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Noninvasive glucose measurement by fluorescence quenching of non toxic gold nanoparticles

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ABSTRACT

Effects of interaction of human body compatible gold nanoparticles with glucose on fluorescence emission spectra of the nanoparticles are investigated experimentally. It is observed that nanoparticles' fluorescence peak quenches and blue shifted because of such interaction. This procedure is sensitive even to low difference of glucose concentration. The results suggest that glucose could seriously affect the optical properties of gold nanoparticles. Furthermore, a linear range of relative shift of different fluorescence spectrum's peaks is obtained. Furthermore, comparison of fluorescence and absorption results shows that the former technique is as much as 20 times more sensitive to the variation of glucose concentration.

1. Introduction

With advent of using nanoparticles in medicine and biology, there have been increasing interests in understanding interactions of such particles with various molecules [1–4]. Interaction between nanoparticles and biological cells may be useful to diagnose and control different diseases [5]. One of the most common diseases which can lead to serious complications, such as cardiovascular diseases, retinopathy, nephropathy, and neuropathy is "Diabetes" which annually takes the lives of 3.4 million people. Statistics predicts that in 2025 more than 380 million people will suffer from Diabetes across the world [6].

The oldest technique for diabetes detection, which is about one century old, is urine test. Nowadays blood glucose measurement is performed by punching patient's finger with a sharp needle and instilling a drop of blood on a special paper. This method is invasive, painful, with high risk of infection, and without enough accuracy. On the other hand, blood glucose measurement should be often performed several times per day. So it is desirable to find a way in order to fabricate a precise and noninvasive household device.

Among different attempts for exact measurement of blood glucose measurement, those based on optical methods are more accurate and with larger diversity [7]. In optical methods, different techniques based on near infrared absorption [8], mid-infrared absorption [9], Raman shift [10], photo acoustic near-infrared absorption [11], and optical rotation [12] are introduced. Using those techniques, inherent characteristics of glucose molecules, directly and independently from other ingredients of blood, are determined. On the other hand, in some methods, such as measuring tissue scattering coefficient [13], ISF (Interstitial fluid; the fluid found in the intercellular spaces) refractive index, and sound propagation in tissue [14], effect of glucose on optical properties of tissue are studied. Furthermore, most of optical methods mentioned above, deal with optical absorption and Rayleigh scattering.

In the majority of new noninvasive optical techniques used in clinical applications to detect disease progression, nanoparticle traces are often used. In the past decade, nanoscience and technical progress to fabricate different nanoparticles have created new horizons in nonlinear optical measurement [15]. Different types of nanaoparticles can be used in optical techniques, such as fluorescence spectroscopy [16] and surface-enhanced Raman scattering [17]. On the other hand, spectroscopic techniques based on fluorescence of nanoparticles are more advantageous with respect to other techniques, such as absorption spectroscopy. For example, in the former technique, in contrast to absorption techniques; fluorescence and illumination wavelengths are different from each other, also detection and illumination systems are not in a line which results to larger signal to noise ratio. Furthermore, fluorescence technique offers greater range of linearity [18].

Another advantage of the proposed technique is that for smaller nanoparticles used in fluorescence spectroscopy, surface to volume ratio increases, and the quantum efficiency of fluorescence intensity is over a million times higher than that of the bulk metal [19]. Such increase is due to excitation of surface Plasmon in metals [20].

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In this paper we introduce a new method based on application of metallic nanoparticles, without need on CTAB (Cetyl trimethylammonium bromide, $C_{19}H_{42}BrN$) is a cationic detergent which extensively use in nanoparticle fabrication process) surfactant [21]. We study fluorescence spectra of the synthesized nanoparticles and their interaction with glucose to diagnose glucose concentrations. The synthesized nanoparticles are non-toxic and compatible with human body, which makes them interesting in medical applications. Furthermore, since the fluorescence spectrum emitted by nanoparticles changes when they attach to glucose, their use as a noninvasive agent in determining of glucose concentration seems promising.

The proposed technique is fast and noninvasive and can be used in vivo, while others are time-consuming and complex and need costly chemical reaction. Furthermore, the most important drawback of other methods is usage of CTAB during synthesis of nanoparticles, which make them useless as a sensor in human body [22,23]. Since the substantial step in glucose measurement is interaction of nanoparticle and glucose, the nontoxic fabricated nanoparticles by this method can be prepared in form of a cream to be adsorbed from skin which makes the technique noninvasive.

2. Material and methods

2.1. Chemicals and reagents

Due to the effects of the size and the shape of a nanoparticle on its emitted fluorescence spectra, it is important to synthesize and characterize it for possible application in blood glucose detection. Different techniques, e.g. electrolytic, chemical reduction, and photo-reduction can be used for that purpose. The important drawback of all these three methods is their need for surfactants, such as CTAB, to induce anisotropic particle growth in aqueous solution. Since the substance is toxic and even very low quantity of it is harmful for human body, one should find a nontoxic synthesis method of fabrication. In this study we introduce a technique to synthesize gold nanoparticle without using any CTAB.

An element can be inherently toxic, e.g., silver nanoparticles [24], or becomes toxic during manufacturing process because of using toxic materials such as CTAB [22]. On the other hand, gold is not toxic inherently and we did not use any toxic substance in manufacturing process. Therefore, fabricated gold nanoparticles are immune and biocompatible. Furthermore, Ghanavi et al. used such nontoxic nanoparticles as sensor for in vivo [27]. They estimate cell cytotoxicity/viability, the cells were plated at a density of 1×104 cells/well in a 96-well plate at 37 °C in 5%CO_2 atmosphere. After 24 h of culture, the medium in the wells was replaced with fresh medium containing nanoparticles in varying concentrations.

For measuring of viability of cell dye solution used and cell viability (%) determined. Reaction sample is prepared by mixing a polar solvent and saturated fatty acid, e.g. Stearic acid ($C_{18}H_{36}O_2$), and $HAuCl_4$ as a metallic salt. Then, a mixture of reducing agents is prepared by use of Ascorbic acid. For the next step, these two mixtures are combined and heated solvo-thermally for 10–30 min in 50–160 °C.

For preparation of glucose with different concentration, we solve different amount of glucose in high quality distilled water.

2.2. Apparatus and measurement

Transmission electron microscope (TEM) of gold nanoparticle was obtained by using an electron microscope (JEOL, Japan), operating at 120 kV. The UV–Vis and fluorescence spectra of the samples were taken both using Perkin Elmer spectrophotometer (Perkin Elmerλ20 and Perkin Elmer 50.2). A quartz cell of 1 cm optical path length was used for all spectrum measurements. The nanoparticles sample was prepared as mentioned above and were dissolved with different concentration of glucose solution (varying from 0 to 11.11 mM). Then, samples were contained in 1-cm path length quartz, and the fluorescence intensities of the solution were recorded by spectrophotometer.

3. Results and discussion

Gold nanoparticles are fabricated by the method explained in the last section. Fig. 1 illustrate TEM image of the fabricated nanoparticles. One can estimate the size of the nanoparticles to be less than 100 nm in diameters.

After characterizing the size of the fabricated nanoparticles, we measure their absorption spectra. Fig. 2 shows UV–Vis absorption spectra of the fabricated gold nanoparticles acquired by a spectrophotometer (Perkin Elmerλ20). The scan range of the spectrophotometer varies from 400 to 700 nm. The observed peak around 520 nm is related to the resonance of the surface Plasmon of the gold nanosphere [18].

Next, the nanoparticles are impregnated to the glucose with different concentrations. Then, both, bare gold nanoparticles and those impregnated to glucose are separately illuminated and excited by light from a spectrophotometer (Perkin Elmer50.2) with wavelength of 260 nm. After excitation, the nanoparticles

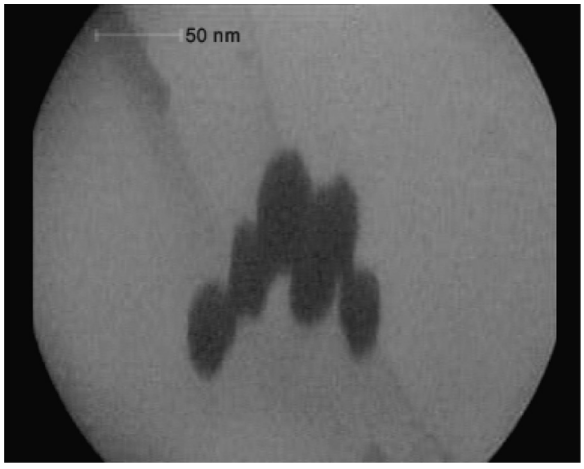

Fig. 1. TEM image of gold nanoparticles.

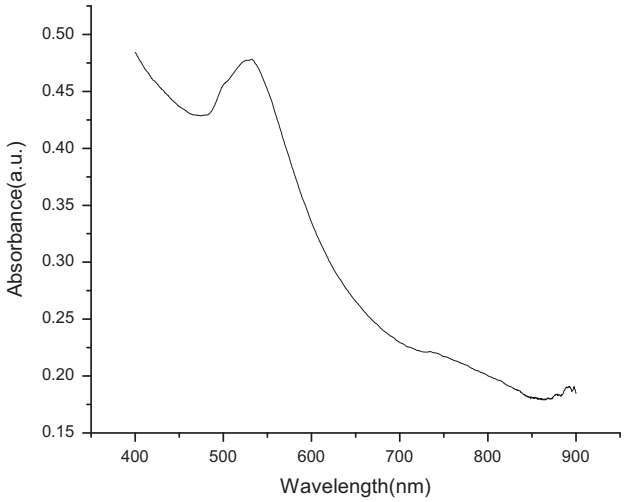

Fig. 2. UV–Vis absorption spectra of gold nanosphere.