Fluorescence based Sensors for Heparin

▪ A widely used blood anticoagulant

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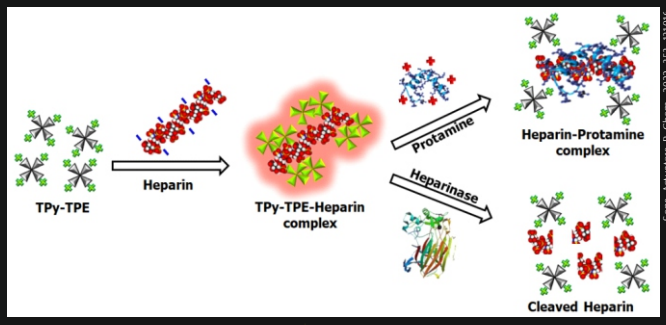
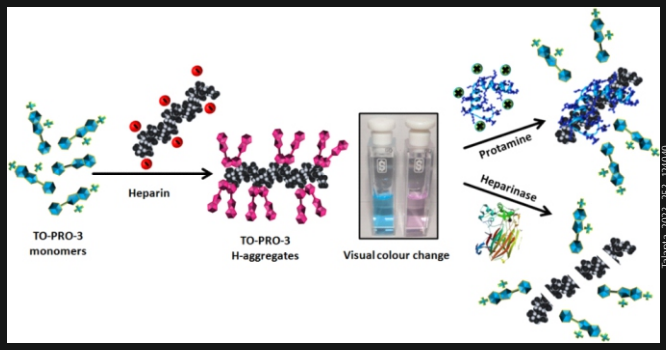
Heparin is one of the most widely used blood anti-coagulant and an antithrombotic drug. Heparin treatment is required to maintain blood fluidity, and to prevent blood clot formation during major surgical procedures that require extracorporeal circulation, for example, hemodialysis or cardio-pulmonary bypass surgeries. Considering the raising instances of cardiovascular diseases and the maturing population, an estimated one billion doses of Heparin are produced every year. This has led to a rapid increase in the development of Heparin market. Heparin is generally administered in ranges of 1.7–10μM (0.2–1.2 U/mL) for long-term post-operative care and 17–67μM (2–8 U/mL) during cardiovascular surgery. However, Heparin overdose can lead to serious adverse effects, such as, Heparin-induced thrombocytopenia, hemorrhages, osteoporosis and hyperkalemia. Thus, it is vital to detect and control the Heparin level and its activity during and after surgery, and to manipulate the amount of Heparin used for anticoagulation therapy.

We have developed a fluorescence-based sensor for Heparin detection where we have utilized a tetraphenylethylene derived AIEgen, named tetrapyridinium-tetraphenylethylene (TPy-TPE), for sensing Heparin. TPy-TPE carries four positive charges and forms aggregates in presence of negatively charged Heparin to form highly emissive aggregates of TPy-TPE (Scheme 1). Most importantly, the tetracationic nature of TPy-TPE provides a stronger binding affinity towards Heparin compared to the previously reported monocationic or dicationic fluorophores. The improved interaction between Heparin and TPy-TPE has proved to be advantageous in terms of improved sensitivity (lower LODs in aqueous and serum samples), higher fluorescence enhancement and better performance in complex matrices. While TPy-TPE is utilized for Heparin determination, its sole U.S. Food and Drug Administration (FDA) authorized antidote, Protamine, and Heparinase, which specifically degrades Heparin to produce clinically important Low Molecular Weight Heparin (LMWH) have also been detected through our probe molecule. Overall, the photophysical investigation for the detection of Heparin is a successful attempt and is expected to enhance Heparin related biosensing research in the biomedical fields.

In another contribution, we report a naked-eye detection of Heparin in aqueous and in complex human plasma samples by using a cyanine based probe, TO-PRO-3, which records a huge blue shift (~115 nm) in its absorption maximum, and marks the highest reported absorption spectral shift for any Heparin sensing system, known till date leading to visual detection of Heparin (Scheme 2). The probe has been also shown to be useful for sensing the only clinically approved Heparin antidote, Protamine as well as a Heparin degrading enzyme, Heparinase, which serves as an important biomarker for inflammation. Overall, we have been able to develop a very simple, highly sensitive and selective assay for a widely used blood anti-coagulant drug, Heparin, which can even perform well in complex bio-samples and promises potential applications in real life scenario and Heparin related biochemical research.



▲ Scheme 1: Schematic representation of Fluorescence turn-on detection of Heparin.



▲ Scheme 2: Schematic representation of visual detection of Heparin.

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Dr. Prabhat K. Singh, is currently working as a Scientific Officer/G at Radiation and Photochemistry Division, Bhabha Atomic Research Centre (BARC), Mumbai, India. His current research interest includes ultrafast spectroscopy, supramolecular chemistry and use of self-assembled materials for designing optical sensors for bio-sensing and chemo-sensing applications. Prof. Singh has authored about 115 publications in peer-reviewed international journals. He is a recipient of young scientist award of Department of Atomic Energy, Indian Science Congress Association (ISCA) and National Academy of Science, India (NASI). In recognition of his work, he was selected as a Member of Indian National Young Academy of Sciences (INYAS), and National Academy of Sciences, India (NASI) recently. Prof. Singh is also a member of prestigious Global Young Academy, Berlin, Germany.