CHITOSAN NANOPARTICLES LOADED WITH MINOCYCLINE TARGETING OSTEOMYELITIS

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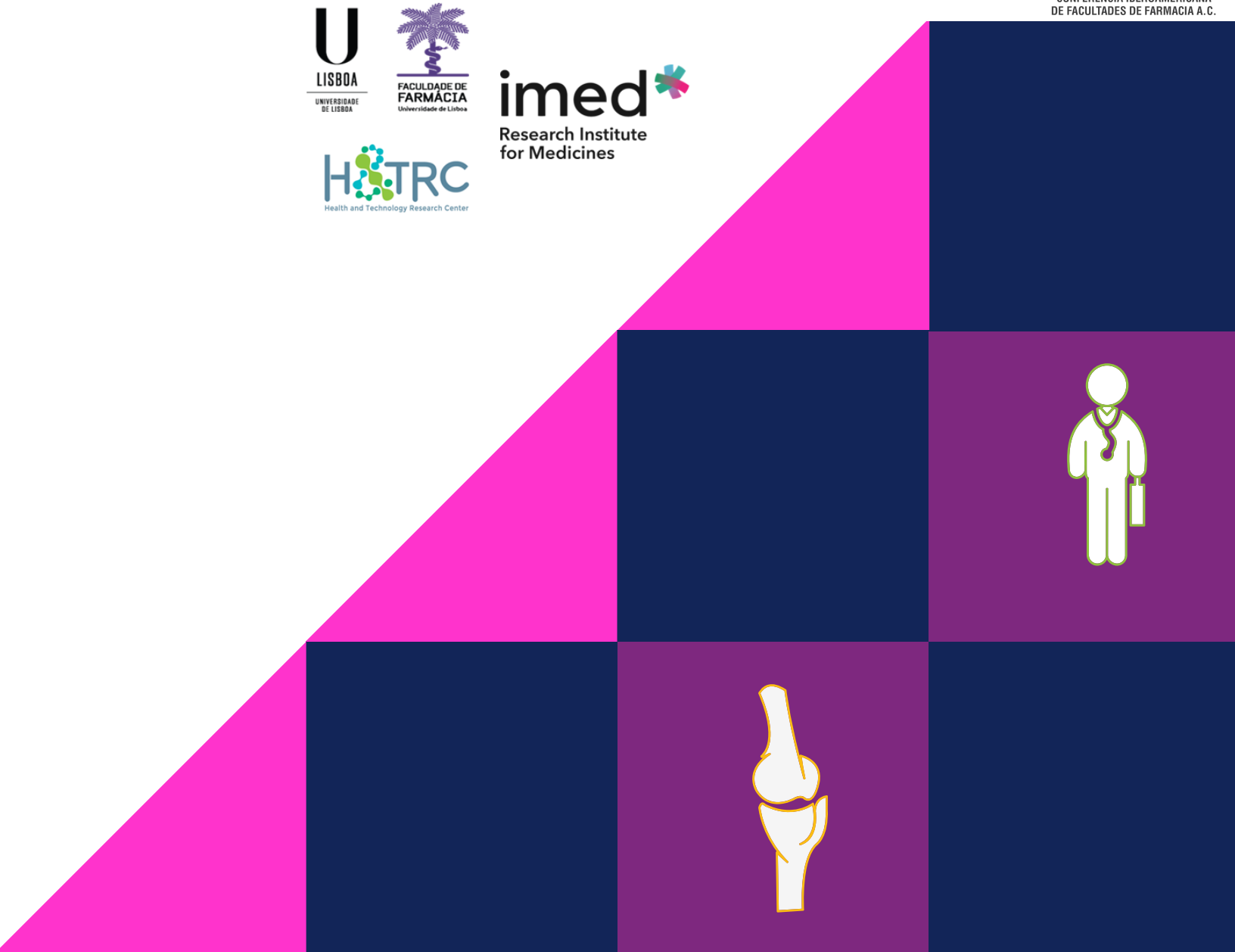

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Introduction

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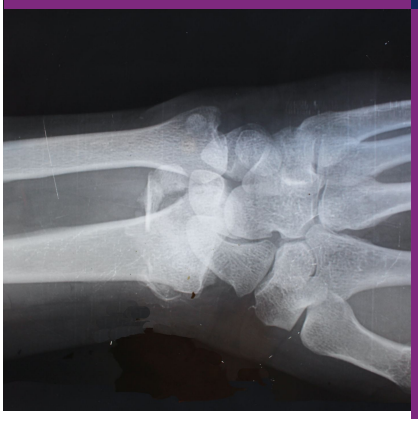

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Introductioin

Effective control of osteomyelitis (bone infection) with reduced toxicity is an current challenge

Targeted and controlled drug delivery systems allow:

- Decreased toxicity
- Upgraded drug targeting
- Improved therapeutic effect [1]

♦ Strategy

Innovative chitosan nanoparticulate system

Nanoparticles loaded with minocycline (antibacterial)

Alternative as a local delivery system

Nanoparticles and biofilms: advantages

Enhanced bioavailability

Targeted delivery of antibiotics magnification

Local release of antibiotics

Controlled and sustained release

Protection against deactivating enzymes

Materials and Method

Chitosan nanoparticles preparation (Fig. 1)
Ionic gelation technique optimized [2]
Encapsulation efficiency increased
Chitosan and sodium tripolyphosphate (TPP) matrix
Bioactive pluronic F68 polymer

♦ **Nanoparticles physicochemical characterization**
Mean particle size
Polydispersity index (PDI)
Zeta potential
Drug loading (DL)

♦ **Minocycline quantification**
Spectrophotometry (λ = 350 nm)

♦ **Antimicrobial activity test**
Dilution method (modified)
Minimal inhibitory concentration (MIC)
Chitosan nanoparticles tested with S. aureus

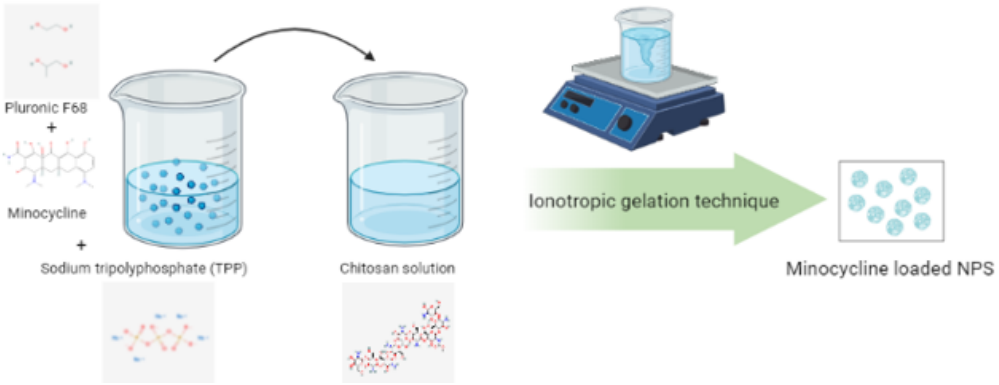

Figure 1. Preparation of chitosan nanoparticles loaded with minocycline by ionotropic gelation technique

Results

Se incluyeron datos de 3795 personas que acudieron boticas y farmacias de Perú. La prevalencia de búsqueda de atención farmacéutica fue de 82,7%. Los factores asociados a una menor probabilidad de buscar atención farmacéutica fueron tener una de edad de 65 a más años, proceder de Lima Metropolitana y usar permanentemente un medicamento.
Los factores asociados a una mayor probabilidad de buscar atención farmacéutica fueron proceder de la región de la Sierra, atenderse en el MINSA, tener una percepción favorable hacia la automedicación y comprar medicamentos sin receta médica.

Nanoparticles physicochemical characterization (Figure 2)

- Nanoparticles (NPs) within nanometric size
- Stable positive zeta potential observed
  - Greater electrostatic repulsion between particles in dispersion
  - Possible aggregation prevented
- Stable formulation and monodisperse in nature (low value of polydispersity index)

Antimicrobial activity test

- Blank nanoparticles showed no effect
- Minocycline loaded nanoparticles showed a MIC of 16 µg/mL

Formulation	Size average (nm)	PDI	Zeta potential (mV)	DL%	EE%
b-NPs	529.4 ± 32.0	0.679 ± 0.1	+33 ± 0.9	-	-
Min-NPs	320.6 ± 5.7	0.415 ± 0.0	+39 ± 1.6	0.46 ± 0.13	8.91 ± 2.49

Figure 2. Characteristics of b-NPs and Min-NPs. Results are presented as mean ± SD (n = 3).
PDI – polydispersion index. DL% - drug loading. b-NPs – blank nanoparticles. Min-NPs – minocycline loaded nanoparticles. EE% - encapsulation efficiency.

Conclusions

A suitable nanoparticulate formulation of minocycline (Min-NPs) was developed by an optimized ionic gelation technique, using chitosan-TPP stabilized with pluronic F68.

The Min-NPs' formulation exhibited adequate features for local delivery, with particle size in the nanorange, and polidispersity index and zeta potential values depicting formulation stability.

Transmission electron microscopy (TEM), in vitro drug release and citocompatibility studies are ongoing and may improve the formulation potential role in drug targeting adressing osteomyelitis.

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Figure 1 was created with Biorender.com.

References / Contact

Matos, et al., Int J Pharm, 2015, 490(1-2), 200–208.

Yasmin, et al., Nanotechnol Rev, 2017, 6(2), 191–207.

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