Optical properties of selected Chinese Traditional Patent Medicines and Western Medicines terahertz range

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Abstract The spectral characteristics of Sang Ju Gan Mao Granules, Gan Mao Jie Du Tablet, Fu Fang Jin Yin Hua Granules and Compound Paracetamol, and Amantadine Hydrochloride Tablets are studied by terahertz time-domain spectroscopy (THz-TDS) technologies in the spectral range of 0.2—1.7 THz. The absorption spectra and the indexes of refraction are obtained. It can be seen that the three samples of Chinese Traditional Patent Medicines have almost the same absorption peaks at 1.44 THz. However, the absorption peaks of the three western medicine samples are at 0.73, 1.01, and 1.18 THz, respectively. The large spectral differences between different drugs are strong evidences that THz time-domain spectroscopy is a useful fingerprint technique in the study of pharmaceutical compounds and the crack down on the fake medicines.

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1 Introduction

It is well known that illicit drugs endanger both human healthy and public security, so it is of crucial importance to detect and study illicit drugs and fake medicines. Over the decades, the capability to analyze drug has become increasingly convenient owing to the improvement and advancement of the technologies. At present, several techniques such as scanning electron microscopy, conventional optical microscopy, and near infrared (NIR) and Raman are being used to analyze and characterize solid pharmaceutical materials, but they are destructive, not fully-automated, and not able to resolve multiple coating layers or provide only limited information [1-3]. So a safe and nondestructive method is needed for the detection and identification of illicit drugs. In this respect, terahertz (THz) time-domain spectroscopy shows great advantages and has recently been demonstrated to be an interesting novel technique for the investigation of pharmaceutical materials and products [4].

The THz region of the electromagnetic spectrum is commonly considered the frequencies ranging from 0.1 to 10 THz, between the infrared and microwave regions. One of the most interesting properties of THz radiation is that it can induce low frequency crystal lattice vibrations, crystalline phonon vibrations, torsion vibrations, and weak intermolecular interactions such as hydrogen bonding and vander waals force [5]. Because of the inherent rotation vibration states of many organic molecules in gas and the low frequency vibration of crystal lattice in solids [6], it is possible that THz spectroscopy can be used to detect illicit drugs. However, historically spectroscopy measurement in THz region has been challenging owing to the lack of suitable detector and the difficulty associated with generating and detecting photons in the THz region and so on. Recent advances are now allowing THz technology to be applied to many fields such as the semiconductor, security, and medical [7]. In particular, THz spectroscopy has become more prevalent in the study of pharmaceutical materials in recent years. THz time-domain spectroscopy, compared with conventional spectroscopic techniques, can provide both absorption coefficient and refractive index of a sample with high signal-to-noise ratio (SNR) and high sensitivity with room temperature sources and detectors. In addition the low energy of THz radiation minimizes the risk of sample degradation. Absorption characteristics within the mid-IR (MIR) region are dominated by intramolecular vibrations involving the motion of bonds within the sample molecule. In the microwave region, THz photons have not enough energy to make molecules vibrate in stretch or bend modes but torsional low energy motions may be excited. Perhaps more importantly the forces that hold molecules together in the crystal lattice are much weaker than intramolecular vibrations—these so-called phonon modes may be excited by THz radiation and thus cause absorption features in the THz spectrum. A consequence of this is that crystalline samples have distinct THz spectra while amorphous materials are too disordered to sustain phonon modes, hence are relatively transparent in the THz spectral region. Usually, crystalline pharmaceuticals have unique phonon modes so that different polymorphic forms have different THz spectra [8]. These spectral fingerprints can be used for drugs identification using THz time-domain spectroscopy as many pharmaceutical materials have adequate spectral fingerprints in THz range.

In this letter, we report an experimental investigation for the identification of Chinese Traditional Patent Medicines and Western Medicines using THz time-domain spectroscopy (THz-TDS). The refraction indices and absorption coefficients of these drugs were measured. The THz spectra showed distinct differences between different medicines due to the differences in arrangements and intermolecular interactions. This research demonstrates that study on the optical properties of selected Chinese Traditional Patent Medicines using THz-TDS is greatly significant and effective in the field of security. In particular, this study makes a contribution to establish fingerprint database of medicines.

2 Experiment

The reflecting-emitting THz system [9] was used in our experiments in measuring transmit THz time domain spectra as shown in Fig. 1. The laser source is a commercial mode-locked Ti: sapphire laser (Spectra Physics Mai Tai) producing 100-fs pulses at 800 nm with a repetition rate of 80 MHz and an average power of 960 mW. A p-type InAs wafer with 〈1 0 0〉 orientation was used as the THz emitter and a 2.8-mm-thick 〈1 0 0〉 ZnTe was employed as the sensor. A standard lock-in technology was used in this system. The samples are located in the focus of the two Si lens and are held in a 5-mm-thick quartz cuvette. The width and height size of the quartz cuvette are equal to 2.5 and 30 mm, respectively. Here, the relative humidity in the chamber was less than 4% and the temperature was 298 K in the experiments.

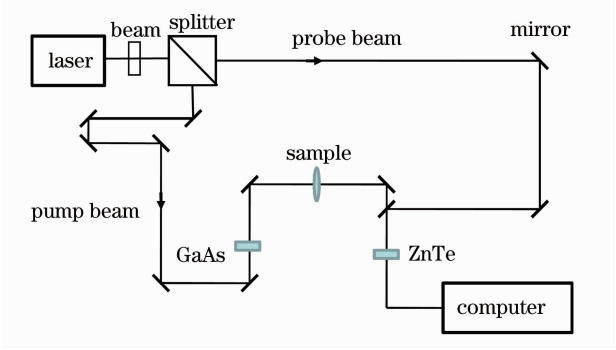

Fig. 1. Schematic diagram of the THz-TDS system

Detials of the experimental samples are included in Table 1. These medicines were firstly triturated with an agate mortar and then pressed under a pressure of 12 tons to form thin circular slices with a diameter of 0.013 m and thickness of about 0.001 m.

Table 1 Detials of the Experimental Samples

Number	Name	Manufacturer
A1	Sang Ju Gan Mao Granules	Lishizhen Medicine Group Co., Ltd.
B1	Gan Mao Jie Du Tablet	Tonghua Zhenghe Pharmaceutical Co., Ltd.
C1	Fu Fang Jin Yin Hua Granules	He Bei Gogin Pharmaceutical Co., Ltd.
S1	Compound Paracetamol and Amantadine Hydrochloride Tablets	Wutai Pharmaceutical Co., Ltd.
S2		Asia Pharmaceutical Group (Hai Nan)
S3		Changchun Haiwai Pharmaceutical Group Co., Ltd.

3 Results and discussion

Figure 2 shows THz time-domain spectra of selected Chinese Traditional Patent Medicines (A1, B1, C1) and reference. The reference pulse of free cell without sample is shown with dotted line while the solid lines are the THz signals that have passed through the sample cells, showing a drop in amplitude and a delay in time because of reflection, dispersion, and absorption. The different delay time suggested that the physical and chemical properties of the samples are unlike [10].

In the crystal, the molecules are held together by vander waals forces to maintain the rigid crystal structure. Owing to the weak potential forces and the large moving masses involved, translational and torsional motions of the molecules fall into the far-IR (FIR) part of the spectrum. Their absorption and refractive index spectra are shown in Figs. 3 and 4, respectively. It is seen that all three samples show a steep rise in absorption with frequency. This behavior, seen in many amorphous materials, can be caused by the coupling of radiation into the acoustic phonon modes of the materials

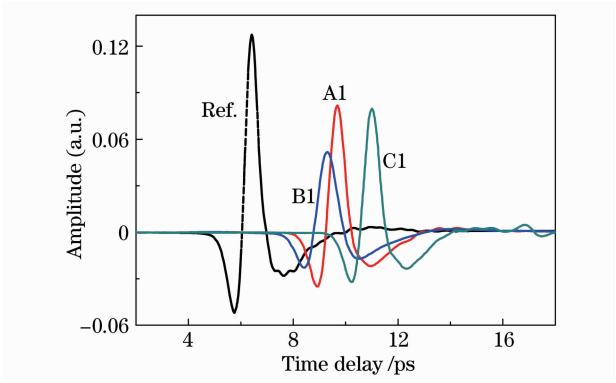

Fig. 2. THz time-domain spectra of selected Chinese Traditional Patent Medicines (A1, B1, C1) and reference

[11]. And the three medicine samples have almost the same absorption peaks at 1.44 THz. Corresponding to every absorption peak, a characteristic change is shown in the refractive index spectrum, which means that an abnormal dispersion is always accompanied with an obvious absorption. Take 1.44 THz for an example, the refractive indices of A1, B1 and C1 are 1.98, 1.90, and

2.40, respectively. By contrast, medicines with different compositions, due either to additives or to a different refining process, have markedly different refractive indices. These results suggest that medicines with different compositions can be identified and analyzed by THz spectroscopy.

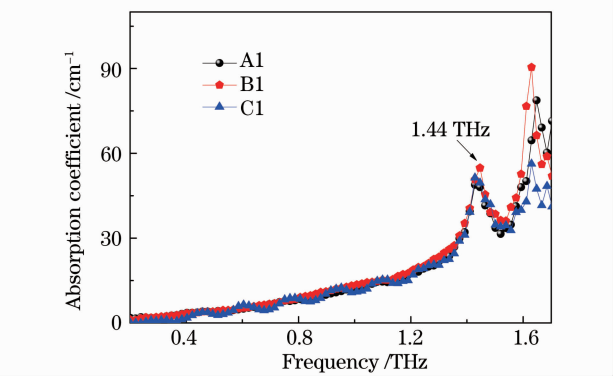

Fig. 3. Absorption coefficient of selected Chinese Traditional Patent Medicines

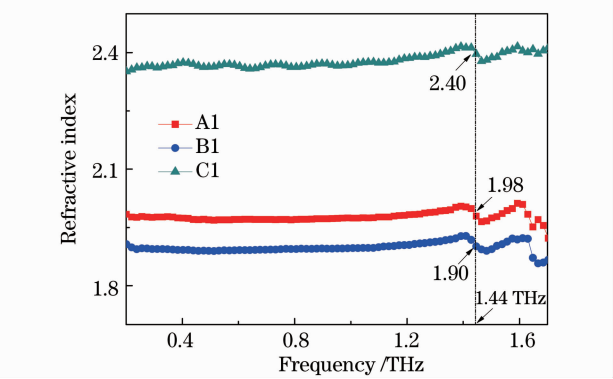

Fig. 4. Refractive index of selected Chinese Traditional Patent Medicines

The strong structure dependency of low-frequency modes allows to distinguish even structurally closely related compounds. So while both samples, different arrangements can change the intermolecular modes and therefore the FIR spectra dramatically [12]. As an example, Fig. 5 compares the compound paracetamol and amantadine hydrochloride tablets from three different companies. THz time-domain spectra of S1, S2, S3, and reference are shown in Fig. 5. It is observed that the delay time of the same thickness samples is different, while their amplitudes are same.

As in the previous section, it can be seen that their spectra have differences because of different intermolecular orders in the crystalline lattice and so on, indicating THz spectra are sensitive to structure and arrangement. Figures 6 and 7, respectively, show the absorption coefficients and refractive indices of the three samples from 0.2 to 1.4 THz. The three Western Medicine samples are seen to have almost the same absorption peaks at 0.73, 1.01, and 1.18 THz. And the absorption peaks are more evident. In addition, all absorption

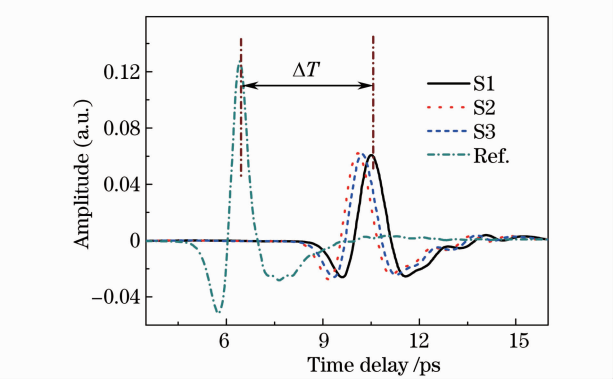

Fig. 5. THz time-domain spectra of Compound Paracetamol and Amantadine Hydrochloride Tablets S1, S2, S3 and reference

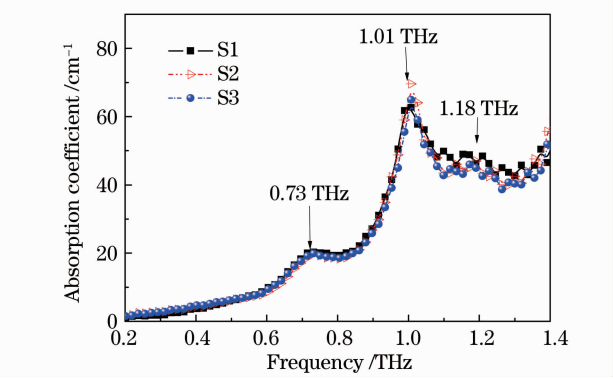

Fig. 6. Absorption coefficient of S1, S2, and S3

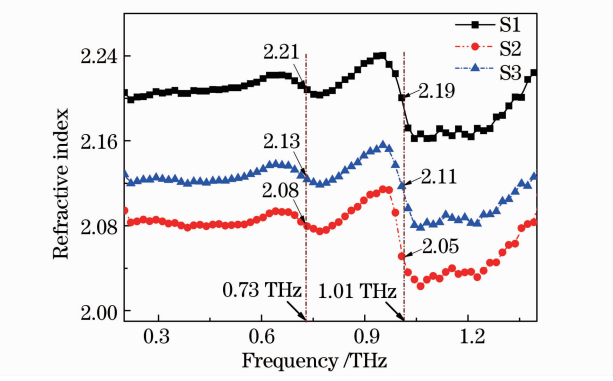

Fig. 7. Refractive index of S1, S2, and S3

peaks are associated with a characteristic phase shift in the refractive index. The refractive indices are very different. Take 0.73 THz for an example, the refractive indices of S1, S2, and S3 are 2.21, 2.08, and 2.13, respectively. Hence, THz-TDS enables a spectroscopic discrimination between even structurally closely related compounds, which may have useful applications in the chemical and pharmaceutical industry.

4 Conclusion

THZ-TDS is used to obtain the absorption coefficients and refractive indices of selected Chinese Traditional Patent Medicines and three Western Medicines. And the three Western Medicine samples have almost

the same absorption peaks at 0.73, 1.01, and 1.18 THz. The pharmaceutical examples show that a variety of different Chinese Traditional Patent Medicines and Western Medicines are readily differentiated by their THz absorption spectra and refractive spectra. Their spectral differences arise solely from the different intermolecular orders in the crystalline lattice, which indicates the sensitivity of THz spectra to structure and arrangement in medical materials. THz spectroscopy therefore enables a clear discrimination among Chinese Traditional Patent Medicines and Western Medicines. With advances continuing in the technology behind the spectroscopy, and the growing utilization of chemometrics, THz technique is expected to become one of the industry standards for future pharmaceutical endeavors.

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