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Development of a technique for studying trimethylamine oxide solutions using planar SERS structures

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Abstract: This work is devoted to revealing the parameters of preparing SERS substrates for studying a low concentration trimethylamine oxide (TMAO) solution by Raman spectroscopy. A study was made of the effect of treatment with a 3,5% HCl solution, deionized water, and isopropanol vapor of planar surface enhance Raman spectroscopy (SERS) structures on the resulting Raman spectra of TMAO. We used a SERS substrate representing a multilayer structure: a mirror silver layer, a thin dielectric SiO_2 insulating layer, and an array of plasmonic Ag nanoparticles about 25 nm in size. The influence of the duration of the substrate soaking in the analyte solution on the quality of the Raman spectra was established. Raman studies of SERS substrates with TMAO were carried out using 532 and 785 nm lasers.

Keywords: nanoparticles, silver, trimethylamine oxide, SERS

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Разработка методики исследования растворов триметиламин оксида с использованием планарных ГКР-структур

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Аннотация. Данная работа посвящена выявлению параметров подготовки ГКР-подложек для исследования раствора триметиламин оксида (ТМАО) малой концентрации методом Рамановской спектроскопии. Было проведено исследование влияния обработки 3,5% (масс.) раствором HCl , деионизованной водой и парами изопропанола планарных структур гигантского комбинационного рассеяния (ГКР) на получаемые спектры ТМАО. В работе использовалась ГКР-подложка, представляющая многослойную структуру: зеркальный серебряный слой, тонкий диэлектрический слой-изолятора SiO_2, массив плазмонных наночастиц Ag размером порядка 25 нм. Установлено влияние длительности вымачивания подложки в растворе аналита на качество рамановских спектров. Рамановские исследования ГКР-подложек с ТМАО производились с использованием лазеров 532 и 785 нм.

Ключевые слова: наночастицы, серебро, триметиламин оксид, гигантское комбинационное рассеяния

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Introduction

Today, the medical industry needs faster, more sensitive, and more accurate methods for analyzing biological samples. Effective methods have already been found to detect and determine the concentration for most components of human blood (cells, large proteins, inorganic salts) [1]. However, there are biomarkers that require long and painstaking analysis for their detection. One such substance is trimethylamine oxide. The risk of atherosclerosis, thrombosis and even stroke increase if the concentration of TMAO exceeds 2,25 μM [2]. TMAO detection is possible using the High Performance Liquid Chromatography (HPLC) method [3]. HPLC has disadvantages that prevent the effective use of this method everywhere - a significant amount of human blood, complex equipment, high price, complicated sample preparation, analysis duration (more than 2 days) [3].

Surface enhanced Raman spectroscopy is an alternative method for diagnosing and detecting biomarkers [4]. This method is highly sensitive due to SERS-substrates based on nanoparticles of plasmonic metals (Au, Cu, Ag) [4]. The resulting spectrum makes it possible to judge the concentration of one or another component of the sample in the case of a study of a complex composition. However, high sensitivity may require compliance with a number of conditions: tight contact between the surface of the nanoparticle and the molecules under study; using a laser of a suitable wavelength; substrate pretreatment. Thus, there is an increased interest in determining these parameters for a quick and inexpensive study of TMAO in human blood.

In this work, we used planar SERS substrates based on a metal–dielectric mirror and an array of Ag nanoparticles. TMAO at a concentration of 10 mM used as the analyte. A weakly concentrated solution of hydrochloric acid and vapors of boiling isopropanol were used to treat the substrates. Lasers of two different wavelengths were used to study TMAO.

Materials and Methods

The SERS substrate was created in accordance with the method presented in earlier works [5]. Si(100) substrate with 300 nm SiO_2 thickness was used as the basis for the SERS structure. The adhesive layer Cr 50 nm deposited by magnetron sputtering. Then, a 100 nm Ag reflective layer formed on the substrate by vacuum thermal evaporation. After that, the reflective layer coated

with 20 nm SiO_2 as an insulator by the method of electron beam evaporation. The final step was the formation of an monolayer of uniformly distributed silver nanoparticles (NP) with average diameter 25 nm by annealing a 5 nm thin dispersed Ag film in vacuum at a temperature of 230 °C for 10 minutes. The size and distribution of nanoparticles were controlled by a Helios NanoLab 660 FEI scanning electron microscope. The formed monolayer of nanoparticles repeats the result obtained in previous work [5].

Before applying the analyte, some of the finished substrates were not processed. The second part was soaked in 3.5% (mass.) solution of hydrochloric acid (HCl) and washed in a slow flow of deionized water. The use of an identical technique by the authors in [6] showed that the treatment of Ag NPs in a weak solution of hydrochloric acid makes it possible to restore the intensity of the SERS signal for structures with different storage periods in air to the initial values. Thus, it can be assumed that the sulfide-oxide layer removed during the treatment from the surface of the nanoparticles is so small, so the treatment does not significantly affect the surface morphology. The third part treated with hot vapors of isopropyl alcohol 98.5%.

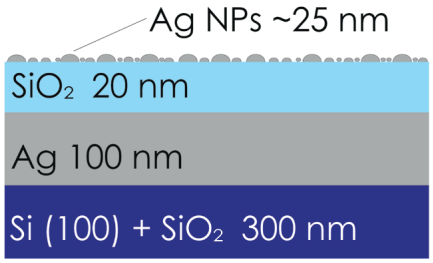

Fig. 1. SERS-substrate scheme

In this work TMAO with a concentration of 10 mM solutions used as analyte. The analyte was applied in two ways: by soaking the finished SERS structure in an analyte solution and by a drop from a dispenser. The substrates were soaked in the analyte solution for 5, 30, and 60 minutes. The substrates with the applied analyte dispenser dried in a fume hood at room temperature. Part of the samples with drops was covered with a cover slip for distribution and preservation in liquid form until the moment of examination.

The study was carried out on an inVia confocal microscope from Renishaw with the following parameters: wavelengths of 532 and 785 nm; laser power 5 mW; light spot diameter 4 μm; spectrum accumulation time 60 s.

Results and Discussion

Considering the effect of soaking on untreated substrates (see Fig. 1) in the solution, we found that the most rational approach is to expose the sample for 30 minutes (Fig. 2). Increasing the exposure time to 60 minutes (in 2 times) increases the intensity of the SERS spectrum by only 18%. It should be noting that the soaking of the samples made it possible to distribute the analyte much more uniformly than when applied by a drop.

The study of the pretreatment effect showed that the use of dilute hydrochloric acid makes it possible to increase the efficiency of SERS substrates due to the removal of oxide and sulfide layers from silver nanoparticles that appear as a result of annealing and in a natural way, respectively (Fig. 3). Processing for 30 seconds and subsequent washing in a weak stream of deionized water for 10 seconds showed the following results: reduction of noise level; an increase in the intensity of characteristic TMAO peaks; reduction of the thermal decomposition [7]. The use of an isopropanol led to a drop in the quality of the spectrum to the level of noise.

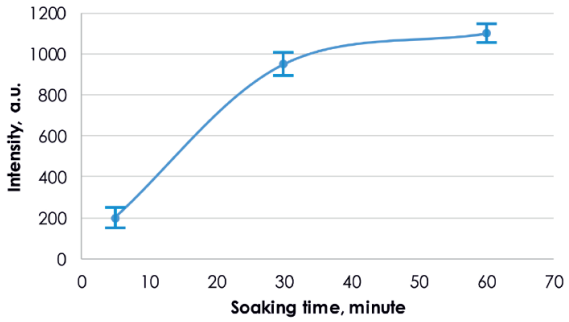

Fig. 2. Dependence of the SERS intensity of the 760^{-1} cm TMAO peak on the soaking time, wavelength 532 nm

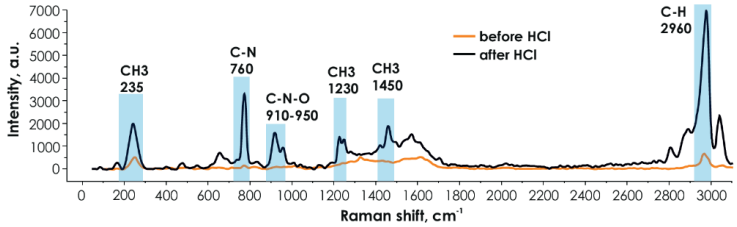

Fig. 3. Raman spectra of TMAO without and with preliminary treatment of the SERS-substrate in 3,5% HCl solution for 30 s, wavelength 532 nm

The study of the influence of the treatment time on the intensity of the SERS spectrum showed that the optimal time for holding the substrate in the acid solution is from 15 to 30 seconds (Fig. 4). A further increase in the treatment time of the substrate leads to a rapid decrease in the intensity.

Fig. 5 demonstrates the influence of the laser wavelength on the efficiency of recording the Raman spectrum of TMAO. The TMAO spectra are of a high quality at 532 and 785 nm. The wavelength of 532 nm provides better visibility of more peaks, due to the greater plasmonic activity of Ag NPs in the blue-green region of the spectrum. The 785 nm wavelength provides better visibility of C-N and C-N-O bond peaks and reduces the thermal degradation of the analyte.

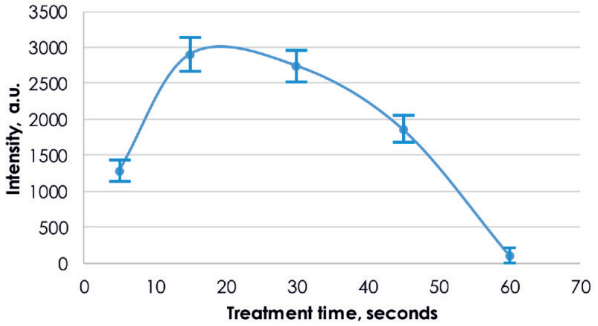

Fig. 4. Dependence of the intensity of the 760 cm^{-1} peak on the treatment time, wavelength 532 nm

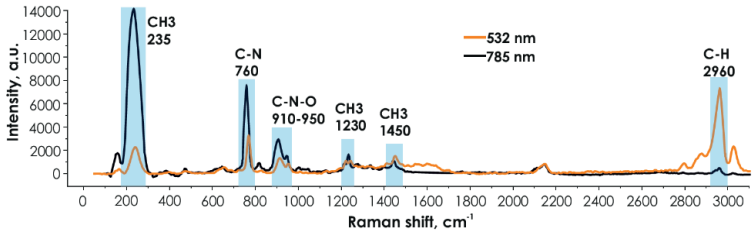

Fig. 5. TMAO spectra at different laser wavelengths, treatment time in acid solution ~30 s

Conclusion

In the course of the work, it was possible to establish the importance of a pre-treatment, soaking time and the laser used on the effectiveness of the study of TMAO. It was founding that the greatest effect in the study of TMAO using SERS-substrate based on Ag NPs will be provided that the following parameters are observed: treatment of the substrate in a 3,5% HCl solution for 15 to 30 seconds, followed by washing in a weak stream of deionized water; soaking time in TMAO solution for at least 30 minutes; using a 532 nm laser to search for C-H bonds of TMAO; using a 785 nm laser to search for C-N and C-N-O bonds of TMAO.

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