PHYSICAL, CHEMICAL AND MICROBIOLOGICAL STABILITY OF SIROLIMUS 0.4% IN TOPICAL FORMULATIONS

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OBJECTIVES
To improve the galenic formulation of sirolimus 0.4% for treatment of facial angiofibromas in tuberous sclerosis
To determine the validity period of proposed formulations according to:
- Physical stability
- Chemical stability
- Microbiological stability

METHODS
3 formulations of sirolimus 0.4% (each in duplicate, A and B), Conservation 2-8ºC

Gel
Sirolimus 0.4%
Transcutol 10%
Hydroxypropyl methylcellulose 2%
WFI (water for injection) q.s. 20 g

Ointment
Sirolimus 0.4%
Transcutol 10%
Lanolin 10%
Shea butter 20%
Vitamin E 1%
Vaseline q.s. 20g

Emulsion
Sirolimus 0.4%
Transcutol 10%
Absorption base W/O 20%
WFI q.s. 20 g

Physical stability
- pH of A and B with reactive strips at t=15 and 30 days
- Galenic Properties:
  Uniformity, extensibility, absence of crystals, absence of phase separation according to 3 levels:
  Level 1 (less favorable) and Level 3 (most favorable)

Chemical stability
- Sirolimus remnant content (RC%) of A and B at t=0, 1, 2 days and alternate days until t=30 days. \( T_{90} \) when %CR was ≤ 90%. Extraction (hexane, acetonitrile y WFI)
Analytical method High-resolution liquid chromatography

Microbiological stability
Microbiological culture of A and B at t=15 and 30 days

RESULTS

Physical stability

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<tbody>
<tr>
<td>pH (t=15 and 30 days)</td>
<td>6.0</td>
<td>7.0</td>
<td>6.0</td>
</tr>
<tr>
<td>Uniformity</td>
<td>Level 3</td>
<td>Level 3</td>
<td>Level 3</td>
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<tr>
<td>Extensibility</td>
<td>Level 3</td>
<td>Level 1</td>
<td>Level 2</td>
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<tr>
<td>Absence of crystals</td>
<td>Level 3</td>
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<td>Absence of phase separation</td>
<td>Level 3</td>
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Chemical stability

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<tr>
<td>Sirolimus RC% at day 30:</td>
<td>96.1 ± 1.6</td>
<td>101.2 ± 4.6</td>
<td>90.3 ± 6.3</td>
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Microbiological stability
Negative cultures of A and B at t=15 and 30 days

CONCLUSIONS

Ointment validity period
30 days at 2-8 ºC