A comparative study of sericin and gluten for magnetic nanoparticle-mediated drug delivery

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Introduction

The presence of the blood-brain barrier (BBB), a tightly interconnected network of blood vessels and endothelial cells that restricts the entry of foreign particles larger than 100 nm into the brain, poses considerable challenges and complexities in advancing therapeutic strategies for neurodegenerative diseases (NDs) 1. 2. Gene therapies, specifically DNAzymes, post-transcriptional gene silencing technique, have shown promising results in treating neurodegenerative diseases 5. DNAzymes are single-stranded DNA-based catalytic molecules functioning as efficient RNA-silencing agents; they target, bind to, and degrade disease-associated mRNAs, reducing the levels of proteins implicated in specific pathological conditions 6. Thus, the study aimed to synthesize nanoliposomes from soy lecithin using the ethanol injection method, serving as carriers to deliver DNAzymes for targeted brain modification and enhancing their ability to cross the BBB by more than 6%. To this end, after synthesizing and investigating the physicochemical properties of DNAzyme-loaded nanoliposomes (DNZ-NLPs), both in vitro and in vivo studies were performed using SH-SY5Y brain cells and BALB/c mice, respectively.

Methods

This comprehensive research navigates the landscape of nanomedicine, specifically focusing on the potential of magnetic nanoparticles (MNPs), with magnetite (Fe3O4) taking center stage. MNPs, encapsulated in biocompatible polymers like silica known as magnetic silica nanoparticles (MSN), are augmented with phosphotungstate (PTA) for enhanced chemodynamic therapy (CDT). PTA is recognized for its dual role as a natural chelator and electron shuttle, expediting electron transfer from ferric (Fe3+) to ferrous (Fe2+) ions within nanoparticles. Additionally, protein- based charge-reversal nanocarriers like silk sericin and gluten are introduced to encapsulate (MSN- PTA) nanoparticles,.

offering a dynamic facet to drug delivery systems for potential revolutionization of breast cancer therapy. Various analyses, such as DLS, SEM and TEM, Fourier Transform Infrared Spectroscopy (FTIR), X-Ray diffraction analysis (XRD), and Thermogravimetric analysis (TGA), were analyzed.

Results

This study successfully formulates and characterizes protein-coated nanocapsules, specifically MSN-PTA-SER, and MSN-PTA-GLU, with optimal physicochemical attributes for drug delivery applications. The careful optimization of sericin and gluten concentrations results in finely tuned nanoparticles, showcasing uniform size, enhanced negative zeta potential, and remarkable stability. Various analyses, from DLS, SEM, TEM, FTIR, XRD, and TGA, provide insights into structural integrity and surface modifications. Vibrating Sample Magnetometer (VSM) analysis underscores superparamagnetic behavior, positioning these nanocapsules as promising candidates for targeted drug delivery. In vitro evaluations demonstrate dose-dependent inhibition of cell viability in MCF-7 and Zr-75–1 breast cancer cells, emphasizing the therapeutic potential of MSN-PTA-SER and MSN-PTA-GLU. The interplay of surface charge and pH-dependent cellular uptake highlights the robust stability.

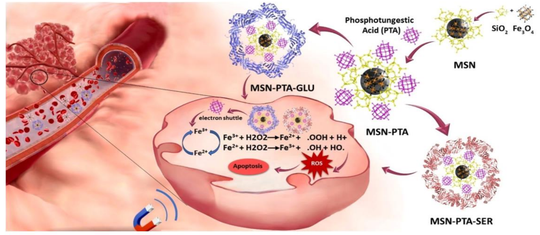

Figure 1. General schematic of MSN-PTA-SER and MSN-PTA-GLU and their functional mechanism in targeted drug delivery.

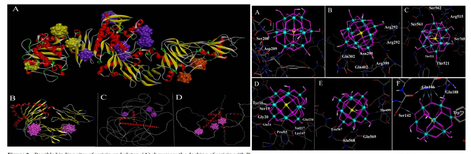

Figure 2. Possible binding sites of sericin and gluten. (**A**) showcases the docking of sericin with P, highlighting possible binding sites indicated by boxes 1, 2, and 3, depicted in yellow, purple, and red respectively. (**B**–**D**) Similarly, purple represents the binding sites for the three subtypes of gluten.

Figure 3. Most important amino acids involved in interactions with PTA. The clusters with the highest stability in terms of energy and reproducibility along with the critical amino acids engaged in interactions, have been illustrated. Sericin interactions (A–C) correspond to sericin polymers 1, 2, and 3, respectively. Similarly, gluten interactions (D–F) are linked to gliadin, glutenin high molecular weight, and glutenin low molecular weight, respectively.

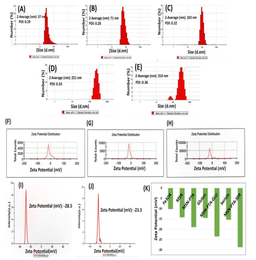

Figure 4. DLS analysis of (**A**) Fe_3O_4, (**B**) MSN, (**C**) MSN-PTA, (**D**) MSN-PTA-SER, and (**E**) MSN-PTA-GLU. Zeta potential analysis of (**F**) Fe_3O_4, (**G**) MSN, (**H**) MSN-PTA, (**I**) MSN-PTA-SER, (**J**) MSN-PTA-GLU and (**K**) Overall comparison of zeta potential of mentioned nanoparticles with zeta of sericin and gluten alone.

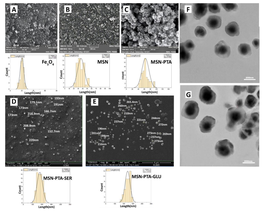

Figure 5. SEM and TEM analyses with size distribution assessment performed using Image J. SEM images include: (**A**) Fe_3O_4, (**B**) MSN, (**C**) MSN-PTA, (**D**) MSN-PTA-SER, and (**E**) MSN-PTA-GLU. SEM size distribution analysis using Image J. TEM images include: (**F**) MSN-PTA-SER, and (**G**) MSN-PTA-GLU.

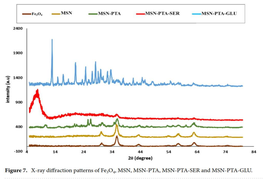

Figure 7. X-ray diffraction patterns of Fe_3O_4, MSN, MSN-PTA, MSN-PTA-SER and MSN-PTA-GLU.

Figure 9. The TGA examination of Fe_3O_4, MSN, MSN-PTA, MSN-PTA-SER and MSN-PTA-GLU.

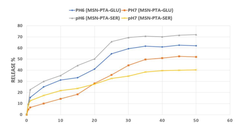

Figure 10. The in vitro release of MSN-PTA at pH value of 7, 6.

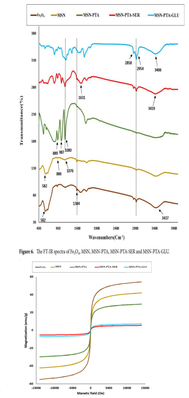

Figure 6. The FT-IR spectra of Fe_3O_4, MSN, MSN-PTA, MSN-PTA-SER and MSN-PTA-GLU.

Figure 8. The VSM examination of Fe_3O_4, MSN, MSN-PTA, MSN-PTA-SER and MSN-PTA-GLU.

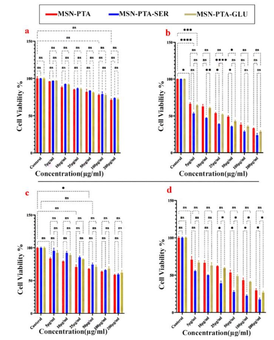

Figure 11. Viability of MCF-7 cells at 24 h (**A**) and 48 h (**B**), and ZR-75–1 cells at 24 h (**C**) and 48 h (**D**) following exposure to different concentrations of MSN-PTA, MSN-PTA-SER, and MSN-PTA-GLU. Results represent the mean ± SD from three independent experiments, with statistical significance denoted by *P ≤ 0.05 compared to the respective controls.

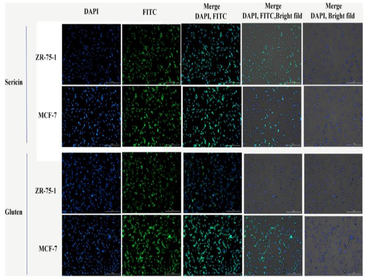

Figure 12. Fluorescence microscopy revealed intracellular uptake of FITC-labeled MSN-PTA-SER and MSN-PTA-GLU at pH 6 in MCF-7 cells, alongside DAPI staining for visualizing cell nuclei, presented with a bar scale of 200 nm.

Conclusions

In summary, this study successfully formulates and characterizes protein-coated nanocapsules, specifically sericin-based and gluten-based, exhibiting optimal physicochemical attributes for drug delivery applications. The meticulous optimization of sericin and gluten concentrations results in finely tuned nanoparticles, with sericin and gluten coated nanoparticles showcasing uniform size, enhanced negative zeta potential, and remark- able stability. The comprehensive analyses, spanning from DLS and SEM measurements to FTIR, XRD and TGA examinations, provide a thorough understanding of structural integrity and surface modifications. VSM analysis underscores superparamagnetic behavior, positioning these nanocapsules as promising candidates for targeted drug delivery. In vitro evaluations highlight the dose-dependent inhibition of cell viability, underscoring the therapeutic potential of MSN-PTA-SER and MSN-PTA-GLU. The interplay of surface charge and pH-dependent cellular uptake further accentuates the versatility of these nanocarriers, paving the way for advancements in targeted drug delivery and personalized nanomedicine. Overall, the sericin-based nanocarrier, distinguished by its charge reversal property, emerges as a smaller and more stable alternative, showcasing a significantly more negative zeta potential.