# Terahertz Spectroscopy of Furosemide

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***Abstract*-Low frequency vibrational modes of furosemide were measured with terahertz time domain spectroscopy at room temperature. The different crystalline forms of furosemide were also measured. A clear difference between their spectra was observed. This makes the identification of polymorphs of furosemide easy and quick.**

## I. INTRODUCTION

Terahertz time domain spectroscopy (THz-TDS) is becoming an important technique in the pharmaceutical industry especially in the identification of polymorphs and the imaging of drug coatings.

The polymorphism of furosemide has been extensively investigated with x-ray powder diffractometry (XRD) and fourier transform infrared spectroscopy. In this paper, the different crystalline forms of furosemide were studied using THz-TDS. The absorption coefficients of these samples were obtained in the range of 0.2-1.7 THz at room temperature.

## II. EXPERIMENT

The experimental setup for THz-TDS has been described in the literature [1]. Furosemide was purchased from Sigma–Aldrich Co. and used without further purification. Different crystalline forms of furosemide were prepared carefully and named according to [2] and were proved by XRD. Samples were mixed with polyethylene powder in a mass ratio of 1:5 and made into disks of thickness about 1.0 mm by applying a pressure of 22 MPa.

## III. RESULTS AND DISCUSSION

The absorption coefficient and refractive index of furosemide are shown in Fig.1. Furosemide shows two wide peaks centered at 1.13 THz and 1.52 THz. Fig. 1 also shows the THz spectra of three crystalline forms of furosemide. The difference between these samples is clear. Form I has nearly the same spectrum shape as the purchased compound. Form III has a stronger 1.35 THz peak than form I. Form V shows two peaks which have positional shift and lower strength compared with form I.

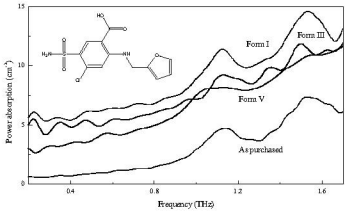


Fig.1. Terahertz spectra of three crystalline forms of furosemide

To further understand the relationship between THz spectra and the structure, density functional theory (DFT) calculations were performed at B3LYP/6-311G level of theory by using the Gaussian 03 program package [3]. Primary results on the single molecule are shown in Table 1. The 0.94 THz mode is associated with rotation of the furan group and the carboxylic group. The 1.32 THz mode is associated with rotation of the substituted groups except the furan part. The 1.50 THz mode is caused by the vibration of the whole molecule. The peak position shift is due to the difference of crystalline forms. The missing 1.32 THz mode in form I and V may be explained by DFT calculations based on x-ray crystallographic data.

Table 1. Calculated and experimental frequencies of furosemide

| Single molecule | Form I | Form III | Form V |
|---|---|---|---|
| 0.94 THz | 1.13 THz | 1.12 THz | 1.05 THz |
| 1.32 THz | | 1.35 THz | |
| 1.50 THz | 1.5 THz | 1.49 THz | 1.57 THz |

## IV. SUMMARY

The experimental and theoretical investigation of furosemide and its polymorphs were presented in 0.2-1.7 THz. THz-TDS is confirmed to be a useful tool in the identification of drug polymorphs. The low frequency modes of furosemide are attributed to intra-molecule collective motions based on DFT calculations performed on single molecule at the B3LYP/6-311G level.

## REFERENCES

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