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Differentiation of illicit drugs with THz time-domain spectroscopy

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Abstract The terahertz time-domain spectroscopy (THz-TDS) was used for sensing and identifying illicit drugs. The absorption spectra of seven illicit drug samples (morphine and its hydrochloride, cocaine hydrochloride, codeine phosphate, papaverine hydrochloride, pethidine hydrochloride, and thebaine) were studied by THz-TDS at 0.3–2.0 THz at room temperature. The geometric structure and vibration frequencies of morphine were calculated by density functional theory. The four absorption features were dominated by intra-/inter-molecular collective or lattice vibration modes. Each illicit drug has a distinct signature in its THz spectra. The results indicate that the THz-TDS can be used to identify and discriminate illicit drugs by their characteristic fingerprints.

Key words Terahertz, THz-TDS, Illicit drugs, DFT, Morphine

1 Introduction

Drug abuse has been a serious problem throughout the world. Several techniques have used for inspection of illicit drugs, such as X-ray scanner, canine detection, and trace drug detection. Terahertz (THz) technology has drawn an increasing attention due to its wide applications in various fields[1–5]. THz spectroscopy is a promising technique for detecting and identifying explosives and illicit drugs in mails, with their fingerprint spectra. THz rays penetrate plastics, clothing, luggage, paper products, and other non-conductive materials, and the transmission or absorption spectra can be recorded for seeing the drugs in an envelope. In some major airports in Europe and America, terahertz imaging has been used for security inspection. Terahertz imaging detects firearms and knives, but not the drugs and explosives due to poor mass resolution of them. A new approach is to combine terahertz imaging and spectroscopy in the security checks, using the imaging to find suspicious samples and the spectroscopy to identify them.

THz absorption spectroscopy is good at sensing illicit drugs. Experiments were done on methylenedioxy methamphetamine (MDMA) and methamphetamine (MA) with THz rays using the wave parametric oscillator on three amphetamine-type stimulants[6,7]. Sun *et al*[8] used 0.2–2.5 THz absorption spectra to indentify MDMA, MA, and methylenedioxy amphetamine (MDA). Li *et al*[9] studied MA using terahertz time-domain spectroscopy (THz-TDS) and simulation with the Gaussian 03 code package. THz absorption spectra was also used to detect acetyl codeine and heroin[10], ketamine hydrochloride[11], and methadone hydrochloride[12].

Morphine, a common drug, has been widely studied by using the mass spectra[13], infrared and Raman spectra[14], but its THz spectrum has been less known. In this work, 0.3–2.0 THz absorption spectra of seven illicit drugs were studied using THz-TDS. The results show that the drugs can be detected by their fingerprint spectra in a THz system. The density functional theory (DFT) was used to predict and understand the THz spectra of morphine.

2 Methods and materials

2.1 The THz-TDS system

The transmitted THz-TDS apparatus and data analysis of experimental were given in our previous paper[15].

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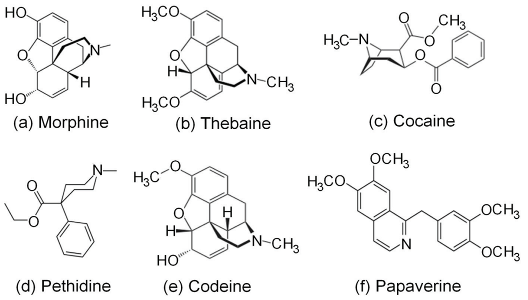
Briefly, it is of a model-locked Ti: sapphire laser (Mai-tai, Spectra Physics), with a 80-MHz repetition rate, 100-fs pulse duration, and 600-mW average power at the 800-nm center wavelength. The laser light is divided into two beams, that is, a pump beam focused onto a biased GaAs photoconductive emitter for THz generation, and another beam as a functional probe for electro-optic detection using a ZnTe crystal of 2-mm thick. The setup has a usable bandwidth of 0.3–2.0 THz, in spectral resolution of better than 40 GHz. To eliminate the influence of ambient water vapor on data collection, the measurements were done in nitrogen atmosphere, and temperature and humidity near the sample was controlled at 20±0.5°C and <4%.

2.2 Sample preparation

The illegal drugs (Fig.1), were from the National Institute for Control of Pharmaceuticals and Biological Products, China, and used without further purification. The drugs were well mixed with polyethylene (PE) powder in different proportions. The mixtures were pressed into Φ13 mm×1.2 mm sample pellets under 2.943×10^4 N to minimize the multi-reflection effects.



(a) Morphine (b) Thebaine (c) Cocaine

(d) Pethidine (e) Codeine (f) Papaverine

Fig.1 Structural formulas of the illegal drugs.

2.3 Predication of theoretical frequencies

To better understand the THz absorption spectrum for morphine, the frequencies were predicated using the Gaussian 03 code[16]. Geometric optimizations were performed at the B3LYP/6-31G(d) level, without imaginary frequency in harmonic approximation.

3 Results and discussion

Fig.2 shows the THz absorption spectra of the drugs at 0.3–2.0 THz. The absorption coefficients below 0.3 THz were not given due to multiple reflections inside the sample. A slight difference in structure should result in a large spectral difference, such as the morphine and morphine hydrochloride.

In Fig.2(a), the morphine has a well-defined spectral feature, with four absorption peaks at 1.32, 1.50, 1.66, and 1.97 THz. Its low frequency vibrations of morphine were calculated at the B3LYP/6-31G(d) level, and compared with the experimental data at 600 –3000 cm^{-1} in Ref.[14]. Our results agree with the experiment data, with the 0.960 scale factor cited from the Computational Chemistry Comparison and Benchmark Database. Form the geometry optimized by the B3LYP/6-31G(d) level, an unique “T” structure, can be seen, with two rings locating at the right angles relative to the other three rings of approximate plane.

In Fig.2(b), the morphine-HCl has a clear spectral distinction without discrete frequency band except for two weak absorption peaks of 0.82 and 1.71 THz, indicating that the solid-state crystal structure probably dominated the determination of THz spectra, which was used by Fischer *et al*[17] who demonstrated their detection of morphine-HCl inside an envelope.

Thebaine, which is similar to morphine, has weak absorption peaks at 0.59, 1.03, 1.55, 1.66, and 1.78 THz in Fig.2(c), indicating that THz-TDS is sensitive to crystalline structures[18,19] and can be used to identify compounds with similar substitutes.

As a powerful addictive stimulant, cocaine typically exists in the form of cocaine hydrochloride, which has the spectral features at 0.85, 1.20, 1.47, 1.56, and 1.96 THz in Fig.2(d). While the 0.85 and 1.56 THz absorptions were reported[17,20], the 1.47 and 1.96 THz absorptions are observed for the first time. Cocaine hydrochloride has similar chemical structure with cocaine freebase, but its spectrum difference is distinct. They share a common peak at 1.54 THz, but cocaine hydrochloride has more absorption peaks because the large Cl counter ion increases the magnitude of dipole moment in normal mode vibration [21]. The THz-TDS spectrum of the chemically similar ecgonine was distinct from that of cocaine[22].

The pethidine hydrochloride exhibits a weak absorption peak at 1.15 THz and a small peak at 1.84 THz (Fig.2(e)). In Fig.2(f), the THz-TDS spectrum of codeine phosphate has major peaks at 0.81, 1.01 and 1.25 THz, two small peaks at 1.39 and 1.87 THz, and a strong peak at 1.98 THz. Dobroiu *et al*[23] indentified codeine in an envelope in THz transmission spectra.

Papaverine is pharmacologically an alkaloid as a muscle relaxant and vasodilator extracted from opium, and its Raman and IR spectroscopy has been reported[24,25]. The papaverine hydrochloride in Fig.2(g) has complicated absorption features of five absorption peaks at 1.06, 1.42, 1.62, 1.75, and 1.89 THz.

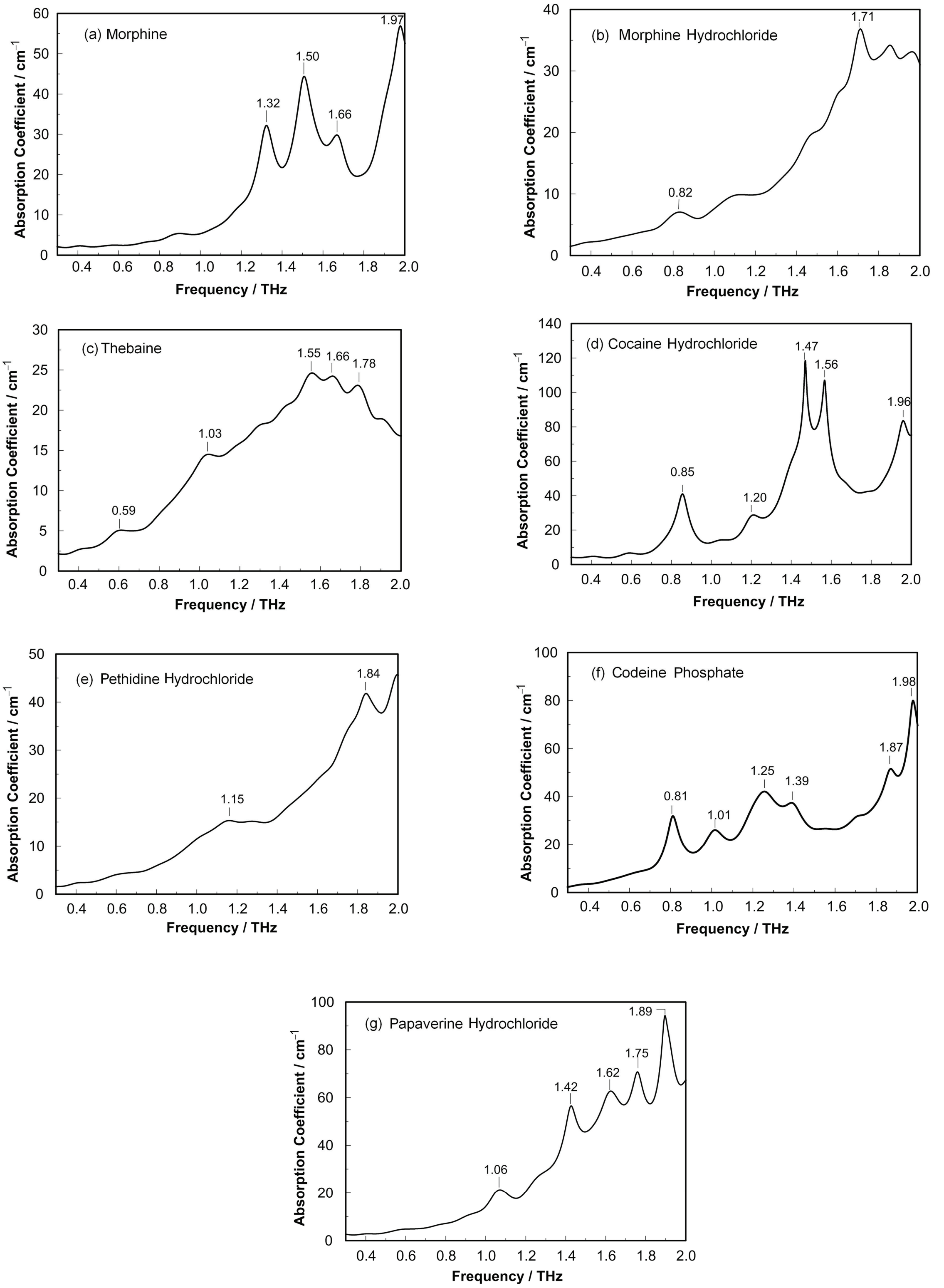


Fig.2 THz absorption spectra of seven drugs at 0.3–2.0 THz.

To the authors' knowledge, the THz-TDS spectra for pethidine hydrochloride, codeine phosphate, and papaverine hydrochloride at 0.3–2.0 THz have not been reported yet. The THz frequency obtained in this study could not be compared and clearly discriminated due to crystal interactions. Predicting theoretically the vibration frequencies at low-energy modes should consider the combination of inter/intra-atom vibrations. For instance, the THz spectra of (+)-methamphetamine hydrochloride could be accurately assigned under calculations of solid-state DFT[26].

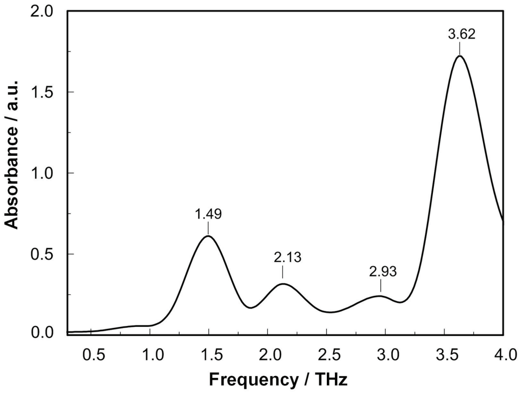


Fig. 3 THz spectra of morphine calculated by B3LYP/6–31G(d) level at regions of 0.3–4.0 THz.

In order to reveal the relationship of structures with vibration modes of morphine, theoretical calculations were carried out using Gaussian 03 program. The morphine belongs to the C_1 symmetry point group, and has 114 modes of normal vibration aside from three translations and three rotations. Fig.3 shows that the THz spectra of morphine calculated by B3LYP/6-31G(d) level at 0.3–4.0 THz without scales were located at 1.49, 2.13, 2.93, and 3.62 THz, respectively. The 1.49 THz absorption at 0.3–2.0 THz agrees well with the experimental data of 1.50 THz. This is tentatively attributed to intra-molecular vibrations, and the 2.13 THz absorption seems close to the experimental data of 1.97 THz. The 2.13 THz peak is theoretically weaker than that of the 1.49 THz, and the measured 1.97-THz peak is the strongest, but there are no calculated absorption peaks at 1.32 and 1.66 THz. This is ascribed to the different effect of solid, temperature, and vibration anharmonicity, because the calculation is based on the vibration modes of gas molecule at 0 K, while the condensed sample is the polycrystalline materials at room temperature. The absence of the O-H stretching at 3607 and 3534 cm^{-1} in the IR spectrum could be related to morphine molecules forming intermolecular hydrogen bonds. Therefore, the absorption peaks at 1.32, 1.66, and 1.97 THz are caused by inter-molecular modes or lattice vibration but not the intra-molecular affects.

4 Conclusions

In this study, the THz absorption spectra of seven illicit drugs were measured by THz-TDS system at 0.3–2.0 THz, and differentiated sufficiently each other. Fingerprints in relation to the intra-/inter-molecular vibration or phonon modes were identified, and their absorption coefficients were measured. These could be belonged to a database. The results are of great importance for identifying illicit drugs, and have been demonstrated by characteristic THz absorption of many drugs. The THz spectra may be a promising inspection for illicit drugs.

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