Journal of Pharma Research
Available online through
www.jprinfo.com

Research Article
ISSN: 2319-5622

# Formulation and Evaluation of Candesartan Oral Disintegrating Tablets

**Lakshmi Prasad J*, Sivaram Prasad Akurathi, Ram Bhramha Reddy**
*Department of Pharmaceutics, Nalanda Institute of Pharmaceutical Sciences, Kantepudi, Sattenapalli, Andhra Pradesh, INDIA.*

**Received on: 11-12-2015; Revised and Accepted on: 21-12-2015**

## ABSTRACT

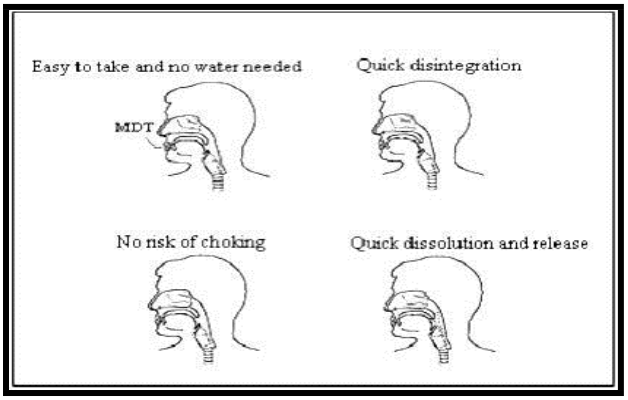
*The bioavailabilities of Oral disintegrating tablets (ODT's) drugs are significantly greater than those observed from conventional solid forms such as tablets and capsules. Therefore, in the present study an attempt will be made to design mouth dissolving tablets of Candesartan ODT(anti-hypertensive)with a view to provide a convenient means of administration to those patients suffering from difficulties in swallowing such as pediatric and geriatric patients and uncooperative mentally ill patients.The mouth dissolving tablets (MDT) of CANDESARTAN will be designed using co-processed directly compressible excipients developed in our laboratories with the prime objective of arriving at cost –effective product. The designed MDT of CANDESARTAN will be evaluated for hardness, friability, weight variation, invitro dispersion time wetting time, water absorption ratio, drug content uniformity, in vitro dissolution rate.All the formulations F1 to F12 were prepared by employing different superdisintegrants of which F9 was found to have better activity.*

***Key words:****Oral disintegrating tablets (ODT's), Candesartan, Mouth dissolving tablets (MDT), Superdisintegrants.*

## INTROUDUCTION

### 1. Orally Disintegrating Tablets:

The concept of Fast dissolving Drug Delivery System emerged from the desire to provide patient with more conventional means of taking their medication. It is difficult for many patients to swallow tablets and hard gelatin capsules. Hence they do not comply with prescription, which results in high incidence of non-compliance and ineffective therapy. In some cases such as motion sickness, sudden episodes of allergic attacks or coughing and unavailability of water, swallowing conventional tablets may be difficult. Particularly the difficulty is experienced by pediatric and geriatric patients. Such problems can be resolved by means of Fast Dissolving Tablet. When put on tongue, this tablet disintegrates instantaneously, releasing the drug, which dissolves or disperses in the saliva. The center for drug Evaluation and Research states an ODT to be: "A solid dosage form containing medicinal substances, which disintegrate rapidly, usually within a matter of seconds, when placed upon the tongue."These tablets are distinguished from conventional, sublingual tablets, lozenges and buccal tablets which require more than a minute to dissolve in the mouth. In the literature these are also called orally disintegrating, Orodisperse, Mouth dissolving, Quick dissolving, Fast-melt and rapidly disintegrating tablets and freeze- dried wafers.




### 2. Types of ODTs

For ease of comparison, ODTs may be categorized into two main groups:
a) Lyophilized formulations
b) Loosely compressed tablets.

### 3. Conventional Techniques Used in the Preparation of Fast Dissolving Drug Delivery Systems:

Various technologies used in the manufacture of Fast dissolving tablets include: 1) Freeze –drying or lyophilization, 2) Tablet Molding, 3) Direct compression, 4) Spray drying, 5) Sublimation, 6)Taste masking, 7) Mass extrusion.

### *4. Direct compression:*

It is the easiest way to manufacture tablets. Conventional equipment, commonly available excipients and a limited number of processing steps are involved in direct compression. Also high doses can be accommodated and final weight of tablet can easily exceed that of other production methods. This technique can now be applied to fast dissolving tablets because of the availability of improved tablet excipients, especially tablet disintegrants and sugar-based excipients.

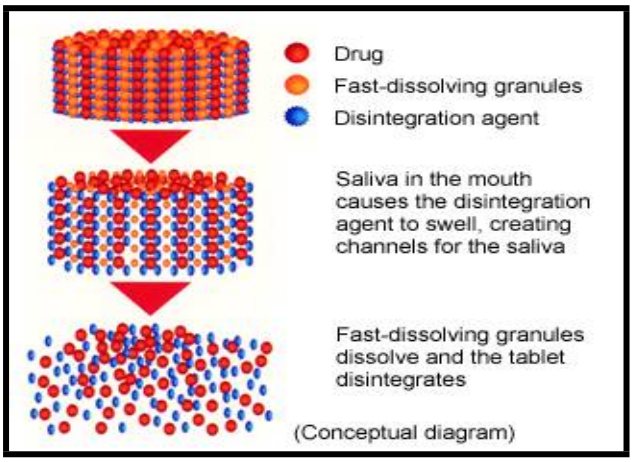



**Fig. 1: Disintegration Mechanism of ODT drugs**

***Corresponding author:**
***Lakshmi Prasad J***
*Department of Pharmaceutics,*
*Nalanda Institute of Pharmaceutical Sciences, Kantepudi,*
*Sattenapalli, Andhra Pradesh, INDIA.*
**E-Mail: jarugulakshmiprasad7@gmail.com*

## MATERIALS AND METHODS

**Materials:**

| Sl. No. | Materials |
|---|---|
| 1 | Candesartan |
| 2 | Sodium starch glycolate |
| 3 | Microcrystalline cellulose |
| 4 | Croscarmellose sodium |
| 5 | Amberlite IPR 88 |
| 6 | Crospovidone |
| 7 | Sodium saccharine |
| 8 | Aerosil |
| 9 | Lactose |
| 10 | Magnesium stearate |

**Methods Used:**

**1. Evaluation of Precompressional and Post Compressional Parameters of Oro Dispersible Tablets:**

***Bulk density:*** Apparent bulk density was determined by pouring the blend into a graduated cylinder. The bulk volume($V_b$) and weight of the powder was determined.

$$\text{Bulk density} = M / V_b$$

***Tapped density:*** The measuring cylinder containing a known mass of powder blend was tapped for a fixed number of times as per USP apparatus-11. The minimum volume occupied by the powder after tapping was measured.

Tapped density = weight/tapped volume

***Compressibility index:*** Compressibility index is calculated as follows

Tapped density- Bulk density/ Tapped density*100

The value below 15% indicates a powder with good flow characteristics where as above 25% indicates poor flowability.

***Haussner's ratio:*** It is an indirect index of ease of powder flow, it is calculated as follows. Tapped density / Bulk density

Haussner's ratio <1.25 indicates good flow properties, whereas >1.5 indicates poor flowability.

***Angle of Repose:*** Angle of repose was determined using funnel method. The blend was poured through funnel that can rise vertically until a maximum cone height (h) was obtained. Radius of the heap(r) was measured and angle of repose was calculated as follows. The results post compression parameters are shown in Table-4.

$$\text{Ø} = tan^{-1}\,\text{h/r}$$

**Compression of Tablets:**

To the mixed blend of powder and excipients finally add magnesium stearate and glycerylbehanate and then mixed for 5 min. The mixed blend was compressed with sixteen (16) station tablet punching machine using 7 mm flat punches with break line.

**2. Evaluation of tablets:**

***Weight variation:*** Twenty tablets from each formulation were selected randomly and average weight was determined. Individual tablets were then weighed and compared with average weight.

***Hardness test:*** The force required to break a tablet in a diametric compression was determined by using Pfizer tablet hardness tester.

***Friability:*** The weight of twenty tablets was noted and placed in the friabilator and then subjected to100 revolutions at 25 rpm. Tablets were dedusted using a soft muslin cloth and reweighed.

Percent friability = [initial weight - final weight/initial weight] × 100

**Wetting timeand Water absorption ratio:**

A piece of paper folded twice was kept in a petri dish ( internal diameter 6cms) containing 6ml of purified water. A tablet was put on the paper and time required for complete wetting was measured. The wetted tablet was weighed. Water absorption ratio, R was determined using the following equation.

$$R = [Wa - Wb / Wb] \times 100$$

Where Wa, Wb are the weights of tablets before and after wetting.

***Invitro dispersion time:*** Tablet was added to 10ml of distilled water at 37± 0.5°C, time required for complete dispersion of tablet was measured.

**Drug content uniformity:**

The drug content uniformity was determined by taking the powder equivalent to 10mg, then it was (n=3) dissolved in $P^H$6.8 phosphate. Required dilution (10µg/ml) was prepared and absorbance was taken against the blank at 205nm.

**Invitro disintegration time:**

The disintegration was performed using an I.P disintegration apparatus with distilled water at 37±0.5 °C. The time taken for disintegration of all formulations was noted in table

**Dissolution studies:**

Dissolution rate of Enalapril maleate from all formulations was performed using LABINDIA DISSO 2000 an eight stage dissolution rate testing apparatus with paddle. The dissolution fluid was 900 ml of $P^H$6.8 phosphate buffer with a speed of 50 rpm and temperature of 37±0.5°C were used in each test. 5 ml of sample was withdrawn at different time intervals ( 2.5, 5, 10, 15 & 20 mins) and fresh medium was replaced to maintain sink conditions.

**Drug- Excipients interaction:**

The drug- excipients interaction was studied using FTIR. IR spectra for drug and powderedtablets were recorded in a Fourier transform infrared spectrophotometer using KBr pellet technique.

**3. Methodology For formulation:**

***Preperation of Taste masked granules using Amberlite IPR 88:***

The drug weighed in specified quantities has to be dissolved in water, To this weighed specified ratio of Amberlite IPR 88 should be added and sonicated for 6 hours. The resulting solution has to be filtered and dried for 8 hours and then has to be used for direct compression.

***Preparation of Orodispersible Tablets by Direct Compression Method:***

Orodispersible tablets are prepared by direct compression. The various disintegrants like crospovidone, croscarmellose, Sodium starch glycolate are used. All the ingredients are passed through sieve no. 40. Required quantity of each ingredient is taken for each specified formulation and all ingredients are mixed. Aerosil and magnesium stearate are then passed through mesh no.80 mixed and blended with initial mixture. The resulting mixture is compressed into tablet using 16 station rotary press.

**Table No. 1: Formulation of Different batches**

| Formulation (mg) Ingredients | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 | F10 | F11 | F12 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Candesartan | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 |
| Amberlite IPR88 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 |
| Microcrystalline cellulose | 57.8 | 56.8 | 55.8 | 53.3 | 57.8 | 56.8 | 55.8 | 53.3 | 57.8 | 56.8 | 55.8 | 53.3 |
| Lactose | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Crospovidone** | 3 | 4 | 5 | 7.5 | - | - | - | - | - | - | - | - |
| **Croscarmellose sodium** | - | - | - | - | 3 | 4 | 5 | 7.5 | - | - | - | - |
| **SSG** | - | - | - | - | - | - | - | - | 3 | 4 | 5 | 7.5 |
| **Aerosil** | 0.6 | 0.6 | 0.6 | 0.6 | 0.6 | 0.6 | 0.6 | 0.6 | 0.6 | 0.6 | 0.6 | 0.6 |
| **Sodium saccharine** | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| **Magnesium stearate** | 0.6 | 0.6 | 0.6 | 0.6 | 0.6 | 0.6 | 0.6 | 0.6 | 0.6 | 0.6 | 0.6 | 0.6 |
| **Peppermint flavor** | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s |
| **Total** | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |

**Melting point:**

It can be determined by using micro controller based melting point apparatus. Melting point of Candesartan was found to be **158°C.**

**Solubility studies:**

Candesartan it is practically insoluble in water and sparingly soluble in methanol and freely soluble in acetonitrile.

**Standard graph of Candesartan:**

$\lambda_{max}$of Candesartan cilexetil was found to be **232nm** as it shows maximum absorbance in this wavelength.

**Preparation of standard calibration curve in 0.1 N Hcl :**

50 mg of Candesartan was dissolved in 25 ml of 0.1N HCL by slight shaking (2000 mcg/ml). 2 ml of this solution was taken and made up to 50 ml with water, which gives 80 mcg/ml concentration (stock solution).

From the stock solution, concentrations of 10, 20, 30, 40 and 50 µg/ml in water were prepared. The absorbance of these solutions were measured at 232 nm and standard plot was drawn using the data obtained. The correlation coefficient was calculated. The absorbance data of the above concentrations are shown in Table.

## RESULTS AND DISCUSSION

**Table No. 2: Standard graph of Candesartan in 0.1N HCL ($\lambda_{max}$ 232 nm)**

| S. No. | Concentration (mcg/ml) | Absorbance |
|---|---|---|
| **1** | 2 | **0.132** |
| **2** | 4 | **0.279** |
| **3** | 6 | **0.405** |
| **4** | 8 | **0.569** |
| **5** | **10** | **0.729** |

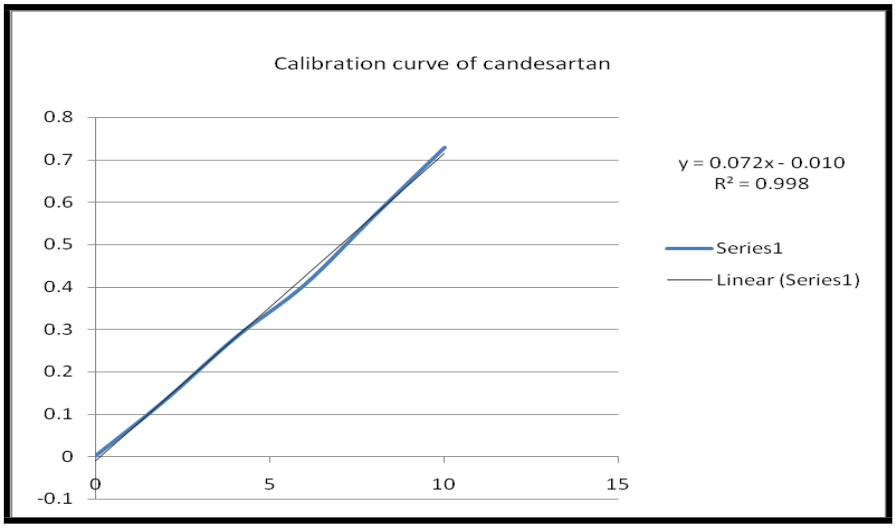



**Fig. 2: Calibration curve of Candesartan**

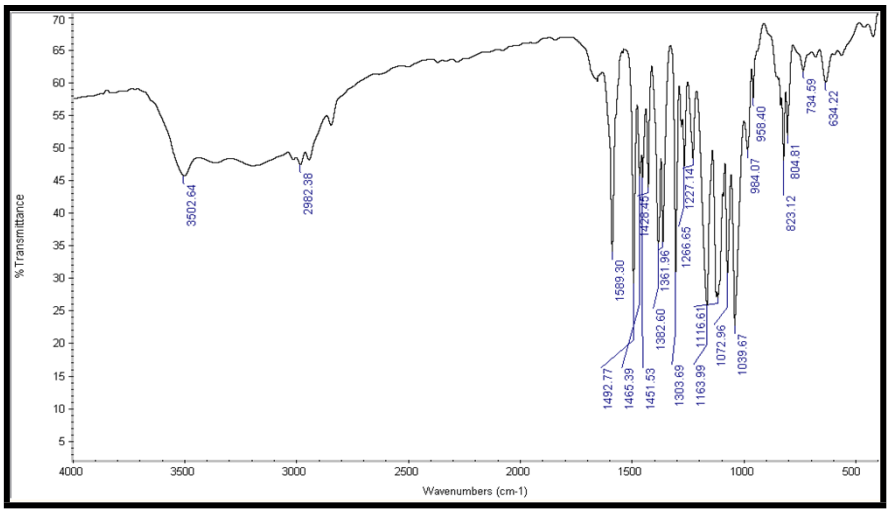



**Fig. 3: FT-IR Spectra of Candesartan**

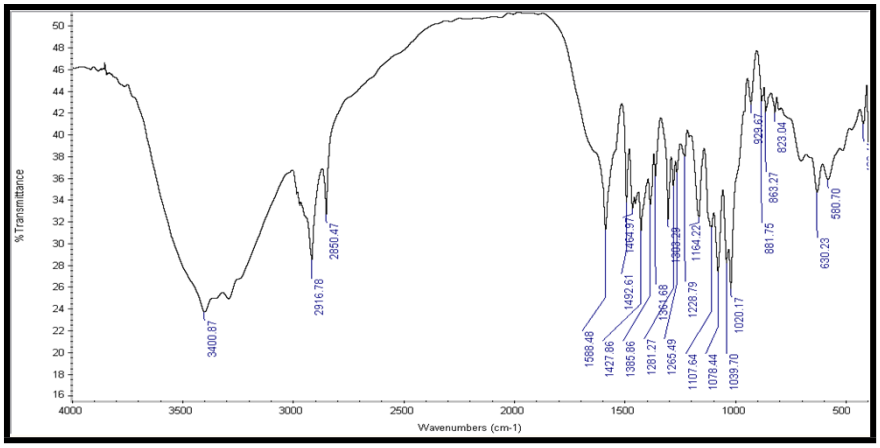



**Fig. 4 :FT-IR characteristic peak of Candesartan Drug ( Drug+ Excipients) Physical mixture of Formulation F9.**

**Table No. 3: FT-IR characteristic peak of Candesartan Drug, Drug + Excipients**

| Sl. No | IR Observed Peaks | | | |
|---|---|---|---|---|
| | Functional Group | IR Range ($cm^{-1}$) | Pure Drug | Physical mixture of Formulation(F9) |
| 1 | N-H | 3400-3500 | 3502.64 | 3400.87 |
| 2 | C-H | 2960-2850 | 2982.38 | 2916.78 |
| 3 | C=N | 1630-1690 | 1589.30 | 1588.48 |
| 4 | C=C | 1450-1600 | 1492.77 | 1492.61 |
| 5 | C-O | 1310-1410 | 1303.69 | 1303.29 |

**Table No. 4: Precompressional characteristics of the powder blend:**

| Formulation code / Parameters | Bulk Density gm/cc | Tapped Density gm/cc | Hausners ratio | %Compressibility /carrs index (%) | Angle of Repose (degrees) | Porosity (%) |
|---|---|---|---|---|---|---|
| F1 | 0.50 | 0.625 | 1.25 | 20 | 29.26 | 14.39 |
| F2 | 0.52 | 0.55 | 1.057 | 15.45 | 19.24 | 11.2 |
| F3 | 0.45 | 0.55 | 1.22 | 18.18 | 20.42 | 18.2 |
| F4 | 0.462 | 0.539 | 1.16 | 14.46 | 29.72 | 16.64 |
| F5 | 0.46 | 0.55 | 1.195 | 16.36 | 19.17 | 18.2 |
| F6 | 0.56 | 0.69 | 1.23 | 18.84 | 20.24 | 16.7 |
| F7 | 0.53 | 0.59 | 1.113 | 12.01 | 19.17 | 15.3 |
| F8 | 0.52 | 0.62 | 1.192 | 16.12 | 18.24 | 11.2 |
| F9 | 0.5 | 0.62 | 1.25 | 19.35 | 22.26 | 20 |
| F10 | 0.53 | 0.62 | 1.19 | 16.120 | 29.24 | 17.6 |
| F11 | 0.39 | 0.44 | 1.12 | 11.36 | 26.48 | 15.8 |
| F12 | 0.48 | 0.55 | 1.14 | 12.72 | 28.06 | 18.9 |

**Table No. 5: Postcompressional characteristics of the Formulated ODT**

| Formulation code / Parameters | Weight variation | Hardness ($Kg/cm^2$) | Thickness (mm) | Friability (%) | Content uniformity (%) | Disintegration time (Sec) | Wetting time (sec) |
|---|---|---|---|---|---|---|---|
| F1 | passes | 3.00 | 0.210 | 0.12 | 99.92 | 26 | 29 |
| F2 | passes | 3.01 | 0.213 | 0.15 | 98.3 | 24 | 28 |
| F3 | passes | 3.02 | 0.212 | 0.14 | 100.01 | 20 | 24 |
| F4 | passes | 3.00 | 0.212 | 0.19 | 98.5 | 16 | 20 |
| F5 | passes | 3.03 | 0.214 | 0.21 | 98.9 | 28 | 32 |
| F6 | passes | 3.02 | 0.213 | 0.10 | 100.02 | 21 | 25 |
| F7 | passes | 3.01 | 0.210 | 0.11 | 98.6 | 19 | 22 |
| F8 | passes | 3.03 | 0.212 | 0.14 | 100.01 | 17 | 21 |
| F9 | passes | 3.01 | 0.213 | 0.12 | 99.2 | 20 | 22 |
| F10 | Passes | 3.01 | 0.214 | 0.18 | 99.63 | 26 | 30 |
| F11 | passes | 3.00 | 0.213 | 0.11 | 99.28 | 27 | 26 |
| F12 | passes | 3.00 | 0.213 | 0.09 | 99.38 | 25 | 31 |

**Table No. 6: Invitro dissolution studies of formulated ODT's:**

| Time (min) | Cumulative Percentage Drug Release(%) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 | F10 | F11 | F12 |
| 5 | 53.68 | 55.42 | 65.34 | 70.43 | 47.24 | 52.43 | 61.53 | 72.19 | 45.28 | 50.23 | 60.21 | 65.26 |
| 10 | 58.94 | 62.57 | 72.90 | 89.45 | 58.96 | 61.89 | 70.82 | 86.13 | 56.47 | 60.96 | 68.90 | 70.19 |
| 15 | 68.23 | 76.24 | 90.56 | 94.56 | 67.34 | 74.21 | 84.90 | 92.39 | 68.21 | 72.10 | 75.17 | 82.83 |
| 30 | 74.69 | 90.06 | 93.5 | 97.56 | 75.56 | 86.12 | 98.31 | 97.34 | 98.42 | 80.43 | 85.62 | 95.84 |

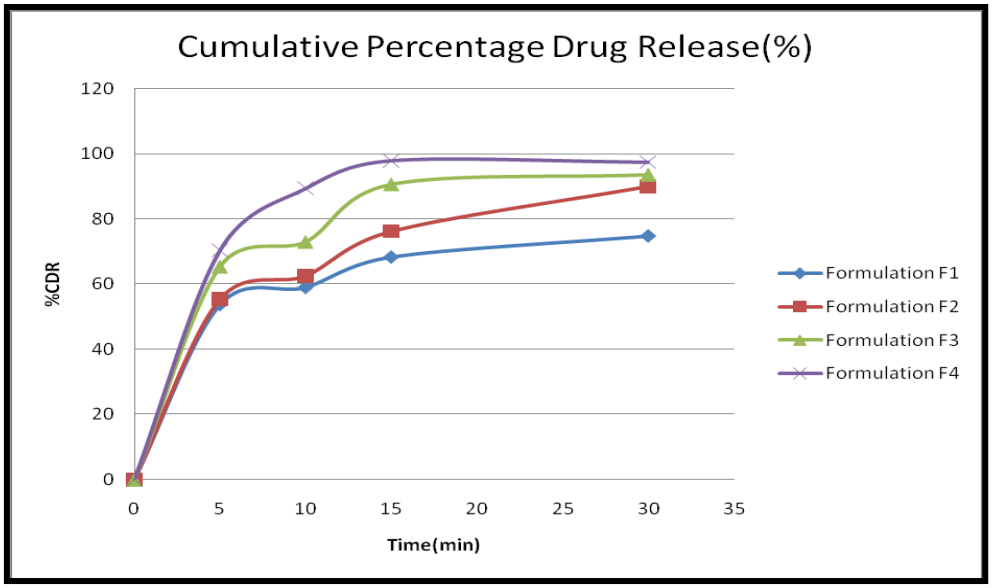



**Fig. 5: Graphical Representation of Percentage Cumulative Drug Release for Formulations F1, F2, F3& F4.**

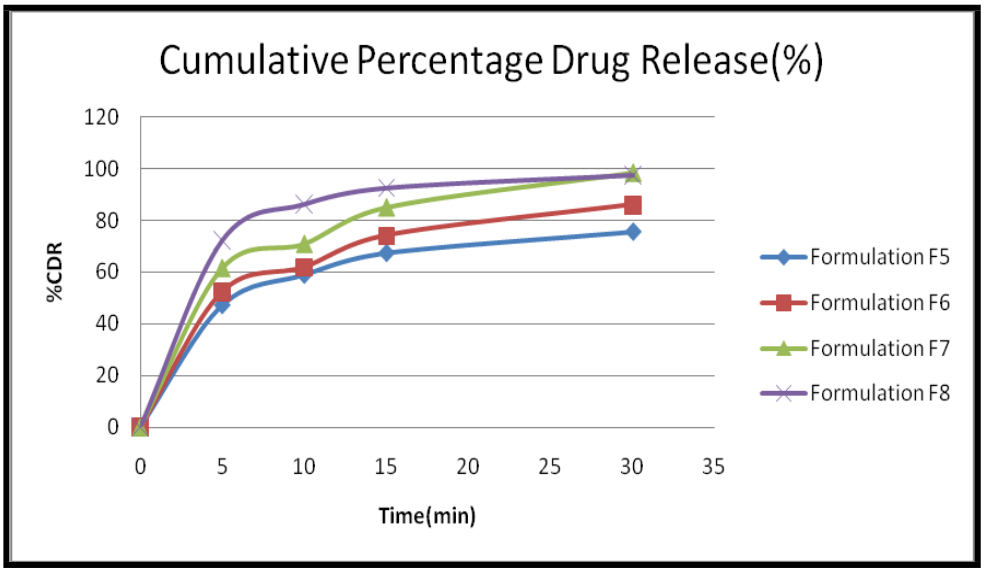



**Fig. 6: Graphical Representation of Percentage Cumulative Drug Release for Formulations F5, F6, F7& F8.**

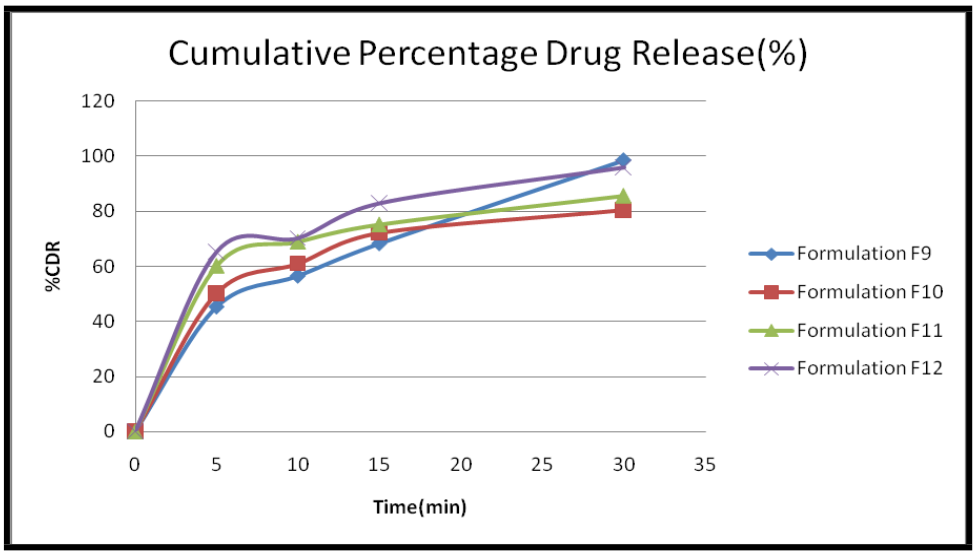



**Fig. 7: Graphical Representation of Percentage Cumulative Drug Release for Formulations F9, F10, F11& F12.**

## CONCLUSION

In the present work, mouth dissolving tablets candesartan were prepared by direct compression method. All the tablets were subjected to weight variation, drug content uniformity, hardness, friability, water absorption ratio, wetting time, *in vitro* dispersion time, dissolution, Based on the above study following conclusions can be drawn:

- The drug Candesartan is a bitter drug which was taste masked with amberlite IPR 88.
- Tablets prepared by direct compression method were found to be good without any chipping, capping and sticking.
- The hardness of the prepared tablets was found to be in the range of 3.00 to 3.03kg/cm$^2$.
- Thefriability values were found to be in the range of 0.11 to 0.21%.
- The low values of standard deviation for average weight and drug content of the prepared tablets indicate weight and drug content uniformity within the batches prepared.
- The *in vitro* dispersion time of Candesartan tablets prepared by direct compression method was found to be in the range of 0 to 30 min.
- Based on the *in vitro* dispersion time, formulations F9 and F7 were found to be promising and displayed *in vitro* dispersion with in 30min. Wetting time of promising formulations was found to be within 1 minute, which facilitates their faster dispersion in the mouth.
- All the formulations F1 to F12 were prepared by employing different superdisintegrants of which F9 was found to have better activity.
- Overall F9 formulation has emerged as the superior activity orodispersible tablet formulation for the drug Candesartan

**REFERENCES:**


1. Chien YW. Novel drug delivery system. New York – Marcel Dekker Inc., **1992**; 139-40.
2. Indurwade NH, Rajyaguru TH, Nakhat PD. Novel approach – Fast dissolving tablets. Indian Drugs, **2002**; 39(8): 405-9.
3. Watanabe Y, Koizumi K, Zama Y, Matsumoto Y, Motsumoto M. New compressed tablet rapidly disintegrating in saliva in the mouth using crystalline cellulose and a distinegrant. Bio Pharm Bull, **1995**; 18(9): 1308-10.
4. Dobetti L. Fast melting tablets: Developments & Technologies. Pharm. Tech., **2001**; (Suppl): 44-50.
5. Bhandari S, Mittapalli RK, Ganu R, Rao. YM. Orodispersible tablets: An overview. Asian Journal of Pharmaceutics, **2008**; 2(1): 2-11.
6. Kuchekar BS, Badhan AC, Mahajan HS. Mouth dissolving tablets: A novel drug delivery system. Pharma Times, **2003**; 35: 7-9.
7. Kuchekar BS, Aruagam V. Fast dissolving tablets. Indian J. Pharm. Edu., **2001**; 35: 150-52.
8. Reddy LH, Ghosh B, Rajneesh. Fast dissolving drug delivery system; a review of the literature. Indian J. Pharm. Sci., **2002**; 64(4): 331-6.
9. Tritthart W, Piskering MA. Solid, rapidly disintegrating cetrizine formulations. US Patent, 6, 245, 353, 2001.
10. Liberman HA, Lachmann L and Shwartz JB (editors), Pharmaceutical Dosage Forms: Tablets. Vol. 1, 2$^{nd}$ed, Marcel Dekker Inc., USA; 285-327.
11. Lindgreen S, Janzon L. Dysphagia: Prevalence of swallowing complaints and clinical findings. Med. Clin. North Am., **1993**; 77: 3-5.
12. Bhushan SY, Sambhaji SP, Anant RP, Kaka Saheb RM. New drug delivery system for elderly. Indian Drugs, **2000**; 37: 312-8.
13. Wilson CG, Washington N, Peach J, Murray GR, Kennerley J. The behaviour of a fast-dissolving dosage form (expidet) followed by g-scintigraphy. Int. J. Pharm., **1987**; 40: 119-23.
14. Brahmaiah Bonthagarala, Pasam Venkateswara Rao, Pusuluri Dharani Lakshmi Sai, K. VenkataSivaiah, G. Anil Kumar, B. NageswaraRao, Varun Dasari. Enhancement of dissolution rate of Clofibrate (BCS Class –II drug) by using liquisolid compact technology, Int. J. Biomed. and Adv. Res., **2015**; 6(03): 288-298.
15. Brahmaiah Bonthagarala, Prasanth Pasumarthi, Katta Vamshi Kiran, SathramNataraja, Sudarshan Donthiboina. Formulation and evaluation of orodispersable Atenolol Maleate Tablets: A comparative Study on Natural Super disintegrents and Synthetic Super disintegrents, Int. J. Res. in Ayr. and Pharma., **2014**; 5(2): 185-192.
16. Sweetman SC, editor. Martindale: The complete drug reference, Thirty-third edn. Pharmaceutical Press, London. **2002**; 125-6.
17. Scheirmeier S, Peter Christian Schmidt. Fast dispersible ibuprofen tablets. Eur. J. Pharm. Sci., **2002**; 15: 295-305.
18. HisakadsuSuanada, Yunxia Bi. Preparation,evaluation and optimization of rapidly disintegrating tablets. Powder Technology, **2002**; 122: 188-98.



**How to cite this article:**

Lakshmi Prasad J et al.,: Formulation and Evaluation of Candesartan Oral Disintegrating Tablets, J. Pharm. Res., 2015; 4(12): 393-398.

**Conflict of interest:** The authors have declared that no conflict of interest exists.

**Source of support: Nil**