LAYERSOMES FOR ORAL DELIVERY OF AMPHOTERICIN B*
A. C. Rana, Abhinav Singh Rana
Institute of Pharmaceutical Sciences, Kurukshetra University, Kurukshetra, Haryana, India
E-mail: acrana4@yahoo.com

Background

Leishmaniasis is caused by a protozoal parasite of the genus leishmania which multiplies in certain vertebrates that act as reservoirs of the disease. Leishmaniasis is considered endemic in 88 countries in the world and 350 million people are considered at risk. An estimated 14 million people are infected, and each year about two million new cases occur. Amphotericin B (Amp-B) is potent antifungal agent which is considered first line drug for the treatment of the systemic fungal infections, in visceral leishmaniasis. Amp-B is selected as the drug for treatment of systemic fungal infection, because it shows lower resistance development tendency with high potency. The current therapy involves IV administration which is often associated with infusion and drug related side-effects.

Objective

The objective of the present work was to exploit the potential of polyelectrolytes stabilized liposomes in oral delivery of Amp-B.

Methods

Water

Sonication

Vortexing

Liposome dispersion

Coated Liposome

PAA Polymer addition

Poloxamer

Cholesterol

Diatyl ether

Methods

Charaterization
• Size, PDI, zeta potential and Entrapment efficiency
• Surface morphology by TEM

Freeze drying

• Different cryoprotectants were screened to make fluffy easy to redisperse cake

In vitro release

• Release behavior of different formulations was measured in PBS (pH 7.4)

Stability studies

• Layersomes: stability in simulated biological fluids (SGF and SIF)

Pharmacokinetic & Toxicity studies

• Pharmacokinetic was assessed in SD rats following the oral administration of different formulation
• Toxicity was assessed in Swiss mice following single administration of different formulation

Results

Shape and Morphology

Freeze drying studies

Fluffy, easy to re-disperse cake was obtained with trehalose at 10% w/v ratio

Stability in SGF and SIF

Formulation

Size (nm)

Initial size

SGF (pH 1.8)

SIF (pH 6.8)

Liposomes

161.4±10.2

319.4±14.6

288.7±12.9

PAA-liposomes

200.5±8.4

aggregation

223.4±14.9

Layersomes

238.4±15.1

247.2±15.6

251.4±10.8

Table 1: Trehalose

<table>
<thead>
<tr>
<th>Trehalose (%)</th>
<th>Reconstitution ratio (5/5)</th>
<th>Liposome</th>
<th>PAA-liposome</th>
<th>Layersomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>2.37</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>1.23</td>
<td>1.13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>1.54</td>
<td>1.94</td>
<td>0.99</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>2.24</td>
<td>2.17</td>
<td>1.19</td>
<td></td>
</tr>
</tbody>
</table>

Parameter

Cmax 16.2 41.9 42.8 49.2 60.6
Tmax 4 3 4 4 6
AUC tot 148.6 306.9 358.6 534.5 592.8

Toxicity studies

• AUC for layersomes was 3.39, 2.41 and 2.06 folds higher in comparison to Oral-Amp-B, Amp-B loaded liposomes and PAA-liposomes, respectively.
• Cmax of layersome in fasted and fed state were 49.27, and 60.65 respectively.
• At lower doses (1mg/kg) change in BUN and creatinine was not significantly increased in comparison to control

Conclusion and future direction

✓ In conclusion the positive outcomes of the proposed strategy is expected to add some toolbox in designing lipid based drug delivery system for oral delivery of other difficult to deliver drugs.

References