DOI: 10.1017/S1431927603446254
Microsc Microanal 9(Suppl 2), 2003

The Integrated Microscopy Approach for Pharmaceutical Science

D. Scott Aldrich*

*Pharmacia Corp., Pharmaceutical Science - Trace Analysis, Kalamazoo, MI 49001

The presentation describes the approach, microscopy tools and methods utilized for pharmaceutical product development. Based on concepts of ultramicroanalysis promoted by McCrone, the study of fundamental material nature is sought, often in singular analyte species, using chemical microscopy as the primary tool [1]. Figure 1 compares the contamination condition for a highly-concentrated, localized analyte versus traditional trace analysis perspective. This application has an important role in the pharmaceutical development process and commercial manufacturing support. The origin, variability and form of all components in the final product are key to good process control and to ensure product stability. The ultimate product process must be chosen on the premise that material character is well known. The nature or properties of raw component, intermediate and final batch substances constitute the intrinsic character of the product form. Condition of the components, such as the filler D-mannitol crystals shown in Figure 2, may provide clues to the origin of a batch failure or processing incident.

Microscopy-based instrumental techniques are configured in an integrated approach for material identification. Optical polarized, infrared, laser and electron microscopical tools provide an orthogonal and comprehensive developmental approach to verify the intrinsic nature of the new product form. Hot-stage microscopy has proved essential in drug phase transition studies [2, 3]. The integrated approach is also effective in a troubleshooting role to identify extrinsic, or foreign matter that may contaminate raw materials or the process. Analytical electron microscopy and associated mapping and elemental compositional tools are integral in this effort.

References

[1] McCrone WC. Microscopy and ultramicroanalysis, Amer Lab, April (1986) 22.

[2] Schinzer WC, et al. Characterization and interconversion of polymorphs of premafloxacin, a new quinolone antibiotic, J Pharm. Sci. Vol 86:12 (1997)1426.

[3] Kuhnert-Brandstätter M. Thermomicroscopy in the Analysis of Pharmaceuticals, Pergamon Press, Oxford, Great Britain,1971.

[4] Yoshinari, T, et al. Moisture induced polymorphic transition of mannitol and its morphological transformation, Int'l. J. Pharm. 247, (2002), p. 69-77.

[5] Jones FT and Lee KS. The optical and crystallographic properties of three phases of mannitol. The Microscope, 197018:279-285.

Highly-concentrated unknown per unit volume	Homogeneous, trace concentration per unit volume

Figure 1. Localized concentration of a contaminant versus trace level contamination per unit volume.

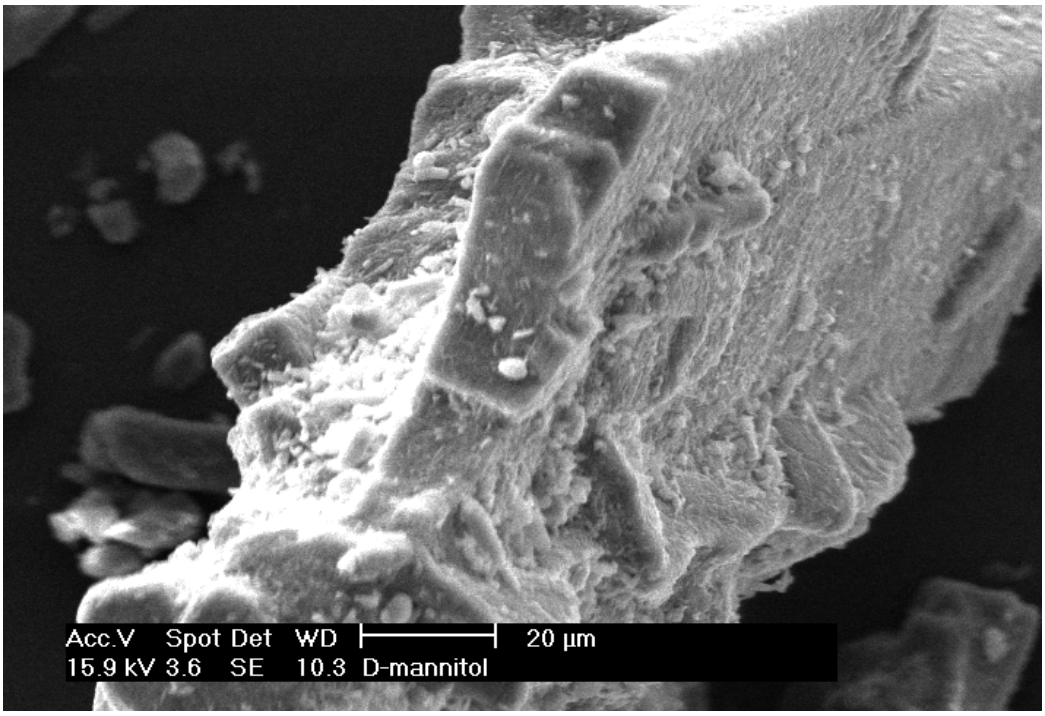

Figure 2. D-mannitol crystals with post-crystallization erosion and damage evident.

https://doi.org/10.1017/S1431927603446254 Published online by Cambridge University Press