

## Structure, stability, toxicity and anti-inflammatory activity of a complex of 5-hydroxy-6-methyluracil with 5-aminosalicylic acid

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### Abstract

UV spectroscopy was used to study complex formation of 5-hydroxy-6-methyluracil (5-OH-6-MU) with 5-aminosalicylic acid (5-ASA) in an aqueous medium. Two spectral methods (the method of isomolar series and the method of molar ratios) proved that aqueous solutions see 5-OH-6-MU and 5-ASA forming a complex compound of 1:1, i.e it takes one uracil molecule per one molecule of the acid under study. The method of molar ratios in the temperature range of 20-44 °C calculated the equilibrium constants of complexing reactions of 5-OH-6-MU...5-ASA (complex compound stability constant – K). The analysis of the results showed that 5-hydroxy-6-methyluracil forms a sufficiently strong complex with 5-aminosalicylic acid: K values in the temperature range under study vary within  $(2-9) \cdot 10^4$  l/mole. It was found that with increasing temperature the value of the stability constant of a complex compound is reduced. The study of the temperature dependence of K allowed to define standard values of thermodynamic parameters (change in Gibbs free energy –  $\Delta G^\circ$ , enthalpy –  $\Delta H^\circ$  and entropy –  $\Delta S^\circ$ ) of complexing. The negative values of  $\Delta G^\circ$ ,  $\Delta H^\circ$  and  $\Delta S^\circ$  indicate, respectively, spontaneous complexing formation of 5-OH-6-MU...5-ASA, its exothermic properties and certain restrictions on vibrational and rotational motions of molecules, resulting from the formation of the complex compound. The obtained data about the composition, equilibrium and the thermal stability of the investigated complex 5-OH-6-MU...5-ASA were employed to develop the methods of its synthesis, to design the prototype of the compound and to examine its anti-inflammatory activity and toxicity. Pharmacological studies (on the model of carrageenan inflammation) found that a complex compound formed by 5-hydroxy-6-methyluracil and 5-aminosalicylic acid demonstrates a higher anti-inflammatory activity compared to the starting materials (5-OH-6-MU, 5-ASA). The study of the acute toxicity of the complex of 5-OH-6-MU...5-ASA showed that it may be related to hazard category 4 (low-hazardous substances), while one of the starting materials – 5-aminosalicylic acid – belongs, according to GOST 12.1.007 – 76 to hazard category 3 (moderately hazardous substances).

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