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Monaco, D., Omar, C., Reynolds, G.K. et al. (3 more authors) (2021) Drying in a continuous wet granulation line: Investigation of different end of drying control methods. *Powder Technology*, 392. pp. 157-166. ISSN 0032-5910

<https://doi.org/10.1016/j.powtec.2021.07.004>

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1 the drying, and was compared to the available fixed drying time and temperature controlled end of
2 drying methods. The method was successful in targeting a specific moisture content and could be
3 used to locate the optimal drying temperature for a target moisture content in the future. The moisture
4 content during the filling of the dryer was also recorded and provided further insight into the drying
5 behaviour of the granules in the segmented dryer; this characteristic behaviour could later be used to
6 detect problems during the filling time. The drying rate was also calculated making it possible to
7 predict the optimal drying time at different operating conditions in the granulator and to assess the
8 impact on drying of the different liquid to solid ratio used.

9 **KEYWORDS**

10 Continuous manufacturing, drying, fluidised bed, Consigma-25.

11 **1. INTRODUCTION**

12 In the past few years the pharmaceutical industry has been moving from batch to continuous
13 manufacturing, this change has been pushed by the increase in competition, decrease in profit margin
14 and by the push of various regulatory bodies such as the Food and Drug Administration (FDA) on
15 quality by design and continuous manufacturing [1]. Continuous manufacturing has several
16 advantages such as faster product development, lower waste production, higher energy efficiency,
17 smaller production facilities and the ability to control the product quality during the process [2].
18 Continuous manufacturing has also presented both formulation scientists and equipment designing
19 companies with new challenges. One of the problems encountered was the design of a process able
20 to continuously dry granules produced using wet granulation techniques [3].

21 Wet granulation is a size enlargement technique that turns small particle powder into bigger
22 agglomerates called granules. It utilises liquid binder and is commonly used in the pharmaceutical
23 industry especially for products with particularly high or low percentages of active pharmaceutical

1 ingredients, or particularly poor flowing materials [4]. A common wet granulation process execution
2 uses a twin screw granulator to produce granules [5], the wet granules need to be dried to remove the
3 moisture and form granules acceptable for further processing.

4 The dryer has the biggest impact on the residence time of the material along the line taking up to
5 an order of magnitude more time than any other operations. It is also one of the highest energy draw
6 unit operations, as it requires multiple fans and heating elements to operate. For these reasons, it is
7 important to understand the drying behaviour in this particular fluidised bed to be able to optimise
8 the time required for drying, not only to have a smaller residence time but also to optimise the power
9 efficiency of the fluidised bed. The understanding of the behaviour of this fluidised bed could also
10 lead to a simple model that could be used in a control system to obtain dry granules up to specification
11 even when fluctuations are detected.

12 A few studies on the segmented fluidised bed present in the Consigma-25 line have been published,
13 showing similar drying performances between the different fluidised bed cells and over time during
14 continuous runs [6,7]. An earlier study focused on the use of NIR techniques to detect final moisture
15 content and the effect of different drying condition on the final moisture[8]. Two studies focused on
16 developing mass balances around the segmented dryer in order to better understand and control the
17 drying process in the dryer [9,10], while a more recent study further developed the model in order to
18 predict the final moisture content[11]. Another recent study focused on the granule breakage
19 phenomena during the drying, reporting a noticeable effect mostly due to the pneumatic transport
20 lines utilised [12]. Work on a different twin screw-fluidised bed dryer combination consisting of a
21 ThermoFisher twin screw and a continuous Glatt fluidised bed dryer has also been published; the
22 differences in the dryer design provide insight on different strategies that can be adopted in order to
23 monitor and control the drying process in a continuous line [13–15]. While most of these studies

1 focus on adjustment of process parameters in the dryer, some work includes the effect of granule size
2 on the drying endpoint [3].

3 In this study, the temperature profiles of the granules produced at different liquid to solid ratios in
4 each cell are analysed. The liquid to solid ratio (L/S) and therefore the amount of liquid binder was
5 selected as the variable as it is one of the main parameters affecting both the quality of the granules
6 produced in a twin screw granulator [16] and the drying load. The two different control methods
7 available to control the length of the drying in the line are also tested to have a full comparison of the
8 methods available and how they deal with the different L/S. The first method utilises a fixed drying
9 time set as a parameter while the other control method uses a target temperature to define the end of
10 the drying process. An online NIR probe is also employed to measure the residual moisture content
11 in the granule throughout the drying cycle. The average drying rate at different condition is also
12 calculated and used to compare the drying between the different liquid to solid ratios.

13 **2. MATERIALS**

14 Microcrystalline cellulose (Chemical PH 101, Field Group, Nagpur, India, $d_{50}=50\mu\text{m}$) and α -
15 lactose monohydrate (Pharmatose 200M, DMV-Fonterra Excipient GmbH and Co., Goch, Germany,
16 $d_{50}=55\mu\text{m}$) were used as raw materials. For granulation, a 1:1 blend of MCC and lactose was blended
17 using a helical ribbon blender, and water was used as liquid binder. The initial moisture content of
18 the powder before granulation was recorded to be 2.4%. The blend was processed in a Consigna-25
19 line varying the L/S ratio in the twin screw granulator in order to observe the drying behaviour in the
20 segmented fluidised bed dryer of granules with different water contents.

21 **3. METHOD**

22 **3.1 Experimental**

1 A Consigma-25 (GEA Pharma Systems, Collette™, Wommelgem, Belgium) was used in these
2 experiments. The continuous powder to tablet line Consigma-25 (GEA Pharma Systems, Collette™,
3 Wommelgem, Belgium), used in this study has a twin screw granulator necessitating the utilisation
4 of a dryer.

5 The twin screw granulator was run at a constant speed of 500 rpm with a constant barrel
6 temperature of 25°C. The L/S was varied from 0.25 to 0.475. Three samples were taken for every
7 condition. In Figure 1a the granule size distribution is shown for the three L/S utilised in the drying
8 experiments where p3 indicates the % for size class based on the volume of the granules. The granules
9 produced at lowest L/S are mostly monomodal while the one produced at higher L/S showed a more
10 prominent second peak at around 1350 µm with the highest L/S having a more pronounced second
11 peak. The amount of fines (<200 µm) (L/S 0.25= 24.2%, L/S 0.35= 26.1% and L/S 0.475= 22.1%)
12 and coarse fractions (1200-1600 µm) (L/S 0.25= 9.0%, L/S 0.35= 13.1% and L/S 0.475= 19.5%) were
13 used to quantify this behaviour showing similar amount of fines between conditions, especially at
14 0.25 and 0.35 L/S with a more pronounced difference in the percentage of bigger granules. Figure 1b
15 shows the granule size distribution based on the surface area of the granules, this distribution leans
16 strongly towards the fines as smaller particles contribute more towards the total area. Although no
17 assay was conducted in this study, literature shows [17] that bigger granules tend to contain a higher
18 percentage of binder. This inhomogeneity coupled with the fact that the majority of the surface area
19 available for drying is present in the smaller size classes can lead to uneven drying of the material in
20 the granules which can affect the drying behaviour. Although this is important to fully understand the
21 drying behaviour of the different granules in the dryer was not part of the study, which focuses on the
22 average moisture content after drying. The granule size distribution was obtained using a Camsizer
23 (Retsch Technology GmbH, Haan, Germany).

1 Using a μ CT 35 (Scanco Medical AG, Switzerland) X-ray scans of dried granules produced at
2 different L/S ratio are shown in Figure 2. The granules chosen were part of the coarse fraction, and
3 therefore might not represent the porosity present at smaller size classes. Granules from the coarse
4 fraction were chosen due to the higher percentage of moisture usually present in this fraction leading
5 it to have a greater effect on the overall drying. At a close inspection, the granules produced at the
6 low and mid L/S were similar while those produced at higher L/S appeared more compacted. The
7 overall porosity of the granules, calculated using the x ray images, were 60% at L/S 0.25, 57% at L/S
8 0.35, and 51% at L/S 0.475, this porosity includes the large void present in some granules[18]. Local
9 porosities for the granules were also determined by calculating the porosities for smaller areas of the
10 granules which didn't contain large voids, the local porosities obtained were 56% at L/S 0.25, 55%
11 at L/S 0.35, and 44% at L/S 0.475. These numbers confirm the initial visual inspection of the x-ray
12 images. As X-ray scans do not provide a direct measurement of porosity this was calculated via image
13 analysis using ImageJ [19] using the following methodology . An empty part of the scan was used to
14 obtain a threshold black value for empty space, the ratio of the pixels with values under the threshold
15 over the total pixel of the granule area was then considered to be the porosity.

16 The segmented fluidised bed dryer is divided in 6 cells as shown in Figure 3, each segment is
17 referred to as a cell. Wet granules from the granulator are directed to a cell via a valve positioned at
18 the top of the fluidised bed and the cell is then filled for a finite filling time. When the filling time for
19 one cell has been reached the valve turns and the next cell is loaded. After the granules have been in
20 a cell for a specified drying time (which includes the filling time) or when they reach a target
21 temperature the cell is unloaded via a rotary valve at the bottom of the fluidised bed dryer connected
22 to a pneumatic conveying system. The process can continue indefinitely as the cells are loaded and
23 unloaded sequentially. Each cell of the fluidised bed dryer is equipped with a temperature probe
24 situated just above the air distribution plate in the centre of each cell. Given its location the probe will
25 measure a combination of the air and product temperature depending on its coverage.

1 Granulation and drying condition were kept constant as shown in Table 1 while the liquid to solid
2 ratio was varied. The variation of L/S at a constant powder feed rate means only the amount of liquid
3 binder, in this case water, was altered during the experiment. To analyse the drying behaviour of the
4 granules the temperature readings of each cell were taken. The temperatures were automatically
5 recorded every 2 seconds. The L/S used were 0.25, 0.35 and 0.475. For each L/S the line was run
6 continuously for 6 cells. To ensure steady state operation one cell before and one cell after were also
7 run but not considered in the data analysis. For the experiments utilising the set temperature to
8 discharge, the cell target temperature was set to 47°C, while for the experiment using constant drying
9 time the time was set to a constant 840s. The final moisture content for each cell was automatically
10 measured by Near Infra-Red (NIR) moisture content probe (FP710e, NDC Technology, Dayton,
11 Ohio, USA) located after the discharge of the granules and before the milling process at the end of
12 the drying. The probe was calibrated using LOD measurement (M35, Sartorius GA, Germany). Eight
13 samples with moisture content varying from 0 to 35% were used to produce the calibration curve.
14 The LOD measurement used 3g of sample and was run at 100°C with automatic end point detection.
15 Each measurement was repeated 5 times. The probe integration rate was set at its standard value of
16 1s and data was collected every 2 seconds.

17 For the experiments involving the continuous online measurement of moisture content the NIR
18 probe was fitted to the measurement port located at cell number 5. All experiments were run starting
19 the granulator at cell 4 to avoid any noise from the start-up process. The drying times were altered
20 based on the L/S in order to capture the full drying curve. The twin screw was paused after the filling
21 of cell 6 was complete in order to minimise material requirement. Although this is different from
22 usual continuous operation, it was deemed acceptable as a similar single cell approach showed good
23 correlation with continuous runs in literature [20]. As the experiments were repeated back to back it
24 is important to note that the temperature of the cells in the dryer, when empty, remained stable over
25 the course of the experiment.

1 **4. RESULTS AND DISCUSSION**

2 **4.1 Drying behaviour**

3 The mass of dry material in each cell was kept constant at 0.5 kg for all the experiments while the
4 mass of water present in each cell varied based on the selected liquid to solid ratio (Wet mass L/S
5 0.25: 625g, L/S 0.35: 675g, L/S 0.475: 732.5g). Figure 4 shows that when the temperature behaviour
6 is plotted for the three conditions, the temperature behaves similarly throughout the range of
7 conditions. Although only the temperature of one cell per condition is shown, the behaviour was
8 consistent between the 6 cells. In all cases a sharp decrease in temperature is detected when the cell
9 starts filling with granules, with the decrease in temperature being slightly less steep when less liquid
10 is present. After the cell is loaded with granules, the temperature remains constant for a period of
11 time. The length of this period is related to the L/S, with higher L/S ratio corresponding to a longer
12 temperature plateau. This represents the constant rate drying period. The temperature remains
13 relatively constant near the wet bulb equilibrium temperature until all surface moisture is evaporated.
14 This process takes longer for the higher L/S runs as there is more water to evaporate. After most of
15 the surface water is evaporated the temperature starts to rise. For experiments using a temperature
16 end point for drying, the cell discharge was triggered when the temperature reached 47°C.

17 The small downward spike found at the end of the drying process is due to the activation of the
18 filter cleaning system which pushes air through the filter to clean it. The final moisture content for
19 each cell when using the constant drying time of 840s was measured giving readings between 1.4%
20 to 3% with the probe located before the milling process. This wide range indicates that this method
21 is not capable of producing consistent final moisture content when such a change in L/S is present
22 and so it would have to be optimised for each L/S, especially if the target moisture is different to
23 equilibrium.

24 **4.2 NIR online measurements**

1 In order to further characterise the drying behaviour in the segmented fluidised bed dryer, online
2 moisture content measurements were taken with an FP710e moisture content probe fitted in the probe
3 port located at cell 5 of the fluidised bed. This probe measures both the moisture content of solids and
4 the amount of material around the probe utilising the total amount of light reflected, which is referred
5 to as product presence. The moisture content reading against the temperature is shown in Figure 4.
6 The experiments were performed at different L/S to assess the impact on the moisture content reading
7 and the drying behaviour. In this case the drying time were varied in order to fully obtain the drying
8 curve of the granules.

9 The filling time is characteristic for this type of dryer and differs from typical batch dryers as granules
10 are simultaneously loaded in the cells while also drying. Due to this behaviour during the filling time,
11 the overall moisture content increases as the rate of addition of moisture outweighs the drying rate.

12 At the beginning of the cell filling the moisture content is observed to spike and drop before rising
13 again. This was due to initial material entering the fluidised bed getting detected by the probe but
14 then fluidised away making the probe incapable of providing a consistent reading. This was confirmed
15 by the product presence reading available with the FP710e, which gives an indication of the amount
16 of material near the probe capable of reflecting the NIR light. Figure 4 and Figure 5 show respectively
17 that the moisture content reading and the product presence value drop at the same time confirming
18 the previous hypothesis. This also highlights the fact that during the filling time, the conditions of the
19 granule bed are constantly evolving and therefore extra care should be taken to avoid excessive
20 elutriation or potential blockage of the distributing plate caused by overwettted granules as this can
21 impact the final product qualities or lead to equipment malfunction.

22 After the filling time was completed (highlighted with a vertical solid line), the moisture content
23 decreased as expected at a fairly constant rate until the critical moisture content was reached, where

1 the drying rate drastically reduced. In this case the moisture content never dipped below 1.4% and
2 remained constant at the end of the drying indicating being close to equilibrium.

3 The product presence also decreased over time after the filling was completed with a larger impact
4 shown in the lower L/S; this is likely due to the larger proportions of fines present at the lower L/S,
5 which get pushed towards the top of the bed and away from the probe. In addition to this, over the
6 course of the drying process, granule density decreases as water is evaporated which causes more
7 granules to float higher towards the filter, away from the probe range. This behaviour was confirmed
8 via observation of the fluidising behaviour during the drying process through the glass window on
9 the side of the cell. In Figure 6, where the pressure drop over the top filters is shown, it is possible to
10 see how the pressure drop increases over the drying time while the product presence decreases due to
11 the build-up of material on the filters.

12 An experiment was also performed, where the fluidised bed cell was filled for 360 s instead of 180 s
13 at a L/S of 0.35 in order to achieve a higher amount of material in the cell and ensuring probe coverage
14 throughout the drying process. The result of this is shown in Figure 7. This shows how the product
15 presence graphs were nearly identical in the first 180 seconds as expected but the product presence
16 then stabilised when more material was added, remaining constant throughout the drying time. This
17 again highlight the importance of the filling process in producing a stable bed and should be
18 investigated in further research.

19 The spikes present at the end of the drying in Figure 5 and Figure 6 are caused by the activation of
20 the filter cleaning system (blowback) which pushes air through the filter while the cell is emptying.
21 This ensures that the all the material that was in the cell leaves. The use of blowback also keeps the
22 filters clean for longer periods which is shown by the reduced drop in pressure over the filters after
23 its activation. The spike of material and the reduction in product presence which can be observed
24 during the drying process is due to the elutriation of the fines from the granules. Although this was

1 not the focus of the study, this behaviour might affect the drying and should be taken in consideration
2 especially in the context of manufacturing where it could lead to problems in material tracking. Also,
3 the pressure drop over the filters of the dryers can be used to monitor the extent of material remaining
4 on the filter. Overall, the product presence reading tends to be particularly noisy because of the
5 turbulent environment present near the probe.

6 The drying time was considered to be completed when the residual moisture content detected was
7 below 2% as this would be lower than the residual moisture content recorded for the blend before
8 granulation, which was recorded by positioning the probe in the material before granulation.

9 **4.3 Optimal drying time estimation**

10 One of the objectives of the study was to optimise the drying efficiency of the process. The use of
11 the derivative of the cell temperature over time was investigated as an indicator of drying efficiency.
12 Figure 8 shows the derivative over the drying cycle; the first negative variation is caused by the
13 beginning of the filling process which causes a steep drop in the cell temperature which then
14 stabilises. After around 400s the temperature starts to increase as the surface moisture is mostly
15 evaporated and the drying transitions to the falling drying rate period. The derivative peaks at around
16 580s, after that the change in temperature slows down as it approaches the drying air inlet temperature.
17 The time between the two peaks was considered an optimal drying time in this study. NIR moisture
18 data was collected for 6 drying runs at each L/S at the peak derivative time (Table 2). The overall
19 moisture content average obtained via this method was $2.4\pm 0.2\%$. At longer times than detected the
20 drying is less efficient as shown in Figure 4, although more time is required to reach the 2.0% moisture
21 target. To improve the method further, a study focusing on the correlation of the derivative peak and
22 the process variables, e.g. dryer inlet temperature is needed.

23 The optimal drying times for each cell were averaged and plotted against the L/S (Figure 9). The
24 data shown in Table 2 suggest that the differences in the reported temperatures in the different cells

1 have little effect on the method performance. This suggest the derivative method is a robust approach
2 for control and optimization of dryer. In addition, the linear trend found between L/S and drying time
3 can be used to predict optimal drying time as a function of L/S when the other parameters are kept
4 constant.

5 **4.4 Average drying rate**

6 To be able to calculate the optimal drying time for different conditions such as higher throughput
7 or higher filling time of the cells which might be required by the process and to assess if the
8 differences in L/S affected the drying, an average drying factor was utilised. This was calculated from
9 the mass of water evaporated and the optimal time. The mass of evaporated water was obtained by
10 subtracting the residual mass of water in the granules, derived from the moisture content reading,
11 from the mass of water added to the process during granulation. The amount of water evaporated was
12 then divided utilising the time obtained via the derivative method. As shown in Table 2, the rate of
13 drying remained the same at L/S of 0.25 and 0.35 and was slightly lower at 0.475. Further studies
14 focusing on the effect of the particle size and the liquid distribution across the granule size is required
15 to fully understand the effect of the larger granules and lower porosity [21] at the higher L/S.

16 **4.5 Target temperature discharge**

17 In this set of experiments, the fluidised bed was set to unload a cell when it reached a specific
18 temperature. The temperature selected was 47°C. This temperature was selected based on the previous
19 experiments where the profile plateaued above this based on the 60°C air temperature used in the
20 study. This temperature is strongly related to the drying conditions, especially the drying temperature,
21 and therefore the collection of new drying curves would be required if the conditions were varied.

22 The moisture content readings obtained when utilising this method were consistent (L/S 0.25=
23 1.9±0.1%, L/S 0.35= 1.9±0.2% and L/S 0.475= 1.8±0.1% and an average overall of 1.9±0.1%, with

1 ± indicating the 95% confidence interval) indicating that this method can be successfully employed
2 to dry granules produced with varying amount of liquid to obtain a target moisture content without
3 the need for trial and error when drying conditions, especially temperature, are kept the same.

4 The previously discussed derivative method to detect the optimal drying time and the time to reach
5 2% residual moisture in the NIR experiment are also shown in Figure 9. The lines are nearly parallel
6 with the difference in offset caused by the different final moisture content that the different methods
7 target with longer times leading to lower moisture contents. Both the NIR and derivative method
8 drying time showed an average variability of less than 2.5% across the different L/S tested while the
9 temperature method showed a higher average variability at 8.2%. This is most likely because each
10 cell temperature reading at steady state was slightly different and needs to be considered if the
11 residence time across the line requires consistency. The bigger time variability did not translate to a
12 higher final moisture content variability. The lower final moisture content achieved by the
13 temperature method might contribute to smaller variability in the measurement as it is closer to the
14 equilibrium moisture content.

15 The difference in final moisture content value between methods shows that although the derivative
16 method can be used to detect an efficient end of drying it does not detect the point of equilibrium as
17 further drying can be achieved.

18 **4.7 Methods comparison**

19 The two methods to select the discharge time in the fluidised bed of the Consigma-25 line have
20 both advantages and disadvantages. Setting a constant drying time ensures that the process performs
21 at a constant residence time. It is also a robust system which does not rely on any sensor that could
22 deviate during the process. The lack of sensor utilisation is also the main downfall of this method as
23 it is not able to react to disturbances such as environmental changes or upstream deviation from the

1 set point, requiring the drying time to be optimised every time a parameter that influences the drying
2 is changed.

3 Conversely, operating the dryer using the end temperature setting, managed to obtain consistent
4 drying of the granules at different L/S, making it a versatile option capable of responding to
5 fluctuations. This stability might also be partly due to the temperature that was selected driving the
6 granules very close to the equilibrium point, so careful attention should be taken to consistency if
7 aiming for a higher moisture content at a lower target temperature, especially if the temperature
8 recorded differs between cells. In the case of a change in the drying air temperature the ideal target
9 temperature for the process will have to be located again via trial and error or via recording a new
10 drying curve using NIR moisture reading, this also applies to the derivative method as it will point at
11 a different moisture content.

12 The method using the derivative of the temperature and detecting the minima and maxima devised
13 in this paper is an attempt to create a method which reduces trial and error to obtain the optimal drying
14 time. This approach can be used to identify when the drying rate drops considerably and was able to
15 target a consistent moisture content. If a different moisture content was required for the final product,
16 the method could be used to identify the optimal inlet air temperature where the derivative would
17 peak at the moisture content required. The applicability of the method at different working conditions
18 and with different materials is outside the scope of the study but will be part of future investigations
19 to further refine and test the application limits of the method. As the derivative can be calculated in
20 real time a control system sensing the second peak could be also put in place to detect the end of the
21 drying and initiate the unloading of the cell automatically.

22 Continuously recording the moisture content of the granules with a NIR probe was also confirmed
23 to be possible, giving a direct reading of the moisture content in real time. This method also has
24 disadvantages, as shown in Figure 4 and Figure 5 where insufficient material present in the vicinity

1 of the probe can lead to unrepresentative readings. Other concerns are both location and cost. In the
2 current configuration only cell number 2 and 5 can be equipped with extra probes and these would
3 need additional investment as they are not fitted to the equipment as standard.

4 **5. CONCLUSIONS**

5 The drying behaviour of the granules was observed via the inbuilt temperature sensor and moisture
6 content probe. The drying time appears to correlate linearly with the amount of water present in each
7 cell. The effect of particle size was not a focus of this study and seems to have an effect on the drying
8 rate at the highest L/S and should be investigated further.

9 The behaviour of the moisture content during the filling time was captured providing further
10 insight in the drying operation of the fluidised bed dryer while it is filled continuously. The
11 characteristic behaviour of the moisture content stabilising during the filling time could provide
12 further information particularly on the efficiency of the drying. For example, a reduced drying
13 capacity due to clogging or bad fluidisation should result in a higher moisture content during the
14 filling phase. Being able to detect this issue quickly presents the possibility of controlling parameters
15 both in the dryer or twin screw granulator to minimise the impact on the final moisture content and
16 also to monitor correct operation of the dryer. The importance of sufficient coverage of the NIR probe
17 was also shown, which is particularly important at the beginning of the filling time.

18 The alternate end of drying detection method showed similar trends in drying time. The target
19 temperature method produced granules with consistent final moisture content although the method is
20 dependent on determining a suitable selection based on experimental trials. The model devised in this
21 study utilising the derivative of temperature also managed to obtain consistent moisture content
22 values and showed a smaller variability in predicted drying times. This could be due to the difference
23 in the temperature readings from each cell, which has a greater impact on the target temperature

1 method, which utilised the absolute temperature value, while the derivative method relies on
2 temperature difference. However, this difference did not seem to affect the consistency in the final
3 moisture content of either method. As the derivative method identifies the point where the efficiency
4 of drying diminished drastically it could be further developed to select an optimal inlet air temperature
5 for a specific moisture content.

6 The simplicity of the derivative method allows it to be used in real time making it viable to be
7 implemented in an online control system after further testing its robustness over more drying
8 conditions. Although other more complex soft sensing techniques can be considered, there is a real
9 challenge for these to be adopted in industry. The derivative method simplicity and relative ease of
10 integration can act as a stepping stone towards more advanced control strategies during production in
11 the pharmaceutical industry.

12 As the interplay of different units and their parameters on critical attributes is critical in this kind
13 of equipment, flowsheet models comprising of the different unit operation would be a powerful
14 modelling tool in the future. These could not only be used to reduce the amount of experimental
15 work required but also run alongside the equipment as a soft sensor for a variety of properties such
16 as moisture content during the drying process in each cell. These sensors could then be implemented
17 in control strategies to further improve performance and to make the control systems more reliable.

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