Interactions of purine derivatives with 1-naphthol and 1,5-naphthalenediol in aqueous solutions

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The equilibrium constants of complexes of 7 purine derivatives with 1,5-naphthalenediol and of 5 purine derivatives with 1-naphthol were established in aqueous solutions at 20°C by using electron absorption spectrometry. The study of interactions has shown that the equilibrium constants of the complexes of the studied purines with 1,5-naphthol are generally higher than those of the complexes with 1-naphthalene and that the presence of further methyl and oxo groups, respectively, in the purine molecule results in significant increase of equilibrium constants of the formed complexes.

Были определены равновесные константы комплексов 7 производных пурина с 1,5-нафталендиолом и 5 производных пурина с 1-нафтолом в водных растворах при 20°C методом электронной абсорбционной спектрометрии. Изучение взаимодействий показало, что константы равновесий комплексов, изучаемых пуринов с 1,5-нафтолом, в общем случае выше, чем константы равновесий комплексов с 1-нафталеном и что присутствие добавочных метильных и оксо групп в молекуле пурина приводит к значительному увеличению равновесных констант образованных комплексов.

Purine bases form complexes with a number of compounds [1—4]. The formation of complexes is explained by stacking interactions, interactions based on charge transfer or formation of hydrogen bondings.

Interactions of purine bases with polycyclic aromatic hydrocarbons in aqueous solutions are reflected in increased solubility of aromatic hydrocarbons [4—6]. On the basis of solubility properties of purine bases and study of bond energies, the formation of complexes with aromatic hydrocarbons is attributed to dispersive power and interactions of the "charge transfer" type [7, 8].

With majority of purine derivatives, self-association was observed at higher concentrations in aqueous solutions [9—11]. The predominant driving forces responsible for this association are the vertical-stacking interactions of bases [11]. Authors of several works have demonstrated that the extent of associations of

purine and pyrimidine derivatives is directly related to polarizability of bases [12, 13]. The association constants of dimers of these bases are relatively low in aqueous solutions [9, 10, 14].

In our work we studied the interactions of chosen purine bases, *i.e.* purine, caffeine, 8-methylcaffeine, theophyline, its 7-(2-hydroxyethyl) and 7-(2,3-dihydroxypropyl) derivatives, and tetramethyluric acid with 1-naphthol and 1,5-naphthalenediol, respectively, in aqueous solutions.

Experimental

1-Naphthol (1-N) and 1,5-naphthalenediol (1,5-ND; Lachema, Brno), caffeine and 8-methylcaffeine (8-MC; Health Supply), theophyline (Gane's Chemical Works), 7-(2-hydroxyethyl)theophyline (HET; Slovakofarma, Czechoslovakia), 7-(2,3-dihydroxypropyl)-theophyline (DHPT; Beyer) were crystallized before use. Tetramethyluric acid (TMUA) was synthesized after [15] and crystallized from diluted ethanol several times. Purine (Aldrich) was used without further purification.

Determination of equilibrium constants of complexes

The equilibrium constants of complexes of purine bases with hydroxy derivatives of naphthalene in aqueous solutions were determined by electron absorption spectrometry at 20°C. The absorption spectra were recorded on a Specord UV VIS (Zeiss, Jena) spectrophotometer. The equilibrium constants of the studied complexes have been calculated after the *Ketelaar* equation [16] which is a modification of the *Benesi—Hildebrand* equation [17] and is valid provided that $C_d > C_a$

$$C_a/(A - A_0) = [K_c \cdot C_d(\varepsilon_c - \varepsilon_a - \varepsilon_d)]^{-1} + (\varepsilon_c - \varepsilon_a - \varepsilon_d)^{-1} \qquad (1)$$

where C_a is the concentration of the acceptor, C_d is the concentration of the donor, ε_c, ε_a, ε_d are the molar absorption coefficients of the donor-acceptor complex; A is the absorbance of the system, related to unit of length, A_0 is the sum of the absorbances of free components, and K_c is the formal equilibrium constant. The equilibrium constants were evaluated from the linear relationship of $C_a/(A - A_0)$ *vs.* $1/C_d$; the equation of straight line was solved by the method of least squares.

The concentrations of 1-naphthol and 1,5-naphthalenediol in aqueous solutions were determined spectrophotometrically (with 1-naphthol $\varepsilon = 2.879 \times 10^6$ cm^2 mol^{-1} at $\lambda = 322$ nm; with 1,5-ND $\varepsilon = 4.030 \times 10^6$ cm^2 mol^{-1} at $\lambda = 329.5$ nm).

Results and discussion

In the interactions of purine bases with the studied hydroxy derivatives of naphthalene, shifts of the absorption bands to higher wavenumbers and changes in

their intensities were observed in the absorption spectra of 1-naphthol and 1,5-naphthalenediol in aqueous solutions. The nature of these changes in the spectra of 1-N and 1,5-ND was very similar in the interactions with all the investigated purine derivatives. The absorption spectra of 1-naphthol and 1,5-naphthalenediol in distilled water as well as the spectra changed in consequence of the interaction with 8-methylcaffeine are presented in Figs. 1 and 2. The

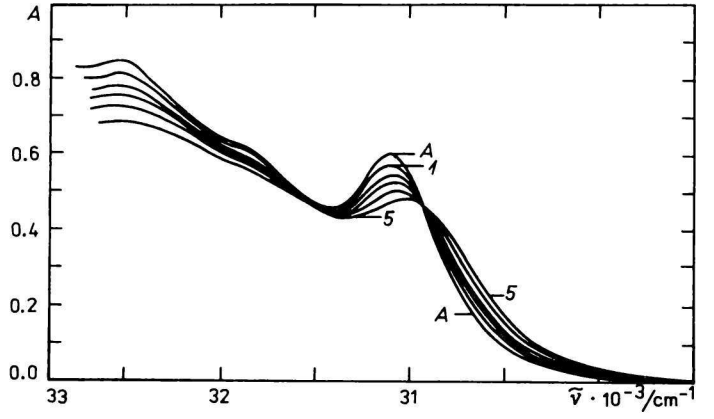

Fig. 1. Absorption spectra of 1-naphthol in water (curve *A*), $C_{1\text{-N}} = 0.268 \times 10^{-3}$ mol dm^{-3}, and in the systems of 1-naphthol—8-methylcaffeine; $C_{MC} = 1.126 \times 10^{-3}$ mol dm^{-3} (curve *1*) to 9.38×10^{-3} mol dm^{-3} (curve *5*); the width of the used cell $d = 1.004$ cm.

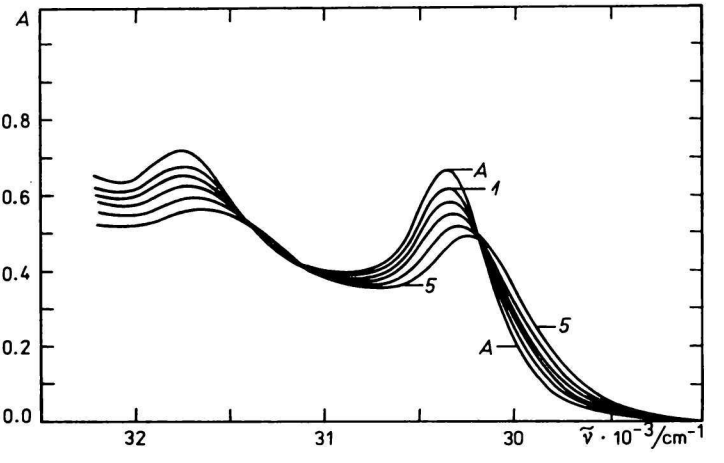

Fig. 2. Absorption spectra of 1,5-naphthalenediol in water (curve *A*), $C_{1,5\text{-ND}} = 0.165 \times 10^{-3}$ mol dm^{-3}, and in the systems of 1,5-ND—8-methylcaffeine; $C_{MC} = 0.747 \times 10^{-3}$ mol dm^{-3} (curve *1*) to 6.226×10^{-3} mol dm^{-3} (curve *5*); $d = 1.004$ cm.

course of these changes in the absorption spectra of hydroxy derivatives of naphthalene due to interaction with the studied purine bases is characteristic of the formation of hydrogen bondings, the hydroxy derivatives being the proton-donors [18].

The concentrations of 1-naphthol and 1,5-naphthalenediol in the systems for the determination of equilibrium constants of the complexes varied from 0.13 to 0.29×10^{-3} mol dm^{-3}. Except for theophyline and purine, the suitable concentrations of purine derivatives in the systems were found to be generally $0.5—16 \times 10^{-3}$ mol dm^{-3}. The necessary concentration of theophyline in the system with 1-naphthol was $2.2—22.5 \times 10^{-3}$ mol dm^{-3} and that of purine in the system with 1,5-ND varied in the range $3.7—37.5 \times 10^{-3}$ mol dm^{-3}.

The relationship of the quantities $C_a/(A - A_0)$ *vs.* $1/C_d$ of eqn (*1*) is illustrated in Fig. 3 for the systems of 1-naphthol with 8-methylcaffeine.

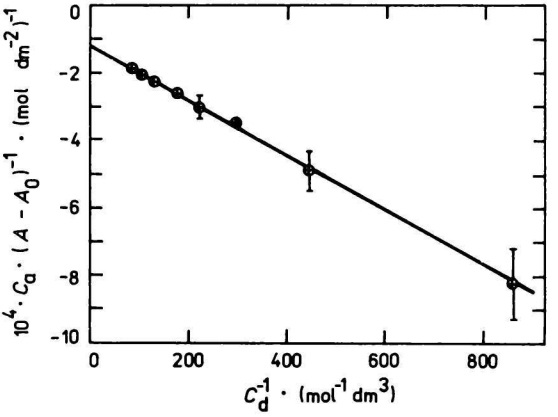

Fig. 3. Relationship of the quantities $C_a/(A - A_0)$ *vs.* $1/C_d$ of eqn (*1*) in the systems of 1-naphthol—8-methylcaffeine.

The evaluated equilibrium constants and their standard deviations σ for the studied complexes of hydroxy derivatives of naphthalene with purine derivatives and the changes of molar absorption coefficients of hydroxy derivatives of naphthalene, caused by interactions, are presented in Table 1.

In the studied systems the competition of bonds, namely those between purines and 1-naphthol or 1,5-naphthalenediol and the mutual bonds of purines formed by self-associations, should be considered. We failed to identify the interactions of the studied purines originating from self-associations by electron absorption spectrometry. The equilibrium constants of dimers of these bases are relatively low in

Table 1

Equilibrium constants of the complexes of 1-naphthol and 1,5-naphthalenediol, respectively, with purine derivatives in aqueous solutions at 20°C and changes of molar absorption coefficients of hydroxy derivatives of naphthalene (with 1-N at $\lambda = 322$ nm and with 1,5-ND at $\lambda = 329.5$ nm)

Complex	K dm^3 mol^{-1}	σ	$\Delta\varepsilon \cdot 10^{-3}$ cm^2 mol^{-1}	σ
1-N—caffeine	73.3	11.7	− 857	311
1-N—8-MC	160.0	24.6	− 809	165
1-N—theophyline	32.6	4.7	− 948	309
1-N—HET	81.6	10.9	− 653	107
1-N—DHPT	78.7	8.0	− 635	115
1,5-ND—caffeine	157.0	25.0	−1736	297
1,5-ND—8-MC	197.4	20.1	−2342	599
1,5-ND—theophyline	86.6	11.2	−1562	136
1,5-ND—HET	73.9	7.1	−1790	384
1,5-ND—DHPT	85.5	18.4	−2018	380
1,5-ND—TMUA	228.2	37.1	−2860	644
1,5-ND—purine	12.2	2.5	−1509	596

aqueous solutions. Using ^{1}H-n.m.r. spectrometry, *Thakkar et al.* [14] established the value of the association constant of theophyline to be 6.0 dm^3 mol^{-1}. The association constant of the caffeine dimer, determined also by ^{1}H-n.m.r. spectrometry, was 8.6 dm^3 mol^{-1}. Essentially lower association constant, 2.1 dm^3 mol^{-1}, has been found for purine [9, 10]; the association constant of the 6-methylpurine dimer was 6.7 dm^3 mol^{-1}.

It is probable that in the presence of hydroxy derivatives of naphthalene in aqueous solutions, preferably the complexes of purine derivatives with these compounds are formed as their association constants are orderly higher than those of the complexes formed by self-associations of purines. The evident linearity of the relationship $C_a/(A - A_0)$ *vs.* $1/C_d$ of the complexes of the studied purines with the hydroxy derivatives of naphthalene also proves that self-associations of purines are insignificant in the given systems.

Interactions of 1,5-naphthalenediol were studied with 7 purine derivatives. In comparison with 1-naphthol, the equilibrium constants of the complexes of 1,5-ND with the studied purine derivatives are noticeably higher. It is evidently due to stabilization of the bond by interaction with hydrogen bonds of both hydroxy groups of the 1,5-ND molecule. The appearance of isosbestic points (Fig. 2) proved that one complex was formed.

The lowest equilibrium constant of the 1,5-ND complex was found with purine (12.2 dm^3 mol^{-1}). Markedly higher equilibrium constants of the 1,5-ND complexes

with the other studied purine derivatives point to the importance of the contribution of interactions of the oxygen atom having significant proton-acceptor properties.

The equilibrium constants of the 1,5-ND and 1-naphthol complexes, respectively, with caffeine were almost twice higher than those of the corresponding complexes with theophyline. The methyl group present in the position 7 of the caffeine molecule influences its dipole moment and significantly decreases the hydration of its molecule in aqueous solutions with regard to the theophyline molecule. The change in hydration is probably the reason of the markedly increased values of equilibrium constants of the 8-methylcaffeine complexes with the studied hydroxy derivatives of naphthalene when compared to those of the caffeine complexes. The difference in equilibrium constants was particularly remarkable with the complexes of these compounds with 1-naphthol. The highest equilibrium constant found for the complex of 1,5-ND with tetramethyluric acid is in accordance with the above-mentioned facts.

Comparison of the association constant values of dimers of purine, theophyline, and caffeine [9, 10, 14] with the equilibrium constant values of complexes of these compounds with 1,5-ND has shown a simultaneously increasing tendency in the equilibrium constants of complexes from purine to theophyline and caffeine. Consequently, it can be assumed that not only hydrogen bondings but also stacking interactions, which are thought to be determining in dimerization of the studied purine derivatives, are significant in the interactions of purine bases with hydroxy derivatives of naphthalene.

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