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A Novel Application of Solids Characterization by Environmental Scanning Electron Microscopy (ESEM) Utilizing a Peltier Stage

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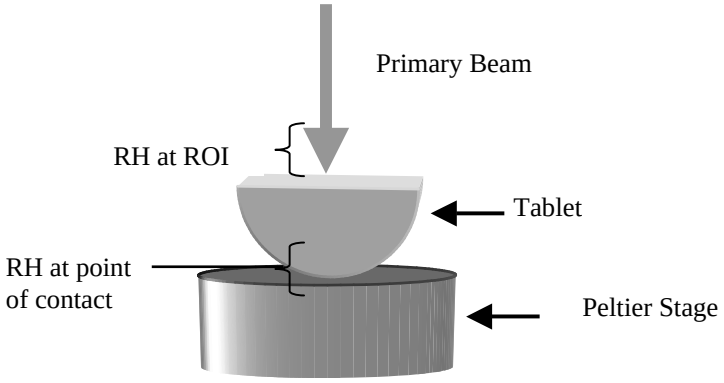
The advent of the Environmental Scanning Electron Microscope (ESEM) has brought about new opportunities to utilize this technique to characterize pharmaceutically active compounds. The ability to examine materials under a partial pressure of water vapor allows for imaging an uncoated specimen. This flexibility allows for the routine nondestructive examination of a variety of materials that could not be achieved with a coated specimen (e.g., hydrated and/or solvated crystal lattices. By utilizing an uncoated specimen, dynamic imaging of the surface during dehydration and or desolvation can now be routinely observed. With the addition of a Peltier stage, the specimen can be exposed to a wide range of relative humidity (RH) conditions by varying the stage temperature and/or pressure of the gas within the environmental chamber.

Using this technique for *in situ* monitoring a pharmaceutical sample environment, specifically a solid dosage form, was of considerable interest to understand the affects of humidity on sample integrity. Given the typical tablet size, the Peltier stage sample capacity, and the concern about a suitable cross-section to represent the bulk sample, a fundamental question arose: “Is the effective RH at the analysis site on a tablet surface the same as at the tablet/Peltier contact site for a given temperature/pressure combination?” Scheme 1 summarizes this question. The high degree of temperature control provided by the Peltier stage coupled with ESEM pressure controls, allows the operator to span the entire RH scale and maintain conditions for prolonged periods of time. However, the instrumental data output for temperature/pressure/RH conditions are only accurate within the Peltier stage environment. For situations where samples extend beyond the Peltier stage, a method for determining RH at the site of analysis is useful.

Thus a quick and sensitive technique for estimating the actual temperature/RH at the analysis site is critical for a better understanding of observed specimen effects. This was achieved by placing a few salt grains (see Figure 1A for established deliquescence conditions) on the elevated surface of a compressed tablet and recording the deliquesce point. By recording the output conditions at which deliquesce was achieved and factoring in the known deliquescence conditions for the salt, the temperature/RH at the analysis site (see Figure 1B) can be calculated.

Scheme 1:



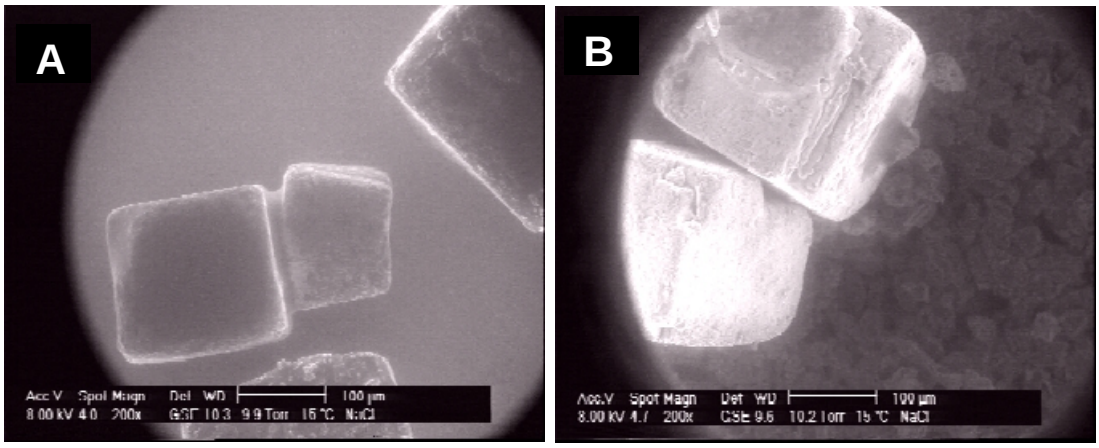


Figure 1: (A) NaCl crystals on the Peltier Stage starting to deliquesce. (9.9Torr/ 15°C/~77%RH). (B) View of NaCl crystals on Surface of a Tablet at 10.2Torr/15°C corresponding to 80%RH at the sample/Peltier contact point

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