doi:10.1017/S1431927610054218
Microsc. Microanal. 16 (Suppl 2), 2010

Application of Forensic Science Methodology to Pharmaceutical Investigations

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Drug development by the Pharmaceutical Industry is regulated by the Food and Drug Administration (FDA) in the U.S. and various other government agencies throughout the world, primarily to ensure that drugs are safe for human consumption and effective for the specified indication. Drug development involves numerous scientific disciplines, including chemistry, biology, pharmacy, and engineering, fields that are also represented in forensic science. In much the same way as forensic science utilizes various scientific disciplines to identify materials' and determine their source to support criminal investigations, a part of pharmaceutical sciences has a similar objective to support investigations that come out of manufacturing plants [1,2]. Furthermore, greater efforts have been put forth by the FDA and the Pharmaceutical industry in identifying counterfeit drugs and manufacturing tools used to make drugs [3]. Examples of identification of unknown particles and fibers and authenticity testing will be presented.

A typical investigation involving particulate requires the identification and determination of the source of that material. Common techniques used to identify materials in our labs include stereomicroscopy (SM), polarized light microscopy (PLM), scanning electron microscopy (SEM), energy dispersive x-ray spectroscopy (EDS), and Fourier transform infrared spectroscopy (FT-IR). Following identification, a thorough review of the manufacturing process can determine the source.

In one such study, particulate was observed in two tablets (Fig. 1). The particle in one tablet was about 0.8 mm in length and was flush with the surface of the tablet, while the particle in the second tablet was just beneath the surface with a very small portion exposed and about 0.5 mm in length. Both particles were reflective and had a metallic luster. The particles were isolated and examined and photographed by SM, and were ideal for elemental analysis by EDS. EDS results indicated that one particle was stainless steel (primarily Cr, Fe, Ni) and the other particle was an organic material with inorganic components. EDS and FT-IR spectra of the organic particle were consistent with the components of the tablet. As various grades of stainless steel are used in the manufacturing equipment EDS was used to rule out some equipment and direct the investigation towards specific equipment.

Extraneous fibers can be particularly troublesome in liquid filled capsules. In a second example, PLM was used to identify the fibers found adhered to liquid filled capsules. Fiber identification is routinely done using PLM to characterize the fiber structure (Fig. 2). The fibers in this study were consistent with cotton, human hair, animal hair, and synthetic. The cotton and synthetic fibers were likely associated with clothing as from a lab coat, the human hair from a person working in the manufacturing facility, animal hair from a brush.

"Rapid" analysis of a tablet, for example, to determine if it is authentic, is done by several methods including near infrared spectroscopy, thin layer chromatography, dissolution, and chemical reactions to name several [4]. High performance liquid chromatography and gas chromatography are more conclusive techniques, but take more time to perform. To assess authenticity of a suspect tablet, we used SM, SEM/EDS, and FT-IR to compare results of a suspect tablet to those of a known, authentic tablet. The tablet and logo dimensions, morphology (SM & SEM), elemental composition (EDS), and chemical composition (FT-IR) were consistent with those of known tablets.

The inks used on the tablets were also examined to determine how they differ. Except for hue, the inks on the suspect tablet and the known tablet were chemically similar to each other (Fig. 3). In spite of this difference, the scientific evidence from this work suggests the material is authentic.

The objective in forensic investigations and pharmaceutical investigations is the same: to identify a material and to assist in determination of its source. Forensic science is typically used to support a criminal investigation, whereas in this context, pharmaceutical science is used to support manufacturing defect investigations and authenticity testing.

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FIG. 1. Left, Middle: Tablets showing embedded particles; Right: EDS spectra of particles.

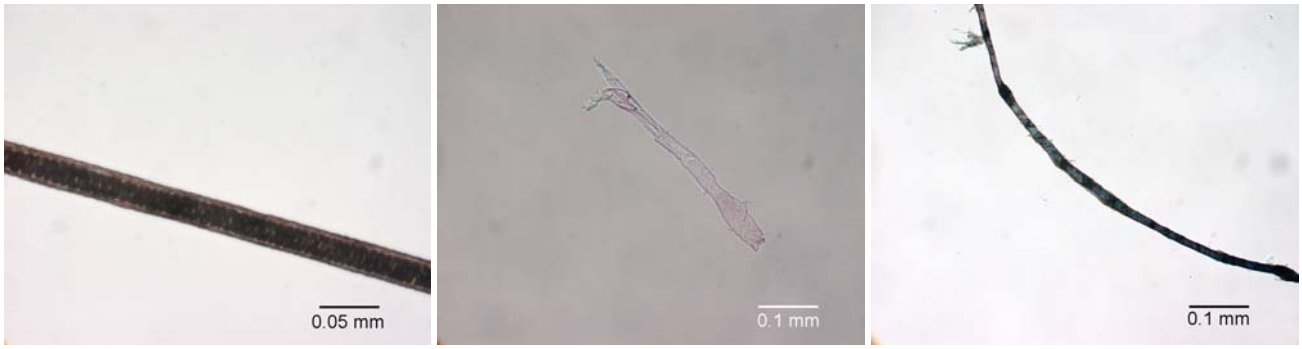

FIG. 2. Left: animal hair fiber; Middle: cotton fiber; Right: synthetic fiber.

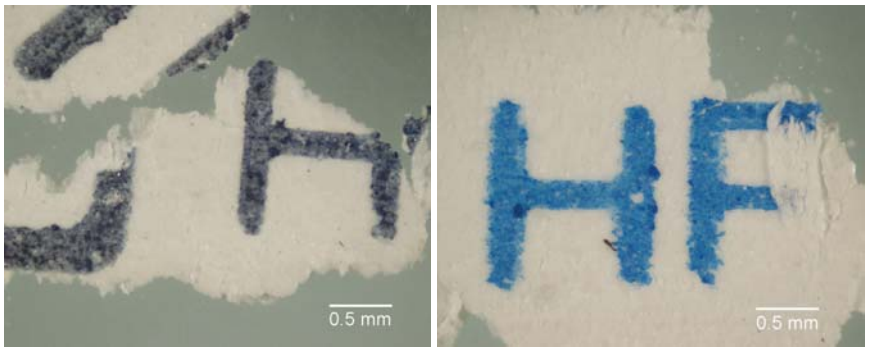

FIG. 3. Left: logo on coating from suspect tablet; Right: logo on coating from authentic tablet.

https://doi.org/10.1017/S1431927610054218 Published online by Cambridge University Press