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Application of stimuli responsive polymers for sustainable ion exchange chromatography

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ABSTRACT

Ion exchange processes are widely used in the food, bioprocessing and related industries for the isolation of proteins and other ionic species. Traditional ion exchange resins require salts, acids or bases for releasing adsorbed molecules creating a strong saline waste stream with negative environmental and economic impact. Stimuli responsive polymers (SRPs) with ion exchange functional groups can be used to selectively capture and release charged molecules from a complex mixture using physical stimuli to trigger conformational transitions in the polymer. The structural change of the polymers in response to a stimulus may lead to reduced ligand–target molecule interaction resulting in the release of the captured molecule without the use of chemical reagents, thereby reducing the environmental burden associated with ion exchange processes. The use of temperature responsive polymers has already been demonstrated for such applications at analytical scale. However, little progress has been made to extend these discoveries to the development of materials and methods amenable to industrial scale processing. So far, other SRPs such as, electric, magnetic and light responsive polymers remain largely unexplored for such application. This article discusses the potential of temperature responsive and other SRPs for developing sustainable ion exchange processes. It also highlights the material science and engineering challenges that need to be overcome to bring such processes to industrial application.

Keywords: Stimuli responsive polymers; Stimuli responsive resins; Ion exchange chromatography; Temperature responsive polymers; Magnetoresponsive polymer composites; Electroresponsive polymers; pH responsive polymers; Ultrasound responsive polymers

1. Introduction

Ion exchange chromatography is widely used in the food and pharmaceutical industries to capture ionic molecules from complex solutions for the purposes of isolating such molecules as valuable products (e.g., isolation of a protein) or removing them to demineralise or purify the unbound stream (e.g., removal of minerals or impurities from water streams) (De Silva et al., 2003; Etzel, 2004; Houldsworth, 1980; Keogh et al., 2010). Although ion exchange chromatography has proven to be a very efficient industrial processing step for many applications in biomolecule purification and demineralisation, it has limitations such as low binding capacity of the ion-exchange resins, high costs associated with the resins and regeneration chemicals (acids or bases) (Chanda et al., 2010; Gorshkov and Ivanov, 1999; Tikhonov and Zagorodni, 1998), and creation and disposal of "secondary" waste streams (Gorshkov and Ivanov, 1999; Khamizov et al., 2010).

The economic and environmental impact of the technology has an important bearing on its sustainability in large scale industrial applications. In many instances, elution of molecules bound onto the sorbents is achieved with the use of salt solutions of increasing ionic strengths. After elution, purification of the eluate requires further processing such as desalting which uses energy and creates a salt effluent stream that needs disposal, requiring additional equipment

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and increasing cost of production. Similarly, regeneration of ion exchange sorbents used for demineralisation of liquid streams typically require the use of acids and bases, which results in the creation of salt effluent streams that require treatment and disposal, incurring additional costs (Chanda et al., 2010; Gorshkov and Ivanov, 1999; Maharjan et al., 2009, 2008). Due to the dilute nature of the effluent salt streams, recovery of the salts for recycling adds significant costs and in most situations recovery is uneconomical. As costs and environmental pressures mount, the sustainability of industrial ion exchange chromatography could be significantly improved if chemical reagent-free elution and regeneration technologies are developed. Therefore, developing more efficient and environmentally friendly, reagent-free “green” ion exchange technologies has been the focus of much research over the past two decades (Chanda et al., 2009, 2010; Gorshkov and Ivanov, 1999; Kobayashi et al., 2001, 2002, 2003; Maharjan et al., 2009; Müller et al., 2013; Muraviev et al., 1999; Tikhonov and Zagorodni, 1998). Stimuli responsive polymers offer an attractive route to achieving ion exchange processes that meet the green chemistry goals (Ayano et al., 2001) of the factories of the future.

Stimuli responsive polymers (SRPs) are polymers which reversibly alter their structure in response to a change in environmental conditions such as temperature, pH, presence of chemicals, electric, or magnetic fields. SRPs respond to small changes in their environment with major changes in their physical structure and properties such as individual chain dimensions, secondary structure, solubility or the degree of intermolecular association (Roy and Gupta, 2003). These may be manifested as dissolution/precipitation, degradation, change in hydration state, swelling/collapsing, hydrophilic/hydrophobic surface, conformational change, and micellization (Bajpai et al., 2011a). The fact that external stimuli can be applied to tune and modulate the structure of such polymers in an accurate and predictable manner makes them suitable for applications such as controlled drug delivery, bioseparation, biocatalysis, and the development of biosensors and microfluidic devices (Mendes, 2008). SRPs functionalised with ion exchange groups can be used to develop resins that selectively capture charged biomolecules (Ayano et al., 2001; Maharjan et al., 2009). The structural alteration of the polymers in response to a stimulus may lead to reduced ligand–biomolecule interaction resulting in the release of the captured biomolecule without the use of chemical reagents. Thus, the development of stimuli responsive ion exchange sorbents will have a significant positive impact on the sustainability of industrial ion exchange processes.

The objective of this article is to highlight the potential of SRPs for intelligent design of environmentally friendly ion exchange processes for the food and other bioprocessing industries. SRPs are briefly reviewed with focus on polymers that hold promise for bioseparation applications. Our aim is not to elaborate on the chemistry and synthesis of such polymers but to draw attention to their structural features and functionality. These discussions are followed by an evaluation of the current status of the knowledge on the application of SRPs for ion exchange chromatography, followed by suggested further research.

2. Stimuli responsive polymers (SRPs)

A variety of naturally occurring and synthetic stimuli responsive materials exist including temperature, pH, electric and magnetic field, light and chemical responsive materials. Multiresponsive materials that respond to two or more stimuli are also being continually identified and developed. On the basis of their physical forms, stimuli-responsive polymers may be classified as (i) linear free chains in solution which undergo reversible collapse in response to an environmental stimulus, (ii) covalently crosslinked gels where shrinking or swelling is triggered by a stimulus, and (iii) chain-adsorbed or surface-grafted forms where reversible collapse of the polymers occurs on the surface in response to a stimulus (Bajpai et al., 2011a; Kumar et al., 2007). Various geometrical and chemical architecture (supramolecular morphology) are designed depending on application and desired functionality such as nanoparticles (Yoshimatsu et al., 2012), hydrogels (Al-Manasir et al., 2009; Burba et al., 2008), self assembled monolayers (SAMs) (Lahann et al., 2003a; Mu et al., 2007) and grafted polymeric hydrogels and brushes (Ebara et al., 2006; Kumar et al., 2013; Mierczynska et al., 2012).

2.1. *Temperature responsive polymers*

The term temperature responsive polymers refer to polymers which exhibit sharp and discontinuous changes in solubility and other physical or mechanical properties either upon heating or cooling to a lower critical solution temperature (LCST) or an upper critical solution temperature (UCST) (Lee et al., 2010; Seuring and Agarwal, 2012). For obvious reasons, polymers which exhibit such changes in aqueous solutions are of particular interest in biological applications including separation. So far, most basic and applied research focused on polymers that exhibit LCST in water (Seuring and Agarwal, 2012). Such polymers are composed of hydrophobic and hydrophilic moieties and their temperature response arises from the temperature dependence of hydrogen bonding and hydrophobic interactions. At lower temperature, the water molecules surrounding the hydrophobic polymeric network are highly structured (hydrogen-bonded). Since that lowers the free energy of mixing, the polymer will be in the solution state. As the temperature increases, the hydrogen bonding becomes weaker while hydrophobic interaction increases. When the temperature reaches the LCST of the system, the polymer collapses and precipitates out of the solution (Al-Manasir et al., 2009; Bajpai et al., 2011a; Lopez-Perez et al., 2010; Maeda et al., 2000). This phase transition is fully reversible and the polymer returns to the solution state once the temperature is reduced below the LCST. The LCST of such polymers is dependent on the composition of the polymer as well as solvent properties such as pH, ionic strength and the type of ions present in the system (Al-Manasir et al., 2009; Boutris et al., 1997; Lopez-Perez et al., 2010; Mao et al., 2004; Saeed et al., 2010; Zhang et al., 2007). Examples of thermoresponsive polymers include poly(N-isopropylacrylamide) (PNIPAAm), Poly(N,N′-diethylacrylamide) (Barroso et al., 2012), poly(N-vinylcaprolactam) (Song et al., 2011) and oligo (ethylene glycol)-based co-polymers such as the co-polymer of 2-(2-methoxyethoxy) ethyl methacrylates (MEO_2MA) and oligo(ethylene glycol) methacrylates (P(MEO_2MA-*co*-OEGMA)) (Tan et al., 2009). PNIPAAm is by far the most known and investigated thermoresponsive polymer (Saeed et al., 2010; Seuring and Agarwal, 2012; Tan et al., 2012). It combines hydrophilic amide groups that are able to form hydrogen bonds with the hydration water and hydrophobic N-propyl group that force hydration water to assume a more organised structure (Lopez-Perez et al., 2010). The LCST of PNIPAAm in water occurs