Formulation and evaluation of sublingual tablets of lisinopril

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This study presents formulation and evaluation of sublingual tablets of lisinopril for treatment of hypertension. Sublingual route offers faster disintegration and dissolution of drug than oral route, because of increasing bioavailability as it bypass GIT (gastrointestinal tract). Sublingual tablets, prepared by direct compression method, were found in accordance with standards. Out of three batches (A, B, C), batch B having fastest disintegrating time was most suitable as sublingual tablet.

Keywords: Bioavailability, Faster disintegration, Hypertension, Sublingual route

Introduction

Sublingual route (SR), faster than other routes except parenteral route, ensures that substance will degrade only by salivary enzymes before entering bloodstream, whereas orally administered drugs must survive through harsh environment of gastrointestinal tract (GIT). Lisinopril (1-[N2-{(S)-1-carboxy-3-phenylpropyl}-L-lysil]-L-proline dihydrate), an angiotensin-converting enzyme (ACE) inhibitor, is used in treatment of hypertension, which is caused by obesity, stress, decreased physical activity, increased salt intake and decreased calcium & potassium intake. Lisinopril is very less bio available (25-30%) due to incompletely absorption from GIT and first pass metabolism. SR offers fast disintegration of tablet, faster onset of action and rapid absorption by sublingual mucosa blood vessels. Among different techniques (freeze drying technology, spray drying method, sublimation technology and direct compression method) used for formulating sublingual tablets (STs), direct compression method does not require water or heat during formulation and is an ideal method. Excipients (superdisintegrants) and spray dried form of excipients promote rapid disintegration and dissolution of tablet, giving faster onset of action. This study presents formulation and evaluation of STs of lisinopril for treatment of hypertension.

Experimental Section

Materials

Lisinopril was obtained as a gift sample from Ranbaxy Pvt Ltd, Gurgaon, India. Avicel pH101, DCP (Dicalcium phosphate) anhydrous, Na starch glycolate (SSG), Magnesium (Mg) stearate and talcum powder were obtained from Central drug house (CDH), New Delhi, India, and Aspartame was obtained from Himedia. All other chemicals used were of analytical grade, procured from standard sources.

Methods

Three batches (A, B, C) of tablets were prepared by varying concentration of Avicel (pH-101) and SSG (Table 1). Accurate amount of drug and other excipients were weighed, sieved through sieve no. 35 and blended homogenously. To this mixture, talc and Mg stearate were added in appropriate quantity following geometric dilution method. Finally, mixture was directly compressed into tablet (wt, 200 mg; diam, 8.4 mm) using multi punch Rotary Press Machine (Madhur).

Evaluation Parameters

Table 1

Weight Variation Test and Drug Content

Weighed 20 tablets were selected randomly and their average weight was calculated. None average weight deviates by more than the percentage and none deviates by more than twice that percentage. Tablets (20) from each batch were randomly selected and powdered. Powder containing lisinopril (25 mg) was dissolved in water, filtered, and filtered solutions were analyzed...
Table 1—Composition of Lisinopril sublingual tablets

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>A1</th>
<th>A2</th>
<th>A3</th>
<th>B1</th>
<th>B2</th>
<th>B3</th>
<th>C1</th>
<th>C2</th>
<th>C3</th>
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<td>145</td>
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<td>163</td>
<td>143</td>
<td>123</td>
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</tbody>
</table>

Transmittance, %

Wavenumbers, cm⁻¹

a)

b)

Contd—
spectrophotometrically (Shimadzu, UV-1700) at 257.4 nm.

**Hardness and Friability Tests**

Hardness of tablets was tested using Monsanto hardness tester and their average hardness was determined (Table 2). Tablets (6) were selected from each batch and placed in Roche Friabilator (Singhla Scientific industries Pvt Ltd, Ambala) and revolved at 25 rpm and equipment was run for 100 revolutions. Tablets were reweighed and after brushing of powder on surface of tablet, loss% was calculated (Table 2).

**Disintegration and Dissolution Tests**

Disintegration test was carried out in tablet disintegration apparatus (Sunbim, India). Tablets (6) were selected and 1 tablet in each of 6 tube of disintegration tube was placed. Distilled water was used as disintegrating medium maintained at 24 ± 0.2°C. Time for complete disintegration of tablet was noted (Table 2). In vitro drug release profile (Table 2) was checked by dissolution rate USP apparatus type II (Paddle method, Electrolab TDT-08L). Phosphate buffer (900 ml; pH, 7.4) was taken as dissolution medium at 50 rpm at 37±0.5°C for 30 min. Samples (5 ml each) were withdrawn and same volume was replaced with equal volume of fresh dissolution medium. Amount of API (active pharmaceutical ingredient) in samples was determined using spectrophotometer (Shimadzu, UV-1700) at 254.7 nm.

**Results and Discussion**

Three batches (A, B, C) of STs were prepared by direct compression method. Each batch contained different composition of ingredients [Avicel (pH101) and SSG]. All batches were tested for different evaluation
parameters. Weight variation of tablets was -1.4% to +5.2% (Table 2).

**IR Spectrum Study**

IR spectra of pure drug lisinopril (Fig. 1a) and IR spectra of lisinopril with excipients Avicel (Fig. 1b) and DCP (Fig. 1c) reveal the presence of peak at 1390.93 cm\(^{-1}\), indicating that there was no interaction between drug and excipients used.

**In vitro Drug Release Study**

Formulation B3 (Batch-B) showed maximum (88%) drug release in 30 min (Fig. 2, Table 2).

**Conclusions**

STs of lisinopril were prepared by direct compression method using DCP, Avicel (pH-101), SSG, Aspartame, talc and Mg stearate. B3 (Batch B) formulation gave maximum drug release (88%) in 30 min.

**References**


