Formulation and evaluation of gas powered systems of cefdinir tablets for controlled release

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ABSTRACT

The present work is aimed to formulate Cefdinir floating tablets using different hydrophilic and hydrophobic polymers like HPMC, Ethyl cellulose, Xanthum gum, guar gum and gas generating agent Sodium bicarbonate. The develop gastro retentive dosage form that could retain the agent namely Cefdinir in the stomach for longer periods of time delivering the drug to the site of action, i.e., stomach. HPMC is used as a swelling agent, Guar gum and Xanthum gum is used as binding agent. Ethyl cellulose is used as matrix form agent. PVP is used as a suspending agent. Sodium bicarbonate is used as a gas forming agent. MCC is used as a disintegrant and diluent. Magnesium stearate is used as a lubricant. The prepared Cefdinir tablets will be evaluated for drug content, entrantment efficiency, post compression studies, In-vitro buoyancy studies, swelling index studies, In-vitro dissolution studies, release kinetics, stability studies. All these parameters were found to be within the pharmacopoeial limits. Formulation F5 was selected for drug release and stability study on the basis of appropriate results of post compression study. In-vitro dissolution study was carried out and showed controlled release pattern.

Keywords: Gas Powered Systems, Cefdinir, Controlled release, Floating drug delivery.
gastric residence time seems to offer a greater safety of use compared to the other approaches. The tablets were prepared with effervescent component (sodium bicarbonate) using hydroxypropylmethylcellulose (HPMC) as a binder. The prepared Cefdinir tablets evaluated for drug content, entrapment efficiency, pre compression studies, in-vitro buoyancy studies, swelling index studies, in-vitro dissolution studies, release kinetics, stability studies.

**MATERIALS AND METHODS**

Cefdinir was supplied as a gift from M/s Hetero Drugs Ltd, Hyderabad, India. HPMC, Xanthum Gum, Guar Gum, PVP, Ethyl Cellulose, Sodium Bicarbonate, Micro Crystalline Cellulose, Magnesium Stearate were used of pharmaceutical grades. All other chemicals were used of analytical grade.

**Preparation of calibration curve of Cefdinir**

100 mg of Cefdinir was accurately weighted into 100 ml volumetric flask, dissolved in 0.1N HCL and volume was made up with 0.1N HCL. Pipette 1ml of this solution into another 10 ml volumetric flask and the volume was made with 0.1N HCl and marked as Stock. From this Cefdinir standard stock solution (1000µg/ml), 1ml solution was diluted to 10 ml using 0.1N HCl solution to get concentrations of 100 µg/ml from this solution, aliquots of 0.2 ml, 0.4 ml, 0.6 ml, 0.8 ml, 1.0 ml, 1.2 ml and 1.4 ml from standard drug solution were diluted to 10 ml with 0.1M. The absorbance of these solutions was measured at 206 nm 0.1N HCL as a blank.

**Pre compression studies**

**Bulk density**

It is a ratio of mass of powder to bulk volume. The bulk density depends on particle size distribution, shape and cohesiveness of particles. Accurately weighed quantity of powder as carefully poured into graduated measuring cylinder through large funnel and volume was measured, which is called initial bulk volume. It is expressed in gm/ml and is given by the formula:

\[
\text{Bulk density} = \frac{M}{V_0}
\]

Where, \( M \) = mass of the powder, \( V_0 \) = bulk volume of the powder

**Angle of repose (θ)**

It is defined as the maximum angle possible between the surface of the pile of the powder and the horizontal plane. Fixed funnel method was used. A funnel was fixed with its tip at a given height \( h \), above a flat horizontal surface to which a graph paper was placed. Powder was carefully poured through a funnel till the apex of the conical pile just touches the tip of the funnel. The angle of repose was then calculated using following equation:

\[
\text{Angle of repose } \theta = \tan^{-1}\left(\frac{h}{r}\right)
\]

Where, \( h \) = height of the pile, \( r \) = radius of the pile

**Tapped density**

Ten gram of powder was introduced into a clean, dry 100 ml measuring cylinder. The cylinder was then tapped 100 times from a constant height and the tapped volume was read. It is expressed in gm/ml and is given by:

\[
\text{Tapped density} = \frac{M}{V_t}
\]

Where, \( M \) = mass of the powder, \( V_t \) = final tapping volume of the powder

**Compressibility index (Carr’s index)**

Compressibility index is used as an important parameter to determine the flow behavior of the powder. It is indirectly related to the relative flow property rate, cohesiveness and particle size. It is Simple, fast and popular method for predicting flow characteristics. Carr’s index can be represented by Equation:

\[
\text{Compressibility index} = \frac{M}{V_0} - \frac{M}{V_t}
\]
**Compressibility index (%)** = \[ \frac{TD - BD}{TD} \times 100 \]

**Hausner's ratio**

Hausner's ratio is used to predict the flow ability of the powders. This method is similar to compressibility index. Hausner's ratio can be represented by Equation:

\[
\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}
\]

**Evaluation of Prepared Formulation**

**Weight variation**

Randomly selected twenty tablets were weighed individually and together in a single pan balance. The average weight was noted and standard deviation calculated. The tablets pass the test if not more than two tablets fall outside the percentage limit and none of the tablet differs by more than double percentage limit.

\[
PD = \left( \frac{\text{Wavg} - \text{Winitial}}{\text{Wavg}} \right) \times 100
\]

Where, PD = Percentage deviation, Wavg = Average weight of tablet, Winitial = Individual weight of tablet

**Thickness**

The thickness and diameter of tablets was determined using Vernier Caliper. Twenty tablets from each batch were used and average values were calculated.

**Hardness**

The Monsanto hardness tester was used to determine the tablet hardness. The tablet was held between affixed and moving jaw. Scale was adjusted to zero; load was gradually increased until the tablet fractured. The value of the load at that point gives a measure of the hardness of the tablet. It is expressed in kg/cm². For each formulation, the hardness of six tablets was determined and average value was calculated.

**Drug content**

Tablets were crushed and the powder equivalent to 100mg of drug were accurately weighed and transferred to 50 ml volumetric flask. To this flask, sufficient amount of distilled water was added to dissolve the tablets completely. Then, the volume of flask was made up to the mark with same solvent. From this solution, 1ml of the sample was pipetted out and transferred to 10 ml volumetric flask. The volume in the second flask was made up to the mark with distilled water. From this 0.6ml, 0.8ml and 1ml samples were withdrawn and volume was made up to 10ml to maintain concentration within the beer’s range. This final diluted solution was estimated UV spectrophotometrically at 286 nm.

**Friability**

Twenty tablets samples were weighed accurately and placed in friabilator (Roche Friabilator). After the given specification (4 min at 25 rpm), loose dust was removed from the tablets. Finally tablets were weighed. The loss in weight indicates the ability of the tablets to withstand this type of wear. The % friability was then calculated by:

\[
\% \text{ Friability} = \left( \frac{\text{Loss in weight / Initial weight}}{1} \right) \times 100
\]

**In-vitro buoyancy studies**

The in-vitro buoyancy was determined by floating lag time, and total floating time. The tablets were placed in a 100ml beaker containing 0.1N HCl. The time required for the tablet to rise to the surface and float was determined as floating lag time (FLT) and the duration of the time the tablet constantly floats on the dissolution medium was noted as the Total Floating Time respectively (TFT).

**Swelling index studies**

The swelling behavior of a dosage unit was measured by studying its weight gain. The swelling index of tablets was determined by placing the tablets in the basket of dissolution apparatus using dissolution medium as 0.1N HCl at 37±0.5°C. After 1, 4 and 6h each dissolution basket containing tablet was withdrawn, blotted with tissue paper to remove the excess water and weighed on the analytical balance (Schimuzu, AX 120). The experiment was performed in triplicate for each time point. Swelling index was calculated by using the following formula

\[
\text{Weight gain} = \frac{\text{Weight at time (t)} - \text{Initial weight}}{\text{Initial weight}} \times 100
\]

**RESULTS AND DISCUSSION**

**Calibration curve of cefdinir**

The linearity was observed in the concentration range of 2 to 14μg/ml and thus it follows the Bear-Lambert’s law of absorbance at 328 nm.

**Pre compression studies**

Precompression studies of powdered blend were performed on parameters like bulk density, tapped density, compressibility index, Hausner’s ratio and angle of repose as shown in the table below. Angle of repose was found to be 26.62, 27.46, 28.32, 28.06, 27.58 and 28.44. Bulk density was found to be 0.721, 0.710, 0.415, 0.454, 0.458 and 0.445 g/cm3, tapped density 0.872, 0.879, 0.483, 0.525, 0.505 and 0.502 g/cm3, Hausner’s ratio 1.206, 1.251, 1.178, 1.155, 1.119 and 1.123, Carr’s index 19.714, 15.113, 15.602, 12.234 and 12.585 was found for F1, F2, F3, F4, F5 and F6 formulation respectively and reported in Table 2.
Table 2: Precompression Studies

<table>
<thead>
<tr>
<th>Formulation code</th>
<th>Bulk density (gm/mL)</th>
<th>Tapped density (gm/mL)</th>
<th>Compressibility index (%)</th>
<th>Hausner’s ratio</th>
<th>Angle of repose (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>0.721</td>
<td>0.872</td>
<td>17.126</td>
<td>1.206</td>
<td>26.62</td>
</tr>
<tr>
<td>F2</td>
<td>0.710</td>
<td>0.879</td>
<td>19.714</td>
<td>1.251</td>
<td>27.46</td>
</tr>
<tr>
<td>F3</td>
<td>0.415</td>
<td>0.483</td>
<td>15.113</td>
<td>1.178</td>
<td>28.32</td>
</tr>
<tr>
<td>F4</td>
<td>0.454</td>
<td>0.525</td>
<td>15.602</td>
<td>1.155</td>
<td>28.06</td>
</tr>
<tr>
<td>F5</td>
<td>0.458</td>
<td>0.505</td>
<td>12.234</td>
<td>1.119</td>
<td>27.58</td>
</tr>
<tr>
<td>F6</td>
<td>0.445</td>
<td>0.502</td>
<td>12.585</td>
<td>1.123</td>
<td>28.44</td>
</tr>
</tbody>
</table>

### Organoleptic and Hardness

The formulated tablets were evaluated for their organoleptic characters. The tablets are round in shape and white in colour. All the tablets showed elegance in appearance. The hardness of the tablets was measured by Monsonto hardness tester. The hardness of all the formulations was found to be in the range of 7.2 to 7.6 kg/cm². It indicates all the tablets have adequate mechanical strength.

### Total floating time and *in-vitro* buoyancy studies

*In-vitro* buoyancy of the tablets from each formulation (F1 to F6) was evaluated (Figure). Where, the highest and lowest floating lag time (FLT) was observed with the formulation F1 and F6 respectively. The concentration of the natural polymers increases the floating lag time also increases and total floating time observed for all the formulations was >10 hours.

### Weight variation

Twenty tablets of each formulation were selected for weight variation test. The accepted percentage deviation was ±7.5 for 130-324mg weight tablets. It was within the LP. limit and all the tablets passed the weight variation test. Friability test was carried out by Roche friabulator. The maximum weight loss should be not more than 1%. All the tablets passed the friability test.

### Total floating Time (hr.)

Figure 3: Hardness studies of cefdinir floating tablets formulations

Figure 4: Average weight of cefdinir floating tablets formulations

Figure 5: Total floating time studies of cefdinir floating tablets formulations

Figure 6: Buoyancy lag time (min.) studies of cefdinir floating tablets formulations
Figure 7: Welling index ratio (%) studies of floating tablets formulations

Figure 8: Photographic representation of swelling index ratio (%) studies
In-vitro drug release studies
In-vitro drug release studies were done for the selected study formulations. The drug release was found to show maximum drug release in case of F5 with 97.4% in 10 hrs as shown in figure 9.

**CONCLUSION**

The Cefdinir is antimicrobial agent. In this study the gastroretentive Cefdinir tablet formulation with different excipients for controlled release is successively prepared and evaluated. Formulation showed good release results thus, results of the current study clearly indicate, Cefdinir floating tablet was a stable dosage form and a promising potential of the cefdinir gastroretentive system as an alternative to the conventional dosage form for controlled release. However, further clinical studies are needed to assess the utility of gastroretentive Cefdinir floating formulation.

**REFERENCES**