Research Article

Hongling Wang, Xuejing Si, Tunhua Wu*, Ping Wang*

Silver nanoparticles enhanced fluorescence for sensitive determination of fluoroquinolones in water solutions

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Abstract: A new type of silver nanoparticle (AgNPs) was prepared with simple and fast methods and low-toxic compounds. With the addition of different concentrations of AgNPs, the effects of AgNPs on the fluorescence properties of three different kinds of fluoroquinolones (enrofloxacin ENR, lomefloxacin LMF and norfloxacin NOR) in water solutions were studied, respectively. The experimental results demonstrated that the fluorescence intensity for each of the fluoroquinolones (FQ) was firstly enhanced and then quenched with the increased concentration of AgNPs in water solutions. The possible mechanisms about the AgNPs on the fluorescence behaviors of each FQ were also investigated, respectively. In addition, new silver enhanced nanoparticles materials fluorescence methods were established for the separate determination of ENR, LMF and NOR in water solutions. As compared with the identical control fluorimetric methods with no addition of AgNPs, the new enhanced fluorimetric methods were also investigated, respectively. The experimental results indicated that the new enhanced methods could detect lower concentrations of ENR, LMF and NOR in water solutions. Moreover, the newly enhanced fluorimetric methods were validated and successfully applied for the quantitative assay of ENR, LMF and NOR in different kinds of medicinal preparations, respectively.

Keywords: Metal-enhanced fluorescence; Silver nanoparticles; Fluorimetry; Enrofloxacin; Lomefloxacin; Norfloxacin.

1 Introduction

Metal-enhanced fluorescence (MEF) is usually generated by the interactions of fluorophores with metal. It has been widely used in many research areas, including protein labeling, single molecule detection, immunoassay, fluorescence sensors and the detection of DNA [1-3]. In order to achieve MEF, metal nanomaterials, especially silver and gold, are considered as the critical factor for the fluorescence enhancement of fluorescent chemicals. Due to the wide application of MEF, many studies about precious metals have been correspondingly increased [4,5]. However, development of enhancing fluorescence by looking for new nanomaterials is still lacking. It has been reported that most of those studies based on MEF have been performed on the surface of solid substrates [6]. However, most of the life activities, physiological and biochemical reactions are carried out in water solutions [7]. Therefore, it is of great significance to study the effects of several metallic nanomaterials through the MEF in the water solutions [7, 8]. Silver nanomaterials (AgNPs) have been widely used due to their short absorption wavelength and wide wavelength range about their applications [9,10]. In addition, a large amount of research has been devoted to the synthesis and characterization of stable AgNPs [11-14]. However, most of the conventional methods for the synthesis of AgNPs always use organic solvents, which might be prone to secondary pollution in the environment [11,13,14].

As the third generation of quinolone antibiotics, the drugs of FQs are effective against both Gram-negative and Gram-positive bacteria. One example is ciprofloxacin, one of the most widely used antibiotics worldwide [17,18]. Thus, most of these drugs have led to a significant increase into the environment as prototypes or active metabolites in recent years. In addition, some experimental results demonstrated that these FQs might change the structures of microorganisms in the soil and aquatic environment, which eventually lead to drug resistant bacteria [19,20].

*Corresponding author: Tunhua Wu, First Affiliated Hospital of Wenzhou Medical University, Wenzhou 325035, China; Ping Wang, School of Pharmaceutical Sciences, Wenzhou Medical University, Wenzhou, 325035, China E-mail: me_54@163.com
Hongling Wang, Xuejing Si, School of Pharmaceutical Sciences, Wenzhou Medical University, Wenzhou, 325035, China

According to the reports, the aquatic environment serves as one of the most important sinks of trace FQs [21]. Up until now, many analytical techniques have been used for the detection of FQs. For instance, high performance liquid chromatography [22,23], capillary electrophoresis [24,25], liquid chromatography tandem mass spectrometry [26,27] and ultraviolet spectrophotometry [28,29]. Nevertheless, most of the above methods tend to require expensive and sophisticated instruments and complicated pretreatment processes. Among those methods, the fluorimetry is relatively simple, time-saving, sensitive and low-cost. It is reported that almost all the FQs contained in the conjugated heterocyclic ring could produce fluorescence. However, because of their low quantum yield, the fluorimetric methods are limited in the determination of FQs in water solutions. Therefore, it is very important to establish some methods for enhancing the fluorescence intensity of FQs in water solutions.

And in our previous studies, two different types of AgNPs were prepared by “green” methods. In the meantime, new AgNPs enhanced fluorescence methods were established for the determination of some fluoroquinolones and tetracyclines in water solutions, respectively [15,16]. Herein, for the first time, the sodium dihydrogen citrate and β -cyclodextrin (β -CD) as the low-toxic compounds were utilized for synthesis of a new type of AgNPs. In addition, with the increasing concentrations of AgNPs, three different kinds of FQs (enrofloxacin ENR, lomefloxacin LMF and norfloxacin NOR) (Figure 1) were investigated in water solutions, respectively. And the possible mechanisms about the AgNPs on the fluorescence behaviors of each FQ were also studied, respectively. Moreover, new silver enhanced nanoparticles fluorescence methods for the determination of trace ENR, LMF and NOR in water solutions were established, respectively. What is more, these new established fluorescence methods were validated and applied to the separate determination of ENR, LMF and NOR in medicinal preparations.

2 Materials and methods

2.1 Chemicals and instrumentations

All chemicals about ENR, LMF and NOR were of analytical reagent grade; Deionized water was used in this experiment. Stock solutions consisting of ENR, LMF and NOR were stored in a refrigerator (4 °C), respectively. The stock solutions were further diluted as working solutions prior to use. The medicinal preparations were all bought

Figure 1: Chemical structure of ENR, LMF and NOR.

from hospital in Wenzhou, China. For comparison, two different kinds of medicinal preparations of ENR injections (A and B) LMF (ear drops C and ear drops D) NOR capsules (E and F) were used.

Fluorescence measurements were performed using a spectrofluorophotometer (F-4600, Hitachi, Japan). A program was developed to obtain the values of maximum excitation wavelength (λ_{ex}) and emission wavelength (λ_{em}) at any constant fluorescence intensity value. In addition, all the UV absorption spectra were obtained using a spectrophotometer (UV-2550, Shinadzu, Japan). Moreover, the morphology and particle size of the AgNPs solutions were described by the transmission electron microscope (TEM, JEM-2100F, JEOL, Japan) and scanning electron microscope (SEM, LEO-1530, Oxford, UK). All experiments were carried out at room temperature.

2.2 Preparation of the AgNPs solutions

A new type of AgNP was prepared as follows: a certain amount of tartaric acid was added to the sodium dihydrogen citrate for preparation of the sodium tartrate

solutions. Briefly, in a 250-ml three-necked flask, 0.25 g β -CD, 1 ml of 38.8 mol/L sodium tartrate, 2 ml of 0.1 mol/L silver nitrate, and 47 ml of ultrapure water were mixed and heated; the reaction was vigorously stirred at 100°C for 1 h. Finally, the yellow AgNPs (1×10^{-3} mol/L) solutions were obtained and stored at 4°C. All experiments were carried out at room temperature.

2.3 Establishment of new silver enhanced nanoparticles materials fluorescence methods four determination of FQ in water solutions

In this work, the fluorescence behaviors of the three kinds of FQs dissolved in the AgNPs solutions were investigated, respectively. Moreover, with the addition of AgNPs in the appropriate dilution, the strongest fluorescence intensities of each FQ were observed. Finally, new enhanced fluorometric intensities of each FQ were observed. Finally, the new silver enhanced nanoparticles fluorescence method for determination of each FQ was established in water solutions, respectively.

2.4 Analysis of each FQ in the medicinal preparations

In this section, the procedures for the medicinal preparations of each FQ were as follows: (1) A certain volume of the ENR injections with two different kinds were diluted by the deionized water and added with a certain amount of AgNPs. Then the mixture for each of the ENR injections was directly determined of their fluorescence intensity, respectively. (2) The ear and eye drops of LMF were separately diluted by the deionized water by adding of certain volume of AgNPs. Then the mixed solution of the ear and eye drops was placed into the fluorescence spectrophotometer for direct determination of their fluorescence intensity, respectively. (3) Ten pieces of NOR capsules with two kinds were separately selected and ground into homogenized powders. Then the homogenized powders for the ten pieces of NOR capsules were weighted, and the content for each of the capsule for each of the NOR capsules could be accurately measured, respectively. Then the powders were diluted by the deionized water with 5×10^{-5} mol/L sodium dihydrogen citrate solutions, respectively. In addition, the mixed solutions for each of the NOR capsules were separately filtered through the membranes. And some volume of the filtered product

Table 1: Performance date for determination of ENR, LMF and NOR in aqueous solutions.

Method	Liner range (mg L ⁻¹)	Calibration equation	Correlation coefficient	Detection limit (μg L ⁻¹)
1	0.10-0.60	$y^b=15915x^a+452.7$	R=0.9993	0.14
2	0.0050-0.30	$y=31963x+17.911$	R=0.9993	0.058
3	0.10-0.70	$y=13476x-273.71$	R=0.9991	0.19
4	0.050-0.50	$y=17283x-11.639$	R=0.9993	0.15
5	0.050-0.50	$y=15105x-150.01$	R=0.9991	0.14
6	0.010-0.45	$y=21131x+151.89$	R=0.9997	0.12

1: Fluorimetric method for determination of ENR with no addition of AgNPs in water solutions

2: New silver enhanced nanoparticles materials fluorescence method for determination of ENR in water solutions

3: Fluorimetric method for determination of LMF with no addition of AgNPs in water solutions

4: New silver enhanced nanoparticles materials fluorescence method for determination of LMF in water solutions

5: Fluorimetric method for determination of NOR with no addition of AgNPs in water solutions

6: New silver enhanced nanoparticles materials fluorescence method for determination of NOR in water solutions

a: Concentration of each FQ (mg L⁻¹)

b: Relative fluorescence intensity of each FQ

was separately added with a certain amount of AgNPs. Finally, the fluorescence intensities for each of the NOR capsules could be obtained, respectively. Each experiment repeated three times. All of the data were obtained at room temperature.

Ethical approval: The conducted research is not related to either human or animal use.

3 Results and discussion

3.1 Characterizations of fluorescence spectra of the FQs in water solutions

Steady-state fluorescence spectra of the three kinds of FQs were firstly determined in water solutions. It was obvious that the experimental results indicated that the fluorescence excitation and emission spectra of ENR, LMF

Figure 2: Fluorescence excitation and emission spectra of each FQ mixed with AgNPs (a) and in water (b), (c): water, (d): AgNPs solution.

Figure 3: the alongside with the approximation line for each of the FQ.

and NOR were basically identical, because of their similar molecular structures. Figure 2 shows the λ_{ex} and λ_{em} of the ENR, LMF and NOR in the water solutions, respectively. As can be seen from Figure 2, the determination wavelengths for the three kinds of FQs were chosen as: ENR: $\lambda_{\text{ex}}=277$ nm, $\lambda_{\text{em}}=442$ nm; LMF: $\lambda_{\text{ex}}=285$ nm, $\lambda_{\text{em}}=450$ nm; and NOR: $\lambda_{\text{ex}}=276$ nm, $\lambda_{\text{em}}=440$ nm. Simultaneously, the autofluorescence of the solvent was very weak, which could not affect the accuracy of the measurements for the ENR, LMF and NOR in water solutions.

In the present study, a series of the standard solutions for the ENR, LMF and NOR with different concentrations were prepared and their fluorescence intensities were determined under identical experimental conditions. The results demonstrated that, within a certain range, good linear relationships were obtained between the concentrations for each of the FQ and their fluorescence intensities in water solutions. The experimental results were shown in Figure 3. Therefore, the fluorimetric methods for determination of ENR, LMF, and NOR in water solutions were established, respectively. And the experimental results were shown in Table 1.

3.2 Characterizations of the AgNPs in water solutions

In our previous studies, two different types of AgNPs were prepared by “green” methods [15, 16, 30]. In this study, a new type of AgNPs synthesized with simple technical processes and low-toxic compounds produced brilliant

Figure 4: Characteristics of AgNPs in water solutions
a: UV-vis absorption spectrum of the AgNPs
b: TEM image of the AgNPs
c: SEM image of the AgNPs.

yellow colloidal solutions. Further studies showed that the AgNPs could steadily survive at room temperature for two months. In addition, the spectra feature and the morphology of the AgNPs were investigated by UV spectrophotometry, TEM and SEM, respectively (Figure 4). As shown in Figure 4(a), the maximum absorption peak of AgNPs was located at 410 nm, which was the typical surface plasmon resonance absorption peak of AgNPs [15, 16, 31]. Figure 4(b) and Figure 4(c) showed the TEM and SEM images of AgNPs, which indicated that the AgNPs had similarly spherical particles with good sample dispersibility. Moreover, the average diameter was approximately 50 ± 1 nm.

3.3 The fluorescence behaviors for each of the FQ influenced by AgNPs in water solutions

In this section, the influences of different concentrations of AgNPs on the fluorescence behaviors of ENR, LMF, and NOR were investigated, respectively. The experimental results were shown in Figure 4. And with the increased concentration of AgNPs, the fluorescence intensity for each of the FQ was firstly enhanced and then quenched, respectively. In addition, the concentration of AgNPs was 1×10^{-3} mol/L, and the initial concentrations of the three kinds of FQs were all 0.3 mg/L. And the experiment for each of the FQ was taken in a colorimetric tube (10 mL). Thus, the concentration of AgNPs in the experiment was 1×10^{-4} mol/L, the concentrations of the three kinds of FQs were all 0.03 mg/L. Moreover, the fluorescence sensitization effect of each FQ reached the maximum with the addition of AgNPs at the volume ratio of 5%. And the fluorescence peak shapes about the excitation and emission spectra of ENR, LMF, and NOR with the addition of AgNPs were almost the same as each of the standard solutions of FQ (Figure 2).

However, the λ_{em} for each of the FQ produced a slight red-shift in water solutions (Figure 2). Moreover, with the increase concentration of AgNPs, the red-shift of the λ_{em} for each of the FQ became much bigger. With the addition of AgNPs at the volume ratio of 100%, the red-shift of the λ_{em} for ENR, LMF, and NOR reached the maximum for about 5 nm, 5 nm and 7 nm, respectively. And, the red-shift of the λ_{em} becoming much bigger for each of the FQ might be due to the increase of the polarity of the solution for each of the FQ with the increased concentration of AgNPs [32].

In this work, a little amount of β -CD was added into the preparation of the AgNPs. It has been reported that β -CD is a special material; it has a hydrophobic cavity in its

Figure 5: Effects of different volume ratios of β -CD and the mixture of AgNPs and β -CD on the relative fluorescence intensities of each FQ.

structure, which could affect the fluorescence behaviors of organic compounds [33, 34]. Our previous experimental results have shown that the stability of AgNPs can be enhanced with the addition of a little amount β -CD. And the β -CD as the protective reagent was not involved in the

Figure 6: Fluorescence emission spectra of ENR and absorption spectra of AgNPs in water solutions.

synthesis of AgNPs [15, 16, 30]. Therefore, the synthesized AgNPs solutions were actually the mixture of AgNPs and β -CD. In order to study the interference of β -CD in this experiment, the effects of β -CD at the same volume concentrations (5%) on the fluorescence behaviors of each FQ were investigated, respectively. As can be observed from Figure 4, the fluorescence effects of the β -CD on the ENR, LMF and NOR were almost negligible, respectively. Thus, the fluorescence sensitization for each of the FQ in the water solutions was achieved totally by AgNPs through the MEF.

In this study, ENR was selected as the representative of FQ in water solutions. Figure 5 shows the surface plasmon resonance absorption spectra of AgNPs and the fluorescence emission spectra of ENR. The experimental results revealed that there was seriously overlapping between the AgNPs and ENR in water solutions. It might be that the fluorescence emitted by ENR could be reabsorbed by the excess AgNPs, which might lead to the decrease of the fluorescence intensity of the ENR [35].

3.4 Mechanisms of the AgNPs on the fluorescence behaviors of each FQ in water solutions

These experimental results showed that the fluorescence intensities for ENR, LMF, and NOR were firstly enhanced and then quenched with the increased concentration of AgNPs. And the fluorescence effects of being quenched for each of the FQ were more obvious with the further concentration increase of AgNPs. Additionally, the fluorescence effects of being quenched for each of the

FQs were more obvious with the further concentration increase of AgNPs. Though there is no absorption maximum of AgNPs at 276–285 nm where the fluorescence of fluoroquinolones was excited, there is still some absorption at these wavelengths that could give a significant inner filter effect at high AgNPs concentrations, leading to an apparent decrease in fluorescence intensity; this could be the reason for the fluorescence quenching at high AgNPs concentrations. In this study, the working concentration of AgNPs was very low. The initial concentration of AgNPs was 1×10^{-3} mol/L. Based on our experimental results, the strongest fluorescence intensity for each of the FQ added to the concentration of AgNPs was about 5% (5×10^{-5} mol/L), respectively. Therefore, the additional concentration of AgNPs was very low for each of the FQ. Our experiments also showed that the fluorescence effects of the β -CD on the each of the FQ was almost negligible, respectively. Therefore, the FQ would not bind with the AgNPs by intercalation in the β -CD. Thus, the inner filter effect of AgNPs might lead to the quenching effects of all the FQs.

3.5 New enhanced fluorimetric methods for sensitive determination of each FQ in water solutions

According to the above achievements, new fluorimetric methods for separately determination of ENR, LMF and NOR were established based on the silver nanoparticles enhanced fluorescence in water solutions. And the concentration of AgNPs was added at the volume ratio of 5%. In addition, the standard equations, linear ranges, correlation coefficients, and the detection limits of the new methods are also shown in Table 1. Moreover, compared with the fluorimetric methods without the addition of AgNPs, the new established silver nanoparticles-enhanced fluorimetric methods could detect lower concentrations of ENR, LMF, and NOR in water solutions, respectively.

3.6 Detection of each FQ in medicinal preparations using the new fluorimetric methods in water solutions

In this work, the new established fluorimetric methods were employed for determination of each FQ in medicinal preparations, respectively. For comparison, the contents of ENR, LMF, and NOR in medicinal preparations produced by different manufacturers, including two different kinds of ENR injections (A and B), one kind of LMF ear (C) and

Figure 7: The emission spectra of the solutions with ENR injections (A and B), LMF ear (C) and eye drops (D) and NOR capsules (E and F).

eyedrops (D) and two different kinds of NOR capsules (E and F) were selected, respectively. In this experiment, the working solutions for the medicinal preparations of each FQ were obtained with the addition of AgNPs at the volume ratio of 5%. The experimental results are shown in Figure 7. It can be seen from Figure 7 that the fluorescence spectra of the medicinal preparations about ENR, LMF, and NOR were consistent with the fluorescence spectra of the standard solutions of ENR, LMF, and NOR. Additionally, under these optimized conditions, those coexisting substances in the medicinal preparations did not emit fluorescence, thus could not affect the determination of the contents of ENR, LMF, and NOR in medicinal preparations.

Therefore, the contents of ENR in A and B, LMF in C and D and NOR in E and F could be easily determined by the new fluorimetric methods, respectively. The experimental results were as follows: (1) The contents of ENR in A and B were 26.0 mg ml^{-1} and 95.0 mg ml^{-1} , which were generally the same with the concentrations listed in medicine specifications of the A (25.0 mg ml^{-1}) and B (100 mg ml^{-1}). (2) The contents of LMF in C and D were 2.9 mg ml^{-1} and 2.7 mg ml^{-1} , which were not different with the concentrations listed in medicine specifications of C (3.0 mg ml^{-1}) and D (3.0 mg ml^{-1}). (3) The contents of the NOR in E and F were 0.1 g per capsule and 0.1g per capsule, which had no difference to the concentrations listed in medicine specifications of E (0.1g per capsule) and F (0.1g per capsule). Therefore, the new fluorimetric methods had been widely used for direct determination the contents of three kinds of FQs in medicinal preparations. It also provides new research methods and ideas for the actual detections of such medicines.

4 Conclusions

In this assay, a new type of AgNPs was prepared for the first time with simple and easy synthetic processes, and environment-friendly compounds. In addition, the fluorescence intensities of ENR, LMF, and NOR were greatly enhanced with the addition of AgNPs at the volume ratio of 5% in water solutions, respectively. Under the optimal experimental conditions, the new silver enhanced nanoparticles materials fluorescence methods for sensitive determination of ENR, LMF, and NOR in water solutions were established, respectively. Additionally, compared with the fluorimetric method without the addition of AgNPs, the new fluorimetric method could detect lower concentrations of each FQ

in water solutions. Moreover, the possible mechanisms about the AgNPs on the fluorescence behaviors for each of the FQ has also been discussed, respectively. Finally, the new established fluorimetric methods were successfully applied to the directly determination of ENR, LMF, and NOR in two different kinds of medicinal preparations, respectively. And the preparation processes were not more complicated than most assays for FQs required. In conclusion, the studies in this work provided not only the determination of different kinds of FQs in water solutions but may also be great potential methods and ideas to determine FQs in other environmental samples.

Conflicts of Interest: We declare that we have no conflicts of interest to this work.

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