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**RESEARCH ARTICLE**

# DESIGN AND CHARACTERIZATION OF FAST DISSOLVING TABLETS OF VALSARTAN USING SYNTHETIC AND NATURAL SUPERDISINTEGRANTS

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## *Abstract*

The present study has a design the formulation of the valsartan fast dissolving tablets and evaluate which was prepared by using synthetic and natural superdisintegrants. Fast dissolving drug delivery is currently the gold standard in the pharmaceutical industry where it is regarded as the fastest, safest,convenient and most economic method of drug delivery having the highest patient compliance and preferred over conventional tablets. Valsartan fast dissolving tablet formulations prepared by the direct compression method by using crosspovidone synthetic and gum karaya natural superdisintegrant .Formulations were evaluated for precompressional and postcompressional parameters like uniformity of weight, thickness, hardness, friability, drug content, wetting time, water absorption ratio, *in vitro* dispersion time, *in vitro* disintegration time and *in vitro* dissolution study.Results revealed that among the 6 formulations, the formulation S3 containing 7.5% of crospovidone and formulation N 3 containing 7.5% of Gum karaya was found to be promising formulation. S3 shown disintegration time of 9.22 seconds and the drug release was up to 96.78% in 30 minutes and N3 shown disintegration time of 16.34 seconds and the drug release was up to 75.60% in 30 minutes.



## INTRODUCTION

Solid dosage forms are popular because of ease of administration, accurate dosage forms, pain avoidance and most importantly the patient compliance. The most popular solid dosage forms are being tablets and capsules; one important drawback of this dosage forms for some patients, is the difficulty to swallow.[1]

The unpleasant taste can be masked by sugar coating. As some drugs resist compression into dense compacts, remaining to their amorphous nature, low-density character and drugs with poor wetting, slow dissolution properties, intermediate to large dose, or any combination of these features may be difficult or impossible to formulate and manufacture as a tablet that will still provide adequate bioavailability.2,3 Bitter tasting drugs, drugs with objectionable odour, or drugs sensitive to oxygen or atmospheric moisture may require encapsulation or entrapment prior to compression the tablets may require coating.Valsartan is an angiotensin II receptor antagonist and is widely used in the management of hypertension to reduce cardiovascular mortality in patients with left ventricular dysfunction following myocardial infarction, and in the management of heart failure. Valsartan is rapidly absorbed after oral dose with a bioavailability of about 23%.Peakplasma concentrations occur 2 to 4 hours, and its plasma half-life is about 7.5 hours after an oral dose. In management of hypertension, Valsartan is given in a dose of 80 mg once daily.Present aim to determine the effect of natural and synthetic superdisintegrant on disintegration and dissolution rate of Valsartan tablet.[4]

## Material and Method:

Valsartan obtained as a gift sample from Dr.Reddy's laboratories, Hydarabad. Crosspovidone, gum karaya, Talc, Magnesium stearate, Mannitol, Orange flavor from Research lab Fine chemical industries Islampur. All the ingredients were of pharmacopeial grade and used as supplied.

**Preparation of Tablets**:

Fast dissolving tablets of valsartan were prepared by direct compression method, using synthetic disintegrant crosspovidone and natural gum karaya in different ratio 4.5%-7.5% and also used directly compressible mannitol as diluents to enhance the mouth feel.

All the ingredients were passed through ≠ 60 meshes separately. The drug and mannitol were mixed small portion and blending it to get a uniform mixture and keep aside.Then ingredients were mixed to geometrical order. Mixed blend of excipients was compressed using 8mm flat edged punches to get tablet of 200 mg weight in 8 station compression machine.

**Characterization:**

**Pre compression Parameters:**

**1. Bulk Density (Db):**

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weight powder (passed through standard sieve # 20) into a measuring cylinder and initial weight was noted. This initial volume is called the bulk volume. From this the bulk density is calculated according to the formula mentioned below. It is expressed in g/ml and is given by

$$Db = M / Vb$$

Where, M is the mass of powder

Vb is the bulk volume of the powder.

**2. Tapped Density (Dt):**

It is the ratio of total mass of the powder to the tapped volume of the powder. Volume was measured by tapping the powder for 750 times and the tapped volume was noted if the difference between these two volumes is less than 2%. If it is more than 2%, tapping is continued for 1250 times and tapped volume was noted. Tapping was continued until the difference between successive volumes is less than 2 % (in a bulk density apparatus). It is expressed in g/ml and is given by

$$Dt = M / Vt$$

Where, M is the mass of powder

Vt is the tapped volume of the powder.

**3. Angle of Repose (θ):**

The friction forces in a loose powder can be measured by the angle of repose (q). It is an indicative of the flow properties of the powder. It is defined as maximum angle possible between the surface of the pile of powder and the horizontal plane.

$$\tan(\theta) = h / r$$

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

Where, q is the angle of repose.

h is the height in cms

r is the radius in cms.

The powder mixture was allowed to flow through the funnel fixed to a stand at definite height (h). The angle of repose was then calculated by measuring the height and radius of the heap of powder formed. Care was taken to see that the powder particals slip and roll over each other through the sides of the funnel. Relationship between angle of repose and powder flow property.

**4. Carr's index (or) % compressibility:**

It indicates powder flow properties. It is expressed in percentage and is give

$$I = \frac{Dt - D}{Dt} \times 100$$

Where, Dt is the tapped density of the powder and
Db is the bulk density of the powder.

**5. Hausner ratio:**

Hausner ratio is an indirect index of ease of powder flow. It is calculated by the following formula.

$$\text{Hausner ratio} = \frac{Dt}{Db}$$

Where, Dt is the tapped density.
Db is the bulk density.

**Lower hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25)**

**In vitro Evaluation of Fast Dissolving Tablets:**

**1. Weight variation:**[7,8]

20 tablets were selected randomly from the lot and weighted individually to check for weight variation. Weight variation specification as per I.P. is shown in table No.5

**2. Hardness:**[7,8]

Hardness or tablet crushing strength (fc ), the force required to break a tablet in a diametric compression was measured using Monsanto tablet hardness tester. It is expressed in kg/cm2.

**3. Tablet thickness:** [7,8]

Tablet thickness can be measured using Varnier calipers (mitutoyo). The thickness was measured by placing tablet between two arms of the Varnier calipers.

**4. Content of acive ingredient:**[9]

25 mg of powder valsartan is weighed accurately and mixed with 25 ml of methanol, from that taken 1ml of solution and make up with 50ml of water and assayed for the drug content by UV Spectrophotometric method.

**4. Friability (F):**[6,7]

Friability of the tablet determined using Roche friabilator. This device subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping a tablet at I height of 6 inches in each revolution. Preweighted sample of tablets was placed in the friabilator and were subjected to the 100 revolutions. Tablets were dusted using a soft muslin cloth and reweighed. The friability (F) is given by the formula.[5]

$$F = \frac{\text{Winitial} - \text{Wfinal}}{\text{Winitial}} \times 100$$

**5. Wetting Time**[10,11]**:** A piece of tissue paper folded twice was placed in culture dish containing 6 ml phosphate buffer pH 7.4. A tablet was carefully placed on the surface of tissue paper and time required for phosphate buffer pH 7.4 to reach the upper surface of the tablet was noted **as** wetting time.

**6. Water Absorption Ratio**[10,11]**:** A test was done with the same procedure of wetting time. In this weight of tablet was noted before placing it on a petridish .After complete wetting the wetted tab lets was weighed. The water absorption ratio R was determined using equation,

R= Wa –Wb/ Wb X100

Where Wa= weight of tablet before water absorption
Wb = weight of water after water absorption

**7. In-vitro disintegration test**[10,11]**:**

The test was carried out using Tablet disintegration tester in distilled water at 37ºC ± 2ºC was used as a disintegration media and the time in second taken for complete disintegration of the tablet with no palable mass remaining in the apparatus was measured in seconds.

**8. In-vitro dissolution study**[12]

The release rate of Valsartan from fast dissolving tablets was determined using United State Pharmacopoeia (USP) XXIV dissolution testing apparatus II (paddle method).(Model TDL 06T)

The dissolution test was performed using 900 ml of phosphate buffer pH 7.4 was used as dissolution medium.,temperature was at 37± 0.50C and stirrer was adjusted to rotate at 50 rpm. 5ml of dissolution media were withdrawn through a filter (0.45µ) at regular time intervals. Samples are diluted and assayed for valsartan at 250 nm. The withdrawn sample was filled with fresh fluid. Each dissolution rate replicated three times.

## RESULTS AND DISCUSSION:

**Table 1: Formulation Table**

| Ingredients ( mg ) | S1 | S2 | S3 | N1 | N2 | N3 |
|---|---|---|---|---|---|---|
| **Valsartan** | 40 | 40 | 40 | 40 | 40 | 40 |
| **Crospovidone** | 9 | 12 | 15 | - | - | - |
| **Gum Karaya** | - | - | - | 9 | 12 | 15 |
| **Magnesium Sterate** | 2 | 2 | 2 | 2 | 2 | 2 |
| **Talc** | 2 | 2 | 2 | 2 | 2 | 2 |
| **Mannitol** | 95 | 92 | 89 | 95 | 92 | 89 |
| **Orange Flavour** | 2 | 2 | 2 | 2 | 2 | 2 |
| **Microcrystalline Cellulose** | 50 | 50 | 50 | 50 | 50 | 50 |
| **Total** | 200mg | 200mg | 200mg | 200mg | 200mg | 200mg |

**Table No. 2 Pre-compression Parameters of Formulations Prepared by Direct Compression Method**

| Sr No. | Formulation code | Angle of Repose(θ) | Bulk Density (gm/cc) | Tapped Density (gm/cc) | Carr's Index (%) | Hausner's Ratio |
|---|---|---|---|---|---|---|
| 1 | S1 | 29.18 | 0.36 | 0.438 | 16.6 | 1.2 |
| 2 | S2 | 25.45 | 0.34 | 0.414 | 16.6 | 1.01 |
| 3 | S3 | 26.42 | 0.34 | 0.46 | 25.0 | 1.33 |
| 4 | N1 | 28.30 | 0.41 | 0.52 | 20.0 | 1.25 |
| 5 | N2 | 26.15 | 0.40 | 0.52 | 21.0 | 1.27 |
| 6 | N3 | 24.20 | 0.41 | 0.46 | 9.50 | 1.10 |

**Table No.3 Post-compression Parameters of Formulations Prepared by Direct Compression Method**

| Parameters | Formulation code | | | | | |
|---|---|---|---|---|---|---|
| | S1 | S2 | S3 | N1 | N2 | N3 |
| **Hardness±SD (kg/cm)** | 3.20± 0.24 | 2.94± 0.12 | 3.4± 0.30 | 3.68± 0.10 | 3.60± 0.8 | 3.20± 0.12 |
| **Thickness±SD (mm)** | 2.20± 0.04 | 2.22± 0.4 | 2.27± 0.8 | 2.24± 0.8 | 2.32± 0.05 | 2.12± 0.05 |
| **Friability (%)** | 0.52 | 0.86 | 0.51 | 0.82 | 0.68 | 0.84 |
| **In-vitro disintegration time±SD(sec)** | 21.34±0.42 | 14.22±0.62 | 9.22±0.16 | 30.32±0.08 | 24.26±0.68 | 16.34±0.86 |
| **Wetting Time±SD(sec)** | 14.00±0.86 | 11.33±0.62 | 9.08±0.58 | 22.00±0.44 | 18.46±0.65 | 12.00±0.16 |
| **Water Absorption ratio±SD(%)** | 44.34±0.16 | 38.56±0.86 | 40.62±0.72 | 36.82±0.36 | 40.24±0.48 | 42.64±0.62 |
| **Percent Drug Content±SD** | 99.72±0.42 | 97.66±0.14 | 99.92±0.92 | 101.32±0.86 | 98.24±0.26 | 99.22±0.64 |
| **In vitro Drug release %** | 85.22 | 92.46 | 96.78 | 70.68 | 72.62 | 75.60 |
| **Weight Variation(%)** | (182.4-214.8) Within the IP Limits of ±7.5% | | | | | |

All values are expressed as mean ± SD, n=3

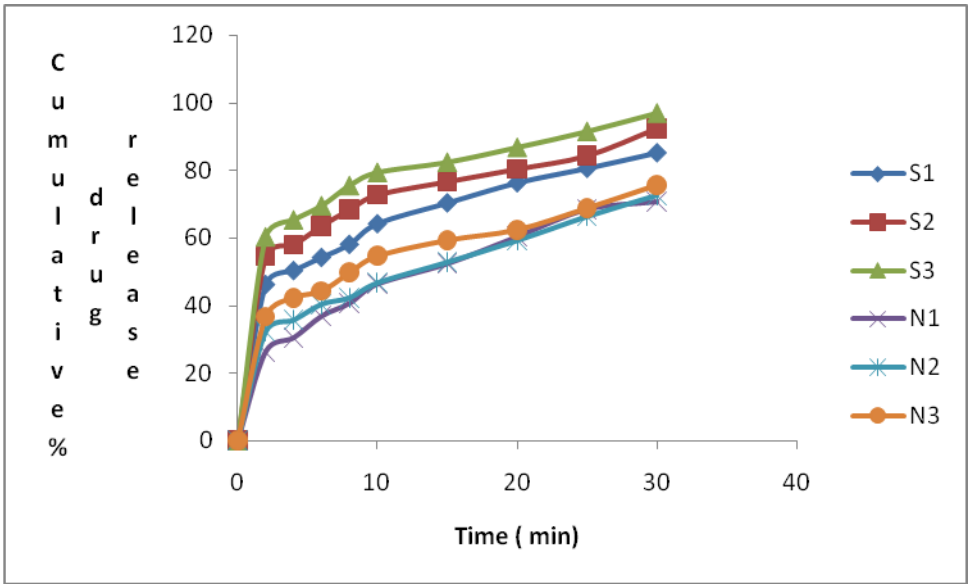


**Fig 1 : Cumulative % drug release Vs time of S and N in phosphate buffer**

The present study was undertaken to formulate and evaluate fast dissolving tablet of Valsartan by direct compression method using different concentrations of crospovidone (4.5% - 7.5%) as synthetic superdisintegrant and Gum karaya (4.5% - 7.5%) as natural superdisintegrant.

The angle of repose and the compressibility values varied from 24.20 to 29.18 respectively. Bulk densities of various formulations varied 0.34 to 0.41 gm/cc. From these values, it was evident that these blends had good flow properties. Hardness, thickness and friability of all the tablet formulations were observed in the range of 3.20 to 3.68 kg/cm2, 2.12 to 2.27 mm and 0.51 to 0.86%, respectively. Weight variation was found within the specification of the IP limits of • } 7.5%. Average weight of 20 tablets of all ten formulations was found in the range of 182.4 to 214.8 mg. Wetting time and water absorption ratio was found in the range of 9.08 to 22.00 sec and 36.82 to 44.34%, respectively, which facilitate the faster dispersion in the mouth. Drug content of all the formulations was found in the range of 97.66 to 101.32%. The *in-vitro* disintegration time was measured by the time taken to undergo complete disintegration and was observed rapid with the batches containing crospovidone (9.22 to 21.34 sec) and delayed with the batches containing *gum karaya* (16.34 to 30.32 sec). The rapid disintegration may be due to the rapid

uptake of water from the medium, swelling and bursting effect. *In vitro* dissolution studies of various formulations at different time intervals are reported in (Table-8).

The formulation N3 showed the maximum dissolution rate of 98.79% drug release in 30 min, whereas the N3 formulation released up to 77.50% in 30 min. From the overall observations, formulation S3 containing 7.5% w/w crospovidone was considered to be the best formulation, which releases up to 98.79% of the drug in 30 min.

## CONCLUSION:

The present work was aimed to formulate the fast disintegrating tablet Of valsartan by using synthetic and natural superdisintegrants, crospovidone and *Gum karaya* respectively. The results from *in vitro* disintegration time, *in vitro* release study, wetting time and water absorption ratio showed that crospovidone is more beneficial than the Gum karaya. Thus it can be concluded that, the formulation S3 containing crospovidone (7.5% W/W) is most acceptable.

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