Chemistry of Natural Compounds, Vol. 35, No. 5, 1999

REACTION OF LIGNOSULFONATE WITH THE ANTIHELMINTIC PREPARATION MEDAMINE

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UDC. 547.99

Grafting known medicines (MD) to appropriate macromolecular supports is one way of optimizing their effectiveness. Thus, in several instances the effectiveness of MD has been prolonged, the toxicity lowered, the activity elevated, the solubility changed, etc. [1, 2]. Certain requirements apply to the use of polymeric supports. These include nontoxicity of the macromolecule and its metabolites and the ability to be eliminated from the organism after a certain time interval. From this viewpoint, lignin might be a completely suitable macromolecule. Hydrolyzed lignin (Polyphepanum) is currently used in medicine as a means for eliminating toxins from an organism [3].

The polymer-support used in the present work is lignosulfonate (LS). This lignin derivative was chosen primarily because of its good solubility in water. Furthermore, LS contains reactive sulfonate groups in addition to carboxylates. The medamine molecule contains N atoms and exhibits basic properties [3]. Therefore, ionic bonds can form between the reagents in the lignosulfonate—medamine system. Potentiometric titration was used to study the formation of ionic bonds between the positively charged $-NH^+$ ions of protonated medamine and the acidic groups of lignosulfonate.

Figure 1 shows the titration curves of LS by medamine at various reagent ratios. It can be seen that the titration curve shifts to the acidic region in the presence of LS. This is consistent with a shift of the acid—base equilibrium and the formation of ionic bonds. The results also indicate that LS complexes with medamine are present in weakly acidic, neutral, and strongly basic media.

The solubility of free medamine and that complexed with LS changes as a function of pH. Thus, free medamine dissolves at pH $\leq$ 3.5 whereas complexed medamine is soluble at pH $\leq$ 7.6 (the complex with LS:medamine = 25:1), i.e., the medicinal compound becomes soluble at neutral pH values. Naturally this helps to increase its effectiveness. Thus, the pH of the medium is one of the factors that affects the course of the complexation reaction of medamine with LS.

Hydrogen bonds (medamine)NH...OH(LS) are apparently formed according to the decrease in the frequency of the absorption band observed in the spectrum of the LS:medamine complex for OH and NH (3300 cm^{-1}) vibrations relative to the νNH and νOH observed in the spectra of medamine and LS. A shift of the absorption maximum at 1700 cm^{-1} of carboxylates to a frequency 10 cm^{-1} lower compared with that in the spectrum of LS can be explained by an electrostatic interaction (medamine)NH^+-OC(LS). Therefore, both electrostatic and H-bonds are involved in the reaction of medamine with LS.

Medamine is a low-molecular-weight compound. Therefore, LS binding can be represented as the grafting of medamine to the LS macromolecule. Two scenarios are possible: 1) Medamine binds functional groups within one LS macromolecule. 2) Medamine is situated between two different LS macromolecules. Viscometry was used to clarify this question. The data indicate that the characteristic viscosity is practically constant during complexation at $0.35 \cdot 10^{-2}$ dl/g. This suggests that medamine under the experimental conditions ([LS] = 10^{-2} M) is obviously situated within (on) one LS macromolecule.

The molecular masses of the starting LS and that complexed with medamine were determined by ultracentrifugation. These were 44,150 and 47,700, respectively (the complex produced with LS:medamine = 25:1). The data are consistent with the viscosimetry results because the molecular mass of the complex otherwise should have increased by at least two times, which is not observed.

Thus, the medicinal compound medamine is capable of forming complexes with LS in aqueous media through ionic and H-bonds over a wide pH range. The solubility of the preparation increases with pH up to neutral values.

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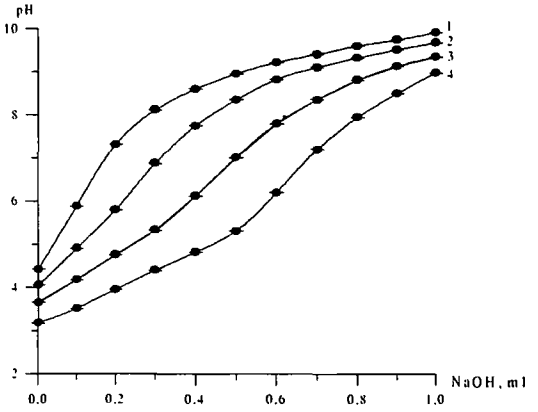

Fig. 1. Potentiometric titration curves: LS, 0.5 M (1); LS:medamine = 50:1 (2); 25:1 (3), 16.6:1, NaOH 0.1 N (4).

Potentiometric titration was performed using a pH-340 potentiometer with a glass reference electrode and an AgCl working electrode. The accuracy of the measurements is 0.05 pH units.

The IR spectra were recorded on a Perkin—Elmer Specord UR-75 system 2000 IR-Fourier spectrometer in KBr pellets.

The solution viscosities were measured using an Ubellohde viscometer at 20°C.

The authors thank T. Sadykov for supplying medamine.

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