Silicone-based drug reservoirs manufacturing process – Critical quality attributes evaluation using NIR and Raman spectroscopy.

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Purpose: To investigate the use of near infrared (NIR) and Raman spectroscopy as Process Analytical (PAT) tools for the evaluation of 3 critical quality attributes of the reservoirs: the crosslinking state, the API content and homogeneity.

Methods: NIR spectroscopy was interfaced with crosslinking experiments performed at different temperatures. Principal Component Analysis (PCA) and conformity tests were carried out with the collected data to visualize the spectral variations occurring during the process. The API homogeneity within the reservoirs was analyzed with Raman spectroscopy (mapping). To compare the spectra collected during the mapping acquisition, a common polymer peak was set to the same ordinate limit in all the spectra. The area variations of the 2090 cm^{-1} API peak were derived as the mapping test result. In order to quantify the API content of the reservoirs, a NIR model based on Partial Least Squares (PLS) regression was built with the calibration set. HPLC was used as the reference method. Further, the model ability to quantify accurately was tested with the validation set.

Results: Conformity tests and PCA both highlighted the spectral modifications occurring during the crosslinking process. Compared to the conformity test method, PCA had the advantage to discriminate the heating effect from the crosslinking effect occurring together during the monitored process. Raman mapping was able to detect poor and good product performance related to the API distribution. For the API quantification, the 1.2 % Root Mean Squared Error of Prediction (RMSEP) of the NIR model indicated the global accuracy of the NIR model. The 95 % tolerance interval calculated on the validation results accuracy profile indicated that each future result will have a relative error below ± 5 % with a probability of at least 5 %.

Conclusion: Within the framework of silicone-based reservoirs manufacturing process, 3 critical quality attributes of silicone-based drug reservoirs were quickly and efficiently evaluated by NIR and Raman spectroscopy. The developed PAT tools can advantageously be used for process optimization leading to the definition of Process Design Space or and/or represent the first steps towards a Real Time Release quality based system.