Journal of Molecular Structure 1062 (2014) 185–188

Contents lists available at ScienceDirect

Journal of Molecular Structure

journal homepage: www.elsevier.com/locate/molstruc

Glass transition dynamics of anti-inflammatory ketoprofen studied by Raman scattering and terahertz time-domain spectroscopy ☆

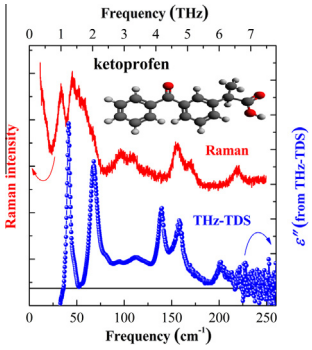
Tomohiko Shibata *, Hikaru Igawa, Tae Hyun Kim, Tatsuya Mori, Seiji Kojima *

Graduate School of Pure and Applied Sciences, University of Tsukuba, Tsukuba, Ibaraki 305-8573, Japan

HIGHLIGHTS

- Vibrational properties of pharmaceutical racemic ketoprofen were investigated.
- Low-frequency Raman scattering spectra clearly showed the boson peak.
- Remarkable change of Raman spectra was observed through a liquid–glass transition.
- The THz-TDS spectra of crystalline state were compared with Raman scattering spectra.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Available online 24 January 2014

Keywords:
Ketoprofen
Boson peak
Raman scattering
THz-TDS
Glass transition
Crystal

ABSTRACT

A liquid–glass transition and a crystalline state of pharmaceutical racemic ketoprofen were studied by Raman scattering and the broadband terahertz time-domain spectroscopy (THz-TDS) in the frequency range from 9 to 260 cm^{-1}. The low-frequency Raman scattering spectra clearly shows the remarkable change related to a liquid–glass transition at about $T_g = 267$ K. After melt-quenching at liquid nitrogen temperature, a boson peak appears at about 16.5 cm^{-1} near and below T_g and the intensity of quasi-elastic scattering related to structural relaxation increases markedly on heating. The crystalline racemic ketoprofen of "conformer *A*" shows the noncoincidence effect of mode frequencies below 200 cm^{-1} between Raman scattering spectra and dielectric spectra observed by THz-TDS.

© 2014 Elsevier B.V. All rights reserved.

1. Introduction

In the pharmaceutical research, there is a growing interest currently in the development of glassy pharmaceuticals, because they often show a better solubility than crystalline pharmaceuticals [1,2]. However, one concern is the instability of a glassy state originating from the disordered structure and aging effect. Therefore, it is important to make clear the molecular dynamics in glassy states of pharmaceutical system for getting predictable stability. Up to now, vibrational spectroscopy such as FTIR and Raman scattering has been applied to study liquid–glass transitions of organic and inorganic glass forming materials [3–6]. In particular, the inelastic scattering spectra of glasses have generally shown a low-frequency response called "boson peak" and have never been satisfactorily understood. The investigation of the low-frequency Raman spectra of glassy pharmaceuticals will give new insights into the low-energy excitation of glassy materials and physical properties of glassy pharmaceuticals.

Terahertz time-domain spectroscopy (THz-TDS) and low-frequency Raman scattering spectroscopy have been successfully

☆ Selected paper presented at XIIth International Conference on Molecular spectroscopy, Kraków – Białka Tatrzańska, Poland, September 8–12, 2013.

* Corresponding authors. Tel.: +81 29 853 5040.
E-mail addresses: s1320438@u.tsukuba.ac.jp (T. Shibata), kojima@bk.tsukuba.ac.jp (S. Kojima).

http://dx.doi.org/10.1016/j.molstruc.2014.01.050
0022-2860/© 2014 Elsevier B.V. All rights reserved.

used for the identification and quantification of various solid state of drug, such as enantiomer, polymorphic, amorphous state [7–10]. It is because the spectral features in the low-frequency region below 100 cm^{-1} are associated with intermolecular vibration modes of molecules. For the characterization of pharmaceutical materials, it is important to measure both THz-TDS and low-frequency Raman scattering. The two methods have the complimentary selection rules which enable the full information on vibrational properties related to the crystalline structure, and their strength of intermolecular interactions.

Ketoprofen is one of nonsteroidal anti-inflammatory drugs (NSAIDs) used for the treatment of inflammation and pain. It was found by calorimetric measurements that the glassy ketoprofen can be easily achieved by rapid cooling from the liquid without crystallization [11,12]. Dynamical properties of glassy state and liquid–glass transition were studied by Sailaja et al. using dielectric spectroscopy in the frequency range from a few Hz to MHz [13]. Besides the primary α-relaxation process above T_g, secondary γ-relaxation related to the localized motion was reported in a glassy state. High frequency vibrational properties of glassy and supercooled liquid states of ketoprofen are still unexplored. Vibrational properties of crystalline ketoprofen were investigated by infrared, Raman scattering and inelastic neutron scattering spectroscopy in the frequency range of 100–3500 cm^{-1} [14–17]. In addition to the Raman and FTIR spectra of crystalline states, DFT calculations were reported by Vueba et al. [17]. It was reported that the bands assigned to C=O and O—H stretching vibrations display a downward shift from the calculated values for the isolated molecules due to the interaction of intermolecular hydrogen bonds. To get more information of the intermolecular interaction, the study of low-frequency vibrational properties below 100 cm^{-1} is required.

The present study is focused on the vibrational properties of both glassy and crystalline states of ketoprofen in the frequency range from 9 to 260 cm^{-1} using low-frequency Raman scattering and THz-TDS. In this paper, we report the experimental results of the temperature dependence of low-frequency Raman scattering spectra in glassy, supercooled and liquid states of ketoprofen. The THz-TDS and Raman spectra of crystalline ketoprofen of the low-frequency vibrations have been measured and compared at room temperature.

2. Experimental

Ketoprofen ((*RS*)-2-(3-benzoylphenyl) propanoic acid, $C_{16}H_{14}O_3$, a molar mass of 254.28 g/mol) was purchased from Sigma Co. (catalogue No. L1751 (CAS 22071-15-4), 98% GC assay). It is a racemic mixture of S-(+)-ketoprofen and R-(−)-ketoprofen (see Fig. 1) and the studied (±)-ketoprofen mixture is referred as ketoprofen. Ketoprofen is white crystalline powder at room temperature and used for measurements without further purification.

Raman scattering spectra were measured in the frequency range from 9 to 260 cm^{-1}, in *VV* and *VH* geometry under a scattering angle $\theta = 180°$, using a single frequency green-YAG laser with wavelength 532 nm. The spectrometer is a triple-grating monochrometer (T64000, Horiba–Jobin–Yvon) with additive dispersion [5] and the spectral resolution of the Raman spectrometer was 1.6 cm^{-1}. A heating/cooling stage (Linkam, THMS600) was used to control the temperature of the sample from 90 to 373 K. The temperature stability of a sample was within ±0.1 K. In order to investigate the Raman scattering of crystalline, glassy, supercooled and liquid states of ketoprofen, the following two series of measurements were performed. First, crystalline ketoprofen was measured at room temperature, using a pressed pure pellet with 0.5–1.5 mm thickness. Crystalline sample was measured without analyzer. Second, the crystalline ketoprofen was heated and kept 5 min at 373 K (T_m ~ 368 K [11,12]) to get an equilibrium liquid phase and then the liquid ketoprofen was quenched down to liquid nitrogen temperature with the high cooling rate of more than 10 K/min, which was high enough to obtain glassy ketoporfen. The Raman spectra of glassy, supercooled liquid and equilibrium liquid states of ketoprofen were recorded upon heating from 90 K to 373 K.

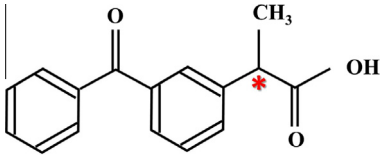


Fig. 1. Chemical structure of ketoprofen molecule, where C* is a chiral carbon atom.

THz transmission spectra were measured in the frequency range from 0.5 to 6.5 THz (16.65–216.45 cm^{-1}) using a THz-TDS equipment (TAS7500SU, Advantest Co.) with a Cherenkov type broadband THz generator and the high-speed AOS technique [18]. Crystalline ketoprofen was measured only at room temperature, using the same sample of Raman measurement.

3. Results and discussion

3.1. Liquid–glass transition

Ketoprofen undergoes a liquid–glass transition at T_g = 267–270 K [11–13]. The temperature dependence of the low-frequency Raman spectra was measured upon heating from a glassy state into a supercooled liquid state through a liquid–glass transition.

Boson peak is a common nature of the low-energy excitations of glassy materials and observed in inelastic scattering spectra such as Raman spectra of various glass formers, for example, lower alcohols and oxide glasses [5,6]. As a general trend, a strong glass shows an intense boson peak and a weak fast relaxation process, while a fragile one shows a weak boson peak and an intense fast relaxation process [19]. The degree of fragility is given by the fragility index m [13,20] defined by:

$$m = \lim_{T \to T_g} \left| \frac{d \log \tau}{d(T_g/T)} \right| \tag{1}$$

where τ is the relaxation time of α-relaxation.

Fig. 2(a) shows the temperature dependence of *VH* depolarized Raman scattering spectra of a glassy state of ketoprofen below T_g. A boson peak appears at about 16.5 cm^{-1} and two weak vibration modes appear at 75 and 220 cm^{-1}. The boson peak spectrum of reduced intensity was fitted by log-normal function and shown in Fig. 3. The reduced intensity $I_r(\omega)$ of Stokes component was defined by:

$$I_r(\omega) = \frac{I(\omega)}{\omega\{n(\omega)+1\}}, \tag{2}$$

where $I(\omega)$, $n(\omega)$ is the Raman scattering intensity and the Bose–Einstein factor, respectively.

The intensity of a boson peak is weaker than that of glycerol, and the peak frequency is about a half of glycerol. Considering the fragility of glycerol is m = 50–54 [21], weaker intensity is reasonable. Since the large value of fragility index of ketoprofen, m = 86, was reported very recently [13], the boson peak intensity can be rather weak. The strong correlation is known between the boson peak frequency with the shear modulus [6], and the recent simulation predicted that the boson peak frequency is Ioffe-Regal limit of transverse acoustic mode [22]. Therefore, the lower boson peak frequency of ketoprofen may be caused by smaller shear modulus of glassy ketoprofen than that of glassy glycerol, which has a strong network of hydrogen bonds.

Download English Version:

https://daneshyari.com/en/article/1402726

Download Persian Version:

https://daneshyari.com/article/1402726

Daneshyari.com