Pyrene-modified Cyclic Peptides Detect Specific Metal Ions by Fluorescence in Water

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Some diseases caused by accumulating metal ions in cells, for example Wilson disease and hemochromatosis, were reported. Therefore, we considered that design of a probe which detected a metal ion selectively in cells would contribute to come true of swift diagnosis and treatment of these deseases. To this purpose, we prepared the fluorescent cyclic probe **1** modified with histidine and two pyrenes (fluorescence groups) as shown in Fig. 1A. The histidine used in **1** is known to stabilize complex formation with Cu^{2+} and we used them to improve the metal ion selectivity with the probe.[1]

In this study, we synthesized **1** using a solid-phase peptide method. Cyclization of **1** was carried out by forming an amide bond between the amino group at the N-terminus of the peptide and glutamic acid from which a protective group was selectively removed on the solid-phase support. RP-HPLC and MALDI-Tof-Mass were used for purification and identification of the crude product.

Detection of metal ions was evaluated by mixturing 100 equivalents of these metal ions with **1** (final concentration: 500 nM) dissolved in HEPES buffer solution at room temperature and measuring these fluorescence spectra. The fluorescence intensity at 377 nm derived from pyrene monomer obtained from the fluorescence spectra of the mixture solution was shown in Fig. 1B. **1** mixed with metal ions except Cu^{2+} showed the fluorescence of pyrene monomer, but the fluorescence of **1** with Cu^{2+} was remarkably quenched. This result suggests that **1** selectively captures Cu^{2+} and forms a complex. We also assessed Job plot of the mixture of **1** with Cu^{2+} and we confirmed its 1:1 complex.

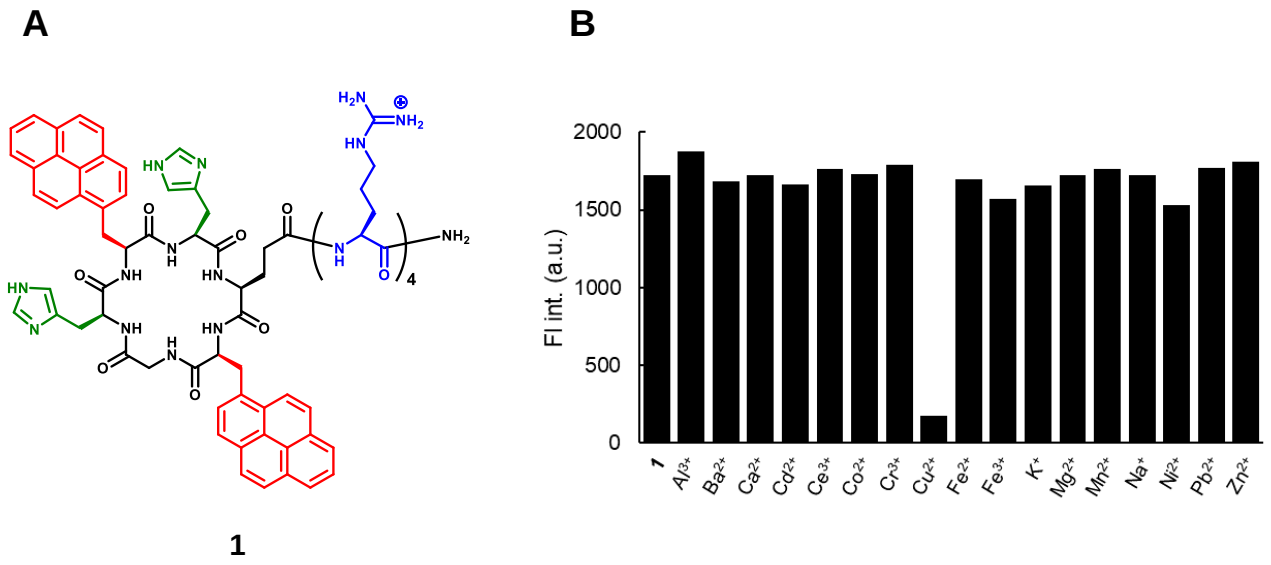

Figure 1. (A) Chemical structure of **1**. (B) Fluorescence intensity at 377 nm derived from pyrenes contained in an aqueous solution of **1** (final concentration: 500 nM) with/without 100 equivalents of various metal ions at room temperature (excitation wavelength: 340 nm).

References

[1]Zhang, Y.; Cai, Y.; He, Y.; Lin, Q.; Ren, J.; Cao, D.; Zhang, L. *RSC Adv.* **2021**, *11*, 7426-7435.