Development of a Magnetic Nanostructure for Co-delivery of Metformin and Silibinin on Growth of Lung Cancer Cells: Possible Action Through Leptin Gene and its Receptor Regulation

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Introduction

- Chemotherapeutic combinational approaches would be more efficient in decreasing toxicity of the drug, preventing tumor progression in relation to either drug alone.
- Hence, the aim of this study is to construct magnetic PLGA/PEG nanoparticles (NPs) co-loaded with Metformin (Met) and Silibinin (Sil) to investigate their cytotoxicity as well as their impact on mRNA expression levels of leptin and leptin receptor genes in A549 lung cancer cells.

Material and methods

- The synthesized NPs were characterized by FTIR, FE-SEM, and VSM, and then, MTT assay was utilized to assess and compare the cytotoxicity of various concentrations of the chemotherapeutic molecules in pure and nano formulated forms as well as in alone and combination state after 48 h exposure time.
- Moreover, the mRNA levels of leptin and its receptor genes expression were studied by quantitative real-time PCR. By co-encapsulation of Met and Sil into PLGA/PEG/ Fe_3O_4 , the cytotoxic efficiency of the compounds was considerably augmented for all concentrations.

RESULTS

Cytotoxicity assay displayed that a combination of Met and Sil had a synergistic concentration-dependent effect on A549 lung cancer cells.
Moreover, qPCR data revealed that the expression levels of the leptin and leptin receptor was considerably reduced with increasing concentrations of drug-encapsulated magnetic NPs, especially Met/Sil-encapsulated PLGA/PEG/ Fe_3O_4 NPs.

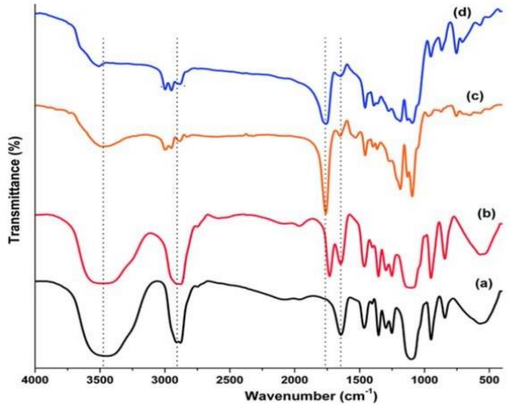

Figure 1. FTIR Spectra of (A) PLGA/PEG/ Fe_3O_4NPs, (B) Sil-loaded PLGA/PEG/ Fe_3O_4 NPs, (C) Met-loaded PLGA/PEG/Fe Fe_3O_4 NPs, and (D) Met/Sil-loaded PLGA/PEG/ Fe_3O_4 NPs.

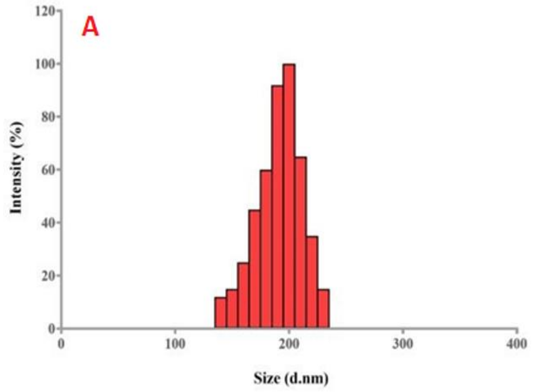

Figure 2. A) DLS histogram showing the size distribution of Met/Sil-loaded PLGA/PEG/ Fe_3O_4 NPs. The average size ranged from 160 to 220 nm.

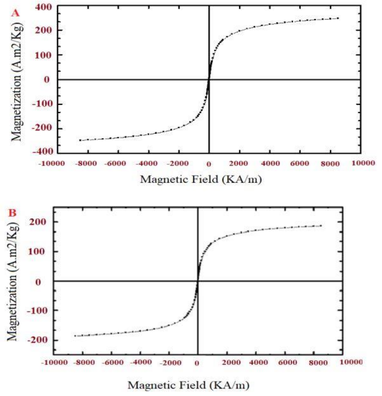

Figure 3. Magnetic Hysteresis Curve of Pure Fe_3O_4 NPs (A), and Met/Sil-loaded PLGA/PEG/F Fe_3O_4 NPs (B).

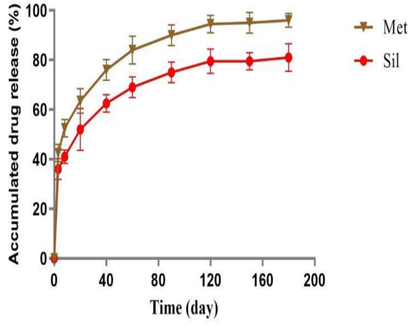

Figure 4. Dischage Profile of Sil and Met from Met/Sil-loaded PLGA/PEG/ Fe_3O_4 NPs at pH 7.4. The data are presented as mean ± SD (n=3).

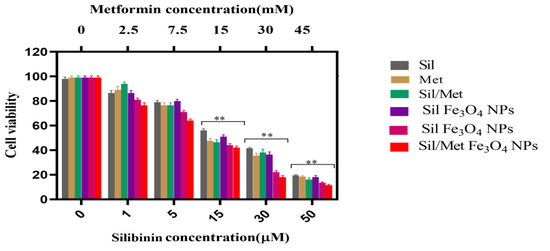

Figure 5. (A) *in vitro* cytotoxicity of pure Met, pure Sil, pure Met/Sil, Met-loaded PLGA/PEG/F Fe_3O_4 NPs, Sil-loaded PLGA/PEG/ Fe_3O_4 NPs, and Met/Sil-loaded PLGA/PEG/ Fe_3O_4 NPs against A549 cells incubated for 48 h. The data are presented as mean ± SD (n = 3).

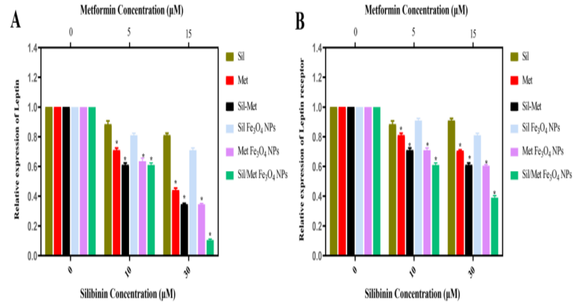

Figure 6. Expression Levels of (A) leptin and (B) leptin receptor in A549 lung cancer cells by treatment with different concentrations of pure Met, pure Sil, pure Met/Sil, Met-loaded PLGA/PEG/ Fe_3O_4 NPs, Sil-loaded PLGA/PEG/ Fe_3O_4 NPs, and Met/Sil-loaded PLGA/PEG/ Fe_3O_4 NPs. *p < 0.05 vs. other groups was considered significant. The data are presented as mean ± SD (n = 3).

Conclusion

Present preliminary study shows that co-incorporating Met, Sil, Fe3O4 into PLGA/PEG NPs might provide a more promising and safe treatment strategy for lung cancer.

References

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