Disstacking of Phthalocyanine in Water by Poly(ethylene Oxide)

To Ngai,[†] Guangzhao Zhang,[†,‡] Xi-you Li,[†] Dennis K. P. Ng,[†] and Chi Wu*,[†,‡]

Department of Chemistry, The Chinese University of Hong Kong, Shatin N. T., Hong Kong, and The Open Laboratory of Bond Selective Chemistry, Department of Chemical Physics, University of Science and Technology of China, Hefei, Anhui, China

It was found that use of hydrophilic poly(ethylene oxide) (PEO) as a dispersion agent could disstack phthalocyanine (PC) in water and enhance its luminescence quantum yield. A combination of laser light scattering, UV–vis, and fluorescence spectroscopy was used to study the PEO/PC interaction. Our results revealed that, for a given weight concentration, long PEO chains were more effective than shorter ones to disstack PC into individual molecules. The PEO concentration dependence of UV–vis and fluorescence emission spectra showed that one long PEO chain ($M_w \sim 10\,000$ g/mol) is as effective as 25 short PEO chains ($M_w \sim 2000$ g/mol).

Introduction

Due to their intense absorption in the red visible region (ca. 700 nm) and superior photophysical properties,[1,2] phthalocyanines as efficient photosensitizers have been used in photodynamic therapy for various diseases,[3,4] virus sterilization of red blood cells,[5–7] and photooxidation of mercaptans in petroleum distillates.[8] However, their large π conjugation leads to a strong stacking tendency, especially in aqueous media, which affects their sensitizing ability,[9,10] because such stacking provides an efficient nonradiative energy relaxation pathway, reducing the triple-state population and therefore inhibiting the generation of singlet oxygen, which is directly related to the death of tumor cells.[11–14] The stacking of phthalocyanines in water was attributed to the high dielectric constant of water.[10,15] Therefore, it is a remaining challenge to disstack phthalocyanines into individual molecules in water for their biomedical applications.

In the past, two physical methods, i.e., the addition of organic solvents (e.g., ethanol, pyridine, and dimethyl sulfoxide)[16] and the incorporation of phthalocyanines into cationic micelles,[17–19] were used to reduce the stacking. The disstacking usually reflects in a stronger emission and a longer lifetime of the excited state. For example, the addition of the surfactant *n*-hexadecyltrimethylammonium bromide (CTAB) greatly increases the excited-state lifetime of zinc(II) tetrasulfonated phthalocyanine in water from <80 ps to >1 ns.[19] The influence of different surfactants on the stacking of some dendritic phthalocyanine molecules terminated with carboxylate groups was also studied.[20] It was found that cationic surfactant, e.g., *n*-hexadecyltrimethylammonium bromide, was more effective in disstacking phthalocyanines than anionic surfactant, which was attributed to the electrostatic interaction between the anionic ends of the dendritic fragments and cationic surfactant. Another strategy was to chemically modify phthalocyanine by attaching bulky and hydrophilic substituents either at the axial positions or on the periphery of phthalocyanines.[21,22] Brooks and co-workers,[22] for example, prepared the water-soluble ruthenium phthalocyanines $Ru(PC)L_2$ [PC = phthalocyaninate; L = $PPh_2(3-C_6H_4SO_3^-)$ or 3-pyridinesulfonate], which are relatively nonaggregated in water as shown by UV–vis spectroscopy. Recently, we reported a series of zinc(II) phthalocyanine molecules substituted with four dendritic fragments terminated with carboxylate groups.[23] The absorption and fluorescence spectroscopic studies showed that the stacking was reduced when the size of the dendrons became bigger. Phthalocyanine with the second generation of dendritic fragments could exist mainly as individual molecules even in a highly polar

* To whom correspondence should be addressed.

† The Chinese University of Hong Kong.

‡ University of Science and Technology of China.

(1) *Phthalocyanines – Properties and Applications*; Leznoff, C. C., Lever, A. B. P., Eds.; VCH: New York, 1989 (Vol. 1), 1993 (Vols. 2 and 3), and 1996 (Vol. 4).

(2) Ali, H.; van Lier, J. E. *Chem. Rev.* **1999**, *99*, 2379.

(3) Bonnett, R. *Chem. Soc. Rev.* **1995**, 19.

(4) Milgrom, L., MacRobert, S. *Chem. Br.* **1998** (May), 45.

(5) Rywkin, S.; Ben-Hur, B.; Malik, Z.; Prince, A. M.; Li, Y. S.; Kenney, M. E.; Oleinick, N. L.; Horowitz, B. *Photochem. Photobiol.* **1994**, *60*, 165.

(6) Abe, H.; Wagner, S. J. *Photochem. Photobiol.* **1995**, *61*, 402.

(7) Allen, C. M.; Weber, J. M.; van Lier, J. E. *Photochem. Photobiol.* **1995**, *62*, 184.

(8) Kimura, M.; Yamaguchi, Y.; Koyama, T.; Hanabusa, K.; Shirai, H. *J. Porphyrins Phthalocyanines* **1997**, *1*, 309.

(9) Iliev, V.; Ileva, A. *J. Mol. Catal. A: Chem.* **1995**, *103*, 147 and references therein.

(10) Ball, D. J.; Wood, S. R.; Vernon, D. I.; Griffiths, J.; Dubbelman, T. M. A. R.; Brown, S. B. *J. Photochem. Photobiol. B: Biol.* **1998**, *45*, 28.

(11) Spikes, D. J. *Photochem. Photobiol.* **1986**, *43*, 691.

(12) Vacus, J.; Simon, J. *Adv. Mater.* **1995**, *7*, 797.

(13) Howe, L.; Zhang, J. Z. *J. Phys. Chem. A* **1997**, *101*, 3207.

(14) Dhami, S.; Phillips, D. *J. Photochem. Photobiol. A: Chem.* **1996**, *100*, 77.

(15) Yang, Y.-C.; Ward, J. R.; Seiders, R. P. *Inorg. Chem.* **1985**, *24*, 1765.

(16) Juarranz, A.; Stockert, J. C.; Canete, M.; Villanueva, A. *Cell. Mol. Biol.* **1985**, *31*, 379.

(17) Gu, Z. W.; Omelyanenko, V.; Kopecková, P.; Kopecek, J.; Konák, C. *Macromolecules* **1995**, *28*, 8375.

(18) Dhami, S.; Cosa, J. J.; Bishop, S. M.; Phillips, D. *Langmuir* **1996**, *12*, 293.

(19) Howe, L.; Zhang, J. Z. *Photochem. Photobiol.* **1998**, *67*, 90.

(20) Li, X.-Y.; He, X.; Ng, A. C. H.; Wu, C.; Ng, D. K. P. *Macromolecules* **2000**, *33*, 2119.

(21) Kimura, M.; Nakada, K.; Yamaguchi, Y.; Hanabusa, K.; Shirai, H.; Kobayashi, N. *Chem. Commun.* **1997**, 1215.

(22) Bossard, G. E.; Abrams, M. J.; Darkes, M. C.; Vollano, J. F.; Brooks, R. C. *Inorg. Chem.* **1995**, *34*, 1524.

(23) Ng, A. C. H.; Li, X.-Y.; Ng, D. K. P. *Macromolecules* **1999**, *32*, 5292.

Chart 1. Structure of the First-Generation Dendritic Phthalocyanine PC-1

First generation dendritic fragment
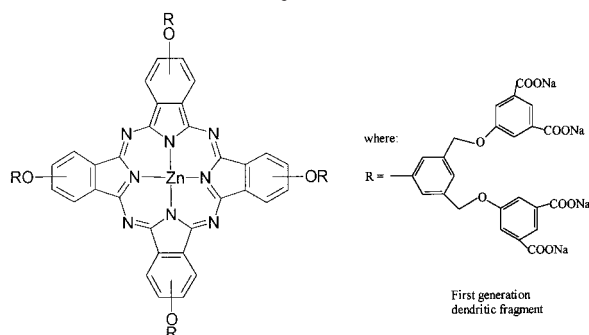
aqueous solution, but not phthalocyanine with the first generation of dendritic fragments.

However, the chemical modification of phthalocyanine with a higher generation of dendritic fragments is not only time-consuming but also expensive. On the other hand, the addition of organic solvents or ionic surfactants often complicates their biomedical applications. This led us to search for a better way to disstack phthalocyanine. Using biodegradable and biocompatible polymer is certainly a good choice. It has been known that biocompatible poly(ethylene oxide) (PEO) can strongly interact with anionic surfactants, such as sodium dodecyl sulfate (SDS), in aqueous solution to form charged complexes in which small SDS micelles are wrapped by PEO chains.[24] Inspired by this complexation, in the present study, we study the feasibility of using PEO to disstack phthalocyanine in water. It is worth noting that the use of PEO in the human body has already been approved by the Food and Drug Administration (FDA).

Experimental Section

Sample Preparation. The preparation of the first-generation dendritic phthalocyanine (PC-1) terminated with carboxylate groups can be found elsewhere.[23] Chart 1 shows its chemical structure. Three poly(ethylene oxide) (PEO) samples (from Aldrich) with different molar masses of 400, 2000, and 10 000 g/mol are, respectively, denoted as PEO400, PEO2000, and PEO10000 hereafter. The polydispersity of PEO is close to 1.2. The solution mixtures of PC and PEO were prepared by adding a PC aqueous solution dropwise into a PEO aqueous solution under stirring. The molar ratio of PEO to PC ranged from 0.2 to 25. The absorption and fluorescence emission spectra of different PC/PEO mixtures were recorded on a Hitachi U-3300 spectrophotometer and a Hitachi F-4500 spectrofluorometer, respectively.

Laser Light Scattering. A modified commercial light scattering spectrometer (ALV/SP-125) equipped with an ALV-5000 multi-τ digital time correlator and an ADLAS DPY425II solid-state laser (output power = 400 mW at λ = 532 nm) was used. In dynamic LLS, the Laplace inversion of each precisely measured intensity–intensity time correlation function $G^{(2)}(t,q)$ in the self-beating mode resulted in a line width distribution $G(\Gamma)$. The CONTIN Laplace inversion algorithm in the correlator was used. For a pure diffusive relaxation, $G(\Gamma)$ can be converted to a translation diffusion coefficient distribution $G(D)$ by $\Gamma = Dq^2$ or a hydrodynamic radius distribution $f(R_h)$ by use of the Stokes–Einstein equation. The PC/PEO mixtures were clarified with 0.2-μm Millipore filters to remove dust. All the LLS measurements were done at 25.0 ± 0.1 °C. The details of the LLS instrumentation and theory can be found elsewhere.[25,26]
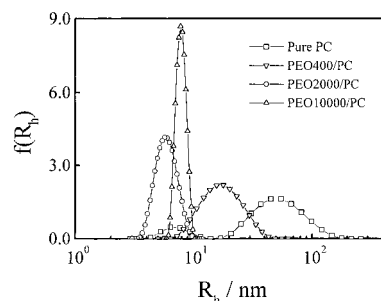

Figure 1. Hydrodynamic radius distributions $f(R_h)$ of PEO/PC complexes in water, where C_{PC} = 0.284 mg/mL and C_{PEO} = 5.00 mg/mL.
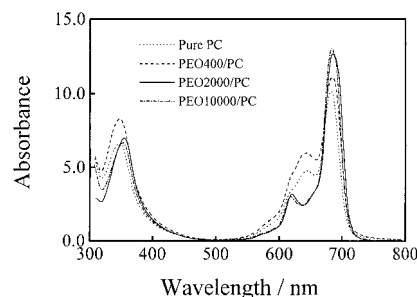

Figure 2. Absorption spectra of PEO/PC complexes in water, where C_{PC} = 0.284 mg/mL and C_{PEO} = 5.00 mg/mL.

Results and Discussion

Figure 1 shows that in the absence of PEO the hydrodynamic radius distribution of PC-1 in water has two peaks, indicating that there exist two kinds of aggregates with different sizes. Both of them are larger than individual PC-1 molecules ($\sim$3–4 nm). The peak located at $\sim$7 nm can be attributed to PC-1 dimers, a common form in water because two planar macrocycles can easily stack into a face-to-face structure.[15,27] The molecular modeling also showed a similar calculated size for a PC dimer.[28] The aggregation reveals that the first-generation dendritic fragment is too small to sterically disstack PC into individual molecules. The addition of PEO clearly reduces the size of the PEO/PC-1 complex, especially the large aggregates. Note that the PEO10000/PC-1 complexes are larger than the PEO2000/PC-1 complexes, which can be attributed to the fact that PEO10000 is 5 times longer than PEO2000. The PEO/PC complexes are narrowly distributed. The complexation between PC and PEO can also be viewed in UV–vis and fluorescence spectroscopies.

Figure 2 shows that, in the absence of PEO, the UV–vis spectra of PC-1 shows a rather strong blue-shifted dimer band at 639 nm, indicating the existence of a significant amount of dimers in pure water.[15,29,30] As the length of the PEO chains increases, this board dimer band diminishes, while the monomeric Q-band at 685 nm and a vibronic band at 617 nm become more and more intense. Figure 3 shows that upon excitation at 617 nm, the fluorescence emission of PC-1 increases with the PEO length. It is known that PC in its stacking states is normally not emissive.[27] Therefore, the fluorescence at 702 nm mainly comes from individual PC-1 molecules. Both the UV–vis and fluorescence spectra clearly dem-

(24) Brown, W.; Fundin, J.; Miguel, M. G. *Macromolecules* **1992**, *25*, 7192.

(25) Chu, B. *Laser Light Scattering*, 2nd ed.; Academic Press: New York, 1991.

(26) Berne, B.; Pecora, R. *Dynamic Light Scattering*; Plenum Press: New York, 1976.

(27) Kaneko, Y.; Arai, T.; Tokumaru, K.; Matsunaga, D.; Sakuragi, H. *Chem. Lett.* **1996**, 345.

(28) PCMODEL version 6.0, Serena Software, 1996.

(29) Osburn, E. J.; Chau, L.-K.; Chen, S.-Y.; Collins, N.; O'Brien, D. F.; Aronstrong, N. R. *Langmuir* **1996**, *12*, 4784.

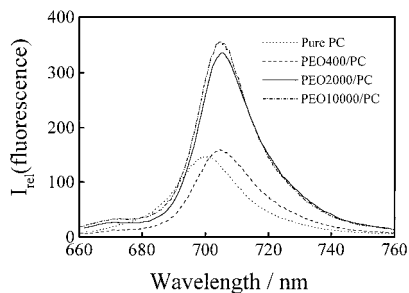(30) Reddi, E.; Jori, G. *Res. Chem. Intermed.* **1988**, *10*, 241.

Figure 3. Fluorescence spectra of PEO/PC complexes in water, where C_{PC} = 0.284 mg/mL and C_{PEO} = 5.00 mg/mL.
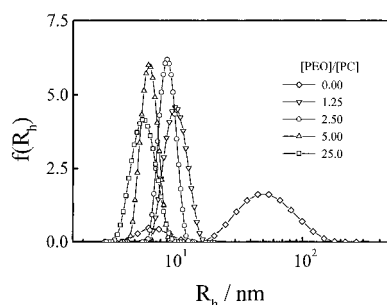

Figure 4. PEO concentration dependence of hydrodynamic radius distribution $f(R_h)$ of PEO/PC complexes in water, where [PC] was kept as 0.100 mM and PEO has a molar mass of 2000 g/mol.

onstrate that PEO can effectively disstack PC-1 into individual molecules, presumably by wrapping each PC-1 molecule with its hydrophilic chain. To elucidate the interactions between PC and PEO, we further studied the PEO concentration dependence of the PEO/PC complexation.

Figure 4 shows that the size of the PEO/PC complexes decreases as the PEO-to-PC molar ratio increases, clearly revealing the disstacking of PC-1 in water. Figure 5 reveals that both the relative absorption and fluorescence emission intensity increase with the PEO concentration, indicating the disstacking of PC-1 into individual molecules. For PEO10000, the absorption and fluorescence emission intensity reach their respective maximum when [PEO]/[PC] ~ 1, showing that each PEO10000 chain is sufficient to wrap one PC-1 molecule to prevent the stacking, while in the case of PEO2000, only when [PEO]/[PC] reaches about 25 can the same disstacking efficiency be achieved. This means that even for a given PEO weight concentration, a longer PEO10000 chain is still 5 times more effective than a shorter PEO2000 chain. Such a phenomenon has been observed in the adsoprtion of polymer chains on surface.[31] This is because for the same energetic gain, there is less cost of the translational entropy when longer chains are adsorbed on a surface. The complexation between PC and PEO with different lengths is schematically shown in Figure 6.

In summary, a combination of laser light scattering, UV−vis absorption, and fluorescence spectroscopies shows that hydrophilic poly(ethylene oxide) (PEO) chains can
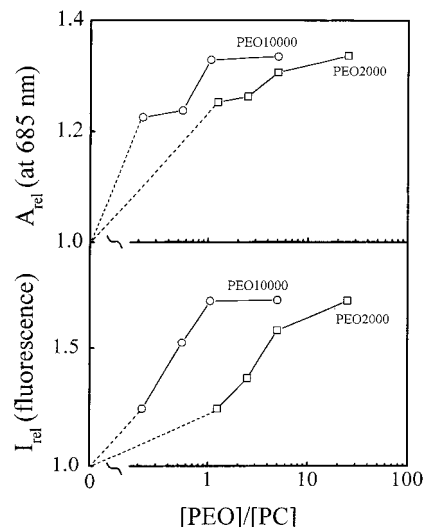
(31) Gao, J.; Wu, C. *Macromolecules* **1999**, *32*, 1704.

Figure 5. PEO concentration dependence of relative absorption intensity at 685 and relative fluorescence emission intensity of PEO/PC complexes in water, where [PC] = 0.100 mM. The values of both A_{rel} (at 685 nm) and I_{rel} (fluorescence) in the absence of PEO are fixed as unity for reference.
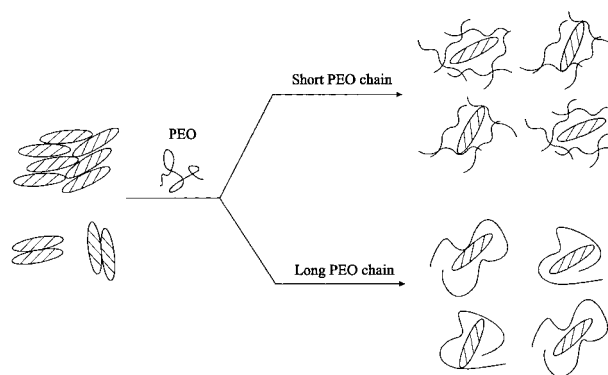

Figure 6. Schematic of complexation between PC and PEO with different chain lengths.

effectively disstack phthalocyanine into individual molecules via complexation. The disstacking leads to a high luminescence quantum yield, which makes such PEO/PC complexes useful in biomedical, photophysical, and chemical applications. Our results reveal that, for a given weight concentration, longer PEO chains are more effective than shorter ones in the disstacking. This is attributed to a strong adsorption of long PEO chains on PC. The effectiveness of long polymer chains in the disstacking revealed in this study can also be applied for the dissolution of other organic/inorganic compounds.