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Raman mapping analysis of multi-component pharmaceutical tablet

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Application Specialists

Applications & Keywords

Cold tablets

Pharmaceutical product quality control

Techniques

Dispersive Raman

Raman imaging / mapping

Instrument Solution

XperRAM S Series

NanoSpectrum software

Background

As the fast development in pharmaceutical research continues, an accurate characterization of not only raw materials but composites is thoroughly demanded in terms of safety and stability [1].

While the in-line analysis of manufacturing processes in real time poses a challenge for traditional analytical methods such as HPLC and similar techniques that require time-and-work-intensive sample preparation, Raman spectroscopy, the on-line measurement application, is in the limelight as a well-suitable analytical technique for identifying the distribution of constituents across a sample in a non-destructive way [4]. In addition, Raman spectroscopy can analyze subtle structural changes such as polymorphism and crystallinity, both of which can greatly affect drug dissolution and efficacy [3].

Here, we observed pharmaceutical composites which are a well-known painkiller with a confocal Raman spectroscopy system.

Materials & Methods

Bearcet Semi Tab (BST) is composed of 18.75 mg of tramadol hydrochloride, 162.5 mg of acetaminophen, and several additives including cellulose (HPMC, Hydroxypropyl Methylcellulose) [4].

Raman spectra and Raman mapping of BST were obtained with the confocal micro-Raman spectroscopy instrument, XperRAM S Series.

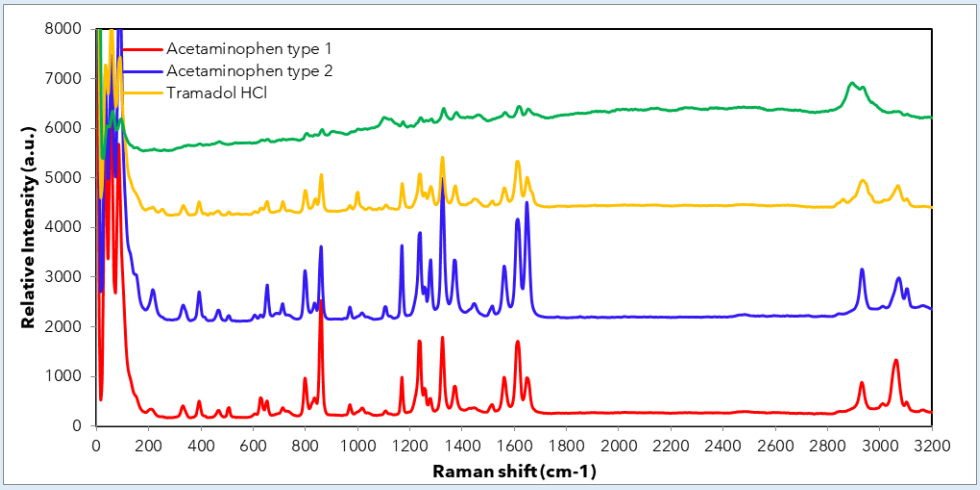
Raman imaging was performed with specific vibration modes at 1650 cm^{-1} (N-H bending vibration) [3] and 3064 cm^{-1} (C-H stretching vibration of phenyl ring) [3] of acetaminophen, 995 cm^{-1} of tramadol hydrochloride (C-N bending vibration) [5], and 2900 cm^{-1} of cellulose (C-H stretching vibration) [6].

To evaluate the dispersion of two types of Acetaminophen, two modes at 1650 cm^{-1} and 3064 cm^{-1} were used to reconstruct the map images. The Raman imaging area was 100 um x 100 um, and the step size was 1 µm. The exposure time was 500 milliseconds; the light intensity was 10 mW; the wavelength of laser was 532 nm; and the lens magnification was 40x (N.A. = 0.75).

Results

In order to investigate the intrinsic Raman spectra of each component, characteristic spectra were exported from Raman map. In *Figure. 1*, four distinguishable spectra were shown. Using the information of the product ingredient label and data of previously conducted research, we identified intrinsic spectra of acetaminophen and cellulose corresponding to each spectra of *Figure. 1*.

Figure. 1



Especially, spectra of acetaminophen showed two different types where the intensity and ratio of a few peaks were distinct. Specifically, the ratio of 797/859, 1280/1326 and 1613/1653 cm^{-1} showed difference between type 1 and 2. Also, peak intensities of 628, 1279 and 3102 cm^{-1} were different in each type, and 3064 cm^{-1} which corresponds to C-H stretch of phenyl ring vibration mode shift to 3073 cm^{-1} in type 2.

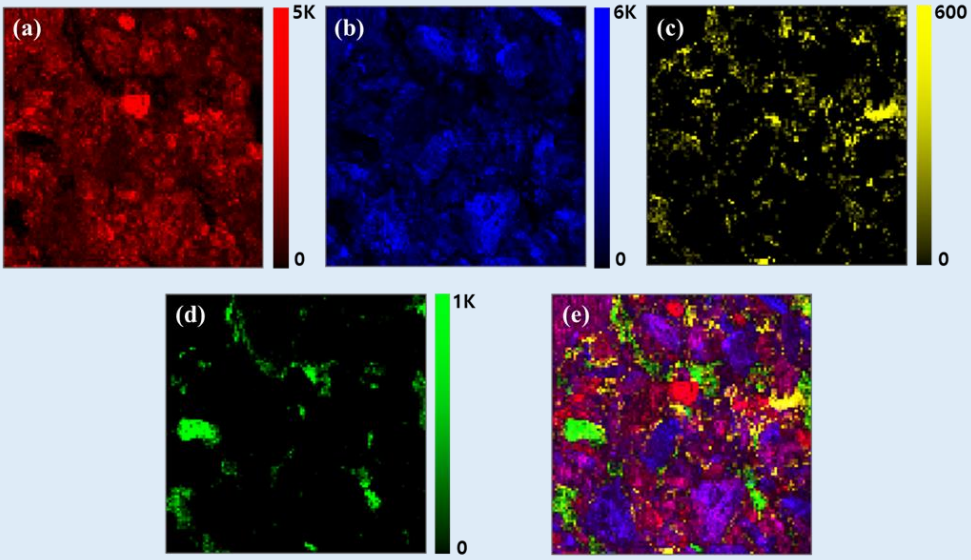
Those results were caused of polymorphism acetaminophen [3,7,8]. Acetaminophen are known that three polymorphic lattice structures exist (monoclinic, orthorhombic and unstable form) [9]. Since form Ⅲ of acetaminophen is thermodynamically unstable, monoclinic and orthorhombic structures are commercially used to manufacture tablet in the pharmaceutical industry.

In comparison to Raman spectra of acetaminophen and cellulose, tramadol hydrochloride are contained with a small amount, so intrinsic Raman spectrum of it was hard to be acquired and mostly overlapped the spectrum of acetaminophen. Only 996 and 2860 cm^{-1} peaks were indicated as the characteristic vibration modes of tramadol hydrochloride.

Results

With those specific vibration modes of the components in BST, Raman maps were reconstructed in *Figure. 2*.

Figure. 2 Raman mapping images of each component in BST



As the map images shown in *Figure. 2 (a)* and *(b)*, acetaminophen was occupied in most of area in tablet. On the other hands, cellulose and tramadol hydrochloride were distributed in a less amount than acetaminophen (*Figure. 2 (c)* and *(d)*). Interestingly, in *Figure. 2 (e)*, merged Raman map image of all components showed that each component was perfectly packed.

For conformation of constituent quantity of BST with Raman spectroscopy, each Raman map images was quantified in *Table. 1*, and the results significantly corresponded with information shown in the ingredient label.

Table. 1 Quantities of ingredients labeling of BST and quantification data by Raman map images

	Acetaminophen	Tramadol HCl	Ratio (Acetaminohen / Tramadol HCl)
Doses (mg)	162.5	18.75	8.667
Pixel counts (pixel)	30481	3564	8.552

Conclusion

Consequently, results as illustrated in page 3 and 4 prove significance of application of Raman spectroscopy as an advantageous analysis technique for the non-destructive, easy to operate, and accurate screening dedicated to the pharmaceutical research industry.

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