The Mutual Effect of Absorption of Biologically Active Substances and Microstructure of Native Cellulose Matrix on the Properties of Resulting Compounds

N. E. Kotelnikova*[1], E. F. Panarin[1], R. Serimaa[2], T. Paakkari[2], G. Wegener[3], E. Windeisen[3]

[1]Institute of Macromolecular Compounds, Russian Academy of Sciences,
St. Petersburg, 199004 Russia
[2]Department of Physics, University of Helsinki, SF-00014 Helsinki, Finland
[3]Institute for Wood Research, University of Munich, 80797 Munich, Germany

Abstract: In order to obtain multicomponent polymer systems exhibiting biological activity microcrystalline cellulose was used as a matrix for biologically active compounds, such as dimethylbenzylalkylammonium chloride, poly-N-vinylpyrrolidone, copolymer of N-vinylpyrrolidone and crotonic acid, and complex of dimethylbenzylalkylammonium chloride with copolymer of N-vinylpyrrolidone and crotonic acid. Adsorption interaction of microcrystalline cellulose with these was studied under various conditions. Adsorption isotherms of compounds of polymer nature are of similar character and are described by the Freundlich equation. The isotherms of dimethylbenzylalkylammonium chloride are described by the Langmuir equation. Characteristics of the resulting compounds were obtained using XPS and IR Fourier spectroscopy, WAXS, and SEM. Chemical interaction between microcrystalline cellulose and dimethylbenzylalkylammonium chloride takes place. This interaction leads to a new labile morphological cellulose structure accessible to penetration, which is confirmed at a morphological level by SEM.

INTRODUCTION

The use of cellulose, a natural polymer, as a matrix for biologically active compounds (BAC) is widely known. A tremendous amount of literature dealing with the problem makes it possible to distinguish two main trends: 1) the development of biologically active cellulose materials by the synthesis of cellulose derivatives containing chemically bound antimicrobial compounds and 2) the preparation of cellulose adsorbates and BAC by their diffusion-adsorption interaction.

The second way is more preferable because diffusion of BAC bound to cellulose by labile bonds during adsorption interaction takes place by desorption mechanism more readily, thus ensuring a rapid therapeutic effect. In our case it was intended to use biomacromolecules of powdered microcrystalline cellulose (MCC) as carrier for drugs.

Antimicrobial drugs bound to MCC may be of practical interest. Among them is dimethylbenzylalkylammonium chloride (DMBAA), a salt of quaternary ammonium base (QAB). It is an organic ammonia derivative, which is a cationic surfactant and is applied for imparting antimicrobial properties to fibre materials including cellulose fibres. DMBAA is known to be highly toxic, which restricts the fields of its application. One of the methods for decreasing its toxicity is to modify it by natural and synthetic polymers including its complexation with polymers. Previously developed method of complexation of DMBAA with a water-soluble copolymer of N-vinylpyrrolidone and crotonic acid (VPCA) has led to the preparation of a medicine, CVPCAD, which exhibits biologically activity, decreases the toxicity of the surfactant, and prolongs its effect (Ref. 1).

 CCC 1022-1360/99/$ 17.50+.50/0

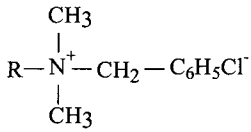
The main aim of the present investigation is to study separately adsorption interaction of MCC with each component of CVPCAD: DMBAA, poly-N-vinylpirrolidone (PVP), VPCA, and DMBAA-VPCA complex (i.e. CVPCAD itself) and a mutual effect of this interaction on the properties of resulting compounds.

EXPERIMENTAL PART

Materials and Methods

Microcrystalline cellulose (MCC) obtained from cotton cellulose has been described elsewhere (Ref. 2).

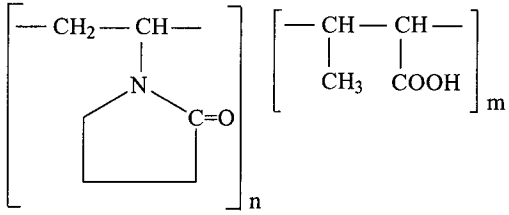
Dimethylbenzylalkylammonium chloride (DMBAA) was used as an aqueous solution the initial concentration of which was 52 wt.-%. DMBAA is a mixture of the individual homologous compounds of dimethylbenzylalkylammonium chloride with the following chemical structure:



where R – $C_{12\text{-}16}$ $H_{25\text{-}33}$

Poly-N-vinylpyrrolidone (PVP) was used in aqueous solutions the concentration of which (C_o) ranged from 0.09 to 0.90 mol/l. The PVP:MCC molar ratio ranged from 0.73 to 7.3. Samples of PVP with molecular mass (M) from $3.0 \cdot 10^3$ to $518 \cdot 10^3$ were studied (Ref. 3).

Copolymer of N-vinylpyrrolidone and crotonic acid (VPCA) has the following chemical structure (Ref. 4):



Polymer complex of DMBAA and VPCA, (CVPCAD) was used in the form of an aqueous-salt solution containing 10 wt% of the principal substance (NaCl concentration 2.8 wt.-%) (Ref. 1, 2).

Adsorption and desorption experiments of the above compounds on MCC were carried out as described elsewhere (Ref. 2).

X-ray photoelectron spectra (XPS) were taken on an electron PHI 5400 (Perkin-Elmer) spectrometer with excitation by Mg radiation. For these study samples of MCC and of modified MCC were used in the form of powders. Solutions of CVPCAD, PVP, and DMBAA before and after adsorption were applied in condensed gel form after vacuum drying on glass support at 40°C to constant weight. The chemical composition of the surface was determined from the overall spectra. The analysis of the chemical state of elements and the calculation of relative atomic concentrations were carried out from the spectra of individual photoelectronic lines with the aid of standard programs. The spectra were calibrated by the C 1s line of hydrocarbon impurities with $Å_{bond}$ = 285.0 eV (Ref. 4).

A Bruker JFS 88 IR Fourier spectrometer was used for spectroscopic study in the IR range (400-3600 cm^{-1}) of modified MCC samples as described elsewhere (Ref. 2).

The wide angle X-ray diffraction experiments were performed using powder diffraction apparatus and monochromatized CuK_α. The measurements were carried out in the scattering angle range $5^\circ < 2\theta < 40^\circ$ with an angle step of 0.25°. The samples in a form of flat cake of sickness of about 1 mm were prepared by slight moulding of powdered samples in a special press mould. The samples were rotated during the experiments in an evacuated chamber.
Electron microscopic study was performed with a scanning electron microscope (SEM) Leitz AMR 1200B.

RESULTS AND DISCUSSION

Fig. 1(A-D) show adsorption isotherms of PVP (A), VPCA (B), of CVPCAD (C) and DMBAA (D) solutions at 18 °C and 50 °C (adsorption time 120 min). The two-stage S-shaped isotherms in the adsorption of PVP and VPCA solutions over the entire M range shows that the adsorption mechanism is of the same character regardless of the M of the polymer. The isotherms for CVPCAD solutions have similar character. These stepwise isotherms belong to type IV and indicate that polymolecular adsorption takes place on the microcrystalline cellulose surface. Adsorption isotherms cannot be described by the Langmuir equation but are adequately described by the Freundlich equation. This equation is used for adsorption from solutions on non-homogeneous surfaces and takes into account the interaction between the adsorbed molecules: $A_s=K\cdot c^{1/n}$, where A_s is the quantity of the adsorbed compound in the surface layer of the adsorbent, c is the equilibrium solution concentration, and K and n are constants. The constant K represents the relative of a given adsorbent to sorb a given adsorbate, and n is the adsorbate affinity for a given adsorbent. Freundlich's equation is expressed logarithmically as $logA_s=logK + (1/n)logc$. Freundlich's constants are listed in the Table.

Table. Freundlich's constants 1/n and K for PVP, VPCA, and CVPCAD and Langmuir's constants K_1 and K_2 for DMBAA adsorption on MCC

Adsorbate	10^{-3} M g/mol	Adsorption temperature, °C	Adsorption constants			
			Freundlich's constants		Langmuir's constants	
			1/n	$K\cdot10^3$	K_1	K_2
PVP	3.0	18	1.62	1.77	-	-
		50	1.32	1.58	-	-
	518.0	18	0.79	3.55	-	-
		50	0.95	4.31	-	-
VPCA	19.0	18	1.85	2.04	-	-
		50	1.73	2.10	-	-
	33.0	18	1.10	4.87	-	-
		50	1.32	5.98	-	-
CVPCAD	-	18	1.95	8.5	-	-
	-	50	2.04	10.3	-	-
DMBAA	-	18	-	-	28.4	29.8
	-	50	-	-	62.5	75.4

Thus, the isotherms of compounds of polymer nature: PVP, VPCA, and CVPCAD, are of similar character. This means that the polymer component of CVPCAD, VPCA, is responsible for its adsorption character on the cellulose matrix. In contrast, the isotherms of DMBAA are quite different and are described by the Langmuir equation (Table). Therefore, one can conclude that the effect of these adsorbed substances on the properties of modified MCC samples will also be different.

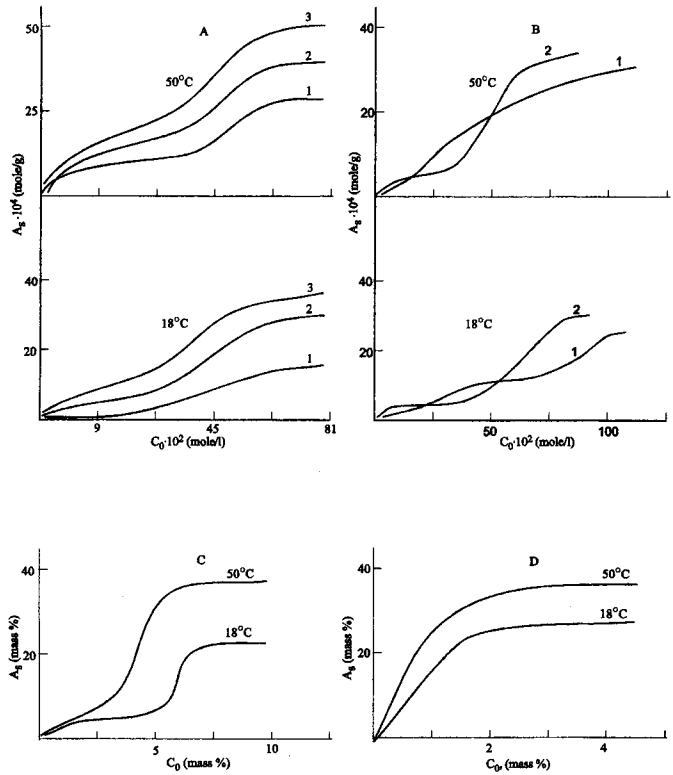


Fig.1. Adsorption isotherms of PVP (A) with 10^{-3} x M=3.0 g/mol (1), 53.9 g/mol (2), and 518.0 g/mol (3); VPCA (B) with 10^{-3} x M=19 g/mol (1), 33 g/mol (2); CVPCAD (C), and DMBAA (D)

Fig. 2 (1-5) show the IR spectra of MCC sample containing adsorbed CVPCAD (19.2 mass %) (1), CVPCAD (2), VPCA (3), DMBAA (4), and that of DMBAA solution after desorption in water at pH 6 of the MCC sample containing 4.1 mass % of DMBAA (release of DMBAA 58.1 %) (5). The spectrum of MCC containing adsorbed CVPCAD (1) exhibits an absorption band at 1650-1674 cm^{-1} but this band is markedly displaced (to 1670 cm^{-1}) compared to the spectra of VPCA and CVPCAD (1680 cm^{-1}) This band is attributed to the stretching vibrations of the –C=O groups of the lactam ring. The shift is due to hydrogen bonding between these groups in vinylpyrrolidone chain and the OH groups on the MCC surface. An interesting feature of the spectrum 5 is the fact that it contains groups of absorption bands at 1000-1200 cm^{-} which can be assigned to the stretching vibrations of C-O and C-O-C groups in the glucopyranose ring. This result appears to indicate that DMBAA reacts with MCC and can partially dissolve it, as it is confirmed by the literature data (Ref. 5).

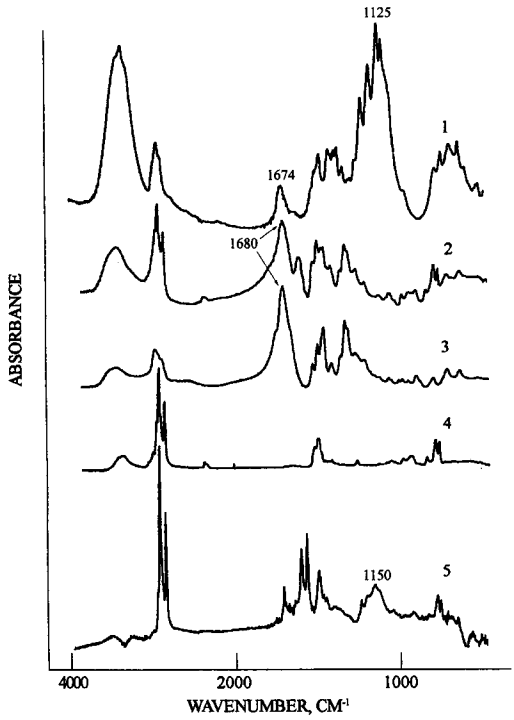


Fig.2. IR spectra of the MCC sample containing adsorbed CVPCAD (19.2 mass %), CVPCAD (2), VPCA (3), DMBAA (4), and DMBAA solution after desorption (release of DMBAA 58.1 %)

XPS spectra (Fig. 3, A and B) of the carbon (C) 1s line (A) of adsorbate complexes of MCC containing PVP (15.4 mass%) (2) and DMBAA (4.1 mass%) (3) compared to the spectrum of initial untreated MCC (1) show that in all cases adsorption takes place on the MCC surface without any change in the electronic configuration of carbon atoms. This is indicated by the splitting of C 1s line into individual photoelectronic lines (dotted line). Similar conclusion can be drawn on the basis of the XPS spectra of the nitrogen (N) 1s line (B). It is seen that the spectra of CVPCAD (1) and DMBAA (2) contain nitrogen in two valence states: quaternary and ternary. The latter possibly is the admixture of ternary amine obtained during the preparation of DMBAA. In the samples of adsorbates of these compounds on MCC nitrogen is in the same two states. Taking as an example adsorbate of MCC and DMBAA (3), it can be seen in contrast that after DMBAA desorption from the adsorbate, changes in the electronic state of carbon and nitrogen atoms in the MCC sample containing 1.7 mass % of DMBAA occur.

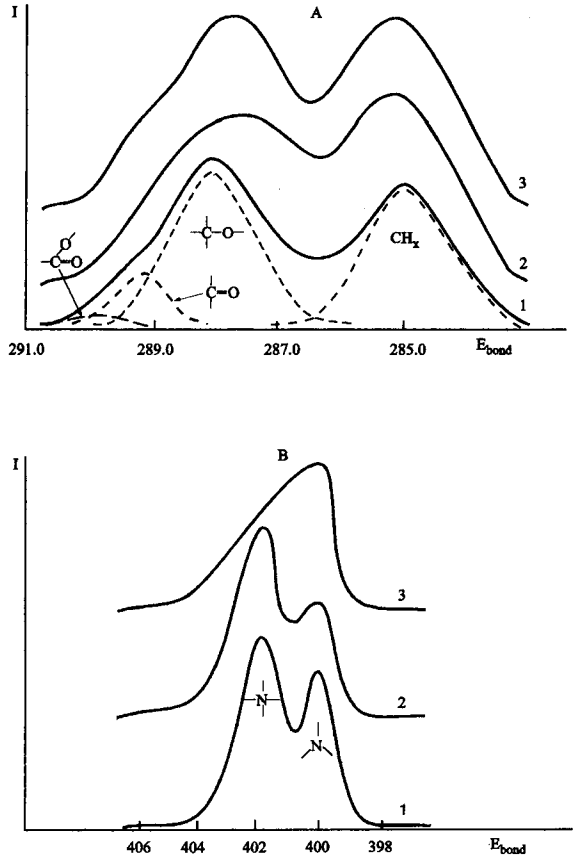


Fig.3. XPS spectra of C line 1s (A) of MCC (1) and adsorbates of MCC and PVP (2) and MCC and DMBAA (3); XPS spectra of N line 1s (B) of CVPCAD (1), DMBAA (2) and adsorbate of MCC and DMBAA (3)

This indicates that nitrogen is chemically bound in the ternary valence state and some of alkyl groups belonging to DMBAA are also bound. Hence, the XPS method shows that DMBAA and MCC chemically interact on the surface forming the adsorption complex on the MCC surface. Consequently, as a result of treatment with DMBAA, OH...N bonds (as energetically more preferable than OH…N bonds) are formed on the MCC surface. Namely, the OH groups of MCC react with the quaternary nitrogen atom of DMBAA, which leads to the formation of the OH...N bond. Some of the short alkyl groups belonging to DMBAA are also adsorbed on MCC.

The chemical interaction of DMBAA with MCC occurring not only on the surface but also in bulk, must lead to changes in the X-ray structure of modified MCC samples. Fig. 4 (1-5) show X-ray diffraction patterns of initial MCC (1) and of MCC samples containing CVPCAD (19.2 mass%) (2), VPCA (23.2 mass%) (3), and DMBAA (4.1 mass%) (4).

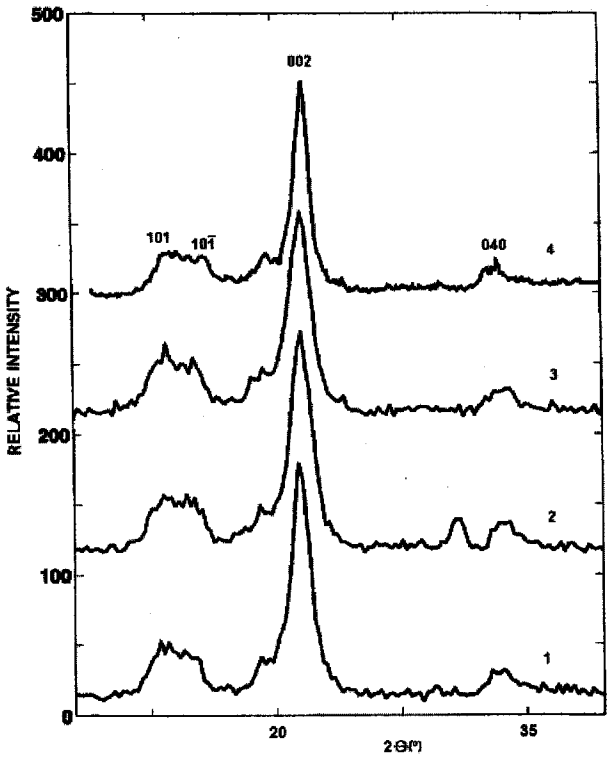


Fig.4. The diffraction patterns of MCC (1), adsorbate of MCC and CVPCAD (CVPCAD content 19.2 mass %) (2), adsorbate of MCC and VPCA (MM of VPCA=19.0·10^3, VPCA content 23.2. mass %) (3), adsorbate of MCC and DMBAA (DMBAA content 4.1 mass %) (4)

The WAXS intensity curve of sample (3) is similar to this of pure MCC (cellulose crystalline modification I). The sample (2) exhibits an additional reflection at 2θ=32°, which can be attributed to crystalline NaCl belonging to CVPCAD. In spite of the fact that all patterns resemble patterns of cellulose modification I, there are differences in reflection intensities in the case of pattern 4: MCC reflections 101, 10$\bar{1}$, 002, and 040 are smaller than those in pure MCC. These changes indicate that crystallites of MCC are partially destroyed after DMBAA adsorption. It is also possible that they are rearranged from cube-like to sheet-like form.

Obtained results were confirmed by the SEM method at a morphological level (Fig. 5). It is seen that the structure of initial MCC fibre (top) greatly changes under DMBAA adsorption (bottom). MCC is partially dissolved and a new morphological design of the fibre with a porous and loose structure is formed. Porosity favour the penetration of reagents inside the cellulose fibre. Therefore, the interaction between the MCC porous structure already formed and the polymer component of CVPCAD, VPCA, takes place. As a result, a multicomponent polymer complex is readily adsorbed on MCC yielding adsorbates with polymer complex content up to 0.2 mol/mol of MCC. This conclusion also explains the adsorption isotherms for PVP, VPCA and CVPCAD appear similar.

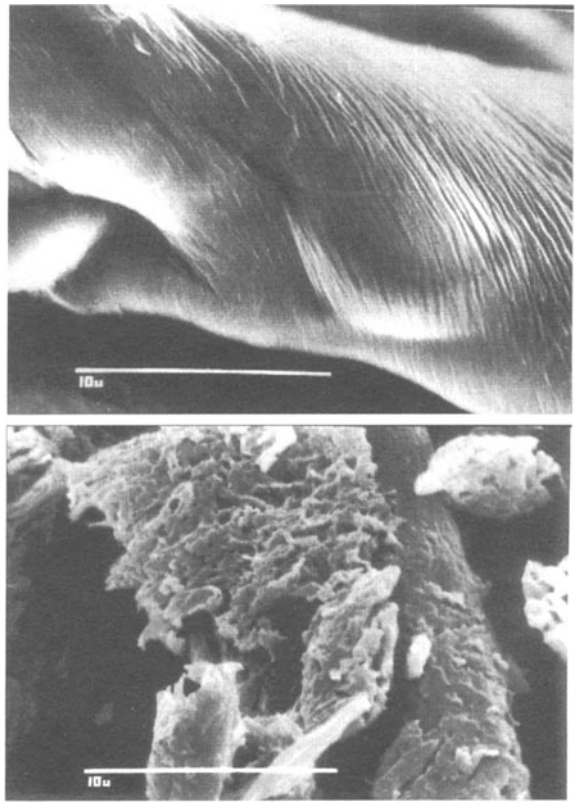


Fig.5. SEM micrographs of the fibres of initial MCC (top) and the MCC sample containing 1.7 mass % of DMBAA after DMBAA desorption (bottom)

Consequently, the mutual effect of BAC adsorption and microstructure of MCC matrix leads to preparing of resulting compounds. They are compatible labile complexes the structure of which depends on the chemical structure of the compounds adsorbed.

ACKNOWLEDGEMENT

This investigation was supported by the joint grant of the Foundation for Basic Research of Russia and of the State Foundation for Natural Sciences of People's Republic of China.

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APPENDIX

Glossary of abbreviations

BAC- biologically active compounds

CVPCAD - polymer complex of dimethylbenzylalkylammonium chloride and copolymer of N-vinylpyrrolidone and crotonic acid

DMBAA - dimethylbenzylalkylammonium chloride

MCC - microcrystalline cellulose

PVP - poly-N-vinylpyrrolidone

QAB - quaternary ammonium base

VPCA - copolymer of N-vinylpyrrolidone and crotonic acid