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Impact of Synthesis Strategy on the Hyperthermic Efficiency of Magnetite-Loaded PLA Nanocarriers for Targeted Drug Delivery

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Multi-functional hybrid nanostructures integrating diagnostic and therapeutic capabilities represent a key advancement in precision medicine. Poly(D,L-lactic acid) nanospheres (PLA-NS) are excellent candidates due to their biocompatibility and tunable degradation. However, their efficacy depends on the spatial distribution of the inorganic phase within the polymer. This study investigates how synthesis strategies influence the magnetothermal efficiency of PLA-NS functionalized with poly-L-lysine-modified magnetic nanoparticles (MFPLL). Two strategies were compared: (i) *in situ* MFPLL incorporation during nanoprecipitation and (ii) post-synthetic modification by mixing preformed PLA-NS with MFPLL. Systems were characterized by morphology, size, magnetic properties, and surface chemistry, followed by magnetic hyperthermia evaluation.

Morphological analysis confirmed spherical hybrid particles (< 200 nm) with high uniformity. Magnetic measurements showed superparamagnetic behavior, while FTIR and thermogravimetric analysis verified successful amino functionalization of the PLA-NS surface, suitable for drug binding. The synthesis method significantly affected the intrinsic loss power (ILP) under an alternating magnetic field. Post-synthetic modification (PLA-NS+MFPLL (post)) maintained the original MFPLL heating efficiency (ILP: 1.09 ± 0.02 nH·m^2·kg^{-1}). Conversely, *in situ* incorporation (PLA-NS–MFPLL (*in situ*)) resulted in an approximately 25% performance reduction (0.81 ± 0.04 nH·m^2·kg^{-1}). This decrease is attributed to nanoparticle immobilization within the rigid polymer matrix, which inhibits Brownian relaxation.

Figure 1: SEM micrograph of the PLA-NS+MFPLL (Post) sample (a), TEM micrograph of the PLA-NS–MFPLL (In situ) sample (b), and intrinsic loss power (ILP) values of the investigated samples (c).

Findings indicate that post-synthetic loading is superior for maintaining high specific absorption rates. With excellent MRI contrast ($r_2 \approx 400$ mM^{-1}s^{-1}), this platform represents a promising theranostic tool for combined thermal therapy and imaging.

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