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TOPICAL RAPAMYCIN IN RARE TUBEROUS SCLEROSIS DISEASE: LIPOSOMAL FORMULATION STABILITY
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AIM
To develop a liposomal formulation and to determine the validity period according to chemical, physical and microbiological stability in rare tuberous sclerosis disease.

METHOD
A LIPOSOMAL FORMULATION of rapamycin 0.4% was prepared in biological safety cabinet.
Packing and conservation: 20G bottle protected of ambient light and stored in a cold room at 5°C±3°C.
Composition: sirolimus 0.4%, transcutol-P 10%, liposomal solution 25%, cholesterol 0.1%, isopropile miristrate 10%, propyleneglycol 10%, carbopol 2%, NaOH 10% q.s. pH 7.5, WFI q.s. 20g.

CHEMICAL STABILITY
Analytical method: extraction of rapamycin with apolar solvents and HPLC analysis. The percentage of remaining sirolimus content (%CR) was determined by triplicate at t=0, 2, 7, 14, 21, 28, 35, 42, 56, 70 and 84 days. T90 was established when %CR was ≤ 90%.

PHYSICAL STABILITY
Parameters: pH, uniformity, extensibility, absence of crystals and absence of phase separations were evaluated on a transparent surface according to 3 levels: level 1, the least favorable and level 3, the most favorable, at t=0 days. Mean particle size, zeta potential and encapsulation efficiency (EE%) was determined by triplicate at t=0 days.

MICROBIOLOGICAL STABILITY
Culture samples in blood-agar media were incubated at 37°C by duplicate at t=28, 56 and 84 days.

RESULTS

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<tr>
<th>CHEMICAL STABILITY</th>
<th>PHYSICAL STABILITY</th>
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<tr>
<td>%CR at t=28 days ± SD 110.1 ± 15.9</td>
<td>pH 7.5</td>
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<td>%CR at t=56 days ± SD 107.5 ± 21.1</td>
<td>Uniformity, extensibility, absence of crystals and absence of phase separations Level 3</td>
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<tr>
<td>%CR at t=84 days ± SD 124.0 ± 20.4</td>
<td>Mean particle size, Pdl 178.9 nm, Pdl 0.093</td>
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<td>T90 &gt; 84 days</td>
<td>Zeta potential (mV) ± SD -41.1 ± 13.4</td>
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<td>EE% ± SD 89.2 ± 4.6</td>
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CONCLUSIONS
This study describes a new liposomal formulation to improve the previously treatment for facial angiofibromas in tuberous sclerosis and it also provides favorable stability data. However, more dermokinetic and clinical studies are needed to confirm that liposomes are most appropriate to ensure effectiveness, safety and high patient satisfaction.