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# DEVELOPMENT OF STABLE DISPERSABLE BI-LAYER TABLET OF MONTELUKAST SODIUM AND LEVOCETRIZINE HCL

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**ABSTRACT**

In the present study an attempt was made to prepare bilayer tablet of Montelukast sodium and Levocetrizine HCL for the treatment of asthma and allergic rhinitis. Bilayer tablet of Montelukast Sodium and Levocetrizine HCL was successfully developed. Immediate release of Montelukast was formulated with crosscaramellose sodium and Levocetrizine layer with starch granules as disintegration. IR spectrum revealed that there is no disturbance in the principle peaks of pure drugs of Montelukast sodium and Levocetrizine HCL. This indicates there was no interaction between the drug and excipient.The formulation showed good flow property and compressibility index. The angle of repose was ranged from 25.0˚±1.40 to 31.4˚±0.97 for Montelukast sodium and 25.2˚±1.40 to 29.5˚± 0.68 for Levocetrizine HCL. The compressibility index was found range from 11.6 to 22.2 for Montelukast sodium and 14.1 to 27.8 Levocetrizine HCL. Hausner's ratio was found to be 1.143 to 1.287 for Montelukast sodium and 14.1 to 27.8 for Levocetrizine HCL. The result of the angle of repose indicates good flow property of the granules and the values of compressibility index further showed support for the flow property. The prepared tablets were evaluated for hardness, friability, weight variation, drug content uniformity. The results were found within the limits. Among the various formulations prepared, Formulation F8 with croscarmellose sodium (20%) shows minimum disintegration time and improved dissolution properties compared to formulation F-1 to F-7. This is because of the dual action of wicking and swelling property of disintegrants. The stability studies were carried out for the optimized formula for three months and it show acceptable results. Hence, Montelukast sodium and Levocetrizine HCL bilayer tablets can be used for alternative dosage form in the effective treatment of patients suffering from allergic rhinitis and bronchial asthma.

**Keywords:** Montelukast sodium, Levocetrizine HCL, Bilayer tablets, Stability study, *In vitro* dissolution.

## INTRODUCTION

The goal of any drug delivery system is to provide a therapeutic amount of the drug to the proper site in the body to achieve promptly, and then maintain the desired drug concentration. Combination products-also known as fixed dose combinations are combinations of two or more active drugs produced in a single dosage form. The preferred treatment option in the treatment of chronic diseases i.e. hypertension, diabetes and allergic rhinitis is combination therapy in the form of bilayer tablets. The advantages include minimization of side effects, and a reduction of dose related risk [1-4].

Bilayered tablets are tablets containing subunits that may be either the same (homogeneous) or different (heterogeneous). These tablets are suitable for sequential release of two drugs in combination, separate two incompatible substances and when the release profiles of the two drugs are different from one another. Levocetirizine HCL is a selective, long acting peripheral H1 receptor antagonist. Allergic rhinitis is a symptomatic disorder of the nose induced by inflammation mediated by immunoglobulin E (IgE) in the membrane lining the nose after allergen exposure [5,6]. Formulating Levocetirizine into an immediate release layer dosage of bilayer tablets would provide fast relief. Montelukast is a leukotriene receptor antagonist (LTRA) used for the maintenance treatment of asthma attacks and to relieve symptoms of seasonal allergies [7]. Montelukast sodium is formulated as immediate release, the reason being that it has to reach systemic circulation very quick so as to provide immediate onset of action.

The aim of the present study is to design and evaluate bilayer tablets of Montelukast and Levocetrizine for the treatment of allergic rhinitis. The Immediate release layer of Montelukast is formulated using MCC PH 102, Pearlitol, L-HPC L-H21 and immediate release layer of Levocetrizine HCL is formulated using super disintegrants like Croscarmellose sodium. Compatibility between drug and excipients is studied by FTIR spectroscopy.

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Evaluation of physiochemical properties of the tablet is performed. An *In vitro* drug release study is performed to optimize the prototype formulations of bilayer tablet [8-10]. A stability studies is conducted for optimized formulation as per ICH guidelines.

## MATERIALS AND METHODS

### Materials

Montelukast sodium and Levocetrizine HCL was a gift sample from Delphin pharmaceuticals and Unilinks chemicals respectively. Other materials used in the study such as MCC (RanQ remedies, Mumbai), Starch (Vijaya enterprises, Mumbai), Colloidal silicon dioxide (Cabot Sanmar Ltd), Croscarmellose sodium (KAPL, Bangalore), Magnesium stearate and Talc (SD fine chemicals) were purchased.

### Methods

### Physiochemical Interaction of drug and polymer:

Physiochemical interaction of drug Montelukast sodium and Levocetrizine HCL and excipients is conducted by Fourier Transform Infra red spectrophotometer (FTIR) specrophotometeric analysis.

### Manufacturing process of Montelukast sodium and Levocetrizine HCL bilayer tablets

### Procedure for montelukast sodium layer

Shift the montelukast sodium, MCC PH 102, pearlitol, CCS (ac-di-sol), L-HPC LH21, colloidal silicon di oxide pass through 30mesh. Geometrically mix montelukast sodium with MCC PH102 and pearlitol (1:2:2 ratio). Load the sifted materials along with geometrical mix blend into blender and mix for 20minutes. Sift magnesium stearate through 60# and load into blender and continue mixing for 5 minutes

### Procedure for Levocetirizine HCL layer

Sift starch, MCC, lactose pass through 30#. Sift separately ponceau 4R lake through 100 #. Add starch plain for paste to a small quantity of water to form a slurry. Boil remaining quantity of water to 80˚C add starch slurry to above boiled water and stir well to form a smooth paste without any lumps. Dry the granules at 60˚C in tray dryer till the solvent is partially evaporated. Sift the semi dried granules through 20 # and continue final drying at 60˚C until required LOD achieved. (LOAD limit: 2-4% at 105˚C). Sift ponceau 4R Lake through 100 # and sift Levocetrizine through 30 # and mix with above dried granules geometrically by 1:5 ratio. Sift purified talc through 30 mesh, magnesium sterate through 60 # load the sifted materials, geometrical mix blend and dried granules into blender and mix for 10 minute Finally add magnesium sterate into blender and then mix for 5minutes. All the formulation compositions were shown in Table 1.

## EVALUATION OF GRANULES

### Bulk density

Bulk density is the ratio of the weight of the powder to the bulk volume it occupies. It is expressed in gm/ml. A weighed quantity of powder blend previously shaken to break any aagglomerates formed, was introduced in to a measuring cylinder and the volume was noted. Bulk density was calculated using the following equation;

Bulk density = Mass of the powder Blend taken/Volume occupied by the powder blend

### Tapped density

A weighed quantity of powder blend previously shaken to break any agglomerates formed, was introduced in to a measuring cylinder and the volume was noted. The cylinder was placed in the tapped density apparatus and allowed to fall under its own weight on to a hard surface (USP-II), that provides fixed a drop of 3mm(±10%) at a nominal rate of 250 drops per minute is used. Tapping was continued until no further change in volume was noted. Td was calculated using the following equation;

Tapped density = Mass of the powder Blend taken/ Tapped Volume of the powder blend

### Carr's compressibility Index

Carr's Index is an important measure that can be obtained from the bulk and tapped densities. In theory, the less compressible a material the more flow able it is. A material having values of less than 20 is defined as the free flowing material. The formula for Carrs Index is as below:

$$\text{Carr's Index } (\%) = 100\ \{1 - Bd/Td\}$$

### Hausner's ratio

It indicates the flow properties of the powder and is measured by the ratio of tapped density to the bulk density

Hausner's ratio= (Tapped density)/(Bulk density)

### Angle of repose

Angle of Repose is an indication of the frictional forces existing between granule particles. The maximum angle possible between the surface of the pile of granules and the horizontal plane gives the angle of repose:

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

where, θ is the angle of repose; h is the height of the heap of powder and r is the radius of the heap of the powder.

Method:

Weighed quantity of granules were poured through the funnel from the fixed height on the graph paper. Then circumference of the heap was marked by pencil. The radius of the circle formed was measured and angle of repose then calculated on the parameter which was found out from the radius of circle and height of the heap.

### Moisture content

Initially 5 g of weighed granules were taken and kept for drying at 105˚C for a required time in a oven. Then removed and again reweighed and noted as final weight. The difference in weight was noted as moisture content.

$$\text{Moisture content} = \frac{\text{Initial weight - Final weight}}{\text{Initial weight} \times 100}$$

**EVALUATION OF TABLETS**

**Description**

Observe and record the colour, shape and scoring or embossing of the tablet.

**Thickness**

Thickness depends on die filling, physical properties of material to be compressed. There is possibility of small variation in the thickness of individual tablet in batch. But it should not be apparent to the unaided eye. The thickness and diameter can be measured by vernier callipers.

**Hardness**

Tablet must possess sufficient strength or hardness and can be measured by Monsanto hardness tester. Ten tablets were randomly picked from each formulation and were evaluated for hardness and can be expressed in kg/cm.[2]

**Friability**

Friability can be performed in Roche friabilator, Preweighed ten tablets were introduced in the friabilator. Then the machine was operated for 100 revolution. Tablets were dropping from a distance of six inches with each revolution. Tablets were then dusted and reweighed. Loss of less than 1% in weight is considered to be within the specifications and acceptable.

$$F\% = \frac{\text{Initial Weight} - \text{Final Weight}}{\text{Initial Weight}} \times 100$$

**Average weight**

Select 20 tablets randomly. Weigh the tablets and calculate the average weight by dividing the total weight by 20.

**Uniformity of weight**

Select 20 tablets randomly and calculate the average weight. Take the individual weight of all tablets. Not more than two of individual weights deviate from average weight by more than the percentage shown in the table given below and non deviates by more than twice that percentage.

**Disintegration [11,12]**

Place 1 tablet in each of the six baskets and suspended assembely in purified water mainted at 37˚C ± 2˚C. Omit the disc, except in case the tablet float on the top of water the disc may be added. Operate the apparatus for 15 minutes. Remove the assembly from the liquid. One or two tablets fail to disintegrate, repeat the test on 12 additional tablets; not less than 16 of the total of 18 tested disintegrate.

**Dissolution test for Montelukast sodium**

Medium : 900ml, 0.5%w/v of sodium dodecyl sulphate in water
Apparatus : USP 11 (paddle)
Speed : 75 rpm
Time : 60 minutes
Temperature : 37˚C ± 0.5˚C

**Chromatographic condition**

Column : L1 (zorbax c18 150 × 4.6mm, 5µ or equivalent)
Wavelength : 240nm
Injection volume : 50 µl
Flow rate : 1ml/min
Column temperature : 40˚C
Sample cooler temperature : 20˚C
Diluent : 1st dilution: methanol
2nd dilution : dissolution medium
Mobile phase : buffer (mobile phase A): methanol (mobile phase B)
Buffer preparation : dilute 6gm of ammonium acetate in 1000ml water and adjust ph to 5.5 with glacial acetic acid.

**Standard preparation**

Weigh accurately 115mg of Montelukast sodium and 55mg of Levocetrizine HCL in 100ml volumetric flask. Add 70 ml 0f methanol to dissolve and make up with volume of methanol. Pipette out 2ml from above solution into 200ml volumetric flask and make up the volume with dissolution medium and filter through 0.45µm membrane filter (11 µg/ ml of Montelukast & 5.5 µg/ml of Levocetrizine HCL)

**Sample preparation**

Set dissolution parameters and place 1 tablet in to each jar containing 900ml of medium taking care to exclude air bubbles from surface of the tablet and immediately start the apparatus. After 60 minutes with draw 10 of the samples 0.45µm membrane filter. Inject 50µl of standard and sample solution and record the chromatogram. Calculate the amount of Montelukast dissolved by using calculation.

**Dissolution calculation**

$$\frac{\text{Spl. Area}}{\text{Std area}} \times \frac{\text{Std.wt}}{100} \times \frac{2}{200} \times \frac{900}{1} \times \frac{1}{\text{Label claim}} \times \frac{\text{std Purity (on dried basis)}}{100} \times \frac{(100\text{-LOD})}{100} \times \frac{586.2}{608.2} \times 100$$

**For Levocetrizine (by HPLC)**

**Dissolution condition**

Medium : 900ml, ph 6.8 phosphate buffer
Apparatus : USP 11 (paddle)
Speed : 75rpm
Time : 45 minutes
Temperature : 37˚C ± 0.5˚C

Preparation of phosphate buffer pH 6.8: dissolve 6.8g potassium dihydrogen phosphate and 0.894gm sodium hydroxide 1000ml water and adjust ph to 6.8 with dilute sodium hydroxide solution or 0.1 n HCL if necessary.

**Chromatographic condition**

Column :L1 (Zorbax c18 150 ×4.6mm, 5µ or equivalent)
Wavelength :240 nm
Injection volume :50µl
Flow rate :1ml/min
Column temperature :40˚c
Sample cooler temperature :20˚c
Diluent :1st dilution: methanol
2nd dilution: dissolution medium Mobile phase: buffer (mobile phase A): methanol (mobile phase B)
Buffer preparation :dilute 6gm of ammonium acetate in 1000ml water and adjust pH to 5.5 with glacial acetic acid

**Standard preparation**

Weigh accurately 115mg of Montelukast sodium and 55mg of Levocetrizine HCL in 100ml volumetric flask. Add 70ml of methanol to dissolve and make up the volume with methanol. pipette out 2ml from above solution into 200ml volumetric flask and make up the volume with dissolution medium and filter through 0.45 µm membrane filter (11 µg /ml of Montelukast and 5.5 µg/ ml of Levocetrizine HCL)

**Sample preparation**

Set dissolution parameters and place 1 tablet in to each jar containing 900ml of medium taking care to exclude air bubbles from the surface of the tablet and immediately start the apparatus. After 45 minutes withdraw 10ml of the sample and filter through 0.45µm membrane filter Inject 50µl of standard and sample solution and record the chromatogram. Calculate the amount of Levocetrizine HCL dissolved by using following calculation.

**Dissolution Calculation:**

$$\frac{\text{Spl. Area}}{\text{Std area}} \times \frac{\text{Std.wt}}{100} \times \frac{2}{200} \times \frac{900}{1} \times \frac{1}{\text{Label claim}} \times \frac{\text{std Purity (on dried basis)}}{100} \times \frac{(100\text{-LOD})}{100} \times 100$$

**Stability Studies**

Bi layered tablet of optimized formulation were packed in Alu-Alu pack and subjected to accelerated stability studies for 3 months at 25˚C±2˚C/60%±5%RH and 40ºC ±2ºC/75%RH±5%RH. At interval of 3 months sufficient number of tablets were taken and evaluated for their Average Weight, Thickness (mm), Disintegration time (sec), Drug content (%) and Dissolution (30 min) studies.

## RESULTS AND DISCUSSION

**Preformulation studies**

Preformulation studies, one of the important prerequisite in development of any drug delivery system. Preformulation studies were performed on the between drug and excipient compatibility studies. The FTIR spectra of drugs and drug with excipients are depicted in the Figure 1.The spectra of standard Monteleukast sodium and Levocetrizine HCL showed sharp charecteristics peaks. These peaks are also prominent in the spectra of the physical mixtures containing the drug and excipients in the formula of individual layers. This results indicates that there is no interaction between the drug and excipients.

**Angle of repose, Carr's compressibility index & Hausner's ratio**

The result of formulations F1 to F8 angle of repose, carr's compressibility index and Hausner's ratio was shown in Table 2 and 3. The angle of repose of Monteleukast and Levocetrizine powder blend was found between 25.0˚±1.40 to 31.4˚±0.97 and 25.2˚±1.40 to 29.5˚±0.68 respectively. The compressibility index of Monteleukast and Levocetrizine powder blend was found between 12.6 to 22.2 and 14.1 to 27.8 respectively. The Hausner's ratio of Monteleukast and Levocetrizine powder.

**Evaluation of Bilayer tablets**

**Hardness test**

The results hardness test of all the formulations F1 –F8 were shown in Table 4**.** The hardness of bilayer tablets was found range between 5.0±0.17 to 7.5± 0.137 kg/cm$^2$.

**Friability Test**

The values of friability test were tabulated. The % friability was less than 1% in all the formulations ensuring that the tablets were mechanically stable. The results were shown in Table 4.

**Weight variation test**

The percentage weight variation of all the formulations F1 – F8 were shown in Table 4. All the formulated tablets passed weight variation test as the percentage weight variation was within the pharmacopoeial limits of 7.5% of the weight. The weights of all the tablets were found to be uniform with low standard deviation values.

**Thickness**

The measured thickness of bilayer tablets F1 to F8 was found range between 3.27 ±0.013 to 3.68±0.015 (mm). The results were shown in Table 4.

**Drug content**

The percentage of drug content of formulations F1 to F8 was found between 96.34% to 99.13% of Montelukast sodium and 95.42% to 100.65% Levocetrizine HCL. The results were shown in Table 4.

***In vitro* dissolution study**

All the eight formulation of Montelukast sodium and Levocetrizine bilayer tablet were subjected to *In vitro* release studies. Dissolution profiles of all formulations were compared by percentage drug release versus time and shown in Figure 2 and 3. The percentage release of Montelukast and Levocetrizine at the end of 30 mins for F1 was found to be 69.4 % and 74.62 % respectively. The low percentage

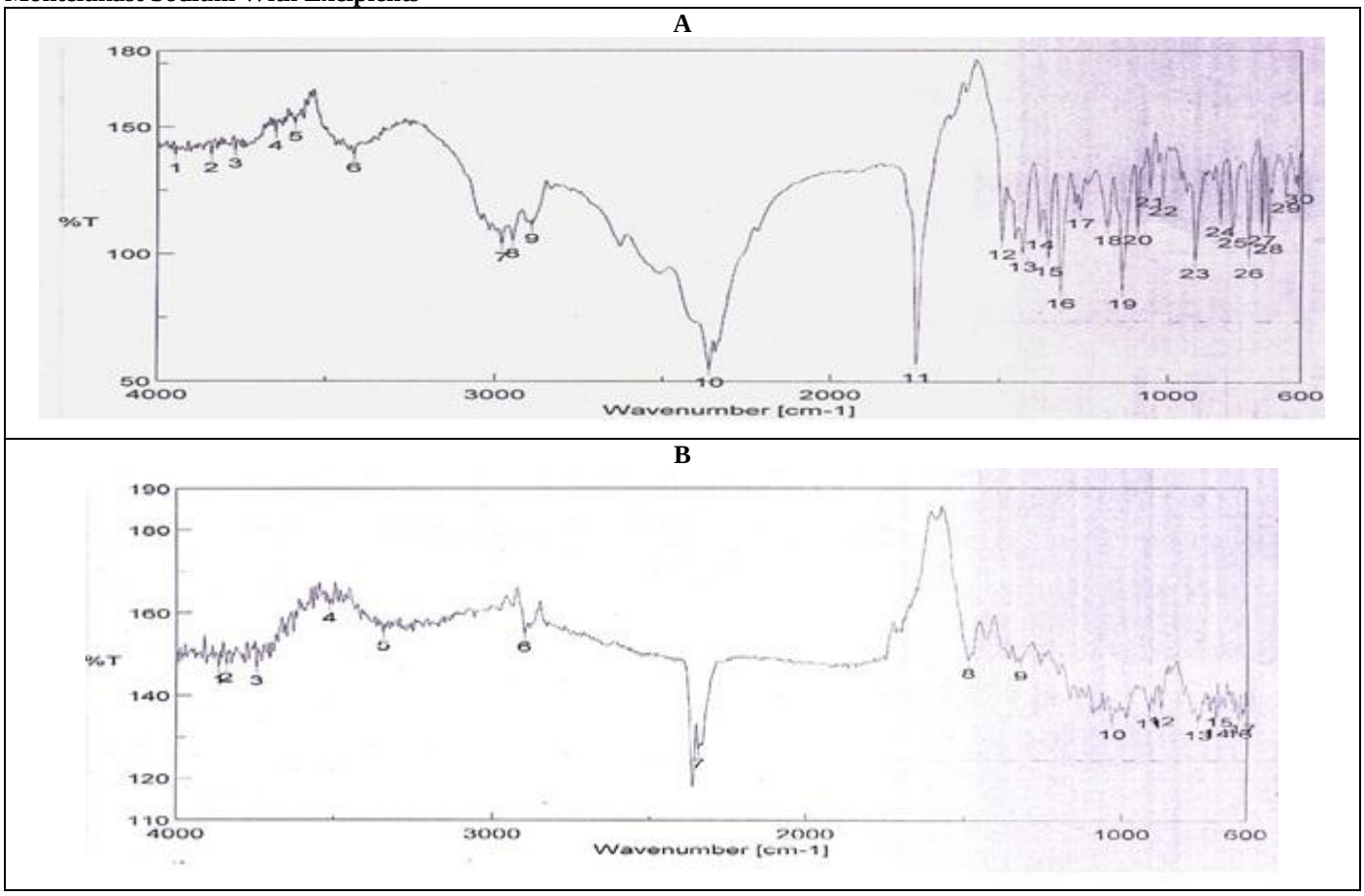
release of montelukast may be due to low concentration of croscarmellose sodium (5%), in case of Levoceterizine higher quantity of starch 40% decreases the release. The percentage release of Montelukast and levocetrizine at the end of 30 mins for F2 was found to be 73.25% and77.15% respectively. Increased release of Montelukast was found due to croscarmellose sodium increase upto 10%. Increased release of Levoceterizine was found due to decrease the starch quantity. The percentage release of Montelukast and Levocetrizine at the end of 30 mins for F3 was found to be 78.59% and 79.81% respectively. Due to MCC increased concentration both layer. The percentage release of Montelukast and Levocetrizine at the end of 30 mins for F4 was found to be 81.29% and 84.23% respectively. Improved release was found after increased addition of pearlitol and lactose. The percentage release of Montelukast and Levocetrizine at the end of 30 mins for F5 was found to be 86.56% and 86.42% respectively.

The release of Montelukast increased due to increased concentration of croscarmellose sodium (12.5%). The percentage release of Montelukast and levocetrizine at the end of 30 mins for F6 was found to be 89.54% and 89.88% respectively. The percentage release of Montelukast and Levocetrizine at the end of 30 mins for F7 was found to be 90.56% and 93.32% respectively. The percentage release of Montelukast and Levocetrizine at the end of 30 mins for F8 was found to be 93.05% and 95.15% respectively. The results revealed that Montelukast release was improved as the concentration of croscarmellose sodium increased. From dissolution results it was confirmed that formulation F8 was shown good dissolution profile when compared with other formulations (F1 to F7).

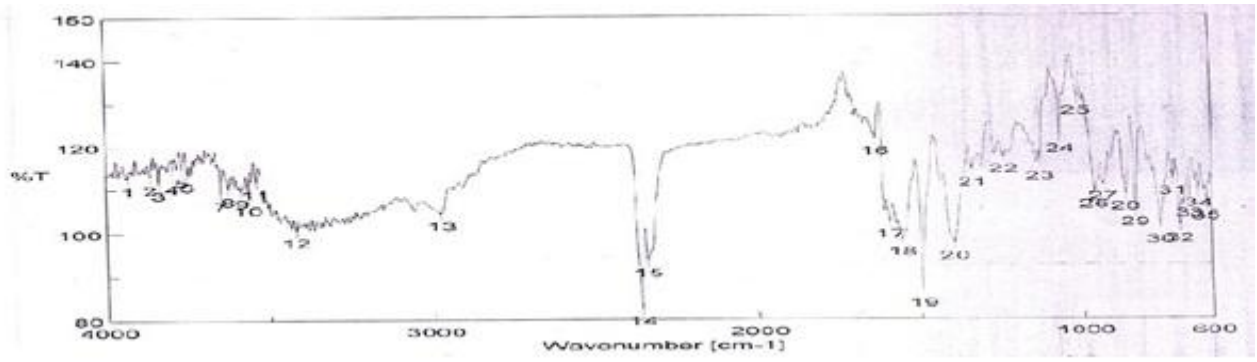
**Stability study**

The result of the stability studies was shown in Table 5. The stability of optimized formulation F8 was monitored up to 3 months at 25˚C±2˚C/60%±5%RH and 40˚C±2˚C/75%RH±5%RH. Periodically (Initial and 3months) samples were removed and evaluated by different parameters like Average Weight, Thickness (mm), Disintegration time (sec), Drug content (%) and Dissolution (30 min). There were no major changes observed during stability of Montelukast sodium and Levocetrizine HCL bilayer tablets.

**Figure 1. FTIR Spectrum Of (A) Levocetrizine Hcl (B) Levocetrizine Hcl With Excipients (C) Montelukast Sodium (D) Montelukast Sodium With Excipients**



**C**




**D**

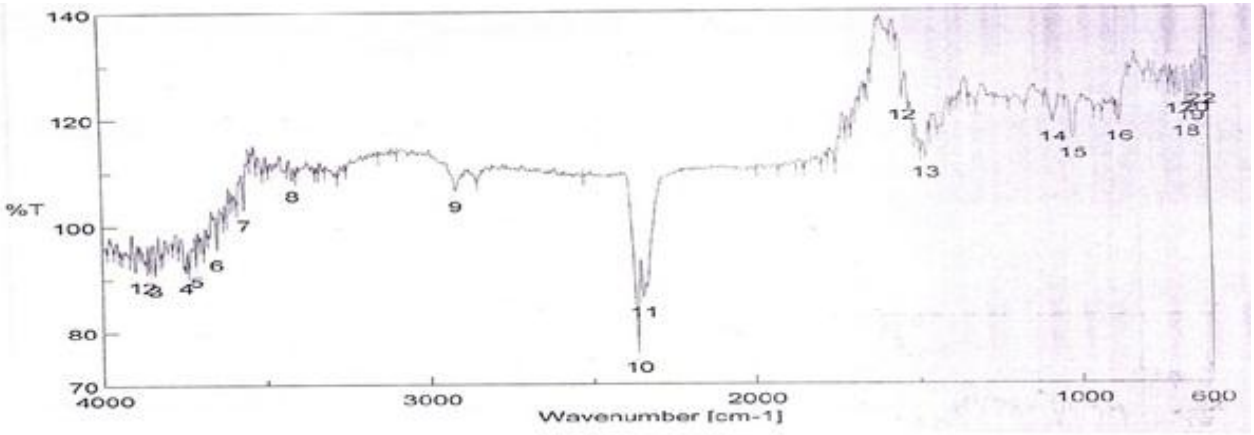



**Table 1. Composition of the Formulation of Bilayer Tablet**

| Ingredients | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 |
|---|---|---|---|---|---|---|---|---|
| | M1+L1 | M2+L2 | M3+L3 | M4+L4 | M5+L5 | M6+L6 | M7+L7 | M8+L8 |
| **Montelukast** | 10.40 | 10.40 | 10.40 | 10.40 | 10.40 | 10.40 | 10.40 | 10.40 |
| MCC PH 102 | 30.00 | 40.00 | 64.60 | 40.00 | 40.00 | 39.60 | 39.60 | 39.60 |
| Pearlitol | 89.60 | 73.60 | 46.00 | 70.60 | 68.10 | 66.00 | 63.50 | 60.00 |
| Croscarmellose Sodium | 5.00 | 10.00 | 10.00 | 10.00 | 12.5 | 15.00 | 17.50 | 20.00 |
| L-HPC L-H21 | 2.00 | 2.00 | 3.00 | 3.00 | 3.00 | 3.00 | 3.00 | 4.00 |
| Aerosil(colloidal | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 |
| Mg. Sterate | 1.00 | 2.00 | 4.00 | 4.00 | 4.00 | 4.00 | 4.00 | 4.00 |
| **Levocetrizine** | 5.00 | 5.00 | 5.00 | 5.00 | 5.00 | 5.00 | 5.00 | 5.00 |
| Starch | 40.00 | 10.00 | 15.00 | 17.50 | 18.00 | 18.00 | 18.00 | 18.00 |
| MCC | 10.00 | 29.00 | 40.0 | 20.00 | 15.10 | 13.60 | 13.60 | 13.60 |
| Lactose | 29.00 | 40.00 | 23.60 | 40.60 | 45.00 | 50.00 | 50.00 | 50.00 |
| Ponceau 4R lake | 0.60 | 0.60 | 0.30 | 0.30 | 0.30 | 0.30 | 0.30 | 0.30 |
| Starch for paste | 3.00 | 3.00 | 3.00 | 3.50 | 3.50 | 4.00 | 4.00 | 4.00 |
| Colloidal silicone | _ | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Ponceau4R Lake | 0.10 | 0.10 | 0.10 | 0.10 | 0.10 | 0.10 | 0.10 | 0.10 |
| Purified Talc | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Mg. Stearate | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| **Total Weight (mg)** | 230 | 230 | 230 | 230 | 230 | 230 | 230 | 230 |

**Table 2. Precompression Parameters of Montelukast Sodium**

| Formulations | Bulk density (g/ml) | Tapped density (g/ml) | Hausner's ratio | Carr's index % | Angle of repose |
|---|---|---|---|---|---|
| M1 | 0.441±0.473 | 0.564±0.566 | 1.278±1.050 | 21.8±0.79 | 33.4˚±0.97 |
| M2 | 0.452±0.471 | 0.582±0.564 | 1.287±1.049 | 19.9±1.14 | 32.4˚±0.84 |
| M3 | 0.473±0.469 | 0.593±0.562 | 1.253±1.053 | 20.4±1.53 | 31.2˚±1.32 |
| M4 | 0.524±0.462 | 0.621±0.559 | 1.185±1.062 | 22.2±1.12 | 29.8˚±0.96 |
| M5 | 0.544±0.460 | 0.643±0.556 | 1.181±1.062 | 20.3±1.25 | 29.2˚±1.24 |
| M6 | 0.572±0.456 | 0.654±0.555 | 1.143±1.067 | 22.0±1.45 | 28.4˚±1.26 |
| M7 | 0.606±0.452 | 0.710±0.548 | 1.171±1.063 | 14.3±1.43 | 26.8˚±1.34 |
| M8 | 0.615±0.451 | 0.728±0.545 | 1.183±1.062 | 12.6±1.54 | 25.0˚±1.40 |

**Table 3. Pre compression Parameters For Levocetrizine HCl**

| Formulation | Bulk density (g/ml) | Tap density (g/ml) | Hausner's ratio | Carr's index % | Angle of repose | Moisture content (%) |
|---|---|---|---|---|---|---|
| L1 | 0.356±0.33 | 0.492±0.44 | 1.382±1.13 | 27.6±0.79 | 29.5˚±0.68 | 3.60±0.2 |
| L2 | 0.362±0.32 | 0.498±0.448 | 1.375±1.136 | 27.3±1.12 | 28.2˚±0.89 | 3.30±01 |
| L3 | 0.368±0.328 | 0.510±0.446 | 1.385±1.134 | 27.8±1.25 | 27.9˚±0.85 | 3.50±0.3 |
| L4 | 0.391±0.324 | 0.532±0.443 | 1.360±1.139 | 14.1±1.28 | 27.4˚±0.96 | 3.40±0.3 |
| L5 | 0.418±0.32 | 0.564±0.437 | 1.349±1.140 | 25.8±0.98 | 26.8˚±1.25 | 3.20±0.2 |
| L6 | 0.420±0.315 | 0.493±0.432 | 1.180±1.141 | 15.0±0.95 | 25.2˚±1.40 | 3.15±0.1 |
| L7 | 0.420±0.315 | 0.493±0.432 | 1.180±1.141 | 15.0±0.95 | 25.2˚±1.40 | 3.15±0.1 |
| L8 | 0.420±0.315 | 0.493±0.432 | 1.180±1.141 | 15.0±0.95 | 25.2˚±1.40 | 3.15±0.1 |

**Table 4. Post Compression Parameters For Bilayer Tablet**

| Formulation | Thickness (mm) | Hardness ($kg/cm^{2)}$ | Friability (%) | Disintegration (Mins and Sec) | Avg Wt | Assay% | |
|---|---|---|---|---|---|---|---|
| | | | | | | Montelukast | Levocetrizine |
| F1 | 3.27±0.013 | 5.0±0.17 | 0.25 | 15m 30s | 230.4±0.21 | 96.34 | 98.65 |
| F2 | 3.30±0.014 | 5.2±0.15 | 0.20 | 8m 10s | 234.5±0.52 | 98.65 | 95.42 |
| F3 | 3.43±0.010 | 5.5±0.11 | 0.18 | 6m 45s | 229.3±0.25 | 97.17 | 98.43 |
| F4 | 3.45±0.016 | 6.4±0.0 | 0.17 | 4m 30s | 228.2±0.23 | 99.96 | 97.05 |
| F5 | 3.55±0.010 | 6.9±0.06 | 0.18 | 3m 45s | 227.8±0.18 | 96.72 | 99.12 |
| F6 | 3.60±0.015 | 7.2±0.1 | 0.20 | 3m 10s | 229.8±0.19 | 95.64 | 99.60 |
| F7 | 3.68±0.015 | 7.5±0.13 | 0.15 | 2m 50s | 227.8±0.43 | 99.06 | 100.05 |
| F8 | 3.72±0.013 | 7.8±0.17 | 0.14 | 2m 35s | 227.5±0.32 | 99.13 | 100.65 |

**Table 5. Stability Studies Report**

| Conditions | Relative Humidity | Months | Average Wt (mg) | Thickness (mm) | Disintegration (min) | Assay (%) | Dissolution (30min) |
|---|---|---|---|---|---|---|---|
| 25±2˚C | 60±5%RH | 0 | 227.5±4 | 3.72±0.013 | 2m 35s | (M)99.13<br>(L)100.05 | M)93.05<br>(L)95.15 |
| | | 1 | 228.5±5 | 3.71±0.025 | 3m 15s | (M)98.42<br>(L)101.25 | (M)93.15<br>(L)95.25 |
| | | 2 | 226.5±6 | 3.74±0.045 | 3m 30s | (M)99.54<br>(L)100.15 | (M)94.25<br>(L)96.35 |
| | | 3 | 225.5±5 | 3.73±0.023 | 3m 45s | (M)99.15<br>(L)100.09 | (M)93.25<br>(L)95.54 |
| $40±2^{0}$C | 75±5%RH | 0 | 227.5±4 | 3.72±0.013 | 2m 35s | (M)99.13<br>(L)100.05 | (M)93.05<br>(L)95.15 |
| | | 1 | 229.5±5 | 3.73±0.024 | 3m20s | (M)98.13<br>(L)100.10 | (M)93.14<br>(L)96.24 |
| | | 2 | 228.5±5 | 3.71±0.023 | 3m 25s | (M)99.54<br>(L)100.08 | (M)99.13<br>(L)93.24 |
| | | 3 | 227.4±5 | 3.74±0.025 | 3m40s | (M)99.25<br>(L)100.09 | (M)99.13<br>(L)94.25 |

**Figure 2. *In vitro* dissolution profile of Montelukast sodium**

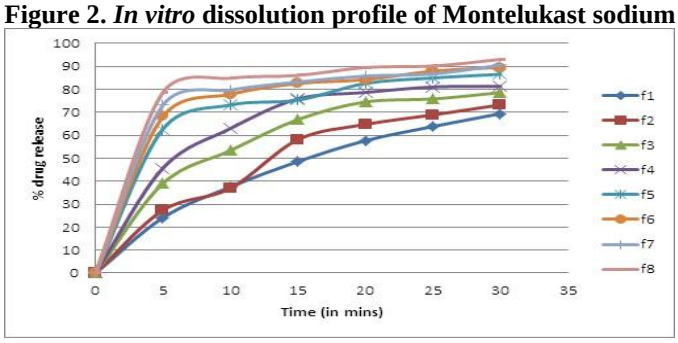
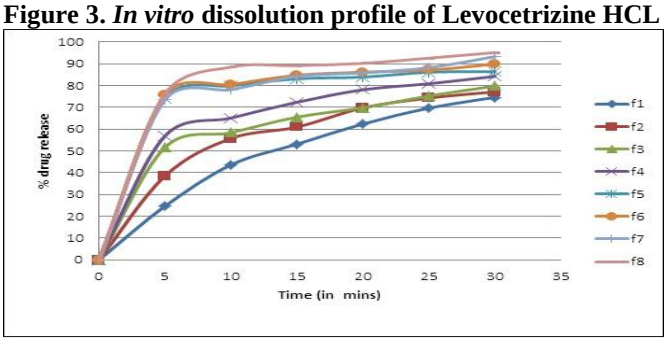



**Figure 3. *In vitro* dissolution profile of Levocetrizine HCL**




## CONCLUSION

The present research was carried out to develop an immediate release bilayer tablet of Montelukast sodium and Levocetrizine HCL which is indicated for the successful treatment and relief of allergic rhinitis and bronchial asthma. Bilayer tablet of Montelukast sodium and Levocetrizine HCL was successfully developed. Immediate release layer of Monteleukast was formulated with croscarmellose sodium and Levocetrizine layer with starch granules as disintegrants. FTIR result indicates that there is no incompatibility between drug and excipients. As per the results of physical characters of Powder blend from F1to F8 was not shown much difference in granules flow property. The values are ranged with in that of the pharmacopeial limits. Formulation characteristics such as content uniformity, Hardness, Friability, Thickness, Disintegration time were found to be satisfactory. *In vitro* dissolution studies of bilayered tablets were conducted in pH 6.8 buffer for 30 minutes. Samples were analyzed by HPLC. The formulation (F8) showed acceptable pharmacotechnical properties and complied with the internal specifications. From accelerated stability studies, bilayer tablets were found to be stable. Hence, it is finally concluded that, the bilayer tablet of immediate release of Montelukast sodium and Levocetrizine HCL can be used for alternative dosage form in the effective treatment of patients suffering from allergic rhinitis and bronchial asthma.

## REFERENCES

1. Rathod RT, Misra D. FDC of Montelukast with Levocetirizine, focus on bilayer technology. *J Indian Med Assoc*, 107(8), 2009, 562-4.
2. Hemanth Kumar A, K. Kavitha, Selvi Arun Kumar, M. Rupesh Kumar and SD. Jagadeesh Singh. Novel Approach of Bilayer Tablet Technology –A Review. *IJPCBS*, 3(3), 2013, 887-893.
3. Pradeep ReddyT, Divya RaoV, Ravi Kumar K. Bi-layer technology- an emerging trend, A review. *International Journal of Research and Development in Pharmacy and Life Sciences*, 2(3), 2013, 404-411.
4. Gopinath C, Hima bindu V, Nischa M. An over view on bilayer tablet technology. *Journals of Global Trends in Pharmaceutical Science*, 4(2), 2013, 1085-1098
5. Hair PI, Scott LJ. Levocetirizine, A review of its use in the management of allergic rhinitis and skin allergies. *Drugs*, 66(7), 2006, 973-96.
6. Day JH, Ellis AK, Rafeiro E. Levocetirizine, a new selective H1 receptor antagonist for use in allergic disorders. Drugs Today (Barc). 2004, 40(5), 415-21.
7. Michael S Benninger and Heather W Montelukast, Pharmacology, Safety, Tolerability and Efficacy. *Clinical Medicine*, Therapeutics, 1, 2009, 1253–1261.
8. Naisarg D Pujara Ronak K Gokani, Jalpa S Paun. Bilayer tablet. An emerging trend. *International Journals of Pharmaceutical Research and Development*, 4(04), 2011, 102 - 111.
9. Shajan A, Narayanan N, Reema N, Aishwarya G. Design and evaluation of bilayer tablets of doxofylline HCL and Montelukast sodium for treatment of asthma. *Int J Pharm and Ind Res*, 3(1), 2013, 70–76.
10. Moiz Mohammed, Prathima Srinivas Maringanti, Sadanandam Mamidi. Formulation and evaluation of bilayered tablets of Montelukast and Levocetrizine dihydrochloride using natural and synthetic polymers. *International Journals of Drug Delivery*, 3(4), 2011, 597-618.
11. Devireddy SR, Gonugunta CS, Veerareddy PR. Formulation and evaluation of taste-masked Levocetirizine dihydrochloride orally disintegrating tablets. *J Pharm Sci Technol*, 63(6), 2009, 521-526.
12. Atul S Rathore L. Sathiyanarayanan and Mahadik KR. Development of Validated HPLC and HPTLC Methods for Simultaneous Determination of Levocetirizine Dihydrochloride and Montelukast Sodium in Bulk Drug and Pharmaceutical Dosage Form. *Pharm Anal Acta PAA*, 1, 2013, 2-6.