Prussian blue analogues within liposomal nanoreactors for glutathione depletion

Fatima Escudero-Amate [1,2,3], Andrea Mosseri[1,2,3,*], Ana Rueda-Flores[1,2,3], Javier Bonet-Aletá[1,2,3], María Sancho-Albero[1,2,3,4], Jesus Santamaria[1,2,3,4], Jose L. Hueso[1,2,3,4,5*]

1 Instituto de Nanociencia y Materiales de Aragon (INMA), CSIC-Universidad de Zaragoza, Campus Río Ebro, Edificio I+D, C/ Poeta Mariano Esquillor, s/n Zaragoza 50018, Spain; 2 Department of Chemical and Environmental Engineering, University of Zaragoza, Campus Río Ebro, C/ María de Luna, 3, Zaragoza 50018, Spain; 3 Networking Research Center in Biomaterials, Bioengineering and Nanomedicine (CIBER-BBN), Instituto de Salud Carlos III, Madrid 28029, Spain; 4 Instituto de Investigación Sanitaria (IIS) de Aragón, Avenida San Juan Bosco, 13, 50009 Zaragoza, Spain; 5 Escuela Politécnica Superior Huesca, Universidad de Zaragoza, Crta. de Cuarte s/n,Huesca 22071, Spain

**Corresponding authors: amosseri@unizar.es / jlhueso@unizar.es*

Highlights

- Direct synthesis of Prussian blue nanoparticles within liposomes.
- Catalytic activity toward glutathione preserved after encapsulation.
- Liposomal integration provides a platform toward vesicle-based catalysis.
- Successful homeostasis disruption via glutathione depletion.

1. Introduction

Catalytic nanomaterials have emerged as promising tools in nanomedicine due to their ability to exploit the biochemical features of diseased microenvironments and trigger localized chemical transformations. In particular, catalytic platforms capable of interacting with the redox balance of cancer cells have attracted increasing attention, as the tumor microenvironment (TME) typically presents elevated concentrations of reducing biomolecules such as glutathione (GSH). Catalytic systems able to modulate these redox pathways can disrupt cellular homeostasis and enhance therapeutic responses. Among the different catalytic nanomaterials investigated for this purpose, copper- and iron-based systems have demonstrated promising activity toward GSH oxidation and related redox processes. However, their integration into biological delivery platforms remains a significant challenge. Conventional strategies typically rely on the post-synthetic encapsulation of preformed nanoparticles into vesicular carriers such as liposomes.

These approaches often require additional processing steps, including extrusion or membrane disruption, which may limit encapsulation efficiency, induce material loss, or compromise structural stability. Recent studies have also highlighted the potential of biological vesicles, such as extracellular vesicles or exosomes, as transport vectors for catalytic nanomaterials due to their intrinsic biocompatibility and ability to interact with biological systems. In this context, developing simplified and robust methodologies to integrate catalytic nanomaterials within vesicular structures represents an important step toward the implementation of vesicle-based catalytic nanomedicine. Here we explore a synthetic strategy that enables the direct formation of catalytic nanoparticles within lipid vesicles, avoiding conventional post-loading procedures and complex processing steps.

2. Methods

Preformed liposomes composed of DPPC and cholesterol were used as vesicular templates for the in situ formation of the catalytic nanoparticles. Liposomes were first prepared and extruded to obtain homogeneous size distributions, and subsequently employed as nanoreactors for nanoparticle growth. A Prussian blue analogue was generated by the sequential addition of metal precursors to the preformed vesicles. This strategy enables the direct nucleation and growth of the catalytic phase within the liposomal system, avoiding conventional encapsulation of pre-synthesized nanoparticles and reducing additional processing steps typically required in liposome loading protocols.

3. Results and discussion

The proposed methodology successfully produced CuFeCN catalytic nanoparticles associated with the liposomal structures. Microscopy and characterization analyses indicate that the catalytic material is located both within the liposomal interior and associated with the lipid membrane, where it forms a belt-like distribution surrounding the vesicles. This spatial organization suggests that the lipid bilayer can act not only as a container but also as a structural environment influencing nanoparticle nucleation and localization. The resulting hybrid nanosystem maintains the catalytic behavior previously reported for the corresponding non-encapsulated CuFeCN materials, including reactivity toward glutathione-containing environments. These observations indicate that the catalytic functionality of the material is preserved despite integration within the vesicular structure. In addition, the liposome–catalyst assemblies exhibit good colloidal stability under refrigerated storage, remaining stable for several days without significant visible aggregation. This stability highlights the potential of the liposomal template as a platform for preparing catalytic vesicle–nanoparticle hybrids, especially to target GSH both under ex vitro and in vitro tumor microenvironments.

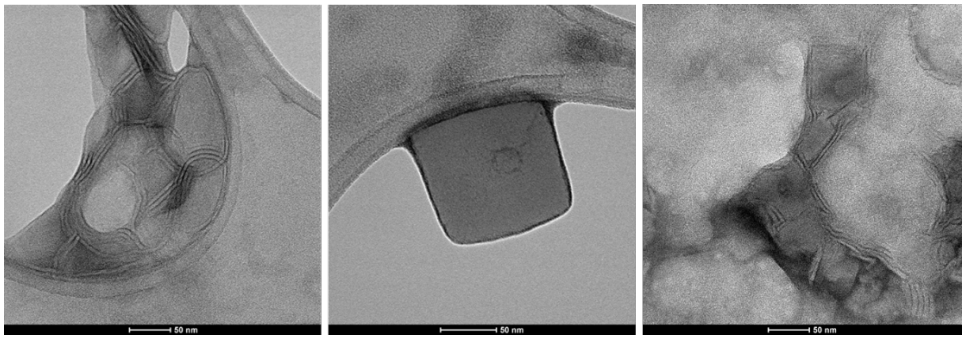

Figure 1. TEM images of liposomes, CuFeCN NPs and the lipid-prussian analogue hybrids.

4. Conclusions

A one-pot methodology for the in situ formation of CuFeCN catalytic nanoparticles within liposomal vesicles has been developed. The approach enables direct nucleation of the catalytic phase without the need for post-synthetic encapsulation or extrusion procedures. The resulting liposome–nanoparticle hybrids retain the catalytic characteristics of the CuFeCN material while exhibiting good colloidal stability and excellent catalytic response towards GSH depletion. Beyond the specific system reported here, this strategy provides a simplified route to integrate catalytic nanomaterials within lipid vesicles and may serve as a useful platform for the development of vesicle-based catalytic nanomedicine systems.

References

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Keywords

Catalytic nanomedicine; liposomes; Prussian blue analogues; glutathione; tumor microenvironment