Applied Surface Science 314 (2014) 301–307

Contents lists available at ScienceDirect

Applied Surface Science

journal homepage: www.elsevier.com/locate/apsusc

Straightforward approach to graft bioactive polysaccharides onto polyurethane surfaces using an ionic liquid

Sandra Bigot[a], Guy Louarn[b], Nasreddine Kébir[a,*], Fabrice Burel[a]

[a] Normandie Université, INSA de Rouen, CNRS UMR 6270 FR 3038, Avenue de l'université BP08, 76801 Saint-Etienne du Rouvray, France
[b] Institut des Matériaux Jean Rouxel (IMN), UMR 6502, CNRS-Université de Nantes, 2 rue de la Houssinière, BP 32229, 44322 Nantes, France

ARTICLE INFO

Article history:
Received 27 February 2014
Received in revised form 13 June 2014
Accepted 17 June 2014
Available online 9 July 2014

Keywords:
Polyurethane
Ionic liquid
Polysaccharides
Antibacterial
Grafting to
Surface treatment

ABSTRACT

Surface properties directly affect the performance of a material in a biological environment. In this study, the goal was to develop a simple procedure allowing the grafting of antibacterial polysaccharides onto biomedical grade polyurethanes (e.g. Tecothane®). Thus, a straightforward chemical pathway involving an isothiocyanate–alcohol reaction in an ionic liquid (IL) was developed. PU isothiocyanted surfaces (PU–NCS) were first prepared by reacting *p*-phenylene diisothiocyanate with the surface urethane groups. Then, unmodified bioactive seaweed polysaccharides were directly grafted onto the surface, in mild conditions. The selected IL, i.e. 1-ethyl-3-methyl imidazolium phosphate, was of particular interest since this liquid worked as solvent for *p*-phenylene diisothiocyanate and the polysaccharides and as catalyst for the grafting reactions. Successful grafting of the different polysaccharides was attested by changes in the surface functional groups, using X-ray photoelectron spectroscopy (XPS). Atomic force microscopy (AFM) showed that polysaccharide grafting, slightly increased the surface roughness from 1.9 to more than 7 nm. Contact angle with water decreased from 88° (for native PU) to around 75° after polysaccharide grafting, attesting a more hydrophilic surface. This procedure would be transposed to the grafting onto PU surfaces of any macromolecule of interest bearing hydroxyl, thiol or amine groups.

1. Introduction

Polyurethanes (PUs) are widely used in the biomedical field as artificial implantable material because of their excellent mechanical properties, relatively good biocompatibility and long-term biostability. However, bio-adhesion may occur on PU surfaces leading to infection and/or thrombogenesis. Chemical modification has been used as a method of choice to improve the surface characteristics of biomaterials without affecting the bulk properties. Thus, during the last decades, much research has been dedicated to develop various surface modification methods such as plasma treatment, photo-oxidization and wet chemical treatment [1–5].

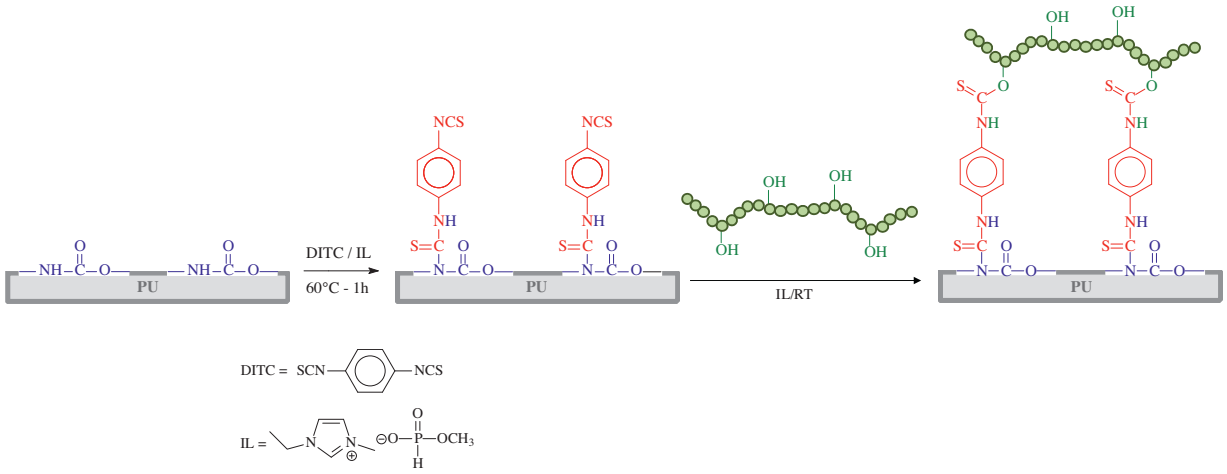
Polymer grafting in wet conditions has been found to be the most attractive, controlled and promising method. Thus, a number of bioactive polymers have actually been grafted onto the PU surface, such as poly(ethylene glycol) (PEG) [6–9], heparin [10–12], hyaluronic acid [13,14], chitosan derivatives [15,16], phospholipid derivatives [17], zwiterionic polymers [18–21], and poly(2-hydroxyethyl methacrylate) derivatives [22–26].

However, from a chemical point of view, the grafting procedures were either multi-steps or employing toxic molecules such as, isocyanate agents, tin catalyst or organic solvents. For instance, Archambault et al. [6,7] and Park et al. [8] have treated PU surfaces with diisocyanate molecules in presence of catalyst (stannous catalyst or triethylamine) and then, they have grafted amino- or hydroxyl-terminated PEG in toluene media. You et al. [9] used a same procedure, assisted by microwave irradiation. Numerous works have used also this procedure [18–20] to subsequently graft, from the chain-end of the immobilized PEG, other bioactive compounds such as lysine, carboxymethyl-chitosan and zwitterions. Jin et al. [23,24] have grafted poly(2-hydroxyethyl methacrylate) and poly(oligo(ethylene glycol) methacrylate) via surface-initiated ATRP in five steps starting by an oxygen plasma activation of the surface. Alferiev et al. [10] grafted heparin onto PU surface in four steps, i.e. bromoalkylation of the urethane nitrogen groups, grafting of 7-carboxy-5-thiaheptyl groups, grafting of polyallylamine and then grafting of heparin. Some authors have described another approach consisting to insert diamine or polyethyleneimine (PEI) on the PU surface to subsequently graft bioactive polymers such as heparin, PEG, dextran and hyaluronic acid [11,13,14].

In this work, we describe a straightforward and alternative chemical process to graft any polysaccharide onto PU surfaces. This

* Corresponding author. Tel.: +33 0232956576; fax: +33 0232956644.
E-mail address: nasreddine.kebir@insa-rouen.fr (N. Kébir).

http://dx.doi.org/10.1016/j.apsusc.2014.06.114
0169-4332/



Scheme 1. The chemical approach for grafting polysaccharides onto PU surfaces.

method can be applied to polyurethane materials of any shape, including tubes and scaffolds, for which physical treatments of the inner surface are difficult to achieve. Bioactive seaweed polysaccharides [27,28] were used as examples. The grafting reaction was conducted in 1-ethyl-3-methyl-imidazolium phosphate i.e. [C2mim][(MeO)(H)PO_2]. This ionic liquid (IL) was used as solvent and catalyst. In a first step isothiocyanate groups were created onto the PU surface. Then, unmodified polysaccharides were directly grafted onto the surface via thiocarbamate links resulting from the reaction of the surface isothiocyanate groups and the polysaccharide hydroxyl groups (Scheme 1).

2. Experimental

2.1. Materials

Tecothane® TPU (TT-1065D) was supplied by Lubrizol (thermedics polymer products), (Wilmington, USA). Seaweed polysaccharides were provided from the CEVA (www.ceva.fr), Pleubian, France. The chemical structures as well as the FTIR spectra of the selected seaweed polysaccharides are given in the supplementary data. One can observe mainly that all the polysaccharides exhibited a band of carbonyl between 1600 and 1700 cm^{-1}, arising from residual proteins and/or carboxylic groups in some polysaccharides (Ulv 815 and Zost 900).

Their characteristics are depicted in Table 1. These polysaccharides contain a small amount of nitrogen owing to the presence of residual proteins coming from their natural media. *p*-Phenylene diisothiocyanate (98%) was supplied by Aldrich (France). *N*-Ethylimidazole (≥95%) and dimethylphosphite (98%) were purchased from Sigma-Aldrich (France) and Alfa Aesar (France), respectively.

2.2. Synthesis of 1-ethylimidazolium phosphate ([C2mim][(MeO)(H)PO_2])

[C2mim][(MeO)(H)PO_2] was prepared as described in the literature [29]. Herein, 225 mL of tetrahydrofuran (THF), *N*-ethylimidazole (622 mmol) and dimethyl phosphite (622 mmol) were introduced dropwise in a round bottom flask, at room temperature, under nitrogen atmosphere. After stirring during 2 days at 90 °C, the medium segregates into two parts. The IL phase (lower phase) was separated from the THF phase (upper phase) and washed with diethyl ether. The obtained IL was dissolved in dichloromethane, filtered over neutral activated alumina and then dried under vacuum.

[C2mim][(MeO)(H)PO_2] characterization: ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 1.58 (t, 3*H*, J = 7.4 Hz, NCH_2CH_3), 3.44 (d, 3*H*, J = 11.8 Hz, $POCH_3$), 4.01 (s, 3*H*, NCH_3), 4.32 (q, 2*H*, J = 7.4 Hz, NCH_2CH_3), 6.96 (d, 1*H*, J = 5.41 Hz, PH), 7.32 (d, 2*H*, J = 11.4 Hz, NCHCHN), 10.40 (s, 1*H*, NCHN). ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm) 15.8, 36.7, 45.5, 50.7, 121.7, 123.6, 139.3.

2.3. Preparation of isothiocyanated PU surface (PU–NCS)

PU films (1 × 1 × 0.1 cm^3) were immersed in 2 mL of a solution of *p*-phenylene diisothiocyanate in [C2mim][(MeO)(H)PO_2] (2 mg/mL). After stirring 1 h at 60 °C, PU films were washed with the IL under sonication.

2.4. Grafting of polysaccharides onto PU–NCS surfaces

Each polysaccharide was dissolved in [C2mim][(MeO)(H)PO_2] (*C* = 2 mg/mL) under the conditions reported in Table 1. Then, PU–NCS sheets (1 × 1 × 0.1 cm^3) were immersed into these solutions at room temperature. After stirring for 24 h, the PU sheets

Table 1
Some characteristics of the used seaweed polysaccharides.

Polysaccharide	Seaweed	*Mw* (g/mol) *	S (%)**	N (%)**	Conditions of dissolution in IL (C = 1 mg/mL)
Laminarin 822	*L. saccharina* parmeat	6990	ND	ND	60 °C (15 min)
Ulvan 815	*U. rotundata*	620,300	3.14	1.2	80 °C (15 min)
Fucan 812	Fucus/Ascophyllum	438,600	ND	ND	80 °C (15 min)
Zosterin 900	Zosteraceae	340,200	ND	ND	95 °C (30 min under sonication)

* Data supplied by the CEVA: $\overline{M_w}$ values were determined by high performance size exclusion chromatography (HP-SEC) using pullulan calibration curve ranged from 5800 to 1600,000 g/mol.
** Data supplied by the CEVA: N (%) was determined by the Kjeldahl technique, S (%) was determined by an internal method (turbidimetry after mineralization).