NIR real-time monitoring of a silicone-based drug reservoir crosslinking process.

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Purpose: First, to monitor the crosslinking process of a silicone-based drug reservoir at different temperatures. Secondly, to determine how the temperature and the crosslinking completion time are related. Finally, to predict the crosslinking state of new samples.

Methods: Thermostated samples were non-invasively interfaced with a NIR reflectance probe during the crosslinking process. Conformity Tests (CTs) were performed with the data collected from each sample. CT is based on the calculation of the spectral differences between the reference and the test spectra, i.e. between the spectra acquired respectively after and before the crosslinking completion. Principal Component Analysis (PCA) was also performed to follow the reaction.

Results: Samples thermostated at temperatures ranging from 20 to 75 °C were scanned during the crosslinking reaction. The latter was considered to be reached when minimal spectral deviations were detected by the CT. Those results were confirmed by the PCA. It was found that PC 3 modeled the crosslinking process while PC 2 represented the sample temperature. A PCA model built with this data set was tested with uncrosslinked and crosslinked samples scanned while thermostated at 80°C. The PCA model predictions agreed with the CTs calculated with each test sample and allowed to discriminate the spectral deviations caused by the crosslinking reaction from those caused by temperature.

Conclusion: The crosslinking of a silicone-based drug reservoir was successfully monitored in real time with NIR spectroscopy. An agreement was found between the CTs results and the PCA results. Finally, PCA successfully predicted the crosslinking state of new samples. Moreover, CTs and PCA approaches were found to be complementary since the CTs illustrate the combined effects of temperature and crosslinking while the PCA can discriminate both effects. Consequently, the present study enables a better process understanding and can therefore be part of a Quality by Design approach.

Session topic: PAT in bioactive production and downstream processing.