

# Pharmaceuticals - homogeneity of active ingredient in a solid phase drug delivery system

## Introduction

Time release drug delivery systems are becoming increasingly important in modern pharmaceuticals.

Subcutaneous insertion of a drug-loaded polymer avoids the need for repeated injections, and provides a much more constant

delivery of drug. This is particularly significant in cases where the difference in concentration between therapeutic and toxic drug levels is quite small. Figure 1 shows the difference in tissue drug concentration for traditional and time-release systems.

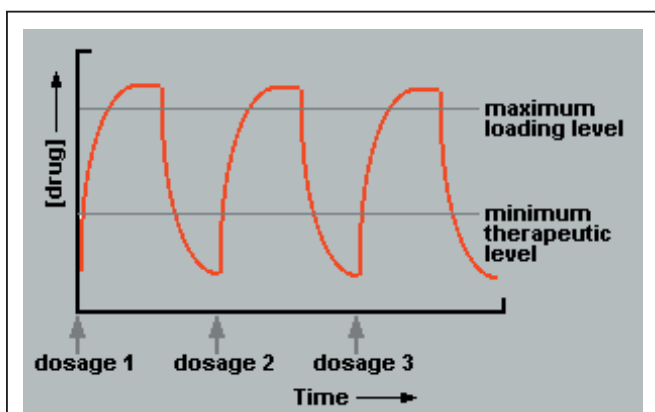


Figure 1a. Traditional dosing methods.

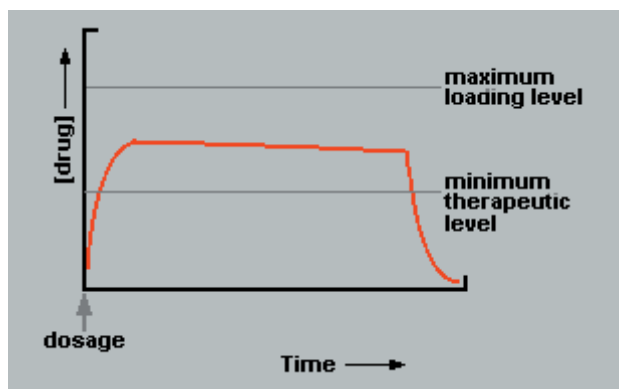


Figure 1b. Time-release delivery methods.

Figure 1.

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Such drug delivery systems are often based on a polymer or 'depot' within which the drug is included. Furthermore, the composition of the polymer itself is chosen to allow biodegradation of the polymer as shown in Figure 2, swelling to produce drug release, or response to physiological environment leading to drug release. The delivery system may be surgically implanted subcutaneously, applied as a surface patch, injected ultrasonically or inhaled.

In each case the structure and stability of the polymer and the concentration and homogeneity of active ingredient distribution must be characterized.

**Results**

The survey scan in Figure 3a shows detail of the end of a typical drug delivery depot. Bubbles caused by the extrusion process can be seen over the entire surface of the depot. A vertical fault line can also be seen at 500 microns on the X axis. This

particular depot sample contains the lowest concentration of active ingredient that will be used commercially.

The red area shown in Figure 3a was defined as a region of interest. Closer observation of this area shows several flat areas, identified by the arrows (Figure 3b).

Bubbles clearly visible in the picture are caused by the extrusion process

and have nothing to do with drug distribution. Furthermore the bubbles are not of analytical interest since they represent material above or below the focal plane of the imaging system.

The identification and distribution of active ingredient throughout the depot are critical to manufacturing quality control of the product.

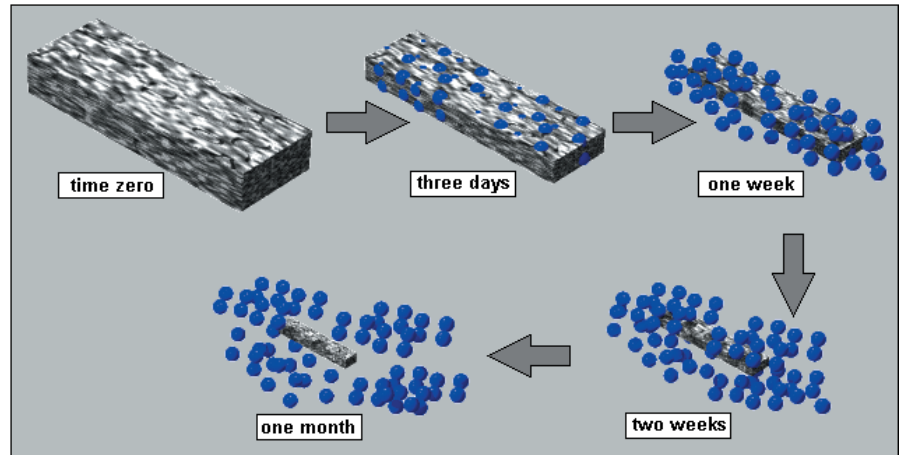


Figure 2. Controlled release of drug from a biodegradable polymer.

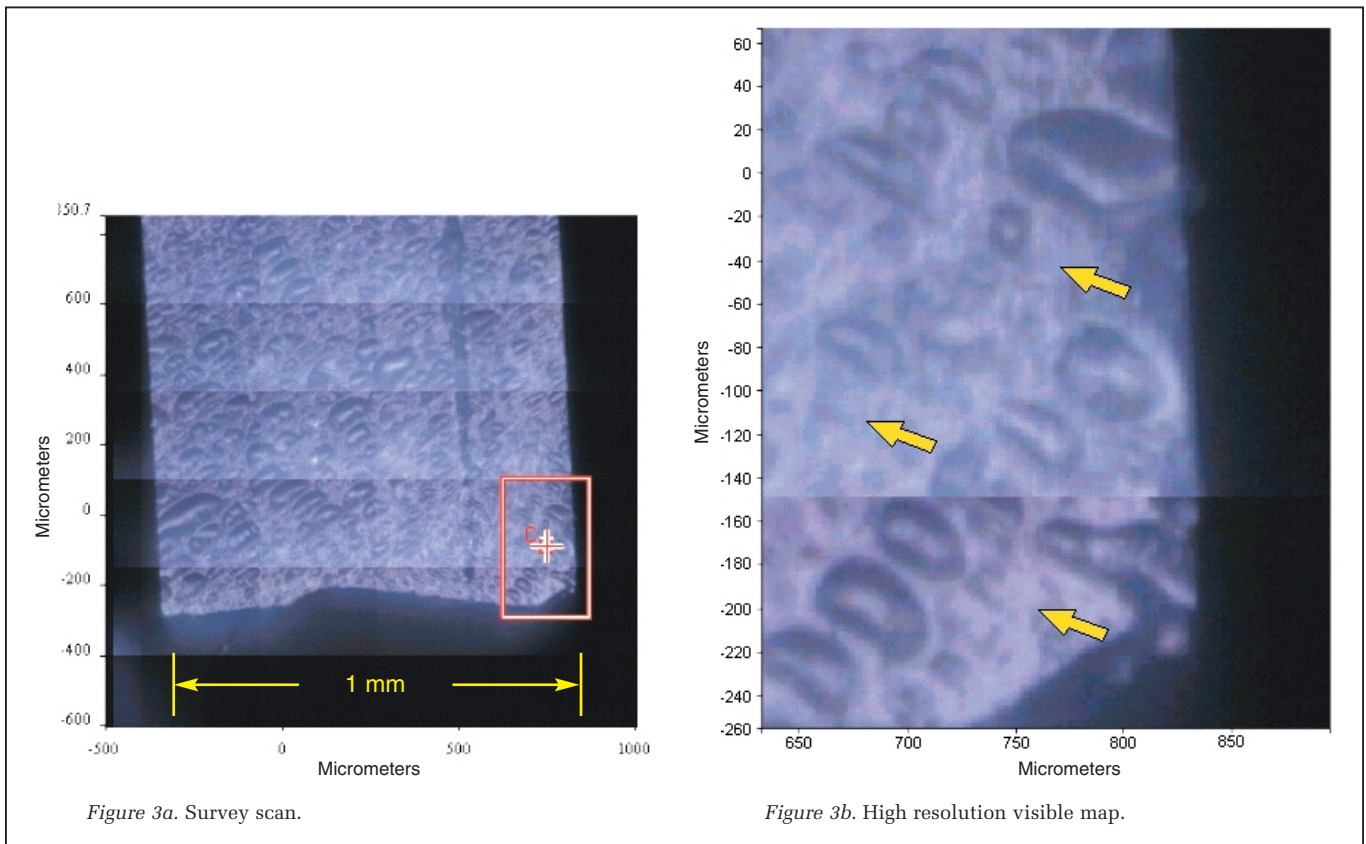


Figure 3.

The infrared image of the selected sample area was collected at 8 wavenumber spectral resolution, 6.25 micron pixel resolution, 16 spectra per pixel. Data collection took 18 minutes.

Features in the total absorbance map can be easily related to the visible image as shown in Figure 4b. The two locations were then chosen from flat regions and spectra from these locations (marked as 7 and 8) were extracted (Figure 5).

Raw spectra showed artefacts due to the thickness of the sample, so the two spectra were transferred into Spectrum and treated with the Kramers-Kronig transform. This produced spectra that both clearly showed the carrier polymer, but only one showed the active ingredient's absorption band (Figure 6).

**Conclusion**

Active ingredient distribution through the depot can clearly be analyzed, allowing accurate quality control of the drug delivery implant product. The Spectrum™ Spotlight is ideally suited to the measurement of time-release drug delivery systems. The sensitivity provided by the system allows for extremely rapid measurement of high quality results.

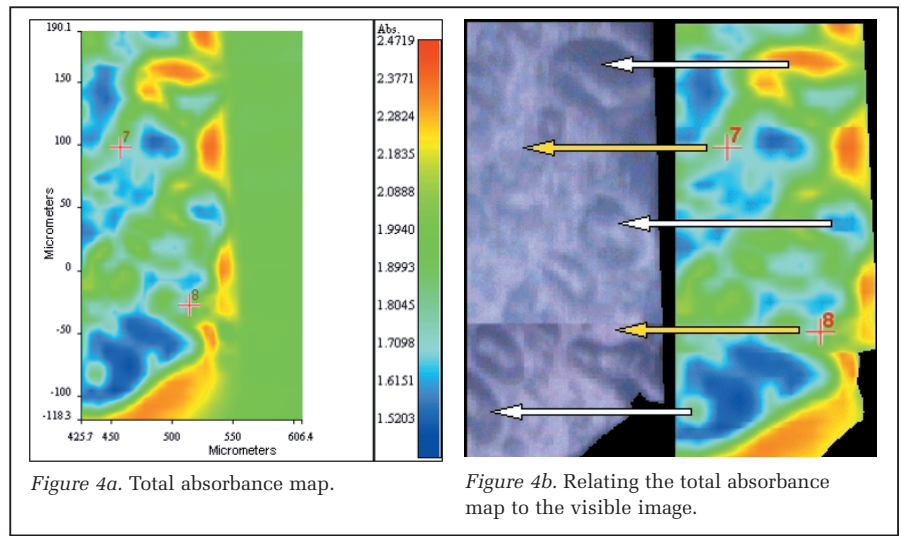


Figure 4.

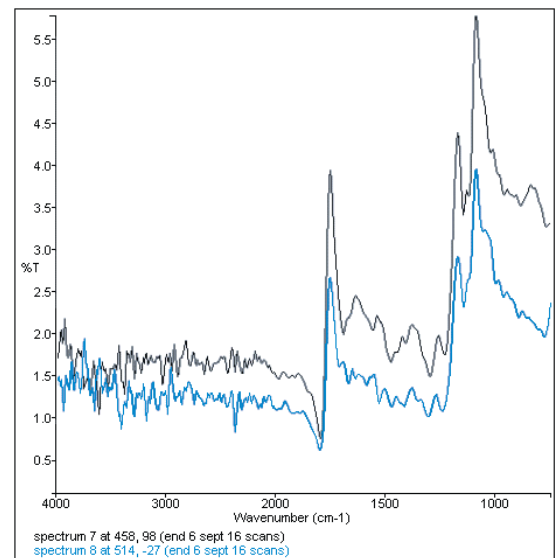


Figure 5. Spectra from Figure 3.

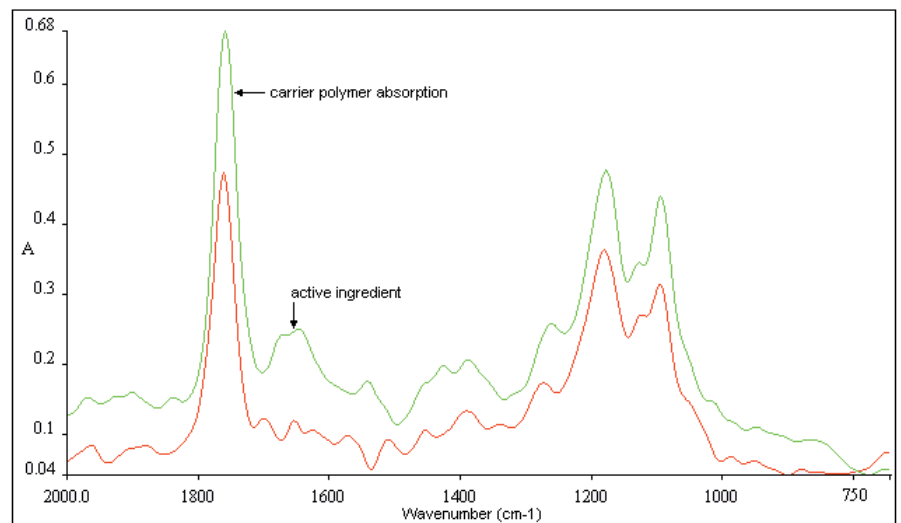


Figure 6. Kramer's Kronig transform applied to spectra from Figure 5.

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