

Accepted Manuscript

Lubricant based determination of design space for continuously manufactured high dose paracetamol tablets

Krista Taipale-Kovalainen, Anssi-Pekka Karttunen, Jarkko Ketolainen, Ossi Korhonen



PII: S0928-0987(17)30687-5
DOI: <https://doi.org/10.1016/j.ejps.2017.12.021>
Reference: PHASCI 4341

To appear in: *European Journal of Pharmaceutical Sciences*

Received date: 15 June 2017
Revised date: 21 December 2017
Accepted date: 22 December 2017

Please cite this article as: Krista Taipale-Kovalainen, Anssi-Pekka Karttunen, Jarkko Ketolainen, Ossi Korhonen , Lubricant based determination of design space for continuously manufactured high dose paracetamol tablets. The address for the corresponding author was captured as affiliation for all authors. Please check if appropriate. Phasci(2017), <https://doi.org/10.1016/j.ejps.2017.12.021>

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.

Lubricant based determination of design space for continuously manufactured high dose paracetamol tablets

Krista Taipale-Kovalainen, Anssi-Pekka Karttunen, Jarkko Ketolainen, Ossi Korhonen

University of Eastern Finland, School of Pharmacy, Promis Centre, Kuopio, Finland

Abstract

The objective of this study was to devise robust and stable continuous manufacturing process settings, by exploring the design space after an investigation of the lubrication-based parameters influencing the continuous direct compression tableting of high dose paracetamol tablets. Experimental design was used to generate a structured study plan which involved 19 runs. The formulation variables studied were the type of lubricant (magnesium stearate or stearic acid) and its concentration (0.5, 1.0 and 1.5%). Process variables were total production feed rate (5, 10.5 and 16kg/h), mixer speed rpm (500, 850 and 1200rpm), and mixer inlet port for lubricant (A or B). The continuous direct compression tableting line consisted of loss-in-weight feeders, a continuous mixer and a tablet press. The Quality Target Product Profile (QTPP) was defined for the final product, as the flowability of powder blends (2.5 sec), tablet strength (147 N), dissolution in 2.5 minutes (90 %) and ejection force (425 N). A design space was identified which fulfilled all the requirements of QTPP. The type and concentration of lubricant exerted the greatest influence on the design space. For example, stearic acid increased the tablet strength. Interestingly, the studied process parameters had only a very minor effect on the quality of the final product and the design space. It is concluded that the continuous direct compression tableting process itself is insensitive and can cope with changes in lubrication, whereas formulation parameters exert a major influence on the end product quality.

Keyword: *Continuous manufacturing, Design of Experiments, Design Space, Paracetamol, High dose, Lubrication, Quality Target Product Profile*

1. Introduction

Batch processing is widely used by the pharmaceutical industry. Most marketing authorizations (MA) for conventional pharmaceuticals are based on batch processing. However, there is a consensus that continuous manufacturing is accepted and supported by regulatory agencies (Nasr et. al, 2017). Still there is a need for harmonization of guidelines to promote the adoption of a continuous manufacturing. ICHQ8 guidance highlights an opportunity for implementation of continuous manufacturing processes into commercial applications. The need to change manufacturing from batch to continuous manufacturing has faced many challenges (Badman et al., 2015, Byrn et al., 2015) with problems encountered in the lack of knowledge, regulatory barriers and investments. The keypoint is to justify how the quality is built into the product and evaluated, how the material traceability is assured, and how the batch is defined (Nasr et.al, 2017). Furthermore, the real-time monitoring gives the opportunity for manufacturers to use performance-based approach to justify the quality of the product and to use the real-time release testing. In addition, a greater assurance of product quality can be achieved during continuous manufacturing process by collecting product information in-line with the aid of process analytical technology (PAT) and adopting the concept of parametric release (EU GMP Annex 17, 2001).

The continuous manufacturing process emphasizes the importance of design of an effective and efficient manufacturing process based on an in-depth understanding of how formulation and process factors impact on the end product quality. Furthermore, this can help to define the design

Download English Version:

<https://daneshyari.com/en/article/8511548>

Download Persian Version:

<https://daneshyari.com/article/8511548>

[Daneshyari.com](https://daneshyari.com)