Application note 11/13

Real-time measurement of nicotine release from dermal patch

Pion have developed a new approach to measuring the amount of nicotine released from a sustained release dermal patch. Rate of release and insight into membrane transport information are explored.

Materials

• Pion SDI system	(P/N SDI)
• Horizontal dissolution insert	(P/N IHFD-2)
• Coring sample tube	(P/N 141-0018)
• 254 nm wavelength filter	(P/N UVFILT254)
• PBS buffer (10 mM phosphate pH 7.4)	(Sigma P4417)
• Nicotine patch (16.6 mg / 20 cm^2)	(Nicorette)

Method

A 2.0 mm diameter cored sample was taken from a Nicorette patch with the adhesive layer surface facing out. After establishing background absorbance at all pixels in the imaged area using PBS buffer in the flow cell, the sample was inserted into the flow cell and the cell was filled with buffer. The flow was turned off for approximately 6 min, giving static conditions for the dissolution medium, and a UV movie was taken during this time. Buffer was then pumped over the sample to move all released sample downstream for post-sample absorbance measurement (intrinsic dissolution rate).

The sample was cored from the patch using a sharpened stainless steel tube with a 2.0 mm ID. The drug surface was level with the top of the tube leaving sides exposed to buffer. This method allows placement of an artificial membrane on top of the patch for more realistic simulation of dermal transport rates. Data was captured with a frame rate of 2.5 frames/s.

Results

Figures 1a and 1b show 254 nm absorbance images at 1.54 and 5.54 min respectively.

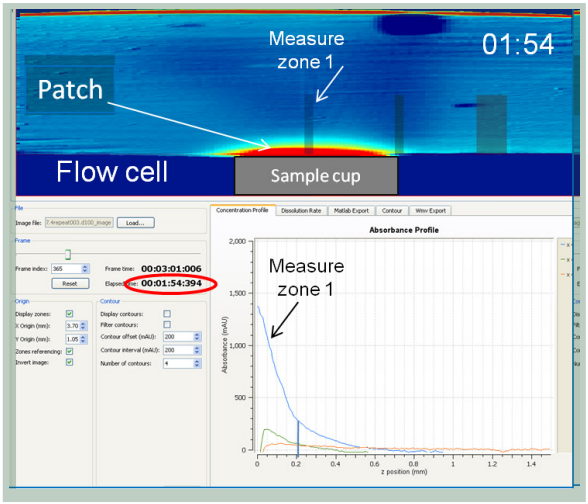

Figure 1a

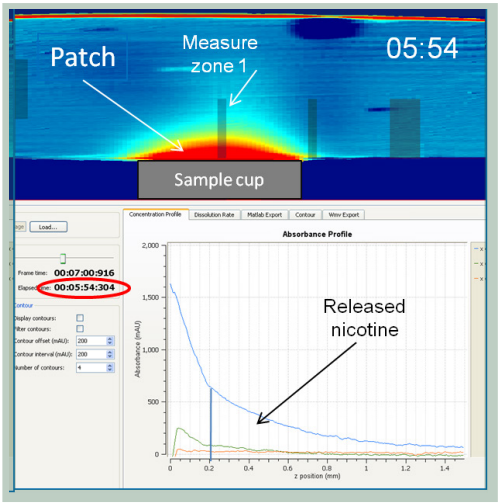

Figure 1b

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In Figures 1a and Ib, the black line on top of the grey rectangle overlaid onto each of the actual SDI images shows the top of the sample cup and the location of the patch, and the measurement zones are shown relative to the holder surface. Absorbance is referenced to the background measured on all pixels with holder and dissolution medium but without sample in the cell, and is rendered on a scale from blue (low) to red (high). The images show the release of nicotine from the surface of the patch. The time-dependent enlargement of the red/yellow/light blue region over the patch is evident in comparing Figure 1a (1.54 min) to Figure 1b (5.54 min).
Figure 2 shows the time-dependent concentration profiles determined at measurement zone 1 of Fig 1. Absorbance is converted into concentration knowing the optical pathlength of the sample cell, 3 mm, and the molar absorption coefficient (Willits et al., Anal. Chem., 1950, 22, 430). Information about the accumulation and spread of the nicotine into the dissolution medium following transport through the membrane barrier of the patch may be obtained from this figure.

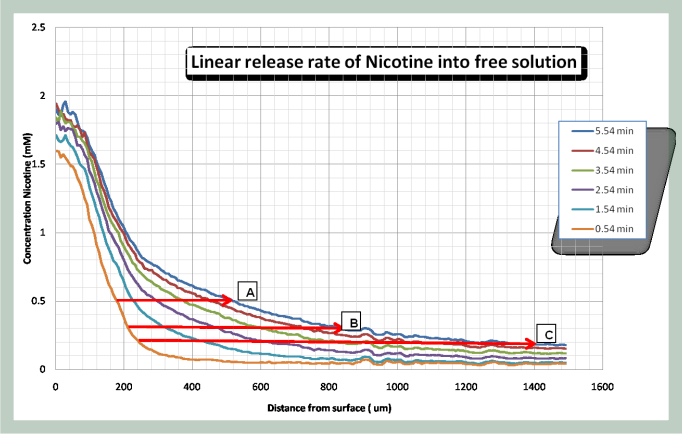

Figure 2. Absorbance traces away from surface in measurement zone 1 (see Figure 1) at 1 min intervals. Lines A, B, and C show the distances moved in 5 min for fixed concentrations of nicotine (0.5, 0.3, and 0.2 mM respectively). These represent rates of 1.1, 2.1 and 3.8 mm/s respectively into PBS buffer (100 mM pH 7.4).

The patch is designed to release 10 mg of nicotine over 16 hours. This corresponds to a release rate of $1x10^{-9}$ mol/s. Data in Fig 2 are concordant with this value. The Nernst Brunner equation is

$$\text{Rate} = DA\,(C_o\text{-}C_b)/h$$

where D if the diffusion coefficient, A the area, h the diffusion layer thickness, and C_o and C_b concen-trations at the surface and in the bulk, respectively. By taking the gradient in concentration $(C_o\text{-}C_b)/h$ from the central part of the curves at 4.54 and 5.54 min, and a literature value for the diffusion coeffi-cient of nicotine, the rate calculated for the whole patch of area 20 cm^2 is $1x10^{-9}$ mol/s, in good agreement with the known release rate.

Conclusion

A new method for measurement of nicotine release from a sustained release dermal patch is described, based on real-time UV imaging of the area containing the patch and the dissolution medium. Because release is observed into a small volume immediately over the patch, the Pion SDI Surface Dissolution System allows results to be obtained more rapidly than when using traditional methods. The time-dependent concentration profiles of nicotine above the patch provide quantitative information on the release process, and good agreement is found with the known release rate. This approach has potential for widespread application to sustained release formulations. Different media (e.g. oils, gels) could be placed above the formulation and release of the active pharmaceuti-cal ingredient visualized using UV imaging. An artificial membrane could be put on top of the patch for more realistic simulation of dermal transport rates.