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Development of surface-enhanced Raman spectroscopy application for determination of illicit drugs: Towards a practical sensor

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ABSTRACT

Surface-enhanced Raman spectroscopy (SERS) has been widely applied to identify or detect illicit drugs, because of the ability for highly specific molecular fingerprint and independence of aqueous solutions impact. We summarize the progress in determination of illicit drugs using SERS, including trace illicit drugs, suspicious objects and drugs or their metabolites in real biological system (urine, saliva and so on). Even though SERS detection of illicit drugs in real samples still remains a huge challenge because of the complex unknown environment, the efficient sample separation and the improved hand-held Raman analyzer will provide the possibility to make SERS a practically analytical technique. Moreover, we put forward a prospective overview for future perspectives of SERS as a practical sensor for illicit drugs determination. Perhaps the review is not exhaustive, we expect to help researchers to understand the evolution and challenges in this field and further interest in promoting Raman and SERS as a practical analyzer for convenient and automated illicit drugs identification.

1. Introduction

The United Nations Office on Drugs and Crime (UNODC) World Drug Report in 2017 pointed out that about quarter of a billion people, or around 5% of the global adult population, used drugs at least once in 2015. More worriedly, harm caused by drug use remains considerable. Estimated 29.5 million of those drug users, or 0.6 per cent of the global adult population, suffer from drug use disorders. In other words, their drug use is harmful to the point that they may experience drug dependence and require treatment [1]. The health consequences of illicit drug use continue to be devastating, which will lead to a variety of problems [2]. Consequently, it is a critical need to rapidly identify the illicit drugs to support the anti-drug campaign.

As one of the earliest tools, chemical color tests could provide toxicologists and criminalists with visible results for the presumptive identification of drugs and poisons [3–6]. While the fact that cannot be ignored is that these tests may be misinterpreted by subjective color perception. Gas Chromatography (GC) and high-performance liquid chromatography (HPLC) are called gold standard analytical tools for illicit drugs detection, especially when they are combined with other techniques that can capture the molecular characteristics, such as ultraviolet-visible spectrophotometry [7], nuclear magnetic resonance [8], or mass spectrometry [9–15]. Above mentioned hyphenated techniques are good at analysis in complex environments, including simultaneous analysis of multiple components and single component analysis in bio-fluids. However, these well-established methods face some disadvantages: 1) the process of sample preparation is complicated and time-consuming; 2) such methods must be conducted by trained personnel in laboratories. So it is hard to achieve large-scale screening. In addition, electrochemical sensors have also been used to detection of illicit drugs [16–18]. But the single position of anodic/cathodic peak is easily influenced. In many instances, commercial test kits (colloidal gold) are usually used as screening tests for urines with advantages of efficiency, sensitivity and good selectivity [19,20]. While the R & D cycle is long and the commercial test kits are only for a limited number of illicit drugs at present. It is difficult to cope with the endless designer drugs and their metabolites. Moreover, the colloidal gold techniques could not be intended for quantitative determination. In terms of various kinds of controlled drugs, spectroscopy techniques (fluorescence spectroscopy [21], ultraviolet spectrum [22,23] and infrared (IR) spectroscopy [24,25],) are also applied.

Here, we introduced another important method, namely surface-

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Table 1
The advantages of the SERS compared to other techniques.

Versus	Nuclear magnetic resonance (NMR)	Infrared spectroscopy (IR)	Electrochemistry (EM)	Mass spectrometry (MS)
SERS	Fast; Inexpensive; On-site detection	Without impact of water; Sensitive	Fingerprint	Fast; Convenient; large-scale screening
Analyte	Heroin	Opiates	Morphine, codeine	Cocaine, Amphetamines
Reference	[8,63]	[24,91]	[18,51,91]	[11,15,53,90]

enhanced Raman spectroscopy (SERS). SERS is a phenomenon in which the Raman signals of molecules are enormously enhanced and fluorescence is suppressed when they are very close to certain SERS-active nanostructures [26–29]. Compared to other analytical techniques, its advantages have been highlighted in Table 1. SERS is one of vibrational spectroscopic methods based Raman spectroscopy free from aqueous impact. SERS not only can provide a highly specific molecular fingerprint, but also can realize ultra-trace analysis. And it just takes only few seconds to collect one SERS spectrum. The SERS technique has potential to resolve a mixture into its individual components because of molecular specificity. Thus, it may develop to a viable method for identification of illicit drugs in complex systems.

In recent years, the demand for SERS techniques that can provide fast, reliable and even quantitative measurements of illicit drugs has increased widely. But to date, there are few reviews comprehensively about SERS application in illicit drugs detection [30–32]. For this reason, this paper mainly reviews the development of SERS as efficient sensor platform for illicit drugs detection, particularly concerning trace amount of drugs and primary form or metabolites in bio-fluid. The review is organized as follows. First, this article will be on focus of the chemical analysis of illicit drugs owing to the increasing availability of suitable nanostructures. Second, SERS applications are highlighted in the determination of illicit drugs or their metabolites in bio-fluids. Finally, the future trends of SERS technique in the field of illicit drugs analysis were mentioned.

2. Chemical analysis of illicit drugs

Many illicit drugs (opiates, cocaine, cannabis, amphetamine-type stimulants and some new psychoactive substances) are good Raman scatterers, and therefore lent to rapid analysis via Raman spectroscopy. However, Raman spectroscopy is intended for molecular structure characterization rather than detection due to its relatively low sensitivity. So SERS as a particular working mode of Raman scattering is imposed in consideration of trace amount existing (as shown in Fig. 1). SERS is a modern technique and allows one to carry out different analysis, even if the quantity of sample available is small. At present, the technique has been applied to quantitative and/or qualitative detection, which can meet the need of rapid, sensitive, and reliable analysis. In this section, the illicit drugs in simple systems mainly concern about standard samples, street drugs, drugs additives and suspicious objects.

2.1. Illicit drugs powder and suspicious objects

Raman spectroscopy is a valuable tool for detailed chemical analysis and it is often applied to identify solid powder [33]. This technique has the benefit of no sample preparation and can be performed on samples without removal from the evidence, thus there is no potential risk of contamination [34,35]. The Raman spectra of many sorts of illicit drugs' standard substances have been recorded, such as a representative range of β-ketophenethylamine, the rapidly growing family of cathinone-related "legal high" recreational drugs [36], cocaine [37] and 3,4-methylenedioxymethamphetamine (MDMA) [35]. And as the development of Raman spectrographs, small contamination of illicit drugs and suspicious objects present on fibers of clothes [38–40] and fingerprints [41,42], can also be analyzed rapidly with direct laser beams, fiber optic probes and microscopes. If trace contamination of prohibited substances were found on weighing scales or used packaging, it might be possible to link with drug related activities, in spite of no bulk powders. The technique promises to be a helpful tool for forensic science.

To promote on-site analysis, transportable Raman spectrometers were gradually applied to in situ detection of seized illicit drugs (including solid or liquid forms of heroin, cocaine and amphetamine) [43]. Moreover, the progress of the software makes it possible to get the pertinent investigative information by nontechnical personnel quickly and conveniently, thereby making field analysis simple. In the cases, such as border controls and airport environment, people usually finished the identification through an automatic identification of the spectral window after digital library was created by reference substances [34,44]. And above approaches inspire researchers to achieve field detection using more portable Raman spectrometer. It should be pointed out that, even though Raman spectroscopy has the ability to distinguish the different substances present in a sample, it is not a very sensitive technique. For this reason, SERS is an important development direction for sensitive detection.

2.2. SERS substrate development

As a kind of nano-analytical technique, the well sensitivity of SERS can be attained by improving metal-dielectric nanoparticle substrates. And various SERS substrates have been fabricated and applied in different fields. There are several review papers on SERS substrate fabrications [45–47]. The theoretical and experimental studies have shown that active substrates possessed nano-size characteristics and broad and

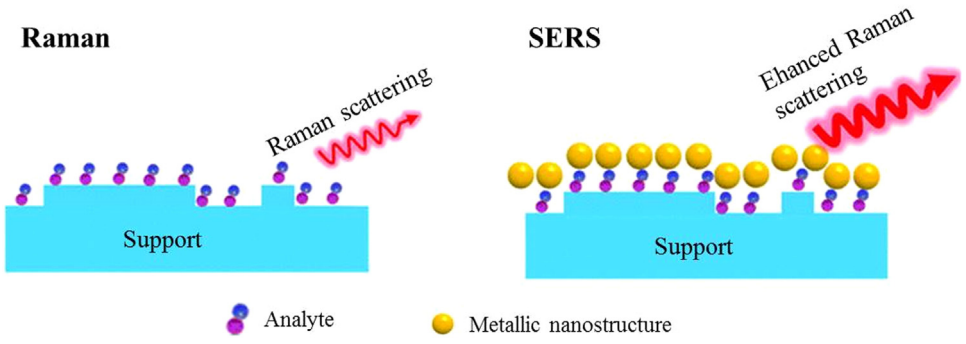

Fig. 1. Schematic of Raman spectroscopy and surface-enhanced Raman [28].