



Selective, switchable fluorescent probe for heparin based on aggregation-induced emission

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INTRODUCTION

Heparin is the most well studied Glycosaminoglycans (GAGs), which is widely used in the practice of modern medicine.¹ There has been an increased interest in developing assays for its detection and analysis based on aggregation induced emission (AIE) fluorogens because of its clinical relevance and its propensity to be contaminated or adulterated with other difficult to detect molecules.^{2,3} However, no probe has been reported that can distinguish heparin from heparan sulfate. Herein, we use an AIE fluorogen, TPE-4MN, to study its interaction with heparin and its selectivity for GAG detection.

RESULTS AND DISCUSSION

Chemical Structure

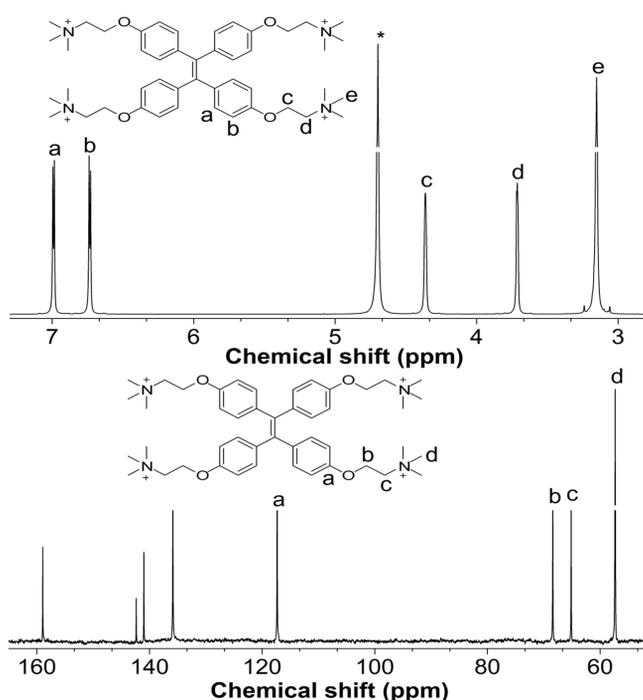
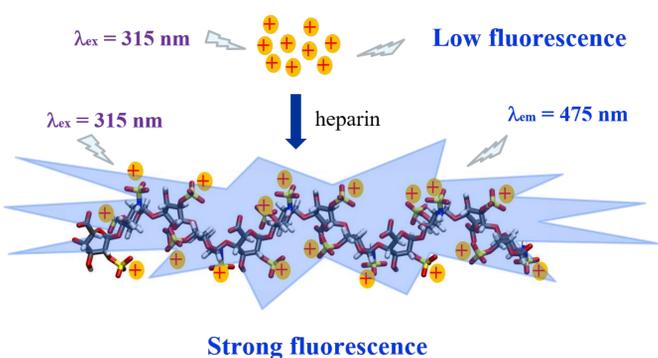


Figure 1. ¹H NMR and ¹³C NMR spectra of TPE-4MN in D₂O.

Mechanism



Scheme 1. Proposed mechanism of the interaction between TPE-4MN and heparin.

Aggregation-Induced Emission

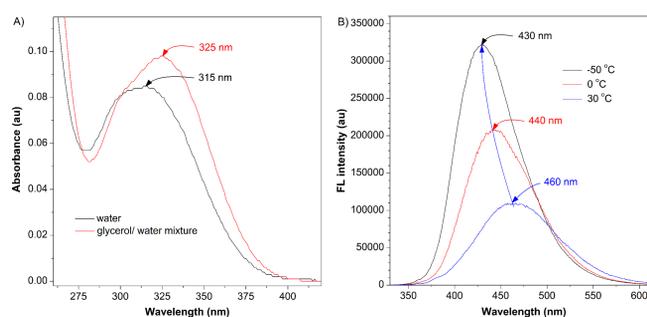


Figure 2. (A) UV-vis spectra of TPE-4MN in water and glycerol/water mixture with 99% glycerol. (B) Fluorescent spectra of TPE-4MN in glycerol/water mixture with 99% of glycerol under different temperature. λ_{ex} : 325 nm; concentration: 10 μ M.

Mechanism Study

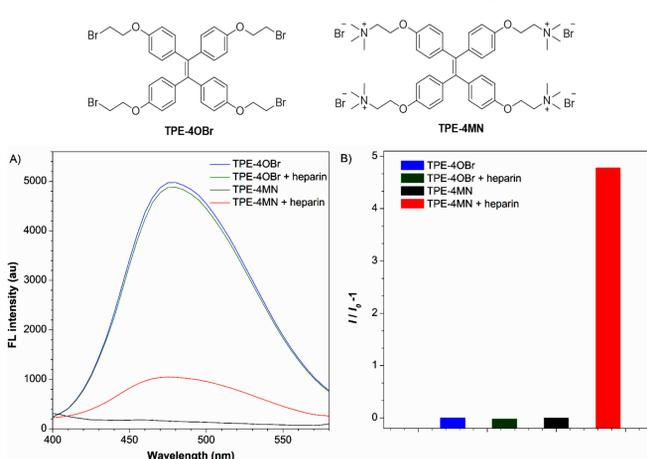


Figure 3. (A) Fluorescent spectra of TPE-4OBr and TPE-4MN in HEPES buffer (pH = 7.4, 5 mM) with 2% of THF with heparin. (B) Column of the fluorescent intensity of TPE-4OBr and TPE-4MN in HEPES buffer (pH = 7.4, 5 mM) with 2% of THF with heparin. λ_{ex} : 315 nm; concentration of heparin: 5 μ g/mL; concentration of TPE-4OBr/TPE-4MN: 10 μ M.

Sensitivity

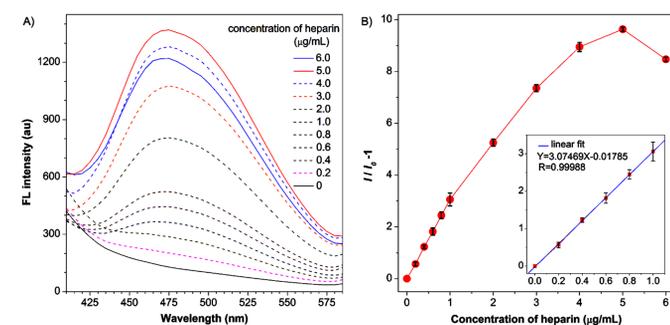


Figure 4. (A) Fluorescent spectra of TPE-4MN in HEPES buffer (pH = 7.4, 5 mM) with different concentration of heparin. (B) Plot of the fluorescent intensity of TPE-4MN in HEPES buffer (pH = 7.4, 5 mM) with different concentration of heparin. Insert: The result of linear fit of plot. λ_{ex} : 315 nm; concentration of heparin: 0 ~ 6.0 μ g/mL; concentration of TPE-4MN: 10 μ M.

Selectivity

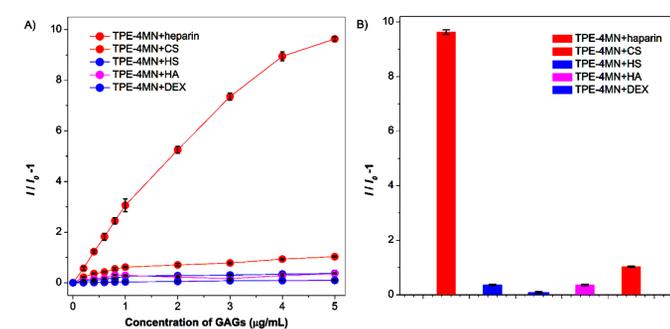


Figure 5. (A) Plot of the fluorescent intensity of TPE-4MN in HEPES buffer (pH = 7.4, 5 mM) with different GAGs. (B) Column of the fluorescent intensity of TPE-4MN in HEPES buffer (pH = 7.4, 5 mM) with different GAGs. λ_{ex} : 315 nm; concentration of GAGs: 0 ~ 6.0 μ g/mL; concentration of TPE-4MN: 10 μ M.

CONCLUSION

A probe for heparin, TPE-4MN, has been prepared and its aggregation induced emission property has been confirmed. The probe has great sensitivity and selectivity on the detection of heparin and its LOD has been calculated to be 0.75 μ g/mL. The mechanism of the detection has been demonstrated to be the interaction between the positive charge from TPE-4MN and the negative charge from heparin.

ACKNOWLEDGMENT

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