PVA-based nanobiosensor for ultrasensitive detection of folic acid by fluorescence quenching

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The present work demonstrates \textit{in vitro} folic acid sensing with a polyvinyl alcohol (PVA) based hybrid hydrogel as an efficient and cost effective fluorescence quenching based sensor. This new sensor PVA-tryptophan-CdTe QDs (PTQ), exhibited better sensing efficiency with an excellent limit of detection (0.57 pg/ml) compared to commercially available ELISA kits. The excellent sensitivity was attributed to a combination of a strong Photoinduced Electron Transfer process and an Inner Filter Effect in the sensor-folic acid interaction. The real time sensing applications of the sensor was investigated for folic acid present in the blood serum samples of healthy mice and human; and cancer infected mice and human. Our sensor exhibited efficient sensing for folic acid in the blood serum samples of acute myeloid leukemia [limit of detection (LOD) 42.29 ng/ml] and ovarian cancer effected patients (LOD 365 ng/ml). The LOD value indicates that our sensor is highly efficient toward sensing of FA in acute myeloid leukemia as its LOD value lies below 110 ng/ml. Such works will help to bring together material chemists, biologists and clinicians in a single platform to develop cost effective, photostable and specific assays for diagnostic purposes.

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1. Introduction

Folic acid (FA) is the synthetic form of the naturally occurring folate, a member of Vitamin B family. It is a water soluble compound which is present in the substrates and coenzymes involved in the acquisition, transport and enzymatic processing of one carbon unit for aminoacid and nucleic acid metabolism [1]. Some previous studies suggest that FA together with vitamin B12 can participate in the synthesis of DNA and RNA [2]. In addition, it plays pivotal role in copying RNA from DNA. Thus, it is essential for accurate replication of DNA [3]. It is well known that FA concentration varies significantly in a number of health disorders like in cancer, cardiovascular disease, alzheimer’s disease, depression, reduced cognition and neural tube defect (NTD) [4–7]. Low or high level concentrations of FA in blood serum, plasma and red blood cells are exploited as an efficient biomarker for diagnosis of various disease conditions.

Since FA is essential for proper functioning of numerous biological functions in human, it is pertinent to develop simple and sensitive methods for detection of FA in biological systems. In this regard, researchers round the globe have developed different kinds of sensor arrays viz. electrochemical sensors, ELISA etc. ELISA kit, which is widely used immunoassay technique with many advantages like high specificity and high sensitivity [8]. But such kits have certain disadvantages like long reaction time, effect of temperature, unstable upon exposure to light etc. [8]. However, in recent years, fluorescence based assays have emerged as an attractive alternative choice for such purposes. In this regard, fluorescence based assays have their own advantages and disadvantages. The main advantages are ability of signal multiplication and amplification, low cost and fast response time while disadvantages are less specificity, temperature effect, ionic concentration effect, light scattering etc. [9]. Keeping these in mind, an effort has been made toward the design of an efficient fluorescence based assay for FA sensing. There also exist few reports where fluorescence quenching based processes has been employed for FA sensing [10–17]. Hu et al. reported the fabrication of graphene oxide and Ag nanoparticles for the detection of FA. Yan et al. reported the use of gold nanoclusters for FA and Zhang et al. reported the application of polyethyleneimine-capped silver nanoclusters for FA [14–16]. However, most of the reported works suffer from many drawbacks like high fabrication cost, expensive precursors, devoid of long term stability, poor detection limit and poor selectivity. Taking these and the cost effectiveness of the sensor into consideration, we have selected a cheap and readily available precursor

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