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Synthesis and application of photo-active carboxymethyl cellulose derivatives

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ABSTRACT

In this work, the polysaccharide carboxymethyl cellulose (CMC) was first activated *via* periodate oxidation then modified by insertion of photo-active cinnamic acid hydrazide moieties to finally produce the photo-crosslinkable CMC-CM with various extents of functionalizations. The chemical structures of the manufactured polymeric materials were entirely investigated utilizing FTIR, ^{1}H, ^{13}C NMR, and UV–vis spectra. Upon irradiation in UV light, the progress and kinetics of the cross-linking were detected using UV–vis spectra. Moreover, the crystallinity changes before and after chemical modification and subsequent UV irradiation were examined by XRD spectra. Also, the obtained hydrogels with various cross-linking densities were freeze dried to visualize the morphological changes using SEM. In addition, the rheological experiments indicated the improvement of the hydrogel mechanical properties by increasing both UV irradiation time and degree of cinnamate functionalization. The obtained hydrogel exhibited good swelling, gelation and biodegradation properties, which indicate a promising potential in different biomedical applications.

1. Introduction

Carboxymethyl cellulose (CMC) is regarded as one of the most commonly used polysaccharide derivatives. As a result of its water solubility, high availability, biocompatibility in addition to non-toxicity, CMC had been widely employed in various industrial applications such as pharmaceutics, cosmetics and textiles [1–3]. Moreover, the biodegradability of CMC enhanced its utility in various biotechnological applications such as drug delivery systems, enzyme immobilization and tissue engineering [4–7]. In most of these biomedical and pharmaceutical applications, CMC had to be cross-linked to form a three dimensional polymeric hydrophilic network, which is able to absorb large amounts of water and swells until reaching equilibrium between the thermodynamic swelling forces and cross-linking elastic retractive force. At this equilibrium point, a polymer–water state called a hydrogel is obtained [8–10].

Many types of cross-linking agents had been utilized for either ionic or covalent cross-linking of CMC such as Al^{3+} ions [11,12], 1,4-butanediol diglycidyl ether [13], polyethylene glycol diglycidyl ether (PEGDE) [14], and dicarboxylic acids [15] in addition to epichlorohydrin (ECH), which is a common CMC cross-linking agent due to the high tendency to form ether linkage with the —OH groups [16–18]. All the aforementioned cross-linking agents were efficiently employed in manufacturing CMC based hydrogels for various biomedical and environmental applications. However, formation of carcinogenic and even toxic byproducts during the biodegradation process is considered a serious drawback and limits the implementation of these hydrogels in some pharmaceutical applications [14]. For these reasons, various attempts had been devoted to the development of novel cross-linking techniques that minimize the formation of these undesirable byproducts. Among these techniques, photo-induced cross-linking is considered one of the most efficient methods employed in safe cross-linking and gelation. The convenient photo-crosslinking process includes the functionalization of the main polymeric chain with polymerizable vinyl moieties such as maleic anhydride or acrylate derivatives. Then, the cross-linking reaction will be performed by irradiation to UV or visible light in the presence of a suitable photo-initiator [19]. Although there are obviously better results obtained from this technique compared to the ordinary chemical cross-linking methods, the difficulty of removing the unreacted photo-initiator in addition to trace initiator byproducts could still restrict the employment of these hydrogels in some applications [20,21].

In this work we describe an efficient method for the synthesis of a novel modified photo-crosslinkable CMC. In the beginning, CMC was oxidized with sodium periodate, which selectively cleaves the C2—C3 bond and form modified dialdehyde CMC [22]. Then, the resulting aldehyde groups were allowed to react with cinnamic acid hydrazide in order to introduce the photo-active cinnamate moieties onto the CMC backbone. The gelation of the obtained cinnamate modified CMC

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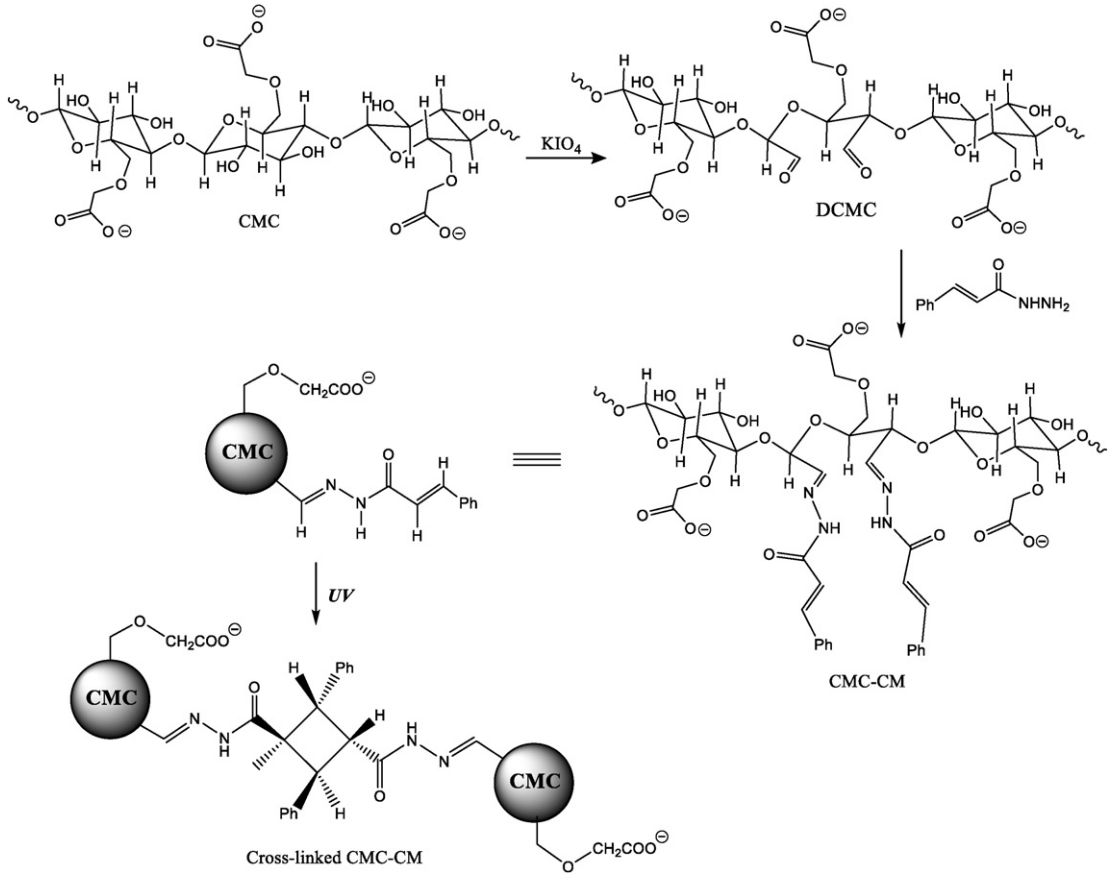

Scheme 1. Synthesis and photo-crosslinking of CMC-CM.

(CMC-CM) was performed upon irradiation in the UV region as a result of the dimerization of the active cinnamate units *via* [2π + 2π] cyclo-addition reaction [23]. The obtained polymeric materials were extensively characterized using Fourier transform infrared (FTIR), nuclear magnetic resonance (^{1}H and ^{13}C-NMR), wide angle X-ray diffraction (XRD) spectra in addition to a scanning electron microscope (SEM).

2. Materials and methods

2.1. Materials

Carboxymethyl cellulose (CMC) sodium salt (degree of substitution 2.34, and $M_w = 7.6 \times 10^5$ mol g^{-1}) was obtained from Sigma-Aldrich (USA), sodium periodate, hydrazine hydrate, cinnamoyl chloride, cellulase (chromatographically purified, T. Reese) and ephedrine hydrochloride were all supplied from Alfa Aesar (USA). The other chemicals were of analytical grade and used as supplied without any further treatments.

2.2. Periodate oxidation of CMC

The modified dialdehyde CMC (DCMC) was prepared according to the procedures proposed by Li et al. [1]. Three different samples with different oxidation extents were prepared as explained in the following; in three 250 mL conical flasks 100 mL 5% (*w*/*v*) aqueous CMC solutions were prepared, the pH 3 was adjusted using acetic acid then the flasks were placed in a shaker fitted with a water bath adjusted at 35 °C. To each flask we added 10 mL aqueous sodium metaperiodate solution with concentrations of 5.0 mM, 7.5 mM and 10 mM and the reaction continued for 4 h. The oxidized DCMC samples with different aldehyde contents were then precipitated by adding excess acetone then filtered and washed with water/ethanol and finally with dimethyl formamide (DMF).

2.3. Determination of aldehyde content

For evaluation of the extent of periodate oxidation, the formed aldehyde groups were estimated by turning it into oxime groups through reaction with hydroxyl amine hydrochloride and titration of the released HCl against standardized NaOH solution [24]. In details, 25 mL 2% (*w*/*v*) aqueous DCMC solution was adjusted to pH 5 and allowed to react with 20 mL 0.75 M aqueous $NH_2OH \cdot HCl$ solution for 4 h at 40 °C. The released HCl was then estimated by titration against 0.1 M NaOH. Another blank sample was prepared and treated in the same manner but using CMC. Eq. (1) was employed for determination of the aldehyde content (*Ald*%).

$$Ald\% = \frac{M_{NaOH}(V_C - V_b)}{m/211} \quad (1)$$

where M_{NaOH} is the molar concentration of NaOH solution (0.1 M), V_C is the consumed volume of NaOH in case of DCMC samples, V_b is the volume of consumed NaOH for the blank CMC and m is the weight of the polymeric samples.

The obtained oxidized CMC samples with aldehyde contents 23%, 47% and 56% are named DCMC1, DCMC2 and DCMC3 respectively.

Table 1
Elemental analysis of modified and unmodified CMC samples.

Sample	C (%)	H (%)	N (%)	DS (mmol/g)
CMC	42.5	5.6	0.003	–
CMC-CM1	48.3	5.5	3.4	1.2
CMC-CM2	52.3	5.4	5.8	2.1
CMC-CM3	57.6	5.3	9.0	3.2