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Adsorption of zwitterionic drugs on oxidized cellulose from aqueous solutions

Dmitry S. Zimnitsky *, Tatiana L. Yurkshtovich, Pavel M. Bychkovsky

Belarusian State University, Research Institute for Physical Chemical Problems, 14 Leningradskaya Street, Minsk 220050, Belarus

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Abstract

Adsorption of zwitterionic drugs (β-lactam antibiotics and amino acids) on samples of oxidized cellulose (OC) with various carboxyl contents and structure characteristics from aqueous solutions was investigated. It was established, that drug binding with OC occurs via proton transfer from carboxyl group of ion exchanger to the carboxylate ion of adsorbed zwitterion. The adsorption process can be described according to the theory of localized stoichiometric adsorption and represented by Langmuir-like isotherms. The constants of sorbate interfacial distribution with some exceptions increase with a growth of sorbate relative hydrophobicity. The drug uptake is shown to increase with an increase of carboxyl content in the OC phase. The degree of crystallinity of sorbent has no considerable effect on drug adsorption from aqueous solutions.

Keywords: Adsorption; Langmuir isotherm; β-Lactam antibiotics; Amino acids; Oxidized cellulose; Degree of crystallinity

1. Introduction

Substantial progress in wound treatment has been achieved recently [1]. However, the development of drugs for local wound treatment and for prevention of wound infections is still of special interest because such drugs should possess several important properties, first of all, they must have haemostatic, antibacterial and reparative activity [2]. The adsorption immobilization of several drugs on a biodegradable polymer carrier is one of the effective ways to prepare wound-healing drugs with combined effects. The principles of drug immobilization on biodegradable polymers and potential application of macromolecular prodrugs have been recently reviewed [3,4].

Oxidized cellulose (OC) containing carboxyl groups is a polymer carrier that has several useful medical characteristics [5]. It is one of the most widespread haemostatic used in almost all types of surgery. OC was shown to possess antitumor [6], immunostimulant [7], wound healing [8] and adhesion-prevention properties [9,10]. The presence of carboxyl groups in the OC permits the immobilization of drugs by adsorption and preparation of polymer drugs with a variety of therapeutic effects [11–14]. These properties, as well as complete bioabsorption [15], characterize OC as a medical material with very high potential.

The development of wound-healing drugs with combined effects on an OC base by means of

* Corresponding author. Tel./fax: +375 17 206 6229.
E-mail address: zimnitsky@tut.by (D.S. Zimnitsky).

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adsorption requires elucidation of nature and regularities of drugs adsorption on OC. Among antibacterial drugs we choose β-lactam antibiotics (cephalexin and ampicillin); among reparative drugs – α-amino acids (AA) – glycine, alanine, proline and tryptophane as a model substances. These substances have various molecule sizes and relative hydrophobicities; in neutral pH range they exist in zwitterionic form.

The aim of this study was to investigate the adsorption of zwitterionic drugs on the OC samples with various carboxyl contents and degrees of crystallinity from aqueous solution; elucidate nature, regularities of adsorption and factors influencing adsorption. The effect of drug structure and hydrophobicity on the adsorption was also of interest.

2. Experimental

2.1. Preparations

The OC samples were obtained by the oxidation of native and mercerized celluloses at 292 ± 1 K over various periods of time. Cellulose, in the form of coarse calico, was taken as a starting material. It has cellulose I structure modification and index of crystallinity (IC) 0.87, which was determined according to Segal [16]. Solutions with different concentrations (10–40%) of N_2O_4 in CCl_4 were used as oxidants. The ratio of cellulose mass to the solution volume was 1:10 (g/mL). The mercerized cellulose was obtained by treatment of cellulose with 20% solution of sodium hydroxide over a period of 3 h at 273 K [17]. The physical form and appearance of cellulose were unchanged after the oxidation procedure. The oxidation conditions and properties of the OC samples are given in Table 1.

2.2. Characterization of adsorbents

The OC samples were analyzed for exchange capacity (carboxyl content) with calcium acetate [18]. The swelling of OC was analyzed gravimetrically by centrifugation [19].

The surface areas S (m^2/g) of the OC samples were determined by nitrogen adsorption at 77 K on a NOVA 2200 device (Quantachrome Corp., USA). The samples were outgassed at 333 K and 1 MPa for 2 h. Because immobilization of AA occurs in water solution, an attempt was made to evaluate surface areas of OC samples swelled in water. The water replacement procedure was used [20]; that is, samples of OC were swelled in water and treated three times with acetone and hexane. After this, samples were dried in vacuo at 323 ± 2 K until they reached a constant weight.

Fourier transform infrared (FT–IR) spectra of samples were obtained as KBr pellets, with a Thermo Nicolet FT–IR Nexus spectrophotometer. The X-ray diffraction measurements were performed using Carl Zeiss diffractometer (Cu Kα, Ni-filter, HZGb-4A).

The acidic properties of OC samples were analyzed by potentiometric titration according to the modified Henderson–Hasselbalch equation [21]. Titration was performed by a separate weights procedure at 298 ± 0.5 K, in the presence of sodium hydrochloride as a background solution (ionic strength of 0.05 mol/L) and with sodium hydroxide as a titrant. The pH changes were measured with a potentiometer (HI 9321) that had a hydrogen function.

2.3. Adsorption procedure

The adsorption of AA from aqueous solutions was studied by a batch method at 298 ± 0.5 K over periods of time required for an achievement of adsorption equilibrium. The range of initial concentration was 5×10^{-4} to 0.05 mol/L and the ratio of sorbent mass to the solution volume was 1:200 (g/mL). The pH values of initial solutions corresponded to isoelectric point of AA and remained the same after the adsorption. The properties of sorbates are given in Table 2.

Table 1
Preparation conditions and characteristics of OC

Sample	Oxidation time (h)	Concentration of N_2O_4 in CCl_4 (%)	Exchange capacity (mmol/g)	IC	Swelling (g/g)	S (m^2/g)	pK_a
OC-1	5	40	1.8	–	0.52	12.5	3.97
OC-2	24	15	1.8	0.82	0.37	6.2	4.16
OC-3	24	40	3.8	–	0.58	14.8	3.80
OC-4[a]	24	10	1.8	0.75	0.42	8.4	4.06

[a] Prepared by the oxidation of mercerized cellulose.