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Surface plasmon resonance based selective and sensitive colorimetric determination of azithromycin using unmodified silver nanoparticles in pharmaceuticals and human plasma

Vijay D. Chavada [a], Nejal M. Bhatt [a], Mallika Sanyal [b], Pranav S. Shrivastav [a,*]

[a] Department of Chemistry, School of Sciences, Gujarat University, Ahmedabad 380009, Gujarat, India
[b] Department of Chemistry, St. Xavier's College, Navrangpura, Ahmedabad 380009, Gujarat, India

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ABSTRACT

In this article we report a novel method for colorimetric sensing and selective determination of a non-chromophoric drug-azithromycin, which lacks native absorbance in the UV–Visible region using unmodified silver nanoparticles (AgNPs). The citrate-capped AgNps dispersed in water afforded a bright yellow colour owing to the electrostatic repulsion between the particles due to the presence of negatively charged surface and showed surface plasmon resonance (SPR) band at 394 nm. Addition of positively charged azithromycin at a concentration as low as 0.2 μM induced rapid aggregation of AgNPs by neutralizing the negative charge on the particle surface. This phenomenon resulted in the colour change from bright yellow to purple which could be easily observed by the naked eye. This provided a simple platform for rapid determination of azithromycin based on colorimetric measurements. The factors affecting the colorimetric response like pH, volume of AgNPs suspension and incubation time were suitably optimized. The validated method was found to work efficiently in the established concentration range of 0.2–100.0 μM using two different calibration models. The selectivity of the method was also evaluated by analysis of nanoparticles-aggregation response upon addition of several anions, cations and some commonly prescribed antibiotics. The method was successfully applied for the analysis of azithromycin in pharmaceuticals and spiked human plasma samples with good accuracy and precision. The simplicity, efficiency and cost-effectiveness of the method hold tremendous potential for the analysis of such non-chromophoric pharmaceuticals.

1. Introduction

Azithromycin (AZT) is an azalide, a subclass of macrolide antibiotics and is one of the world's best-selling antibiotics [1]. AZT is derived from erythromycin yet it shows higher activity against gram-negative organisms preserving good activity against gram-positive microorganisms. Due to its dibasic nature, AZT possesses greater oral bioavailability and improved acid stability compared to erythromycin. It shows excellent pharmacokinetic properties which includes extensive distribution within tissues and high drug concentrations within cells. AZT prevents bacterial growth by blocking bacterial protein synthesis. This action stops the growth of the bacteria and relieves symptoms of the bacterial infection, which include inflammation and pain. Hence, AZT is useful for the treatment of upper and lower respiratory tract infections, skin infections, intestinal infections and sexually transmitted infections [2,3]. The most widely used simple and economical methods for the quantification of AZT are based on spectrophotometric measurements. These methods involve formation of complex between AZT and the reagent by charge transfer and\or ion-pair interactions [4]. Further no direct spectrophotometric measurement is reported for AZT, apparently due to its non-aromatic structure. Other detection and/or quantitative methods are largely based on chromatographic techniques [5–9].

Owing to the unique optical sensing properties of noble metal nanoparticles, particularly those of silver (AgNPs) and gold (AuNPs), they find widespread use in almost every field of chemistry [10–13]. Among these AgNPs has a significant advantage over AuNPs due to their high extinction coefficients and low cost, which make them more favourable compared to AuNPs [14,15]. Basically, the synthesized AgNPs remain in a dispersed state as a result of electrical repulsion among the negatively charged citrate molecules coated on the particle surface, and thus exhibit a bright yellow colour. The colour and optical properties of unmodified AgNPs can be controlled by triggering the surface charges upon reacting with some target molecules. This generally results in the loss of surface charge, aggregation of the AgNPs and thereby changes in colour. The same strategy has been extensively utilized for the colorimetric sensing of various metal ions [16,17] as well as drug molecules [18,19] and bio-molecules [20]. This fundamental strategy was adopted for the present work by explicitly balancing the surface charge of the AgNPs in presence of a target drug to obtain a response

* Corresponding author.
E-mail address: pranav_shrivastav@yahoo.com (P.S. Shrivastav).

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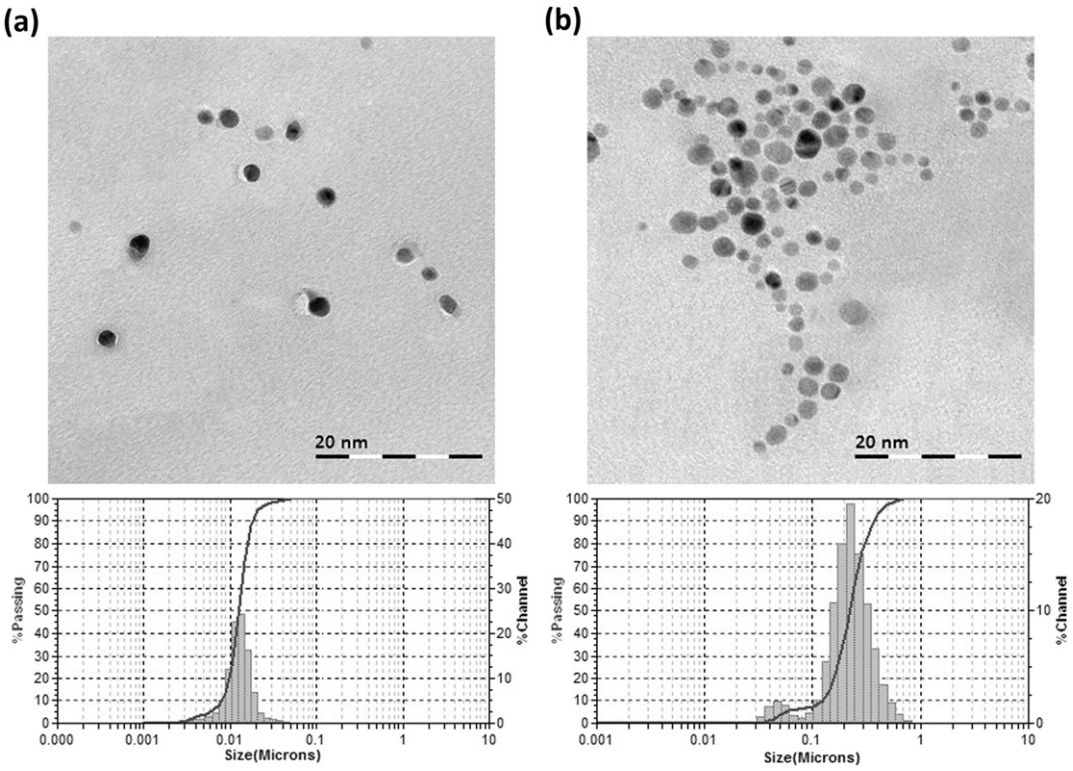

Fig. 1. TEM images and DLS histograms of AgNPs in the (a) absence and (b) presence of azithromycin.

which is visible to the naked eye. Till now, there are no reports on the use of metal nanoparticles for the colorimetric sensing of azithromycin. Therefore, the main objective of the present work was to fabricate a visual colorimetric sensor for highly facile, selective, sensitive and cost-effective determination of azithromycin based on selective aggregation reaction between azithromycin and unmodified AgNPs.

2. Experimental

2.1. Chemicals and materials

Reference standard of azithromycin dihydrate (99.72%) and other drugs used for interference study, erythromycin dihydrate (99.23%), clarithromycin (99.35%), roxithromycin (98.97%) and doxycycline (99.82%) were procured from Clearsynth Laboratories Pvt. Ltd., (Mumbai, India). HPLC grade methanol, dichloromethane, ethyl acetate and analytical reagent grade sodium hydroxide, hydrochloric acid, trisodium citrate, $NaBH_4$ were purchased from E. Merck (Mumbai, India). Analytical grade metal salts were obtained from CDH Pvt. Ltd. (New Delhi, India). Water used in the study was prepared from Milli-Q water purification system from Millipore (Bangalore, India). Twenty tablets of Azintas® (Intas Pharmaceuticals Pvt. Ltd., India) and Azipro® (Cipla Ltd., India) claimed to possess 250 mg of AZT, were purchased from a local pharmacy store. Blank human plasma was obtained from Supratech Micropath (Ahmedabad, India) and was stored at −20 °C until use.

2.2. Instrumentation

A Jasco V-570 double beam spectrophotometer (Kyoto, Japan) with a matched pair of 10 mm quartz cells were used for spectral

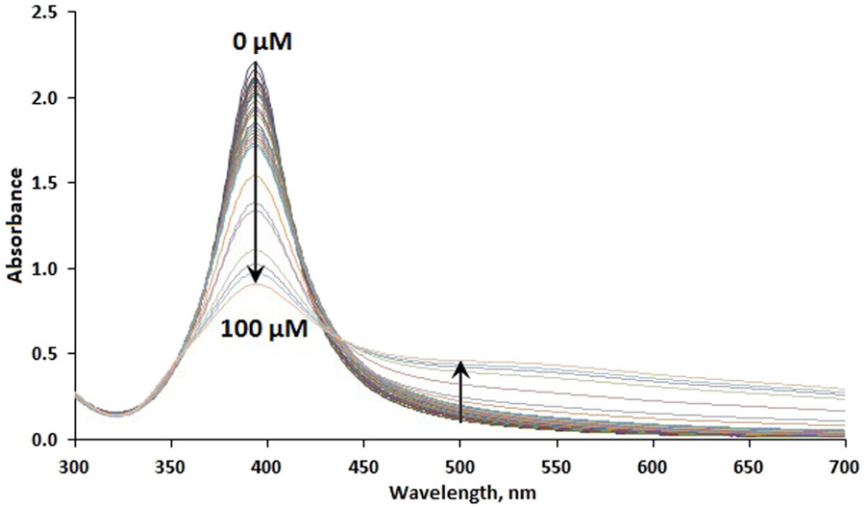

Fig. 2. UV absorption spectra of AgNPs with increasing concentration of azithromycin (0–100 µM).