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The use of graphene quantum dots as detection elements in nanomaterials-based sensors for forensic applications

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Abstract

The large-scale abuse and addiction of narcotics such as amphetamine and cocaine have become a global problem. In this project, we innovatively use graphene quantum dots (GQD) as a fluorescent sensor to detect and quantify amphetamine and cocaine. This technology will have broad forensic application prospects. Compared with metallic quantum dots, graphene quantum dots are green and safe, with excellent biocompatibility and low toxicity.

We used undoped and N-doped GQDs as fluorescent sensing probes for the detection of amphetamine and cocaine, respectively. Using FTIR and FL as characterization methods, the fluorescence luminescence of GQDs under multiple excitation wavelength bands was studied and compared with the fluorescence after adding drugs. The experimental results show that the N-doped GQD has a higher response to the binding substance. The detection concentration of amphetamine ranges from 5 μ M to 5 mM, and the detection concentration of cocaine ranges from 10 μ M-10 mM. Within this range, the fluorescence peak intensity ratio and the drug concentration have a two-stage linear negative correlation.

Keywords

Graphene Quantum Dots, Amphetamine, Cocaine, Chemical Sensor, Forensic Drugs

Sammanfattning

Storskaligt missbruk och missbruk av narkotika som amfetamin och kokain har blivit ett globalt problem. I detta projekt använder vi innovativt grafenkvantprickar (GQDs) som en fluorescerande sensor för att detektera och kvantifiera amfetamin och kokain. Denna teknik kommer att ha breda rättsmedicinska applikationsmöjligheter. Jämfört med traditionella kvantprickar är grafenkvantprickar gröna och säkra, med utmärkt biokompatibilitet och låg toxicitet.

Vi använde odopade och N-dopade GQD: er som fluorescerande avkännande sonder för detektion av amfetamin respektive kokain. Med användning av FTIR och FL som karakteriseringsmetoder studerades fluorescens luminiscens hos GQD under flera exciteringsvåglängdsband och jämfördes med fluorescensen efter tillsats av läkemedel. De experimentella resultaten visar att den N-dopade GQD har ett högre svar på den bindande substansen. Detekteringskoncentrationen av amfetamin sträcker sig från 5 μM till 5 mM, och detektionskoncentrationen av kokain varierar från 10 μM -10 mM. Inom detta område har fluorescens toppintensitetsförhållandet och läkemedelskoncentrationen en tvåstegs linjär negativ korrelation.

Nyckelord

Grafenkvantprickar, amfetamin, kokain, kemisk sensor, rättsmedicinska läkemedel

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Acronyms

GQDs	Graphene Quantum Dots
QDs	Quantum Dots
FL	Fluorescence
PL	Photo-luminescence
FTIR	Fourier-transform Infrared Spectroscopy
NFC	National Forensic Centre
RISE	Research Institutes of Sweden AB
UNDOC	United Nations office on Drugs and Crime
TLC	Thin-layer Chromatography
GC	Gas Chromatography
HPLC	High Performance Liquid Chromatography
DA	Dopamine
APAP	N-acetyl-p-aminophenol
CNS	Central Nervous System
ADHD	Attention Deficit Hyperactivity Disorder
HPLC	High Performance Liquid Chromatography
GC-MS	Gas Chromatography-mass Spectrometer
LC-MS	Liquid Chromatography-mass Spectrometer
CE	Capillary Electrophoresis
ED	Electrochemical Detection
FD	Fluorescent Detection
MA	Methamphetamine
SPE	Solid Polymer Electrolyte
N-GQDs	Nitrogen Doped Graphene Quantum Dots
CQDs	Carbon Quantum Dots

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Chapter 1

Introduction

Graphene is regarded as an ideal sensing material. It has the advantages of low cost, environmental friendliness, and high bio-compatibility. At the same time, graphene can be dispersed in an aqueous solution with good stability. In recent years, application research based on graphene chemical sensors has increased. According to previous work, graphene-based sensors can be used for chemical detection for a series of drugs [1, 2, 3, 4]. A previous project in collaboration with the National Forensic Centre (NFC) and Research Institutes of Sweden AB (RISE) demonstrated that Graphene Quantum Dots (GQDs) are used as amphetamine sensors with fast and inexpensive analytical methods. Based on these results, GQDs for amphetamine detection mechanism, related sensitivity, and selective detection potential are further explored.

1.1 Background

Addictive drug abuse has been a serious societal problem for a long time in most of the world. According to the World Drug Report 2019 published by the United Nations Office on Drugs and Crime (UNDOC), cocaine and methamphetamine dominate the field of stimulants, and the use of these two substances in the market is increasing [5]. Therefore, their detection and identification are very important to control their abuse. Several analytical methods have been used to identify these substances, such as Thin-layer Chromatography (TLC), Gas Chromatography (GC) and High Performance Liquid Chromatography (HPLC). However, their lengthy preparation steps make them difficult and time-consuming, although these techniques can provide accurate results, due to the excellent properties of GQDs: low toxicity, fluorescent properties,

chemical inertness, good photo-stability and adjustable photo-luminescence, GQDs was introduced as a sensitive, fast and green product as nanosensors for stimulants and similar benzene ring derivatives detection [2, 3]. From previous work, The optical band gap of GQDs is determined to be 4.98 eV, due to the $n-\pi^*$ transition part. GQDs can be used as a fluorescence sensor for the determination of morphine and methamphetamine. The detection limits of methamphetamine and morphine were 1.48 and 0.5 $\mu\text{g/ml}$, respectively [3]. Another one-time sensor was reported to simultaneously voltammetric determine Dopamine (DA) and N-acetyl-p-aminophenol (APAP), and the detection limits of DA and APAP are 0.13 mM and 0.25 mM, respectively [2].

1.2 Problem

The drug detection technologies used at this stage are mainly TLC, GC and HPLC. However, these characterization instruments are very expensive and often require a longer detection cycle to complete an accurate measurement. The large-scale equipment also makes it difficult to perform immediate detection. The use of GQDs as a simple, portable, and safe pre-detection tool can greatly shorten testing time and reduce instrument and laboratory costs.

In addition, there are various synthesis methods for GQDs fabrication, different synthesis conditions and environments can affect the structure and properties of the obtained GQDs, and such differences will affect the accuracy and reliability of the GQDs as a chemical sensor.

1.3 Purpose and Goal

There are several goals of the degree project: Based on previous work and results, investigate a GQDs based nanosensor for forensic drugs detection, especially for amphetamine and cocaine; Then it is necessary to do further research to find a possible way to achieve the selective detection between cocaine and amphetamine. In addition, I also aim to compare the drug detection results of different doped GQDs and analyze whether GQDs doping condition affect the drug detection results.

1.4 Benefits, Ethics and Sustainability

These excellent properties of GQDs, such as environmental friendliness, low toxicity, good bio-compatibility and low cost, make it harmless for both environment and the inspectors. The research about the specific detection of GQDs based nanosensors can improve the accuracy and its scope of application. The investigation of the technology can make the portable lab-on-chip come true, and it can provide a more convenient, fast and low-cost alternative, in addition to large-scale instrument test.

1.5 Delimitations

During the project, due to the limitation of laboratory condition, the GQDs samples used were all from different laboratories and were not synthesized in the same laboratory. Therefore, different laboratory environments and road transportation may have an impact on GQDs.

1.6 Outline

Chapter 1 gives an overview of the whole project, including a brief background introduction, research purpose, experimental conditions and the potential of the project. Chapter 2 introduces detailed background information about this research, including forensic drugs and current related detection methods, sensors development, GQDs, and related theoretical and experimental knowledge. Chapter 3 shows the methods and substrates used for GQDs synthesis, as well as the Fluorescence (FL) detection technology and Fourier-transform Infrared Spectroscopy (FTIR) technology used for characterization. The fourth chapter includes experimental results and result analysis. Chapter 5 summarizes the research results and proposes strategies for further research.

Chapter 2

Theoretical Background

2.1 Forensic Drugs

Cocaine and amphetamine are different central nervous system stimulants and have similar effects[6]. Amphetamine is a class of phenethylamines with mainly excitatory effects, including amphetamine, methamphetamine, methcathinone and cathinone. It is a powerful Central Nervous System (CNS) stimulant of phenethylamines. It has been approved for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) and narcolepsy. However, uncontrolled or heavy use may cause serious health risks[7, 8]. Cocaine is a crystalline tropane alkaloid extracted from coca leaves[6]. This is a strong narcotic and stimulant, with strong addiction. Improper use may cause confusion, euphoria or agitation and other psychological effects[9].

According to the data from UNDOC, in 2018, about 19 million people used cocaine, and about 27 million people used amphetamine. Methamphetamine is the most commonly used amphetamine-type stimulant in Southeast Asia[5]. The large-scale illegal use can cause serious society problems and drug abuse also affects the health of both teenagers and adults.

2.2 Current Detection Methods

With the severe proliferation of drugs and the continuous occurrence of drug crimes, the proliferation is severe. Although traditional detection methods have been widely used, they are relatively expensive, time-consuming, and requiring high operational

requirements. Some typical detection method includes HPLC, Gas Chromatography-mass Spectrometer (GC-MS), Liquid Chromatography-mass Spectrometer (LC-MS), Capillary Electrophoresis (CE), Electrochemical Detection (ED) and Fluorescent Detection (FD).

2.2.1 HPLC

HPLC adopts a high-pressure infusion system. The mobile phase is a single or mixed solvent with different proportions and is equipped with a stationary phase chromatographic column. The components in the column are separated and sent to the detector. Over the years, chromatographic columns, derivatization reagents, and detectors have been extensively studied and applied to the detection of Methamphetamine (MA). Falcó [10] et al. used normal phase HPLC with 1,2-naphthoquinone 4-sulfonate sodium as a derivatizing agent to analyze MA in urine and showed a good recovery rate. In recent years, studies have found that pre-processing samples can improve the sensitivity of HPLC methods. Wang [11] et al. established a method based on ionic liquid dispersion-liquid micro-extraction combined with HPLC. The linear range is: 10 to 1000 ng/mL, the detection limit is 1.7 ng/mL. Taghvimi et al. [12] synthesized magnetic nano graphene oxide and used it as an adsorbent. The linear range is 100 to 1500 ng/mL, and the detection limit and quantification limit are 30 and 100 ng/mL, respectively.

2.2.2 FD

Fluorescence chemical sensors are molecules whose molecular interactions rely on fluorescent signals. In recent years, fluorescent chemical sensors have been widely used in detection. Traditional fluorophores (such as fluorescein and rhodamine) have high emissivity in solution, so fluorescence is easily quenched. New fluorophores such as Quantum Dots (QDs) and perylene imide have been discovered. Masteri-Farahani[13] developed a new fluorescent nanosensor, they chemically modified cadmium sulfide quantum dots(CdS-QDs) with anti-methamphetamine antibodies, resulted in a selective detection of methamphetamine receptor sites. The detection limit of this method for detecting MA is as low as 0.006 mg/L, it provides a simple, rapid and effective method. Saberi[14] and others used CoOOH nanosheets combined with carbon dots(CDs) as fluorescence sensors to measure MA. The results show that

CoOOH has a good quenching efficiency, a fluorescence detection limit of 1 nm, and a dynamic range of 5 to 156 nm.

2.2.3 ED

Electrochemical sensors instead of standard chromatography and spectroscopy methods have shown promising results. In recent years, due to the need to develop portable drug field screening equipment, Solid Polymer Electrolyte (SPE) was chosen as the best sensor platform. In 2019, Akhoundian [15] adopted the MIP strategy to mix polymers into multi-walled carbon nanotubes, carbon paste electrodes are obtained. Using Fast Fourier Transform Square Wave Voltammetry, it can measure trace amounts of methamphetamine with a detection limit of $8.3 \times 10^{-10} \text{ mol/L}$. It is a MIP-based voltammetry sensor, which also shows the lowest ever. The detection limit is rapid to screen MA in human urine and serum samples.

2.3 Graphene Quantum Dots

2.3.1 Graphene

Here is the definition of graphene given in recent comments: Graphene is a two-dimensional (2D) honeycomb lattice structure formed by a densely packed single layer of flat carbon atoms, and it is also the basic building block of graphite materials of all other sizes. It can be packaged into zero-dimensional (0D) fullerenes, rolled into one-dimensional (1D) nanotubes or stacked into three-dimensional (3D) graphite[16]. It is almost completely transparent and only absorbs 2.3% of light[17]; the thermal conductivity is as high as 5300 W/m·K. At room temperature, its electron mobility exceeds $15000 \text{ cm}^2/\text{V}\cdot\text{s}$ [16], which is higher than that of carbon nanotubes or monocrystalline silicon, and its resistivity is only about $10^{-6} \Omega \cdot \text{cm}$ [18].

Graphene has unique structural flexibility, which is reflected in its electronic properties. The sp^2 hybridization between the 1s orbital and the two p orbitals results in the formation of a triangular planar structure and the formation of bonds between adjacent carbon atoms. The distance between the bonds is 1.42 Å. Due to the Pauli principle, these bands have a filled outer shell, thus forming a deep valence band. The unaffected p orbitals perpendicular to the planar structure can be covalently bonded to adjacent carbon atoms to form energy bands. Since each p orbital has an extra

electron, the band is filled in half. The half-filled band in the transition element plays an important role in the physics of the strongly correlated system, because due to its strong tight bonding characteristics, the Coulomb energy is large, and the correlation leads to a strong collective effect, which creates a gap.

There are various derivatives of graphene, and graphene oxide is one of the most important ones. Graphene oxide has a similar structure to graphene, but due to uncertain factors such as synthesis conditions, its precise chemical structure is still uncertain. It is generally believed that its oxygen-containing functional groups have epoxy bridges (-O-) and hydroxyl (-OH), carboxyl (-COOH) and carbonyl (C=O), of which carboxyl and carbonyl usually appear on the C atoms at the edge of graphene.

2.3.2 Quantum Dots

Theoretically, QDs are semiconductor nanostructures that bind excitons in three spatial directions. Generally speaking, colloidal nanocrystals are fragments of crystals with a scale of 1-100 nm that exist in a solution in a meta-stable state. Due to its physical size is close to the critical size of many properties, and the considerable surface atomic ratio, many properties of colloidal nanocrystals show unique size-related phenomena [19]. In the traditional sense, colloidal nanocrystals are mainly divided into noble metal colloidal nanocrystals and semiconductor colloidal nanocrystals. According to the classical quantum confinement effect, when the geometric radius of the colloidal semiconductor nanocrystal is smaller than the exciton Bohr radius of its bulk material, the energy levels of the valence band and conduction band will present a discrete distribution, and the properties of the nanocrystal will change.

2.3.3 Graphene Quantum Dots

GQDs refer to an emerging carbonaceous fluorescent material with a graphene sheet size of less than 100 nm and a number of sheet layers of less than 10 layers. The lateral dimension of GQDs is usually a few nanometers. HRTEM and XRD measurements revealed that the graphite in-plane lattice spacing is 0.18 – 0.24 nm, while the inter-layer spacing is approximately 0.334 nm. According to the different synthetic routes, various defects, heteroatoms and functional groups are introduced, which may significantly change the structure and physicochemical properties of GQDs.

Due to the C=C double bond structure in GQDs, it can undergo a π - π transition, so it can absorb a large number of photons in a short wavelength range. Generally speaking, it shows a strong absorption peak in the range of 260-320 nm in the ultraviolet absorption spectrum, accompanied by a tail that extends to the visible light range. At the same time, due to the influence of n- π transition, GQDs may also have shoulder peaks in the range of 270-390 nm. Moreover, due to the influence of surface modification functional groups and surface passivation, the position and peak shape of the ultraviolet absorption peak will be affected. The luminescence performance of GQDs is its most important performance, and it is also the performance that has been studied most extensively and closest to practical applications by researchers. Compared with spherical Carbon Quantum Dots (CQDs), GQDs with a lamellar structure have a more regular crystalline structure, and therefore have a higher FL quantum yield.

GQDs can exhibit unique photo-chemical characteristics due to edge effects and quantum size effects. In addition to the advantages of CQDs, the fluorescence is dependent on the excitation wavelength. When the excitation wavelength is changed from 310 nm to 380 nm, the corresponding fluorescence emission peak position shifts from 450 nm to 510 nm, and the Photo-luminescence (PL) intensity decreases rapidly. Generally speaking, graphene oxide exhibits a broad spectrum of red light emission, depending on the oxygen-containing functional groups it contains. After graphene oxide is reduced, due to the reduction of oxygen-containing functional groups and the change in structure, it mainly presents blue light (first principle simulation speculates that it is caused by carbon vacancy defects). Modified graphene-like has similar laws. The emission spectrum is mainly composed of two parts: blue emission peak position (not moving) and long-wavelength emission (peak position moving). Compared with unmodified graphene, its long-wavelength emission is significantly enhanced. Since the grafted functional group can provide a new excitation transition process and enhance the excitation process of the originally weak sp^2 carbon cluster size effect, the corresponding luminescence process is enhanced.

Nitrogen Doped Graphene Quantum Dots (N-GQDs) are a new type of carbon quantum dots, whose internal electrons are restricted in all directions and exhibit significant quantum confinement effects and edge effect. When their size is less than 10 nm, these two effects will bring them new physical and chemical properties. Compared with traditional GQDs, N-GQDs not only have the characteristics of low price, adjustable

band gap, and stable photoluminescence. The introduction of N heteroatoms will also bring novel electrocatalytic activity, photoluminescence properties, and low Cytotoxicity and good bio-compatibility. Therefore, they have huge application potential in optoelectronic devices, cell imaging, bio-medicine, etc. Although the early research on N-GQDs has made some progress, the N/C atomic ratio of N heteroatoms in quantum dots is usually less than 5%. In addition, the bonding mode of N and C is single, mostly pyridine structure, occasionally pyrrole structure, not easy to be regulated. Another way of bonding between N and C, that is, one N heteroatom replaces the original C atom in the graphene lattice to become a substituted N, and maintains the sp^2 hybrid configuration of the original C.

GQDs has higher bio-compatibility than other nanomaterials. Ajayan's research team has shown that GQD doses as high as 50 $\mu\text{g}/\text{mL}$ do not have any significant toxicity on human breast cancer cell lines.[20].

2.4 Theory

Due to the $\pi-\pi^*$ transition of the C=C bond, GQDs is effective in the collection of photons in the short wavelength region. They usually show strong light absorption in the UV region (260–320 nm), with the tail extending into the visible light range. Functional groups and surface passivation may change the absorption characteristics [21].

The underlying mechanism of GQD tunable PL characteristics is not fully understood, which is mainly due to the inconsistent experimental observations caused by the huge heterogeneity of single particles from the same synthesis and the unique and uncertain characteristics of carbon nano-dots obtained from different processes. By adjusting the synthesis conditions and paths, doping and defects can be adjusted sensitively.

2.5 Methodology

2.5.1 FL

Fluorescence spectrometer is a qualitative and quantitative analysis instrument for detecting substances. The principle is based on the fluorescence effect: laser irradiates atoms, the electrons in the atoms absorb energy and transition to the

first excited singlet state or the second excited singlet state, but these excited states are unstable. When the electrons return from the first excited singlet state to the ground state When time, the energy will be released in the form of light to produce fluorescence, and generally the continuous luminescence time is shorter than 10^{-8} sec (the phosphorescence duration generated at the same time is greater than 10^{-8} sec). Through the detection of a fluorescence spectrometer, information on the excitation spectrum, emission spectrum, quantum yield, fluorescence intensity, fluorescence lifetime, Stokes shift, fluorescence polarization and depolarization characteristics, and fluorescence quenching of the substance can be obtained. Fluorescence spectrum analysis technology is often used in biological research, pharmaceutical analysis, chemical analysis, food inspection, medical inspection, environmental monitoring, mineral analysis, etc.

The fluorescence spectrometer mainly judges the nature and quantity of the substance according to the fluorescence spectrum and the excitation spectrum. The details are as follows: the wavelength and intensity of the excitation light are kept unchanged, and the fluorescence generated by the fluorescent substance is irradiated on the detector through the emission monochromator. Adjust the emission monochromator to various different wavelengths, the corresponding fluorescence intensity is measured by the detector, and then use the fluorescence wavelength as the abscissa and the fluorescence intensity as the ordinate to draw the graph, which is the fluorescence spectrum. Use excitation light of different wavelengths to excite the fluorescent substance to make it fluoresce, let the fluorescence irradiate the detector with a fixed emission wavelength, and then use the excitation light wavelength as the abscissa and the fluorescence intensity as the ordinate to draw the fluorescence excitation spectrum.

2.5.2 FTIR

There are four types of molecular motion: translation, rotation, vibration, and electronic motion. The latter three are quantum motions. The molecule absorbs a photon with energy $h\nu$ from the lower energy level E^1 and can jump to the higher energy level E^2 . The whole movement process satisfies the law of conservation of energy. The smaller the difference between the energy levels, the lower the frequency of light absorbed by the molecule and the longer the wavelength. Infrared absorption spectrum is caused by molecular vibration and rotational transition. The atoms that make up

chemical bonds or functional groups vibrate (or rotate) constantly, and their vibration frequency is equivalent to infrared light. Therefore, when molecules are irradiated with infrared light, the chemical bonds or functional groups in the molecules will undergo vibrational absorption. Different chemical bonds or functional groups have different absorption frequencies, and their positions on the infrared spectrum are also different, so that information about the chemical bonds or functional groups contained in the molecule can be obtained. It is worth noting that the dipole moment changes only when the molecule vibrates, and the vibration has infrared activity.

2.6 Related Work

2.6.1 Amphetamine affinity to graphene

Majid and his colleagues used fluorescent GQDs as nanosensors to characterize morphine and methamphetamine [3]. They used XRD, UV-vis spectroscopy and fluorescence spectroscopy to detect its microstructure, optical properties and energy band structure. Similar to our project, GQDs are also used as fluorescent sensing probes for the determination of morphine and methamphetamine. The detection limits of methamphetamine and morphine were 1.48 and 0.5 $\mu\text{g/ml}$, respectively.

2.6.2 Graphene nanoplatelet-based sensor for the detection of dopamine and N-acetyl-p-aminophenol

Francis and his colleagues used separate and simultaneous voltammetry for the determination of dopamine (DA) and N-acetyl-p-aminophenol (APAP) and developed a new type of single-sex sensor [2]. The sensor is fabricated by dip-coating (GNPs)-Nafion (Naf) nanocomposites made of graphene nanosheets onto screen-printed electrodes (SPE). The sensor can simultaneously analyze DA and APAP by differential pulse voltammetry (DPV), and in their mixture, the sensor shows excellent sensitivity and specific detection.

Chapter 3

Methodologies and Methods

3.1 Research Process

In the project, GQDs aqueous solution is used as chemical sensor for amphetamine and cocaine detection. In order to discuss the effect of doping condition and differentiation of synthesis, GQDs are obtained by several different method: pyrolysis of citric acid, electrochemical exfoliation using graphite rod electrodes in NaN_3 electrolyte and microwave pyrolysis of NH_4F , citric acid and urea. Prepared GQDs samples are mixed with a series concentration gradient drug solution and then detect the FL response intensity to achieve the determination purpose of the GQDs based chemical sensor. In addition, FTIR is also used for characterization for functional groups for drug chemicals and GQDs.

3.2 Synthesis of GQDs

In order to discuss influence of different GQDs synthesis paths on the detection results, Three different synthesis methods are used and four types of GQDs samples are obtained. GQDs synthesized by the direct pyrolysis method was synthesized by the previous researcher Carl Fredrik Åslund in the laboratory of KTH, while the other three synthesized GQDs were synthesized with two methods in the laboratory of the University of Latvia, especially, these two synthesis methods in University of Latvia can form nitrogen-doped products, while the product from the laboratory of KTH are non-doped GQDs. The undoped GQDs synthesized by Carl in the KTH laboratory is

abbreviated as CGQDs, and the other three GQDs synthesized by the University of Latvia are abbreviated as L3, L4 and L5. Among them, CGQD is obtained by direct pyrolysis of citric acid in the KTH laboratory, L3 and L4 are obtained by electrolysis of graphite rods in NaN_3 , and L5 is obtained by microwave pyrolysis of citric acid.

3.2.1 Direct pyrolysis of citric acid

Here we used a simple and environmentally friendly synthesis method of GQDs, the synthesis process is modified according to the process reported by Yongqiang Dong in 2012[22]. The main mechanism of the synthesis method is heating citric acid to be pyrolyzed and carbonized to generate GQDs, then obtained GQDs solution is neutralized with add NaOH solution, the final product is GQDs aqueous solution. In the process steps, at first 2g citric acid pure anhydrous crystal is added in a beaker with heating and stirring until the temperature reach 200 °C. At this step, the citric acid solid start melting then become orange color. Then we stop heating but continue to stir, at the same time, prepared 1 mol/L NaOH solution is added until the pH of the solution detected by the pH strips is around 7. Finally, the solution turns to red brown. The mechanism is that sufficient heating make citric acid pyrolysis, and one citric acid molecule interacts with the hydroxide (-OH) group of another citric acid molecule, and then they form a water molecule that binds the carbon atoms together. The structure of citric acid makes these carbon bonds form a hexagonal carbon ring, which is the basic structure of graphene. After continuing to heat for proper carbonization and increasing the carbon content, these structures will form nano-scale graphene "flakes". These "flakes" are graphene quantum dots. GQDs will leave many surface carboxyl (-COOH) and hydroxyl groups. These surface groups will stabilize the GQDs and make them soluble in water. For ease of understanding, the undoped GQDs produced by the direct pyrolysis of citric acid are abbreviated as CGQD in this thesis.

3.2.2 Electrochemical Exfoliation for GQDs synthesis

This synthesis method is using electrochemical exfoliation using graphite rod electrodes in NaN_3 electrolyte to form N-GQDs. Through this electrolytic synthesis method, we obtained N-GQDs samples L3 and L4.

3.2.3 Microwave Pyrolysis of GQDs

Another synthesis method used is to synthesize GQDs by pyrolysis of citric acid in a microwave oven. See 3.2.1 for detailed drug dosage. In this project, the sample synthesized by this method is called L5.

Table 3.2.1: Microwave pyrolysis. The detailed chemical composition and dosage for the synthesis of graphene quantum dots by microwave pyrolysis of citric acid.

Component	Amount, g
Distilled water	24.165
NH_4F (ammonium fluoride)	2.04
$C_8H_8O_7$ (citric acid)	2.02
CH_4N_2O (urea)	1.02

3.3 Use of Forensic Drugs

In the project, pure solid amphetamine sulfate and cocaine hydrochloride are used as amphetamine and cocaine source respectively. Both of these two forensic drugs are provided by NFC.

3.4 Experimental Characterization

3.4.1 Fluorescence detection

The project mainly uses fluorescence luminescence analysis technology to characterize the photoluminescence of GQDs and the response of GQDs to amphetamine sulfate and cocaine hydrochloride. In order to analyze the response of GQDs luminescence to different drug concentrations, a relatively wide concentration range is used for observation. First, dissolve the chemical powders in Milli-Q water, When the powder is completely dissolved, the solution is gradually diluted into a series of concentration gradient tested solutions. In the final test, the quantum dot solution and the test liquid are mixed to form a composition Sample solution. In order to obtain a better luminous effect, the solution of GQDs is also diluted to different degrees. GQDs with different synthesis conditions will have the best luminescence response at different concentrations. The specific dilution concentration is determined according to the photoluminescence pre-detection results of various types of quantum dots with different concentrations, as shown in 3.4.1.

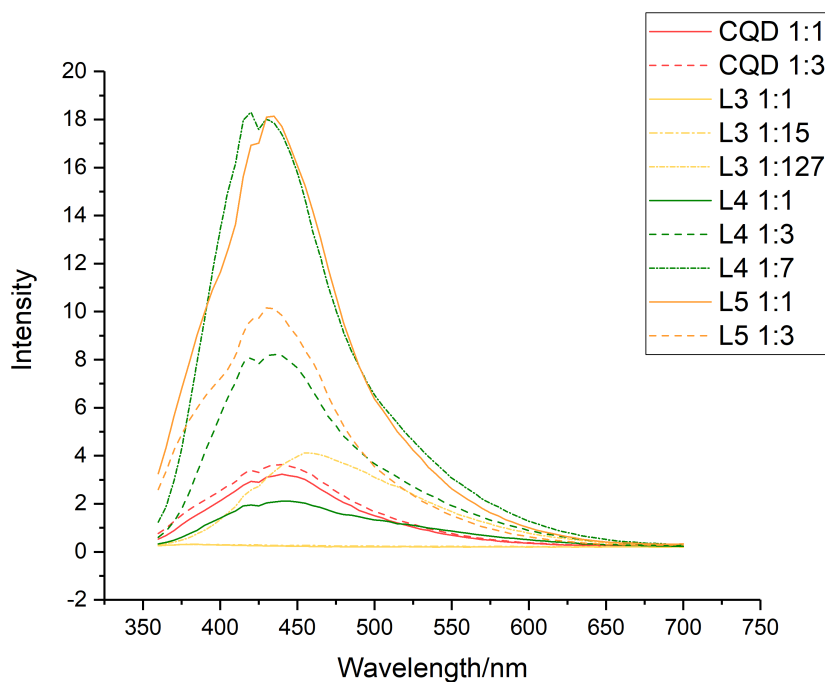


Figure 3.4.1: Fluorescence spectra of graphene quantum dots with different dilution ratios

For GQDs synthesized in the laboratory of KTH, we use a 1:3 dilution. For the GQDs we received from the laboratory of the University of Latvia, we use a 1:127 dilution ratio for L3, a 1:3 dilution ratio for L4 and a 1:1 dilution ratio for L5. The diluted liquid is Milli-Q water. Then, the prepared GQDs solution and the drug solution to be tested are mixed in a volume ratio of 1:1. The sample solution has a volume of about 200-250 μL . The sample solution is placed on a plastic sample plate and allowed to stand for 1 hour to ensure a sufficient reaction and stabilization. After that, the measurement is performed. The characterization is measured using a plate reader: SpectraMax M2. Put the sample plate into the spectrometer carefully and set the excitation wavelengths to 280 nm, 300 nm, 320 nm and 335 nm respectively, so that we can detect the different effects of different excitation wavelengths on the luminescence of the GQDs. The choice of excitation wavelength is based on the report on the previous work of the project[23], and the results show that different excitation wavelengths may lead to different emission spectra 3.4.2. Pre-vibration is applied before detection for 5 seconds, and the scan range is from 360 to 700 nm, the step is 5 nm.

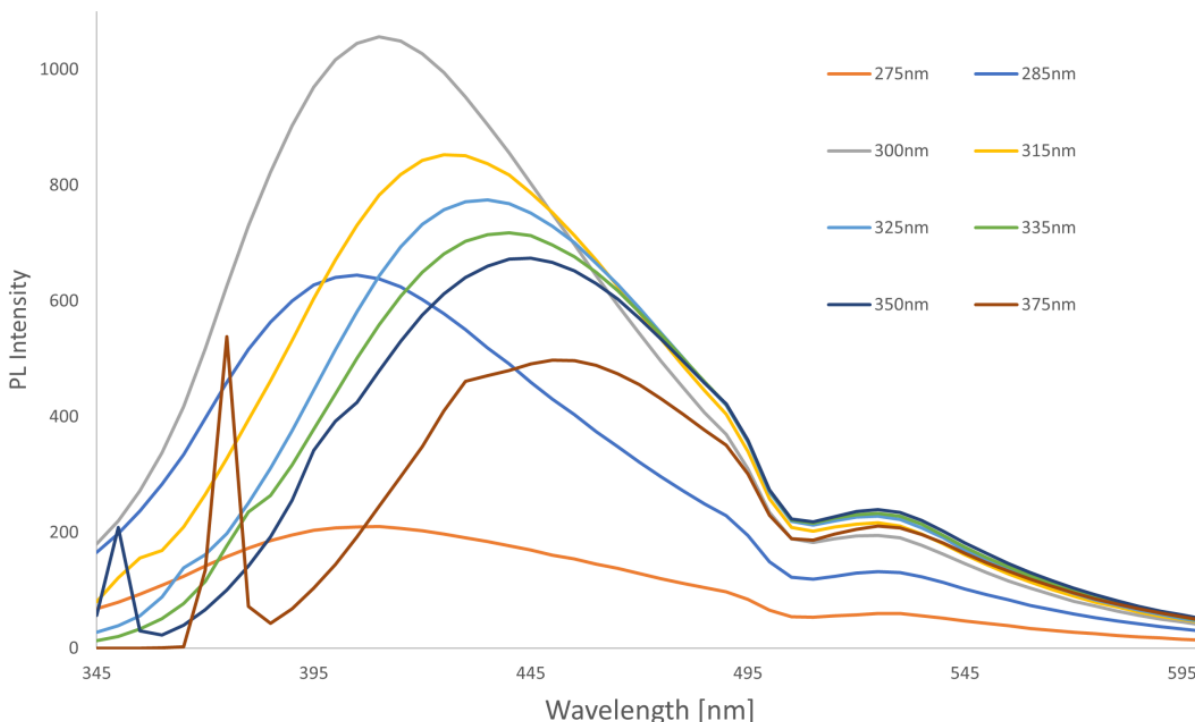


Figure 3.4.2: GQDs response to different excitation wavelength

3.4.2 FTIR detection:

FTIR can be used to characterize the molecular structure and functional groups inside the sample. The graphene quantum dot sample and the target drug mixed sample are tested and compared with their original spectra respectively, and the chemical bond formed during the reaction between the graphene quantum dot and the target drug can be analyzed. Clean Si wafer is used as detection background in the project. A complete Si wafer is divided into square pieces with a side length of approximately 2 to 3 cm. These small Si wafers are used as sample substrates for FTIR inspection. Firstly 5 μL of the sample solution to be tested is dropped on the small Si wafer, and then samples are dried for more than 1 hour in ambient conditions (room temperature, air). The prepared samples are placed on the sample stage for testing. The same setup parameters are used in all FTIR characterizations of this project. See the table 3.4.1 for detailed parameter settings.

ALL data was normalized to transmittance 1 at 4000 cm^{-1}

Table 3.4.1: FTIR characterization setup.

Setup	Parameter
Type	Transmittance spectra
Background	Double polished Si wafer
Resolution	4cm^{-1}
Scan time	64
Scan range	$4000 - 380\text{cm}^{-1}$
Source	MIR
Beam-filter	KBr-broadband
Aperture	2 mm
Scan velocity	10 kHz

3.5 Experimental Environment

All the FL detection and FTIR detection are finished in RISE, Electrum Kista in Stockholm. All GQDs are stored in the fridge. Solid amphetamine sulphate, cocaine hydrochloride powder are store in glass sample tubes, their solutions are stored in plastic sample tubes in room temperature.

Chapter 4

Result and Discussion

4.1 GQDs Characterization

We firstly characterized obtained 4 GQDs samples with FL and FTIR to research the photoluminescence properties and internal molecular structure. Here in the project, CGQD is GQDs pyrolyzed by citric acid in the laboratory of KTH, and L3, L4, L5 are GQDs synthesised by University of Latvia.

4.1.1 Fluorescence Detection

In order to study the relationship between the luminescence characteristics of GQDs and the wavelength of excitation light, we used a series of wavelengths from 335 nm to 280 nm to excite the QDs, and obtained the corresponding fluorescence spectrum. As shown in the figure 4.1.1, with the decreasing of excitation wavelength, second peak appears in L3, L4 and L5, and for L3 and L4, the intensity of second peak keep increase. For CGQDs, the peak location varies slightly with changing excitation condition, and the strongest signal response appears when the sample are excited at 300 nm. In addition, for L3 and L4, the second peak appear at a longer wavelength (about 515 nm), but for L5, the second peak appears at a shorter wavelength at about 380 nm.

In general, for nitrogen-doped GQDs such as L3 and L4, the decrease in excitation wavelength will cause a significant red shift in the overall fluorescence spectrum, which is embodied in that the intensity of low-wavelength peaks gradually decreases, and the peak intensity of the high-band increased significantly. For the L5 sample, the opposite result was shown. The decrease of the excitation wavelength would

cause the fluorescence spectrum to appear blue shift, the peak intensity of the high-band decreased and the intensity of the low-wavelength peak gradually increased. In addition, the peak position of CGQD is not greatly affected by the change of excitation wavelength, but adjusting the excitation wavelength within a certain range can affect the peak intensity.

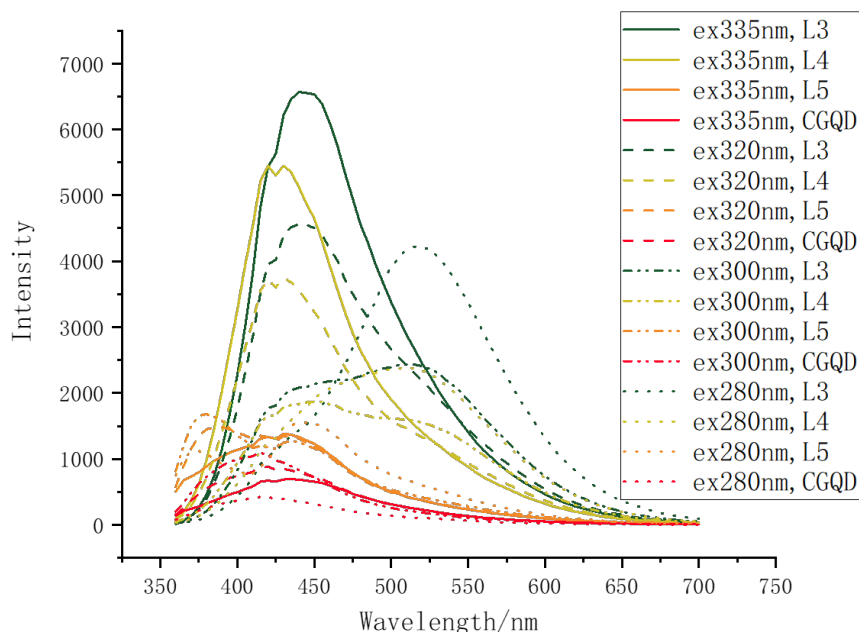


Figure 4.1.1: Fluorescence spectrum of different GQDs samples with variable excitation wavelength. The excitation wavelengths are set as 335 nm, 320 nm, 300 nm and 280 nm respectively. CGQD is GQDs polysynthesised by citric acid, and L3, L4, L5 are GQDs synthesised by University of Latvia.

4.1.2 FTIR Results

FTIR detection is used for L3, L4, L5, CGQD and their mixture with amphetamine sulphate respectively. Si wafer is used as background in all the detection and results range of transmittance are normalized between 0 to 1. FTIR spectrum for CGQD has significantly more defined absorption features. The broad peak ranging from 3700 cm^{-1} to 2700 cm^{-1} can be attributed to the C-H and O-H stretching. CGQD, L3 and L4 exhibited a expected broad peak there while L5 had only minor more defined peaks from 3000 cm^{-1} to 2900 cm^{-1} . All samples show decreased CO_2 absorption at 2394 cm^{-1} compared to the Si background. CGQD also show a broad absorption 2300 cm^{-1} to 2100 cm^{-1} which could result from variations of C=N=O, $\text{C}\equiv\text{N}$, C=C stretches, from

CO that has gaseous peaks from 2200 cm^{-1} to 2100 cm^{-1} or from Si-H stretching at 2100 cm^{-1} . Sample L5 does not show absorption at 1400 cm^{-1} as the other samples but it exhibits a continuously increasing absorption from 1600 cm^{-1} to 400 cm^{-1} (end of the measurements range).

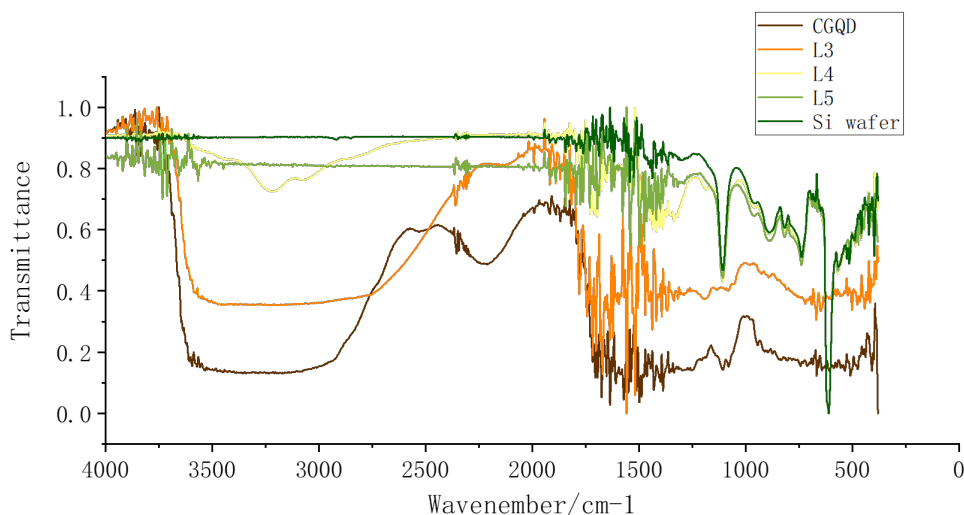


Figure 4.1.2: FTIR spectra of different GQDs samples.

4.2 Sensor Testing

In this section, we use FL to do further detection about the sensing ability of GQDs towards amphetamine sulphate, including the relationship between the fluorescence response intensity of graphene quantum dots and the concentration of added amphetamine, the stability of graphene quantum dots as a drug detector, and the time-dependent detection reaction.

4.2.1 Sensor Test with amphetamine sulphate

4 GQDs samples (L3, L4, L5 from Riga and cGQD from KTH) are prepared with appropriate detection concentration, then amphetamine sulphate solution (amphetamine sulphate with Milli-Q water) is added. The concentration of amphetamine sulphate varies from 5 mM to 0.05 mM. GQDs with same volume water

are used as control samples. In order to explore the fluorescence mechanism and binding behaviour of GQDs and amphetamine sulphate, the excitation wavelength is set as 335 nm, 320 nm, 300 nm and 280 nm.

As shown in the figures 4.2.1, with the decreasing of excitation wavelength, the FL spectrum shows similar trend as the previous fluorescence spectrum 4.1.1 of pure GQDs. In addition, as the concentration of amphetamine decreases, the fluorescence response intensity of GQDs gradually increases, and it can be clearly seen from the figures 4.2.1 that when the concentration of amphetamine decreases to the same extent, the fluorescence intensity of L3 and L4 rises more accordingly, and the fluorescence response intensity of L5 and CGQD rises less.

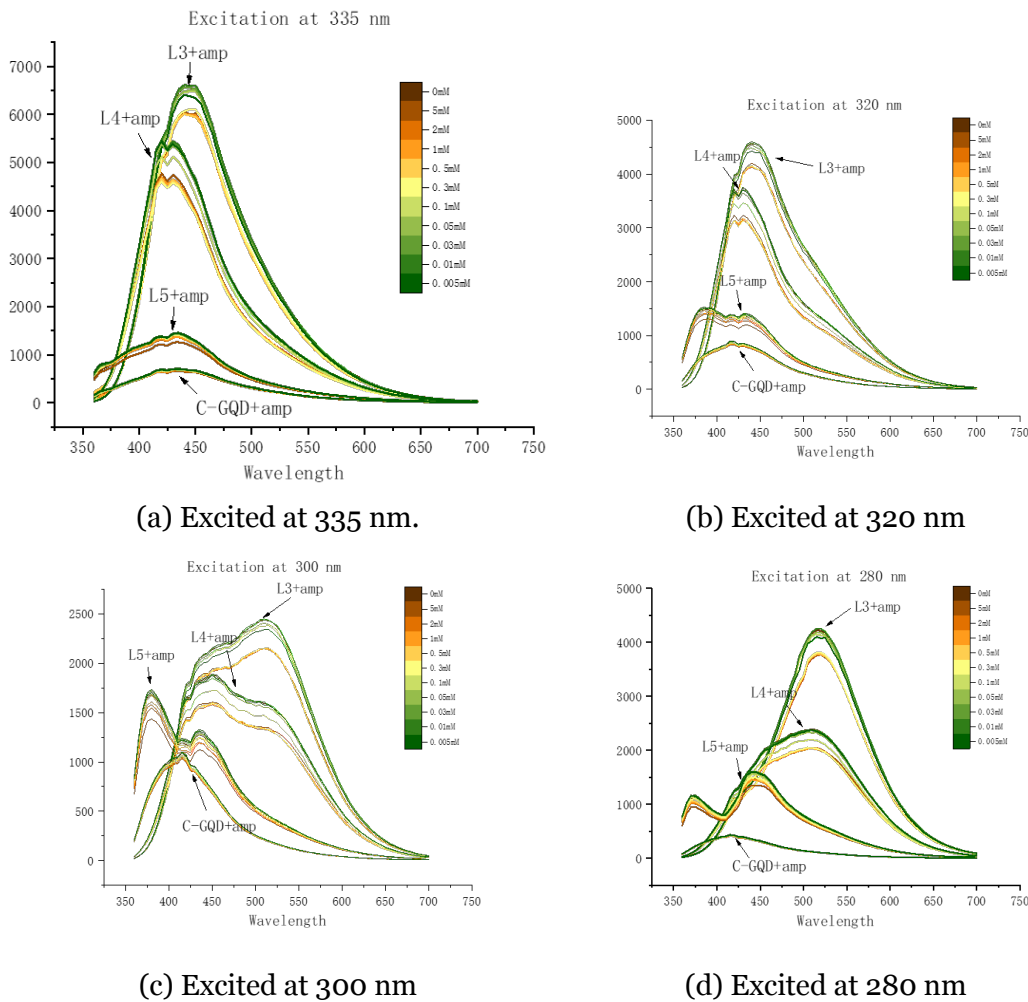


Figure 4.2.1: FL spectrum of different GQDs sensors with amphetamine, the concentration of amphetamine group varies from 0 to 5 mM and different excitation wavelengths are applied. The concentration of amphetamine here refers not to the concentration of amphetamine sulfate in the solution, but the concentration of amphetamine groups in the solution, because one part of amphetamine sulfate contains two parts of amphetamine groups.

FTIR

Similar FTIR detection is used for pure amphetamine sulphate solution and the mixture of amphetamine sulphate with GQDs respectively, results are shown in the figure 4.2.2

For L4, L3 and CGQD adding amphetamine, obvious broad peaks can be found from 2900 to 3000 cm^{-1} and sharp peak at about 1000 cm^{-1} , but for L5 adding amphetamine, these two peaks are not shown in the spectrum.

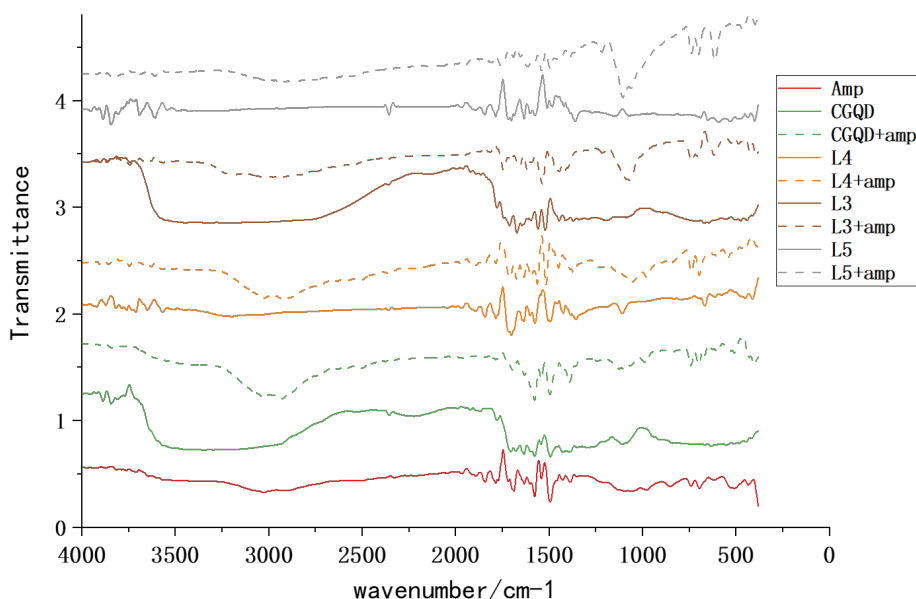


Figure 4.2.2: FTIR spectra of different GQDs samples with amphetamine.

Concentration and fluorescence intensity

The relationship between peak intensity and amphetamine sulphate concentration is explored also. In order to study the trend of peak intensity in GQDs with changeable amphetamine concentration, results excited by 300 nm excitation wavelength are chosen. By analysing data, the scattering plots can be obtained in the figures 4.2.3. Two behaviours can be easily observed in low concentration range (0 - 0.5 mM) and high concentration range (1 - 5 mM). Generally speaking, with the increasing of amphetamine concentration, the intensity ratio F_0/F increase, which means that the increase in drug concentration actually leads to a decrease in the fluorescence intensity of GQDs. However, in the low-concentration area, the intensity ratio increases faster, and in the high-concentration area, the ratio increases slowly. The four quantum dot

samples all showed the same trend, but the fluorescence intensity ratio of L4 increased most obviously, and the fluorescence intensity ratio of CGQD increased the least.

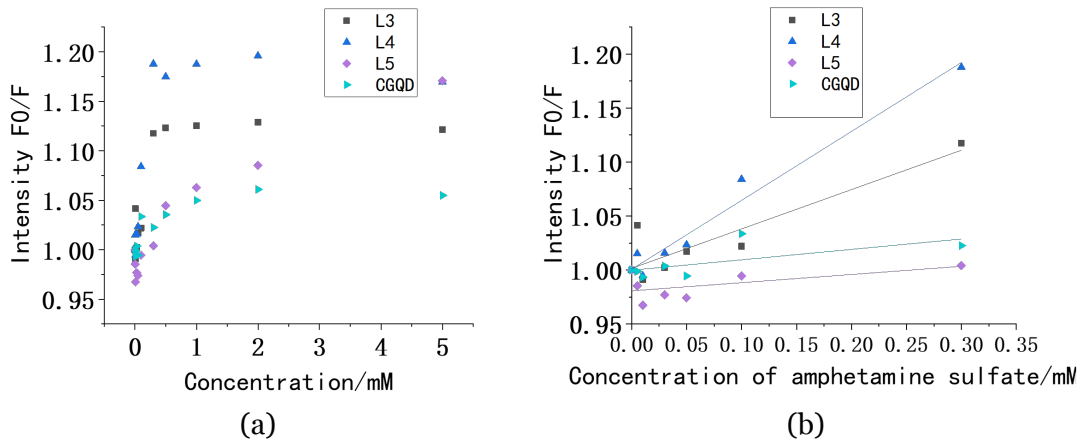


Figure 4.2.3: Relationship between concentration and intensity of GQDs with amphetamine sulphate solution. (a) Full range scattering plot, from 0 to 5 mM. (b) Concentration dependence analysis between 0 to 0.3 mM. F_0 and F are the FL intensities in the absence and presence of narcotic drugs, respectively. These are results with 300 nm excitation wavelength.

In addition, further quantitative analysis was carried out, and the scattered points in the low concentration area were selected for linear fitting, as shown in the figure 4.2.3b. See 4.2.1 for the fitting results. The drug concentration is roughly linearly related to the ratio F_0/F of fluorescence intensity, but the degree of fit needs to be further strengthened to reduce errors.

Table 4.2.1: Linear fitting relationship between amphetamine concentration correlation and fluorescence intensity under the action of graphene sensors.

GQDs	Intercept	Error	Slope	Error	R square
L3	1.00156	0.00947	0.36463	0.07786	0.77724
L4	1.00065	0.00582	0.63859	0.04788	0.9672
L5	0.98066	0.00579	0.07577	0.04763	0.20319
CGQD	0.99978	0.00581	0.09643	0.04777	0.33889

Stability and Time analysis

The intensity at the peak location is monitored for 10 min, and collect the results each 10 seconds, the results are summarized below. The intensity keeps stable with 10-minute continuous excitation. Similar results can be obtained under different excitation wavelength conditions. Here, a spectrum with an excitation wavelength of 335 nm is selected for kinetic analysis. In the process of continuous excitation, the peak

fluorescence intensity did not change in a wide range. The mixed samples of L3 and L4 and amphetamine at various concentrations showed good stability, and the peak fluorescence intensity only showed slight fluctuation.

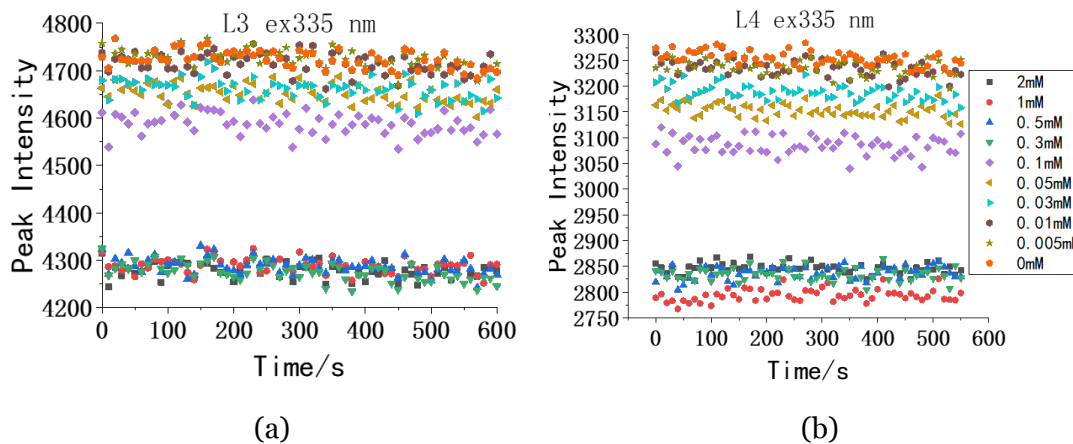


Figure 4.2.4: Stability analysis of L3 and L4 sensor for amphetamine detection, both of those two samples are continually excited at 335 nm for 10 minutes. The peak intensity is the fluorescence intensity at about 430 nm, which is the position of the peak of maximum fluorescence intensity. (a) L3 GQDs and amphetamine sulphate. (b) L4 GQDs and amphetamine sulphate. The concentration amphetamine in the samples varies from 0 mM to 2 mM.

In order to study the stability of amphetamine and GQDs solution at resting states, L3 and L4 are mixed with amphetamine sulphate solution and keep in ambient environment for several days, detection results in second day and the seventh day are compared with the results in first day.

These figures 4.2.5 show the results with different excitation wavelength. It is obvious that samples from second day show shrinking variation range. When the excitation wavelength is 335 nm, the increase of the storage time makes the emission peak of the fluorescence spectrum tend to blue shift, and the fluorescence intensity is obviously reduced, and the attenuation degree of the L3 sample is higher than that of the L4. When the excitation wavelength is 300 nm, for the L3 sample, the emission peak at 415 nm is significantly reduced, and the peak intensity decreases more obviously with the length of the storage time, but the emission peak at 510 nm does not change significantly. See the figure 4.2.5d for details. But for L4, the peak intensity did not decrease significantly. When the excitation wavelength was reduced to 280 nm, both L3 and L4 showed a significant decrease in fluorescence intensity compared to the result of the first day.

For further analysis, the peak intensities are selected for each curve of L3 at 300 nm excitation and plot with the concentration. The details of the specific emission peak intensity changes with the storage time can be seen in the figure 4.2.6. For L3 samples, the longer storage time makes the fluorescence response intensity of the sample decrease significantly, although the trend of its fluorescence intensity changing with the concentration of the drug is not affected. For L4, at high concentration range, second day results have higher intensity and at low concentration, second day results have slightly lower intensity than the first day.

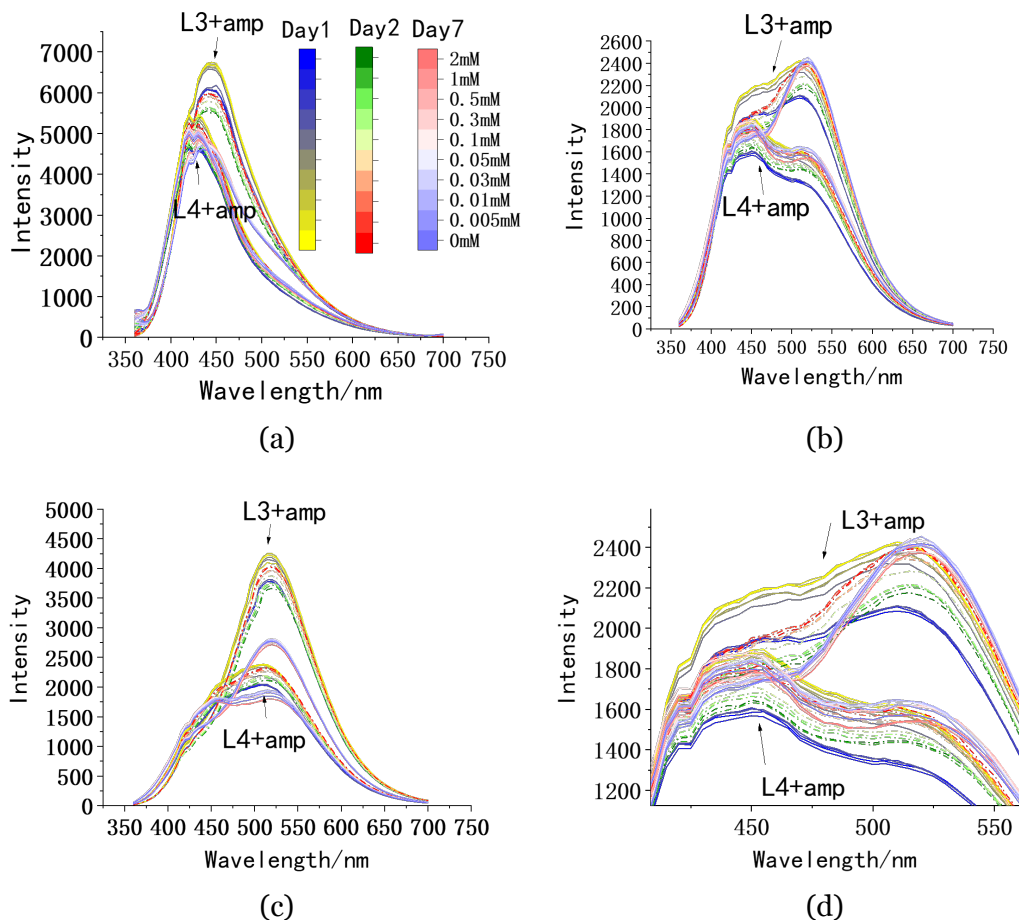


Figure 4.2.5: The fluorescence response spectrum of GQDs-based chemical sensors to amphetamine affected by the reaction time. The figures shows results with different excitation wavelength. (a) Excited at 335 nm. (b) Excited at 300 nm. (c) Excited at 280 nm. (d) Zoom of time dependence analysis with excitation wavelength of 300nm

However, one idea common to all results is that as the storage time gets longer, the fluorescence response of GQDs becomes more insensitive to changes in drug concentration. Compared with freshly mixed samples, with the change of drug concentration, the interval of fluorescence response of long-term samples becomes significantly smaller. In the samples that have been placed for seven days, we can

observe that there are obvious black deposits in the solution 4.2.7. Therefore, we infer that the decrease in the detection sensitivity of quantum dots may be caused by the deposition of graphene dots due to long-term storage, which affects the photoluminescence ability of GQDs.

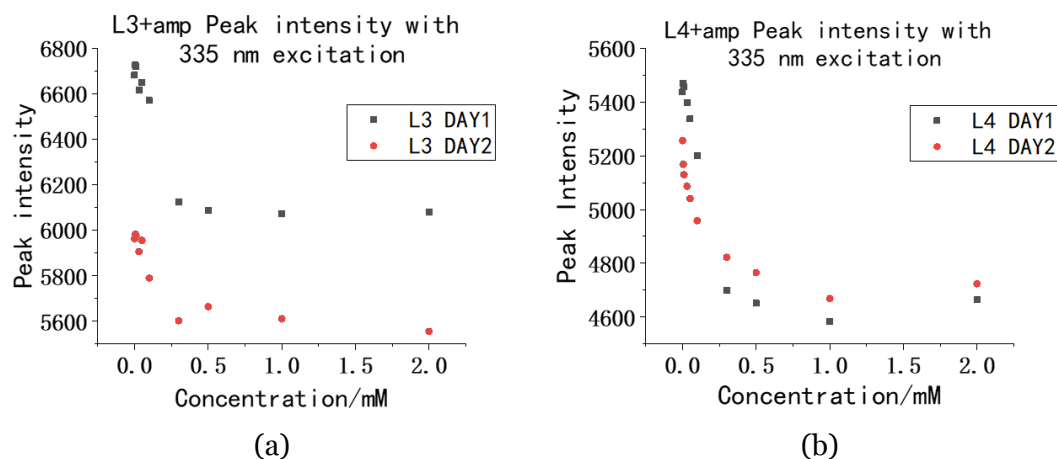


Figure 4.2.6: Peak intensity of fluorescence responses of L3 and L4 with amphetamine sulphate samples on first day and second day.

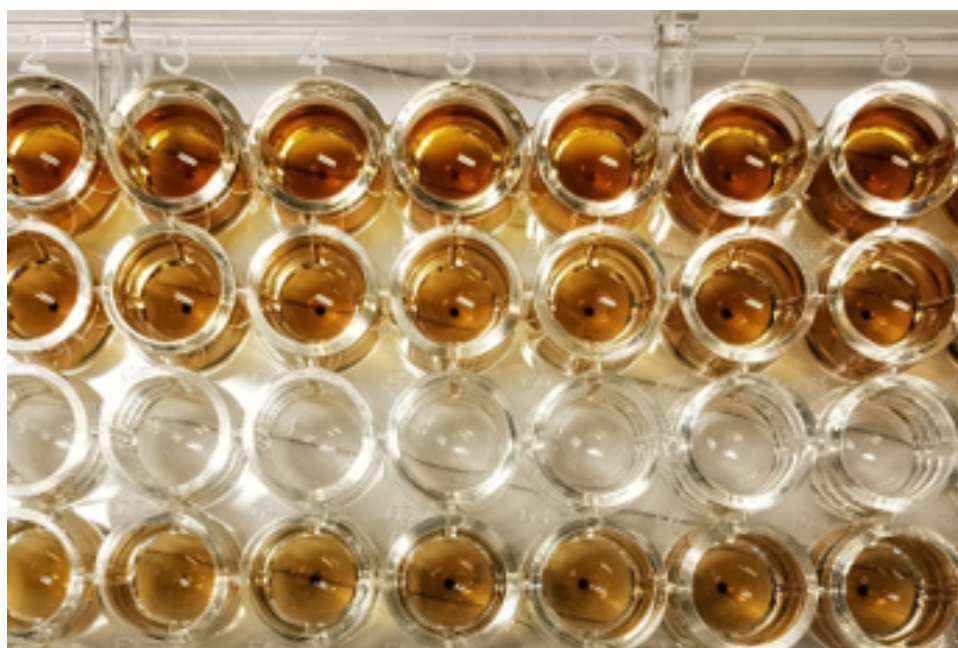


Figure 4.2.7: GQDs samples after 7 days.

4.3 Sensor test with cocaine hydrochloride

In order to explore the application of GQDs for further drug detection, we select cocaine as a comparison target drug. To detect the sensor performance towards cocaine. As

with the previous characterization methods, we also used fluorescence spectroscopy to analyze the fluorescence response intensity of GQDs and cocaine samples, and perform further stability and time-dependent analysis. In addition, FTIR technology is also suitable for the analysis of the internal valence bond structure of the sample. Considering the response intensity of GQDs sample, L3 is chosen as the detected sample for cocaine detection. In addition, the concentration of cocaine in the project means the concentration of cocaine group rather than the concentration of cocaine hydrochloride, because One molecule of cocaine hydrochloride contains one molecule of cocaine, which is different from amphetamine sulfate, since the concentration of cocaine varies from 0 to 10 mM.

Fluorescence comparison

Here we compared the FL response intensity of cocaine and amphetamine towards L3, results are shown in 4.3.1. The change of the fluorescence reaction intensity of cocaine and GQDs with the concentration of the detected drug is similar to the FL result of amphetamine. As the concentration of cocaine increases, the peak fluorescence response intensity of quantum dots gradually decreases, and the decrease degree is faster than the decrease of FL intensity of amphetamine. It can be seen from the figure that the peaks of pure amphetamine and cocaine do not overlap with the peaks of the quantum dot sample.

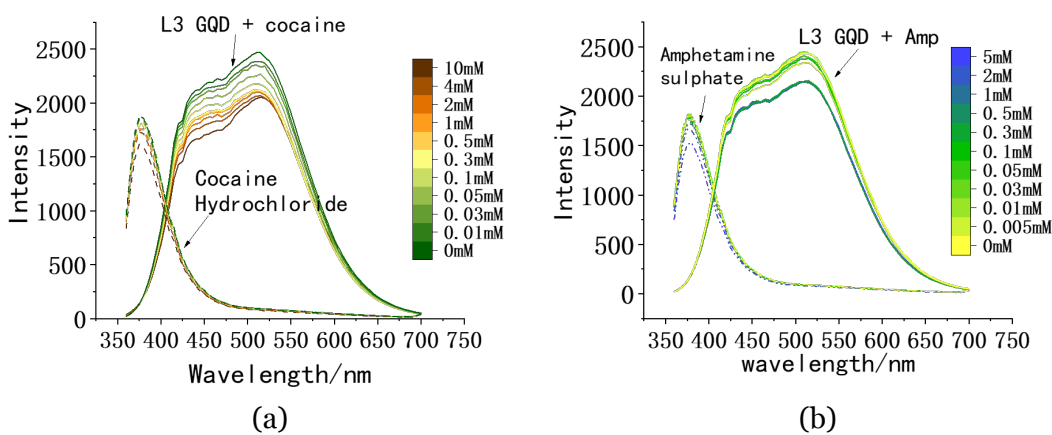


Figure 4.3.1: Fluorescence response comparison of two target drugs towards GQDs-based sensors. (a) Fluorescence response of cocaine drug to L3 GQDs. (b) Fluorescence response of amphetamine drug to L3 GQDs. These two plots show results with 300 nm excitation wavelength.

In order to further analyze the relationship between the cocaine concentration and the

measured fluorescence intensity ratio, the maximum peak intensity of the curve and the corresponding cocaine concentration are selected as a scatter plot, and linear fitting analysis is performed. The fitting result is shown in the figure 4.3.2. Since the intensity ratio of the maximum emission peak and the change trend of the concentration are obviously different in the low-concentration stage and the high-concentration stage, it is divided into two parts and fitted separately, and the fitting results also show two different linear relationships. This phenomena is quite similar with the linear fitting results of amphetamine results, the peak intensity ratio shows good linear fitting relationship with cocaine concentration, and the error of the fitting result is also small.

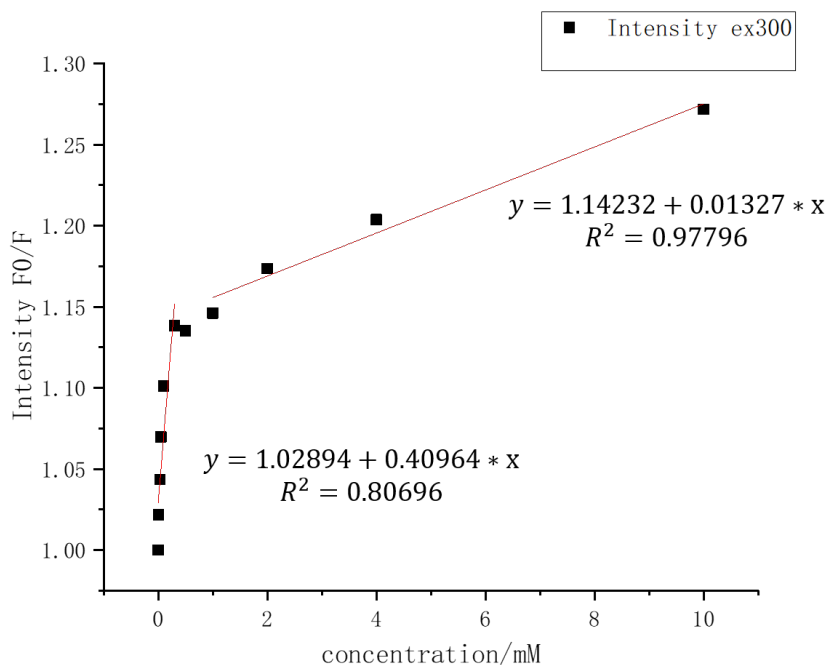


Figure 4.3.2: Relationship between concentration and intensity of GQDs with cocaine hydrochloride solution. F_0 and F are the FL intensities in the absence and presence of narcotic drugs, respectively. These are results with 300 nm excitation wavelength.

Stability and Time analysis

For the stability analysis, the freshly mixed L3 and cocaine samples are detected with FL spectroscopy, and then it is left for another seven days for the second test, and the result is compared with the first test spectrum. It can be seen from the figure that the sensitivity of the fluorescence reaction is significantly reduced with the longer storage time, and the interval of the fluorescence peak intensity with the change of the cocaine

concentration is significantly narrowed, and there is a significant decrease in the peak intensity at the positions of the two peaks, but the intensity of the emission peak at 440 nm decreases faster.

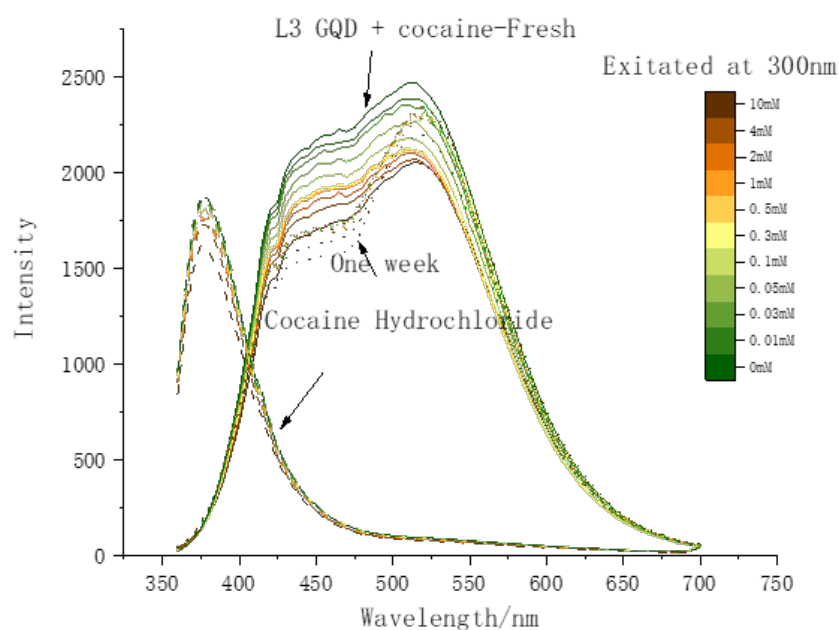


Figure 4.3.3: The fluorescence response spectrum of L3 GQDs-based chemical sensors to cocaine affected by the reaction time.

FTIR comparison

Here the FTIR spectrum of cocaine and amphetamine samples are compared. Unlike the FTIR spectrum of amphetamine, in the FTIR spectrum of cocaine, a smaller absorption peak appears at about 3300 cm^{-1} , which may be caused by the vibration of the secondary amide NH. In addition, the amphetamine and L3 samples show a much boarder peak between 2500 to 3200 cm^{-1} .

4.3.1 Comparison and Selective Detection

According to the research on drug-specific detection based on GQDs sensor, the fluorescence spectra of the reaction between GQDs and amphetamine and cocaine were compared, and the results showed that except for very similar change trends, they were all in the high concentration and low concentration ranges, respectively, which shows two negative linear relationships with different slopes.

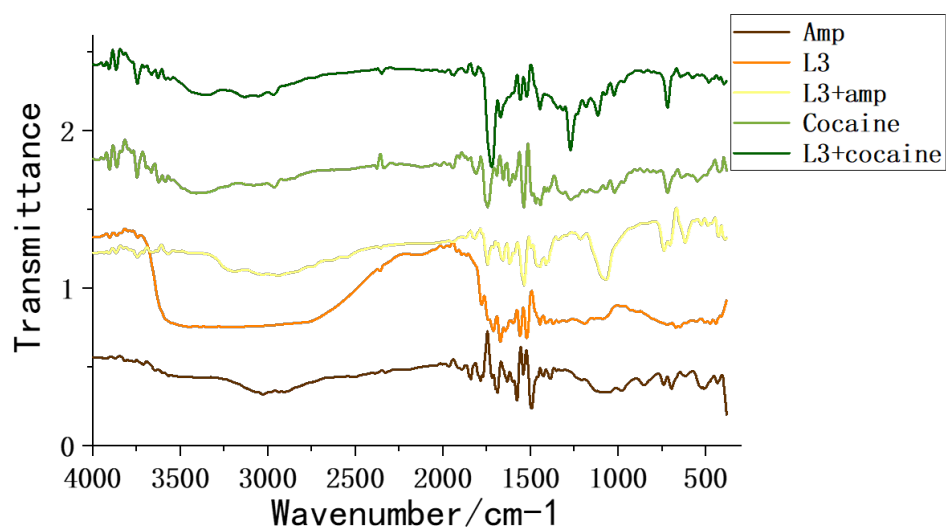


Figure 4.3.4: FTIR spectra comparison between L3+cocaine and L3+amp samples.

Chapter 5

Conclusions

Based on previous work and results, we investigated a GQDs based nanosensor for forensic drugs detection, such as amphetamine and cocaine; The drug detection results of amphetamine and cocaine are also compared. Response range of GQDs sensors for amphetamine and cocaine is between 0.01 mM to 10 mM. With excitation wavelength of 300 nm, the relationship between peak intensity ratio and drug concentration shows good linear fitting results, which shows the great potential of the future application of GQDs-based sensors for forensic detection.

Generally, the fluorescence intensity shows quench with the increasing of drug (amphetamine and cocaine) concentration, but two different decreasing trend exists in low and high concentration range, respectively.

The shift of excitation wavelength can cause the appearance of dual peaks, especially for L3, L4 and L5, in addition, it also cause the red shift on the FL spectrum of L3 and L4, and also cause the blue shift on the FL spectrum of L5.

The mixture of GQDs and target drugs are not stable in ambient environment, therefore, in the process of putting the sensor into use, it is necessary to pay attention to the instant detection after instant mixing, so as not to affect the sensitivity of the detection. However, the continuous excitation emission spectrum test results show that under the condition of long-term light excitation, the quantum dot sensor shows good stability for the drug test results.

5.1 Future Work

The FL detection sensitivity and the results are significantly affected by the synthesis condition and doping condition of GQDs. Therefore, how to well control the morphology and structure of the synthesized quantum dots to ensure that the GQDs-based sensors can work stably and provide accurate concentration detection results is a topic worthy of study.

In the future, selective detection might be achieved by involving antibodies corresponding to the target drugs, the adding of antibodies to GQDs may provide a new view towards the sensor structures and detection mechanism towards drugs.

Bibliography

- [1] Mikael Karlsson, Carl Strandqvist, Johnny Jussi, Olof Öberg, Ingemar Petermann, Louise Elmlund, Simon Dunne, Ying Fu, and Qin Wang. Chemical sensors generated on wafer-scale epitaxial graphene for application to front-line drug detection. *Sensors*, 19(10):2214, 2019.
- [2] Francis D Krampa, Yaw Aniweh, Prosper Kanyong, and Gordon A Awandare. Graphene nanoplatelet-based sensor for the detection of dopamine and n-acetyl-p-aminophenol in urine. *Arabian Journal of Chemistry*, 13(1):3218–3225, 2020.
- [3] Majid Masteri-Farahani and Faezeh Askari. Design and photophysical insights on graphene quantum dots for use as nanosensor in differentiating methamphetamine and morphine in solution. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, 206:448–453, 2019.
- [4] Ülle-Linda Talts. Characterization of graphene-based sensors for forensic applications: Evaluating suitability of cvd graphene-based resistive sensor for detection of amphetamine. *Master thesis at Royal Institute of Technology, TRITA-EECS-EX 2019:789*.
- [5] IDS UNODC et al. World drug report. *United Nations New York, NY*, 2019.
- [6] Jean-Paul Grund, Philip Coffin, Marie Jauffret-Roustide, Minke Dijkstra, Dick De Bruin, and Peter Blanken. The fast and furious—cocaine, amphetamines and harm reduction. *Monographs*, page 191, 2010.
- [7] Gregory H Jones, Michael A Carrier, Richard T Silver, and Hagop Kantarjian. Strategies that delay or prevent the timely availability of affordable generic drugs in the united states. *Blood*, 127(11):1398–1402, 2016.
- [8] David G Liddle and Douglas J Connor. Nutritional supplements and ergogenic aids. *Primary Care: Clinics in Office Practice*, 40(2):487–505, 2013.

- [9] Cristoforo Pomara, Tommaso Cassano, Stefano D'Errico, Stefania Bello, Antonino Davide Romano, I Riezzo, and Gaetano Serviddio. Data available on the extent of cocaine use and dependence: biochemistry, pharmacologic effects and global burden of disease of cocaine abusers. *Current medicinal chemistry*, 19(33):5647–5657, 2012.
- [10] P Campins Falco, C Molins Legua, R Herraiez Hernandez, and A Sevillano Cabeza. Improved amphetamine and methamphetamine determination in urine by normal-phase high-performance liquid chromatography with sodium 1, 2-naphthoquinone 4-sulphonate as derivatizing agent and solid-phase extraction for sample clean-up. *Journal of Chromatography B: Biomedical Sciences and Applications*, 663(2):235–245, 1995.
- [11] Dandan Ge and Hian Kee Lee. Ionic liquid based dispersive liquid–liquid microextraction coupled with micro-solid phase extraction of antidepressant drugs from environmental water samples. *Journal of Chromatography A*, 1317:217–222, 2013.
- [12] Arezou Taghvimi and Hamed Hamishehkar. The application of magnetic nano graphene oxide in determination of methamphetamine by high performance liquid chromatography of urine samples. *Journal of the Iranian Chemical Society*, 13(8):1471–1480, 2016.
- [13] Majid Masteri-Farahani and Nazanin Mosleh. Modified CdS quantum dots as selective turn-on fluorescent nanosensor for detection and determination of methamphetamine. *Journal of Materials Science: Materials in Electronics*, 30(24):21170–21176, 2019.
- [14] Zeinab Saberi, Behzad Rezaei, Hossein Faroukhpour, and Ali Ashghar Ensafi. A fluorometric aptasensor for methamphetamine based on fluorescence resonance energy transfer using cobalt oxyhydroxide nanosheets and carbon dots. *Microchimica Acta*, 185(6):1–10, 2018.
- [15] Maedeh Akhoundian, Taher Alizadeh, Mohammad Reza Ganjali, and Parviz Norouzi. Ultra-trace detection of methamphetamine in biological samples using fft-square wave voltammetry and nano-sized imprinted polymer/mwcnts-modified electrode. *Talanta*, 200:115–123, 2019.

- [16] Andre K Geim and Konstantin S Novoselov. The rise of graphene. In *Nanoscience and technology: a collection of reviews from nature journals*, pages 11–19. World Scientific, 2010.
- [17] Rahul Raveendran Nair, Peter Blake, Alexander N Grigorenko, Konstantin S Novoselov, Tim J Booth, Tobias Stauber, Nuno MR Peres, and Andre K Geim. Fine structure constant defines visual transparency of graphene. *Science*, 320(5881):1308–1308, 2008.
- [18] Fredrik Schedin, Andrei Konstantinovich Geim, Sergei Vladimirovich Morozov, EW Hill, Peter Blake, MI Katsnelson, and Kostya Sergeevich Novoselov. Detection of individual gas molecules adsorbed on graphene. *Nature materials*, 6(9):652–655, 2007.
- [19] Greg Tegart et al. Nanotechnology: The technology for the 21st century. *APEC, Center for Technology Foresight, Bangkok, Thailand*, 2001.
- [20] J Ajayan, D Nirmal, P Mohankumar, M Saravanan, M Jagadesh, and L Arivazhagan. A review of photovoltaic performance of organic/inorganic solar cells for future renewable and sustainable energy technologies. *Superlattices and Microstructures*, page 106549, 2020.
- [21] Konstantinos Dimos. Carbon quantum dots: surface passivation and functionalization. *Current Organic Chemistry*, 20(6):682–695, 2016.
- [22] Yongqiang Dong, Jingwei Shao, Congqiang Chen, Hao Li, Ruixue Wang, Yuwu Chi, Xiaomei Lin, and Guonan Chen. Blue luminescent graphene quantum dots and graphene oxide prepared by tuning the carbonization degree of citric acid. *Carbon*, 50(12):4738–4743, 2012.
- [23] Carl Fredrik Åslund. Detection of amphetamine with graphene quantum dots. *Master thesis at Royal Institute of Technology, TRITA-SCI-GRU 2020:378*.