NIR AND RAMAN SPECTROSCOPY AS PAT TOOLS FOR THE MANUFACTURING OF SILICONE-BASED DRUG RESERVOIRS

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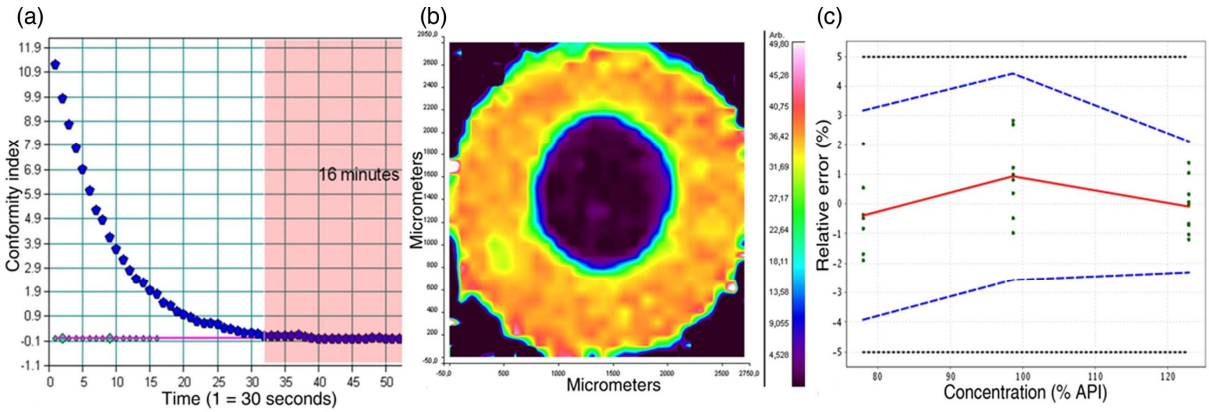
FDA's Process Analytical Technology (PAT) aims at "improving the pharmaceutical development, manufacturing and quality assurance trough innovation in product and process development, process analysis and process control" [1-2]. Using Raman and Near Infrared (NIR) spectroscopy as PAT tools, 3 critical quality attributes of a silicone-based drug reservoir were studied. First, the crosslinking process was monitored at different temperatures with NIR spectroscopy. Principal Component Analysis (PCA) and Conformity Indexes (CIs) were performed on the collected data to visualize the spectral variations occurring during the process. Using CI, Figure (a) depicts the crosslinking kinetic of a sample thermostated at 80 ℃. The process completion time was determined when the CI of the sample was close to 0, meaning that the difference between a crosslinked and an uncrosslinked sample was minimal. Second, the Active Pharmaceutical Ingredient (API) homogeneity in the reservoir was checked with Raman spectroscopy (mapping) (Figure (b)). Finally, a NIR model able to quantify the API in the drug reservoir was developed. An HPLC method was used as the reference method. Partial Least Squares (PLS) regression on the calibration set was performed to build prediction models of which the ability to quantify accurately was tested with an external validation set. The 1.2 % RMSEP of the NIR model indicated the global accuracy of the model. The accuracy profile based on tolerance intervals was used to generate a complete validation report [3]. Figure (c) displays the accuracy profile based on the external validation results. The 95 % tolerance interval calculated on the validation results (dashed blue lines) is included within the ±5 % acceptance limits (dotted black lines). Therefore, each future result will have a relative error below ±5 % with a probability of at least 95 %. In conclusion, 3 critical quality attributes of silicone-based drug reservoirs were quickly and efficiently evaluated by NIR and Raman spectroscopy.



References.

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