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Cationic amphiphilic microfibrillated cellulose (MFC) for potential use for bile acid sorption

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ABSTRACT

In this work, Micro-fibrillated Cellulose (MFC) was cationically modified by quaternary ammonium groups with different chemical structures aiming to improve the sorption capacity to bile acid. The in-vitro bile acid sorption was performed by investigating various factors, such as quaternary ammonium group content and length of its alkyl substituent of the modified cationic MFC (CMFC), ionic strength, initial concentration and hydrophobicity of bile acid. The results showed that the sorption behavior of the modified CMFC was strongly influenced by the quaternary ammonium group content and the lengths of its alkyl substituent, the sorption capacity for the modified CMFC with a C_{18} alkyl substituent, was approximately 50% of that of Cholestyramine. The experimental isotherm results were well fitted into the Temkin model. The effect of salts in the solution was smaller for the bile acid sorption onto the hydrophobic CMFC than the CMFC. It was also found that the binding capacity of CMFC was higher for more hydrophobic deoxycholate in comparison with cholate.

1. Introduction

It is well-known that cholesterol is critical in cell membrane formation and biosynthesis of bile acids, steroid hormones and vitamin D. On the other hand, too high level of cholesterol in blood would not be desirable, for example, causing atherosclerosis (Kazlauske, Ramanauskiene, & Liesiene, 2014), which is one of the main reasons for illnesses and deaths (Mason, 2011). Bile acid sorbents are polymeric compounds that can be used to control the cholesterol level. When these polymers are ingested, bile acids can be adsorbed onto them, which will lead to increased fecal bile acid excretion and, in turn, decreasing the levels of serum and/or tissue cholesterol (Kahlon & Smith, 2007; Einarsson et al., 1991). Bile acids consist of a curved steroidal skeleton with a hydrophobic face and a hydrophilic face, which includes a carboxylic acid group (Fig. 1). This provides the bile acids amphiphilic character and self-associative behavior (Yañez, Chianella, Piletsky, Concheiro, & Alvarez-Lorenzo, 2010). Bile acid sorbents, such as Cholestyramine, Cholestipol and Cholestimide, have been extensively used in clinic for several decades (Ast & Frishman, 1990; Schulman et al., 1990; Honda & Nakano, 2000). However, the above sorbents are based on synthetic polymers. For example, Cholestyramine is quaternized styrene-divinilbenzene copolymer (Ast & Frishman, 1990); and Colestipol is synthesized from tetraethylenpentamine and epichlorohydrin (Schulman et al., 1990); while Cholestimide is an anion-exchange resin with an imidazolium salt on an epoxide polymer skeleton (Honda & Nakano, 2000). Therefore, in the clinical practice, these sorbents can cause some side effects such as constipation, nausea and meteorism (Scaldaferri, Pizzoferrato, Ponziani, Gasbarrini, & Gasbarrini, 2013).

Cellulose is the most abundant natural polymer on earth. Cellulose-based materials, such as Cellulose Nanocrystal (CNC) and Microfibrillated cellulose (MFC) are emerging biomaterials having many unique properties, including excellent surface area and high aspect ratio (Moon, Martini, Nairn, Simonsen, & Youngblood, 2011). Previous studies have demonstrated that CNC, MFC or modified cellulose material can act as sorbents for various organic compounds, including dyes, aromatic compounds and herbicides (Pei, Butchosa, Berglund, & Zhou, 2013; Sun, Hou, He, Liu, & Ni, 2014; Sun et al., 2013; Maatar, Alila, & Boufi, 2013). Since glucosidic bonds in cellulose cannot be hydrolyzed by human digestive enzymes, once ingested, cellulose material maintains its binding capacity to bile

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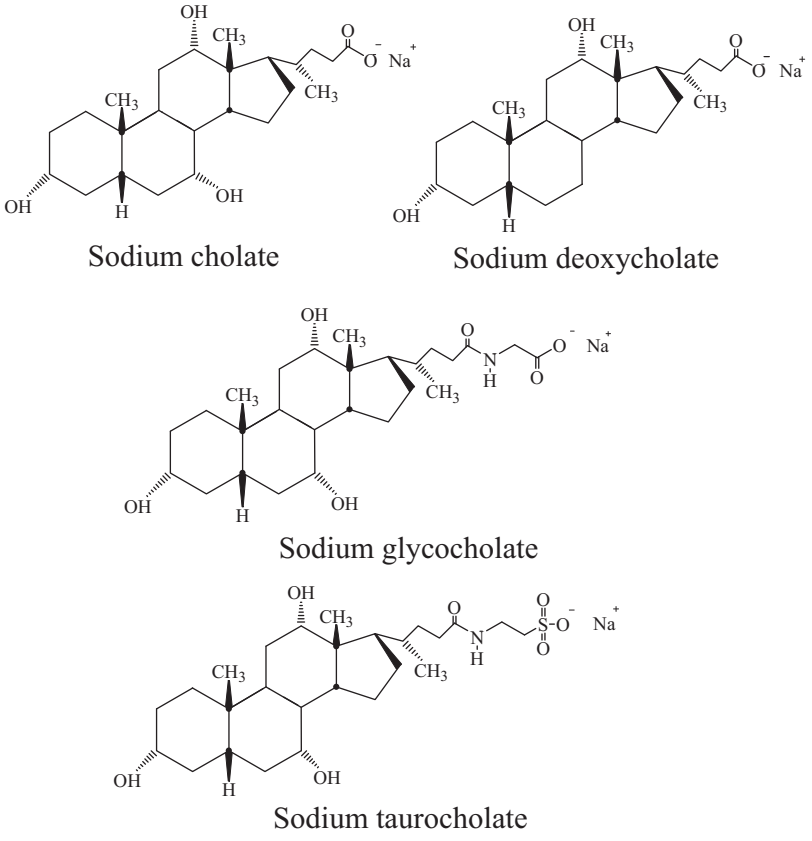

Fig. 1. Examples of bile salts.

acid in the physiological condition of gut, which accordingly makes it an attractive material for food supplement for people with high cholesterol.

In a previous study (Zhu et al., 2014), we have carried out in-vitro bile acid sorption studies of cationic MFC (CMFC) that was cationized using trimethylammonium chloride. It was found that the primary interaction occurred between bile acid and CMFC was electrostatic in nature. However, the sorption capacity of CMFC was lower than that of Cholestyramine under the same condition. In such applications, one would expect that a higher hydrophobic substituent in the CMFC may enhance the interaction with bile acid. Modifications of polymers to increase the hydrophobic interaction have been reported in the literature. For example, when investigating the interaction between cationic dextran hydrogels with *N*-(2-hydroxypropyl)-*N*,*N*-dimethyl-*N*-alkyl ammonium pendant groups and bile acids, Nichifor, Cristea, and Carpov (2000) reported that the increase in the chain length of the alkyl substituent of the modified dextran hydrogel can strongly increase the rate of initial binding constant, K_0 and the binding capacity, K. Also, the ionic strength has a small influence on the bile acid binding by hydrogels with alkyl substituent of C_8 or C_{12} (Nichifor, Zhu, Cristea, & Carpov, 2001). It was suggested that when alkyl substituent is longer than C_4, the binding is governed by hydrophobic interaction between alkyl substituent and bile acid, and aggregation may occur via mixed micelle formation (Nichifor et al., 2001).

The objective of this study was to enhance the interaction of the modified CMFC having cationic groups and long alkyl chains with bile acid. The influences of quaternary ammonium group content (cationic charge density) and length of its alkyl substituent of the modified CMFC, ionic strength, initial concentration and hydrophobicity of bile acid on the binding characteristics were examined.

2. Methods

2.1. Materials

A sulfite- based dissolving pulp used to prepare the CMFC was from a mill in Shandong, China. A endoglucanase sample (Novozym 476, Novozym 435) was used without further purification. Tertiary amines, epichlorohydrin (ECH) and *N*-(2-3-epoxypropyl) trimethylammonium chloride (EPTMAC) were purchased from Sigma Aldrich and were used as received. The Total Bile Acids Test Kit for bile acid measurement was purchased from CY-BIO, Co., Shangyu, China. Other reagents used in this work were supplied by Tianjin Chemical Reagent Co. Ltd., China. Distilled and deionized water was used throughout experiments unless otherwise specified.

2.2. Preparation of sorbents

The preparation of CMFC was as follows: (a) enzyme pretreatment of the sulfite-based dissolving pulp (details will be given in the next section); (b) chemical modification of enzyme-treated sulfite dissolving pulp for the attachment of the first pendant quaternary ammonium group with methyl substitutes (single-modified fibers); (c) chemical modification of single-modified fibers for the attachment of the second quaternary ammonium group with long alkyl chains (double-modified fibers); (d) the cationic pulp was diluted to 1% w/w of mixtures and then homogenized to produce the CMFC. The schematic representation of preparing the cationic amphiphilic MFC and chemical structure of the modified CMFC was illustrated in Fig. 2 and the chemical characteristics were listed in Table 1.