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The implementation of the QbD concept in the development of lipobeads loaded with gemcitabine: the screening study

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The purpose of this study was to incorporate gemcitabine (GEM) into a novel nanosystem, namely lipobeads (LB), which are hydrogel nanoparticles (NG) surrounded by a lipid bilayer. The Quality by Design (QbD) concept was used with the aim to identify and investigate the formulation factors and process parameters with the greatest influence on the quality attributes of the LB loaded with GEM (LB-GEM).

The preparation technique of LB-GEM included two steps: i) the preparation process of NG encapsulated with GEM (NG-GEM) via a free radical precipitation/dispersion polymerization technique; ii) the preparation process of LB-GEM via the thin film hydration technique, where the NG-GEM dispersion served as hydration medium.

Based on a literature review, six factors were identified as potential critical on the critical quality attributes (CQAs) (size, polydispersity index (PdI), zeta potential, encapsulated drug concentration and encapsulation efficiency (EE%)) of both the NG-GEM and LB-GEM, and were studied in a screening experimental design with 19 experiments. In the LB-GEM, the encapsulated drug concentration varied between 0.062 and 0.52 mg/ml, while the EE% varied between 7.11 and 52%; these responses being influenced exclusively by the concentration of the monomer. The size (between 36.31 and 387.16 nm) and PdI (between 0.088 and 0.667) for both NG-GEM and LB-GEM varied significantly with the concentration of the monomer, crosslinker and surfactant.

In conclusion, GEM can be successfully incorporated into LB, and an optimization process will be carried out with the aim to obtain an optimal formulation that meets the quality target profile.