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Investigation of modified plasmon nanoparticles for theranostics application

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Abstract

This paper presents a review and analysis of the possible use of plasmonic gold nanoparticles (GNPs) for theranostics and methods for increasing the most important GNP parameters which are Raman scattering for studying Raman spectroscopy (SERS) and converting light energy into surface heating energy for photothermal therapy (PT). The purpose of this study is to find the condition under which we can obtain the maximum conversion of light energy into heat for PT and at the same time receive a sufficient signal for detecting SERS by examining and analyzing the details of existing works about modified plasmonic nanoparticles. Also, to evaluate the significance of this study for the application of theranostics and the improvement of the quality of cancer tumors treatment. Research methods will include the study, analysis, synthesis, comparison of scientific literature on the topic of the article.

Keywords: Nanoparticles, plasmon resonance, SERS, theranostics, photothermal therapy, laser irradiation;

1. Introduction

Nowadays there is a huge discussion around theranostics and about different methods of medical application [2,3,8]. It is known that plasmon GNPs can be used for cancer tumor treatment and diagnostics – two parts of theranostics. But existing methods works with two component systems: first for the diagnostics and second for the treatment. First GNPs component of this system should have smooth and spherical shape to enhance Raman scattering signal more effective for the SERS most precision detection of the tumor cells. Second component should have more oval shape and some defects inside or outside on the surface to transfer more light energy into heat during the photothermal therapy. Tumor cells are much more sensitive to temperature than other normal cells in organism and the temperature that creates during the photothermal therapy is enough to destroy the tumor cells but it is not harmful for normal cells. Now the question arises: how can we combine and maximize both effects of enhancing Raman scattering signal for SERS and conversion of the light energy into heat during photothermal therapy in one component system (using one plasmon GNPs)?

2. Materials and methods

After determining the objective of this research: "To investigate modified plasmon nanoparticles and their enhanced Raman signal and photothermal heating for theranostics application" we start looking for what other scientists have already done in the context of this topic. In fact, there are a lot of reports, reviews and articles on the applications of nanoparticles for theranostics [2,3,8]. And there is only one report that addresses the question of the simultaneous enhancement and photothermal capabilities of plasmonic nanoparticles [6]. This reports considers a facile one-pot system of gold nanoparticles to prepare dual functional gold nanoparticles.

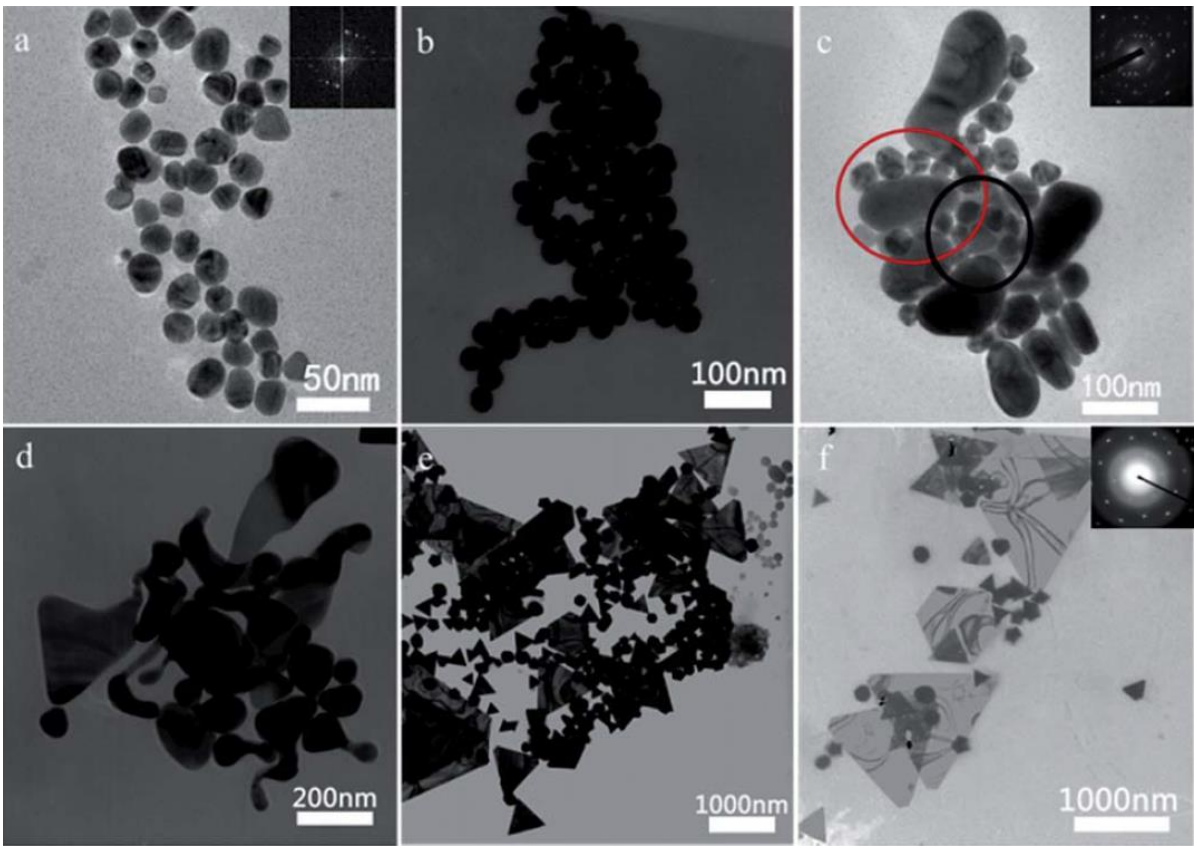

Fig. 1. TEM images of GNPs prepared in the presence of various concentrations of CTAB (a) 0.00, (b) 0.10, (c) 0.15, (d) 0.30, (e) 0.50 and (f) 5.00 mM. The solid circles indicate the core–satellite clusters [6].

This system consists of the combination of large plasmonic GNPs responsible for photothermal heating surrounded by smaller GNPs making hotspots. (Fig. 1). This second GNPs responsible of the hotspots are used for enhancing of SERS signal. The gold nanoparticles were prepared in the mixed system of the zwitterionic surfactant tetradecyldimethyl amine oxide (C14DMAO), n-hexanol (C6OH) and HAuCl4 [6].

It is known that the SERS intensity is a combination effect of chemical enhancement and electromagnetic enhancement (EM). Usually, EM enhancement is dominant since the surface plasmon may produce very strong electromagnetic fields after excitation (Fig. 2). Compared with the Raman spectrum of p-aminothiophenol (PATP) on glass, the Raman shift on gold substrates is

changed and the Raman intensity is significantly enhanced, suggesting the occurrence of chemical bonding between the thiol group in PATP and the surface of the GNPs.

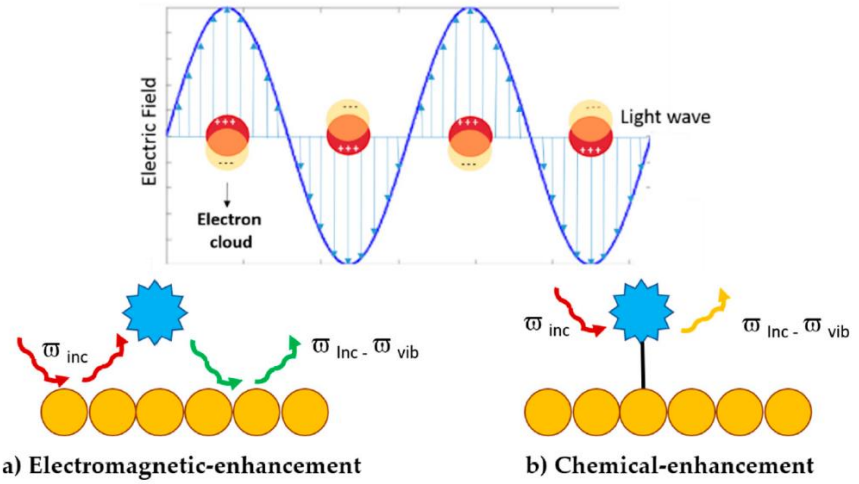

Fig. 2. The concept of electromagnetic enhancement of Raman scattering signal for SERS diagnostics [5].

To test the SERS activity of this plasmon GNPs, the authors used PATP as the probe molecule. A thin layer of the GNPs was deposited on a silicon wafer to serve as SERS substrate. (Fig. 3). It is noticed that the strongest SERS signal occurs in the 0.15 mM cetyltrimethyl ammonium bromide (CTAB) a surfactant system which is about 10 times of that obtained on the directly reduced GNPs. The SERS intensity decreases faster as the size of the GNPs increases [6].

We conclude that the authors decouple the two functions of plasmonic GNPs in one system consisting of two components for two parts of theranostics but there are no any examples of medical application of this system. Nevertheless, the novelty of this research lays on answering the question: How can we modify GNPs to increase the enhanced Raman signal and heating of nanoparticles for theranostics in one component system? To answer this question, we need to investigate PT heating and enhancement for a set of nanoparticles having different modification of structure.

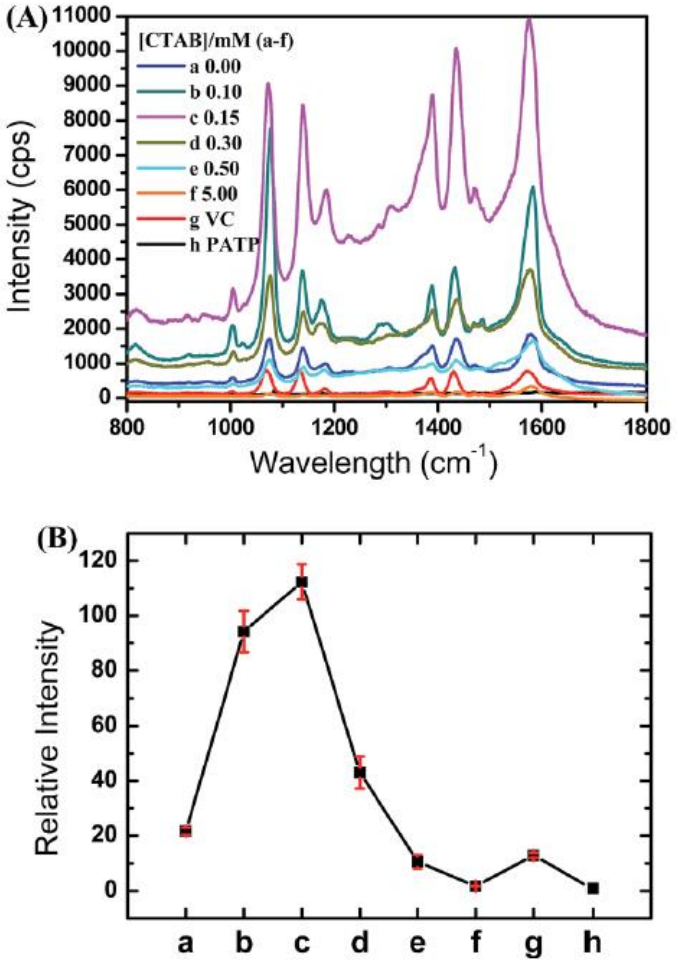

Fig. 3. (A) Raman spectrum of solid PATP (h) and SERS spectra of PATP molecules absorbed on different substrates, thin films of GNPs obtained at various concentrations of CTAB (a)–(f) and reduction by VC (g). Excitation wavelength: 633 nm; laser power: 0.34 mW; acquisition time: 10 s. (B) The comparison of the mean relative Raman signal intensity at 1078 cm^-1 obtained on different substrates. Intensity of sample (h) was used as standard [6].

So, some reports was found [1,4,9] which represent more or less the same idea of changing the crystal structure of plasmonic GNPs. It is shown on the example of two reports [3, 7]. The main idea is investigation of structural transformation of gold nanorods after they have been exposed to low-energy laser pulses by high-resolution transmission electron microscopy (HR TEM). The laser pulses caused gold nanorods melting until the threshold level. These observations suggest that short-laser pulsed photothermal melting begins with the creation of defects inside the nanorods followed by surface reconstruction and diffusion and minimizing of their surface energy (Fig. 4, 5).

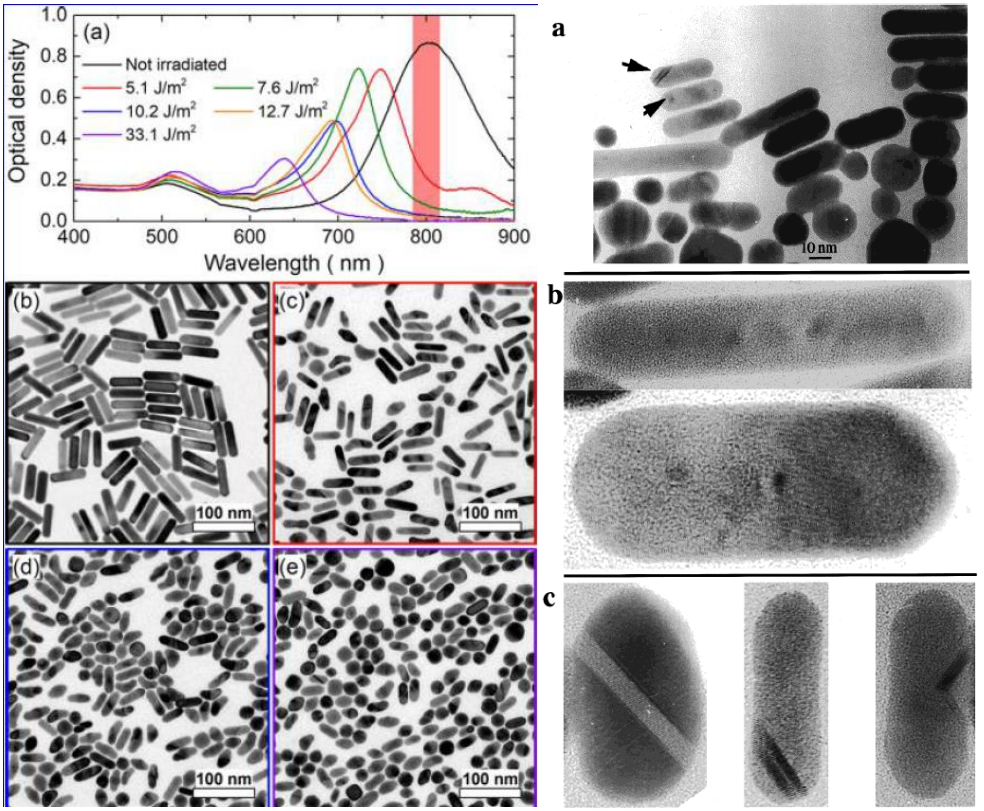

Fig. 4. (a) HRTEM image of gold nanorods after exposure to femtosecond laser pulses with a fluence of 1 mJ cm^-2 (0.5 íJ per pulse). The nanorods show point defects and twins as indicated by arrowheads in (a). This is more clearly seen after further photographic enlargement of individual particles in (b) and (c). (b) shows two examples of nanorods with point defects, while (c) shows three twinned particles [4].
Fig. 5. (a) Optical absorption spectra before and after irradiation at different fluences. The red vertical bar represents the spectral width of the laser pulses. Transmission electron microscopy images of AuNRs (b) before and after irradiation with a laser fluence of (c) 5.1 J/m2, (d) 10.2 J/m2, and (e) 33.1 J/m2 [9].

Regarding the difference in the melting behavior those authors conclude that it is possible to obtain different results after laser irradiation of these gold nanorods. In fact, the surface atoms are less stable, they give rise to surface melting. During the photothermal heating it can cause gradient of the temperature around the surface. So, this leads to the conclusion that this system is less stable and difficult to control melting of the nanorods not to exceed the threshold level.

3. Discussion

Since we came to the conclusion that it is possible to change the crystallinity of GNPs using laser irradiation, it was decided to make a review of existed possible methods. However, the data presented in the researched reports enable us to conclude that GNPs crystallinity can be slightly modified by laser irradiation causing defects in their structure which increase resistance and by this increase conversion of light energy into heat respectively. It may be possible to only induce a change in internal structure (disorder or crystallinity) by following the same procedure but with

lower laser power or lower irradiation time. Finally, if similar experiments have already been done it is necessary to compare the results with data presented in the report.

4. Conclusion

It was shown that there are a lot of experiments of changing the crystallinity of gold nanorods and nanoparticles by laser application and there almost don't exist any reports and research works about increasing Raman scattering signal for SERS diagnostics and photothermal heating for PT therapy by changing or modifying the structure and making it in one component system. Exception is only one article where authors reported about the system which consists of the combination of large plasmonic GNPs responsible for photothermal heating surrounded by smaller GNPs which are used for enhancing of SERS signal. As a result, we were able to suppose that we can obtain the balance between maximum conversion of light energy into heating for PT therapy and good Raman scattering signal for SERS diagnostics by making interstructural defects in plasmon GNPs.

In theranostics both methods: photothermal therapy and diagnostics of scattering signal from the plasmonic nanoparticles can be applied for tumor cells detection and destruction (heating). In this case, the dose of nanoparticles introduced into the human body can be reduced at least twice because nanoparticles will be able to perform both functions that are presented for a two-component system. In medical practice, this will help improve the quality of cancer tumor treatment and reduce the cost of the required plasmonic nanoparticles.

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