Therapeutic drug monitoring

Therapeutic monitoring is an important tool in patient care, with a role in diagnosing illness, optimising treatment and subsequently tracking progress. This process is typically conducted by the collection of blood samples, followed by the analysis and determination of plasma concentrations of the drug or endogenous substance of interest. However, the use of hypodermic needles for sampling is associated with a number of well-characterized disadvantages, including for example, needle-phobia, the need for trained healthcare staff for administration, sharps disposal, the risk of needle-stick injury and transmission of infection (Simonsen et al. 1999). An alternative method of sampling is, therefore, much needed. Due to the intrinsic capacity of hydrogels to imbibe fluid, there is potential for application of such systems in the collection of specific analytes for screening, diagnostic and monitoring purposes. This concept has been employed in tandem with microneedles, in order to extract interstitial fluid, due to the two-way movement of fluid possible with a microneedle platform (Mukerjee et al. 2004). Interstitial fluid levels can be used as surrogate markers for the blood concentration of an analyte, often enabling accurate comparisons to the free concentrations of drugs and endogenous substances in plasma (Kiang et al. 2012). This can then be converted to relevant clinical information, either in one step by a sensor specific to the particular analyte of interest as part of the array, or in two steps by analysis upon removal of the patch and extraction of the specific substance. Typically the movement of interstitial fluid relies on capillary action, in order to extract the fluid, or indeed, more complex mechanisms such as vacuum or osmotic pressure. The use of a hydrogel for this purpose, however, offers an interesting alternative. This potential process is summarized in Fig. 6. Sakaguchi et al. (2012) described pre-treatment of the skin with a poly(carbonate) plastic microneedle array, followed

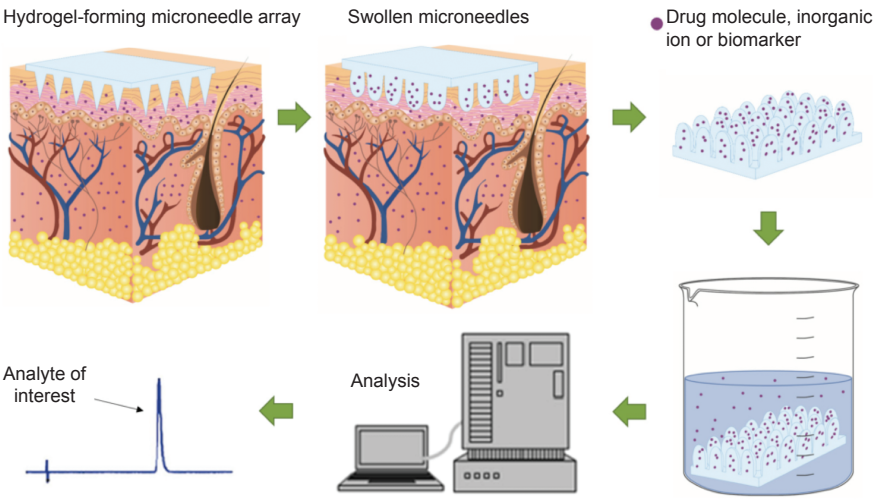

Fig. 6. Schematic representation demonstrating the principle of microneedle-mediated therapeutic drug monitoring. Images display swelling of hydrogel-forming microneedles upon insertion due to interstitial fluid uptake, capture and extraction of analyte of interest and ultimately quantification of analyte (Caffarel-Salvador et al. 2015).