CELLULAR TOXICITY OF A NANOSTRUCTURED EMULSION OF AMPHOTERICIN B.

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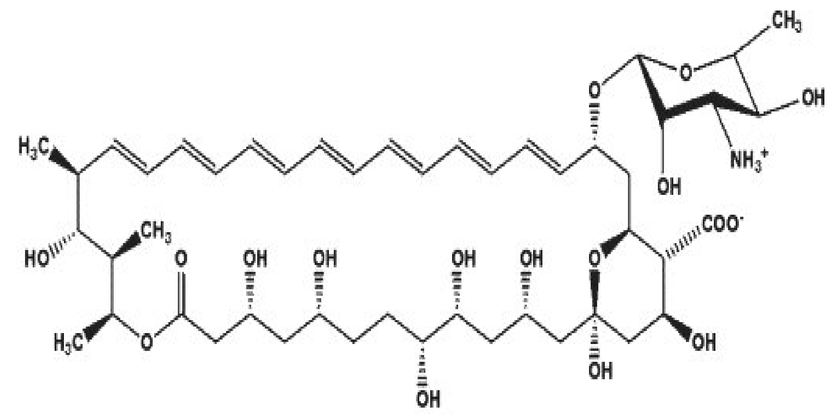
Introduction

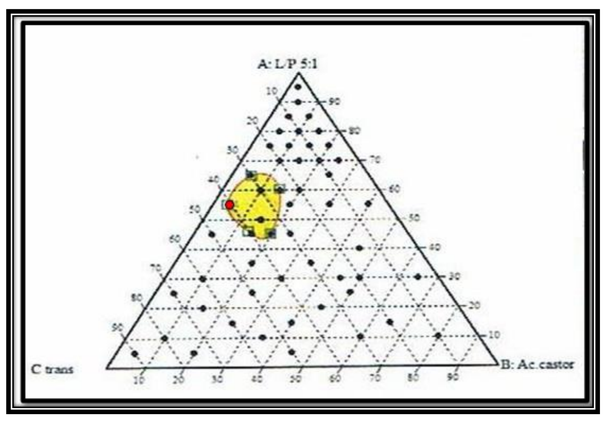
Amphotericin B (AmB) is a potent polyene macrolide antibiotic with high molecular weight (924 Da) and broad-spectrum coverage (1). From a physicochemical point of view, AmB is a poorly hydrosoluble, amphoteric, amphiphilic molecule and is difficult to solubilize in organic solvents. For this reason, there is no topical formulation of AmB commercially available at the moment (2). This fact evidences the need to develop new formulations using excipients with permeation-enhancing properties in order to facilitate the penetration of drug into Stratum Corneum (SC) and its distribution from SC to epidermis and dermis.



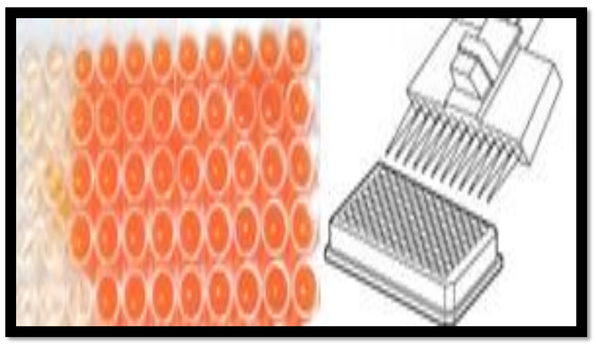
Amphotericin B Chemical Structure

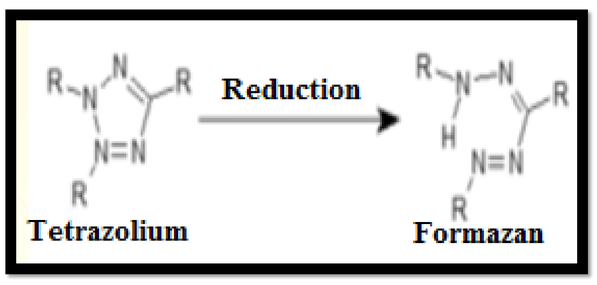
Methods and materials

We have developed an AmB nanoemulsion 0,3% (NE) having as composition: Labrasol® / plurol®5: 1, castor oil® and Transcutol-P® with the following proportions: 55-05-40 (3). To determine the toxicity of this formulation, we have performed cytotoxicity tests through the technique WST-1 (*cell proliferation regente* WST-1 from Roche®) on two cell lines: Raw 264.7 of murine tumor origin and J774 of mouse monocytic tumor origin. Both cell lines were provided by Eucelbanc (Faculty of Biology, UB), respectively. Cytotoxicity tests were performed with: A solution of AmB dissolved in DMSO, the AmB NE and the blank (NE without AmB).



RAW 264,7 (RPMI)
J774 (MEM)
SBF
37 °C, 5 % CO_2

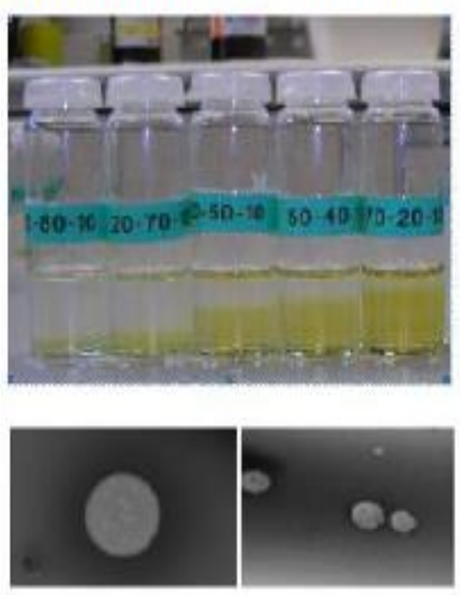




Results

Table 1. Citotoxicity Concentration about AmB solution, AmB NE and NE (blank)

Compounds	CC50 µg/mL	
	RAW	J774
AmB Solution 150-0,14(µg/mL)	56,34 ± 0,29	57,80 ± 0,24
NE AmB 150-0,14(µg/mL)	95,76 ± 0,28	342,13 ± 0,23
Formulation	CC50 % p/p	
NE 12,5-0,02 (%)	> 12,50	38,94 ± 0,20



The results obtained indicate that the AmB NE presented lower cellular toxicity than the AmB in solution in both Cell lines and greater toxicity in J774 cells. The NE without drug was not toxic against raw cells and presented cellular toxicity against J774 cells at a concentration of 38,94 ± 0,20 µg/mL (Table 1). As a future perspective, we will conduct these tests on keratinocytes (HaCaT).

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