Mathematical description of hydrogels' behavior for biomedical applications

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Mathematical description of hydrogels' behavior for biomedical applications

Master's Thesis in Chemical Engineering

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CHALMERS

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Sommario

Negli ultimi anni l'interesse verso gel macroporosi è cresciuto e ad oggi questi materiali vengono utilizzati in diverse applicazioni come, ad esempio, nel rilascio di farmaci, nella medicazione di ferite e nell'ingegneria dei tessuti. Una frazione significativa di queste sostanze è costituita da alginati, polisaccaridi estratti da alghe che, in presenza di ioni bivalenti, sono in grado di reticolare e formare "gel ionotropici". In certe condizioni di gelazione è possibile far sviluppare dei capillari dritti, di dimensioni macroscopiche, lungo tutta l'altezza del gel. L'utilizzo in ambito biomedico di questi particolari materiali fa sì che la loro produzione, e quindi il meccanismo di formazione, debba essere compreso a fondo per poterne modulare le caratteristiche e renderle idonee alle varie applicazioni.
Con lo scopo quindi di far luce su questo fenomeno, la morfologia di gel ionotropici di alginato, prodotti con ioni di tipo Ca^{2+}, Cu^{2+}, Sr^{2+}, è stata analizzata mediante analisi dell'immagine. I risultati ottenuti mostrano un'evoluzione delle caratteristiche di porosità in termini di diametro e densità dei pori e in termini di percentuale di area dei pori al variare dell'altezza del gel.
Visti inoltre i recenti utilizzi di gel ionotropici macroporosi a scopi di vascolarizzazione e rimozione di essudato, in questo lavoro, i gel sono stati anche caratterizzati in termini di permeabilità. Allo scopo è stato messo a punto un metodo basato sulla semplice misura della quantità di fluido che attraversa il gel nell'unità di tempo. I risultati, anche in questo caso, evidenziano caratteristiche differenti a seconda dello ione utilizzato. Il flusso di fluido attraverso questi gel è stato inoltre modellato e comparato ai dati sperimentali.
Infine le diverse teorie proposte in letteratura per la descrizione della formazione dei capillari sono state analizzate e, in particolare una, la "teoria idrodinamica" è stata implementata in un modello. Questo è stato validato su dati sperimentali mostrando delle buone caratteristiche predittive e soprattutto mettendo in risalto le variabili che dominano il processo.

Un'altra importante proprietà impiegata in campo biomedico, che coinvolge idrogeli, è la bioadesione. Questo fenomeno avviene tra una parete biologica e una sostanza adesiva che, solitamente, è un materiale capace di rapida gelazione. Sebbene esistano in commercio farmaci che sfruttano questo meccanismo per rilasciare in modo controllato il principio attivo, non sono stati chiariti i fenomeni chimico fisici alla base del processo di adesione e quali siano i parametri che maggiormente lo influenzano.

In questo lavoro l'attenzione è stata focalizzata sull'importanza del trasporto di acqua dalla parete biologica, simulata da un idrogelo, al materiale bioadesivo.
Diverse prove sperimentali sono state effettuate cercando di modulare la pressione osmotica del gel/adesivo risultante e aumentarne le caratteristiche di *swelling*.
È stato inoltre studiato l'effetto del cambiamento di trasporto dell'acqua, grazie al cambiamento di morfologia del gel simulante la parete biologica, sulle proprietà bioadesive.
Infine è stato sviluppato un modello simulante il trasporto dell'acqua, dello *swelling* e della prima risposta adesiva, di natura elastica, trovando un buon accordo con i dati sperimentali.

Abstract

Over the last years the interest in macroporous gel has been grown and nowadays these materials are used in various applications such as, for example, drug delivery, wounds dressing and tissue engineering. A significant fraction of these substances is constituted by alginates, polysaccharides extracted from algae that, in presence of divalent ions, are able to crosslink and form "ionotropic gels". In certain gelation conditions it is possible to develop straight capillaries, of macroscopic dimensions, along the gel height. Considering that these particular materials are used in biomedical field, their production, and thus the formation mechanism, should be fully understood to be able to modulate their characteristics and to make them suitable for various applications. Therefore with the aim of making light on this phenomenon, the morphology of ionotropic gels of alginate, produced with ions Ca^{2+}, Cu^{2+}, Sr^{2+}, was analyzed with image analysis. The results obtained show an evolution of porosity, in terms of diameter, density of pores and in terms of percentage of holed area, along the gel height. Moreover seeing that in the last years these gels have been used for vascularization and exudate removing purposes, the gels were also characterized in terms of permeability. In order to do that, a method has been conceived and developed based on the simple measurement of the quantities of a fluid passing through the gel in the unit time. The results, even in this case, show different characteristics depending on the used ions. Furthermore the flow through these gels has also been modelled and compared to experimental data. Finally, the different theories describing the capillaries formation has been analysed and, in particular one, the "hydrodynamic theory" has been implemented in a model. This has been validated on experimental data, showing good predictive characteristics and, above all, highlighting the variables that dominate the process.

Another important property, which involves hydrogels in biomedical field, is bioadhesion. This phenomenon takes place between a wall and a biological adhesive substance which, usually, is a material capable of rapid gelation. Although there are several drugs on the market that use this mechanism to release the active substance in a controlled manner, the chemical and physical phenomena at the base of this process have not been clarified yet. In this work the attention has been focused on the importance of water transport from the biological wall, simulated by an hydrogel, to the bioadhesive material. Different experiments have been carried out trying to modulate the osmotic pressure of the resulting gel/adhesive material and increase its swelling characteristics.

It has been also studied the effect of the change in water transport, changing the morphology of the gel simulating the biological wall, on the bioadhesive properties. Finally a model has been developed to simulate the water transport, the swelling and the first adhesive elastic response. A good agreement has been found with the experimental data.

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