

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 2-8°C

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. T₉₀ when %CR was ≤ 90%. Extraction (hexane, acetonitrile y WFI) Analytical method High-resolution liquid chromatography

Microbiological stability

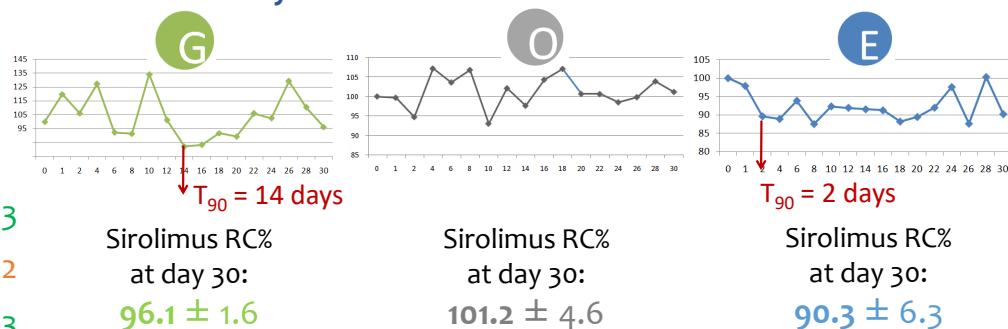
Microbiological culture of A and B at t=15 and 30 days

RESULTS

Physical stability

	G	O	E
pH (t=15 and 30 days)	6.0	7.0	6.0
Uniformity	Level 3	Level 3	Level 3
Extensibility	Level 3	Level 1	Level 2
Absence of crystals	Level 3	Level 3	Level 3
Absence of phase separation	Level 3	Level 3	Level 3

Chemical stability



Microbiological stability

Negative cultures of A and B at t=15 and 30 days

CONCLUSIONS

Ointment validity period
↓
30 days at 2-8 °C

Stability	G	O	E
Physical	✓	✓	✓
Chemical	✗	✓	✗
Microbiological	✓	✓	✓

