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By

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NON DESTRUCTIVE PREDICTION OF DISSOLUTION PROFILES BY NEAR INFRARED SPECTROSCOPY OF TABLETS SUBJECTED WITH DIFFERENT LEVELS OF STRAIN

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The dissolution test is the only test performed in manufacturing with the objective of monitoring whether the product will perform adequately throughout its shelf life. This method is not suitable for predicting in vivo, but is used for batch-to-batch comparisons. However, the dissolution method is time consuming, requires media preparation, and generates a vast quantity of waste. A new method to predict dissolution was developed using non-destructive Near Infrared Spectroscopy (NIRS).

Powder shearing is important in mixing of powders that are cohesive. In continuous mixing, shear strain is developed within the process when powder particles are in constant movement and can affect the quality attributes of the final product such as dissolution test. Shear was applied to powder blends using a Couette cell and tablets were produced using a tablet press emulator. Tablets with different shear levels were measured using NIR spectroscopy in the diffuse reflectance mode. The NIR spectra were baseline corrected to maintain the scattering effect associated with the physical properties of the tablet surface. Principal component analysis was used to establish the principal sources of variation within the samples

A calibration model was developed between the changes in the NIR spectra and dissolution profiles. Principal component analysis was used to study the sources of variation in the spectra

obtained. Partial least squares 2 were used to predict dissolution on tablets with different levels of strain. Statistical methods were used to verify similarity between NIR predictions and dissolution profiles.

Changes in the NIR spectra were observed in diffuse reflectance mode of tablets obtained after compaction at 8, 12, and 16kN for blends of similar composition subjected to the three strain levels: no shear, 160 revolutions, and 640 revolutions. Broad bands are obtained at no shear conditions. As the strain is increased the bands became more define. These spectra show significant differences in two spectral regions: 7450–7000 cm^{-1} and 5600–5100 cm^{-1}. The 7450–7000 cm^{-1} is related to combinations of the first overtones of the C–H stretching modes and the C–H bending modes of cellulose.

Dissolution tests were performed in a USP II dissolution apparatus. From these tests results, a dissolution profile was created as a reference values, and used for calibration model and to predict independent samples. A PLS-2 calibration model was developed with two PLS-2 factors. Predicted dissolution profiles show a high correlation when compared with the reference method achieving a 0.9992 correlation coefficient for 0 and 160 revolutions, 0.9983 for 640 revolutions and 0.9977 for 2560 revolutions. The accuracy of the prediction of dissolution was evaluated through the use of the relative standard error of prediction (RSEP). RSEP for the validation set was 6.3%.

Shear stress applied on the powder mixtures affects the diffuse reflectance spectra and angle resolved light scattering of tablets.The angle-resolved light scattering measurements show significant changes in the material morphology after different levels of shear were applied.

Dissolution is affected by shear. As the blend is sheared for longer times, the dissolution decreases.Model predictions are highly correlated with the reference method values. NIR Spectroscopy, in combination with multivariate techniques and Quality by Design can become an alternate method to predict dissolution profiles

References: (papers published)

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2. Hernandez, E.; Pawar, P.; Keyvan, G.; Wang, Y.; Velez, N.; Callegari, G.; Cuitino, A.; Michniak-Kohn, B.; Muzzio, F. J.; Romañach, R. J., Prediction of dissolution profiles by non-destructive near infrared spectroscopy in tablets subjected to different levels of strain. *J. Pharm. Biomed. Anal.* **2016**, *117*, 568-576.