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Influence of ionic strength on membrane selectivity during the ultrafiltration of sulfated pentasaccharides

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ABSTRACT

Due to their numerous biological properties, natural sulfated polysaccharides have attracted the interest of the food and pharmaceutical industries. Membrane processes were thought to be especially suitable for their production at industrial scale. The aim of this study was to evaluate the effect of sodium chloride, often used as a preservative and a precipitation adjuvant, on the ultrafiltration of sulfated pentasaccharides. In pure water, results showed a complete retention of the polymers on membranes with molecular weight cut-off up to eight times the molecular weight of the studied pentasaccharides. When NaCl was added to a concentration of 0.5 mol L^{-1}, retention rates decreased significantly (≈−50%). As no relevant modification of the molecules size was observed through hydrodynamic radius measurements, these variations of selectivity were fully attributed to the screening of membrane surface charges by the electrolyte. Therefore, optimising the ultrafiltration of charged molecules need absolutely exammining electrostatic interactions.

1. Introduction

In recent years, a wide range of polysaccharides has emerged as an important class of bioactive natural products. Sulfated polysaccharides have particularly aroused the interest of many researchers because of their various applications in food and pharmaceutical industries. Indeed, some of them, such as pectin or carrageenans, have become valuable food additives due to their rheological properties. They are used as gelling agents, thickeners, stabilisers, emulsifiers or fat replacers (Hatziantoniou & Howell, 2002; Hodur, Kertesz, Beszedes, Laszlo, & Szabo, 2009; Moresi & Sebastiani, 2008). In addition, many of these biopolymers exhibit a wide range of biological activities that may find relevance in functional food and pharmaceutical applications. For example, glycosaminoglycans from the extracellular matrix of the vertebrate organisation (Barbucci, Magnani, Lamponi, & Albanese, 1996; Ben Mansour et al., 2009; Chavaroche, Van den Broek, & Eggink, 2013; Cui, Li, & Yuan, 2012; Yang, Chang, Weyers, Sterner, & Linhardt, 2012; Wu & Chen, 2006) or oligosaccharides derived from polysaccharides of seaweed, bacteria, fungi or plant origin (Mellal et al., 2008; Jiao, Yu, Zhang, & Ewart, 2011; Wijesekara, Pangestuti, & Kim, 2011; Cardozo et al., 2011; Chen et al., 2011) possess antitumor, antiviral, immunomodulant, anticoagulant and antioxidant properties. Therefore, many studies have been launched on polysaccharides isolation to improve both selectivity and yield of their production processes.

Sulfated polysaccharides are traditionally extracted by enzymatic hydrolysis and precipitated with ethanol. The purification step is mainly realised by gel filtration or anion exchange chromatography and a high grade of purification is required since only polysaccharides of specific degree of polymerisation show biological activities. Thus, when conventional laboratory techniques are employed, the purification process can become very expensive, which limits the production at industrial scale.

Due to a wide size range, membrane processes have seemed to be especially suitable for initial purification of bioactive and heat-sensitive materials at the industrial scale as they are operated under mild conditions, permit to treat large volumes and can be easily automatised. Furthermore, membrane processes offer a large number of benefits for industries: high product selectivity with consistent quality of permeate and retentate, low energy requirement, reduced operating costs, easy implementation, long operating life and low pollution. The clarification and concentration of sulfated polysaccharide solutions can be achieved by

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microfiltration or ultrafiltration membranes. The following steps of purification are thus facilitated, for example by reducing the volumes to be treated or the amount of alcohol needed for precipitation, and the overall quality of the final product is improved (Hodur et al., 2009). However, the filtrating conditions have to be optimised to control the decline in permeate flux and the variations in selectivity which occur during the filtration of complex natural products. Due to molecules/molecules and molecules/membrane interactions, the determination of the optimised operating conditions is not easy and requires a careful investigation at the laboratory scale (Hatziantoniou & Howell, 2002; El Rayess et al., 2012; Mellal et al., 2008).

Interactions between molecules and membrane during the filtration process are not limited to steric effects. Particularly, in the case of charged molecules, electrostatic phenomena can appear and strongly modify the mass transfer. Most membranes present an electrically charged active surface and these interactions become more and more important with decreasing pore size and thus have to be considered in ultrafiltration (Moritz, Benfer, Arki, & Tomandl, 2001). Regarding ceramic membranes, which are the most frequently employed in industrial filtration plants for this application, the metal oxides composing the active layer become hydroxylated in aqueous solution, leading to the development of an electrical charge at the membrane surface (Zhang, Jing, Fan, & Xu, 2008). Consequently, the pH and ionic strength of the solution may affect significantly the behaviour of sulfated polysaccharides in ultrafiltration (Broeckmann, Wintgens, & Schäfer, 2005; Lo, Yang, & Min, 1996; Pinelo, Moller, Prado-Rubio, Jonsson, & Meyer, 2013). In fact, during the process of polysaccharides isolation, sodium chloride is often added to the solution to prevent microbial development and to strongly reduce the alcohol quantity needed for precipitation (Garcia-Ochoa, Santos, Casas, & Gomez, 2000). The variations of the ionic strength by adding salt can modify the molecular conformation of charged molecules and their interactions with the membrane material. It is then expected that the presence of sodium chloride has an impact on molecules retention.

The present study was undertaken to determine the effect of sodium chloride addition on the membrane efficiency in terms of permeate flux and retention during the ultrafiltration of sulfated pentasaccharides, in order to identify the mechanism(s) controlling the purification and, thus, improve the industrial membrane processing of such molecules.

2. Materials and methods

2.1. Test molecules

Two synthetic polysaccharides provided by Sanofi Chimie (Aramon, France) were selected for ultrafiltration trials because of their structural similitude with natural anticoagulant polysaccharides (Fig. 1). There were a Linear Sulfated Pentasaccharide (LSP) with a molecular weight (M_W) of 1726 g mol^{-1} and the associated Biotinylated Sulfated Pentasaccharide (BSP) with a molecular weight of 2046 g mol^{-1} to determine the impact of their molecular configuration on their behaviour during filtration experiments. The graft of biotin, responsible for a gap of 16% in molecular weight, allows the inhibition of the pentasaccharide activity by adding avidin. These molecules present many sulfated and carboxyl groups, making them highly ionised in aqueous solution.

2.2. Membranes

The ultrafiltration membranes employed in this study were tubular ceramic membranes with molecular weight cut-off (MWCO) varying from 1 to 150 kDa (Inside Ceram™ and Filtanium™ series, Tami Industries, Nyons, France). Each monochanneled porous membrane presented a membrane area of 0.011 m^2, made either of titanium dioxide (TiO_2) or zirconiuim dioxide (ZrO_2). According to measurements of electrophoretic mobility (Verhnet & Grangeon, 2003), which consist in recording the time needed for a suspended compound subjected to an electric field to cross the measuring cell, TiO_2 powder showed isoelectric points (IEP) at pH 3.2 ± 0.5 which is consistent with literature data (Zhang et al., 2008) and ZrO_2 powder had an IEP at pH 3 ± 0.1 which is quite below the values given in literature (6–7). This can be explained by the origin and the treatment of the metal oxides solutions which surely differ from one manufacturer to another. In the study of Verhnet and Grangeon (2003), the oxide powders have been thermally treated in the same way as for the membranes elaboration, before being crushed and sieved. Thus, theses values reflect the surface charge of the membranes with higher accuracy.

2.3. Experimental setup

The ultrafiltration experiments were performed on a filtration module composed of four carters in parallel configuration,

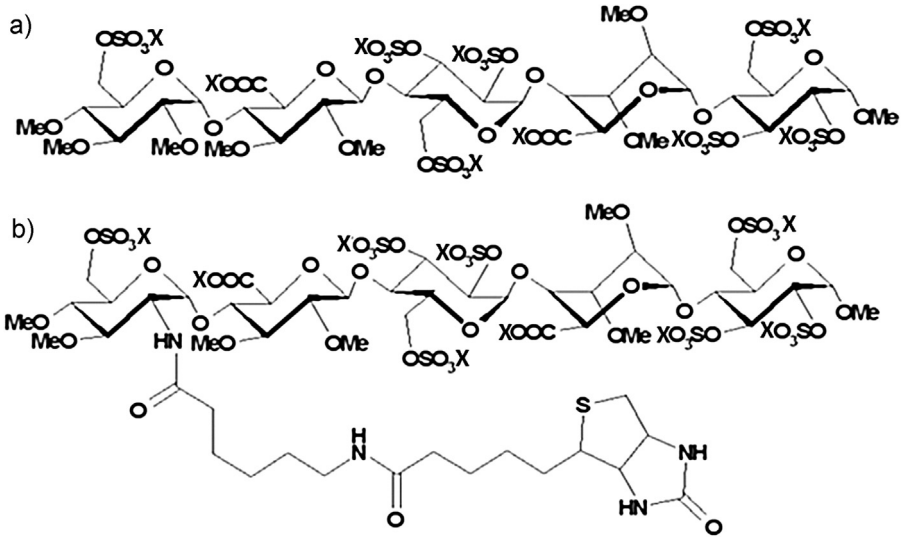

Fig. 1. Chemical structures of the test pentasaccharides (a) linear sulfated pentasaccharide: 1726 g mol^{-1}; (b) biotinylated sulfated pentasaccharide: 2046 g mol^{-1}; X = Na).