STABILITY OF TACROLIMUS ORAL SUSPENSION IN DISPOSABLE POLYPROPYLENE SYRINGE

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BACKGROUND AND IMPORTANCE

Following solid organ transplantation, post-anesthesia care units prioritise tacrolimus administration by enteral route to minimise the neurotoxicity associated with its use via continuous intravenous infusion.

There is no currently tacrolimus liquid dosage form commercially available ready for direct administration per os or via feeding tube.

AIM AND OBJECTIVES

- Design an affordable and ready-to-use extemporaneous tacrolimus oral solution/suspension
- Validate its physical, chemical and microbiological stability in polypropylene syringe
- Limit nurses exposure to this hazardous drug

MATERIAL AND METHODS

1. Design of an appropriate formulation
2. Assessment of stability parameters

- **Design of an appropriate formulation**
  - Search & evaluation of tacrolimus’ physicochemical properties
  - Selection of pharmaceutical form and suitable excipients
  - Preparation and storage: 20 – 25 °C
  - Preparation and storage: 2 – 8 °C

- **Assessment of stability parameters**
  - Every 7 days for a 28-days period, performed in triplicate

<table>
<thead>
<tr>
<th>TESTS</th>
<th>Physico-chemical</th>
<th>Organoleptic properties, sedimentation time, homogeneity, pH, redispersibility, crystal growth and weight variation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Micro-biological</td>
<td>Colony-forming units (CFU) growth: Blood agar cultures read after 24 and 48 h Sabouraud cultures read after 24, 48, 72 and 96 h</td>
</tr>
</tbody>
</table>

RESULTS

Tacrolimus 1 mg/mL oral suspensions

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Composition</th>
<th>Storage Conditions</th>
<th>Organoleptic properties</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Oraplus® + Orasweet® (1:1 ratio)</td>
<td>Stored at 20 – 25 °C</td>
<td>Sheer with yellowish hue and sweet</td>
</tr>
<tr>
<td>B</td>
<td>Simple syrup + 1,5 % CMC aqueous gel (2:1 ratio)</td>
<td>Stored at 2 – 8 °C</td>
<td>Homogeneous</td>
</tr>
</tbody>
</table>

Formulation B underwent validation

Formulation B contains less excipients and is more affordable (8,51 € cheaper per 100 mL)

CONCLUSION AND RELEVANCE

Tacrolimus 1 mg/mL oral suspension in simple syrup and carboxymethylcellulose 1,5% aqueous gel in a 2:1 ratio is stable when conditioned in polypropylene syringe for 28 days and stored at room or refrigerator temperature.

The developed and validated formulation provides safer handling of tacrolimus for nurses when a liquid oral dosage form is needed.

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