IRON OXIDE-POLY(LITHOCHOLIC ACID) NANOPARTICLES WITH FOLIC ACID AND DOXORUBICIN - NANO-WARRIORS TO FIGHT CANCER

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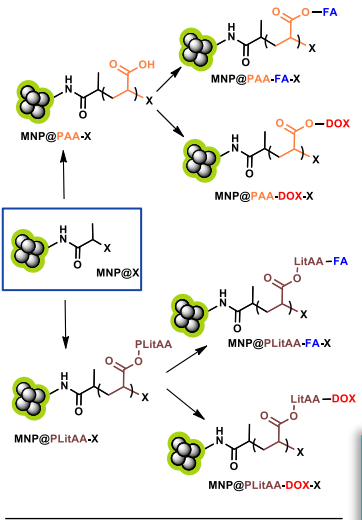
INTRODCTION

Cancer remains one of the greatest challenges of the 21st century. Smart drug delivery systems (SDDS) offer a valuable strategy for improving cancer therapy. Nanoparticle-, polymer-, or liposome-based therapies show superior results compared to conventional methods. These systems enhance treatment efficacy while reducing side effects. A promising approach involves iron oxide nanoparticles (IONPs), which combine multiple therapeutic strategies, including molecular sensitization and physical methods like radiation or phototherapy. Their small size, high surface area, biocompatibility, and modifiability enable targeted drug delivery and specific tumor interaction.

SYNTHESIS OF MNPs

In this study, MNP@X nanoparticles were utilized as chain transfer agents (CTAs) in the surface-initiated polymerization of synthesized lithocholic acid acrylate (LitAA) and acrylic acid (AA), resulting in the creation of two types of polymer-iron oxide hybrid materials (Fig 1. MNP@PAA-X, MNP@PLitAA-X).

Then new formulations based on iron oxide nanoparticles coated by polymeric layers derived from lithocholic acid (LitA) or acrylic acid (AA) and covalently modified with folic acid (FA) (targeting agent) or doxorubicin (DOX) (chemotherapeutic drug) were obtained. FA/DOX was attached to polymer-magnetic hybrids by an amidation reaction between carboxylic acid (on polymeric shells) and amine groups (of FA/DOX).



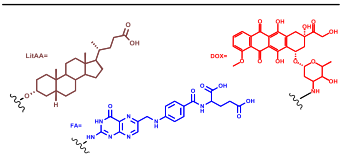


Fig. 1. General presentation of obtained materials.

PHYSICOCHEMICAL ANALYSIS

The synthesized hybrids were characterized using FTIR, UV-Vis, TGA, DLS, ELS, and TEM. The initial material, MNP@NH_2, had a hydrodynamic diameter of ~160 nm. Hybrids modified with biologically active substances ranged from 130 to 270 nm, with particle size increasing alongside shell content. Doxorubicin loading significantly enlarged the hydrodynamic diameter, consistent with TG results. MNP@NH_2 had a ζ-potential of 12 mV, which decreased to −26 mV (MNP@PLitAA) and −32 mV (MNP@PAA) post-polymerization, indicating greater stability. Folic acid further lowered the ζ-potential, while DOX had a minimal effect on it.

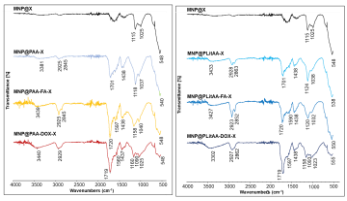


Fig. 2. FT-IR spectra of obtained polymer-inorganic hybrids.

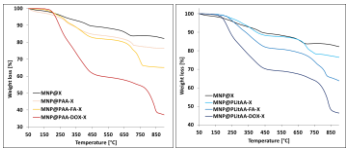


Fig. 3. TG curves of MNPs.

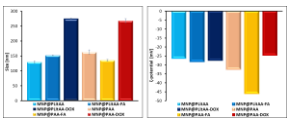


Fig. 4. DLS and ELS results for MNPs.

CONCLUSIONS

Cytotoxicity was assessed against normal (RBCs, THP-1, CCD-1079sk, and H9C2(2-1)) and cancerous (MCF-7, MDA-MB-231, and HeLa) cell lines using MTT and Neutral Red assays. Additionally, transepithelial electrical resistance (TEER), caspase 8 and 9 expression, and the impact on cytochrome P450 enzyme activity were evaluated in cancer cells.

The results demonstrate that the synthesized nanoparticles selectively target cancer cells, inducing apoptosis through caspase activation while sparing normal cells. These findings highlight the potential of these formulations as effective, biocompatible systems for targeted cancer therapy.

BIOLOGICAL STUDIES

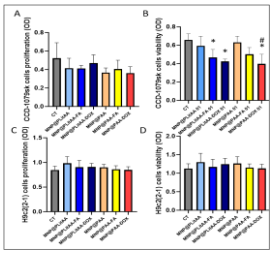


Fig. 5 Compatibility of MNPs against normal cells.

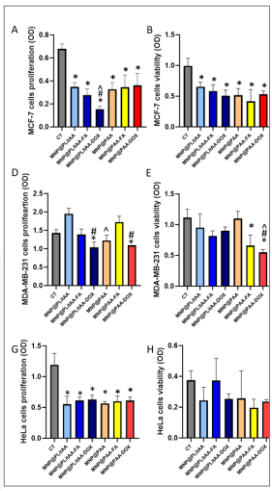


Fig. 6. Anticancer activity of MNPs.

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Reference:

D. Szymczuk, et al. *RSC Advances*, 2025, 15, 14246.