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Application News

No. X272

X-Ray Analysis

X-Ray Fluorescence Analysis of Tablets

Some tablets of drug product have a coating applied to the surface for various purposes, such as preventing deterioration, masking unpleasant taste or smell, or controlling the timing of drug release. Fig. 1 shows an example of a tablet coating. Although inductively coupled plasma-atomic emission spectrometry (ICP-AES) and ICP-mass spectrometry (ICP-MS) are generally used as methods for analysis of the elements in drug products, if an entire tablet is pulverized or dissolved, it becomes difficult to differentiate the elements that originate from the coating and other elements.

X-ray fluorescence analysis makes it possible to analyze tablets as-is without pulverization. This article introduces an example of a simple analysis of unevenly-distributed like those in coatings, based on a comparison of analyses of pulverized and unpulverized tablets.

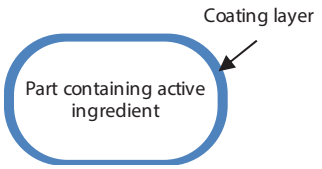


Fig. 1 Example of Tablet Coating Structure

S. Ueno

Sample

Tablet (over-the-counter cold medicine): 1 type

Elements

$_{6}$C to $_{92}$U: Qualitative/quantitative analyses of all elements

Pretreatment

1. Tablet surface

   The tablet surface was analyzed as-is without pretreatment.

2. Tablet cross section

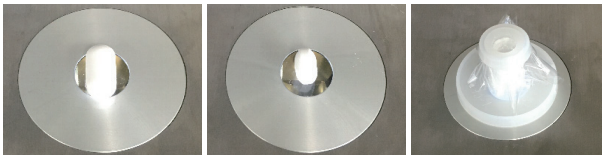
   The tablet was sectioned, and the cross section was analyzed.

3. Pulverized powder

   The tablet was pulverized using an agate mortar, and was then packed in a sample container lined with a 5 μm polypropylene film by lightly pressing and compacting the material until its depth reached 10 mm or more.

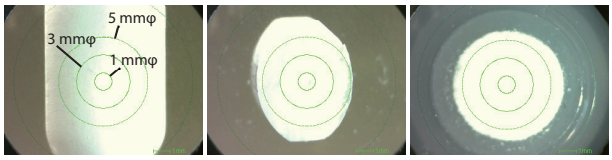
Sample Setting

During the analyses of the tablet surface and cross section, the samples were placed on a polypropylene film that had been glued to the sample setting part. Fig. 2 shows the setting condition in the instrument, and Fig. 3 shows photographic images recorded during the analyses.



(a) As-is (Whole tablet) (b) Cross section (c) Powder

Fig. 2 Setting Condition



(a) As-is (Whole tablet) (b) Cross section (c) Powder

Fig. 3 Photographic Images During Analysis

Qualitative and Quantitative Analyses

Qualitative and quantitative analyses of all elements from $_{6}$C to $_{92}$U were carried out for the tablet surface, cross section, and pulverized powder. The balance automatic setting function [*1] (Fig. 4) was set in the measurement setting conditions.

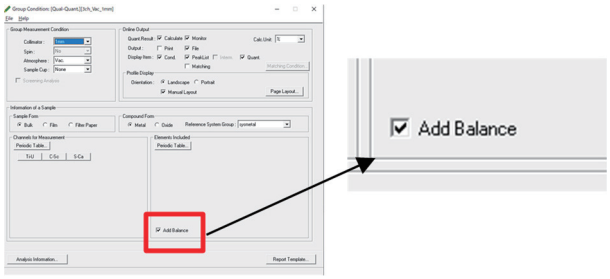


Fig. 4 Balance Automatic Setting Function: Condition Setting Screen

*1 Balance automatic setting function: In cases where the main components include C, H, O, and the like, it is necessary to set "Balance" [(1)] (remaining elements) in the FP method. When the balance automatic setting function is set, balance setting is done automatically by the software in case it is judged to be necessary from the profile shape. Because compensation for differences in shape, thickness, density, and other properties is possible to some extent, this function is also effective in analyses of samples with irregular shapes, small particle sizes, or small quantities.

1. Qualitative Analysis Results

   Fig. 5 shows the superimposed results of the analyses of the tablet surface, cross section, and pulverized powder. Ti was detected relatively strongly from the surface layer, while P and Cl were detected relatively strongly from the cross section. It can be understood that Ti originated from the coating, and P and Cl originated from the active ingredient. The results for the powder were similar to those for the cross section.

   Fig. 6 shows the images of the tablet cross section by laser microscopy. Here, it can be understood that a coating with a thickness of approximately 45 μm was applied to the tablet surface.

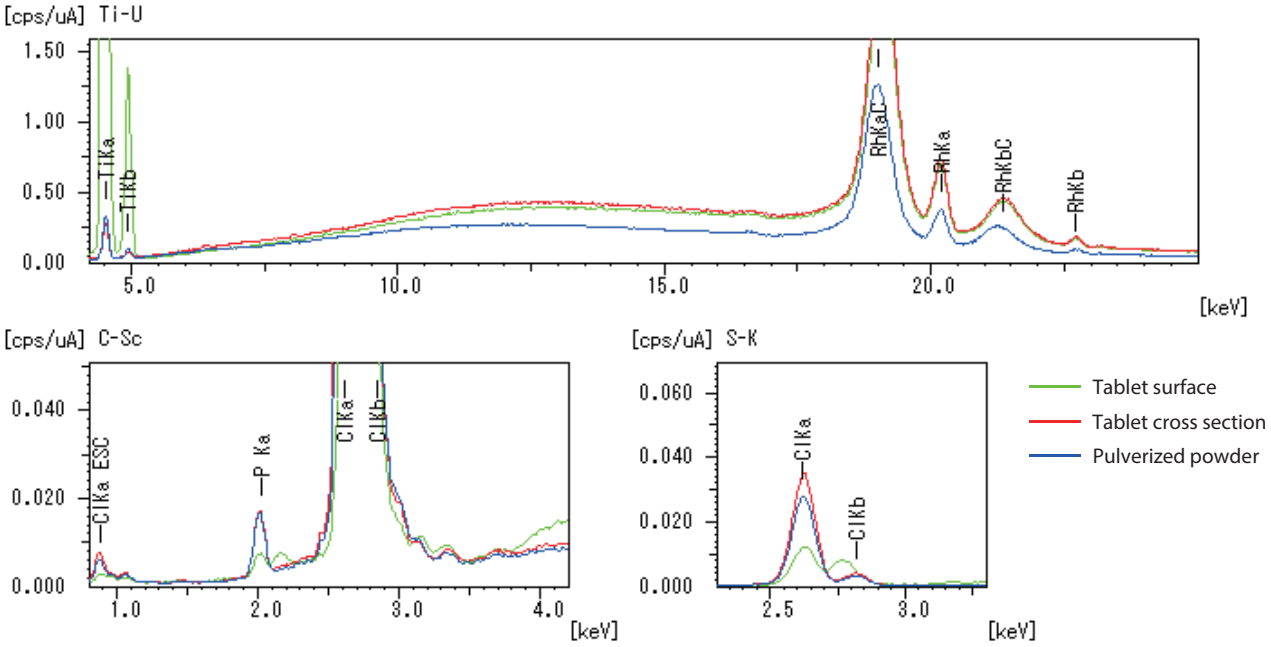


Fig. 5 Superimposed Results of Qualitative Analysis for Elements from $_{6}$C to $_{92}$U

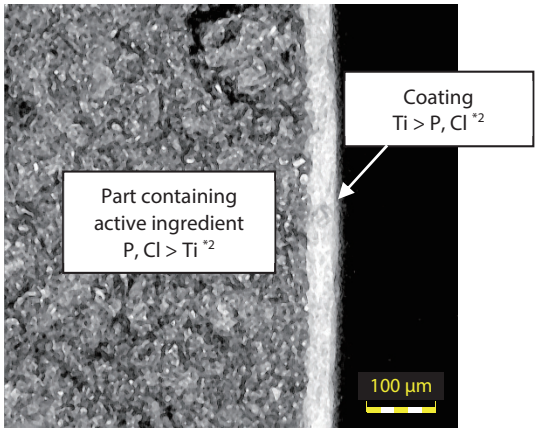


Fig. 6 Laser Microscopy Observation Images of Tablet Cross Section (Instrument: 3D Measuring Laser Microscope OLS)

*2 The relationship of the relative quantities of P, Cl, and Ti reflects the quantitative analysis results.

2. Quantitative Analysis Results

Table 1 shows the results of the quantitative analysis by the FP method, and the quantitative values differ depending on the measurement position. In case the average tablet composition per one tablet is to be obtained, it is necessary to homogenize the sample by pulverizing the tablet.

Table 1 Quantitative Analysis Results [wt%]

Sample	P	Cl	Ti	Balance *3
Tablet surface	0.031	0.51	2.69	96.77
Tablet cross section	0.093	1.68	0.073	98.16
Pulverized powder	0.11	1.48	0.10	98.31

*3 Balance : Fig. 7 shows an example of a quantitative analysis results table. The balance is shown as "Plastic" by balance automatic setting.

Analyte	Result		[3-sigma]	Proc.-Calc.
Ti	2.693	%	[0.009]	Quant.-FP
Cl	0.506	%	[0.013]	Quant.-FP
P	0.031	%	[0.002]	Quant.-FP
Plastic	96.770	%	[------]	Balance

Fig. 7 Example of Quantitative Analysis Results Table: Tablet Surface

Conclusion / Advantages of X-Ray Fluorescence Analysis

When a sample is pulverized, all of the coating layer and the part containing the active ingredient in the interior are mixed, and it becomes difficult to identify the parts where elements were unevenly distributed. When a researcher wishes to analyze a coating layer by ICP-AES or a similar technique, work to remove the outer layer of the tablet is necessary, and pretreatment becomes extremely complicated.

On the other hand, this experiment confirmed that analysis of unevenly-distributed elements is possible with no complicated pretreatment by X-ray fluorescence analysis, as this technique enables analysis of tablets as-is without pulverizing.

Table 2 Measurement Conditions

EDX	
Instrument	: EDX-8000 / (7000)
Analysis method	: FP method
Detector / X-ray tube	: SDD / Rh target
Tube voltage – current	: 50 [kV] – Auto [µA]
Collimator / Primary filter	: 3 [mmφ] / #2
Measurement atmosphere	: Vacuum
Integral time / Dead time	: 100 [s] / Max. 30 [%]

<Reference>
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