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A polysiloxane surfactant dissolves a poorly soluble drug (nystatin) in water

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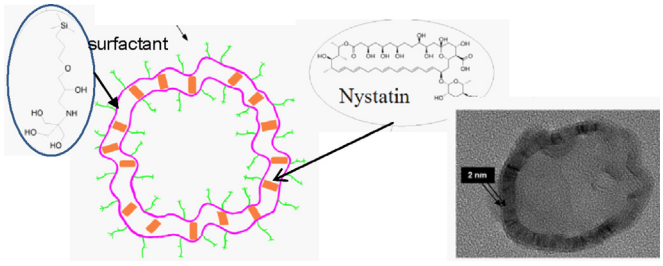
HIGHLIGHTS

- A tromethamol-modified polysiloxane surfactant is investigated.
- A method to dissolve nystatin in water is proposed using this surfactant.
- The drug is physically encapsulated within the surfactant aggregates.
- The in vitro antifungal activity was seriously improved.

GRAPHICAL ABSTRACT



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ABSTRACT

The aqueous dissolution of a poorly soluble drug nystatin (Nys) was achieved by a simple, excipient-free procedure using a tromethamol-modified polysiloxane (ST) as surfactant. Long-term stable Nys aqueous formulation was prepared and investigated by different methods, in order to understand the mechanism of drug solubilization. The cryo-TEM analysis revealed the presence of soft vesicles in the Nyst_ST solution. According to TEM measurements, the drug is contained in the hydrophobic layer of the surfactant vesicles. The dynamic light scattering (DLS) measurements on Nys_ST showed a main population around 134 nm having the Zeta potential of 33.3 mV. FT-IR, UV–vis, and thermogravimetric (TG-DTG-DTA) data point toward physical encapsulation, accompanied by a decrease of H-bonding between the drug molecules. The antifungal activity tested in vitro toward four yeast strains was seriously improved compared to the aqueous dispersion of the native drug, although the availability was diminished compared to DMSO solution.

1. Introduction

The aqueous solubility of drugs is a serious problem that affects, based on some estimation, almost half of the potentially useful drug candidates [1]. To overcome this problem, many types of colloidal delivery systems have been investigated.

Micellar solubilization is generally regarded as a powerful tool for enhancement of the solubility of active compounds in water which is the preferred solvent for medical applications [2–4]. This effect is due to the hydrophobic core of the direct micelles, which represents a more suitable microenvironment for the solubilizate. In this context, as a consequence of their ability to associate in water, new perspectives are opened by using micellar systems based on amphiphilic compounds.

Colloidal lipid emulsions and solid lipid nanoparticles, as well as lipid and surfactant based drug delivery systems (LSBDDS) are largely used for the delivery of poorly water-soluble drugs [5,6].

One class of drugs whose efficacy is drastically reduced because of poor water solubility is represented by polyene antibiotics. This

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