



UNIVERSITY OF SALERNO

Department of Industrial Engineering
Master's degree in Food Engineering

**Micelle-Hydrogel (HyMic) delivery systems: production
and mathematical modeling of their behavior**

Thesis in
Transport Phenomena

Supervisors:

Prof. Eng. Gaetano Lamberti

Prof. Tina Vermonden

Dr. Eng. Diego Caccavo

Dr. Ada Annala

Candidate:

Gianmaria Cantarella

number 0622800429

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“Se saprai mantenere la calma quando tutti intorno a te la perdono e te ne fanno colo. Se saprai avere fiducia in te quando tutti ne dubitano, tenendo però considerazione anche del loro dubbio. Se saprai aspettare senza stancarti di aspettare, o essendo calunniato, non rispondere con calunnia, o essendo odiato, non dare spazio all’odio, senza tuttavia sembrare troppo buone, né parlare troppo saggio. Se saprai sognare, senza fare del sogno il tuo padrone; Se saprai pensare, senza fare del pensiero il tuo scopo, se saprai confrontarti con Trionfo e Rovina e trattare allo stesso modo questi due impostori. Se riuscirai a sopportare di sentire le verità che hai detto distorte dai furfanti per abbindolare gli sciocchi, o a guardare le cose per le quali hai dato la vita distrutte e piegarti a ricostruirle con i tuoi logori arnesi. Se saprai fare un solo mucchio di tutte le tue fortune e rischiarlo in un unico lancio testa e croce, e perdere, e ricominciare di nuovo dal principio senza mai far parola della tua perdita. Se saprai serrare il tuo cuore, tendini e nervi nel servire il tuo scopo quando sono da tempo sfiniti, e a tenere duro quando in te non c’è più nulla se non la Volontà che dice loro: “Tenete duro!” Se saprai parlare alle folle senza perdere la tua virtù, o passeggiare con i Re rimanendo te stesso, se né i nemici né gli amici più cari potranno ferirti, se per te ogni persona conterà ma nessuno troppo. Se saprai riempire ogni inesorabile minuto dando valore ad ognuno dei sessanta secondi, Tua sarà la Terra e tutto ciò che è in essa, e -quel che più conta- sarai un Uomo, figlio mio!”

R.Kipling

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Abstract

The thesis was carried out in collaboration with two universities, the experimental part at Utrecht University, while the modeling part was carried out at the University of Salerno.

In this thesis work the polymers for the production of micelles and hydrogels have been synthesized. Each synthesis step was characterized by different analyzes (¹H-NMR, DLS, swelling analysis). The two triblock polymers used were synthesized PNC (NIPAM-HPMA-cysteine-Peg) and the PNN (NIPAM-NAS-Peg). The two polymers were characterized by analysis ¹H-NMR to investigate the ratio between of the monomers used and also to have a first estimate on the molecular weight.

The synthesis of the micelles exploited the thermoresponsive behaviour of the NIPAM which changes its behaviour from hydrophilic to hydrophobic when the temperature achieves the value of the Cloud Point. The micelles were produced at different concentrations 5, 10, 20 mg / mL and with 2: 3 PNC / PNN polymer ratio and were characterized in terms of Z-average and PDI with DLS analysis.

The micelles produced were used together with PNC (as a linker) for the formation of the polymeric network. In particular, three gels were formed, the first two HyMics were synthesized using an Eppendorf tube and a mold to have a cylindrical shape, the third was produced using exclusively the two polymers. They were then transferred into 2 mL vials and 500 μ L of PBS were added for swelling analysis.

After the experimental part the mathematical study was performed with the formulation of a model for the description of the drug release.

The first step was to define the geometry of the hydrogels. Two geometries (cylinder and sphere) were used which could be the closest to the real shape after injection. The simulation models (2D-axysymmetric and 1D) were chosen, the meshes and sizes were defined. The parameters governing the model have been studied, in particular after the parametric sweeps, k_{er} has been identified as the main parameter, as small variations lead to high differences in terms of amount of drug release and release times. The last step of this thesis work was the analysis of some literature release data. The experimental points have been described with sufficient precision by the written model, with the only addition of a step function for the value of k_{er} . In fact, from physical considerations it was understood that depending on the concentration of enzyme present in the dissolution medium there is an initial latency time in which the k_{er} has very low values tending to zero.

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