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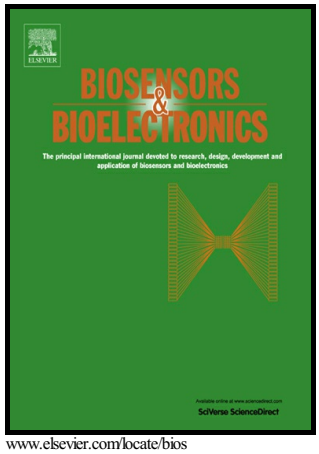

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Simple and label-free pathogen enrichment via homobifunctional imidoesters using a microfluidic (SLIM) system for ultrasensitive pathogen detection in various clinical specimens

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ABSTRACT

Diseases caused by pathogenic microorganisms including bacteria and viruses can cause serious medical issues including death and result in huge economic losses. Despite the myriad of recent advances in the rapid and accurate detection of pathogens, large volume clinical samples with a low concentration of pathogens continue to present challenges for diagnosis and surveillance. We here report a simple and label-free approach via homobifunctional imidoesters (HIs) with a microfluidic platform (SLIM) to efficiently enrich and extract pathogens at low concentrations from clinical samples. The SLIM system consists of an assembled double microfluidic chip for streamlining large volume processing and HIs for capturing pathogens and isolating nucleic acids by both electrostatic and covalent interaction without a chaotropic detergent or bulky instruments. The SLIM system significantly increases the enrichment and extraction rate of pathogens (up to 80 % at 10 CFU (colony forming unit) in a 1 mL volume within 50 min). We demonstrated its clinical utility in large sample volumes from 46 clinical specimens including environmental swabs, saliva, and blood plasma. The SLIM system showed higher sensitivity with these samples and could detect pathogens that were below the threshold of detection with other methods. Finally, by combining our SLIM approach with an isothermal optical sensor, pathogens could be detected at a very high sensitivity in blood plasma samples within 80 min via enrichment, extraction and detection steps. Our SLIM system thus provides a simple, reliable, cost-effective and ultrasensitive pathogen diagnosis platform for use with large volume clinical samples and would thus have significant utility for various infectious diseases.

Keyword: Pathogen Diagnosis, Enrichment, Microfluidic system, Clinical Specimens, Point-of-care testing

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