RESEARCH ARTICLE

# Formulation and Evaluation of Fast Dissolving Tablet of Levocetirizine Dihydrochloride and Montelukast Sodium

Madhu Verma[1,2]*, Iti Chauhan[3], Mohamed Yasir[4]

## Abstract

**Introduction:** Fast disintegrating tablets (FDTs) have received ever-increasing demand during the last decade, and the field has become a rapidly growing area in the pharmaceutical industry.

**Objective:** The aim of present study was to formulate fast dissolving tablets of Levocetrizine dihydrochloride (LEV) and Montelukast sodium (MON) by direct compression method.

**Material And Methods:** An attempt was made to mask the bitter taste of Levocetrizine by preparing ion exchange resin complex by batch method using kyron T-104. The tablets were prepared using mannitol, microcrystalline cellulose as diluents and croscarmellose sodium and crospovidone as superdisintegrants. Parameters like drug: resin ratio, pH & swelling time were successfully optimized to prepare drug resin complex. The fast dissolving tablets were characterized for various pre and post compression parameters along with disintegration time, content uniformity, wetting time, in-vitro drug release, in vivo taste evaluation and compatibility studies.

**Result and Discussion:** The tablets prepared by direct compression method possess hardness of 3.4 to 3.6 Kg/cm$^2$, percentage friability of 0.65 to 0.80, in vitro disintegration time of 29.82 to 51.7 seconds and wetting time of 20.4 to 46.8 seconds. The formulation (F4) containing crospovidone and croscarmellose sodium in 2:4 ratios showed better disintegration time and more than 99% drug release within 6 minutes. Comparative taste evaluation proves the palatability of formulated tables. Results of stability studies were also found in acceptable limits.

**Conclusion:** The prepared orodispersible tablets disintegrate within seconds without need of water and enhance the absorption; this may lead to increased bioavailability of LEV as well as MON.

**Keywords:** Levocetirizine dihydrochloride, Montelukast sodium, Fast dissolving tablet

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## Introduction

Since ages, the oral route of administration continues to be the most desired route due to its multifarious advantages including ease of administration, accurate dosage, self-medication, versatility and above all, patient compliance. Amongst the oral pharmaceutical dosage forms, conventional tablets seem to be most popular, because of ease of transportability and comparatively, lower manufacturing cost.[1]

However, many patient groups such as the elderly, children, mentally retarded, uncooperative, nauseated, or on reduced liquid intake diets face dysphagia. Children may also have difficulty ingesting these dosage forms because of their underdeveloped muscular and nervous systems. Dysphagia nearly affects 35% of the general population. This disorder is also associated with a number of medical conditions like stroke, Parkinson's disease, AIDS, head and neck radiation therapy and other neurological disorders like cerebral palsy.[2] Swallowing conventional tablets will be further hindered by conditions such as unavailability of water, allergic reactions, and episodes of coughing.[3]

The aforementioned issues can be successfully addressed by developing rapidly disintegrating and dissolving tablet dosage forms for oral administration. 3 Mouth dissolving tablets (MDT) are also known as fast dissolving tablets (FDT), orally disintegrating tablets (ODTs), melt-in-mouth tablets, rapimelts, porous tablets, oro-dispersible tablets, quick-dissolving tablets or rapidly disintegrating tablets.[4] United States Food and Drug Administration (FDA) defined 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

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disintegration time for ODTs generally ranges from several seconds to about a minute.[5]

These formulations dissolve in saliva and do not require water for swallowing. Tablet is simple to administer as it is placed in the mouth cavity, allowed to disperse in saliva followed by swallowing.[3] Some drugs are absorbed from the mouth, pharynx, and esophagus as the saliva passes down into the stomach. In these cases, the bioavailability of drugs is significantly greater than those observed from conventional dosage forms due to pregastric absorption of drug dispersed in saliva .[4, 6] The highest priority of any drug delivery system is to successfully deliver the drug in the body to improve patient compliance and MDTs are no exception.[3]

Pharmaceutical marketing also has an impact on the increased demand for fast dissolving/disintegrating tablet products. As the patent ends for a drug entity, it is quite obvious for the pharmaceutical manufacturers to launch a new and improved dosage form of the existing drug entity. It empowers the manufacturer to extend market exclusivity and increased revenue while gifting its patient population with a more convenient dosage form or dosing regimen.[7]

The simplest strategy to achieve the target is the employment of superdisintegrants in the orodispersible tablet formulations. Superdisintegrants have the property to absorb a large amount of water which disintegrates the tablet within seconds. The mechanism of action of superdisintegrants is either swelling or porosity and capillary action or deformation.[7]

Allergic rhinitis (AR) is an inflammatory disorder of the nose induced by Immunoglobulin E (IgE) in the membrane lining of the nose due to allergen exposure such as pollen, dust mites, animal dander, and mould species. Allergic patients some time resist against allergens due to the development IgE antibodies against allergens. The quality of life in case of an individual suffering from AR is considerably reduced due to impaired performance of daily activities, cognitive function amd classroom productivity as well as reduced psychological wellbeing. Poorly treated or untreated AR individual may produce other serious consequences like bronchitis, asthama, sinusitis, or some time infections in ear. Moreover, AR may produce a significant economic burden on the healthcare system as a result of delays in recovery or increased medical care.[8,9]

The H1 antihistaminic is a class of drugs that are used as a major choice of drug to prevent or treat the symptoms associated with allergic reactions. The H1 antagonists are inactive in some severe allergic reactions like bronchial asthma that involves many mediators. In such cases other class of drug like antileukotriene in combination with other drugs are used to treat or to maintenance of asthma or symptoms associated with seasonal allergies. 10 Katzung

Levocetirizine is available as levocetirizine dihydrochloride, is a third-generation non-sedative antihistamine. It is the R- enantiomer of second generation antihistaminic cetirizine. Levocetirizine acts on histaminic receptors and block them. It inhibits the binding of histamine form its receptors rather than inhibiting histamine release from the mast cell. This, in turn, inhibits the release of other allergens as well as enhances blood supply to the affected area, and thus gives relief from the symptoms associated with hay fever. Therefore, It is used to treat the upper respiratory tract allergies, pollinosis, urticaria , atopic dermatitis as well as used as an adjuvant in seasonal asthma.[11]

Montelukast is a leukotriene receptor antagonist (LTRA) that acts by blocking the action of leukotriene D4 on the cycteinyl leukotriene receptor CysLT1 of lungs and bronchial tubes. It is used to treat or maintenance of bronchial asthma and to relieve symptoms of seasonal allergies. It is usually given orally.[12]

A combination of both drugs (levocetirizine + montelukast) is available to treat the sneezing and runny nose due to allergic reactions.

So, in the light of above facts, the main aim of the study is the formulation and evaluation of fast dissolving tablet (FDT) of Levocetirizine Dihydrochloride in combination with Montelukast Sodium. The developed formulation is expected to provide quick relief from “Allergic rhinitis" in the pediatric population. Developed formulation will disintegrate quickly and helps to improve clinical effects through pre-gastric absorption, increase in bioavailability of the drug and fast onset of action. To reduce bitterness of levocetirizine taste, ion exchange resin complex is prepared to mask its bitter taste. To improve the disintegration of FDT, single or combo superdisintegrants will be used.

## Materials and Methods

### Materials

Levocetrizine HCL and Montelukast Sodium were obtained from Paranami drug Pvt Ltd. (Ankleshwar, Gujarat, India) and Matrix Laboratories Limited, (Hyderabad, Telengana, India) respectively as gift sample. Croscarmellose sodium and Talc were obtained from Signet chemicals coprporation Ltd., (Mumbai, Maharastra, India). Microcrystalline cellulose and Magnesium stearate were procured from Albert David Ltd., (Kolkata, WestBengal, India). Kyron T-114 and Crospovidone were purchased from Corel Pharmaceutical Ltd., (Uttarakhand, India) and Aurobindo Pharma (Hyderabad, Telengana, India) respectively. Colloidal Silicon Dioxide and Mannitol was purchased from Sigma-Aldrich (New Delhi, India). Methanol used was of HPLC grade while other solvents and chemicals used were of analytical grade.

### Methods

#### *Instrumentation*

Chromatographic separation was carried out using HPLC (Jasco, Japan) system incorporated with a UV 2075 plus UV/VIS detector and Jasco PU-2080 pump. The data was collected

and processed by Jasco Borwin version (1.5, LC- Net II/ADC System) software. A C-18 Cosmosil packed coloumn (5 C 18 –MS, 250 mm X4.6mm with particle size of 5.0 µm) monitored at 40°C was used for the separation. The mobile phase was methanol: buffer (pH-1.2) (60:40, v/v) at a flow rate of 1.0 mL/min with detection at 290 nm.

Syringe filters (Syringe-driven filters of 0.22 µm, HiMedia Laboratories,Mumbai, India) were utilized for filtration of samples.

### HPLC method for estimation of LEV and MON in formulation

A 10 µg/mL solution of Levocetirizine Dihydrochloride was prepared in methanol. It was scanned at wavelength from 200-400 nm using a UV spectrophotometer.

The same procedure was followed for Montelukast Sodium. The curves obtained were overlapping. Therefore, isobestic point was estimated and employed as λ max for simultaneous estimation of Levocetirizine Dihydrochloride and Montelukast Sodium drugs by HPLC method.

### Preparation of calibration curve using HPLC method

Working standard solutions of LEV and MON were prepared accordingly and injected into the HPLC system at predetermined chromatographic conditions. Linear calibration curve were generated employing least square linear regression analysis by plotting the peak area against concentration of each drug solution. Different calibration curves were plotted for Levocetirizine Dihydrochloride and Montelukast Sodium.[13]

### Preparation of drug resin complex by batch method

Taste masking was done by complexing LEV with Kyron T-114 in different ratios 1:1, 1:2, 1:3, 1:4. Drug- resin complex were optimized by considering parameters such as optimization of resin concentration, optimization of swelling time, optimization of pH and optimization of temperature on maximum drug loading.

### Procedure

The resins were first washed with distilled water till neutralization. Variable amount of resin was placed in a beaker containing 25 mL of deionised water and allowed to swell for variable. Accurately weighed 100 mg of LEV was added to the resin solution and stirred for 4-5 hour. The mixture was filtered through whatman filter paper no. 41 and residue was washed with 75 mL of deionised water and drug loading was calculated.

### Optimization of concentration of resin on drug loading

An accurately weighed 100mg of LEV was added to the different concentration of Kyron T-114 100, 200, 300, 400 mg, the best ratio show maximum adsorption of drug was considered optimized ratio which show maximum drug loading Amount of maximum drug loading was determined at 231 nm by UV spectroscopy.

### Optimization of swelling time on drug loading

Separate batches of Kyron T-114 were soaked in 25 ml of deionised water contained in a beaker for 10, 20, 30, 40, 50, 60, 90 and 120 minutes. The complexation in batch process was performed and the loading efficiency with resin swollen at different time was determined.

### Optimization of pH on drug loading

A series of solutions were prepared which contained fixed quantity of pretreated resin Kyron T-114 (300mg) in deionised water and 100mg of LEV. The pH of the solutions was maintained at 3, 3.5, 4, 4.5, and 5. The solution along with drug and resin was stirred at a magnetic stirrer for 45min.The resinate was collected by filtration and washed with copious amount of deionised water to remove free and uncomplexed drug, followed by drying at 50°C. Drug content was determined as mentioned previously.[14]

### Formulation of ODT Tablet by direct compression

The tablet consists of drug-resin complex, and mannitol was selected as directly compressible material. Croscarmellose sodium (CCS) and Crospovidone were selected as super disintegrant, talc as antiadherent to aid flow, magnesium stearate as lubricant, microcrystalline cellulose as diluent. As show in Table 1, Batch F1 to F6 indicates formulation containing crospovidone and CCS (Croscarmellose sodium) as a superdisintegrants respectively. APIs and all the excipients were weighted in required quantity and passed through 40# sieve to achieve uniform particle size. Powder material (after dry mixing) was compressed to prepare ODT by using punch size 8.0 mm round, flat, one side scored in single punch machine.

### Characterization of formulated ODTs

Powder blends were characterized for parameters such as angle of repose, bulk & tapped density, hausner ratio and carr's index. Table 2 gives a glimpse of the evaluation studies conducted along with the procedure and instrument used.[15,16]

### *In-vivo* taste evaluation

The study was performed on 6 healthy human volunteers, from whom informed consent was first obtained. Drug resin complex equivalent to 2.5 mg LEV was held in the mouth for 180 seconds, and then spat out. The mouth was rinsed with water without swallowing the disintegrated material and, finally, the bitterness levels were recorded on a numerical scale ranging from 0 to 3 where 0, 0.5, 1, 2, and 3 indicate no, threshold, slight, moderate, and strong bitterness, respectively. For ODTs, one tablet containing 2.5 mg LEV and 4 mg MON was held in the mouth until complete

**Table1:** Design of formulations

| *Name of ingredients* | *Formulation code Quantity (in mg)* | | | | | |
|---|---|---|---|---|---|---|
| | *F1* | *F2* | *F3* | *F4* | *F5* | *F6* |
| Montelukast Sodium | 4 | 4 | 4 | 4 | 4 | 4 |
| Levocetirizine Dihydrochloride | 2.5 | 2.5 | 2.5 | 2.5 | 2.5 | 2.5 |
| Kyron T-114 | 7.5 | 7.5 | 7.5 | 7.5 | 7.5 | 7.5 |
| Croscarmellose sodium | 6 | 0 | 3 | 4 | 5 | 1 |
| Crospovidone | 0 | 6 | 3 | 2 | 1 | 5 |
| MCC PH (102) | 20 | 20 | 20 | 20 | 20 | 20 |
| Aspartame | 2.6 | 2.6 | 2.6 | 2.6 | 2.6 | 2.6 |
| Talcum | 2 | 2 | 2 | 2 | 2 | 2 |
| Magnesium stearate | 2 | 2 | 2 | 2 | 2 | 2 |
| Vanilla dry | 2 | 2 | 2 | 2 | 2 | 2 |
| Iron Oxide | 0.4 | 0.4 | 0.4 | 0.4 | 0.4 | 0.4 |
| Mannitol | 131 | 131 | 131 | 131 | 131 | 131 |
| Total | 180 | 180 | 180 | 180 | 180 | 180 |

**Table 2:** Details of Evaluation Parameters for characterization of formulated tablets.

| *S.No.* | *Evaluation Parameter* | *Procedure* |
|---|---|---|
| 1. | General Appearance | Tablet's size, shape, color, surface texture were evaluated |
| 2. | Uniformity of weight | Twenty tablets were taken and their weight was determined individually. The average weight of one tablet was determined. |
| 3. | Disintegration time | Sample- 6 Tablets<br>Disintegration apparatus-<br>Media- Water at 370C ± 20C<br>Time in second taken for complete disintegration of the tablet with no palpable mass remaining was measured. |
| 4. | Wetting Time | A piece of tissue paper (12 cm X 10.75 cm) folded twice was placed in a small Petridish (ID = 6.5 cm) containing water.<br>A tablet was put on the paper, and the time for<br>complete wetting was measured |
| 5. | Friability | Instrument- Roche friabilator<br>Preweighed tablets were placed in the<br>friabilator that revolves at 25 rpm, dropping those<br>tablets at a distance of 6 inches with each revolution. Tablets were rotated for 4 Min and reweighed. |
| 6 | Tablet hardness | Instrument- Pfizer/Monsanto Hardness tester.<br>Hardness is defined as the force applied across the diameter of the tablet in the order to break the tablet. |
| 7 | Content uniformity | 20 tablets were weighed accurately and crushed, tablet powder equivalent to 5 mg of LEV and 8 mg MON was taken in a 100 ml volumetric flask and diluted with mixture of methanol and acidic buffer (60: 40 v/v) and filtered. The filtrate was made up to 100 ml with mobile phase and further dilutions were made to get a concentration of 10 µg/ml of LEV and 16 µg/ml of MON. The resulted solution was used for the estimation by HPLC in the optimized chromatographic conditions. |
| 8 | In-vitro dissolution studies | Instrument- USP II paddle method<br>Dissolution media- 900 ml of 0.1 N HCl at 37±0.50C.<br>5 ml aliquots was withdrawn at the specified time intervals, filtered and assayed by HPLC. Same procedure repeated by taken phosphate buffer<br>pH 6.8 as dissolution media. |

disintegration. Bitterness was recorded immediately and at several intervals for 3 minutes according to the bitterness intensity scale from 0 to 3 where 0, 0.5, 1, 2, and 3 indicate no, threshold, slight, moderate, & strong bitterness and while + sign show palatability. After the study mouth was rinsed well with water.[17,18]

### Reproducibility

To prove the reproducibility of manufacture, the tablets of the optimized batch were manufactured. However, the batch size was increased from 50 to 100 tablets. The tablets were evaluated for dissolution as the rest of the parameters were proved to be reproducible and compared with tablets of the earlier batch.

### Comparison with marketed product

Conventional tablets are taken for comparison. These tablets were subjected to the evaluation of physical properties including drug release pattern. The details are as follows:

- Brand name: ALVOMONT-LC KID TAB
- Company name: Ravenmac Pharmaceuticals Pvt Ltd
- Labelled claim: 2.5 mg Levocetirizine dihydrochloride and 4 mg Montelukast Sodium

### Accelerated stability studies

The stability of optimized formulation was tested according to international conference on harmonization guideline for Zone III and IV. The formulation was stored at accelerated ($40^0 \pm 2^oC/75\% \pm 5\%$ RH) condition wrapped in aluminum foils and kept in at humidity chamber. The stability studies were conducted. Tablet were tested at interval of 10 day till 1 month for physical appearance, DT, hardness, friability, thickness, drug content, and drug release.

## Results and Discussions

### Preparation of calibration curve using HPLC method

LEV and MON, Both displayed linearity in a concentration range of 2-20 µg/ml. LEV showed a straight line equation y=798 x- 15.2 with $R^2$ value of 0.999 whereas MON ehibhited a linear equation y=1233x+132.6 with $R^2$ value of 0.999 (Fig. 1 and 2).

### HPLC chromatogram of LEV and MON

LEV and MON displayed a peak at retention time 4.308 and 7.408 respectively in both standard and sample mixtures (Fig. 3 and 4).

### Drug-excipients interaction

#### *IR Spectroscopy*

The FTIR (Fourier transmission Infrared) spectroscopy study of LEV, LEV-Kyron T114 mixture, MON, physical mixture of LEV, MON, Kyron T- 114 & other excipients were carried out to perform the compatibility studies. (Figs 5–8 )

The spectra indicated that there was no drug-drug and drug-excipients interaction as the peaks of the drug and other excipients were the same in the drug-excipients mixture indicating that the drug molecule was present in an unchanged state in the formulation (Table 3).

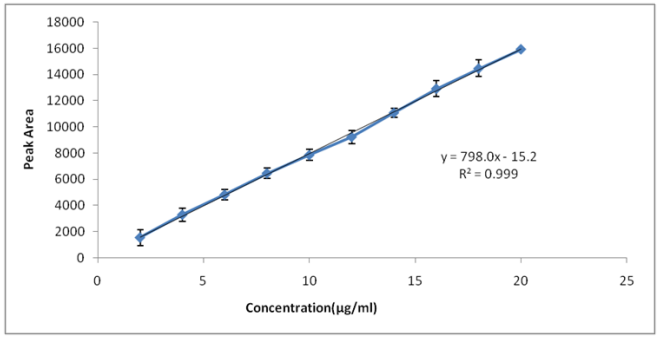


**Fig . 1:** Calibration Curve of LEV in methanol for HPLC

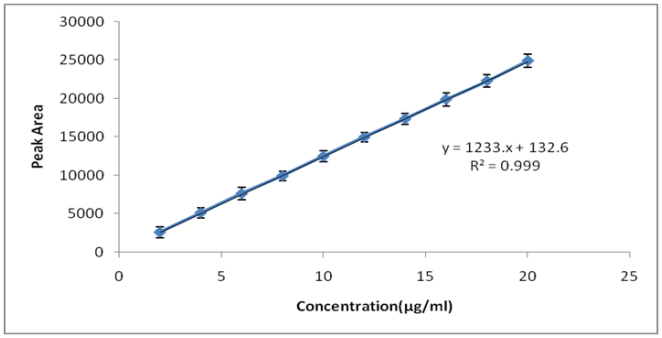


**Fig. 2:** Calibration Curve of MON in methanol for HPLC

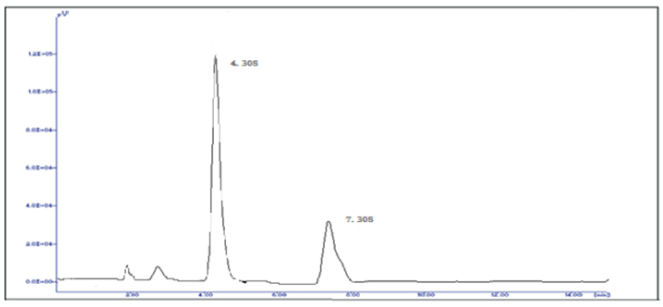


**Fig. 3:** HPLC chromatogram of Standard drug solution of LEV and MON

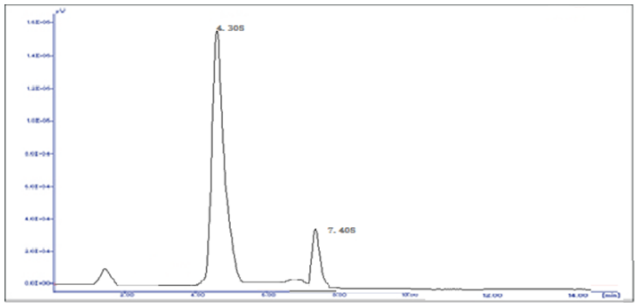


**Fig. 4.:** HPLC chromatogram of Sample drug solution of LEV and MON

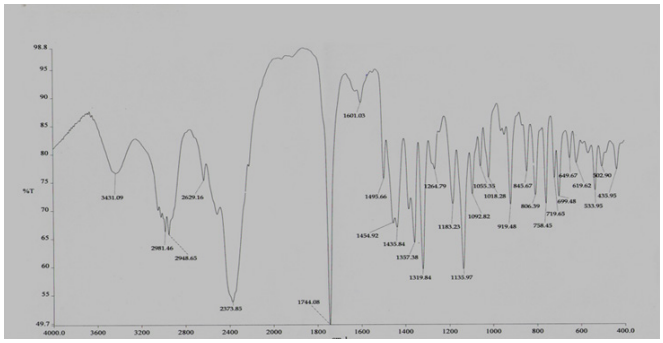

**Fig. 5 :** FTIR spectrum of Levocetirizine dihydrochloride

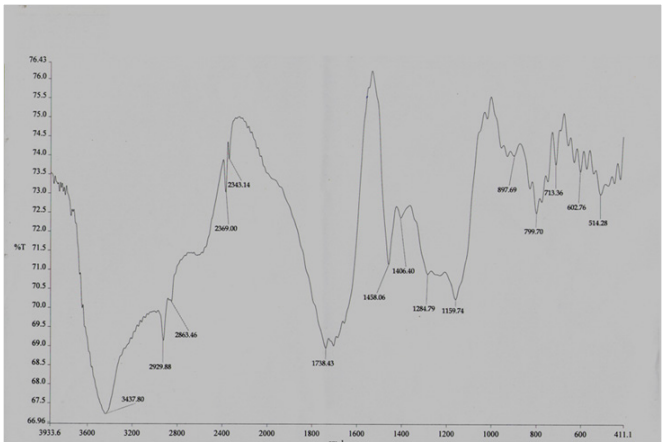

**Fig. 6 :** FTIR spectrum of Levocetirizine dihydrochloride and Kyron T-114

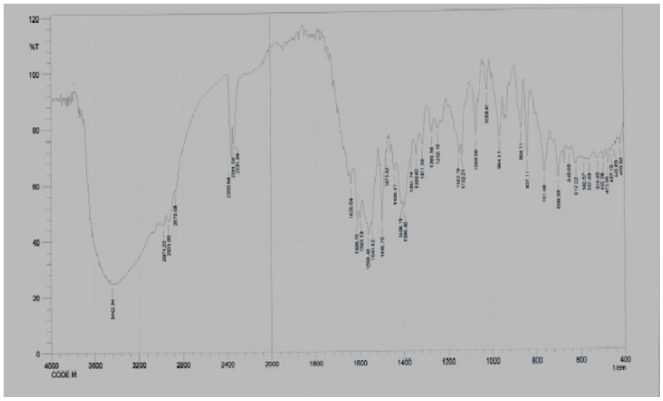

**Fig. 7:** FTIR spectrum of Montelukast sodium

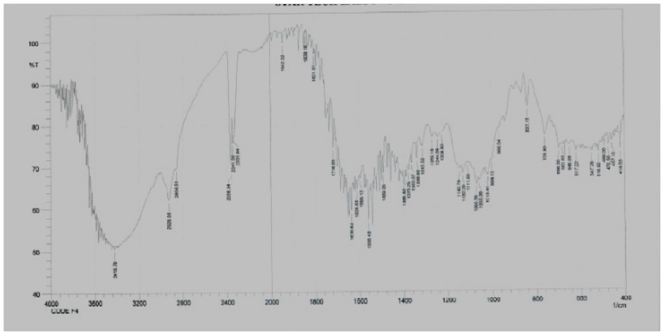

**Fig. 8:** FTIR spectrum of optimized formulation (F4)

## Pre-compression evaluation

### *Optimization of various conditions for maximum drug loading*

Drug-loading process was optimized by considering parameters like optimization of resin concentration, swelling time & pH as shown in Tables 4–6 and Figs 9–11 respectively. It was found that optimum drug loading was achieved at pH 4.0 and decreased at pH higher than this. It was studied that with increase in swelling time resins showed an increase in drug loading capacity. There occurs a surge in the rate and extent of ion exchange process due to swelling. In unswollen state, the exchangeable groups in resins are hidden and stay in coiled form towards their backbone. Swelling and hydration increases the surface area and let these groups exposed to outside.

### Micromeritic properties of powder blends

Powder blends were prepared for all six formulations by mixing all material together. Powder blends which were prepared, under gone for pre-compression parameter evaluation for determining flow related properties like angle of repose, bulk density, tapped density, compressibility index and Hausner ratio. The bulk density of powder blends was found in the range of 0.50–0.59 g/cm$^3$. The value of Hausner ratio lies in the range of 1.135-1.237. From the studies it was concluded that all prepared powder blend batches possessed good flow and compressibility property. The results of precompression properties are displayed in Table 7.

### Post compression evaluation

Formulation were gone under post-compression parameter evaluation like thickness, /weight variation, disintegration time, wetting time, friability, tablet hardness. Results (Table 8) showed that thickness lies in range of 2.43 to 2.53 mm and variations are within acceptable range. Hardness of tablets ranged from 3.4 to 3.6 kg/cm$^2$. The loss in friability varied in the range between 0.65 to 0.80 %. The water absorption ratio of the formulations was found to be between 76.41 to 87.23 %. This was found to be highest in F4 formulation while the wetting time was least for F4 i.e. 20.4 sec. This was certainly due to high water absorbing capacity.

### Uniformity of drug content

The drug content for LEV was found to be in range of 99.04 to 101.26% whereas for MON the value lied between 98.59 to 100.77%. The values were within the acceptable range. The result indicates that there is good uniformity in drug content among all the formulations formed.

**Table 3:** Interpretation of IR Spectras

| *SR. No.* | *IR Spectrum* | *Peaks $cm^{-1}$* | *Groups* | *Stretching / Deformation* |
|---|---|---|---|---|
| 1 | LEV | 758, 804, 847 | - Cl | Stretching |
| | | 2890 | -C-H ar | Stretching |
| | | 1362 | -C-N | Stretching |
| | | 1742 | -COO ar | Stretching |
| | | 1134 | -C-O | Stretching |
| 2 | Physical mixture of LEV and Kyron T- 114 | 705, 758, 804 | - Cl | Stretching |
| | | 2944 | -C-H | Stretching |
| | | 1359, 1390 | -C-N | Stretching |
| | | 1741 | -COO ar | Stretching |
| | | 3373 | -OH | Stretching |
| 3 | MON | 2900-3000 | C-H aromatic | Stretching |
| | | 1700 | -COOH | Stretching |
| | | 3300 | -OH | Stretching |
| 4 | Physical mixture of LEV, MON, Kyron T- 114 & other excipients | 723, 770, 830 | - Cl | Stretching |
| | | 2922 | -C-H ar | Stretching |
| | | 1375 | -C-N | Stretching |
| | | 1745 | -COO ar | Stretching |
| | | 1150 | -C-O | Stretching |

**Table 4:** Effect of resin concentration on % drug loading

| *Resin* | *Code* | *Drug + Resin ratio* | *% of Drug Loading* |
|---|---|---|---|
| Kyron T-114 | A1 | 1:1 | 77.20 ± 3.5 |
| | A2 | 1:2 | 86.30 ± 4.5 |
| | A3 | 1:3 | 91.18 ± 3.7 |
| | A4 | 1:4 | 90.05 ± 6.7 |

**Table 5:** Effect of swelling time on % drug loading

| *Resin* | *Ratio* | *Swelling time (Min)* | *% of Drug Loading* |
|---|---|---|---|
| Kyron T-114 | 1:3 | 10 | 69.50 ± 5.5 |
| | | 20 | 72.81± 4.5 |
| | | 30 | 79.48 ± 4.7 |
| | | 60 | 87.72 ± 6.7 |
| | | 90 | 94.97 ± 4.2 |
| | | 120 | 91.13 ± 4.3 |

**Table 6:** Effect of pH on % drug loading

| *Resin* | *Ratio* | *pH* | *% of Drug Loading* |
|---|---|---|---|
| Kyron T-114 | 1:3 | 1 | 60 ± 3.8 |
| | | 2 | 82 ± 4.2 |
| | | 3 | 92 ± 4.8 |
| | | 4 | 96 ± 2.7 |
| | | 5 | 90 ± 3.9 |
| | | 6 | 84 ± 4.1 |

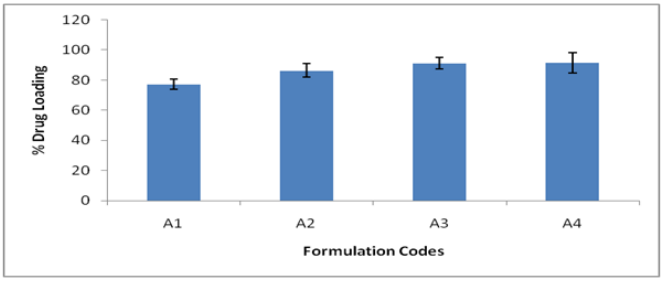


**Fig. 9. Effect of resin concentration on % drug loading**

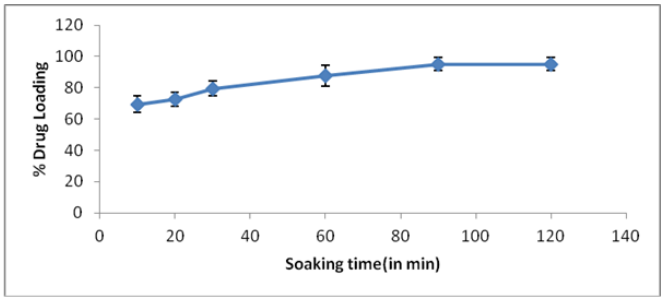


**Fig. 10:** Effect of soaking Time on % Drug loading

## *In-vitro* disintegration time

The disintegration time of all the formulations were found in range from 27.82 to 51.7 sec (Table 9). F4 batch exhibit the least disintegration time.

## *In-vitro* drug release

The results of *in-vitro* drug release are shown in Fig 12 and13. A dissolution study is essential for ensuring drug release and the reproducibility of the rate and the duration of drug release. The result showed that the cumulative % drug

**Table 7:** Results of micromeritic properties

| Properties ↓ / Formulation → | F1 | F2 | F3 | F4 | F5 | F6 |
|---|---|---|---|---|---|---|
| Angle of repose | 30.64 | 31.45 | 24.68 | 23.82 | 23.49 | 30.05 |
| Bulk density | 0.58 | 0.59 | 0.55 | 0.52 | 0.50 | 0.58 |
| Tapped density | 0.71 | 0.73 | 0.64 | 0.59 | 0.55 | 0.70 |
| Hausner ratio | 1.224 | 1.237 | 1.164 | 1.135 | 1.140 | 1.207 |
| % compressibility | 18.31 | 19.18 | 14.06 | 11.86 | 12.28 | 17.14 |

**Table 8:** Results of post compression evaluation

| Properties ↓ / Formulation → | F1 | F2 | F3 | F4 | F5 | F6 |
|---|---|---|---|---|---|---|
| Thickness (mm) | 2.5 ± 0.17 | 2.43±0.19 | 2.56±0.15 | 2.46± 0.18 | 2.5±0.16 | 2.53±0.16 |
| Hardness (kg/cm2) | 3.6 ± 0.65 | 3.5± 0.67 | 3.5± 0.57 | 3.5± 0.43 | 3.6± 0.63 | 3.4± 0.71 |
| (%) Friability | 0.65± 0.071 | 0.66±0.068 | 0.78±0.053 | 0.79± 0.034 | 0.80±0.046 | 0.69±0.04 |
| Weight Variation | 218.4±0.84 | 219.0 ± 0.33 | 219.65± 0.42 | 219.63 ± 0.56 | 220.1± 0.63 | 220.42± 0.25 |
| Water absorption ratio (%) | 78.46± 0.895 | 78.34±0.886 | 83.17±0.767 | 87.23±0.730 | 80.53±0.923 | 76.41±0.780 |
| Wetting Time (sec) | 36.7 ± 0.435 | 30.1± 0.354 | 26.3± 0.532 | 20.4± 0.301 | 27.4± 0.423 | 46.8±0.463 |

**Table 9:** Results of Content uniformity and in vitro disintegration time

| Formulation Batch | Content Uniformity LEV (%) | Content Uniformity MON (%) | In-vitro disintegration time (sec) |
|---|---|---|---|
| F1 | 100.26± 0.25 | 100.77± 0.27 | 35.5± 0.42 |
| F2 | 99.89± 0.37 | 99.77± 0.40 | 30.3± 0.52 |
| F3 | 99.76±0.34 | 99.47±0.35 | 30.6± 0.57 |
| F4 | 100.52±0.15 | 100.21± 0.19 | 29.82± 0.47 |
| F5 | 99.42± 0.47 | 99.02±0.36 | 32.6± 0.61 |
| F6 | 99.04±0.36 | 98.59± 0.31 | 51.7±0.64 |

releases of the ODTs were found in range of 60.84 % to 99.28% for LEV & 60.24 to 99.81% for MON. The highest drug release was obtained with the formulation F4 containing croscarmellose sodium and crospovidone in ratio of 4:2 respectively.

After all the observations, formulation F4 was selected as optimized formulation and further tested for stability.

### Comparison with marketed formulation

Formulation F4 was compared with marked formulation on the basis of evaluation parameters. By studying the in-vitro release profile it was concluded that formulation F4 showed more than 99.81% drug release within 6 minutes while marketed product exhibited 65.82% drug release at the same time, and nearly 98% drug release within 9 minutes (Fig. 14). The results indicate that the prepared tablets (Formulation F4) could improve bioavailability.

### *In-vivo* taste evaluation

The scale of bitterness is represented in Table 10.All the human volunteers experienced bitter taste (score 3) up to 180 sec with pure drug, but with drug resin complex degree of bitterness was from 0 to 0.2 (which was less than threshold score). Taste evaluation of optimized tablet showed a good mouth feel with minimum grittiness. Formulated ODT was found to be palatable after 180 sec.

### Stability study

Stability study of F4 was done for 1 month. Sample was taken on 10 days interval till 1 month, then evaluated for propertied like hardness, disintegration time, uniformity of drug content and in-vitro release of drugs. Study suggested that all parameters were identical as initial (at time 0) indicating a stable formulation.

## FUTURE ASPECTS

Fast dissolving tablets inherit various biopharmaceutical advantages such as improved efficiency, effective at low dose of API, superior absorption profiles and improved bioavailability then conventional dosage forms. In spite of these attributes, there is still room for improvement. The

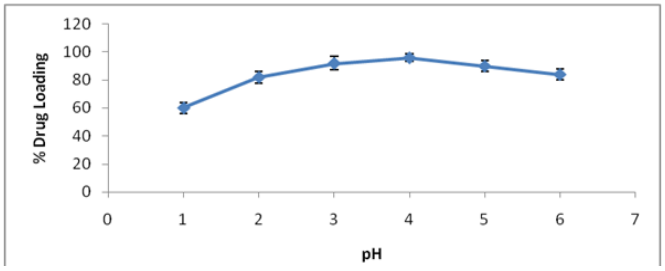


**Fig. 11:** Effect of pH on % drug loading

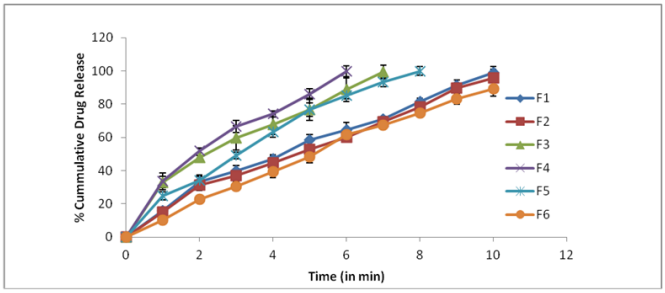


**Fig 12 :** Dissolution profile of LEV formulations in 0.1N HCl

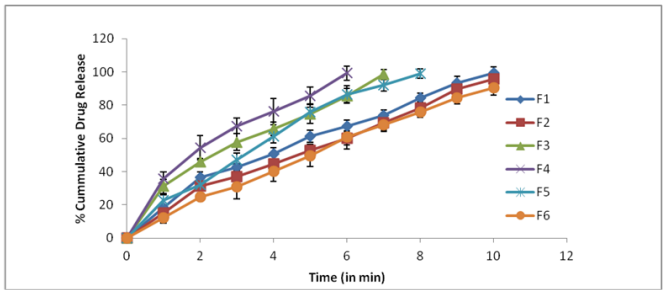


**Fig 13:** Dissolution profile of MON formulations in 0.1N HCl

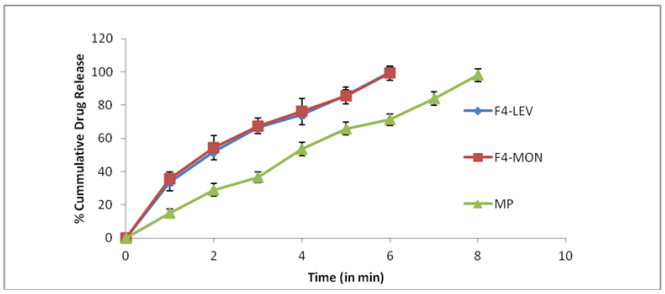


**Fig. 14 Comparison of F4 formulation with marketed preparation**

**Table 10**: Comparative taste evaluation

| *Form of LEV* | *Degree of bitterness after time* | | | | | |
|---|---|---|---|---|---|---|
| | 10 sec | 30 sec | 60 sec | 90 sec | 120 sec | 180 sec |
| Pure LEV | 3 | 3 | 3 | 3 | 3 | 3 |
| LEV-resin complex | 0 | 0.2 | 0.2 | 0.1 | 0 | 0 |
| Formulated ODT | 0 | 0.1 | 0.1 | 0 | 0+ | 0+ |

admissible disintegration time of less than 60 sec for FDTs still have a scope of refinement taking into consideration, the other related formulation attributes. We have still to optimize various characteristics, such as tablet hardness, friability and stability to a mark that MDTs can be packaged and transported in conventional bottles. Despite numerous advancements, FDTs formulation with controlled release mechanism and formulations of hydrophobic drugs with high dose is still a challenge. Strategies should be invented to incorporate large doses of hydrophobic drugs without compromising the fast disintegrating property. It would be a great achievement, if APIs having short half lives can deliver drug for 12-24 h. The combination of abovementioned will be a master stroke with regards to convenience and compliance. Generally, FDTs require large amount of excipients and formulations with large doses will make it difficult to handle. Formulation with fewer excipients will be a major turning point in FDT Technology. By roping in new technologies like Zydis, Wow Tab, Flashtab etc., our aim should be targeting patents. We should also, keep an eye on new market strategies to grab a large chunk of market share and establish orodispersible tablet as a frontline choice of acceptance.

## Conclusion

Levocetirizine Dihydrochloride and montelukast sodium orodispersible tablets were successfully formulated exclusively for pediatrics. . It was found that LEV and MON exhibit maximum absorption at wavelength 231 nm and 350 nm respectively. The IR spectra's revealed that, polymers and excipients used were compatible with drug. The taste masking of bitter drug LEV was successfully achieved by drug-resin complex (Kyron T-114). The Orodispersible tablets were formulated using Crospovidone, Croscarmellose sodium as superdisintegrants by direct compression technique. The powder blend was evaluated for precompression parameters whereas compressed tablets were evaluated for formulation parameters. Flow properties – Angle of repose, loose bulk density, tapped density and also % Carr's compressibility was determined to all the formulations which showed good flow property. All the formulations passed the hardness (3.415± 0.71 to 3.6 ± 0.65 Kg/m2) and friability (0.65 ± 0.071 to 0.80±0.046 %) test indicating mechanical stability.

The disintegration time and wetting time for all the formulations was found to be less than 54 sec and 34 seconds respectively, indicating rapid disintegration. Water absorption ratio showed good absorptivity in all

formulations. Percentage weight variation (218.4± 0.84 to 220.42± 0.25) and drug content uniformity for LEV (99.04 to 101.26%) and MON (98.59 to 100.77%) was also found to be within acceptable range. All the formulations evaluated for in-vitro drug release displayed approximately 100% drug released within 10 min. Best-selected formulation was F4 on the basis of disintegration time (29.82 sec) and in vitro drug release of both drugs (99.81% release of LEV within 6 min & 99.28% release of MON within 6 min).Further, stability studies were conducted for formulations F4 at 40°C ±2°C/75% RH ±5% for 30 days. Various parameters like hardness, friability, drug content uniformity, in vitro disintegration, wetting time were analyzed at a time interval of 10 days till a period of 30 days. Not much variation or change was observed in any parameters throughout the study period. F4 was also found to be stable. The prepared orodispersible tablets disintegrate within seconds without need of water and enhance the absorption; this may lead to increased bioavailability of LEV as well as MON. But still there is scope of improvement and refinement to get superior drug release profiles for other population groups also.

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