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## FORMULATION AND IN-VITRO EVALUATION OF CARBIMAZOLE ORAL DISPERSIBLE TABLETS

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### ABSTRACT

Carbimazole is used to treat hyperthyroidism. Carbimazole is a pro-drug as after absorption it is converted to the active form, methimazole. Methimazole prevents thyroid peroxidase enzyme from iodinating and coupling the tyrosine residues on thyroglobulin, hence reducing the production of the thyroid hormones T3 and T4. In the present work, an attempt has been made to develop oral dispersible tablets of Carbimazole. Novel method of co processed super disintegrating technology was employed to formulate the tablets. All the formulations were prepared by direct compression method. The blend of all the formulations showed good flow properties such as angle of repose, bulk density, tapped density. The prepared tablets were shown good post compression parameters and they passed all the quality control evaluation parameters as per I.P limits. Among all the formulations CBZL5 formulation showed maximum drug release i.e., 97.26% in 10 min hence it is considered as optimized formulation. The CBZL5 formulation contains CP1 as super disintegrate in the concentration of 125 mg. (CP2 contains SSG and CP in 1:2 ratio).

**Key words:** Carbimazole, oral dispersible tablets, co-processed super disintegrating technology

### INTRODUCTION

The oral route stands as the primary and most significant means of administering drugs for systemic effects. Meanwhile, the parenteral route gains prominence in addressing medical emergencies involving comatose individuals or those unable to swallow, as well as for various maintenance therapies. Despite these considerations, approximately 90% of systemic-effect drugs find their administration through the oral route (Debjit Bhowmik, *et al.* 2014). Among orally administered drugs, solid dosage forms emerge as the preferred class, offering optimal protection against temperature, humidity, oxygen, light, and transportation stresses. Solid dosage forms also guarantee dosage accuracy, compactness, portability, a neutral taste profile, and ease of administration (R.D. Rahane, *et al.* 2018)

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### Types of tablets

- ✓ Compressed Tablets
- ✓ Molded tablets or tablet triturates (tt)
- ✓ Dispensing Tablets (Dt)
- ✓ Hypodermic Tablets (Ht)

### Advantages of the tablets

- ✓ Their cost is lowest of all the dosage forms.
- ✓ They are in general the easiest and cheapest to package and ship of all oral dosage forms.

### Disadvantages of the tablets

- ✓ Some drugs resist compression in to dense particles, owing to their amorphous nature or flocculent, low density character.
- ✓ Drugs with poor wetting, slow dissolution properties, intermediate to large dosages, optimum absorption high in the GIT or any combination of these features are very challenging for the formulators (Swati L. Khedeka, Subhash V. 2019).

**Tablet Processing**

- ✓ Direct compression
- ✓ Wet granulation
- ✓ Dry granulation

**Advantages of Oral Disintegrating tablets**

- Ease of administration and Patients compliance
- Rapid onset of action
- Enhanced bioavailability
- Oral Disintegrating tablets are palatable
- Good alternative to conventional tablet and liquid dosage forms

**Disadvantages of Oral Disintegrating tablets**

- **Mechanical strength**

These tablets are very brittle, fragile and porous in nature as they are prepared by low compression force. Thus, requires proper packing and handling while transportation.

- **Unpleasant taste**

If not properly prepared, these tablets can leave unpleasant taste or feeling of grittiness in the mouth.

- **Required dry condition for storage**

These tablets are hygroscopic in nature and thus should be stored in dry condition.

**The Need for Development of ODTs**

- ✓ Patient factors
- ✓ Effectiveness factors
- ✓ Manufacturing and marketing factors

**Characteristics**

FDDTs, as a novel dosage form, have several characteristics to distinguish them from the more traditional dosage forms (Samreen Fathima, Sridhar R. 2019). Traditional tablet formulations generally do not require taste masking, because it is assumed that the dosage form will not dissolve until passing the oral cavity (Greeshma Mohan, *et al.* 2018)

**Excipients Used in Oral Disintegrating Systems**

USFDA defines oral disintegrating tablets as “A solid dosage form containing medicinal substance, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue” (Satpute Vivek M, *et al.*, Satpute Vivek M, *et al.* 2018). As per requirement of Oral Disintegrating tablets, it should disintegrate quickly in the oral cavity.

**Superdisintegrants**

Superdisintegrants can be defined as the substances which help in the faster disintegration in small concentration as compared to disintegrant (Akhil Sharma, *et al.* 2017, Srinivasa Sastry D, *et al.* 2017).

**Properties of a superdisintegrant**

- ✓ Poor gel formation
- ✓ Hydration capacity should be good
- ✓ Molding and flow property should be good Should not form complex with drugs
- ✓ Should be compatible with other excipients
- ✓ Should not be toxic
- ✓ Should be inert

**Technology**

On the basis of fast disintegrating principles, different methods are available for preparation of Oral Disintegrating tablets and they differ from conventional tablets in terms of mechanical strength, stability, mouth feel, rate of dissolution and bioavailability (A.S. Panwar, *et al.* 2011, Basawaraj S. Patil. 2017). Three main approaches used in formulation of Oral Disintegrating tablets. They are:

1. By increasing the tablet matrix porous structure
2. By using water soluble excipients
3. By adding superdisintegrant
  - ✓ Conventional technology
  - ✓ Patented technology
  - ✓ OraSolv Technology
  - ✓ Durasolv Technology
  - ✓ Wow tab technology
  - ✓ Flashdose technology
  - ✓ Flashtab Technology
  - ✓ Oraquick technology

**MATERIALS**

Carbimazole, Sodium starch glycolate, crospovidone, MCC pH 102, Magnesium stearate, Talc.

**METHODOLOGY****Pre-formulation Studies**

The goals of the pre-formulation study are:

- ❖ To establish the necessary physicochemical characteristics of a new drug substance.
- ❖ To determine its kinetic release rate profile.
- ❖ To establish its compatibility with different excipients.

**Determination of absorption maximum ( $\lambda_{\max}$ ):**

Absorption maximum is the wavelength at which maximum absorption takes place. For accurate analytical work, it is important to determine the absorption maxima of the substance under study. Carbimazole was weighed accurately 10 mg and transferred to 100 ml volumetric flask, dissolved in phosphate buffer pH 6.8 and the final volume was made up to 100 ml with phosphate buffer pH 6.8 to get a stock solution (100µg/ml). From the stock solution, 1 ml was pipette out in 10 ml volumetric flask and the final volume was made up to 10 ml with phosphate buffer PH 6.8 to get 10µg/ml. Then this solution was scanned at 200-

[illegible]

|              |    |    |    |    |    |    |    |    |    |
|--------------|----|----|----|----|----|----|----|----|----|
| MCC(mg)      | Qs | Qs | Qs | Qs | Qs | Qs | Qs | Qs | Qs |
| Total wt(mg) | 80 | 80 | 80 | 80 | 80 | 80 | 80 | 80 | 80 |

### Post Compression Parameters

#### Evaluation of uncoated tablets:

##### Shape and colour:

The tablets were examined under a lens for the shape of the tablet and colour by keeping the tablets in light.

##### Uniformity of thickness:

Randomly 10 tablets were taken from formulation batch and their thickness (mm) was measured using a Vernier callipers.

##### Hardness test:

The hardness of the tablets was determined using Monsanto hardness tester. It is expressed in Kg/cm<sup>2</sup>. Six tablets were randomly picked from each formulation.

##### Friability test:

It is the phenomenon whereby tablet surfaces are damaged and/or show evidence of lamination or breakage when subjected to mechanical shock or attrition. The friability of tablets was determined by using Roche friabilator (Lab India, FT 1020). It is expressed in percentage (%). Ten tablets were initially weighed [W<sub>(initial)</sub>] and transferred into friabilator. The friabilator was operated at 25 rpm for 4 min or run up to 100 revolutions. The tablets were weighed again [W<sub>(final)</sub>]. The percentage friability was then calculated by,

$$F = \frac{[W(\text{initial}) - W(\text{final})]}{W(\text{initial})} \times 100$$

##### Weight variation test:

The tablets were selected randomly from each formulation and weighed individually to check for weight variation. The U.S Pharmacopoeia allows a little variation in the weight of a tablet. The % deviation in weight variation is shown in table.

### Results and Discussion

#### Standard Calibration curve of Carbimazole:

**Table 2: Concentration and absorbance obtained for calibration curve of Carbimazole In pH 6.8 Phosphate buffer**

| Concentration (µg/ml) | Absorbance |
|-----------------------|------------|
| 0.2                   | 0.175      |
| 0.4                   | 0.341      |
| 0.6                   | 0.563      |
| 0.8                   | 0.682      |
| 1                     | 0.899      |

#### Drug Content estimation:

The content uniformity test is used to ensure that every tablet contains the amount of drug substance intended with little variation among tablets within a batch.

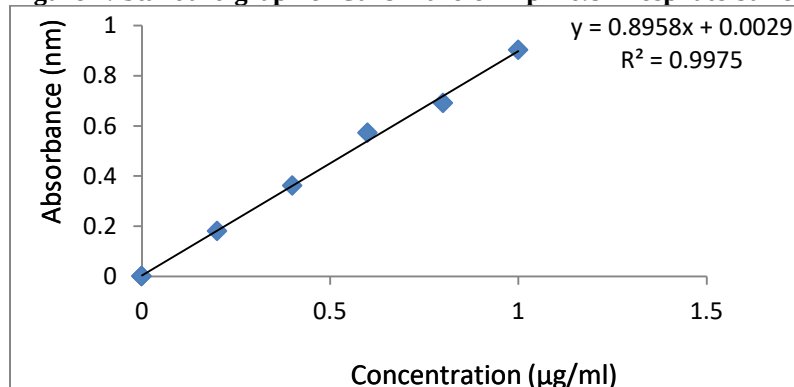
Four tablets were weighed and crushed in the mortar. The powder equivalent to 1.25 mg of the drug were weighed and dissolved in 100ml phosphate buffer pH 6.8 to give a concentration of 12.5 µg/ml. 2ml of this solution was taken and diluted to 10ml to give a concentration of 2.5µg/ml. The absorbance of the prepared solution was measured at 290nm using UV Visible spectrophotometer (Lab India, UV-3200).

#### In -vitro dissolution studies:

*In-vitro* release studies were carried out using a modified USP XXIII dissolution test apparatus (Lab India, DS-800).

The dissolution fluid was 500ml of phosphate buffer pH 6.8 at a speed of 50rpm at a temperature of 37<sup>0</sup>c were used in each test [17]. Samples of dissolution medium (5ml) were withdrawn for every 5min and assayed for Carbimazole by measuring absorbance at 290 nm. For all the tests 5ml of the test medium were collected at specified time intervals and replaced with same volume of phosphate buffer pH 6.8. Details:

|                           |                           |
|---------------------------|---------------------------|
| Apparatus used            | : USP II Lab India DS 800 |
| Dissolution Medium        | : Phosphate buffer PH 6.8 |
| Dissolution Medium volume | : 900ml                   |
| Temperature               | : 37 <sup>0</sup> C       |
| Speed of paddle           | : 50rpm                   |
| Sampling Intervals        | : 2,4,6,8,10 min          |
| Sample withdrawn          | : 5ml                     |
| Absorbance measured       | : 290 nm                  |
| Beers Range               | : 2-10µg/ml               |

**Figure 1: Standard graph of Carbimazole in pH 6.8 Phosphate buffer****Evaluation Parameters for Oral dispersible Tablets of Carbimazole :****Pre-compression parameters****Table 3: Pre-compression parameters**

| Formulations | Bulk Density (gm/cm <sup>3</sup> ) | Tap Density (gm/cm <sup>3</sup> ) | Carr's Index (%) | Hausner ratio | Angle Of Repose(θ) |
|--------------|------------------------------------|-----------------------------------|------------------|---------------|--------------------|
| CBZL1        | 0.47                               | 0.57                              | 16.03            | 1.05          | 24.02              |
| CBZL2        | 0.46                               | 0.56                              | 17.22            | 1.12          | 23.16              |
| CBZL3        | 0.46                               | 0.54                              | 17.11            | 1.14          | 24.53              |
| CBZL4        | 0.47                               | 0.55                              | 18.51            | 1.19          | 21.08              |
| CBZL5        | 0.47                               | 0.56                              | 17.36            | 1.13          | 22.16              |
| CBZL6        | 0.51                               | 0.54                              | 17.71            | 1.15          | 22.14              |
| CBZL7        | 0.48                               | 0.57                              | 16.15            | 1.14          | 24.12              |
| CBZL8        | 0.51                               | 0.58                              | 16.09            | 1.12          | 23.05              |
| CBZL9        | 0.49                               | 0.51                              | 17.05            | 1.11          | 22.78              |

All the pre-compression parameters were found to be within the limits.

**Post compression Parameters:****Table 4: Post-Compression parameters**

| Formulation code | Weight variation (mg) | Hardness (kg/cm <sup>2</sup> ) | Thickness (mm) | Disintegration Time (sec) | Friability (%) | Assay (%) |
|------------------|-----------------------|--------------------------------|----------------|---------------------------|----------------|-----------|
| CBZL1            | 81                    | 2.6                            | 1.06           | 24.03                     | 0.56           | 98.21     |
| CBZL2            | 82                    | 2.5                            | 1.11           | 23.34                     | 0.54           | 99.46     |
| CBZL3            | 79                    | 2.2                            | 1.08           | 22.49                     | 0.52           | 97.37     |
| CBZL4            | 81                    | 2.5                            | 1.11           | 24.91                     | 0.51           | 97.15     |
| CBZL5            | 80                    | 2.7                            | 1.12           | 23.72                     | 0.54           | 98.59     |
| CBZL6            | 82                    | 2.5                            | 1.11           | 25.93                     | 0.53           | 98.67     |
| CBZL7            | 81                    | 2.4                            | 1.13           | 26.54                     | 0.55           | 99.71     |
| CBZL8            | 82                    | 2.7                            | 1.11           | 24.71                     | 0.56           | 99.65     |
| CBZL9            | 83                    | 2.6                            | 1.12           | 22.19                     | 0.51           | 97.81     |

All the post-compression parameters were found to be within the limits.

**In-vitro Dissolution studies:****Table 5: In-vitro dissolution studies of all formulations**

| TIME (min) | % drug release of CBZL1 | % drug release of CBZL2 | % drug release of CBZL3 | % drug release of CBZL4 | % drug release of CBZL5 | % drug release of CBZL6 | % drug release of CBZL7 | % drug release of CBZL8 | % drug release of CBZL9 |
|------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| 0          | 0                       | 0                       | 0                       | 0                       | 0                       | 0                       | 0                       | 0                       | 0                       |
| 2          | 24.25                   | 23.19                   | 24.19                   | 24.45                   | 23.77                   | 26.67                   | 21.45                   | 22.52                   | 21.32                   |
| 4          | 48.06                   | 37.11                   | 39.25                   | 41.41                   | 51.44                   | 41.51                   | 44.51                   | 37.76                   | 44.41                   |
| 6          | 64.41                   | 62.74                   | 74.41                   | 65.16                   | 75.65                   | 72.42                   | 62.74                   | 54.17                   | 64.88                   |

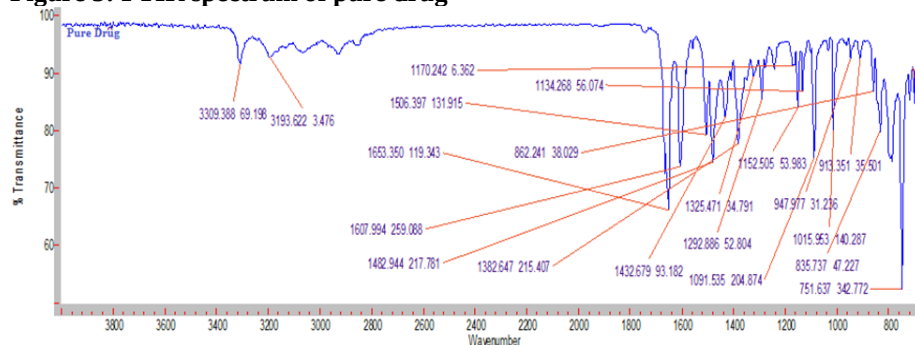


**Figure 6: FTIR spectrum of optimized formulation**

## DISCUSSION

The formulation and in-vitro evaluation of Carbimazole oral dispersible tablets demonstrate their potential as a convenient dosage form. Enhanced disintegration and dissolution profiles suggest improved bioavailability. The findings indicate that these tablets could offer a promising alternative for patients with swallowing difficulties, ensuring effective drug delivery.

## CONCLUSION

In the present work, an attempt has been made to develop oral dispersible tablets of Carbimazole. Novel method of co processed super disintegrating technology

was employed to formulate the tablets. All the formulations were prepared by direct compression method. The blend of all the formulations showed good flow properties such as angle of repose, bulk density, tapped density. The prepared tablets were shown good post compression parameters and they passed all the quality control evaluation parameters as per I.P limits. Among all the formulations CBZL5 formulation showed maximum drug release i.e., 97.26% in 10 min hence it is considered as optimized formulation. The CBZL5 formulation contains CP1 as super disintegrate in the concentration of 125 mg. (CP2 contains SSG and CP in 1:2 ratio).

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