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COMPLEX DERIVATIVES OF GOSSYPOL WITH N-POLYVINYLPYRROLIDONE

L. Biktimirov, Kh. L. Ziyaev, B. Khodzhaniyazov,
D. Ziyamov, N. I. Baram, and A. I. Ismailov

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The results are given of a comparative spectroscopic study of some gossypol derivatives and their complexes with N-polyvinylpyrrolidone,

A number of preparations based on certain gossypol (GP) derivatives have been developed and introduced into public health practice. A disadvantage of GP itself and preparations based on it is their complete insolubility in water, which prevents their use in the form of injections. At the same time, methods are known for imparting to insoluble substances a capacity for dissolving in water by modifying them with the aid of natural biopolymers amd synthetic polymers [1-6].

We have obtained complexes of N-polyvinylpyrrolidone (PVP) with GP and GP derivatives — 1,1′,6,6′,7,7′-hexahydroxy-5,5′-diisopropyl-3,3′-dimethyl-2,2′-dinaphthylidene-8,8′-dibarbituric acid (compound (**1**)) and the disodium salt of 1,1′,6,6′-tetrahydroxy-5,5′-diisopropyl-3,3′-dimethyl-7,7′-dioxo-7,7′,8,8′-tetrahydro-2,2′-binaphthyl-8,8′-bis(methyleneaminoethanesulfonic acid) (compound (**2**)).

On the interaction of PVP with GP and its derivatives there is, apparently, an inclusion of the molecularly dispersed substance in the molecule of the polymer matrix through the formation of hydrogen bonds and coordination bonds between the functional groups of the reagents. As an indirect confirmation of this we may take the shifts in the main absorption maxima in the UV spectra of the complexes with PVP as compared with those of the initial substances (Table 1). A comparative spectroscopic study has been made of GP and compounds (**1**) and (**2**) and of their complexes with PVP.

Absorption bands of stretching vibrations in the 3530 and 3440 cm^{-1} regions in the IR spectrum of GP showed the presence of dimers formed through OH··OH bonds, and an inflection on the low-frequency slope at 3330 cm^{-1} indicated the presence of polymeric structures involving these hydrogen bonds [7].

In the spectrum of PVP there is a broad absorption band at 3350 cm^{-1} with an inflection at 3220 cm^{-1} arising through the vibrations of a hydrate bond.

In the spectrum of the complex of GP with PVP an absorption band was observed at a frequency 3220 cm^{-1} that was more pronounced than the same band in the spectrum of PVP itself, while the band of the carbonyl group had not shifted. This permits the assumption that part of the hygroscopic water usually present in PVP was more strongly bound with the GP.

In the IR spectrum of compound (**1**), in addition to the absorption bands belonging the gossypol part of the molecule, a band was observed at 3170 cm^{-1} the appearance of which may be explained by the formation of NH···NH hydrogen bonds. The stretching vibrations of carbonyl groups and the deformation vibrations of the NH-CO group of compound (**1**) were responsible for the appearance of absorption bands at 1675 and 1530 cm^{-1}.

In the IR spectrum of the complex of compound (**1**) with PVP an absorption band at 3330 cm^{-1} and a well pronounced inflection at 3220 cm^{-1}, as compared with the corresponding inflection in the IR spectrum of PVP itself, also indicated a stronger binding of the water molecules in the complex than in PVP. The absorption band of the carbonyl groups of PVP in the complex had shifted by 5 cm^{-1} in the low-frequency direction as compared with corresponding band in the spectrum of PVP. It is obvious that some of the water molecules in PVP were bound with the molecules of compound (**1**); i.e., hydrogen bonds were formed not only through OH groups, as in the case of GP, but also with the NH groups of the reagent.

A. S. Sadykov Institute of Bioorganic Chemistry, Academy of Sciences of the Republic of Uzbekistan, Tashkent, fax (3712) 62 70 71. Translated from Khimiya Prirodnykh Soedinenii, No. 2, pp. 198-201, March-April, 1996. Original article submitted November 7, 1994.

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TABLE 1. Some Characteristics of Complexes of Gossypol and Gossypol Derivatives with N-Polyvinylpyrrolidone

Parameter	Compound					
	gossypol	gossypol + PVP	**1**	**1** + PVP	**2**	**2** + PVP
mp, °C	178–182	168–170	350	270–275	350	185–187
*R_f	0.35–0.40 (syst. 1)	0.45 (syst. 2)	0.80–0.82 (syst. 2)	0.80–0.85 (syst. 2)	0.35 (syst. 3)	0.40 (syst. 3)
UV spectrum λ_{max}, nm	–	–	496 (DMSO–ethanol (1:9))	320, 480 (DMSO–ethanol (1:9))	385, 404 (acetone–water (1:3))	385 (acetone–water (1:3))
		380 (water)		250, 500 (water)		375 (water)

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*System 1) acetone–benzene–CH_3COOH (9.0:1.0:0.6); system 2) acetone; system 3) acetone–toluene (5.0:2.0)

In the IR spectrum of compound (**2**), in the group of absorption bands arising as the result of stretching vibrations of hydroxy groups we observed a redistribution of intensities in favor of the low-frequency absorption band, as compared with the corresponding group of bands in the spectrum of gossypol. This can apparently be explained by the formation of dimeric and polymeric structures through the hydrogen bonds of hydroxy groups, intensified as a result of the interaction of the S=O groups of compound (**2**). Together with the absorption bands relating to the gossypol part of the molecule, the IR spectrum of compound (**2**) showed absorption bands at 1240 and 1030 cm^{-1} arising from the stretching vibrations of the O=S=O groups.

In the IR spectrum of the complex of compound (**2**) with PVP there was an absorption band at 3330 cm^{-1}, while an inflection at 3220 cm^{-1} more pronounced than the same inflection in the spectrum of PVP itself indicated a stronger binding of the water molecules in the complex. A low-frequency shift of the absorption band of the carbonyl group in the spectrum of this complex by approximately 10 cm^{-1} and a considerably more pronounced peak of the low-frequency slope at 3220 cm^{-1} (in comparison with the corresponding band in the spectrum of PVP), and also changes in the frequencies below 1100 cm^{-1}, not observed in the IR spectrum of the complex of compound (**1**) with PVP, permitted the assumption that in the interaction of PVP with compound (**2**) a stronger complex was formed than in the case of compound (**1**).

On taking what has been said above into account, it may be concluded that in compounds (**1**) and (**2**) the gossypol molecules are present in dimeric and polymeric forms. On the interaction of these compounds with PVP, complexes are obtained the appearance of which becomes possible thanks to the formation of hydrogen bonds by the OH and NH groups and through an intensification of van der Waals interactions of the polar groups of PVP with SO_2O^- groups. A considerable role in the formation of complexes of GP and its derivatives with PVP belongs to the water present in PVP.

EXPERIMENTAL

TLC was conducted on Silufol UV-254 plates. UV spectra were taken on a SF-26 spectrophotometer; in the cases of GP and compounds (**1**) and (**2**), c = 0.002%, and in the case of their complexes with PVP, c = 0.01%. IR spectra were taken on a Specord IR-71 spectrophotometer in paraffin oil mulls.

1,1′,6,6′,7,7′-Hexahydroxy-5,5′-diisopropyl-3,3′-dimethyl-2,2′-dinaphthylidene-8,8′-dibarbituric acid (compound (1)). An alcoholic solution of 3.28 g (0.02 mole) of barbituric acid was added to a solution of 5.18 g (0.01 mole) of GP in 80 ml of ethyl alcohol heated to 70-80°C, and the mixture was heated for another 2 h. The precipitate that deposited after cooling was filtered off, washed with ethyl alcohol and diethyl ether, and dried. Yield 5.92 g (80.2%). Red pulverulent substance. Found%: N 7.60. $C_{38}H_{34}N_4O_2$. Calculation %: N 7.58.

Disodium Salt of 1,1′,6,6′-Tetrahydroxy-5,5′-diisopropyl-3,3′-dimethyl-7,7′-dioxo-7,7′,8,8′-tetrahydro-2,2′-binaphthyl-8,8′-bis(methyleneaminoethanesulfonic acid) (compound (2)). To a solution of 15.0 g (0.37 mole) of caustic soda in 375 ml of abs. ethyl alcohol was added 47.2 g (0.31 mole) of β-aminoethanesulfonic acid, and the mixture was heated in the water bath for 3 h. The resulting solution was treated with a solution of 65.0 g (0.12 mole) of GP in 350 ml of ethyl alcohol, and the reaction mixture was heated in the water bath for 3 h. The precipitate that deposited was filtered off, washed with ethyl alcohol, and dried. Yield 100 g (95.8%). Yellow amorphous powder. Found %: N 3.75. $C_{34}H_{38}N_2O_{12}Na_2S_2$. Calculation %: N 3.46.

The complexes of gossypol and of compounds (**1**) and (**2**) with PVP were obtained as in [8]. The compounds obtained were bright red pulverulent substances readily soluble in water and organic solvents (see Table 1).

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