M1322

Universal Potentiometric Sensors: Application for Real Time Concentration Monitoring in Surfactant Containing Media

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PURPOSE

Up till present the use of universal potentiometric sensors in surfactant containing media was problematic. Typical issues arising are: slow response, limited sensitivity and short lifespan. In this study we will show that the free drug sensors can be used in media containing up to 5% surfactant and that the above mentioned issues can be satisfactory resolved. The products Brij-35® Tween 20® and Tween 80® were tested.

METHODS

The free drug sensors (FDS, Pion Inc.) were used as a potentiometric sensor for the *in situ* measurements. The universal sensor acquired selectivity for the analyte drug by exposing the sensor to a medium containing the drug and the surfactant. All experiments were performed in 20 mL of media using individually stirred and temperature controlled 8 positions of miniaturized dissolution bath of µDISS Profiler™ instrument (Pion Inc., Figure 2). Selected surfactant media were 0.01M HCl containing from 0.5% up to 5% of a neutral surfactant. The model drug compounds used in this study were: Dapoxetine, Loperamide and Cinnarizine; the used surfactants were: Brij-35®, Tween 20® and Tween 80®. Accuracy and reproducibility of the sensors were tested by adding a known amount of drug in the vessel and observing the sensor response. The obtained sensor response was converted to concentration using the algorithm of Bohets et al. (Analytica chimica acta 581 (2007) 181) and compared with the actual concentration. Drift occurring on media change (e.g. 0.01 M HCl 1% Tween20® to 0.01 M HCl 1% Brij-35®) was compensated by a linear drift correction based on the potential of a standard solution acquired just prior and post measurement. For each product the linear range was determined by measuring 5 evenly separated concentrations in the region of interest. This data yielded also a slope, witch can be regarded for practical use as constant over several days.

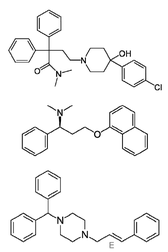

Figure 1. From top to bottom Chemical structure of : Loperamide, Dapoxetine and Cinnarizine

Figure 2. The µDISS Profiler from Pion Inc monitors concentration in real time in 8 temperature controlled vessels using only 1 – 20 mL of dissolution media.

RESULTS

Continuous, reproducible and accurate profiles were obtained using the FDS in the 20 mL of surfactant containing media.
From the addition of standards one could state for all compounds that: the deviation from accuracy was less than 3%, and, the relative standard deviation did not exceed 2%. Typical plots of the known versus calculated concentration resulted in a straight line ($R^2 > 0.999$) with slopes equal to 1.00 ± 0.01. Electrode response time (t95) was typically shorter than 30 seconds. It was noted that after some days the FDS became very sensitive to electrical interference and finally became unresponsive. Using the proprietary Octens fast regeneration mixture one could resurrect the sensors in a matter of minutes. The observed degeneration was not observed when storing the ISE's on Octens proprietary long time storage mixture, even when FDS were stored in excess of 3 months. FDS were interchangeable with regard to nonionic surfactant and also functioned on media not containing surfactant. Conversion from one media to another was fast and didn't affect adversely sensor accuracy when drift correction algorithms were applied.

Dapoxetine long term regeneration

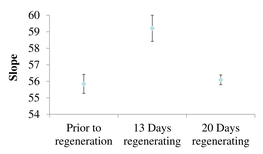

Figure 3. Effect on slope of long term regeneration

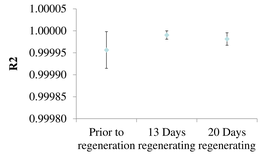

Figure 4. Effect on linearity of long term regeneration

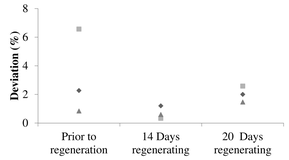

Figure 5. Effect on accuracy of long term regeneration

Depletion of ISE in 1% Tween 20® Cinnarizine

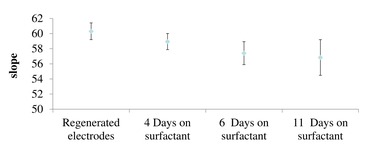

Figure 6. Effect on slope of surfactant exposure

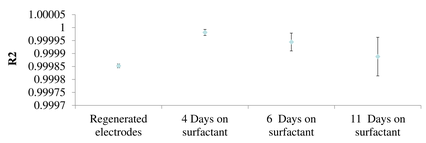

Figure 7. Effect on linearity of surfactant exposure

RESULTS

Addition of Cinnarizine standard in 5% Tween 20®

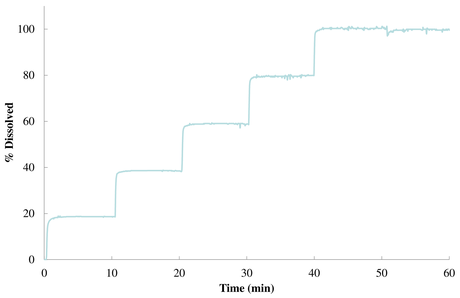

Figure 8. Addition of Cinnarizine standard in 5% Tween 20® 0.01 M HCl . Effects of aging become apparent as spikes on the curve.

CONCLUSIONS

The presented data show that the free drug sensors can be used in surfactant containing media. The sort lifespan of membrane based FDS's in this kind of media can be circumvented by using regeneration and storage solutions. The free drug sensor is universal and can be applied for most drug-like compounds having ionizable functional groups in their molecular structures and a logP > 0.

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