Carbohydrate Polymers 136 (2016) 292–299

Contents lists available at ScienceDirect

Carbohydrate Polymers

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

Liquid-core nanocellulose-shell capsules with tunable oxygen permeability

A.J. Svagan[a,*], C. Bender Koch[b], M.S. Hedenqvist[f,**], F. Nilsson[f], G. Glasser[c], S. Baluschev[c,d], M.L. Andersen[e]

[a] University of Copenhagen, Dept. of Pharmacy, Universitetsparken 2, 2100 Copenhagen, Denmark
[b] University of Copenhagen, Dept. of Chemistry, Universitetsparken 5, 2100 Copenhagen, Denmark
[c] Max Planck Institute for Polymer Research, Ackermannweg 10, 55128 Mainz, Germany
[d] Freiburg Institute for Advanced Studies (FRIAS), Albert-Ludwigs-Universität Freiburg, Albertstraße 19, 79104 Freiburg, Germany
[e] University of Copenhagen, Dept. of Food Science, Rolighedsvej 30, 1958 Frederiksberg C, Denmark
[f] KTH Royal Institute of Technology, Dept. of Fibre and Polymer Technology, 100 44 Stockholm, Sweden

ARTICLE INFO

Article history:
Received 27 June 2015
Received in revised form
12 September 2015
Accepted 12 September 2015
Available online 15 September 2015

Keywords:
Liquid-core capsules
Nanofibrillated cellulose
Cellulose nanocrystals
Low oxygen permeability
Electron spin resonance
Oximetry

ABSTRACT

Encapsulation of oxygen sensitive components is important in several areas, including those in the food and pharmaceutical sectors, in order to improve shelf-life (oxidation resistance). Neat nanocellulose films demonstrate outstanding oxygen barrier properties, and thus nanocellulose-based capsules are interesting from the perspective of enhanced protection from oxygen. Herein, two types of nanocellulose-based capsules with liquid hexadecane cores were successfully prepared; a primary nanocellulose polyurea–urethane capsule (diameter: 1.66 μm) and a bigger aggregate capsule (diameter: 8.3 μm) containing several primary capsules in a nanocellulose matrix. To quantify oxygen permeation through the capsule walls, an oxygen-sensitive spin probe was dissolved within the liquid hexadecane core, allowing non-invasive measurements (spin-probe oximetry, electron spin resonance, ESR) of the oxygen concentration within the core. It was observed that the oxygen uptake rate was significantly reduced for both capsule types compared to a neat hexadecane solution containing the spin-probe, i.e. the slope of the non-steady state part of the ESR-curve was approximately one-third and one-ninth for the primary nanocellulose capsule and aggregated capsule, respectively, compared to that for the hexadecane sample. The transport of oxygen was modeled mathematically and by fitting to the experimental data, the oxygen diffusion coefficients of the capsule wall was determined. These values were, however, lower than expected and one plausible reason for this was that the ESR-technique underestimate the true oxygen uptake rate in the present systems at non-steady conditions, when the overall diffusion of oxygen was very slow.

1. Introduction

Encapsulation is a powerful tool to prolong the lifetime of sensitive molecules and achieve separation of reactive components from each other. For example, the oxidative stability of encapsulated molecules can be increased by hindering the access of oxygen which in turn significantly enhances the life time/shelf life of a formulation/product – a factor that is important in food, pharmaceutical and other technological research areas, e.g. organic optoelectronics (Andersen, Risbo, Andersen, & Skibsted, 2000; Svagan, Busko, et al., 2014). In addition, micro and nanoencapsulation offers the possibility of more efficient drug therapy *via* tailored drug delivery rates (lower dosing frequency), decreased drug toxicity and more convenient administration routes (e.g. oral route).

Cellulose nanofiber, also denoted nanofibrillated cellulose (NFC) or microfibrillated cellulose, is one of the most promising bio-derived, sustainable and abundant materials having excellent mechanical properties (140 GPa crystal modulus), oxygen barrier properties and low toxicity (Alexandrescu, Syverud, Gatti, & Chinga-Carrasco, 2013; Eichhorn et al., 2010; Plackett et al., 2010; Siro, Plackett, Hedenqvist, Ankerfors, & Lindstrom, 2011). NFC based films have oxygen barrier properties that are about two to three orders of magnitude better than the petrochemical synthetic polymer ethylene vinyl alcohol (at 0% RH and 23 °C)

* Corresponding author.
** Corresponding author.
E-mail addresses: svagan@kth.se (A.J. Svagan), mikaelhe@kth.se (M.S. Hedenqvist).

http://dx.doi.org/10.1016/j.carbpol.2015.09.040
0144-8617/

currently used in high oxygen barrier applications (Aulin, Gallstedt, & Lindstrom, 2010). The excellent oxygen barrier properties of NFC films are due to a combination of a high crystallinity, a network structure held together via strong inter and intra molecular hydrogen bonds, a lamellar nanofiber structure and a dense fiber-packing (Fukuzumi et al., 2011; Svagan, Samir, & Berglund, 2007). However, as for EVOH, the oxygen barrier properties are lowered at higher relative humidities (>50% RH). The motivation for using cellulose nanofiber/cellulose nanocrystals in capsule synthesis is that the physical properties, such as the mechanical properties and degree of crystallinity, could easily be directly transferred into the capsule shell properties. Also green chemistry pathways, using water as a medium, can be employed in the capsule synthesis.

The unique properties of NFC have recently stimulated research on novel NFC-based encapsulation technologies (Amin, Abadi, & Katas, 2014). Kolakovic, Laaksonen, Peltonen, Laukkanen, and Hirvonen (2012) manufactured spray-dried microparticles from cellulose nanofibers. They found that the encapsulated drugs were mainly present in an amorphous structure, which improves bioavailability. Furthermore, the particles demonstrated sustained drug release (limited drug diffusion) due to a tight fiber network. The slow release can also be attributed to the presence of chemical interaction between the loaded active molecule and the NFC (Valo et al., 2011). Recently, we developed a novel type of cellulose nanofiber/cellulose nanocrystal (NFC/CNC) based nanocomposite capsule containing a hexadecane liquid core (Svagan, Musyanovych, et al., 2014). The mechanical properties were enhanced significantly by the presence of NFC/CNC demonstrating the potential of fibrous reinforcement of the capsule walls. Such capsules could be used for various applications where liquid mobility is important.

In our previous study (Svagan, Musyanovych, et al., 2014) the focus was on demonstrating improved mechanical properties of the capsule wall when nanocellulose was present. However, that study included only one nanocellulose composition of the capsule wall. The aim herein is to synthesize nanocellulose based capsules with different amounts of nanocellulose in the shell and assess the oxygen permeability properties. But oxygen permeability data for capsules are experimentally harder to acquire compared to films. In this work we test a method based on electron spin resonance (ESR) spectroscopy: an oxygen sensitive spin probe is dissolved in the liquid core of the capsule and the permeation of oxygen is evaluated from its ESR spectrum. The liquid core is hexadecane and the hexadecane/spin-probe system serves as a model material for lipophilic compounds such as polyunsaturated oils. The oxygen permeation is mathematically modeled and by fitting the model to the experimental data, diffusion coefficients are derived and the results are discussed.

2. Materials and methods

2.1. Materials

Bleached sulfite pulp from spruce (never-dried pulp with 14 wt% hemicellulose and <1 wt% lignin) was used in the production of the nanocellulose. The pulp was kindly provided by Nordic Paper Seffle AB, Säffle, Sweden. Methyl 16-doxyl-stearate, isophorone diisocyanate, dibutyltin dilaurate, hexadecane, and the surfactant Span® 80 was purchased from Sigma Aldrich.

Preparation of nanocellulose. (1) *A blend of NFC/CNC*. A modified acid hydrolysis route, as described in detail in a previous study of our group (Svagan, Musyanovych, et al., 2014), was used to obtain a blend of short NFC (<1 μm) and CNC. The surface charge density of the NFC/CNC was 0.031 e nm^{-2} (0.02 mmol g^{-1}) obtained from conductometric titration. The nanocellulose was on average 370 ± 210 nm long and 6.7 ± 2.1 nm thick as assessed in AFM height measurements (Svagan, Musyanovych, et al., 2014). The CNC from spruce has a length of ~140 nm (Beck-Candanedo, Roman, & Gray, 2005) and NFC are longer fibrous entities (herein between 1 μm and 400 nm). A 0.5 wt% NFC/CNC suspension was prepared by diluting the stock suspension (1.71 wt%) and ultrasonicating at 70% amplitude for 120 s (Sonics Sonifier, 750 W, 1/2″ tip) with ice cooling. The ultrasonication step deflocculates the nanocellulose aggregates (Svagan, Musyanovych, et al., 2014).

2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO)-NFC. The TEMPO-NFC was prepared as described by Fukuzumi et al. (2011) with experimental details described in a previous study of our group (Svagan, Busko, et al., 2014). The resulting TEMPO-oxidized NFC suspension had a solid content of 0.90 wt%. The DP was 440, obtained from intrinsic viscosity measurements (Svagan, Jensen, Dvinskikh, Furo, & Berglund, 2010). The dimensions of the TEMPO-NFC were 3.0 ± 1.5 nm in diameter and 200–1000 nm in length (AFM height measurements).

Capsule preparation. The liquid-core capsules were prepared as described before (Svagan, Musyanovych, et al., 2014). Briefly, 0.72 g of a 1 mM spin-probe (methyl 16-doxyl-stearate) solution in hexadecane, 172 mg of isophorone diisocyante (IPDI) and 30 mg of dibutyltin dilaurate were mixed to form the oil phase. A water phase (6.2 g), consisting of a 0.5 wt% NFC/CNC suspension, was added to the oil phase and the two phases were mixed together by ultrasonication at 80% amplitude for 60 s with ice cooling, as depicted in Scheme 1. Before ESR measurements, the capsules were transferred to hexadecane by first mixing the capsule suspension with a 19 mM Span® 80 in hexadecane solution (volume ratio of 1:6 of capsule suspension:Span® 80 solution) and evaporating the water at 50 °C at reduced pressure (11 mbar). The resulting suspension was purified from surfactant by repeated centrifugation and replacing the supernatant with hexadecane (three times).

Larger capsules were prepared by mixing the above capsule suspension in water with a diluted and filtered TEMPO-NFC suspension (0.46 wt%, 5 μm filter) in a weight ratio of 1:20. A water-in-oil emulsion was prepared by passing the TEMPO-NFC/capsule suspension (2.2 mL) through a hydrophobic membrane (membrane pore-size: 10 μm, pressure: 7 kPa, SPG Technology Co, Japan). The continuous phase was a 19 mM Span 80 in hexadecane solution (13 mL). The water was evaporated at 55 °C at reduced pressure (11 mbar). The resulting capsule in hexadecane suspension was purified from surfactant by repeated centrifugation and replacing the supernatant with hexadecane (three times).

2.2. Methods

ESR spectra of capsules in hexadecane or a hexadecane/spin-probe solution were obtained using a Miniscope MS200 (Magnettech, Berlin, Germany) operating in the X-band mode and utilizing an automatic data acquisition program. Cylindrical quartz ESR tubes (height: 21 cm, outer diameter: 0.5 cm) were used in the experiments and the sample height (0.41 cm) was maintained constant. The head space of the ESR tubes was purged gently throughout the experiment with either oxygen (155 mL min^{-1}) or nitrogen (176 mL min^{-1}). By purging the headspace, and not bubbling the sample with gas, we avoided splashing of the sample onto the inner ESR tube walls. The gas composition in the headspace of the ESR tubes was measured using a headspace gas analyzer (CheckMate, PBI Dansensor, Denmark). The samples were initially flushed with nitrogen until a steady signal was measured and also stabilized at this low signal for a long time. Next 100% oxygen was introduced and after 2 minutes the nitrogen in the head space was completely replaced. Modulation amplitudes were in the range 0.57–1.1 G and were always chosen is such a way as to avoid any