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# Selective fractionation of sugar alcohols using ionic liquids

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ABSTRACT

Sugar alcohols, such as xylitol, sorbitol and inositols, are added-value carbohydrates with relevant bioactive and technological properties. These features make their extraction from natural sources of great interest both from the scientific and industrial points of view. However, due to the similarity of the chemical structures of the different carbohydrates and the complexity of the extracted mixtures, the subsequent isolation of these sugar alcohols from other coextracted low molecular weight carbohydrates (LMWC) is still considered a challenging task.

In this article, the solubility of linear sugar alcohols and inositols in selected ionic liquids (ILs), i.e., 1-hexyl-3-methylimidazolium chloride ([HMIM][Cl]), 1-ethyl-3-methylimidazolium dicyanamide ([EMIM][DCA]), 1-ethyl-3-methylimidazolium acetate ([EMIM][OAc]) and 1,3-dimethylimidazolium dimethylphosphate ([MMIM][$Me_2PO_4$]), has been investigated. The experimental results demonstrated widely divergent solubilities (in the 1.7–84.7%, w/w, range) for the several targeted carbohydrates in the different ILs evaluated, with [EMIM][OAc] and [MMIM][$Me_2PO_4$] providing the highest solubility values. These ILs gave also the best results when applied to the selective fractionation of sugar alcohols from other LMWC in 1:1 (w/w) binary mixtures (yields in the 60–98% range). These results show ILs as promising non-volatile and environmental friendly solvents for this type of fractionation process and suggest the interest of further investigation in this particular application field.

## 1. Introduction

Polyols, also called polyhydroxyalcohols or sugar alcohols, are those compounds obtained when either the aldo- or the keto- group of a sugar is reduced to the corresponding hydroxyl group [1]. These carbohydrates occur naturally in plants and can be divided into acyclic (or linear) and cyclic (such as inositols) polyols.

Acyclic sugar alcohols are carbohydrates commonly used as technological ingredients. One of their many applications is as sweeteners, due to their non-cariogenic properties and their lower contribution to raise the glucose levels in blood compared to sucrose [2,3]. The most frequently used acyclic sugar alcohols are mannitol, sorbitol and xylitol. Meanwhile, inositols are considered bioactive carbohydrates used in the treatment of polycystic ovary syndrome and of several affections related to insulin resistance [4,5].

All these added-value carbohydrates coexist in natural sources with other sugars (namely, mono- and disaccharides) which can interfere in their bioactive or technological properties. Several techniques, including solvent-, chromatographic- [6,7] and membrane-based approaches [8] as well as microbiological procedures [9], have been proposed for the selective isolation of these carbohydrates. However, their fractionation is not straightforward due to the complexity of the mixtures and the similarities among the different carbohydrate structures.

The use of volatile organic solvents for carbohydrate fractionation is widespread; differences in their solubility result in the selective precipitation of specific carbohydrates, which can then be easily separated from other components in the extraction mixture [10,11]. However, this type of methodology involves large volumes of volatile organic solvents making research on the development of novel fractionation approaches that contribute to improve the selectivity and efficiency of the process and/or to reduce the consumption of this kind of solvents of great interest for both researchers and industries [12]. In this context, the use of alternative solvents with improved capabilities, such as the ionic liquids (ILs), should be considered advantageous.

ILs are composed of organic cations, and organic or inorganic anions. These solvents exhibit tuneable physicochemical properties, low volatility and viscosity, and high thermal stability [13]. These properties make ILs to be considered promising environmentally friendly alternative solvents in many application fields. In this sense, an additional positive feature is their capacity to be recycled after extraction. This is particularly attractive from the food industry point of view

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where, up to now, ILs have been mainly used as solvents in the synthesis of ingredients or additives [14]. Although information regarding the possible toxicity of food products contaminated with residual ILs is still limited, initial studies in this field have pointed that low doses of some ILs were unable to produce significant toxicological adverse effects [14].

Up to now, ILs have been proved to be more efficient than other conventional organic solvents in dissolving cellulose and other polysaccharides [15–18]. Other studies have demonstrated ILs potential for the depolymerization of these compounds to obtain monosaccharides [19]. However, only a few studies have reported about the solubility of low molecular weight carbohydrates (LMWC) in ILs [16,20–23]. Regarding sugar alcohols, only few works studied the solubility of xylitol, mannitol and sorbitol [22,24–26] in several ILs. Nevertheless, to the best of our knowledge, no other data regarding the solubility of these added value carbohydrates, in particular with regards to cyclic polyols (inositols), in ILs can be found in the literature.

Concerning the use of ILs for the selective fractionation of carbohydrates, most of the reported applications focussed on polysaccharides. Lan et al. [27] used 1-butyl-3-methylimidazolium chloride to dissolve the lignocellulosic material from bagasse. Then, several organic solvents were used for the sequential fractionation of cellulose, hemicellulose and lignin from the mixture. In another application study, ILs were used to release monosaccharides from lignocellulosic wood material. In this case, wood samples were exposed to 1-ethyl-3-methylimidazolium chloride at temperatures in the 80–250 °C range for 0–24 h, depending on the experiment. The highest sugar amounts were obtained at 100 °C after 3–4 h of treatment [19]. Regarding the separation of low molecular weight carbohydrates (LMWC), Al Nashef et al. [28] proposed a method for the separation of fructose from glucose in binary mixtures based on their different solubility in 1,3-dimethylimidazolium dimethylphosphate and 1-ethyl-3-methylimidazolium ethylsulfate at room temperature. More recently, separation of bioactive ketoses from their corresponding aldoses (i.e., fructose/glucose, tagatose/galactose, lactulose/lactose) using ILs have also been investigated [29].

In this study, the solubility of several polyhydroxyalcohols (acyclic sugar alcohols and inositols) in imidazolium-based ILs was evaluated for the first time. Then, this information was used to design a new procedure for the fractionation of these polyols from other LMWC in binary mixtures using ILs.

## 2. Materials and methods

### 2.1. Chemicals and reagents

All chemicals and reagents used in this work were analytical or research grade. *myo*-Inositol, *chiro*-inositol, xylitol, mannitol, phenyl-β-D-glucoside, 1-ethyl-3-methylimidazolium dicyanamide ([EMIM][DCA]), 1-hexyl-3-methylimidazolium chloride ([HMIM][Cl]), 1-ethyl-3-methylimidazolium acetate ([EMIM][OAc]) and trimethylsilylimidazole (TMSI) were obtained from Sigma Chemical Co. (St. Louis, USA). 1,3-Dimethylimidazolium dimethyl phosphate ([MMIM][$Me_2PO_4$]) was from Alfa Aesar (Massachusetts, USA). Pinitol (3-O-methyl-D-*chiro*-inositol), quebrachitol (2-O-methyl-D-*chiro*-inositol) and galactinol (1-O-α-D-galactopyranosyl-L-*myo*-inositol) were from Carbosynth (Berkshire, UK). The chemical structures of the investigated polyols are shown in Table 1. Trimethylsilylimidazole (TMSI), used as derivatization reagent, tetracosane and phenyl-β-D-glucoside, used as internal standards, were acquired from Sigma Chemical Co. *n*-Heptane was purchased from Merck (Darmstadt, Germany).

### 2.2. Water content determination

Before performing the solubility assays, the water content of the evaluated ILs was determined using a C20 Compact Karl Fischer Coulometer (Mettler Toledo; Ohio, US). HYDRANAL®-Coulomat AG (Sigma Chemical Co.) was the reagent used for volumetric titration. The determined water contents for the tested ILs were below 2.04%.

### 2.3. Solubility of polyols in the evaluated ILs

#### 2.3.1. Solubility experiments

For solubility evaluation, each carbohydrate was individually dissolved in the corresponding IL, until a saturated solution was achieved. These mixtures were stirred during 24 h at 1350 rpm and left to stand for another 24 h. Then, an aliquot (10 μL) of the resulting mixture was collected from the upper layer, derivatized as described in Section 2.4 and analyzed by gas chromatography (GC). Solubility was evaluated at two temperatures, 25 and 45 °C, using a Thermomixer (Eppendorf, Hamburg, Germany). All solubility assays were made in triplicate.

#### 2.3.2. Solubility of binary mixtures of LMWC in ILs

Four 1:1 (w/w) binary mixtures containing different polyols and LMWC combinations were studied: fructose:*myo*-inositol (mixture 1), maltose:pinitol (mixture 2), maltose:mannitol (mixture 3) and glucose:mannitol (mixture 4). In each experiment, the corresponding mixture was dissolved in 100 mg of the specified IL with a slight excess (a 10% above the corresponding limit of solubility as experimentally determined in this study or reported in [23]). The resulting mixtures were stirred at 1350 rpm during 24 h at 25 °C and left to stand for another 24 h at this temperature, using a Thermomixer.

### 2.4. Derivatization procedure

Silylation of the tested carbohydrates dissolved in the corresponding IL was carried out as described elsewhere [30]. This procedure allowed direct derivatization of the carbohydrates in the ILs and avoided the use of pyridine. In brief, 10 μL aliquot of the upper liquid layer from the solubility experiments (Section 2.3) were mixed with 0.3 mg of phenyl-β-D-glucoside (used as internal standard) dissolved in the corresponding IL. Then, 100 μL of TMSI was added to the corresponding mixture and was sonicated for 1 h. Afterwards, 200 μL of ultrapure water were added to this mixture to finish the reaction. The derivatized carbohydrates were then recovered by liquid-liquid extraction (LLE) with 100 μL of *n*-heptane containing *n*-tetracosane (0.25 mg). Two more successive LLE with *n*-heptane were performed to ensure quantitative recovery of the derivatized analytes. Extracts were combined and analyzed by GC without any further treatment.

### 2.5. GC analysis

The instrumental determination of the derivatized carbohydrates was carried out by GC using an HP 7890A gas chromatograph equipped with a flame ionization detector (FID), both from Agilent Technologies (Palo Alto, CA, USA). Nitrogen was used as carrier gas (flow rate, 0.7 mL $min^{-1}$). A fused silica capillary column coated with 100% dimethylpolysiloxane (30 m × 0.25 mm i.d. × 0.25 μm *df*) was used (Zebron, Phenomenex, CA, USA). The oven temperature was programmed as follows: 180–250 °C (held for 3 min) at 10 °C $min^{-1}$, and then to 300 °C at 15 °C $min^{-1}$. The final temperature was held for 20 min. The injection port was at 300 °C and injections were performed in the split mode, with a split ratio 1:20. FID temperature was set at 320 °C. Chromatographic peaks were measured using an HPChem acquisition system (Agilent Technologies).

Quantitative analyses were performed in triplicate using the internal standard procedure. For this purpose, calibration curves of the derivatized carbohydrate were constructed in the 0.1–1 mg range. Response factors of these compounds relative to two internal standards (*n*-tetracosane and phenyl-β-D-glucoside) were determined.