

Pharmaceutical imaging solutions offered by the extended pressure scanning electron microscope.

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LEO Electron Microscopy

Introduction

Pharmaceutical enterprises require a range of imaging products that provide high quality information, allowing them to reach their own targets on technology, productivity, and ultimately profitability. With the increasing expectations upon drug delivery systems for efficient and controlled delivery of the active material there is a matching need for analytical tools to provide accurate information on these mechanisms. One of the most effective instruments in this area is the scanning electron microscope (SEM) owing to its unique ability to provide high-resolution images of a specimen under investigation.

After a period of substantial product development at LEO, the SEM can now be used in a pressure regime where water can be condensed easily onto the materials of interest. In the context of SEM operations this pressure regime is known as "extended pressure" or EP.

The **LEO 1450 EP** SEM allows three imaging modes in a single analytical tool. Having the capability of conventional high vacuum imaging (HV), variable pressure imaging (VP), and now extended pressure imaging (EP) this instrument provides a tremendous range of analytical solutions in fields as diverse as pharmaceutical, life-sciences, semiconductor, and materials.

Instrumentation

In the scanning electron microscope a highly focused electron beam is digitally scanned across the specimen and the response of the specimen (emitted current) is measured and is presented as a grey scale image. With a very high depth of field and a large range of magnification up to and beyond 100,000 times, the modern SEM provides an easy and productive tool for microanalysis and materials behaviour. With water vapour in the chamber of the microscope at pressure of only 500 Pa, the specimen can be maintained in a fully hydrated state. Using higher water vapour pressures, liquid water can be condensed onto the specimen leading to studies of the interaction of materials with water.



The LEO 1450EP Extended Pressure SEM

Hydration and dehydration of soluble aspirin

The interaction of water with soluble aspirin demonstrates the mechanisms by which tablets lose mechanical strength and stability and hence release the active material. This process can be observed in real time in the SEM by introducing water vapour into the chamber at sufficiently high pressures that liquid water is condensed onto the specimen. During the wetting phase the particle absorbs water and fragments. During the drying phase the reverse processes can be followed in detail.

Four images from this type of experiment are shown below obtained with a 1400EP instrument. Figure 1, shows a fragment of a dry aspirin tablet, figure 2, shows the same sample at the moment when water is just starting to condense onto the aspirin, you can see a small amount of bubbling taking place. Figure 3 shows the tablet in a pool of liquid allowing the active constituents to dissolve, and figure 4 shows the same fragment after the water has been removed by controlling the pressure and temperature of the SEM chamber, causing the specimen to dehydrate.

The images were taken using a Peltier cooled, cool stage to control the specimen temperature, cooling the specimen to a few degrees centigrade. The use of the cool stage allows water to be condensed at chamber pressures significantly below the saturated water vapour pressure at room temperature allowing good control of the condensing conditions around the specimen.

Summary

Scanning electron microscopes continue to form a core analytical tool in the pharmaceutical industry owing to their unique combination of high-resolution imaging and dynamic experimentation of water interacting with materials. Present and future developments at LEO will continue to serve pharmaceutical enterprises with tools that speed up the development cycle by providing mission critical information on microstructure, composition, and morphology.

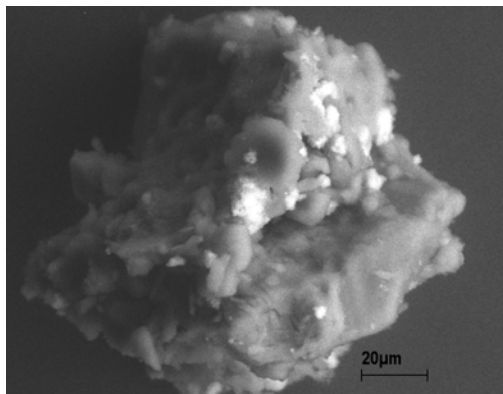


Figure 1, Fragment of an aspirin tablet, dry

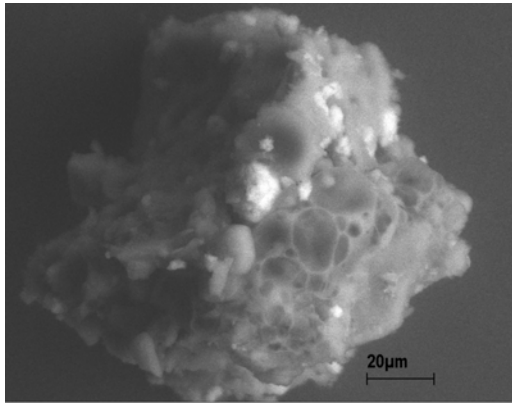


Figure 2, Aspirin as water is just starting to condense, Note : small amount of bubbling taking place.

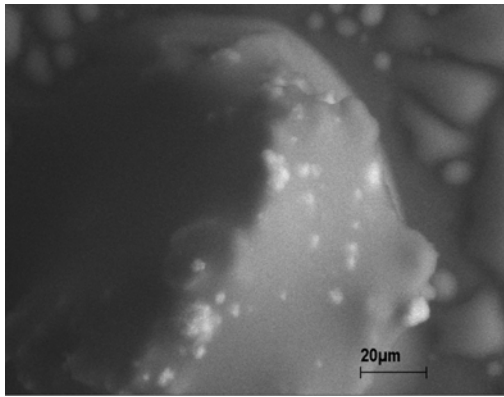


Figure 3, Tablet in a pool of liquid, allowing the active constituents to dissolve.

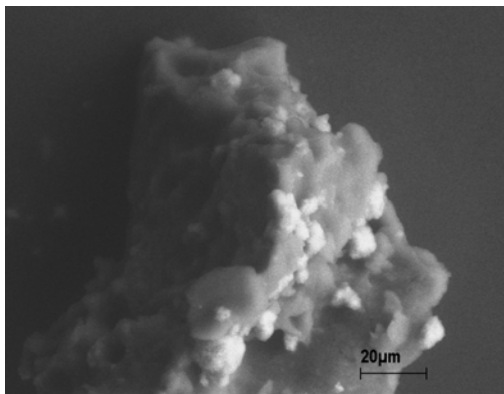


Figure 4, Same fragment after drying.