A SYSTEMATIC APPROACH FOR INVESTIGATION OF
SPRAY DRYING PROCESSES

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parametric sensitivity; post-drying properties; powder properties; spray dryer; thermal
inactivation; two-fluid pneumatic nozzle

ABSTRACT

A systematic approach is developed for investigation of spray drying processes for
chemical and biological systems. The approach involves an in-depth study of atomizer
performance, spray dryer parametric sensitivity, spray-dried powder properties, thermal
inactivation and post-drying properties. The approach helps considerably in rational design
of spray drying experiments and in investigation and optimization of various process aspects
of spray drying of chemical and biological systems, leading to large savings in labor, cost
and time.
INTRODUCTION

Definition and Principle

Spray drying is the transformation of feed from a fluid state into a dried product by spraying the feed into a hot drying medium. It is a one-step, continuous particle-processing operation involving drying. The feed can either be a solution, suspension, emulsion or paste. The resulting dried product conforms to powder, granules or agglomerates, the form of which depends upon the physical and chemical properties of the feed and the dryer design and operation [1,2].

In the spray drying process, the fluid is atomized using a rotating disc or a nozzle and the spray of droplets comes immediately in contact with a flow of hot drying medium, usually air. The resulting rapid evaporation maintains a low droplet temperature so that a high drying air temperature can be applied without affecting the quality of the product. The time of drying the droplets is very short in comparison with other drying processes. The low product temperature and short drying time allow spray drying to process extremely heat-sensitive materials.

Application

Spray drying has direct or indirect association with a large number of products and articles used in daily life. It is used to manufacture a wide variety of foodstuffs such as instant coffee, milk powder, powdered cheese, soups and sweeteners. Among household goods and commodities, the most common spray-dried example is that of detergent powder. Most cosmetics rely on spray drying to provide the basic constituents of face powder and lipsticks. Paints contain spray-dried pigments while wall tiles are manufactured by pressing spray-dried clays. Pharmaceuticals, e.g. antibiotics are produced under aseptic spray drying conditions as finely divided powders which are formed into tablets before marketing. This spray-dried powder form is most suitable for rapid assimilation by body organs. Spray-dried carbides are used in many cutting tools. All these applications demand strict particle size distributions which are met by the spray drying operation.

Finally, spray-dried dyestuffs provide the colors for most fabrics and clothing. Xerox toner is another widely used spray-dried product. The manufacture of plastic utensils includes a spray drying stage while spray-dried enzyme (launder) is associated with the
curing of leather. Spray-dried starch is widely used in the food industry as also in textiles, printing and papermaking. Thus, spray drying processes are indispensable in the building, ceramic, chemical, biochemical, food, pharmaceutical and textile industry [1,3].

Properties of Spray-dried Powders

Spray-dried product properties relevant in the chemical/biochemical field can be listed as:

(i) Mean particle size and particle size distribution
(ii) Free-flowing nature
(iii) Bulk density, particle density and porosity
(iv) Solubility and dispersibility
(v) Moisture content and hygroscopicity
(vi) Appearance and texture
(vii) Particle shape
(viii) Retention of activity, color, aroma and flavor.

By modifying the spray drying process, it is possible to alter and control the above properties of spray-dried powders. An increase in the energy available for atomization (i.e. rotary atomizer speed, nozzle pressure, or air-liquid flow ratio in a pneumatic atomizer) will reduce particle size [1,3]. Particle size is usually increased as the feed concentration or viscosity increases [1,3,4]. Masters [1,3] reports that surface tension has a minimal effect on particle size, although a report on an increase in particle size with an increase in feed surface tension and density as well as with concentration and viscosity is available [4]. If the feed rate is increased, particle size will again increase. The effect of temperature on particle size appears to be highly dependent on the material being dried [4]. It was observed that for crystalline materials, such as sodium sulfate, temperature had very little effect whereas for coffee extract (a film-forming material) the mean particle diameter was significantly reduced by increasing the inlet air temperature. In contrast, reports on studies where the particle size of some materials was shown to increase as the drying air temperature increases [4-6]. High drying air temperatures also seem to be associated with lower bulk densities [3,7]. As a general rule, smaller particles will usually be more dense, and so the bulk density of a powder with a small particle size will be higher. Bulk density
will also increase with a narrower particle size distribution. As would be expected, increased dryer outlet temperature results in a lower final product moisture content.

A major concern in spray drying of biological systems (this complication does not exist for purely chemical systems) is the retention of activity (for enzymes) and aroma/flavor (for foods). Thus, the enzyme activity retention must be close to 100% in the spray drying operation and moreover, the shelf life of the dried enzyme product must be excellent, i.e. enzyme activity must be retained for long times on storage. Since this chapter deals with the development of a systematic approach for spray drying with enzymes as model biological systems (though the work is also applicable to purely chemical systems), the spray drying of enzymes is briefly discussed next.

Spray Drying of Enzymes

Enzymes are nitrogenous organic compounds of high molecular weight. They are normally very heat-sensitive and mild drying temperatures are paramount. Additives, e.g. inorganic salts, are used as protective diluents to further minimize heat damage. Examples of spray-dried enzymes include amylase, protease, glucose oxidase, glucose isomerase, pectinase, rennin, lactase, dextrinase, lipase, pepsin and trypsin. Spray-dried enzymes fall into two categories. Firstly there are the bulk industrial enzymes, which include proteases for detergents, amylases for textile de-sizing and starch hydrolysis, and pectinases for fruit-juice clarification. These uses are tabulated in Table 1. Enzymes for detergents are already spray dried in large quantities. In the second category lie the analytical enzymes. These are invariably dried in small quantities using low temperatures. The spray drying of pancreatin, for example, must not have inlet drying temperatures above 95°C.

Finally we note that it is more difficult to process a thermolabile enzyme compared to a more thermostable system. Further, no systematic, rational approach exists at present to investigate such spray drying processes and a lot of trial and error is resorted to. There are relatively few studies on the spray drying of enzymes, proteins or biopolymers in the chemical and biological literature [8-11]. However, a large number of patents exist in this field. These patents include those granted to Allied Colloids for spray-dried polysaccharide powders [12], CLG Stammvertrieb for single cell protein production [13], Daicel Chem for Chitosan granules production [14], Haarmann and Reimer for granular citric acid [15], Imperial Chemical Industries for various enzyme-containing biocatalysts [16], Institute of Technical and Thermal Physics, Ukraine for production of alkaline protease by spray drying.
TABLE I

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amylase</td>
<td>Baking, milling, paper, textiles, brewing</td>
</tr>
<tr>
<td>Protease</td>
<td>Brewing, meat and fish tenderizing, detergents, cheesemaking, leather tanning, oral hygiene</td>
</tr>
<tr>
<td>Glucose oxidase</td>
<td>Carbonated beverages</td>
</tr>
<tr>
<td>Pectinase</td>
<td>Coffee fermentation, juice clarification</td>
</tr>
<tr>
<td>Lipase</td>
<td>Detergents, digestive aids</td>
</tr>
<tr>
<td>Trypsin</td>
<td>Wound debridement</td>
</tr>
<tr>
<td>Rennin</td>
<td>Cheesemaking</td>
</tr>
<tr>
<td>Lactase</td>
<td>Ice-cream</td>
</tr>
<tr>
<td>Cellulase</td>
<td>Cellulose breakdown</td>
</tr>
</tbody>
</table>

[17] and Takenishi and Teramatsu for ultrafine cellulose powders and their manufacture [18]. Only selected patents where spray drying plays the dominant role in the manufacture of products are listed; those patents where spray drying is used as a unit operation for achieving a certain purpose are not included as their number is extremely large.

Haemoglobin has been successfully spray dried at the laboratory scale with the inclusion of 0.25 M sucrose as a protector [9]. Without a protector, approximately 50% of the haemoglobin was oxidized, even when the inlet and outlet temperatures of the dryer were only 60°C and 30°C respectively. However, when 0.25 M sucrose was included in the formulation, the temperatures could be increased to 100°C and 70°C, with 97% of the haemoglobin remaining in the reduced form. At the higher drying temperature, the moisture content of the product was only 2.7%, compared to 4.7% at an inlet temperature of 60°C. Additionally, these drying conditions increased the product yield and improved its storage stability. The authors used their experience in lyophilization to assist in the selection of potential stabilizers. The stabilizers were generally more effective in freeze drying than spray drying; only sucrose was highly efficient in both. One disadvantage of sucrose, however, is its high hygroscopicity [9].

Finally, Morgan and Armstrong [19] investigated the spray drying of egg yolk while Kitabatake et al. [20] studied the physicochemical properties of spray-dried egg ovalbumin. No attempt is made here to summarize the larger literature on spray drying of drugs, pharmaceuticals and foods.
RESULTS AND DISCUSSION

As pointed out in the previous section, a systematic approach for experimentally investigating spray drying processes has not been established. For biological systems, the situation is worse and research material on the subject is extremely scarce. This could partly be due to the industrial nature of the subject with the concomitant proprietary knowledge and partly to the complexity of the spray drying process itself. Moreover, biological systems have their own peculiar difficulties. For instance, they are often thermolabile and great care needs to be taken to prevent their denaturation during spray drying by proper choice of dryer type, dryer conditions (inlet and outlet temperature, residence time), type of additive etc.

Further, the content of liquid solutions (enzyme, drug, food material) to be dried is often very low in terms of solids percentage, leading to high drying costs per unit weight of the product and low product recoveries. To bring the liquid solution to an economically spray-dryable range (about 25% solids), food-grade additives (carriers, binders) need to be added to the solution before drying. These solids protect the activity, aroma or flavor of the product during drying, increase the dried-product retention and also dictate the nature of product in terms of its physicochemical properties after drying, such as particle size and particle size distribution, free-flowing nature, bulk density and compressibility, solubility, cohesion, moisture content and hygroscopicity. The control of these powder properties is an important problem in chemical and biochemical product engineering.

Systematic Approach

To investigate the spray drying process in a systematic way and obtain a clearer understanding, five subdivisions of the process were made. The blocks are illustrated in Figure 1. They are:

(i) Atomizer performance studies
(ii) Studies on the parametric sensitivity of the spray dryer
(iii) Powder property studies
(iv) Thermal inactivation studies
(v) Post drying studies
SPRAY DRYING PROCESSES

Details of the systematic approach for investigation of spray drying processes for chemical and biological systems are illustrated in a concise manner by the flowchart shown in Figure 2. Expertise on protective carriers and binders, availability of a method for measurement of droplet size, sound knowledge of atomization and atomizer characteristics, and information about parametric sensitivity are important prerequisites for process design (Figure 2). Once spray-dried powder is obtained, its physicochemical properties such as mean particle size and particle size distribution, free-flowing nature, bulk density, compressibility, solubility, moisture content and hygroscopicity, appearance and texture are evaluated. The particle size in the drying chamber is also measured in situ. Carriers and binders that yield the best powder properties are selected for investigating the compatibility of the biological system (e.g., enzyme) with the carrier/binder. The thermal inactivation of the enzyme in the presence of these selected carriers and binders is also studied (Figure 2). This accomplished, the actual spray drying of enzyme in the presence of the selected...
FIGURE 2. Systematic approach for investigating spray drying processes for chemical and biological systems.
SPRAY DRYING PROCESSES

carriers and binders is performed. Finally, post drying studies of powder morphology, shelf life and activation energy are carried out (Figure 2).

At any stage in this flowchart of Figure 2, one can go back to the previous steps and iterate to obtain the desired properties of the spray-dried powder. The approach depicted by Figures 1, 2 minimizes wastage of labor, time and cost. For example, the enzyme is not added until an acceptable spray-dried powder is obtained. The methodology is general and is applicable to both chemical and biological systems. Thus, in the scheme of Figure 2, process steps 8 and 9 can be dispensed with for a purely chemical system.

Selected experimental results for each of the subdivisions of the spray drying process indicated in Figure 1 will now be provided.

Parametric Sensitivity of the Spray Dryer

First, the peristaltic feed pump of the mini spray dryer needs to be calibrated and the graph of liquid flow rate delivered by the pump vs. set point needs to be drawn. For two-fluid pneumatic nozzles, the calibration of the rotameter for air flow through the spray dryer also needs to be determined. A variation of these calibration procedures need to be carried out for other atomizer types (such as the dependence of liquid flow rates on the pressure for a simple pressure nozzle).

Results for the parametric sensitivity of a Büchi mini spray dryer equipped with a two-fluid pneumatic nozzle are represented in Figure 3. The steady-state value of the outlet temperature ($T_o$) is plotted in Figure 3 as a function of the liquid flow rate for fixed values of the inlet temperature ($T_i$ = 140°C, 160°C) and air mass flow rate. For constant load on the spray dryer (fixed liquid flow rates), only one temperature, i.e. $T_i$ or $T_o$, can be varied independently. When water is fed to the spray dryer up to a flow rate of 15 mL/min (for both $T_i$ = 140 and 160°C at constant $r_n$), complete evaporation is found to occur. However, $T_o$ decreases with liquid flow rate as depicted in Figure 3. For both values of $T_i$, a liquid flow rate of about 20 mL/min (for $r_n = 2.12 \times 10^4$ kg/s) leads to condensation in the spray dryer. Thus, the evaporative capacity of the spray dryer under these operating conditions measures about 15 mL/min. Clearly, the dryer should not be overloaded by operating at too high a liquid flow rate (> 15 mL/min in Figure 3) as this would result in a non-dried product. In all parametric sensitivity experiments, the aspirator flow rate was kept at its maximum value of 5.7 m/s at the entrance to the spray dryer and the curves would shift upwards or downwards with changes in aspirator flow rate.
FIGURE 3 Parametric sensitivity studies on a spray dryer: influence of spray dryer load (liquid flow rate) on outlet temperature for constant values of the inlet temperature.

The influence of air flow rate through a two-fluid pneumatic nozzle of a spray dryer is as follows: an increase in the air flow rate ($Q_a$) keeping the liquid flow rate ($Q_l$) constant does not change the outlet temperature, $T_o$, as long as one is operating within the evaporative capacity of the dryer and the air supplied is sufficient to cause atomization in each case. However, the value of $Q_a$ at which condensation begins decreases with decrease in $Q_l$. As a general rule, a decrease in $T_i$ (keeping $Q_a$ and other parameters constant) leads to a fall in the evaporative capacity. These studies provide information on the sensitivity of the spray dryer to various operating parameters and help the investigator to choose a safe region of operation where no condensation takes place and a properly dried product is obtained.

**Nozzle Characterization and Atomizer Performance Studies**

The key measurement in atomizer performance studies is measurement of the droplet size distribution and mean droplet size. The final mean powder particle size after spray drying is related to the mean liquid droplet size produced by atomization, often by a simple factor. Many useful techniques have been developed, each with its own advantages and limitations. These can be classified as follows:
SPRAY DRYING PROCESSES

(i) Mechanical
   (a) Collection of drops on slides
   (b) Collection of drops in cells
   (c) Molten wax techniques
   (d) Drop freezing techniques
   (e) Cascade impactors

(ii) Electrical
    (a) Charged wire techniques
    (b) Hot wire techniques

(iii) Optical
     (a) High speed photography
     (b) Holography
     (c) Light scattering techniques
     (d) Phase Doppler techniques
     (e) Fraunhofer diffraction-based techniques.

Mechanical methods possess the virtues of simplicity and low cost. Their main drawback lies in the collection of representative spray samples. Among electrical methods, the hot wire techniques are the most useful. However, they can only be employed at relatively low velocities (a few metres per second) due to droplet breakup upon impact with the wire. Imaging systems allow the spray to be visualized, but a major difficulty is the determination of the size of the viewing volume to be assigned to given drop sizes. The optical techniques are more expensive and require expertise to correct for multiple scattering errors and errors due to variations in detector sensitivity. For more details on these techniques the reader is advised to consult the excellent treatments provided by Bachalo [21], Chigier [22], Dodge [23], Jones [24] and Lefebvre [25]. Dodge [23] has also compared the performance of seventeen drop size measuring instruments, among which six different types of techniques are included.

Determination of an Empirical Correlation for Atomization from a Two-fluid Pneumatic Nozzle

The importance of empirical correlations in chemical and biochemical engineering is well known. Theory has not yet reached the stage where predictions of complex
atomization processes can be made and one is forced to rely on empirical correlations for
the Sauter mean diameter (SMD) of sprays. The earliest study of two-fluid atomization was
carried out by Nukiyama and Tanasawa [27], who correlated their droplet size data by the
following empirical equation:

\[
\text{SMD} = \frac{0.585}{\sqrt{\text{Fr}}} \left[ \frac{\sigma_1}{\rho_1} \right]^{0.6} + 53 \left[ \frac{\mu_2}{\sigma_1 \rho_1} \right]^{0.225} \left[ \frac{Q_1}{Q_a} \right]^{1.5}
\]

Eq. (1) predicts that the mean droplet diameter is inversely proportional to the
relative velocity between the air and the liquid, while for large values of the air/liquid ratio
the influence of viscosity on SMD becomes negligible. While the above correlation offers
important guidelines for design, it is beset with several difficulties. Firstly, Eq. (1) is not
dimensionally correct, which is a serious flaw. Further, the atomizer dimension does not
appear anywhere in Eq. (1). Attempts to remove these deficiencies have been made [27-35].
For instance, Sakai's correlation for the Sauter mean diameter of the spray [32] has the
form:

\[
\text{SMD} = 14 \times 10^{-6} D_p^{0.75} (m_L/m_a)^{-0.75}
\]

Eq. (2) also has deficiencies: it does not incorporate the effect of fluid physical
properties such as surface tension, viscosity or density on the SMD. Detailed
experimentation in our laboratory on two-fluid pneumatic atomizers using the slide method
[method (i)(a) in our classification] led to the following empirical correlation:

\[
\text{SMD} = 10.26 D_p (R_e)^{-0.869} (\text{Oh})^{-0.709} \left( \frac{m_L}{m_a} \right)^{-0.657}
\]

where \(D_p\) represents the tip diameter of the atomizer and the dimensionless groups in the
correlation represent the Reynolds number (a measure of inertial/viscous forces), the
Ohnesorge number (which takes into account the surface, inertial and viscous forces) and
the ratio of the mass flow rates of air and liquid. The viscosity was varied up to a thousand
times that of water by addition of glycerol while the surface tension was lowered down to
less than one-third that of water by addition of ethanol as described by Nath and Shishodia
[26]. Eq. (3) represents the key result of this section.
Comparison of the Empirical Correlation of this Work with Correlations of Other Workers

A comparison of the power dependence of the mean drop size on different variables with available correlations of other workers is made in Table 2. There exist variations among correlations; however, reasonably good agreement is obtained for all variables as seen on scrutiny of the entries in the table.

Properties of Spray-dried Powders

A glance at the illustrations depicting the systematic approach for spray drying processes (Figures 1, 2) tells us that the inputs of droplet size measurement, atomizer characterization and parametric sensitivity have been studied. Another significant block, i.e. the quantification of physicochemical properties of spray-dried powders in the presence of carriers and binders remains to be investigated. This includes the measurement of angle of slide, angle of repose, angle of spatula, bulk density, compressibility, Kawakita constants, solubility, retention, mean particle size and particle size distribution, color and texture of powders produced by spray drying in the presence of various carriers and binders at different concentrations. This is a vast topic and it is not the aim here to cover each powder property; the interested reader is referred to the excellent articles by Curr [36], Lin and Kao [37], Saleh et al. [38] and Wan et al. [39,40]. We provide a summary table of various powder properties at two values of the inlet temperature for selected systems (Table 3).

Table 3 also demonstrates the dependence of all the powder properties on the inlet drying temperature (T_i) for two selected systems. Almost all powder properties improve with decrease in T_i from 160°C to 140°C. Thus, the values of angle of slide, angle of repose and angle of spatula all register a substantial decrease with decrease in T_i. The bulk densities increase and the compressibility decreases with decrease in T_i suggesting a more free-flowing powder at lower inlet drying temperature (Table 3). This conclusion is further corroborated by the values of the Kawakita constants. The values of both a and 1/b are lower at lower T_i (140°C) suggesting a powder with higher packability at lower T_i. The powder also becomes more cohesive with increase in T_i from 140°C to 160°C (Table 3). Hence, spray drying experiments carried out at the lower inlet drying temperature of 140°C yield superior powder properties for both these salt-polymer additive systems.
TABLE 2

Power Dependence of Sauter Mean Diameter on Different Variables for Various Types of Two-fluid Pneumatic Nozzles

<table>
<thead>
<tr>
<th>Nozzle Type</th>
<th>Investigator</th>
<th>Power Dependence of SMD on Variable Indicated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air Blast</td>
<td>This work</td>
<td>$n_1$, $n_2$, $n_3$, $V_o$, $m_o/m$, $D_o$</td>
</tr>
<tr>
<td></td>
<td>Wigg, 1964</td>
<td>0.2, 0.5, 0, -1.0, -0.75, $D_o^{11}$</td>
</tr>
<tr>
<td></td>
<td>Sakai, 1978</td>
<td>-    , -   , -    , -    , -0.75, $D_o^{17}$</td>
</tr>
<tr>
<td></td>
<td>Kim &amp; Marshall, 1971</td>
<td>0.41, - , - , -1.44, - , 0</td>
</tr>
<tr>
<td></td>
<td>Simpson, 1979</td>
<td>0.375, 0.06, 0.15, -0.5, -0.55, -</td>
</tr>
<tr>
<td></td>
<td>Weiss &amp; Wronsh, 1959</td>
<td>- , - , - , -1.33, - , $D_o^{18}$</td>
</tr>
<tr>
<td>Pneu Jet Air Blast</td>
<td>Rusk &amp; Letheby, 1984</td>
<td>0.4, - , 0, -0.8, - , $D_o^{16}$</td>
</tr>
<tr>
<td></td>
<td>Jantzi, 1982</td>
<td>0.45, - , 0, -0.9, - , $D_o^{13}$</td>
</tr>
<tr>
<td>Prefine Air Blast</td>
<td>El-Shenawwy et al, 1980</td>
<td>0.6, - , 0.1, -1.2, - , $D_o^{14}$</td>
</tr>
</tbody>
</table>

The ammonium sulfate-xanthan gum system leads to the production of granules, which explains the high values of the average particle size (almost 1000 microns) and uniformity coefficient [36] and the low values of the angle of repose, angle of slide and compressibility. All these measurements indicate the superior free-flowing nature of the granulated powder formed under these conditions. Such studies help in optimizing the type and concentration of additive (see Figure 2) to produce spray-dried powder conforming to the desired specifications.

Thermal Inactivation and Shelf Life Studies

The thermal inactivation of a thermolabile model system (yeast alcohol dehydrogenase enzyme) was examined in the presence and absence of additives in the liquid state; the results of these experiments are represented in Figure 4 and Table 4. In Figure 4,
TABLE 3
Quantification of Spray-dried Powder Properties

<table>
<thead>
<tr>
<th>Powder Property</th>
<th>20% Sodium Sulfate + 0.05% Xanthan Gum</th>
<th>20% Ammonium Sulphate + 0.01% Xanthan Gum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angle of Slide 1 (deg)</td>
<td>21.47</td>
<td>38.07</td>
</tr>
<tr>
<td>Angle of Slide 2 (deg)</td>
<td>23.90</td>
<td>38.07</td>
</tr>
<tr>
<td>Angle of Repose (deg)</td>
<td>23.42</td>
<td>48.58</td>
</tr>
<tr>
<td>Angle of Spatula (deg)</td>
<td>53.13</td>
<td>77.47</td>
</tr>
<tr>
<td>( \rho_o ) (g cm(^{-3}))</td>
<td>0.55</td>
<td>0.409</td>
</tr>
<tr>
<td>( \rho_* ) (g cm(^{-3}))</td>
<td>0.97</td>
<td>0.778</td>
</tr>
<tr>
<td>Compressibility (%)</td>
<td>43.20</td>
<td>47.74</td>
</tr>
<tr>
<td>Solubility (%)</td>
<td>35</td>
<td>30</td>
</tr>
<tr>
<td>Kawakita Constant ( a )</td>
<td>0.472</td>
<td>0.532</td>
</tr>
<tr>
<td>Kawakita Constant ( b )</td>
<td>0.111</td>
<td>0.094</td>
</tr>
<tr>
<td>Retention (%)</td>
<td>65.0</td>
<td>72.3</td>
</tr>
<tr>
<td>Average Particle Size (( \mu )m)</td>
<td>26.5</td>
<td>26.5</td>
</tr>
<tr>
<td>Moisture Content (%)</td>
<td>0.10</td>
<td>0.16</td>
</tr>
<tr>
<td>Hygroscopicity (%)</td>
<td>0.0</td>
<td>0.295</td>
</tr>
<tr>
<td>Nature of Powder</td>
<td>White, Fine</td>
<td>White, Amorphous, Lumpy</td>
</tr>
<tr>
<td>Cohesion (%)</td>
<td>19.0</td>
<td>35.1</td>
</tr>
<tr>
<td>Uniformity Coefficient</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
FIGURE 4 Selected experimental thermal inactivation curves for pure yeast alcohol dehydrogenase in the liquid state. 60°C, 0% sucrose (●); 63°C, 0% sucrose (○); 70°C, 44.44% sucrose (■).

<table>
<thead>
<tr>
<th>Temperature (°C)</th>
<th>Sucrose (%(w/w))</th>
<th>$A_e$</th>
<th>$k_e \times 10^2$ (min$^{-1}$)</th>
<th>$A_i$</th>
<th>$k_i$ (min$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>0</td>
<td>0.86</td>
<td>1.30</td>
<td>0.14</td>
<td>0.10</td>
</tr>
<tr>
<td>55</td>
<td>0</td>
<td>0.85</td>
<td>4.70</td>
<td>0.15</td>
<td>0.12</td>
</tr>
<tr>
<td>57.5</td>
<td>0</td>
<td>0.83</td>
<td>7.40</td>
<td>0.17</td>
<td>0.23</td>
</tr>
<tr>
<td>60</td>
<td>0</td>
<td>0.31</td>
<td>8.60</td>
<td>0.69</td>
<td>0.19</td>
</tr>
<tr>
<td>63</td>
<td>0</td>
<td>0.00</td>
<td>--</td>
<td>1.00</td>
<td>1.25</td>
</tr>
<tr>
<td>62.5</td>
<td>44.44</td>
<td>0.93</td>
<td>2.10</td>
<td>0.07</td>
<td>0.06</td>
</tr>
<tr>
<td>65</td>
<td>44.44</td>
<td>0.82</td>
<td>2.30</td>
<td>0.18</td>
<td>0.16</td>
</tr>
<tr>
<td>67.5</td>
<td>44.44</td>
<td>0.55</td>
<td>8.30</td>
<td>0.45</td>
<td>0.19</td>
</tr>
<tr>
<td>70</td>
<td>44.44</td>
<td>0.04</td>
<td>11.20</td>
<td>0.95</td>
<td>0.58</td>
</tr>
</tbody>
</table>

TABLE 4
Kinetic parameters for thermal inactivation of pure yeast alcohol dehydrogenase
the natural logarithm of fractional enzyme activity remaining is plotted against time in the presence and absence of additives at constant temperature. Nonlinear, biphasic behavior was clearly observed at almost all temperatures, i.e., the inactivation curve exhibited a larger slope at short times and a smaller slope at long times. The stable and labile phase rate constants (k_s and k_l) and the stable and labile phase fractions (A_s and A_l) were quantified based on Nath's method [41-43]. The kinetic parameters of pure yeast alcohol dehydrogenase for the temperature range 50-70°C in the presence and absence of sucrose are tabulated in Table 4.

The sum of A_s and A_l is unity in all cases (Table 4). This, along with the high k_s/k_l value, justifies the method used to determine the kinetic parameters. Note that both A and k parameters need to be considered simultaneously (and not singly) for a correct interpretation. A decrease in temperature at constant sucrose concentration or addition of sucrose at constant temperature has the effect of increasing A_s and altering k_s and k_l, and the method of analysis clearly differentiates between these two effects [41-43].

Studies to determine the shelf life of the alcohol dehydrogenase-containing spray-dried powder were conducted by storing the powder in incubators set at constant temperatures of 30, 50 and 60°C for a period of up to four months. At 30°C, <1% activity loss of enzyme resulted after four months. Even on storage at an elevated temperature of 50°C, loss of half the enzyme activity took 25 days. At 60°C, the value of the heat-stable inactivation rate constant, k_s, measured about $10^{-3}$ h⁻¹ in the solid state, compared to a k_s value of approximately $10^{-2}$ min⁻¹ (Table 4) in the liquid state even in the presence of a high concentration of stabilizer. Thus the storage stability of the enzyme was enhanced more than 500-fold by spray drying. This points to the great advantage of storing enzymes in the solid state; the enzyme inactivates slowly due to the substantial decrease in water activity caused by the spray drying process.

SUMMARY

In this chapter, five subdivisions of the spray drying process were made (Figure 1) to obtain a clearer understanding of various process aspects of spray drying. These subdivisions were:

(i) Atomizer performance studies

(ii) Studies on the parametric sensitivity of the spray dryer
(iii) Spray-dried powder property studies
(iv) Enzyme thermal inactivation studies
(v) Post drying studies.

A systematic approach was evolved to investigate spray drying processes (Figure 2).
First, the sensitivity of the spray dryer to various operating parameters, e.g. the inlet (T₁)
and outlet (T₂) temperature and the liquid (ṁₗ) and air (ṁₐ) flow rate was examined. It
was found that for constant load on the spray dryer (ṁₗ fixed), only one temperature, T₁
or T₂, could be varied independently. The evaporative capacity of the spray dryer was
determined under various operating conditions and safe regions of operation were
recommended so that no condensation took place in the drying chamber and a properly
dried product resulted (Figure 3).

Next, the two-fluid pneumatic nozzle was characterized and the droplet Sauter mean
diameter (SMD) was quantified as a function of air and liquid flow rates and the physical
properties of the liquid (viscosity, surface tension). An empirical correlation was developed
for prediction of SMD of the spray in terms of various dimensionless groups (Reynolds
number, Re; Ohnesorge number, Oh; ṁₗ/ṁₐ) (Eq. 3). The developed empirical correlation
was compared with correlations developed by other researchers (Table 2).

Physicochemical properties of the spray-dried powder such as angle of slide, angle
of repose, angle of spatula, bulk density (both loose and tight), compressibility, Kawakita
constants, particle size and particle size distribution, solubility, cohesion, hygroscopicity and
moisture content and nature (color, texture) were quantified (Table 3). The influence of inlet
temperature on the physicochemical powder properties was also explored. Such studies
helped in ensuring that spray-dried product specifications were met.

Thermal inactivation of a model system (yeast alcohol dehydrogenase) in the
presence and absence of additives was investigated in the liquid state (Figure 4). The
enzyme was found to exhibit nonlinear biphasic thermal inactivation behavior. Using Nath’s
method [41-43], the rate constants of thermal inactivation at various temperatures in the
presence and absence of additives were quantified (Table 4).

Finally, post drying studies on the enzyme-containing spray-dried powder were
conducted. The shelf life of spray-dried enzyme was studied at different temperatures for
a period of up to four months and the stability gained by storage in the solid state (vis-a-vis
the liquid state) was quantified.
In summary, the systematic approach developed in this chapter should prove useful for design of experiments and investigation of various process aspects of the spray drying of chemical and biological systems.

REFERENCES


