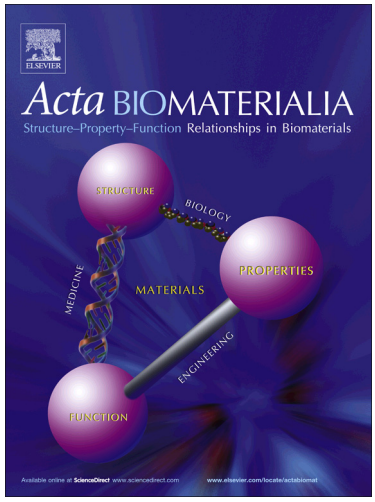

Full length article

Polyion complex hydrogels from chemically modified cellulose nanofibrils: Structure-function relationship and potential for controlled and pH-responsive release of doxorubicin

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Polyion complex hydrogels from chemically modified cellulose nanofibrils: Structure-function relationship and potential for controlled and pH-responsive release of doxorubicin

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KEYWORDS: nanocellulose; cellulose nanofibrils; hydrogel; polyion complex; controlled release; pH-responsive; doxorubicin; cancer

Abstract

Herein, we report the fabrication of a polyion complex hydrogel from two oppositely charged derivatives of cellulose nanofibrils (CNF). CNF was produced from dissolving pulp through subsequent periodate oxidation, chemical modification, and microfluidization. Three different durations for periodate oxidation (30 min, 120 min, and 180 min) resulted in three different aldehyde contents. Further, two types of chemical modifications were introduced to react with the resulting aldehydes: chlorite oxidation to yield anionic CNF with carboxylic acid groups (DCC) and imination with Girard's reagent T to yield cationic CNF containing quaternary ammonium groups (CDAC). Functional group contents were assessed using conductometric titration and elemental analysis, while nanofibril morphologies were assessed using atomic force microscopy (AFM). Longer durations of periodate oxidation did not yield different width profile but was found to decrease fibril length. The formation of self-standing hydrogel through mixing of DCC and CDAC dispersions was investigated. Oscillatory rheology was performed to assess the relative strengths of different gels. Self-standing hydrogels were obtained from mixture of DCC180 and CDAC180 dispersions in acetate buffer at pH 4 and 5 at a low concentration of 0.5% w/w that displayed approximately 10-fold increase in storage and loss moduli compared to those of the individual dispersions. Self-standing gels containing doxorubicin (an anticancer drug) displayed pH-responsive release profiles. At physiological pH 7.4, approximately 65% of doxorubicin was retained past a burst release regime, while complete release was observed within 5 days at pH 4. Biocompatibility of DCC180, CDAC180, and their mixture were investigated through quantification of the metabolic activity of NIH3T3 cells *in vitro*. No significant cytotoxicity was observed at concentrations up to 900 µg/mL. In short, the nanocellulose-based polyion complex hydrogels obtained in this study are promising nature-derived materials for biomedical applications.