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NANOTECHNOLOGY AND THE DIAGNOSIS OF TYPHOID FEVER

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For effective management of typhoid, diagnosis of the disease must be done with speed and accuracy. Laboratory diagnosis of typhoid fever requires isolation and identification of *Salmonella* enterica serotype *Typhi*. In many areas where the disease is endemic, laboratory capability is limited. Recent advances in molecular immunology have led to the identification of sensitive and specific markers. Currently, alternative methods for biological molecular analysis are enzyme immunoassay, surface plasmon resonance and electrochemical immunoassay. With the development of nanotechnology, various nanoparticles and nano-quantum dots have been used as labels to enhance the sensitivity of the electrochemical immunoassay technique.

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1. Introduction

Typhoid fever remains a serious health problem in many regions of the world. The major causes of typhoid fever are caused by *Salmonella enterica* serovar *Typhi* (*S*.Typhi) and also, to a lesser extent, strains of *S*. enterica belonging to serovars Paratyphi (*S*. Paratyphi) A, B and C. This is a highly adapted, human-specific pathogen occurring more frequently in underdeveloped regions of the world where overcrowding and poor sanitation are prevalent.

According to the best global estimates, there are atleast 16 million new cases of typhoid fever each year, with 6,000,000 deaths [1]. Between 1-5% of patients with acute typhoid infection have been reported to become chronic carriers of the infection; depending on age, sex and treatment regimen. Furthermore this chronic carrier state has also been implicated in causation of carcinoma of the gall bladder.

The diagnosis of typhoid fever on clinical grounds is difficult, as the presenting symptoms are diverse [2] and similar to those observed with other common febrile illness, such as malaria and nonsevere dengue fever.

The isolation of serotype *Typhi* from blood remains the method of choice for the laboratory diagnosis [3].

Classical methods are usually used to detect *S. typhi*, including culturing [4, 5], serological methods, such as slide agglutination and the Widal test [6], and polymerase chain reaction (PCR) [7,8]. Even though these methods can provide highly sensitive results for both qualitative and quantitative analysis, they are quite hard- and time-consuming to perform.

With the above-mentioned drawbacks, efforts to develop a method for *S*. typhi determination with increased sensitivity and selectivity and a reduction in analysis time needs to be proposed. Currently, alternative methods for biological molecular analysis are enzyme immunoassay [9, 10], surface plasmon resonance [11], and electrochemical immunoassay [12–14]. In particular, the use of electrochemical immunoassay has attracted considerable interest for *S*.

typhi determination because of its inherent simplicity, high sensitivity, inexpensive instrumentation, and miniaturization.

With the development of nanotechnology, various nanoparticles [15, 16] and nano-quantum dots [17, 18] have been used as labels to enhance the sensitivity of the electrochemical immunoassay technique.

Recently, copper, silver, and gold-enhanced colloidal gold have been reported for immunoglobin G (IgG) determination, which is the model of electrochemical immunoassay with low detection limits ranged from 1.0 ng/mL to 0.25 pg/mL [19–21]. The metal-enhanced colloidal gold electrochemical stripping metalloimmunoassay combines the high sensitivity of stripping metal analysis with the remarkable signal amplification resulting from the catalytic precipitation of metals onto the gold nanoparticles [21–23].

4. Conclusions

Nanotechnology is an emerging field that is potentially changing the way we treat and diagnose diseases.The metal-enhanced colloidal gold has not been previously applied to the detection of bacterial cells in real samples, especially for the detection of *S. typhi*. Therefore, one can employ the electrochemical stripping-metallo-immunoassay based on a copper, silver or gold-enhanced – colloidal gold nanoparticle label for the determination of *S. typhi in* real samples, which will be useful in the diagnosis, follow-up treatment, and controlling in advance the epidemic disease of typhoid fever. The coupling of gold nanoparticles with the advantages of electrochemical stripping analysis can easily be extended for detecting other bacterial cells in real samples with high accuracy and sensitivity.

As someone has truly predicted, there has been plenty of room at the bottom to modify and enhance existing technologies by controlling material properties at the nanoscale. Therefore, with sufficient time and research, the promise of nanotechnology based disease diagnosis may become a reality.

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