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Scaling-up of Multi-Capsule Depth Filtration Systems by Modelling Flow and Pressure Distribution

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Abstract

Scaling-up of filtration systems in the pharmaceutical industry to provide the correct filtration capacity is a complex process. When several filters are used in parallel, the pressure and flow distribution within the system can be modelled using well-established constitutive laws to a high degree of accuracy, as shown in this paper. By combining the model with experimental fouling data, it is also possible to accurately predict the flow and pressure distribution during an entire filtration run. A process is discussed that uses this model to determine how the capacity of a filtration system can be accurately predicted using a minimal set of measurements.

Keywords: Scale-up, Modeling, Depth filtration, filter capacity, fouling

1. Introduction

Scaling-up of filtration processes from R&D to production level in the pharmaceutical industry is a complex undertaking with strong implications on the profitability of the corresponding drug development project [1, 2]. A key challenge lies in providing the appropriate filtration capacity for production-level batch sizes based on laboratory or testing-plant scale measurements [3]. This can, for example, be achieved by using dimensional analysis to scale-up filters used in the laboratory-scale process [4] or by using several filters of standardized size in parallel [5]. When using filters in parallel, in order to accurately predict the capacity of the entire system it is crucial to understand how the different filters in the system affect each other, because the flow and pressure distribution within the system will not be homogeneous. The individual operating conditions of a given filter, such as the pressure difference across it and its resistance due to clogging, depend not only on conditions imposed from the outside but also on factors such as the filter's position within the system and the resistances of the other filters.

In order to be able to make accurate predictions about a scaled-up system, it is necessary to predict the pressure distribution within a given system of parallel filters. This becomes complicated as the filters clog at different rates during the filtration run due to the inhomogeneous pressure distribution within the system, which in turn changes the pressure distribution and vice versa.

In this paper, we derive a mathematical model for calculating the pressure distribution within a scaled-up system composed of a set of depth filters connected in parallel, termed a *multi-capsule depth filter*. The model is validated using experimental data and used to predict scale-up behaviour.

A general approach when considering filter clogging in scaling-up a device is to model the individual membrane fouling using Hermia's laws [6] as in [3, 7], which has the advantage of giving insights into the underlying fouling mechanisms. However, this can be a cause for errors if the model's predictions are not accurate or add complexity if several mechanisms have to be considered to model the fouling accurately [8, 9]. Here we describe how to combine experimental data from the clogging of a single capsule with our model to accurately predict the pressure distribution within a multi-capsule depth filter during an entire filtration run. Our method has the advantage of not requiring knowledge about the underlying clogging mechanisms since all relevant information is provided by the experimental data.

1.1. Multi-capsule depth filtration

By depth filtration we denote the filtration process where the feed flows into and not along the membrane, commonly described as a normal flow or dead-end configuration, and the filtrate is deposited within the entire depth of the filter and

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