The 5Th INTERNATIONAL CONGRESS ON BIOMEDICINE

The effect of different size reduction methods on the doxycycline-containing niosomes, prepared for the skin infection treatments

Fatemeh Kashani-Asadi-Jafari; Master of Biomedical Engineering; Amirkabir University of Technology
Afra Hadjizadeh; Assistant Professor of Biomedical Engineering; Amirkabir University of Technology

Introduction

Niosomes are a type of colloidal particle that can carry hydrophilic and hydrophobic drugs, increase drug bioavailability, prevent drug degradation, reduce the toxic effects of drugs, and deliver drugs to target sites [1].

The outermost layer of the epidermis, the horny layer, acts as a powerful barrier to the penetration of foreign matter. The main challenges of skin infection treatment include: Achieving the ideal balance between the local penetration of the therapeutic agent and its retention at the desired location in the skin layers for the desired duration, increased resistance of microorganisms to common antibiotics, use of conventional medication systems leading to undesirable side effects such as irritation, redness, dryness, and sensitivity to light due to lack of targeted delivery [2].

Doxycycline hyclate, the safest and most effective tetracycline antibiotic, effectively prevents the growth of many gram-positive and gram-negative skin bacteria [3]. In order to increase the therapeutic effects and decrease side effects, we decided to load this drug into niosomal nanoparticles. In this study, a niosomal formulation containing doxycycline, with a molar ratio of 8:2 span60/cholesterol was prepared. Niosomal nano-particles were reduced in size by three methods of bath sonication, probe sonication, and extrusion. Then the sample was characterized in terms of morphology, particle size, drug entrapment efficiency, drug loading capacity, and drug release. Finally, release data were analyzed by several kinetic models.

Methods

Preparation method

The thin-film hydration method was used. (span60 and cholesterol with an 8:2 molar ratio and the total lipid of 700µmol).

Size reduction methods

Three methods were used: Bath sonicator: 5ml of suspension was sonicated for 45 minutes. Extrusion: 5ml of suspension was passed five times through a polycarbonate membrane with a porosity size of 200nm. Probe sonicator: 5ml of suspension was sonicated for 15 minutes at 150watts (8 seconds on and 2 seconds off).

Particle size and morphology

Diameter size was measured with a DLS. The morphology was observed using SEM.

Entrapment efficiency and loading capacity

10ml of suspension was centrifuged via ultracentrifuge at 30,000rpm (100,000 × g) at 25°C for 15 minutes. The supernatant containing the free drug was separated from the pellet. Then its absorption at 276nm was measured with a spectrophotometer. Then the entrapment efficiency and loading capacity were calculated.

Drug release

The synthesized formulation and free-drug (with the equivalent drug) were transferred to a dialysis bag (12,400Mv cut-off) in a beaker with a content of 20 ml PBS. 1ml sample was taken from the beaker at 0.25, 0.5, 1, 2, 4, 8, 16, and 32hours. The absorbance was measured at 276nm. Finally, drug release data were analyzed using Zero-order, Higuchi, and Korsmeyer-Peppas kinetic models.

Results

SEM: The bathing method had almost no effect on reducing the sample size of nanoparticles. The inefficiency of the extrusion method was also observed (Fig1). Span60 is solid at room temperature, and extrusion must be performed at temperatures above Tc of surfactant because it has a low velocity at temperatures below Tc due to the higher gel viscosity of the membrane and reduced ductility. The extrusion method also changed the morphology of the niosomes, which may be due to the low percentage of cholesterol in the sample structure, which loses its flexibility when exposed to high force [4,5]. Therefore, size reduction with the probe sonicator is the best way to reduce sample size (Fig1).

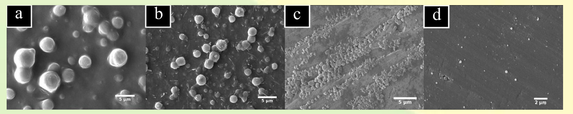

Fig1 (a) Without size reduction, (b) Bath sonication, (c) Extrusion, (d) Probe sonication

Particle size: The DLS results showed an average particle size of 213.76±12.75nm (Fig2).

Entrapment efficiency and loading capacity: The obtained values were 39.7±1.8 and 13.4±0.6, respectively.

Drug release: Controlled and slow drug release from the prepared formulation compared to the free-drug was observed after 32 hours (Fig2). The most consistent release data were with the Korsmeyer-Pappas model ($R^2 \geq 97\%$).

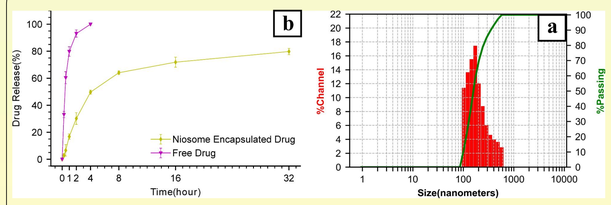

Fig 2 (a) DLS (b) Drug release after 32 h

Conclusions

The sample synthesized by the thin-film hydration method and probe sonication had a suitable size for dermal delivery, and the drug entrapment efficiency was appropriate. In addition, controlled release of the drug prevents skin side effects compared to the free drug and reduces the need for re-dosing. Thus, in general, the synthesized sample can be used in dermal delivery and skin infections.

Bibliography

1. **Yong-Mei Haoa, Ke'an Li. Entrapment and release difference resulting from hydrogen bonding interactions in noisome,2011.**
2. **Rinaldo Patel, Priyanka Prabhu. Nanocarriers as versatile delivery systems for effective management of Acne,2020.**
3. **E. JANTRATID et.al. Biowaiver Monographs for Immediate Release Solid Oral Dosage Forms: Doxycycline Hyclate,2009.**
4. **S. Taymouri and J. Varshosaz. Effect of different types of surfactants on the physical properties and stability of carvedilol nano-niosomes, 2016.**
5. **I. Uchegbu and A. Florence. Non-ionic surfactant vesicles (niosomes): Physical and pharmaceutical chemistry, 1995.**