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Vibrational spectroscopy to support the link between rheology and continuous twin-screw melt granulation on molecular level: a case study

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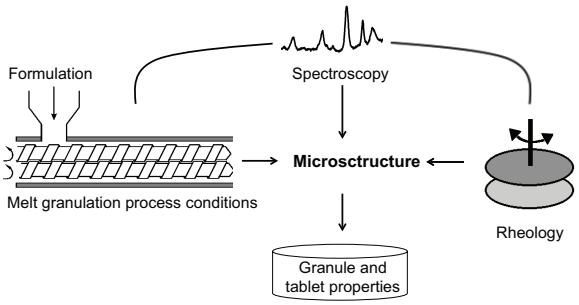
Abstract

Twin screw hot melt granulation (TSHMG) is an innovative and continuous drug formulation process allowing granulation of moisture sensitive drugs. However, due to the lack of experience and in-depth process understanding, this technique is not yet widely used. During the TSHMG process, the microstructure of the granules is generated and modified and strongly depends on the flow behavior of the material. Hence, rheology might be a suitable tool to simulate and examine this process. However, chemical interactions of the material are influencing the physical properties leading to the microstructure. In this research project it is spectroscopically investigated whether the heat applied in a rheometer induces the same molecular effects as these occurring during TSHMG of the model formulation caffeine anhydrous/Soluplus®. Hence, it is evaluated whether rheology can be used as a simulation tool to improve the understanding of the material behavior at molecular level during continuous melt granulation. Therefore, in-line Raman spectroscopy is executed during TSHMG and in situ Fourier Transform Infra-red (FTIR) during oscillatory rheological experiments. The results from the in-line Raman monitoring revealed polymorph transition of caffeine anhydrous during twin screw melt granulation with Soluplus® which is stimulated depending on the binder concentration and/or granulation temperature. A correlation was seen between the FTIR spectra obtained during the rheological temperature ramp and the in-line collected Raman spectra during the melt granulation runs. The polymorphic conversion of caffeine anhydrous could be detected in the same temperature range with both techniques, proving the comparability of plate-plate rheometry and hot melt granulation (HMG) for this case with the used parameter settings. Process simulation using rheology combined with in situ FTIR seems a promising approach to increase process understanding and to facilitate binder and parameter selection for TSHMG.



Keywords: Continuous twin-screw melt granulation, Rheology, Vibrational spectroscopy, Caffeine anhydrous, Polymorphism