

## Advantages of Using Low Voltage for Elemental Mapping by Energy Dispersive X-Ray Spectroscopy in Pharmaceutical Systems

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The advantages of using low energy primary electron beams (low-kV) for imaging by scanning electron microscopy (SEM) have been well established for many years [1]. Until recently [2], elemental analysis by energy dispersive x-ray spectroscopy (EDS) at low-kV was not practical. Use of a low-kV beam results in reduced x-ray signal and the inability to excite higher energy x-ray lines from higher Z elements. The establishment of larger and more efficient silicon drift detectors has addressed the issue of low x-ray signal, and low-kV elemental mapping by EDS is becoming practical and routine. Since most pharmaceutical products are composed of low Z elements, low-kV beams should be a natural choice for elemental analysis and mapping.

A comparison of image quality in elemental maps collected using high (20-30 kV) and low (5-10 kV) primary beams was performed. Several solid oral dosage formulations were selected for testing. Samples tested included tablet coatings, dry blend direct compression tablets and melt extrusion formulations. In addition, a video array from a magnification standard was used to measure spatial resolution of the elemental maps under both beam conditions. All imaging was performed using an FEI Quanta 450 SEM and an Edax Octane EDS system with a 60 mm<sup>2</sup> detector. Mapping conditions were set to collect approximately equal numbers x-ray counts in low-kV and high-kV maps. Thus, the low-kV maps were collected for longer times due to the lower efficiency of x-ray generation.

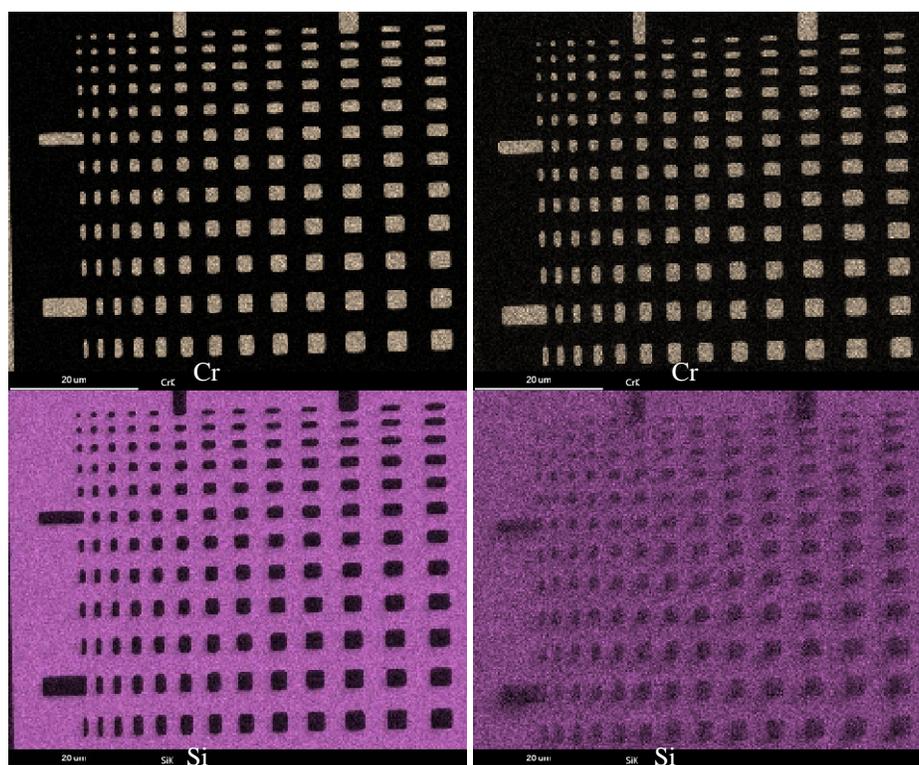
Low-kV elemental maps generally had higher spatial resolution than did high energy elemental maps. This was most apparent for maps of lighter elements. Figure 1 compares elemental maps for silicon and chromium from a video array collected at 10 and 20 kV. There is little difference in the resolution of the chromium map at both accelerating voltages. However there are significant differences in resolution of the silicon map at these two voltages. At 20 kV most squares of the array were blurred and not well resolved. At 10 kV squares down to 1  $\mu$ m were resolved.

Applying the same comparison to direct compression tablets shows the advantages of higher resolution with lower kV beams. Figure 2 shows the distribution of silicon dioxide in a tablet blend by mapping for silicon. At 20 kV the silicon distribution appears as a variety of larger blurred particles. At 5 kV the granular structure within the larger aggregates becomes visible. Other examples of the improved image quality in x-ray maps collected at lower voltages have been observed.

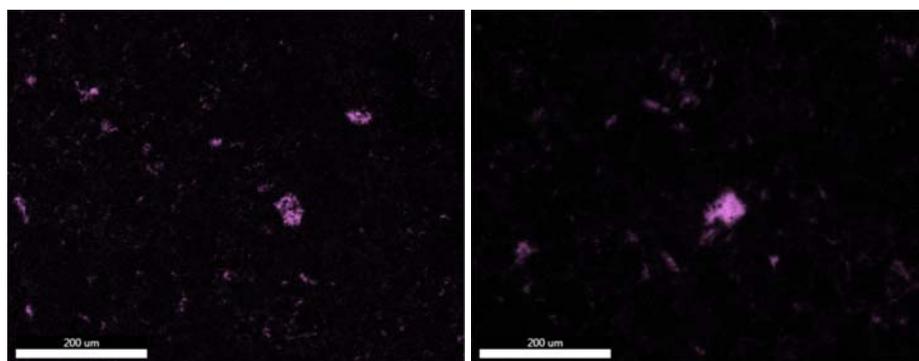
In conclusion, the primary advantage of elemental mapping at lower voltages is the increased resolution due to reduced beam spread within the sample. This not only improves the spatial resolution of elemental mapping, but reduces overlap of data across material boundaries. Lower kV beams also reduce the level of beam damage typical of soft organic materials such pharmaceutical systems. While the x-ray count rate from a low-kV beam is substantially reduced, the use of larger SDD detectors offsets the loss of x-ray signal.

## References:

- [1] J Goldstein *et al* in “Scanning Electron Microscopy and X-Ray Microanalysis”, 3<sup>rd</sup> ed, Plenum New York, 2003, pp 207-209.  
 [2] T Nylese, R. Anderhalt, V. Gorcea, Microsc. Microanal. 19 Suppl 2 (2013), pp. 272-273.



**Figure 1.** Elemental maps for chromium and silicon from a video array from MRS-3 magnification standard composed of chromium squares in glass matrix collected at 5 kV (left) and 20 kV (right).



**Figure 2.** Elemental maps for silicon from a compressed tablet collected at 10 kV (left) and 20 kV (right). Greater detail is visible in the map collected at lower accelerating voltage.

## Disclosures:

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