ELEMENTAL IMPURITY ANALYSIS OF PHARMACEUTICAL PRODUCTS

The Measure of Confidence

Agilent 5100 ICP-OES

ICH and USP tests for elemental impurities provide better indication of potentially toxic contaminants

New, performance-based methods for elemental impurities

The control of elemental impurities is a critical issue in the pharmaceutical industry. Apart from the potential negative health implications, trace inorganic impurities can reduce the stability and shelf life of many pharmaceutical products.

Elemental impurities in pharmaceutical products were previously identified using the heavy metals limit test, defined in USP <231>. This is a subjective, non-specific, colorimetric test applicable to ten sulfide-forming metals and does not provide quantitative concentration data for each individual target analyte. The sample preparation specified in USP <231> can also lead to loss of volatile elements such as mercury, resulting in low recovery, and poor accuracy and reproducibility.

To address the limitations of the USP <231> method, the International Conference on Harmonization (ICH) and USP have drafted new performance-based methods: ICH Q3D, USP<232> (limits), and USP<233> (procedures) for determining elemental impurities in pharmaceutical products. These new performance-based methods are due to be implemented in 2015. ICH Q3D and USP <232> extend the list of elements to 24 and 15 elements, respectively. The USP<233> method references the use of ICP-MS and ICP-OES instruments to replace the antiquated USP <231> colorimetric technique. Unlike USP<231>, the new method's daily exposure limits are directly based on toxicological data and account for differing bioavailability due to routes of exposure.

ICP-MS, with its superior detection limits, can be utilized for a wide variety of pharmaceutical products with different dosage routes, especially parenteral and inhalational products, where the target limits are significantly lower than oral dosage route products.

ICP-OES, on the other hand, has benefits of sensitivity in the presence of high matrix loads, simplicity of operation and high throughput speed. ICP-OES is an ideal technique for oral dosage products and raw materials.

Measure tough samples

Agilent's 5100 ICP-OES is an ideal instrument for pharma labs focused on oral dosage raw material and drug products requiring little to no sample dilution. Its vertical torch allows the analysis of a wide range of samples, including those with total dissolved solids content greater than 25%. The vertical torch gives long term analytical stability on the toughest samples and can easily handle a variety of sample matrices from aqueous to organic solvents.

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Figure 1 demonstrates the resolution and sensitivity capabilities of the 5100 ICP-OES for an organic matrix for pharmaceutical analysis — an oil sample dissolved in an organic solvent. The sample was diluted 10 times and aspirated directly into the instrument. The instrument can easily measure the USP's target limit (J value) of 50 µg/L for Cd at this dilution.

Get accurate results, quickly

The Vista Chip II detector in the 5100 ICP-OES has very wide wavelength coverage with a high clocking speed. It is able to measure all wavelengths, from 167–785 nm in a single measurement. This easily allows the selection of wavelengths that are free from interferences and its fast processing speed reduces analysis time.

This capability allows multiple wavelengths to be used as an unequivocal confirmation of concentration accuracy. This is done by verifying the calculated concentration from primary emission wavelengths against the calculated concentration at alternate emission wavelengths for the same element. Table 1 shows the results of an "in method" verification of Cd concentration, performed by simultaneously measuring two separate Cd emission wavelengths three times, giving the analyst confidence of unbiased analysis.

The 5100 ICP-OES has both Fitted background correction and FACT (Fast Automated Curve fitting Technique), which is a spectral deconvolution algorithm used to correct for spectral overlap. The analyst can use the unique default Fitted background correction, which is an algorithm that automatically selects the best background points. Fitted background correction reduces method development time and reduces the method's complexity for the analyst. The blue dotted line in figure 1 illustrates the automated placement of the Fitted background correction.

FACT is a simple, but powerful tool that does not require special software settings or changes in optics configurations in order to subtract spectral interference. It can be quickly setup to subtract spectral overlaps.

The Agilent 5100 ICP-OES revolutionizes ICP-OES analysis. It is designed to run your samples faster, using less gas (Ar), without compromising performance on your toughest samples. A range of unique hardware and software capabilities easily facilitates elemental impurity analysis of pharmaceutical ingredients/products. The Vista Chip II detector and ICP Expert software creates simple, fast analysis that is reproducible from analyst to analyst and lab to lab.

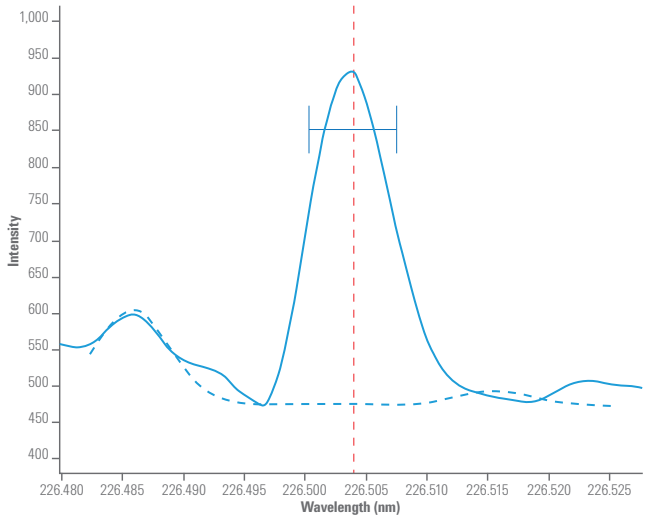

Figure 1: The emission signal of 35 µg/L Cd at 226.502 nm in an oil sample dissolved in an organic solvent. The Cd spectrum is clearly resolved despite the presence of many possible interfering signals.

Table 1. Measured concentration of 35 ppb Cd in an oil sample at two different emission wavelengths. The correlating results give in-method confirmation of the Cd results with no time penalty for the analysis.

Measurement	Measured Concentration (µg/L) of Cd at 214.439 nm	Measured Concentration (µg/L) of Cd at 226.502 nm)
1	37.4	35.4
2	39.3	34.5
3	36.1	34.8

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