A solid dispersion based on milk-micelle as a drug-carrier for the enhancement of the aqueous solubility of ritonavir

Pradip Dhore  
*R.T.M. Nagpur University*

Suprit Saoji  
*R.T.M. Nagpur University*

Nishikant Raut  
*R.T.M. Nagpur University*

M. Bernardez  
*St. John Fisher College*

Rahul V. Haware  
*Campbell University*

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Abstract
The goal of present investigation was to evaluate the feasibility of formulating a solid-dispersion using milk-micelles as drug-carriers, to enhance the aqueous solubility of ritonavir.

Disciplines
Pharmacy and Pharmaceutical Sciences

Comments
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Authors
Pradip Dhore, Suprit Saoji, Nishikant Raut, M. Bernardez, Rahul V. Haware, and Vivek S. Dave
A solid dispersion based on milk-micelle as a drug-carrier for the enhancement of the aqueous solubility of ritonavir

P. W. Dhore1, S. D. Saoji1, N. A. Raut1, M. Bernardez2, R. V. Haware3, V. S. Dave2

1Department of Pharmaceutical Sciences, R. T. M. Nagpur University, Nagpur, Maharashtra, India
2Wegmans School of Pharmacy, St. John Fisher College, Rochester, NY, USA
3College of Pharmacy & Health Sciences, Campbell University, Buies Creek, NC, USA

Objective

The goal of present investigation was to evaluate the feasibility of formulating a solid-dispersion using milk-micelles as drug-carriers, to enhance the aqueous solubility of ritonavir.

Methods

Prototype solid dispersions of ritonavir with milk-micelles, using various drug/carrier ratios (table 1) were prepared by lyophilization technique. Additionally, physical mixtures of ritonavir with the carrier were also prepared using similar ratios.

The influence of the drug/carrier ratio on the improvement of ritonavir solubility was assessed by measuring the saturation solubility of the solid dispersions at 37°C. Briefly, an excess amount (~10 mg) of the prepared solid dispersion was placed in a glass vial containing 5 ml of purified water. The vials were sealed, and continuously shaken on rotary shaker at 37 °C for 48 hours. After 48 hours, the supernatant was collected, filtered through a Millipore™ filter (0.45 μm), suitably diluted, and assayed on a UV-visible spectrophotometer, at 239 nm.

The solid dispersion with the optimized drug/carrier ratio (based on the saturation solubility study) was selected to further evaluate the drug-release behavior in phosphate buffer (pH: 6.8) using USP apparatus II (paddle method).

Additionally, the prepared solid dispersions were characterized by Fourier Transformed Infrared (FTIR) Spectroscopy, Differential Scanning Calorimetry (DSC), Powder X-Ray Diffraction (PXRD), and Scanning Electron Microscopy (SEM).

Results

The formation of a solid dispersion was confirmed by the disappearance of the ritonavir melting endotherm (DSC, 122°C), and the FTIR peak (3000 cm⁻¹) in the solid dispersion. The measured values of apparent aqueous solubility of ritonavir, and the prepared solid dispersions are shown in table 1.

Results (contd.)

The results showed that increasing levels of the carrier in the solid dispersion resulted in a concomitant, and a significant increase in the aqueous solubility of ritonavir. This increase in the solubility was observed up to the drug: carrier ratio of 1:4, beyond which, the solubility of ritonavir was found to decrease. The drug: carrier ratio of 1:4 was thus considered optimal for the prepared solid dispersion.

The in-vitro dissolution profiles of free ritonavir, and the prepared solid dispersions are shown in figure 1. From the results it was observed that, at the end of 120 min, free ritonavir showed a ~10% release; whereas, ritonavir release from the solid dispersions was found to increase progressively with an increase in the carrier level.

This increase in the dissolution rate of ritonavir was observed up to the drug: carrier ratio of 1:4 (> 98% ritonavir released in 2 hours). The drug release was found to be slower from the solid dispersion with a drug/carrier ratio of 1:5.

Conclusions

The prepared solid dispersions showed a significant (up to 17-fold) enhancement in the apparent aqueous solubility, as well as the dissolution behavior of ritonavir. Solid dispersions, using milk micelle as a drug carrier can serve as potential alternative strategy for enhancing the aqueous solubility of poorly water soluble drugs such as ritonavir.

Table 1: Apparent aqueous solubility of the samples

<table>
<thead>
<tr>
<th>Drug: carrier ratio</th>
<th>Apparent aqueous solubility (µg/ml)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pure ritonavir</td>
<td>0.37 ± 0.03</td>
</tr>
<tr>
<td>1:1 (SD-1)</td>
<td>3.61 ± 0.02</td>
</tr>
<tr>
<td>1:2 (SD-2)</td>
<td>6.39 ± 0.05</td>
</tr>
<tr>
<td>1:3 (SD-3)</td>
<td>8.27 ± 0.06</td>
</tr>
<tr>
<td>1:4 (SD-4)</td>
<td>11.36 ± 0.06</td>
</tr>
<tr>
<td>1:5 (SD-5)</td>
<td>6.81 ± 0.03</td>
</tr>
</tbody>
</table>

* Data expressed as mean ± Std. Dev., n = 3

Figure 1: Influence of the drug: carrier ratio on the dissolution of ritonavir. Data expressed as mean ± Std. Dev., n=3

Results (contd.)

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