Multifunctional p(NIPAM-co-NIPMAM)-Fe3O4 nanocubes hydrogel patches integrating antimicrobial activity and magnetic hyperthermia-controlled drug release

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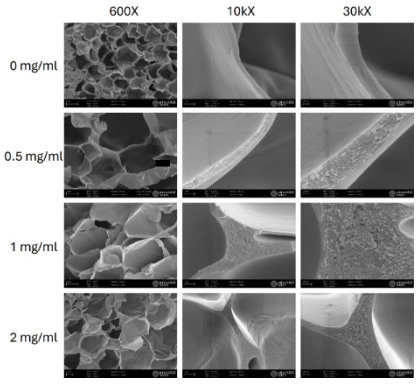
Hydrogels are three-dimensional soft materials formed from natural or synthetic polymers that can absorb large amounts of water while retaining their structure [1]. Due to their tunable properties and biocompatibility [2], hydrogels have attracted significant interest for biomedical applications, including antimicrobial purposes [3,4]. Antimicrobial activity can be achieved through two main strategies: (i) "inherently active" hydrogels, in which the three-dimensional polymer network itself has antimicrobial properties [5], and (ii) "carrier" hydrogels that encapsulate and release active agents. In carrier hydrogels, several cargos have been investigated, including antibiotics [6] and antimicrobial nanoparticles such as zinc oxide, copper oxide, titanium oxide, and iron oxide [7]. Most cargos are released passively from hydrogels; however, uncontrolled release can reduce therapeutic efficacy and promote antimicrobial resistance. Therefore, controlled delivery of agents and drugs is highly desired to improve their efficiency and safety. To overcome the limitations of passive release, several advances have been made in recent years, primarily using pH- or temperature-responsive hydrogels. Temperature-responsive hydrogels can be triggered by laser irradiation in the presence of a photothermal agent [8] or by an alternating magnetic field in magnetically active materials [9]. Thus, iron oxide nanoparticles offer a unique opportunity to design dual-function systems that combine on-demand drug release with direct antimicrobial activity.

In this work, we developed p(NIPAM-co-NIPMAM) based hydrogel patches containing iron oxide nanocubes and antimicrobial drugs (gentamicin and vancomycin). Due to the known magnetic properties [10], superior to those of standard iron oxide nanoparticles, the nanocubes allow a fast and controlled release of drugs under an alternating magnetic field, while simultaneously exhibiting antimicrobial activity against Gram-positive Staphylococcus aureus and Gram-negative Escherichia coli. Overall, this system provides a versatile approach to combine local antimicrobial treatment with controlled drug delivery, as demonstrated by its dual ability to eradicate bacterial populations and modulate the spatiotemporal release of antibiotics.



SEM micrographs at various magnification of the hydrogels with different nanoparticle concentrations

References:

[1] Ho, T.-C.; Chang, C.-C.; Chan, H.-P.; Chung, T.-W.; Shu, C.-W.; Chuang, K.-P.; Duh, T.-H.; Yang, M.-H.; Tyan, Y.-C., *Molecules,* **2022** . [2] Sannino, A.; Madaghiele, M.; Ambrosio, L., *Cellular Response to Biomaterials,* **2009.** [3] Li, Y.; Han, Y.; Li, H.; Niu, X.; Zhang, D.; Wang, K., *Small,* **2024.** [4] Yang, K.; Han, Q.; Chen, B.; Zheng, Y.; Zhang, K.; Li, Q.; Wang, J., *Int. J. Nanomedicine* **2018.** [5] Wang T., Zhu X.-K., Xue X.-T., Wu D.-Y., *Carbohydr. Polym.* , **2021** . [6] Saeed, S.; Barkat, K.; Ashraf, M.U.; Shabbir, M.; Anjum, I.; Badshah, S.F.; Aamir, M.; Malik, N.S.; Tariq, A.; Ullah, R., *Gels,* **2023.** [7] Farag, R.K.; Labena, A.; Fakhry, S.H.; Safwat, G.; Diab, A.; Atta, A.M. , *Materials,* **2019** . [8] Matai I., Kaur G., Soni S., Sachdev A., Vikas, Mishra S., *J. Photochem. Photobiol. B, Biol,* **2020** .[9] Zhou T.. Liu X., Wu Z., Lyu R., Peng C., Zhang H., Xia Y., *ACS Omega* , **2025** . [10] Gavilán, H., Rizzo, G.M.R., Silvestri, N., Mai B. T., Pellegrino T, *Nat Protoc,* **2023** .

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