Refereed Proceedings

The 12th International Conference on Fluidization - New Horizons in Fluidization Engineering

Engineering Conferences International *Year* 2007

Investigation of the Sources of Variability in the Wurster Coater: Analysis of Particle Cycle Times using PEPT

Sarah Palmer* Andy Ingram† Xianfeng Fan‡
Shaun Fitzpatrick** Jonathan Seville††

*University of Birmingham, sep896@bham.ac.uk
†University of Birmingham, a.ingram@bham.ac.uk
‡University of Birmingham
**Merck Sharp & Dohme Ltd.
††University of Birmingham, j.p.k.seville@bham.ac.uk

This paper is posted at ECI Digital Archives.
http://dc.engconfintl.org/fluidization_xii/52

INVESTIGATION OF THE SOURCES OF VARIABILITY IN THE WURSTER COATER: ANALYSIS OF PARTICLE CYCLE TIMES USING PEPT

Sarah Palmer[1], Andy Ingram[1], Xianfeng Fan[2], Shaun Fitzpatrick[3], Jonathan Seville[1]
[1]Department of Chemical Engineering, University of Birmingham, Birmingham, B15 2TT
[2] Positron Imaging Centre, University of Birmingham, Birmingham, B15 2TT
[3]Merck Sharp & Dohme Ltd, Hertford Road, Hoddesdon, Hertfordshire, EN11 9BU

ABSTRACT

Positron Emission Particle Tracking (PEPT) has been used successfully to study pellet motion within the Wurster coater. PEPT experiments were undertaken to understand how the parameters of batch size and partition gap interact with each other; and to determine their effects on the particle cycle time and the components of the particle cycle time: the flight and annulus times and their respective distributions. This enabled the determination of optimum operating conditions for a given set of process conditions.

INTRODUCTION

Fluidised beds with internal draft tubes – commonly known as bottom-sprayed Wurster coaters (Figure 1) – are widely used in the pharmaceutical industry to apply coatings to pellets and tablets.

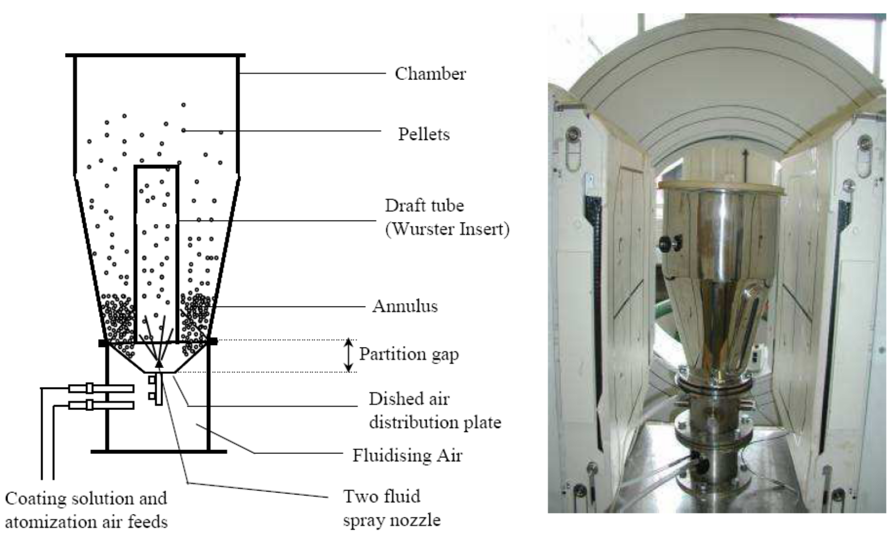

Figure 1: Schematic Diagram of the Wurster Coater (left) and Photograph of Wurster Coater in the PEPT camera (right).

The quality of the coating is of considerable importance, whatever its function, and it is desirable to minimise variation in coating thickness, both on a particle-to-particle basis and from point-to-point on each single particle. Among the principal factors which adversely affect such uniformity are (a) the variation in the particle cycle time within the device, and (b) the variation in particle entry point into the spray region (1,2), which determines the extent of exposure of the particle to the spray. It is known (3) that both factors are affected by:

- the amount of gas flow delivered to the bed and the distribution of this flow between the centre and the annulus of the bed
- the magnitude of the coating spray rate, gas flow and nozzle design
- the dimensions of the equipment, particularly the gap between the bottom of the draft tube and the gas distributor (the partition gap), through which the particles must pass prior to entering the spray region.

Analysis of the problem is complicated by interrelations between these and other variables, e.g. increasing the batch size changes the gas flow distribution between the draft tube and the annulus.

The main focus of this paper is to understand how the parameters of batch size and partition gap interact with each other and to determine their effects on the particle cycle time, the flight time, the annulus time and their respective distributions, using the technique of positron emission particle tracking (PEPT). This will enable the determination of optimum operating conditions for a given set of process conditions based on very detailed studies of pellet motion within the Wurster coater.

Particle motion is difficult to study directly because of the opaque nature of the bed (and usually the walls of the equipment). Several techniques exist to study particle motion; some of those which are well suited and capable of determining the particle cycle time and its distribution are video imaging techniques, the magnetic tracer technique, the computer automated radioactive particle tracking (CARPT) technique and the positron emission particle tracking (PEPT) technique.

A video imaging technique has been utilised with semi-cylindrical spouted beds (4) to determine particle cycle time distributions. However, the majority of measurements were restricted to the time spent in the annulus for two reasons (i) it represents most (80-95 %) of the total particle cycle time and (ii) they could not easily follow the coloured tracer particles in the spout. The disadvantages of video imaging techniques are that the walls of the equipment must be transparent, and the parameters measured near the wall are not necessarily representative of the full column.

The magnetic tracing technique has been used to measure particle cycle time and particle cycle time distribution (1,2,5). The technique consists of detection coils placed at regular intervals around the draft tube insert (2) or at the top of the insert (1,5). When the magnetically-tagged tracer particle passes upwards through the insert an electromagnetic force (emf) signal is induced within the detector coil, which is recorded and stored for post-processing. Having filtered the data, successive detected signals can be converted into a series of particle cycle times. The limitations of this technique are that (i) for smaller particles larger coils and more powerful filtering equipment are required to separate the emf signal from unwanted electronic background noise (ii) the trajectory of the particle is not determined and (iii) the technique is unable to distinguish between the flight and annulus periods of the particle cycle.

The major source of coating variation is the variation in spray coating that each individual particle receives per pass through the spray zone (1,2), however, there is very limited data relating to the residence time, the position of entry and exit and the trajectory of particles during 'flight' through the spray zone and the draft tube. In the present study, the motion of a single pellet of microcrystalline cellulose (MCC) is followed, within a bed of identical particles, using the technique of PEPT. The considerable advantages of this technique over the others discussed are: (i) it enables the non-invasive 3D observation of a single particle within dense particulate systems, and (ii) it is capable of tracking the precise locations of the pellet within the entire boundaries of the Wurster coater. For example, at a speed of 1 m/s it is possible to locate the particle with a precision of about ± 1mm and at a location frequency of about 100 times/s.

EXPERIMENTAL

Equipment & Materials

The Wurster Coater used in this work consists of a lower conical chamber (the diameter of the base is 115 mm) with an upper cylindrical expansion chamber (diameter 250 mm), which has an overall height of 376 mm. The inner draft tube (Wurster insert) is 249 mm in length, 50 mm in diameter and may be positioned *x* mm from the distributor.

The MCC pellets utilised in this study were supplied by NP Pharm S.A.S, France, and have the trade name of Ethispheres 850. The physical properties are: a particle diameter size range of 710-1000 μm, a particle density of 1600 kgm^{-3} and a minimum fluidisation velocity of 0.33 ms^{-1}.

The Positron Emission Particle Tracking (PEPT) Technique

The tracer particle used for PEPT is identical with other particles in all its physical properties, but it is labelled with a positron emitting radioisotope. In this study, the tracer particle is created by irradiating water within a cyclotron, which produces the positron emitting radionuclide ^{18}F. The radioactive water is then adsorbed onto the MCC pellet surface.

The radioactive tracer undergoes radioactive decay (β^+ decay), whereby the nucleus, rich in protons, converts a proton into a neutron, a positron and a neutrino. Each emitted positron annihilates with a local electron, leading to the production of two collinear, back-to-back gamma rays. The gamma rays are detected simultaneously (i.e. within 7.5 ns) by two parallel detectors and used to reconstruct the position of the tracer by triangulation. However, in practice many detected events are corrupt, for example because one of the detected gamma rays has been scattered. In practice, 50-100 sets of lines are used to find the location, using an algorithm which successively removes the outliers.

The 12th International Conference on Fluidization - New Horizons in Fluidization Engineering, Art. 52 [2007]

The raw data obtained from the PEPT technique consist of tracer particle x, y and z co-ordinates as a function of time. Upon processing this data, it is possible to determine relevant information concerning particle trajectories, particle velocity profiles, cycle time distributions within specific zones and the frequency at which particles enter different zones.

Experimental Design

All experiments were undertaken without coating spray solution and at a fluidising air flow rate of 14.2 m^3h^{-1}, which is equivalent to a superficial gas velocity of 0.38 ms^{-1} at the base of the chamber. In order to ensure statistical reliability of the data as well as to make certain the Wurster coater had reached steady operation, each PEPT experiment was conducted for approximately 60-90 minutes. Within this time period an average of 120 particle cycles was achieved per experiment.

Experimental PEPT Data Analysis

As illustrated in Figure 2, the particle cycle time consists of two components; the flight time and the annulus time (time spent in the annulus). During the flight period, it was observed that the pellet often re-circulates within the draft tube. This behaviour is undesirable because it is likely to increase the variation in coating thickness. A Fortran code was developed to identify the duration of the flight, annulus, and therefore, particle cycle periods as well as to quantify the number of re-circulations within the draft tube per particle cycle. Knowing the geometry of the equipment (the height and radius of the draft tube) and the magnitude of the velocities within the annulus it was possible to distinguish between the flight and annulus periods of the complete particle cycle.

The annulus period is identified when the magnitude of the vertical particle velocity is below a certain threshold (typically 0.5 ms^{-1}), which is characteristic of the operating conditions, and the radial position of the tracer is greater than the radius of the draft tube. The start of the flight period is identified when the vertical particle velocity is higher than the specified threshold and the radial position of the tracer is less than that of the draft tube. The end of the flight period is identified once the vertical y-position of the tracer is greater than the height of the draft tube and the tracer has returned to the annular bed (i.e. the start of the 'annulus period'). During the flight period, the number of re-circulations within the draft tube is quantified by calculating the sum of the number of times the tracer passes a vertical 'y-jump'-threshold, which is approximately 40% of the height of the draft tube, before leaving the draft tube.

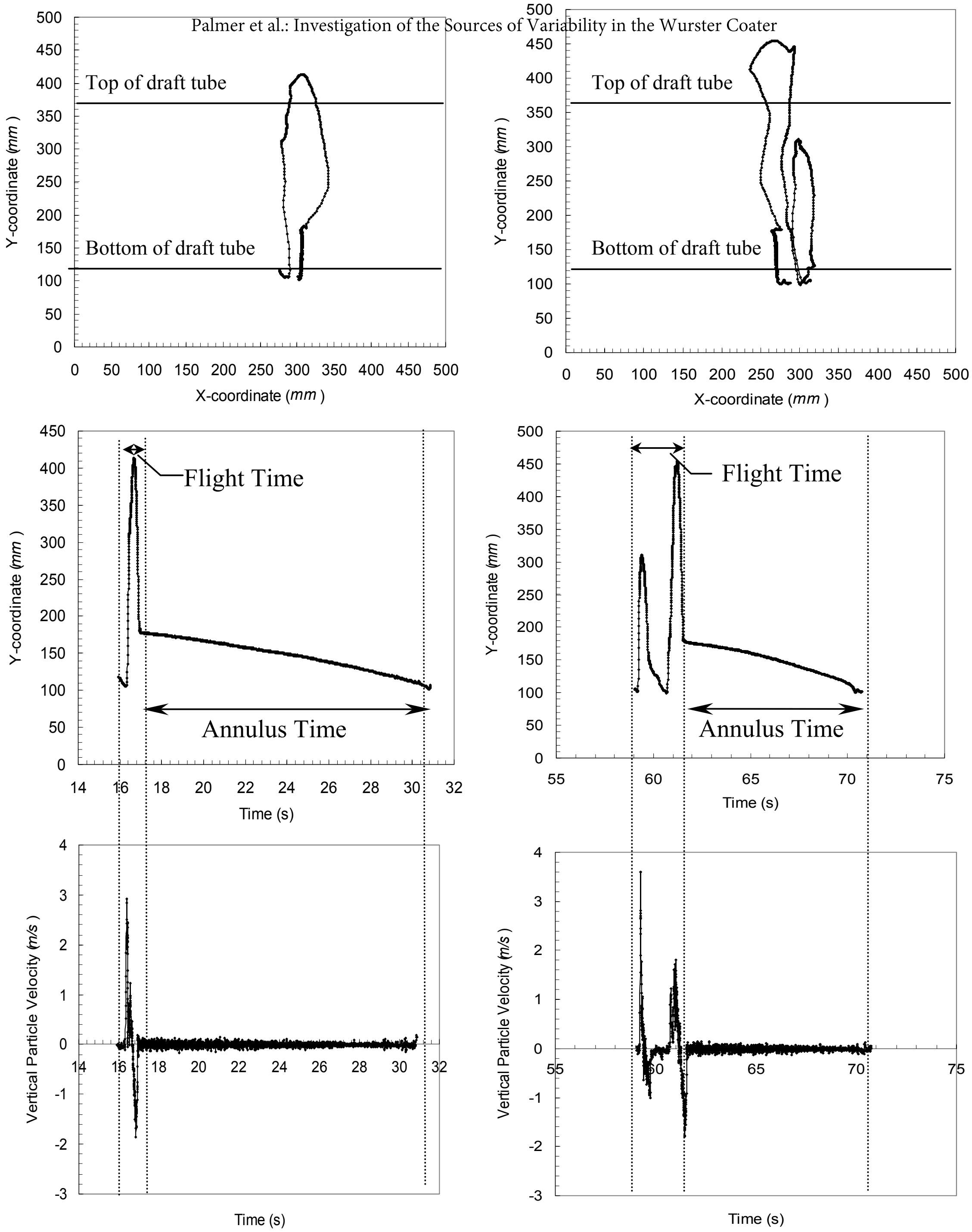

Figure 2: Left column: One complete particle cycle *without* recirculation within draft tube: trajectory, y-coordinate vs time, vertical particle velocity vs time. Right column: One complete particle cycle *with one* recirculation within draft tube: trajectory, y-coordinate vs time, vertical particle velocity vs time.

RESULTS AND DISCUSSION

The 12th International Conference on Fluidization - New Horizons in Fluidization Engineering, Art. 52 [2007]

Table 1. The effect of batch size and partition gap on particle cycle time, flight time and annulus time determined from PEPT experiments.

Batch Size (g)	Partition Gap (mm)	Particle Cycle Time (s)		Flight Time (s)		Annulus Time (s)		% Flight / Particle Cycle Time Ratio
		Mean	% RSD	Mean	% RSD	Mean	% RSD	
400	8	34.5	68.5	8.1	105.4	26.4	87.7	23.5
400	10	26.2	154.2	5.00	93.3	21.2	190.3	19.1
400	15	66.2	72.6	13.7	101.0	52.5	87.8	20.7
600	5	107.0	98.7	19.5	77.0	87.5	116.5	18.2
600	8	70.2	93.9	16.8	110.8	53.5	121.2	23.9
600	10	26.0	77.4	4.2	125.0	21.8	92.4	16.2
600	15	25.5	94.4	4.3	108.7	21.2	112.4	16.9
600	20	59.5	105.1	14.2	175.0	45.3	124.1	23.9
800	8	22.9	85.9	3.0	138.3	19.9	96.7	13.1
800	10	31.6	62.3	5.8	127.8	25.8	66.8	18.4
800	15	34.7	58.2	4.9	120.0	29.7	64.2	14.1
800	20	43.7	83.2	6.3	126.7	37.5	95.0	14.4

Effect of Partition Gap

The results shown in Table 1 demonstrate that the lowest mean particle cycle, flight and annulus times were achieved at a partition gap of 10 mm for the batch sizes of 400 g and 600 g. However, for a batch size of 400 g the percentage relative standard deviation (% RSD) in the particle cycle time is highest at a partition gap of 10 mm, whereas for 600 g it is the lowest. By analysing the components of the particle cycle time it is possible to identify the major source of variation. With reference to the %RSD for the annulus time, it is clear that the behaviour of the pellets within the annulus, rather than the draft tube, is the major source of variation in the overall particle cycle for a batch size of 400 g and a partition gap of 10 mm. This is not the case for a batch size of 600 g, since, for the range studied, the lowest %RSD for the annulus time is achieved at a partition gap of 10 mm. For the batch sizes of 400 g and 600 g, Figures 3a and 3b demonstrates that 40-50% of the particle cycles are completed with zero re-circulations within the draft tube respectively. This is significantly higher than that for the partition gaps of 8 mm and 15 mm for 400 g and the partition gaps of 5 mm, 8 mm and 20 mm for 600 g.

The particle resides within the annulus for longer for the partition gaps below 10 mm, because the reduced size of the gap restricts flow. This may in turn affect the way in which the pellets are delivered to the nozzle, which causes the increased recirculation within the draft tube, thus the duration of the flight period is longer. Figures 3a and 3b demonstrates that the percentage number of particle cycles with zero re-circulations within the draft tube is below 25% for the batch sizes of 400 g and 600 g at partition gaps below 10 mm. This behaviour would be detrimental in terms of minimizing the variation in coating thickness.

At a partition gap of 15 mm, the durations of the flight and annulus periods are the longest for a batch size of 400 g. At a partition gap of 20 mm, the mean flight and annulus time is longer than that for a partition gap of 10-15 mm for a batch size of 600 g (Table 1). One possible explanation is that with increasing partition gap sizes air increasingly by-passes from the draft tube towards the annulus. The increased air throughput towards the annulus may act to oppose the flow of particles through the partition gap and possibly cause 'over-fluidization' of the annular bed, thus the particle resides within the annulus for longer. The decreased air throughput through the draft tube leads to increased pellet recirculation within the draft tube, as shown in Figure 3a, hence longer flight periods.

Effect of Batch Size

With increasing batch size there is an increase in pressure drop across the annular bed. As a consequence, air is increasingly directed towards the draft tube. At large batch sizes (800 g), Table 1 shows that the mean particle cycle time increases with partition gap at a batch size of 800 g. This trend is significantly different to those found for the lower batch sizes of 400 g and 600 g. This may be due to the fact that at large batch sizes the distribution of air towards the draft tube is more dominant than for smaller batch sizes.

As explained previously, increasing the partition gap has a dual effect (even with increased batch sizes):

- An increase in airflow towards the annulus which opposes particle flow through the gap and therefore longer residence times within the annulus; and
- A reduction of air flow in the draft tube causing increased internal circulation and therefore longer residence times within the draft tube.

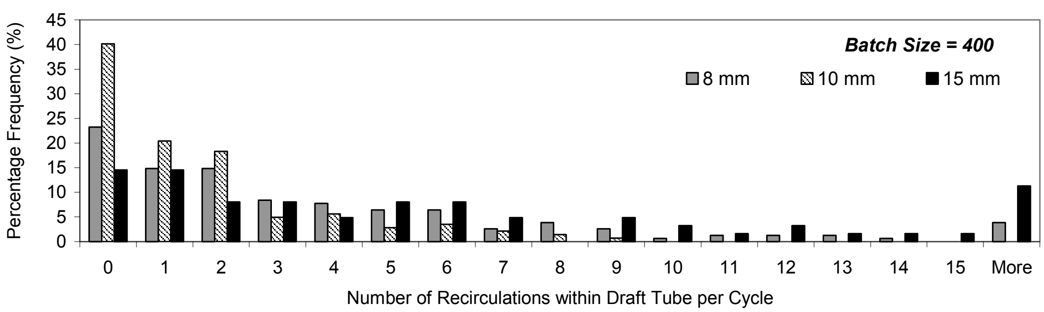

Figure 3a: Effect of partition gap on the distribution of re-circulations within the draft tube at 400g

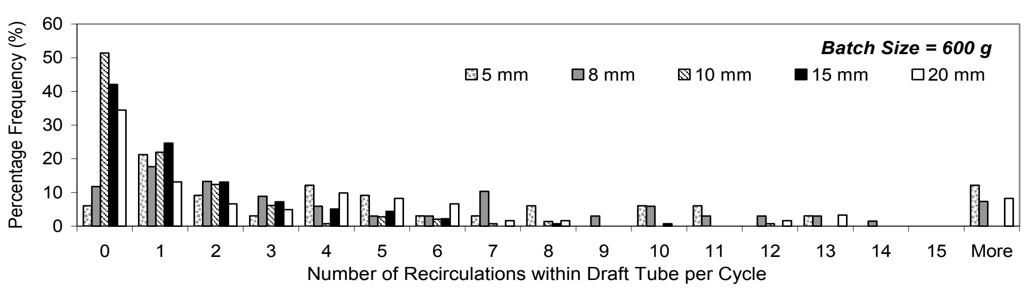

Figure 3b: Effect of partition gap on the distribution of re-circulations within the draft tube at 600g

The 12th International Conference on Fluidization - New Horizons in Fluidization Engineering, Art. 52 [2007]

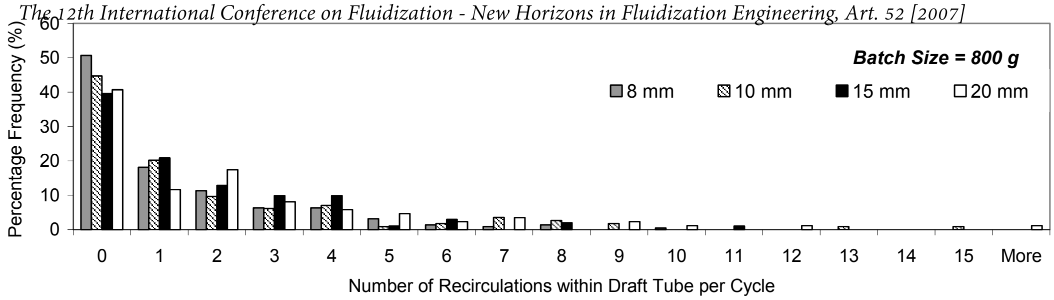

Figure 3c: Effect of partition gap on the distribution of re-circulations within the draft tube at 800g

CONCLUSIONS

The results show that there is a complex relationship between partition gap and batch size, which affects particle motion and therefore the variation in pellet coating thickness. At low batch sizes, optimum operating conditions in terms of minimal re-circulation within the draft tube were achieved at a partition gap of 10 mm, but wide particle cycle time distributions existed. At medium and large batch sizes, optimum operating conditions with respect to minimal re-circulation within the draft tube and narrow particle cycle time distributions were achieved at a partition gap of 10-15 mm. To overcome the issue of re-circulation within the draft tube, independent air supplies to the annulus and central region beneath the draft tube may minimize this effect; work is underway to investigate this further.

REFERENCES

1. Cheng, X. X. and Turton, R. (2000) *Pharm. Dev. Technol.* **5,** 311-322
2. Shelukar, S., Ho, J., Zega, J., Roland, E., Yeh, N., Quiram, D., Nole, A., Katdare, A., and Reynolds, S. (2000) *Powder Technol.* **110,** 29-36
3. Christensen, F. N. and Bertelsen, P. (1997) *Drug Dev. Ind. Pharm.* **23,** 451-463
4. Robinson, T. and Waldie, B. (1978) *Can. J. Chem. Eng.* **56,** 632-635
5. Mann, U. and Crosby, E. J. (1975) *Can. J. Chem. Eng.* **53,** 579-581