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Validation of fluid bed granulation utilizing artificial neural network

Sharareh Salar Behzadi[a], Johanna Klocker[b], Herbert Hüttlin[c], Peter Wolschann[b], Helmut Viernstein[a,*]

[a] *Institute of Pharmaceutical Technology and Biopharmaceutics, University of Vienna, Althan Strasse 14, 1090 Vienna, Austria*
[b] *Institute of Theoretical Chemistry and Structural Biology, University of Vienna, Währinger Strasse 17, 1090 Vienna, Austria*
[c] *Innojet Technologies, Rümminger Strasse 15, 79539 Lörrach, Germany*

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Abstract

Three innovative components (an annular gap spray system, a booster bottom and an outlet filter) have been developed by Innojet Technologies to improve fluid bed technology and to reduce the common interference factors (clogging of nozzles and outlet filters, spray loss, spray drying and fluidized bed heterogeneity). In a fluid bed granulator, three conventional components have been replaced with these innovative components. Validation of the modified fluid bed granulator has been conducted using a generalized regression neural network (GRNN). Under different operating conditions (by variation of inlet air temperature, liquid-binder spray rate, atomizing air pressure, air velocity, amount and concentration of binder solution and batch size), sucrose was granulated and the properties of size, size distribution, flow rate, repose angle and bulk and tapped volumes of granules were measured. To confirm the method's validity, the trained network has been used to predict new granulation parameters as well as granule properties. These forecasts were then compared with the corresponding experimental results. Good correlation has been obtained between the predicted and the experimental data. From these findings, we conclude that the GRNN may serve as a reliable method to validate the modified fluid bed apparatus.

Keywords: Generalized regression neural network; Fluid bed granulation; Innovative components; Non-linear calculation methods

1. Introduction

Current good manufacturing practices as well as validation requirements, necessitate the development of predictable and controllable wet granulation procedures having as few processing steps as possible. Fluidized bed granulation as the economical, state-of-

* Corresponding author. Tel.: +43 1 4277 55400; fax: +43 1 4277 9554.
E-mail address: helmut.viernstein@univie.ac.at (H. Viernstein).

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the-art method of granulating, offers the advantage of combining the various stages of conventional wet granulation in one process. It prevents contamination and saves processing space, time and cost. Development of other methods of fluidized bed technology enables the utilization of this technique also for coating, spheronization and layering (Funakoshi et al., 1980; Jäger and Bauer, 1982; Jones, 1988; Jozwiakowski et al., 1990; Egermann and Flögel, 1995; Achanta et al., 1997; Vertommen and Kinget, 1997; Bauer et al., 1998; Pisek et al., 2000).

The benefits of fluidized bed technology are well enough known to display the importance of innovative improvements to reduce the interference factors and to make fluidized bed processes more economic and safer. Some disadvantages have been discussed before. These include the high energy consumption, the enhanced risk of explosion due to the large amount of oxygen conveyed by the fluidizing air and the problem of air pollution by dust and solvents due to the structure of the standard fluidized bed equipments, where the fluidizing air is blown to the atmosphere. Different methods have been suggested to reduce these problems: methods of preventing explosions in fluidized bed granulators have been recommended by Külling (1977a, 1977b). In order to retain dust of highly toxic materials, a secondary high-efficiency filter has been suggested (Kristensen and Schaefer, 1987). Pollution of air by solvents can be prevented by using a specially constructed fluidized bed operating in a closed system, where the solvent is recovered by cooling (Kristensen and Schaefer, 1987). However, problems still exist: such as clogging of nozzles and outlet filters, spray loss, spray drying and fluidized bed heterogeneity especially with the use of the top spray method, which causes heterogeneous granulation with overwetting of some portions and underwetting of other portions of the feed material. The innovative components (spray system, booster bottom and outlet filter) have been developed by Innojet Technologies to reduce these interference factors. In a fluid bed granulator, the conventional nozzle, the outlet filter and the perforated base plate have been, respectively, replaced with the aforesaid novel devices. The aim of the presented study was the investigation of process and product parameters required to validate the modified apparatus.

In fluid bed granulation technology, the parameters that influence the granule properties have been classified as apparatus, process and product parameters (Kristensen and Schaefer, 1987). The process of size enlargement of particles in the fluidized bed is a complex interaction involving these parameters, which affect the final quality of the granules. Given such complex relationships, conventional data-processing methods are not suitable for investigation of the process of size enlargement. They often lead to unsatisfactory results due to non-linear relationships within the parameter set. This problem can be overcome by the use of non-linear calculation methods like artificial neural networks (Murtoniemi et al., 1994; Watano et al., 1994, 1997b).

Artificial neural networks have been formerly applied in different areas of studies (Veng-Pedersen and Modi, 1993; Klocker et al., 2002). They constitute a set of mathematical methods and algorithms designed to mime the functions (association, learning and generalization) of the human brain (Zupan and Gasteiger, 1999). From the large number of different network-learning processes, a generalized regression neural network (GRNN) has been selected for the presented study.

2. Materials and methods

2.1. Equipment

For wet granulation, (a) the "Innojet annular gap spray nozzle Rotojet type IRN 2" with 2 mm annular gap diameter, 6.28 mm developed length, 0.25 mm gap width, 1.57 mm^2 free spraying cross-section and 2.09 nl/s air consumption at 1 bar spraying pressure, (b) the "Innojet booster Opojet type ITS 140" with 140 mm diameter, four dividing gaps, 1.5 mm gap length and 80–160 m^3/h air velocity, and (c) the "Innojet filter Sepajet type 280" have been incorporated into a laboratory fluid bed granulator with a product container of 5 l feed material capacity.

The annular gap spray nozzle consists of rotating annular gaps. Each rotating annular gap liquid cross-section is both internally and externally surrounded by additional annular gap cross-sections for spraying and supporting air. The three media gap widths were defined or dimensioned at a constant ratio to each other (Fig. 1).