Accepted Manuscript

Control of Three Different Continuous Pharmaceutical Manufacturing Processes: Use of Soft Sensors

Jakob Rehrl, Anssi-Pekka Karttunen, Niels Nicolaï, Theresa Hörmann, Martin Horn, Ossi Korhonen, Ingmar Nopens, Thomas De Beer, Johannes G. Khinast

PII: S0378-5173(18)30174-1
DOI: https://doi.org/10.1016/j.ijpharm.2018.03.027
Reference: IJP 17370

To appear in: International Journal of Pharmaceutics

Received Date: 30 November 2017
Revised Date: 26 February 2018
Accepted Date: 14 March 2018


This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.
Control of Three Different Continuous Pharmaceutical Manufacturing Processes: Use of Soft Sensors

Jakob Rehrl\textsuperscript{1,6}, Anssi-Pekka Karttunen\textsuperscript{2,6}, Niels Nicolaï\textsuperscript{3,7}, Theresa Hörmann\textsuperscript{5,6}, Martin Horn\textsuperscript{4,6}, Ossi Korhonen\textsuperscript{2,6}, Ingmar Nopens\textsuperscript{7}, Thomas De Beer\textsuperscript{3,6}, Johannes G. Khinast\textsuperscript{1,5,6}

\textsuperscript{1} Research Center Pharmaceutical Engineering, 8010 Graz, Austria
\textsuperscript{2} University of Eastern Finland, School of Pharmacy, PROMIS-Centre, FI-70211 Kuopio, Finland
\textsuperscript{3} Laboratory of Pharmaceutical Process Analytical Technology, Ghent University, 9000 Ghent, Belgium
\textsuperscript{4} Institute of Automation and Control, Graz University of Technology, 8010 Graz, Austria
\textsuperscript{5} Institute of Process and Particle Engineering, Graz University of Technology, 8010 Graz, Austria
\textsuperscript{6} European Consortium on Continuous Pharmaceutical Manufacturing (ECCPM), 8010 Graz, Austria
\textsuperscript{7} Department of Mathematical Modelling, Statistics and Bioinformatics, Ghent University, 9000 Ghent, Belgium

* corresponding authors: Martin Horn (martin.horn@tugraz.at), Thomas De Beer (Thomas.DeBeer@UGent.be), Ossi Korhonen (ossi.korhonen@uef.fi), Johannes Khinast (khinast@tugraz.at, phone: +43 316 873 30400, fax: +43 316 873 1030400)

Abstract
One major advantage of continuous pharmaceutical manufacturing over traditional batch manufacturing is the possibility of enhanced in-process control, reducing out-of-specification and waste material by appropriate discharge strategies. The decision on material discharge can be based on the measurement of active pharmaceutical ingredient (API) concentration at specific locations in the production line via process analytic technology (PAT), e.g. near-infrared (NIR) spectrometers. The implementation of the PAT instruments is associated with monetary investment and the long term operation requires techniques avoiding sensor drifts. Therefore, our paper proposes a soft sensor approach for predicting the API concentration from the feeder data. In addition, this information can be used to detect sensor drift, or serve as a replacement/supplement of specific PAT equipment. The paper presents the experimental determination of the residence time distribution of selected unit operations in three different continuous processing lines (hot melt extrusion, direct compaction, wet granulation). The mathematical models describing the soft sensor are developed and parameterized. Finally, the suggested soft sensor approach is validated on the three mentioned, different continuous processing lines, demonstrating its versatility.

Key words: Continuous manufacturing, soft sensor, process analytical technologies, near infrared spectroscopy, residence time distribution, control strategy
دریافت فوری
متن کامل مقاله
امکان دانلود نسخه تمام متن مقالات انگلیسی
امکان دانلود نسخه ترجمه شده مقالات
پذیرش سفارش ترجمه تخصصی
امکان جستجو در آرشیو جامعی از صدها موضوع و هزاران مقاله
امکان دانلود رایگان ۲ صفحه اول هر مقاله
امکان پرداخت اینترنتی با کلیه کارت های عضو شتاب
دانلود فوری مقاله پس از پرداخت آنلاین
پشتیبانی کامل خرید با بهره مندی از سیستم هوشمند رهگیری سفارشات