility with different excipients.

Preformulation studies on the drug sample obtained, therefore, cover color, taste, solubility analysis, melting point determination, and compatibility studies [13].

Identification of levocetirizine dihydrochloride

1. Melting point determination: Melting point of levocetirizine dihydrochloride was set to determine by open cup capillary method
2. Infrared absorption spectrum: The infrared absorption spectrum of levocetirizine dihydrochloride was recorded with a KBr disc.

Preparation of standard calibration curve of levocetirizine dihydrochloride in 0.1 N hydrochloric acid (HCl).

Procedure

One gram of sodium bicarbonate was accurately weigh and transferred it into 100 ml amber colored volumetric flask and dissolved in a small quantity of 0.1 N HCl. To this, a solution 100 mg of levocetirizine dihydrochloride dissolved in approximately 2–5 ml of water was added. To get a concentration, the volume was composed with the 0.1 N HCl of 1000 µg/ml (standard stock -I [SS-I]).

From this, 1 ml was separated and diluted to 100 ml to obtain a concentration of 10 µg/ml (SS-II). From SS-II aliquots of 2 ml, 4 ml, 6 ml, 8 ml, and 10 ml were pipette out into 10 ml volumetric flasks. The volume was made up with 0.1 N HCl to get the final concentration of 2, 4, 6, 8, and 10 µg/ml, respectively. When scanning the solution in the ultraviolet (UV) range, that is, from 200 nm to 800 nm λ_{max} was found to be 230 nm for levocetirizine dihydrochloride in 0.1N HCl as a blank in UV-visible spectrophotometer (UV-1800 Shimadzu). The absorbance of each concentration was measured at 230 nm.

The same solution was stored at room temperature and absorbances of the solutions were measured at 230 nm using a UV-visible spectrophotometer after every ½ h.

Beer's range: 2–100 µg/ml.

Formulation of effervescent tablets of levocetirizine dihydrochloride

Levocetirizine dihydrochloride effervescent tablets were prepared using direct compression method:

All ingredients were individually passed and retrieved through 60 # mesh sieve. The drug was weighed along with the other excipients and was mixed in geometrical order. Sodium bicarbonate and citric acid were pre-heated at a temperature of 80°C for 2 h to remove absorbed/residual moisture and thoroughly mixed in a mortar to get a uniform powder, then transferred to the blend above. Magnesium stearate and Aerosil were added at last and this mixture was shaken for few minutes to ensure proper mixing of all the ingredients. The blend thus obtained was directly compressed into tablets of 200 mg weight on a 10-station rotary tablet machine (Clit, Ahmadabad) using 7 mm round flat punches.

Evaluation of effervescent tablets

Pre-compression parameters

The mixture of powder and granules was evaluated before compression and parameters include the angle of repose for flow property, bulk density, Carr's compressibility index, and Hausner's ratio.

Angle of repose (θ)

The angle of rest is known as the maximum possible angle between the surface of a powder pile and the horizontal plane [14]:
Tan^{-1} (h/r)
Where, angle of repose,
h = height of the pile.
r = radius of the base of the pile.

Bulk density

The bulk density is defined as a powder mass divided by the volume of the bulk. The bulk density of a powder depends primarily on the distribution of particle size, the particle form, and the propensity of the particles to conform to each other and the particle packaging and changes as the powder consolidates. Tap density tester was used to assess both loose bulk density (LBD) and tapped bulk density (TBD). LBD and TBD were calculated using the following formula [15,16]:

Bulk density = Weight of the powder/tapped volume of powder

Carr's compressibility index

Carr's compressibility index determined the compressibility value for the granules. The formula for Carr's index is as follows [17]:
Compressibility index (%) = [(TD-BD) × 100]/TD
Where TD = tapped density, and
BD = Bulk density.

Hausner's ratio

It is used to determine the flow property and is also a type of index. It can determine by the following formula:
Hausner's ratio tapped density/bulk density

Evaluation of tablets

After the direct compression of evaluated granules, the tablets are subjected for evaluation that is shape and color, uniformity of thickness, hardness test, and friability test.

Shape and color

The tablets were analyzed under a lens by holding the tablets in light for tablet form and color.

Uniformity of thickness

The individual tablet's crown thickness can be determined with a Vernier Caliper, which allows precise measurements and provides details on the difference between tablets. Many techniques used in production control involves positioning 5 or 10 tablets in a holding tray, where a sliding caliper scale may be used to measure their total crown thickness. The thickness of the tablet was measured using Vernier Caliper [18].

Hardness test

Tablets need to have a certain amount of strength, or hardness and friability protection, to withstand mechanical handling shocks in manufacturing, packaging, and shipping. The tablet's hardness has been determined using a Monsanto Hardness tester. It is expressed in kg/cm^2. Three tablets were chosen randomly from each formulation, calculating the mean and standard deviation values [19,20].

Weight variation test

From each formulation, the tablets were picked at random and weighed individually to test for weight variability. The U.S Pharmacopoeia makes a small variance of a tablet's weight [21]. The percentage deviation in weight variation is shown in Table 5.

The tablet weight was more than 130 mg and <324 mg in all formulations and therefore a maximum difference of 7.5% was allowed.

Friability test

This is the phenomenon where tablet surfaces are weakened and/or when exposed to mechanical shock or fatigue, show signs of lamination or breakage. Using Roche Friabilator, the friability of the tablets was calculated. It is expressed in percentage (%). Initially, ten tablets were weighed [W (initial)] and put into a friabilator. The friabilator was operated at 25 rpm for 4 min or run up to 100 revolutions. The tablets were weighed again [W (final)]. The percentage friability was then calculated by,

Drug content uniformity

The uniformity examination of content is used to confirm that each tablet contains the amount of drug substance intended for a batch, with little difference between tablets. The content uniformity analysis has been included in the monographs of both coated and uncoated tablets designed for oral administration due to a better understanding of clinical availability where the range of size of the dosage type available involves 50 mg or smaller sizes. Representative samples of 30 tablets are chosen for content uniformity evaluation, and 10 are randomly tested. At least 9 must be evaluated below ±15% of the stated power, but none should cross ±25% [22,23].

The amount of active ingredient(s) is estimated by the process mentioned in the assay and it estimates the amount of active ingredient since the active ingredient of the present investigation is not official in any pharmacopeia the following method was used for the determination of drug content [24].

Twenty tablets were weighed and powdered. The blend equivalent to 20 mg of pantoprazole sodium was weighed and dissolved in a sufficient quantity of 0.1N HCl. The solution was filtered through Whatman filter

Table 1: Formulation of effervescent tablets of levocetirizine dihydrochloride

S. No.	Ingredients	Quantity used in mg					
		F1	F2	F3	F4	F5	F6
1.	Levocetirizine	5	5	5	5	5	5
2.	Sorbitol	30	30	30	30	30	30
3.	Sodium bicarbonate	20	50	50	30	50	60
4.	Citric acid	60	50	30	50	50	20
5.	Mannitol	47	32	32	32	27	47
6.	Crospovidone	12	10	8	6	14	10
7.	CCS	8	10	12	14	6	10
8.	Aspartame	15	10	10	10	15	15
9.	Aerosil	1	1	1	1	1	1
10.	Magnesium stearate	2	2	2	2	2	2

Table 2: Flow properties of the powder according to their angle of repose

Angle of repose (θ) (degrees)	Flow
<25	Excellent
25=30	Good
30–40	Passable
>40	Very poor

Table 3: Flow properties of the powder, according to Carr's index

Consolidation index (Carr's %)	Flow
5–15	Excellent
12–16	Good
18–21	Fair to passable
23–35	Poor
33–38	Very poor
>40	Very very poor

Table 4: Flow properties of powders, according to Hausner's ratio

HR	Flow
<1.2	Free-flowing powder
>1.6	Less free-flowing

Table 5: Percentage deviation in weight variation

Average weight of a tablet	Percentage deviation
<130 mg	10
130–323 mg	7.5
324 mg and above	5

paper (No.41), suitably diluted with 0.1N HCl and assayed at 230 nm, using a UV-visible double beam spectrophotometer (UV-1800 Shimadzu).

In-vitro disintegration time

A tablet's process of breaking up into smaller particles is called as disintegration. A tablet's *in vitro* disintegration period was calculated using a standardized disintegration test which was used only for rapid disintegration agents [25].

Methods

The disintegration took place in a beaker which included a 200 ml medium. The medium consisted of water at a temperature between 15 and 25°C. Just one tablet was tested at a time and was deemed disintegrated when fragments were obtained fully dispersed [26,27].

In vitro dissolution studies

In vitro release studies were carried out using a USP XXIII type-II dissolution test apparatus.

Two aims in the design of *in vitro* dissolution tests are to demonstrate that,
1. The release of the drug from the tablet is up to 100% as near as possible
2. The rate of release of drugs is standardized from batch to batch, which is the same as the rate of release shown to be bioavailable which clinically efficient [28].

Methods

The normal USP XXIII type-II dissolution apparatus was used employing a paddle stirrer at 50 rpm. As a dissolution medium, 900 ml of the pH 6.8 phosphate buffer was used. The temperature of the dissolution medium was maintained at 37±0.5°C throughout the experiment. One tablet was used in each test. Samples of dissolution medium (5 ml) were withdrawn using a syringe fitted with pre-filter at known intervals of time and analyzed for drug release by measuring the absorbance at 230 nm. The volume withdrawn was filled with a fresh volume of dissolution medium at each interval of time. Cumulative percent of levocetirizine released was calculated and plotted against time [29,30].

Stability studies

A drug's stability was characterized as the potential of a particular formulation to remain within its physical, chemical, therapeutic, and toxicological specifications in a particular container. Stability studies were conducted as per the specified ICH guidelines, the selected best formulation. The goal of the stability testing was to provide evidence as to how the nature of a drug material or drug product changes with time under the influence of various environmental factors, such as temperature, humidity, and sunlight, enable appropriate storage standards, re-test duration, and shelf life to be determined.

In the present study, the effervescent tablets were packed in suitable packaging material and stored under the following conditions for a period of 90 days at 40±2°C and RH 75±5%.

The tablets were withdrawn and analyzed for physical characterization (visual defects, hardness, friability, disintegration, dissolution, etc.) and drug content [31].

RESULTS AND DISCUSSION

The present study was aimed at formulating effervescent tablets of levocetirizine dihydrochloride. This is a novel approach to improving patient compliance with a rapid onset of action as opposed to traditional formulations that are currently primarily used.

Identification of levocetirizine dihydrochloride

Melting point

The melting point of levocetirizine dihydrochloride sample was found to be 218.5°C.

Fourier-transform infrared (FTIR) studies

FTIR is one of the most widely used methods for checking the compatibility between substances and for the identification of the drug. Levocetirizine dihydrochloride, excipients, and the selected formulations were analyzed using an infrared spectrophotometer (Shimadzu FTIR 8-400, S model).

All of the samples were screened using the KBr disk method at a resolution of 4 cm^{-1} over the wavenumber range of 4000–400 cm^{-1}. These KBr disks are developed in a ratio of 1:100, respectively, using drug and KBr. Then, this mixture was mixed well in mortar for 3–5 min. A very small amount of this mixture was uniformly spread and sandwich between the pellets and pressed using KBr pellet press at a pressure of 20,000 psi for 1 min. Then, the pressure was released and the pellet was inserted into the pellet holder and scanned in the IR zone.

The drug sample FTIR spectroscopy had shown the identical peak characteristics as that of the levocetirizine dihydrochloride standard which verified that our drug sample was levocetirizine dihydrochloride.

Solubility of drug

Levocetirizine dihydrochloride solubility was calculated in various solvents that were listed in the Table 8 as follows.

Levocetirizine dihydrochloride was freely soluble in water, soluble in ethanol, methanol, and HCl and insoluble in methylene chloride and acetone.

Standard calibration curve

Preparation of calibration curve of levocetirizine dihydrochloride

Evaluation

Pre-compression parameters

The results of angle repose, bulk density, tapped density, and compressibility index evaluation for different blends of formulations shown in Table 10.

The results of the evaluation of pre-compression parameters showed that varies from compressibility index 8.72±0.53% to 15.65±0.53% and angle of repose varies from 16.36±0.59° to 20.33±0.71°. Thus, all formulation blends comprised excellent flow as well as very good compressibility profile which are a prime requisite for direct compression.

Post-compression parameters

Physical appearance

Uncoated white-colored tablets are round, flat, and plain in appearance.

Table 6: The acceptable limit of friability, according to Indian Pharmacopoeia

Percent friability	Acceptable limit
<1	Acceptable
>1	Not acceptable

Table 7: Characteristic peak with their functional group

Peak	Theoretical (cm^{-1})	Standard (cm^{-1})	Drug sample (cm^{-1})
-Cl	740–880	758, 804, 847	758.05, 808.20, 844.85
-C-N	1350–1390	1362	1356
-COOH	1730–1700	1742	1742.05
-C-O	1120–1170	1134	1136.11

Table 8: Solubility of levocetirizine dihydrochloride in different solvent systems

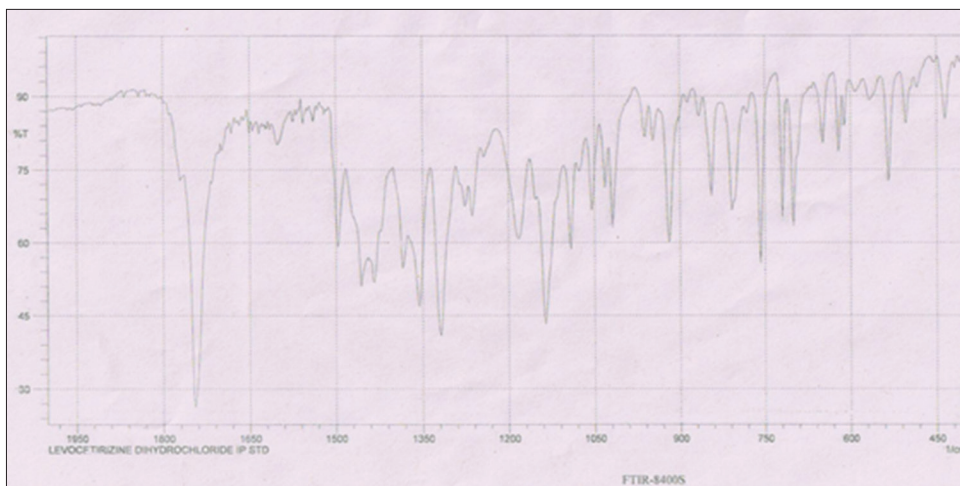| S. No.	Solvents	Quantity of solvent (ml) used to solubilize 1 g drug	Solubility parameter
1.	Distilled water	8	Freely soluble
2.	Methanol	17	Soluble
3.	Ethanol	26	Soluble
4.	Hydrochloric acid	21	Soluble
5.	Acetone	>10000	Practically insoluble
6.	Methylene chloride	>10000	Practically insoluble

Fig. 1: Fourier-transform infrared spectra of levocetirizine dihydrochloride
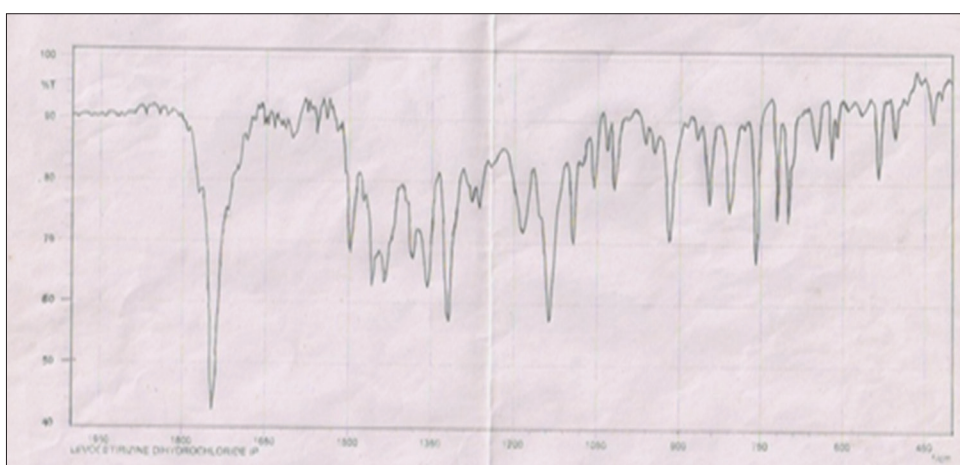

Fig. 2: Fourier-transform infrared spectra of dug sample (levocetirizine dihydrochloride)
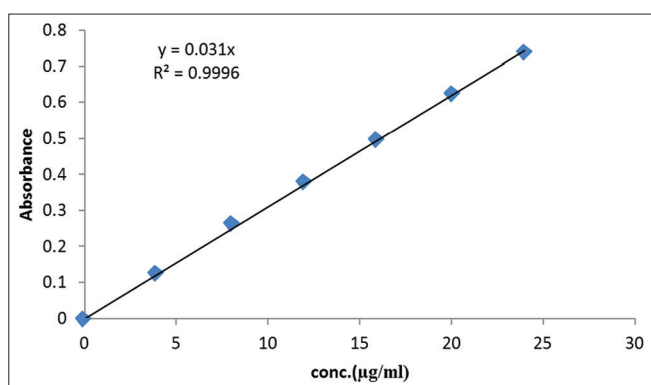

Fig. 3: Calibration curve of levocetirizine dihydrochloride in phosphate buffer (pH6.8)

Table 9: Concentration and absorbance of levocetirizine dihydrochloride in the phosphate buffer (pH 6.8)

S. No.	Concentration (µg/ml)	Absorbance
1.	0	0
2.	4	0.121
3.	8	0.258
4.	12	0.375
5.	16	0.490
6.	20	0.623
7.	24	0.742

The hardness for all the formulation was varied from 2.5±0.35 to 3.3±0.28 kg/cm^2. Overall there was no significant change in this parameter which indicates that blending was uniform.

The disintegration time was significantly improved with an increase in concentration in super disintegrants, which ultimately affect the dissolution of the drug.

Stability studies for optimized formulation

Accelerated stability studies are carried out on the optimized batch (F6). The batch was evaluated at the intervals of 1 month and 3 months, respectively, at 40±2°C and 75±5%RH. The formulation F6 (tablets) was subjected for the evaluation of physical parameters such as description, thickness, diameter, average weight, weight uniformity, hardness, friability, taste, drug content, disintegration time, and *in-vitro* drug release.

Values are means±SEM, for **n=3, ***n=6 and ****= values in range
The prepared tablets from all six formulations were subjected–post-compression parameter, that is, thickness, diameter, average weight, uniformity of weight, and drug content. All the post-compression parameters of all the formulations were compared with the compendial specification for effervescent tablets. The results are shown in Table 11.

The post-compression test results of various tablet formulations indicated that the thickness for all the formulation ranged from 3.03±0.119 to 3.12±0.32 mm and from 8.00±0.010 to 8.06±0.041 mm in diameter.

Table 10: Results of pre-compression evaluation of formulation blend

Formulation	Bulk density (g/cm³)	Tapped density (g/cm³)	Compressibility index (%)	Angle of repose (θ)
F1	0.959±0.010	1.143±0.057	15.65±0.53	20.33±0.71
F2	0.951±0.051	1.096±0.045	13.30±0.48	19.03±0.31
F3	0.944±0.053	1.076±0.015	12.29±0.44	17.5±0.25
F4	0.936±0.057	1.053±0.057	11.16±0.46	16.77±0.15
F5	0.930±0.056	1.033±0.058	9.66±0.85	16.63±0.16
F6	0.932±0.058	1.037±0.055	10.25±0.47	16.36±0.59

*Values are means±SEM, n=3

Table 11: Results of post-compression evaluation of effervescent tablets

Formulation	Thickness (mm) ***	Diameter (mm) ***	Average weight (mg)	Uniformity of weight (%) ****	Hardness (kg/cm²) ***	Friability (%) **	Drug content (%) ****	DT (s) **
F1	3.08±0.031	8.02±0.836	200.60	−4.4–+2.6	2.5±0.35	0.72±0.025	98.23–99.62	22.00±4.39
F2	3.09±0.054	8.04±0.418	206.50	−3.2–+1.4	2.7±0.23	0.60±0.021	97.76–102.13	21.50±3.10
F3	3.05±0.010	8.06±0.041	198.25	−3.6–+2.2	3.1±0.41	0.45±0.015	99.33–99.13	20.00±5.09
F4	3.03±0.119	8.04±0.014	199.02	−1.8–+1.1	3.2±0.27	0.35±0.025	95.56–98.16	18.00±4.96
F5	3.12±0.327	8.00 ±0.010	201.45	−2.5–+1.5	3.3±0.28	0.33±0.02	99.16–102.29	22.75±2.98
F6	3.08±0.277	8.04±0.089	200.67	−2.1–+1.3	3.1±0.22	0.35±0.03	98.81–100.60	18.00±4.61

Table 12: Results of *in-vitro* drug release study of effervescent tablet formulations

Time (min)	Cumulative percent drug released					
	F1	F2	F3	F4	F5	F6
2	11.39±1.66	10.63±2.24	12.72±3.25	13.99±1.95	13.84±1.41	14.36±2.32
5	40.83±2.52	43.39±2.30	46.27±4.27	50.51±1.32	54.68±0.74	59.84±1.52
10	73.35±3.09	78.72±2.16	79.57±2.52	85.33±1.01	91.57±0.59	91.86±1.20

*Values are means±SEM, n=3

Table 13: Accelerated stability testing of optimized formulation (F6) at the storage condition, that is, 40°C±2°C/75±5%RH

Parameters	Time in month		
	0 (Initial)	1 month	3 month
Shape	Round	Round	Round
Color	White	White	White
Thickness (mm) **	3.04±0.207	3.01±0.008	3.12±0.16
Diameter (mm) **	8.04±0.089	8.08±0.047	8.06±0.025
Hardness (kg/cm²) **	3.0±0.35	2.9±0.50	2.7±0.47
Average weight (mg)	198.02	199.33	199.51
Uniformity of weight	−2.32–1.72%	−1.25–3.82%	−1.9–2.4%
Friability (%) *	0.37±0.03	0.46±0.058	0.57±0.083
Drug content ##	98.43–100.67%	94.64–99.81%	92.05–96.32%
Disintegration time (s)	18.00±12.58	20.18±4.84	21.13±3.46

*Values are means±SEM, for *n=3, **n=6 and ## = values in range

Table 14: Results of *in-vitro* cumulative drug release of optimized formulation (F6) at the storage condition i.e. 40°C±2°C/75±5%RH

Time (min)	Cumulative % drug release		
	0 month	1 month	3 month
2	13.84±1.41	11.81±2.36	9.63±2.75
5	54.68±0.74	47.28±2.91	44.96±3.61
10	91.57±0.59	88.4±1.46	85.49±1.69

There had been no major change in physical parameters, product quality, and the levocetirizine dihydrochloride effervescent tablet formulation (F6) cumulative product release profile stored at 40±2°C/75±5 percent RH when compared from the same formulation before storage.

CONCLUSION

In the present work, an attempt was made to prepare an effervescent tablet of levocetirizine dihydrochloride. Effervescent tablets have an advantage over conventional tablets in elderly, pediatric and patients with dysphagia.

The parameters of pre- and post-compression of all formulations were evaluated. The effect of formulation variables such as different classes of super disintegrants in varying ratios on various pre- and post-parameters was evaluated using parameters such as disintegration time, uniformity of weight, content uniformity, friability, hardness, thickness, and stability studies.

ACKNOWLEDGMENT

AUTHORS' CONTRIBUTIONS

The authors announce together declares that all have contributed toward this research work. All the studies conducted by all the authors together.

CONFLICTS OF INTEREST

The authors announce that there are no conflicting interests concerning this work and its publication.

SOURCE OF FINDING

Nil.

REFERENCES

1. Dhiman S, Verma S. Optimization of melt-in-mouth tablets of levocetirizine dihydrochloride using response surface methodology. Int J Pharm Pharm Sci 2012;4:176-84.
2. Tripathi KD. Essentials of Medical Pharmacology. 8th ed. New Delhi: Jaypee Brothers Medical Publishers; 2018.
3. Beale JM, Block J. Wilson and Gisvold's Text Book of Organic Medicinal and Pharmaceutical Chemistry. New Delhi: Wolters Kluwer; 2011.
4. Triggiani M, Gentile M, Secondo A, Granata F, Oriente A, Taglialatela M, *et al*. Histamine induces exocytosis and IL-6 production from human lung macrophages through interaction with H receptors. J Immunol 2001;166:4083-91.
5. Giustizieri ML, Albanesi C, Fluhr J, Gisondi P, Norgauer J, Girolomoni G. H1 histamine receptor mediates inflammatory responses in human keratinocytes. J Allergy Clin Immunol 2004;114:1176-82.
6. Lachman L, Liberman HA, Kaing JL. The Theory and Practice of Industrial Pharmacy. 3rd ed. Bombay: Varghese Publishing House; 1987.
7. Bagul U, Gujar K, Patel N, Aphale S, Dhat S. Formulation and evaluation of sublimed fast melt tablets of levocetirizine dihydrochloride. Int J Pharm Sci 2010;2:76-80.
8. Tokola RA. The effect of metoclopramide and prochlorperazine on the absorption of effervescent paracetamol in migraine. Cephalalgia 1988;8:139-47.
9. Liberman HA, Lachman L, Schwartz JB. Pharmaceutical Dosage Forms Tablet. 2nd ed. New York: Marcel Dekkerinc; 2005.
10. Ipci K, Öktemer T, Birdane L, Altintoprak N, Muluk NB, Passali D, *et al*. Effervescent tablets: A safe and practical delivery system for drug administration. ENT Updates 2016;6:46.
11. Aslani A, Jahangiri H. Formulation, characterization and physicochemical evaluation of ranitidine effervescent tablets. Adv Pharm Bull 2013;3:315-22.
12. Niazi SK. Hand Book of Preformulation. New York: Informa Health Care; 2007.
13. Sinko PJ. Martin's Physical Pharmacy and Pharmaceutical Sciences. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006.
14. Aslani A, Eatesam P. Design, formulation and physicochemical evaluation of acetaminophen effervescent tablets. JRPS 2013;2:140-9.
15. Aulton ME. Pharmaceutics the Science of Dosage Form Design. 2nd ed. Philadelphia, PA: Churchill Livingstone; 2005.
16. Zhou Q, Armstrong B, Larson I, Stewart PJ, Morton DA. Improving powder flow properties of a cohesive lactose monohydrate powder by intensive mechanical dry coating. J Pharm Sci 2010;99:969-81.
17. Manthena PK, Artham S. Formulation and evaluation of sustained release tablets of quinapril HCL. Pharm Innov J 2014;2:13.
18. Amareshwar S, Vishwanadham Y, Prashanthi Y, Sreekanth D. Development and *in vitro* characterization of probenecid rapidly disintegrating tablets by using different co-processed super disintegrants. Nov Appro Drug Des Dev 2017;3:555611.
19. Neeharika J, Kishore BR, Reddy BM. Formulation and evaluation of candesartan cilexetil immediate release tablets. IRJP 2012;3:271-84.
20. Kumar YG. Preparation and evaluation of sustained release matrix tablets of bosentan by using wet granulation technique. Int J Pharm Sci Rev Res 2015;31:155-61.
21. Jagdale S, Gattani M, Bhavsar D, Kuchekar B, Chabukswar A. Formulation and evaluation of chewable tablet of levamisole. Int J Res Pharm Sci 2010;1:282-9.
22. Manikandan M, Kannan K, Thirumurugu S, Manavalan R. Design and evaluation of amlodipine besilate and atorvastatin calcium tablets. RJPBCS 2012;3:425-34.
23. Kumare MM, Marathe RP, Kawade RM, Ghante MH, Shendarkar GR. Design of fast dissolving tablet of atenolol using novel co-processed super disintegran. Asian J Pharm Clin Res 2013;6:81-5.
24. Babu VR, Mallikarjun R, Sayeed A, Rao PR. Design and evaluation of mini-tablets-pulsatile drug delivery system of ramipril. Indo Am J Pharm Sci 2018;5:1839-49.
25. Guggilla SG. Fast Dissolving Tablets. Available from: http://www.lulu.com.
26. Schiermeier S, Schmidt PC. Fast dispersible ibuprofen tablets. Eur J Pharm Sci 2002;15:295-305.
27. Design and *in-vitro* Evaluation of Mouth Dissolving Tablets of Rosiglitazone Maleate by Using Novel Coprocessed Superdisintegrants. Available from: https://www.pharmatutor.org/articles/design-and-invitro-evaluation-of-mouth-dissolving-tablet-of-rosiglitazone-maleate-by-novel-coprocessed-superdetergants?page=1%2C0.
28. Devi NA, Priya PV, Sharma JV, Rao AS. Formulation optimization and evaluation of tramadol oral disintegrating tablets. Int J Pharm Sci Rev Res 2013;18:38-41.
29. Shirsand SB, Shivanand, Shailashri, Keshavshetti G, Jonathan V. Hibiscus sabdariffa mucilage as a disintegrant in formulating fast dissolving tablets. J Pharm Sci 2016;15:143-9.
30. Stops F, Fell JT, Collett JH, Martini LG. Floating dosage forms to prolong gastro retention-the characterisation of calcium alginate beads. Int J Pharm 2008;350:301-11.
31. Kulkarni AR, Soppimath KS, Aminabhavi TM, Rudzinski WE. *In vitro* release kinetics of cefadroxil loaded sodium alginate interpenetrating network beads. Eur J Pharm Biopharm 2001;51:127-33.