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Formation and thermodynamic stability of (polymer + porphyrin) supramolecular structures in aqueous solutions

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ABSTRACT

Optical properties of porphyrins can be tuned through (polymer + porphyrin) (host + guest) binding in solution. This gives rise to the formation of supramolecular structures. In this paper, the formation, thermodynamic stability and spectroscopic properties of (polymer + porphyrin) supramolecular structures and their competition with porphyrin self-association were investigated by both isothermal titration calorimetry (ITC) and absorption spectroscopy. Specifically, reaction enthalpies and equilibrium constants were measured for meso-tetrakis(4-sulfonatophenyl) porphyrin (TPPS) self-association and TPPS binding to the polymer poly(vinylpyrrolidone) (PVP, 40 kg/mol) in aqueous solutions at pH 7 and three different temperatures (12, 25 and 37 °C). ITC, compared to spectroscopic techniques, provides two independent means to determine reaction enthalpies: direct measurements and Van't Hoff plot. This was used as a criterion to assess that (1) self-association of TPPS is limited to the formation of dimers and (2) TPPS binds to PVP in its monomeric state only. The formation of TPPS dimers and (PVP + TPPS) supramolecular structures are both enthalpically driven. However, (polymer + porphyrin) binding was found to be entropically favored compared to dimerization. Furthermore, the reaction enthalpies of these two processes significantly depend on temperature. This behavior was attributed to hydrophobic interactions. Finally, the limiting absorption spectra of monomeric, dimeric and polymer-bound states of TPPS were extracted from our spectroscopic measurements combined with the thermodynamic parameters obtained by ITC. The observed spectral shifts indicate that the two hydrogens in the central porphyrin are involved in (PVP + TPPS) binding. This work provides valuable information on thermodynamic stability of (polymer + porphyrin) supramolecular nanostructures and the general understanding of complex competing associative processes in solution.

1. Introduction

Porphyrins are tetrapyrrolic macrocycles known for their interesting spectroscopic properties [1,2], supramolecular polymeric structures (*e.g.* J and H aggregates) [1,3] and catalytic applications [1,4]. In relation to spectroscopy, porphyrins display very strong absorption around (400 to 430) nm (Soret band) and relatively weaker absorption around (500 to 650) nm (Q bands) [2,5,6]. Excited singlet porphyrins show interesting photophysical properties leading to storage of energy and its transfer to their surroundings [7]. These properties are very valuable for applications in photodynamic therapy [7–10] and photoelectrical devices [11,12].

The formation of supramolecular structures of porphyrins in solution [13–20] have been mainly investigated by examining the red shift (J aggregates, edge-to-edge stacking) and blue shift (H aggregates, face-to-face stacking) of their absorption spectra [14–18]. However, supramolecular structures with their own spectroscopic properties can be also obtained by introducing polymers that can bind porphyrins. These mesoscopic materials can find applications in nanotechnology, catalysis, medicine and separation technologies. However, (polymer + porphyrin) binding competes with porphyrin self-association in solution, and accurate thermodynamic studies are critical for the characterization of the thermodynamic stability of related supramolecular structures. Here, spectroscopic techniques alone provide a limited understanding on the energetics of these complicated associative processes.

In this paper, isothermal titration calorimetry (ITC) is successfully used for characterizing both (polymer + porphyrin) binding and porphyrin self-association for meso-tetrakis(4-sulfonatophenyl) porphyrin (TPPS) in water at pH 7.0 [14–21]. UV/visible spectra were also obtained in similar experimental conditions and discussed in relation to our ITC results.

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Compared to spectroscopic techniques, ITC has the advantage of providing both the equilibrium constant (or standard reaction Gibbs free energy) of a reversible chemical reaction and the corresponding reaction enthalpy [22,23]. Note that reaction enthalpies can be also obtained by determining equilibrium constants from spectroscopic measurements as a function of temperature (Van't Hoff plot). Consequently, if equilibrium constants are measured by ITC as a function of temperature, two independent means of determining the same reaction enthalpy become available from ITC. This unique feature is very important for assessing the accuracy of the binding models chosen to describe complex chemical equilibria. Furthermore, reaction enthalpies extracted from individual ITC measurements as a function of temperature offers a precise way to determine the reaction heat capacity. This thermodynamic parameter is known to be important for evaluating the contribution of hydrophobic interactions to binding processes in aqueous solutions [22]. To our knowledge, there is only one qualitative ITC study related to TPPS binding to ferric myoglobin, [24] and there are only few ITC investigations on porphyrins in general [25,26].

TPPS has four negatively charged sulfonate groups that compensate for the hydrophobicity of the aromatic tetrapyrrolic system and the attached four phenyl groups. The amphiphilic properties of this porphyrin lead to complex self-association behavior in aqueous solutions, depending on physicochemical parameters such as concentration, temperature, ionic strength and pH [14–19,21,27]. Furthermore, additives such as polymers [20,27–30] and surfactants [31–33] may non-covalently bind to porphyrins thereby providing another way to modulate their aggregation state and solubility in solution. Two pK_a points near pH 5 can be associated with TPPS [34]. These characterize the effect of pH on the protonation state of the two pyrrole nitrogens in the central porphyrin ring. Thus, TPPS displays a net charge of -4 at pH ≈ 7 (free base state) and -2 at pH ≈ 3 (diacid state). The reduction of electrostatic repulsion at low pH facilitates self-association of the diacid state compared to that of the free base porphyrin at neutral and high pH [17]. The spectroscopic behavior of TPPS in aqueous solutions has been utilized to characterize TPPS self-association in aqueous solution as a function of pH [14–17]. This process may be described by employing a dimerization model at neutral and high pH, while the self-association occurring at low pH is more complex and normally involves the formation of large J-aggregates.

In this paper, poly(vinylpyrrolidone) (PVP) is used to obtain (PVP + TPPS) supramolecular structures at physiological pH. Specifically, we provide an accurate thermodynamic characterization of TPPS self-association, (PVP + TPPS) binding and related stoichiometry. PVP is a hydrophilic neutral polymer extensively employed in pharmacological applications [35]. For example, PVP is used as a binder in tablet formulations and as a solubilizing agent for active ingredients. There is one spectroscopic study [30] reporting on (PVP + TPPS) binding. However, this investigation was limited to acidic pHs and neglects the very important contribution of TPPS self-association. These (PVP + TPPS) binding studies will also provide the basis for investigating, by ITC, the more complex self-association behavior of TPPS at low pH. Here, PVP can be employed to dissociate individual units from porphyrin aggregates, thereby probing their binding energy.

2. Experimental section

2.1. Materials

5,10,15,20-Tetraphenyl-21*H*,23*H*-porphine-*p*,*p*′,*p*″,*p*‴-tetrasulfonic acid tetrasodium hydrate (TPPS) was purchased from Sigma-Aldrich, and used as supplied, without further purification. (TPPS + water) stock solutions with a composition of ≈1% (w/w) were prepared by weight. Poly(vinylpyrrolidone) (PVP) with nominal molecular weight of 40 kg · mol^{-1} was purchased from Sigma-Aldrich and used without further purification. Complete specification of materials is listed in table 1. Deionized water was passed through a four-stage Millipore filter system to provide higher purity water for all the experiments. (PVP + water) stock solutions with a composition of ≈10% (w/w) were prepared by weight. The solutions for ITC and spectroscopic measurements were gravimetrically prepared by mixing known amounts of TPPS and/or PVP stock solutions with water and buffer. A 0.10-M, pH 7.0 sodium phosphate buffer was also added so that the final phosphate concentration was 0.010 M. TPPS and PVP weight fractions were converted into the corresponding molar concentrations using the molecular weights of (1023 and 111.14) kg · mol^{-1} for TPPS and PVP monomeric unit respectively and the solution specific volume calculated using the specific volumes of (0.78 and 0.999) cm^3 · g^{-1} for PVP [36] and 0.010-M aqueous buffer respectively. The small contribution of TPPS to the solution specific volume was neglected.

2.2. Isothermal titration calorimetry

ITC measurements were performed using the MicroCal iTC200 System from GE Healthcare Life Sciences. All experiments were performed at $T = (12,\ 25$ and $37)$ °C and atmospheric pressure (≈0.99 bar). For dissociation experiments, small aliquots (2.0 μL) of a TPPS aqueous solution (titrant, 3.69 mM) were sequentially injected (≈20 injections) from a rotating syringe into the vigorously stirred sample cell (syringe rotation, 1000 rpm) containing porphyrin-free 0.010-M buffer (titrand). The reaction cell volume is 203.4 μL according to factory specifications. TPPS dilution into the cells leads to porphyrin disaggregation, which resulted in the isothermal absorption of heat from the surroundings. For (PVP + TPPS) binding experiments, small aliquots (2.0 μL) of a PVP aqueous solution (titrant, 91.0 mM) were sequentially injected into the ITC cell containing a TPPS aqueous solution (titrand, 0.244 mM). The choice of PVP instead of TPPS as the titrant was imposed by the large contribution of TPPS dilution to the recorded heat (due to porphyrin dissociation). On the other hand, blank experiments, in which PVP solutions were injected into pure buffer, showed that the contribution of PVP dilution to the overall heat involved in the (PVP + TPPS) mixing process is very small.

Each injection corresponds to a peak on a plot showing the power required to maintain the sample and reference cells at the same temperature as a function of time. The differential heat associated with each injection is calculated as the area of the corresponding measured peak and normalized with respect to the titrant number of moles. The differential heat $q^{(i)}$ associated with injection i is linked to the cumulative heat $Q^{(i)}$ absorbed or released by the sample inside the stirred cell after injection i by applying

$$q^{(i)} = \left[(V + v/2)(Q^{(i)}/V) - (V - v/2)(Q^{(i-1)}/V)\right]/(vC'_{\mathrm{TITRANT}}), \qquad (1)$$

where $Q^{(0)} = 0$, $V = 203.4\ \mu\mathrm{L}$ is the volume of sample cell, $v = 2.0\ \mu\mathrm{L}$ is the volume of individual titrant injections and C'_{TITRANT} is the titrant concentration. The volumetric factors $(V + v/2)/V = 1.005$ and $(V - v/2)/V = 0.995$ represent small corrections taking into account that the titrant addition to the sample cell displaces a small fraction ($v/V \approx 0.01$) of solution outside the stirred sample cell. Thus, the experimentally recorded differential heat corresponds to an overestimate of $Q^{(i)}$ because a small contribution to heat will also come from the sample displaced outside the cell, and an underestimate of $Q^{(i-1)}$ because this displaced sample contributed to the cumulative heat after injection $i - 1$. Thus $Q^{(i-1)}$ does not represent the correct starting point for injection i. The two factors $(V \pm v/2)/V$ represent the average between two