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Development of Electrochemical Biosensor Based on Dendrimer-Magnetic Nanoparticles for Detection of Alpha-Fetoprotein

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Abstract : Liver cancer is one of the most common malignant tumors with poor prognosis. This is because liver cancer does not exhibit any symptoms in early stage of disease. Increased serum level of AFP is clinically considered as a diagnostic marker for liver malignancy. The present diagnostic modalities include various types of immunoassays, radiological studies, and biopsy. However, these tests undergo slow response times, require significant sample volumes, achieve limited sensitivity and ultimately become expensive and burdensome to patients. Considering all these aspects, electrochemical biosensors based on dendrimer-magnetic nanoparticles (MNPs) was designed. Dendrimers are novel nano-sized, three-dimensional molecules with monodispersed structures. Poly-amidoamine (PAMAM) dendrimers with eight $–NH_2$ groups using ethylenediamine as a core molecule were synthesized using Michael addition reaction. Dendrimers provide added the advantage of not only stabilizing Fe_3O_4 NPs but also displays capability of performing multiple electron redox events and binding multiple biological ligands to its dendritic end-surface. Fe_3O_4 NPs due to its superparamagnetic behavior can be exploited for magneto-separation process. Fe_3O_4 NPs were stabilized with PAMAM dendrimer by in situ co-precipitation method. The surface coating was examined by FT-IR, XRD, VSM, and TGA analysis. Electrochemical behavior and kinetic studies were evaluated using CV which revealed that the dendrimer-Fe_3O_4 NPs can be looked upon as electrochemically active materials. Electrochemical immunosensor was designed by immobilizing anti-AFP onto dendrimer-MNPs by gluteraldehyde conjugation reaction. The bioconjugates were then incubated with AFP antigen. The immunosensor was characterized electrochemically indicating successful immuno-binding events. The binding events were also further studied using magnetic particle imaging (MPI) which is a novel imaging modality in which Fe_3O_4 NPs are used as tracer molecules with positive contrast. Multicolor MPI was able to clearly localize AFP antigen and antibody and its binding successfully. Results demonstrate immense potential in terms of biosensing and enabling MPI of AFP in clinical diagnosis.

Keywords : alpha-fetoprotein, dendrimers, electrochemical biosensors, magnetic nanoparticles
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