Analysis of the Improvement of Termination Property of VALSARTAN using Solvent Deposited Systems

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Abstract
The aim of the current study is to prepare and estimate solvent deposited systems (SDS) of valsartan (VAL) and to find out the effect of various formulation variables like polymers and solubilizing agents on drug release properties of VAL. Microcrystalline cellulose (MCC) and sucrose were used as polymeric carriers and sodium lauryl sulfate (SLS) and polyvinyl pyrrolidone (PVP) as solubilizing agents. The arranged SDS were characterized for inflexibility, weight variation, dissolution time, FTIR and drug release behavior for tablets. FTIR studies confirm the compatibility of VAL with excipients used in the formulation. In-vitro drug release studies indicate that the formulations consist of MCC as carrier showed slower VAL release compared to formulations containing sucrose as carrier. Addition of SLS and PVP brought a significant increase in VAL release compared to formulations without them. The formulation F6 showed quicker disintegration (within 32 sec) and VAL release rates (complete release was obtained within 180 sec) along with good physico-mechanical properties.

Keywords: Valsartan, solvent deposited systems, formulation variables, compatibility

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1. Introduction
Modern improvements in combinatorial science and improved throughput technique utilized in drug discovery brought about increase number of novel drugs with poor fluid solvency. Roughly 90% of the novel substance elements are measured inadequately dissolvable by means of high or low penetrability. BCS class II drugs are extremely porous and low soluble in nature. Thereby their absorption or bioaccessibility is incomplete by termination rate. Therefore termination improvement is the key factor in for emulating BCS class II drugs. Valsartan (VAL), \( N - (1 - oxopentyl) - N [21 - (1H - tetrozol - 5 - yl)]1,1, - biphenyl] - 4 - yl]methy] - L - valine,a powerful and selective AT1 receptor antagonist used in the treatment of hypertension. VAL is a BCS class II drug and is highly hydrophobic in nature. The deprived aqueous solubility of drug is linked by measured drug termination and measured...
erratic amalgamation important to slow down oral bioavailability. Till date several approaches has been developed to improve the suspension properties of weakly soluble drugs like complexation, solid dispersions, and soft gels. Solvent deposited systems (SDS) in view of powder arrangement innovation demonstrates capable probable in humanizing the disintegration pace of inadequately solvent medications like VAL. SDS upgrades the medication disintegration as well as can be monetarily suitable and has mechanical scale-up possibility because of minimal effort and simplicity of handling [8-9]. In this way, the current examination was aimed at identifying the detail VAL SDS and to assess its adequacy.

2. Materials and methods:
VAL is given as contribution example by Hetero Drugs Pvt ltd, Hyderabad. Ethanol, micro crystalline cellulose (MCC), sucrose, and sodium laurel sulfate (SLS) purchased from Qualigens fine chemicals, Mumbai.

**Groundwork of VAL SDS**

The VAL SDS was prepared by Spraying Technique. The required quantities of drug and carrier as given in Table 1 were taken. Initially carrier was taken in a mortar and VAL was sprayed on carrier (MCC or sucrose) which was dissolved in ethanol with intermittent mixing and dried at 40°C for 10 min. 40 mg equivalent of VAL was accurately weighed and compressed into tablets by direct compression method.

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Ingredients (mg)</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
<th>F5</th>
<th>F6</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>VAL</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>2.</td>
<td>MCC</td>
<td>150</td>
<td>200</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3.</td>
<td>Sucrose</td>
<td>-</td>
<td>-</td>
<td>150</td>
<td>200</td>
<td>200</td>
<td>200</td>
</tr>
<tr>
<td>4.</td>
<td>SLS</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>30</td>
<td>-</td>
</tr>
<tr>
<td>5.</td>
<td>PVP</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>30</td>
</tr>
</tbody>
</table>

**FTIR Studies**

FTIR studies were carried out by ATR-FTIR spectrometer (Bruker, Germany). ATR spectra estimated more than the wave number scope of 4000-500 cm⁻¹ at a goal of 1.0 cm⁻¹. The powder test was basically positioned onto the ATR gem and the example range was gathered.

**VAL content**

The VAL content in tablets was determined by dissolving one tablet in 20ml ethanol and 20 ml of pH 6.8 phosphate support is included and the substance are sonicated intended for 10min and made sufficient with cushion in 100 ml volumetric flagon. This step is correctly dilute by pH 6.8 phosphate buffer and was assayed at 250nm for VAL.10
Rigidity
The rigidity of the prepared tablets are deliberated by means of the Pfizer tablet rigidity tester and the hardness of the each tablet was recorded\(^{11}\).

Weight Variation
Weight variety was determined according to technique described in USP. Twenty tablets are selected aimlessly and their usual load is determined using an electronic equalization. The tablets be weighed separately and distinction with usual load [12].

In-vitro Disintegration analysis
The disintegration time is given by means of USP tablet breakdown analysis equipment with 900 ml of pH 6.8 phosphates buffer and preserved at 37±0.5\(^{0}\)C\(^{13}\).

2.7 In-vitro Dissolution
The disintegration rate testing of VAL details was examined utilizing USP XXII disintegration rate testing device, (paddle type) (LAB INDIA DISSO 2000). The oar was pivoted at a speed of 50 rpm and the disintegration medium (900 ml pH 6.8 Phosphate cradle) was kept up at a temperature of 37.50 ± 0.5 0C. At explicit time stretches a 5 ml aliquot was gathered and was supplanted with new amount of disintegration medium. The examples were tested for VAL content by estimating the absorbance at 250 nm utilizing U.V Spectrophotometer (ELICO SL 159). The percent of VAL disintegrated at different time stretches was determined and plotted against time [3].

3. RESULTS AND DISCUSSION

Preparation of VALSDS
VAL SDS prepared by spraying technique on carrier gave porous powder due evaporation of ethanol leaving the drug on the surface of the carrier which resulted in faster drying rates. This porous powder was equivalent to 40 mg VAL (250 mg), weighed and then compressed into tablets by direct compression method. The VAL SDS thus prepared were stable and porous indicating the easiness of the method compared to other methods used for the enhancement of solubility\(^{14}\).

FTIR Studies
The FTIR spectra of VAL and VAL SDS F6 were shown in Figure 1. VAL showed characteristic peaks at 3393 cm\(^{-1}\) (N-H stretching), 2981 cm\(^{-1}\) (C-H stretching), 2931 cm\(^{-1}\) (O-H stretching), 1695 cm\(^{-1}\) (C-O stretching), 1653 cm\(^{-1}\) (C-N stretching), and 753 cm\(^{-1}\) (C-H bending) respectively. The VAL SDS also showed the same characteristic peaks as of pure VAL indicating that there is compatibility between the VAL and the recipients used in the formulation\(^{15}\).
**Hardness**
For the most part the tablets ought to be adequately difficult to oppose the breaking during ordinary dealing with but delicate enough to deteriorate appropriately subsequent to gulping. All the formulations showed acceptable hardness (3.8-4.4 kg/cm²). The results were shown in Table 2.

**Weight Variation**
The weight of the individual tablet will be implying the VAL dose for effective therapy. The prepared VAL tablets were checked for weight variation and from the results it is observed that all the formulations showed uniform weight and the percent of error is found to be in the variety of -1.49 to +2.1. The consequences are shown in Table 2.

**Disintegration**
The disintegration time of VAL SDS were shown in Table 5. From the results it is observed that formulation F6 disintegrates within 3 min; added formulations take roughly 3-10 min, whereas the formulation F4 showed a higher disintegration of about 13 min. The longer breakdown time might hold back the discharge rate of the drug. The results were revealed in Table 2.

<p>| Table 2: Evaluation limit of VAL SDS |
|-------------------------|-----------------|-----------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th>S.No.</th>
<th>Formulation</th>
<th>Hardness kg/cm²</th>
<th>% Error of Weight Variation</th>
<th>% Drug content</th>
<th>Disintegration time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>3.8</td>
<td>-1.49</td>
<td>99.13</td>
<td>10</td>
</tr>
<tr>
<td>2</td>
<td>F2</td>
<td>4.2</td>
<td>0.07</td>
<td>104.1</td>
<td>8</td>
</tr>
<tr>
<td>3</td>
<td>F3</td>
<td>4.1</td>
<td>-0.58</td>
<td>96.5</td>
<td>8</td>
</tr>
<tr>
<td>4</td>
<td>F4</td>
<td>4.4</td>
<td>1.68</td>
<td>100.5</td>
<td>6</td>
</tr>
<tr>
<td>5</td>
<td>F5</td>
<td>4.0</td>
<td>2.1</td>
<td>101.5</td>
<td>4</td>
</tr>
<tr>
<td>6</td>
<td>F6</td>
<td>4.2</td>
<td>-1.2</td>
<td>99.6</td>
<td>3</td>
</tr>
</tbody>
</table>

**In-vitro Dissolution Studies**
In the present investigation, termination of VAL SDS was predicted by using Type II dissolution apparatus and 900 ml of pH 6.8 phosphate buffer is used as termination average. The effect of various formulation variables like carriers and solubilizing agents on VAL release from SDS was studied and the comparative release profiles were shown in Figure 2. Totally 6 different formulations were prepared using MCC and sucrose as carriers and SLS and PVP as solubilizing agents. F1 and F2 formulations were prepared with MCC as carrier. Cumulative percent of VAL unrestricted at the end of 5 min is 64.31±1.21 and 70.43±0.89 for F3 and F4 respectively. Complete VAL release was obtained at finished of 30 and 20 min respectively for F3 and F4 and the relative shape is revealed in Fig 2b. The VAL release from F4 is higher than F3. Overall, the VAL release is higher for F4 (containing sucrose as carrier) than F2 (containing sucrose as carrier).
Effect of solubilizing agents on VAL release was also observed. Both SLS and PVP were added to the formulations. The cumulative percent of VAL unrestricted at the ending of 5 min is 86.47±0.26 and 90.31±1.3 respectively for F5 and F6. Complete release of VAL was observed at the end of 10 min and 7 min respectively for F5 and F6 respectively indicating that the addition of solubilizing agents showed significant effect on VAL release from the formulation, which might be due to effective decrease in surface tension. Overall sucrose was selected as carrier because F4 shows higher dissolution properties than F2. VAL SDS with PVP and SLS demonstrated better disintegration properties looked at than definitions without PVP and SLS. SDS with PVP (F6) gave higher disintegration properties when contrasted with SLS detailing (F5). The comparative release profiles for SDS with and without PVP and SLS are given in Figure 2.

4. CONCLUSION

In the present investigation VAL SDS were successfully formulated. The effect of carriers on dissolution rate of VAL was studied and found that sucrose is a better carrier than MCC and the effect of solubilizing agents also studied which enhanced the dissolution profile of VAL from SDS. Overall formulation F6 containing sucrose as carrier and PVP as solubilizing agent showed better dissolution properties.
REFERENCES

