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# FORMULATION AND *INVITRO* EVALUATION OF MOUTH DISINTEGRATING TABLETS OF MONTELUKAST AND DESLORATADINE

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**ABSTRACT**

Montelukast sodium is a leukotriene receptor antagonist, used in the treatment of asthma and Desloratadine is a drug used to treat allergies. The combination formulation is used for the treatment of allergic rhinitis, chronic urticaria. The aim of the present study is to Formulate and evaluate the oral disintegrating tablets of Montelukast sodium and Desloratadine. ODTs were prepared by direct compression method and by using crospovidone, croscarmellose sodium and sodium starch glycollate as superdisintegrants which disintegrates in matter of seconds in the oral cavity, thereby reducing the time of onset of pharmacological action and to reduce the first pass metabolism . Magnesium stearate was used as a lubricant, aspartame as sweetener and orange flavour is used to improve mouth feel.

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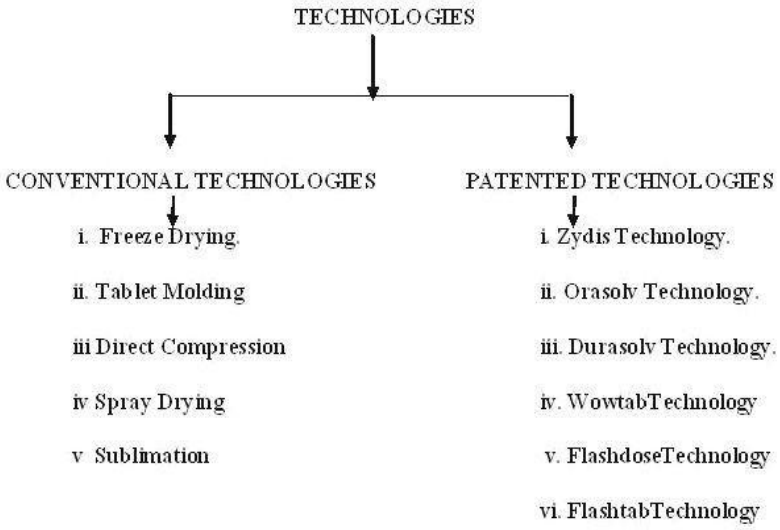
## INTRODUCTION

Orally disintegrating tablets are also called as oral dispersible tablets[1,2]., quick disintegrating tablets, mouth dissolving tablets, fast disintegrating tablets, fast dissolving tablets, rapid dissolving tablets, porous tablets, and rapimelts [3]. However, of all the above terms, United States pharmacopoeia (USP) approved these dosage forms as ODTs. Recently, European Pharmacopoeia has used the term orodispersible tablet for tablets that disperses readily and within 3 min in mouth before swallowing.

**Techniques Used in the Preparation of Fast Dissolving Drug Delivery System:**

Various technologies used in the manufacture of Fast dissolving tablets include:




## MATERIALS AND METHODS:

Montelukast sodium & Desloratadine, Avicel PH102, Mannitol(cyclose), Crospovidone, Aspartame, Cross carmellose sodium, Sodium starch glycollate, Aerosil, Orange flavor, Mondeslor.

**Formulation of Montelukast sodium & Desloratadine MDTs:**

In direct compression method the amount of active ingredient Montelukast sodium & Desloratadine were taken and cross povidone, cross caramellose sodium, sodium starch glycollate were used as super disintegrants, MCC was used as a diluent and sweetening agent like aspartame were passed through the sieve no.40. These ingredients were mixed well for 5 min after that lubricants such as Magnesium stearate is added to the above blend [4]. Then it was transferred for compression[5]. The efficiency of mixing was verified by the determination of percentage purity. percentage purity.

**Table-1: Formulations for Montelukast sodium &Desloratidine oral disintegrating tablets.**

| S.NO | INGREDIENTS | QUANTITY OF INGREDIENTS(mg) | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 | F10 | F11 |
| 1. | Montelukast sodium | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| 2. | Desloratadine | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| 3. | Sodiumstarch glycolate | 2 | 4 | 6 | 8 | - | - | - | - | - | - | - |
| 4. | Crosscarmellose sodium | - | - | - | - | 4 | 6 | 8 | - | - | - | - |
| 5. | Crospovidone | - | - | - | - | - | - | - | 2 | 4 | 6 | 8 |
| 6. | MCC Ph 102 | 158 | 156 | 154 | 152 | 156 | 154 | 152 | 158 | 156 | 154 | 152 |
| 7. | Mannitol(cyclosel) | 20.0 | 20.0 | 20.0 | 20.0 | 20.0 | 20.0 | 20.0 | 20.0 | 20.0 | 20.0 | 20.0 |
| 8. | Sillicon dioxide | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 |
| 9. | Aspartame | 4.0 | 4.0 | 4.0 | 4.0 | 4.0 | 4.0 | 4.0 | 4.0 | 4.0 | 4.0 | 4.0 |
| 10. | Magnesium stearate | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 |
| 11. | Orange flavor | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 |

**Pre-compression properties:**

**Bulk density: -**

Bulk density was determined by pouring gently 25 gm of sample into 100 ml graduated cylinder. The volume occupied by the sample was recorded [6]. Bulk density was calculated as:

***Bulk density* = weight of sample in gram /volume occupied by the sample**

**Tapped density: -**

Tapped density was determined by using Electro lab density tester, which consists of a graduated cylinder mounted on a mechanical tapping device[7]. The Volume was noted and tapped density is calculated using following Formula:

**Tapped density = Wt. of sample in gm / Tapped volume**

**Compressibility Index and Hausner ratio: -**

Both the compressibility index and the Hausner ratio were determined by using bulk density and the tapped density of a powder [8].
density

**Carr'sindex = Tapped density- Bulk density/ Tapped×100**

**Hausner's Ratio=Tapped density (ρt) / Bulk density (ρb)**

**Angle of Response: -**

The angle of repose has been used to characterize the flow properties of solids [9]. Angle of repose is a characteristic related to inter particulate friction or resistance to movement between particles[10]. This is the maximum angle possible between surface of pile of powder or granulesand the horizontal plane.

$$\text{Tan } \theta = h / r$$

$$\theta = \text{Tan}^{-1} h / r$$

Where$\theta$ = angle of repose,

$h = height, r = radius$

**Post compression parameters:**

**Thickness**

The thicknesses of the tablets were determined by using Vernier Caliper and the results were expressed in millimeter [11].

**Hardness test**

The hardness of tablet was measured by Pfizer hardness tester [12]. Ten tablets from the batch were used for hardness studies and resultsareexpressedinKg/cm2.

**Weight variation test:**

Ten tablets were selected at random, individually weighed in a single pan electronic balance and the average weight was calculated[13]. The uniformity of weight was determinedaccording to I.P specification.

**Friability test**

It was performed in Electro lab Friabilator apparatus. Pre weighed samples of 20 tablets were placed in the Friabilator, which is then operated for 100 revolutions[14]. The percent friability was calculated by using the formula:

**%F = 1- (loss in weight/ initial weight) 100**

**Disintegration:**

By using USP device which consists of six glass tubes that are 3inches long, open at one end and held against 10 mesh screen at the bottom end of basket rack assembly[15]. To test for disintegration time, one tablet is placed in each tube and the basket arch is positioned in 1 litre beaker of water at 37°c±2°c. A standard motor driven device is used to move the basket assembly up and down.

**Dissolution studies**

For dissolution of the Montelukast sodium and Desloratadine USP type II paddle type dissolution apparatus is used[16]. One tablet each were placed in each bowl and rotated at 50 rpm in 900ml of the dissolution medium (Distilled water at 37±0.50C) for 20 minutes and the time intervals for withdrawing the sample are 3,6,10,15,20. mins and was replaced with an equal amount of fresh medium, to maintain the constant volume of dissolution method throughout the experiment[17]. The samples were assayed by HPLC.

**RESULTS AND DISCUSSION:**

**Table-2: Pre-compression properties.**

| S.No. | Formulation code | Bulk density(gm/ml) | Tapped density(gm/ml) | Angle of repose | Carr's index (%) | Hausner's ratio |
|---|---|---|---|---|---|---|
| 1 | F1 | 0.674±0.004 | 0.780±0.003 | 27.43±0.47 | 13.5±0.04 | 1.157±0.004 |
| 2 | F2 | 0.686±0.006 | 0.787±0.001 | 24.72±0.43 | 12.8±0.06 | 1.147±0.003 |
| 3 | F3 | 0.694±0.003 | 0.796±0.004 | 24.20±0.52 | 12.8±0.07 | 1.146±0.004 |
| 4 | F4 | 0.697±0.005 | 0.803±0.003 | 22.30±0.25 | 13.2±0.03 | 1.152±0.005 |
| 5 | F5 | 0.652±0.003 | 0.760±0.006 | 27.67±0.54 | 14.2±0.02 | 1.165±0.002 |
| 6 | F6 | 0.666±0.004 | 0.774±0.004 | 25.59±0.29 | 13.9±0.04 | 1.162±0.002 |
| 7 | F7 | 0.681±0.002 | 0.793±0.007 | 24.30±0.28 | 14.1±0.03 | 1.164±0.003 |
| 8 | F8 | 0.626±0.007 | 0.724±0.004 | 28.72±0.33 | 13.5±0.01 | 1.156±0.001 |
| 9 | F9 | 0.647±0.005 | 0.743±0.001 | 24.20±0.54 | 12.9±0.05 | 1.148±0.004 |
| 10 | F10 | 0.656±0.003 | 0.753±0.002 | 23.43±0.48 | 12.8±0.06 | 1.147±0.003 |
| 11 | F11 | 0.664±0.002 | 0.768±0.005 | 24.67±0.51 | 13.5±0.01 | 1.156±0.002 |

**Table-3: Cumulative percent *in-vitro* drug release for Marketed formulation.**

| TIME(MINS) | CUMMULATIVE % DRUG RELEASED | |
|---|---|---|
| | DESLORATIDINE | MONTELUKAST SODIUM |
| 0 | 0 | 0 |
| 3 | 18.2±0.9 | 14.2±1.4 |
| 6 | 34.7±3.2 | 31.7±2.1 |
| 10 | 59.2±2.4 | 53.5±1.3 |
| 15 | 79.6±2.8 | 71.2±2.4 |
| 20 | 93.14±1.6 | 89.5±1.6 |

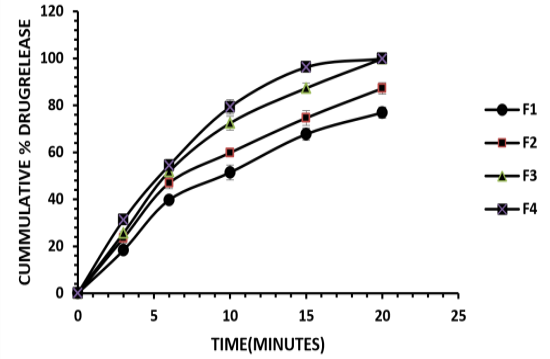
**Table-4: Cumulative percent *in-vitro* drug release of Desloratidine in different formulations.**

| TIME (MINS) | Cumulative percent drug release | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 | F10 | F11 |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 3 | 18.3±1.2 | 23.4±2.1 | 25.6±0.3 | 31.2±0.7 | 16.2±2.3 | 20.2±2.4 | 22.3±0.8 | 22.4±1.4 | 27.3±2.4 | 32.4±2.1 | 36.2±0.9 |
| 6 | 39.7±0.6 | 46.9±2.4 | 51.8±0.6 | 54.4±1.2 | 34.3±2.1 | 39.4±0.4 | 40.6±2.4 | 43.6±2.2 | 49.7±3.1 | 59.5±2.7 | 63.4±1.4 |
| 10 | 51.4±3.2 | 59.8±1.3 | 72.4±0.5 | 79.3±2.9 | 47.2±0.9 | 57.4±1.3 | 54.3±3.2 | 55.4±2.7 | 68.4±2.2 | 80.1±2.4 | 87.2±2.7 |
| 15 | 67.7±2.6 | 74.6±3.1 | 87.3±0.3 | 96.2±2.2 | 61.2±0.6 | 74.6±2.8 | 71.4±1.7 | 72.6±3.1 | 81.2±2.5 | 90.4±1.3 | 98.4±0.9 |
| 20 | 76.9±2.4 | 87.2±2.4 | 99.8±0.4 | 99.6±0.6 | 78.4±2.6 | 91.4±1.6 | 85.6±1.5 | 83.5±1.6 | 92.4±1.7 | 99.7±0.7 | 100.2±0.3 |

**Table-5: Cumulative percent drug release of Montelukast in different formulations.**

| TIME (MINS) | Cumulative percent drug release | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 | F10 | F11 |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 3 | 14.7±2.2 | 19.8±2.6 | 22.8±1.4 | 25.6±1.6 | 15.6±1.4 | 17.9±0.8 | 23.3±2.1 | 20.8±1.4 | 23.4±1.2 | 25.7±2.3 | 29.5±2.2 |
| 6 | 36.3±3.2 | 41.3±3.2 | 44.2±3.4 | 46.7±2.3 | 31.7±2.3 | 37.2±2.4 | 41.8±1.6 | 39.7±0.5 | 40.8±2.3 | 47.9±0.6 | 50.7±1.6 |
| 10 | 49.3±3.6 | 55.4±1.8 | 58.4±2.2 | 64.3±3.1 | 44.3±0.4 | 54.3±3.1 | 56.4±0.8 | 54.1±2.2 | 59.6±1.8 | 61.2±0.5 | 69.8±3.2 |
| 15 | 66.2±2.6 | 71.2±2.8 | 74.9±1.8 | 81.2±2.4 | 58.4±2.2 | 70.9±2.2 | 74.8±2.4 | 70.6±2.6 | 74.7±1.5 | 78.7±2.4 | 90.4±1.8 |
| 20 | 74.3±3.4 | 83.4±3.1 | 87.2±2.3 | 99.4±0.4 | 76.8±2.1 | 83.7±1.5 | 91.2±1.1 | 81.7±1.4 | 82.4±1.8 | 92.3±1.8 | 99.8±0.3 |

**Invitro Dissolution Profiles of Desloratidine**:



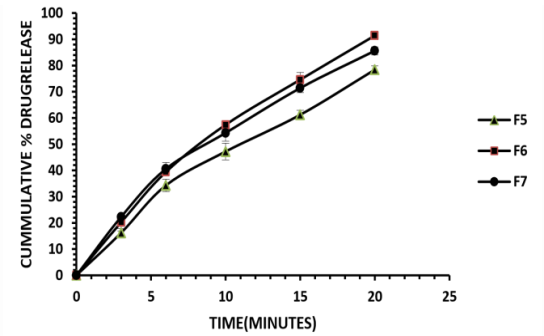
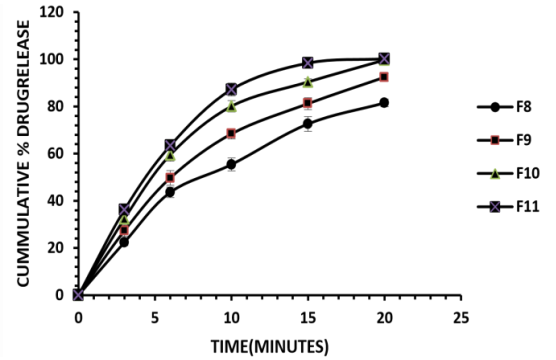




**Fig.F1-F4** **Fig.F5-F7**

**Fig.no.1, no2:Dissolution profile comparison of formultions made using SSG and CCSas super disintegrant.**



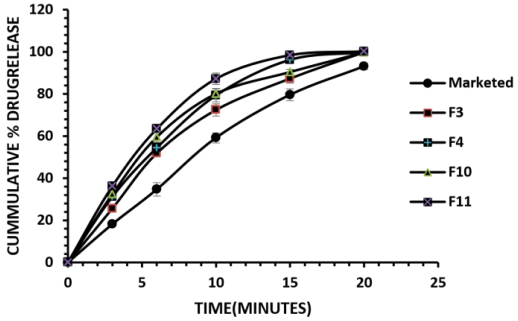
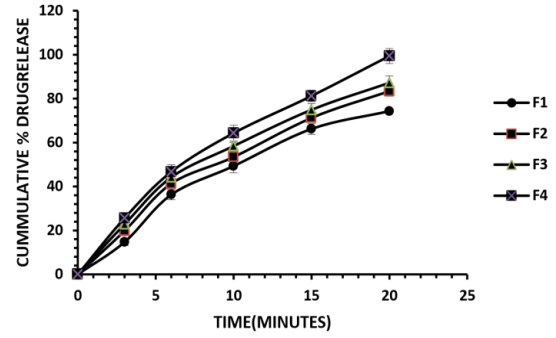




**Fig.F8-F11** **Fig.F3,F4 and F10,F11**

**Fig.no.3, no, 4:Dissolution profile comparison of formulations made using CP as superdisintegrant and comparison of optimized formulations with marketed formulation.**

**Invitro Dissolution Profiles of Montelukast Sodium:**



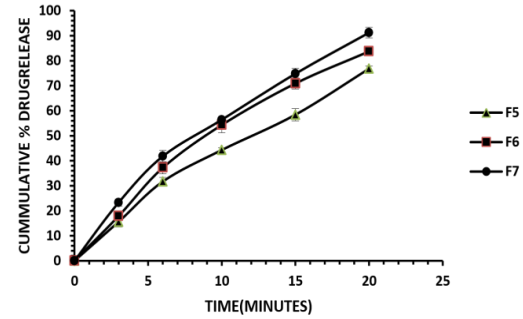




**Fig.F1-F4** **Fig.F5-F7**

**Fig.no.5,no.6: Dissolution profile comparison of formulations made using SSG and CCS as superdisintegrant.**

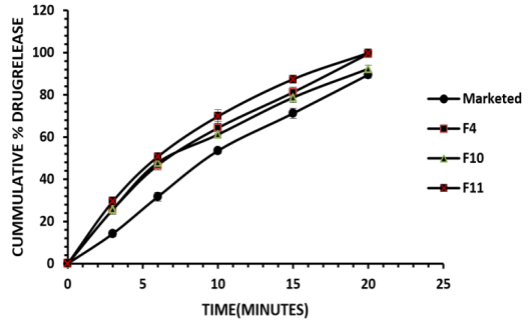



Fig.F8-F11

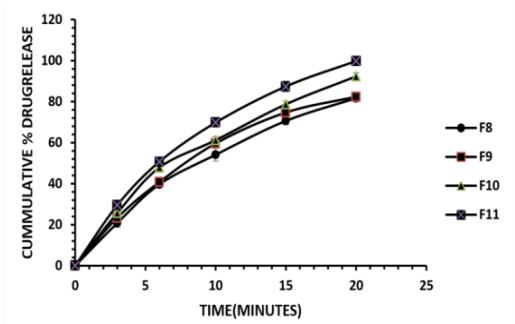



Fig.F4,F10 and F11

**Fig.no.7,no.8: Dissolution profile comparision of formulations made using CP as super disintegrant and comparison of Montelukast sodiumoptimized formulations with marketed formulation.**

**In- vitro dissolution studies:**

- Total eleven formulations were formulated using three superdisintegrants like SSG, CCS, CP. Dissolution studies were performed for these formulations to find the percent drug release of Desloratidine and Montelukast sodium.
- In case of Desloratidine the formulations F3(SSG 3%), F4(SSG 4%), F10(CP 3%), F11(CP 4%) have shown better dissolution than marketed formulation. Of them F4 showed 96.2±0.4% dissolution in 15 minutes and F11 showed 98.4±0.4 dissolution in 15 minutes.
- In case of Montelukast sodium the formulations F4(SSG 4%), F10(CP 3%), F11(CP4%) have shown better dissolution than marketed formulation. Of themF11showed90.4±0.5 dissolution in 15minutes.
- Of the formulations F11, F10, F4 the dissolution rate was found to be more for F11 formulation and dissolution rate was in the order of F11>F4 >F10.
- By considering the above discussions F11(CP 4%) was found to be optimized formulation.
- The data for dissolution profiles compared with marketed formulations were shown in the figures 7.4.4 and 7.4.8 to show that optimized formulations of Desloratidine and Montelukast sodium were effective and suitable than conventional tablets.

## CONCLUSION

The drug polymer compatibility was confirmed by FTIR studies. The results obtained by FTIR studies revealed that there was no chemical interaction between drug and excipients. Direct compression method was used to formulate the tablets, because of its cost effectiveness and to reduced number of manufacturing steps.

The pre compression parameters like angle of repose, Cars index, Hausner's ratio, tapped and bulk density were performed and were found to be within the limits. The post compression parameters were also studied including the Weight variation, Hardness, friability, Thickness, wetting time, *In vitro* disintegration and the water absorption ratio and the values were found to be within the limits.

*In-vitro* dissolution studies showed that formulations F4, F10, F11 showed better dissolution of Desloratidine and Montelukast when compared with marketed formulation and among them F11 was found to be better formulation when compared to others. Based on the formulation development and results, F11 formulation was considered as the desired formulation which contains crospovidone 4 % as a super disintegrant

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