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Amoxicillin-loaded lipid nanoparticles: a novel approach to treat *Helicobacter pylori* infections

Helicobacter pylori affect around 50% of the world population and are the main cause of peptic ulcers and gastric cancer, being classified as a human carcinogenic by the World Health Organization [1, 2]. Unfortunately, the eradication rates for these bacteria are far from the desirable, due to the decline of the efficacy of the standard therapy against the emergent antibiotic resistant bacterial strains [2]. However, there are other factors that also affect the therapeutic efficacy, namely the degradation of antibiotics under acidic conditions, their low diffusion across the mucus layer, their insufficient residence time in the stomach, among others [2]. Lipid nanoparticles emerged as a promising biocompatible drug delivery system. They can improve drugs pharmacokinetic properties, leading to an improvement of the efficacy and a decrease in the incidence of side effects [2].

In this work, amoxicillin-loaded solid lipid nanoparticles (SLNs) were prepared by the double emulsion technique to protect amoxicillin against acidic degradation and to improve its local release and, consequently, its bioavailability. A three-factor, three-level Box-Behnken design was used to optimize the particle size, the polydispersity index and the loading capacity of the SLNs. The characterization of the optimized nanoparticles revealed a mean size diameter around 200 nm and a zeta potential superior to |30| mV. Additionally, the SLNs revealed a low polydispersity index around 0.137 and a satisfactory high loading capacity of nearly 7%. The SLNs were also characterized by transmission electron microscopy revealing a spherical morphology and aqueous vacuoles.

The optimal formulation was stable in suspension when stored at 4ºC during at least 6 months. *In vitro* release studies revealed a high stability under harsh conditions of the mimetic gastric medium (pH 1.6, bile salts, lecithins and 37ºC). Further, a sustained and controlled phase was observed at simulated physiologic medium (pH 7.4) for a total of 26 hours. The *in vitro* methylthiazolydiphenyl-tetratozium bromide (MTT) assay revealed that the optimal SLNs suspension does not have cytotoxic effects in both L929 fibroblasts and MKN28 gastric cell lines.

Figures

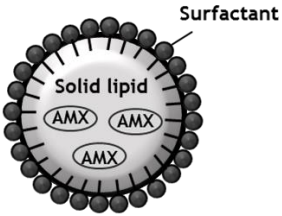

Figure 1: Composition of the amoxicillin-loaded SLNs. AMX, amoxicillin.

References

1. Bouvard, V., et al., Lancet Oncology, **10**(4) (2009) p. 321-322.
2. Lopes, D., et al, Journal of Controlled Release, **189** (2014) p. 169-186.