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Quantitative Detection of Aminoglutethimide by Electrochemical Surface Enhanced Raman Spectroscopy

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Abstract:
In this work, we have investigated the detection of aminoglutethimide (AGI) drug based on its adsorption on the SERS-active screen-printed electrode employing the Electrochemical Surface-Enhanced Raman Spectroscopy (E-SERS) technology. E-SERS spectra exhibits the different absorption of AGI onto the substrate. At the -400 mV of applied potential, the E-SERS peaks of 1147 cm^{-1} shows the strongest intensity among the other peaks. The limit of detection (LOD) is 40 ng/mL and the square R of linear curve is 0.98. This work aims to optimize the trace detection of this drug with possible application in the deterrence and prevention of dopant usage and for point-of-care diagnostics (POCD).

Key words: aminoglutethimide, electrochemical SERS, anti-doping, point-of-care diagnostics.

Introduction

Aminoglutethimide (AGI) is an aromatase inhibitor which is used clinically for the treatment of hormone-dependent metastatic breast cancer [1]. However, it can also be used as dopant and thus the consumption of AGI by sportsmen in official competitions is banned by the World Anti-Doping Agency [2].

The electrochemical SERS (E-SERS) sensors have been rapidly developed and widely used in a range of applications due to its enhanced chemical detection. Benefited from the adjustable potentials on the electrode, the orientation of the molecules on the substrate can be changed which affects the intensity of SERS signal. Both chemical and physical enhancements of SERS can be influenced to a certain extent by applying an electrode potential. In this study, the electrochemical SERS sensor offers the advantages of enhanced signal intensity and more selectivity to the AGI molecule.

Methodology

The screen-printed electrode (SPE) consists of a reference electrode (Ag / AgCl), a counter electrode (carbon) and a working electrode (carbon or gold) shown in Fig. 1.

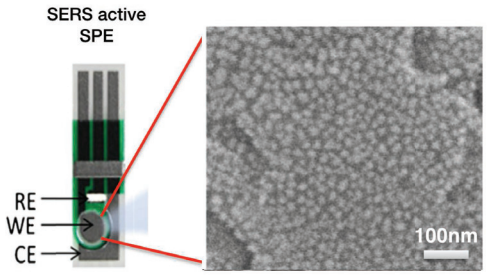

Fig. 1. The photo of SERS active SPE used in this work which is composed of a working electrode (WE), a counter electrode (CE) and a reference electrode (RE). SEM image of silver-deposited carbon working electrode. The diameters of silver nanoparticles are approximately ranging from 20 nm to 30 nm.

The SPEs were mounted to a customized mask so that only the areas of the working electrode were exposed for sputtering deposition by in-line sputtering machine (V0005, Optorun, Japan). The silver nanoparticles were deposited onto the working electrode of the screen-printed electrode. The target power was set to 250 kW for the sputtering process. The deposition time of sputtering process was 12 s. To avoid melting the carbon electrode and the plastic masks, the

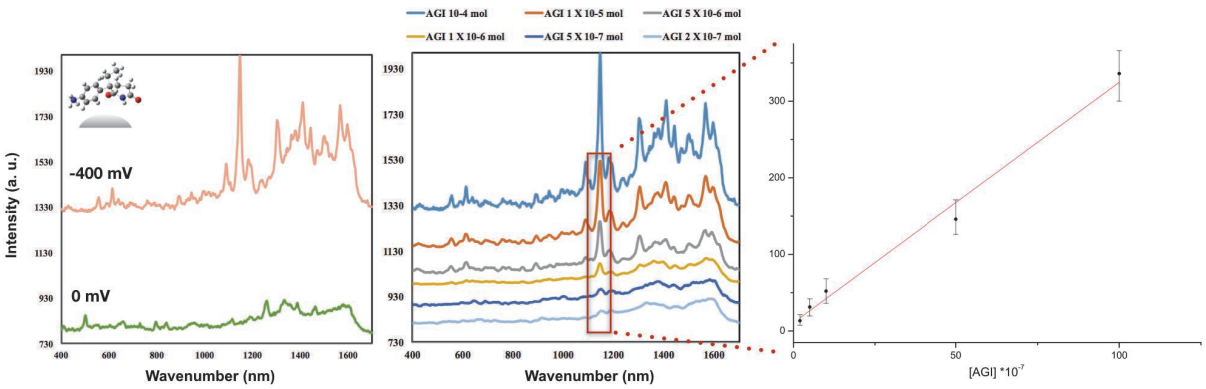

Fig.2. Left graph: Comparison of the SERS (0 mV) and E-SERS (-400 mV vs Ag/AgCl) spectra of 0.1 mM AGI solution. Middle graph: E-SERS spectra of AGI at the applied potential of -400 mV vs Ag/AgCl with enhanced peak signal at 1147 cm-1. Right graph: Calibration curve of different drug concentrations of AGI with good linear dependence (0.98). Error bar represents standard deviation where n = 4.

whole sputtering process was done under 50 degrees centigrade. The 30 µL of solution was placed on the substrate. The Raman spectra and Raman images were obtained with a laser Raman confocal microscope (RAMAN-11, Nanophoton, Japan) equipped with an Olympus 20x, water-immersion objective lens. The sample was illuminated with a line-shaped laser (532 nm was about 2.8 mW / line (400 pixels) focused through the objective lens and Raman scattering from the samples was collected by the same objective lens and guided to a spectrophotometer with a slit width of 15 µm. The Raman signal was diffracted by a 600-grooves/mm grating (spectra resolution, 1.6 cm^{-1}) and was detected by an air-cooled CCD camera (-70 ˚C). Raman spectra were obtained from 1.25 µm x 167 µm (3 x 400 pixels) area. The potentiostat system was a USB portable device. By applied different potentials (from 0 to -1000mV with the increment of -200 mV) to the SERS-active substrate, different absorption of the AGI molecule onto the silver nanoparticles brought the benefits of enhanced signals and more selective SERS peaks.

Result

The AGI was successfully detected on the E-SERS chip shown in Fig. 2. Compared with the SERS spectra (without applied potential), the signal intensities of E-SERS spectra were enhanced at the applied potential of -400 mV vs Ag/AgCl. The C-H in-plane bending of the AGI (corresponding to the wavenumber of 1147 cm^{-1}) showed the strongest peak intensity among the other peaks at the -400 mV applied potential. The limit of detection (LOD) is 2 x 10^{-7} (40 ng/ml) and the square R of linear fitting curve equivalent to 0.98; indicating a good linear relationship.

Conclusion

E-SERS sensor successfully detects the AGI molecule at the low level of concentration. A linear dependence of different concentrations in the [AGI] range occurs from 2 x 10^{-7} to 1 x 10^{-5}, which corresponds to the range from 40 ng/ml to 2 µm/ml. Besides the enhanced signal, more selective peak signals of the AGI can be observed by the applied different potentials which exhibit the possibility for SERS technique applying to some complex case, even for clinical application in the future.

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