Drying Technology
An International Journal

ISSN: 0737-3937 (Print) 1532-2300 (Online) Journal homepage: https://www.tandfonline.com/loi/ldrt20

Gaining insight on spray drying behavior of foods via single droplet drying analyses

Maarten A. I. Schutyser, Eline M. Both, Isabel Siemons, Evelien M. J. Vaessen & Lu Zhang

To cite this article: Maarten A. I. Schutyser, Eline M. Both, Isabel Siemons, Evelien M. J. Vaessen & Lu Zhang (2019) Gaining insight on spray drying behavior of foods via single droplet drying analyses, Drying Technology, 37:5, 525-534, DOI: 10.1080/07373937.2018.1482908

To link to this article: https://doi.org/10.1080/07373937.2018.1482908

Published online: 28 Jun 2018.

DRYING TECHNOLOGY
2019, VOL. 37, NO. 5, 525–534
https://doi.org/10.1080/07373937.2018.1482908

Taylor & Francis
Taylor & Francis Group

Gaining insight on spray drying behavior of foods via single droplet drying analyses

Maarten A. I. Schutyser, Eline M. Both, Isabel Siemons, Evelien M. J. Vaessen, and Lu Zhang

Laboratory of Food Process Engineering, Wageningen University, Wageningen, The Netherlands

ABSTRACT

A continuous challenge for spray drying operations is the optimal control of product quality despite the complex process removal of water and particle formation. In general, high product functionality (e.g. in terms of reconstitution behavior, high enzyme activity or appropriate living probiotic bacteria) is key to the success of spray-dried powders. In this article, we review scientific studies that employ single droplet drying approaches to unravel underlying phenomena of spray drying process. Moreover, we identify scientific challenges to advance single droplet drying studies and thus contribute to development of mechanism-based guidelines for spray drying of functional food powders.

ARTICLE HISTORY
Received 10 January 2018
Revised 26 April 2018
Accepted 28 May 2018

KEYWORDS
Single droplet drying; spray drying; particle formation; bioactive ingredients; probiotic bacteria; morphology

Introduction

Spray drying technology is well-known for its powders with high stability throughout shelf-life, desirable bulk properties, and excellent functional properties, such as reconstitution behavior. Throughout the last decades, spray drying operations have been optimized following trial and error approaches, which is usually justified because of the complexity of the underlying physical phenomena. Mechanistic understanding of the spray drying process itself is often lacking, where especially the physical phenomena behind the fast removal of water and particle formation and its relation to final product quality are not well understood. The fast-drying kinetics, the scale of the drying equipment, and the wide range of polydisperse droplets flying in a stream of hot air make it challenging to investigate the complex phenomena at the particle scale.[1,2]

In view of the challenges to study underlying mechanisms during actual spray drying, many scientific studies have employed single droplet drying (SDD) experimental approaches. In recent years, these studies have established useful insight on the effect of multiple parameters during droplet drying such as droplet temperature, size, and formulation on the drying kinetics, particle morphology, surface composition, and activity of bioactive components. Although numerous reviews on SDD and spray drying are available, to the best of our knowledge, no comprehensive review has addressed the relationship between SDD and particle properties that lead to powder functionality.

The objective of this article is therefore to provide a comprehensive review of the application of SDD approaches in scientific studies to establish better understanding of the relationship between SDD conditions and particle characteristics related to functional powder behavior. In the introduction, we elaborate on the impact of spray drying on powder particle characteristics and desired functional behavior in terms of physicochemical powder properties and properties of bioactive ingredients in spray-dried powders. We review the different SDD methods in relation to establishing relevant insight to advance spray drying operations and resulting powder quality. We discuss how SDD studies are used to investigate the effects of formulation and drying conditions on morphology development and component migration and on inactivation of enzymes and living probiotic bacteria. Finally, we identify scientific challenges to advance SDD methods and complement these with other experimental and modelling approaches to address relevant research questions related to spray drying of foods.

CONTACT Maarten A. I. Schutyser maarten.schutyser@wur.nl P.O. Box 17, 6700 AA Wageningen, The Netherlands.
Color versions of one or more of the figures in the article can be found online at www.tandfonline.com/ldrt.

The influence of spray drying on powder functionality

Particle properties and functional powder behavior

The spray drying process ensures removal of water from the product, while influencing the final functional powder properties. These properties are determined by both the properties of individual particles and the bulk powder. Particle properties include size distribution, shape, particle density, (surface) composition, and internal structure. Functional properties of the powder are affected by these particle properties and comprise amongst others reconstitution behavior, flowability, and bulk density.

Identification and measurement of the aforementioned particle and functional properties can help to define the quality of the powder and it may give an indication on the behavior of the powder during storage, handling and processing. Powder flowability, for instance, is often key for manufacturers as it influences the process efficiency, including blending, transfer, and storage. Furthermore, it is imperative to take into account the reconstitution behavior of a powder as most of the food powders are intended for rehydration with water or in an aqueous system after processing.[10]

According to Valdek et al. particle size and morphology (primarily shape) are the main characteristics of powders as these dictate functional powder properties.[11] Fu et al. [12] investigated the influence of both particle properties for three different lactose powders on their respective flow and bulk characteristics. Two of the lactose powders tested had a different particle size, yet similar shapes, and the third sample had a similar size to one of the other two samples, but differed in shape. The powder flow characteristic measurements performed in this research revealed that differences in particle size and in particular particle shape, significantly affected the flow properties of lactose powder over a wide range of stress conditions. Other studies specifically focussed on the effect of the particle shape on the final powder properties. Takeiti et al. studied the morphology of 12 different commercial maltodextrin powders and concluded that particle morphology influences particle surface area, porosity, and bulk density, ultimately influencing the reconstitution behavior of these powders.[13] Bumiller et al. studied glass spheres, calcium carbonate crystals, and plate-shaped talc powders, with particles similar in size, while differing in shape.[14] Also here a correlation between particle shape and powder flowability was demonstrated. Given these studies, controlling particle size and morphology is thus key for establishing functional powder properties.

Bioactive ingredients

In food and pharmaceutical industries, spray drying is typically applied to produce high-value bioactive ingredients (e.g. enzymes, living bacteria) in powder form. The usage of spray drying brings advantages such as low production cost and high energy efficiency, making it an economical alternative for freeze drying.[15–19] However, the activity of those bioactive ingredients may get lost during spray drying and subsequent storage of the dry formulations.

Loss of bioactivity during spray drying may occur especially due to the increased temperatures during the process, due to unfolding of proteins at the large liquid–gas interface of the small droplets, and/or due to shear stress during atomization in the nozzle. Rational design of the spray-dried formulations and optimization of drying conditions are essential to retain the activity of the bio-active ingredients during drying and subsequent storage.[20] With respect to the formulation often a sugar, polyol, or protein is added to stabilize bioactive ingredients. For example, the enzyme activity of lipase from *Cercospora kikuchii* was retained after spray drying under optimal conditions in the presence of maltodextrin DE10 as a protectant.[19]

Retention of enzyme activity or survival of living bacteria during spray drying is highly depending on the individual drying trajectory of droplets. The droplet–particle conversion during actual spray drying occurs quasi-instantaneously, therefore it is not possible to trace the drying kinetics of the droplets and the degradation of bioactive components *in situ*. Hence, representative SDD experiments have been introduced to mimic the highly complex spray drying process.

Single droplet drying experimentation

Single droplet drying approaches can approximate drying behavior of droplets during spray drying, if carried out under well-defined and relevant conditions (controlled drying air temperature, air velocity, and humidity). Multiple SDD methodologies exist, commonly divided in levitation methods and free flight drying methods. Levitation methods immobilize a droplet through either contact levitation (droplet suspended on a filament or deposited on a flat surface) or through non-contact levitation (acoustic wave). The SDD

Table 1. Comparison between different SDD set-ups.

	Pending droplet	Sessile droplet	Acoustic levitation	Free falling
Methodology	Droplet pending on a (glass) filament	Sessile droplet on hydrophobic surface	Droplet levitated in an acoustic field	Droplets falling through a column
Pros	Allows monitoring of droplet mass and morphology	Allows monitoring of droplet morphology Facilitates high-throughput experimentation	Free suspended droplet in air Allows monitoring of the droplet mass and morphology	Closely resembles the drying conditions in a spray dryer -allows for collection of a larger sample
Cons	The presence of the wire has small effect on the heat transfer and morphology	The mass of the droplet cannot be monitored The surface influences the air temperature and flow pattern near the droplet	Acoustic waves affect heat transfer and shape of the droplet	Impossible to continuously track the dynamics of the drying droplet

methodologies have different pros and cons, which should be considered when designing or performing SDD experiments (Table 1).

Levitation SDD

Amongst the contact levitation methodologies, suspended SDD experiments have been used most frequently.[21–25] In this intrusive method, a single droplet is suspended at the tip of a thin filament or a thin thermocouple and subsequently dried by convective air flow. This SDD approach allows for monitoring the droplet diameter, the temperature of the droplet, and the mass loss simultaneously, therewith collecting important drying kinetics data.[22] The mass loss can be determined by the different degree of deflection of the filament due to the changing droplet mass.[21] Alternatively, the droplet mass may be monitored via an accurate mass balance, which however poses limitations to the minimum size of the droplet.[26] A more advanced SDD device was developed that suspends a single droplet on the tip of a polyamide wire and employs humidity sensors and optimal imaging to monitor droplet mass and morphology, respectively.[27] Advantage of the latter approach is that the droplet mass measurements do not need any calibration in contrast to the deflection method.

In addition to the drying kinetics, droplets suspended from filaments have been used regularly to study the morphology development during drying.[25,28–31] A downside of using this technique is that often relatively large droplets are required (within the millimetre diameter range).[32] This limitation is set by the difficulty to suspend small droplets onto the filament tip and by the lower contribution of heat input via the filament if the droplet is relatively large ($\geq$1 µL).

Another contact levitation method is referred to as sessile SDD, in which a single droplet is deposited onto a surface and dried by well-defined drying air.[2,33] The sessile SDD platform employs a (pneumatic) dispenser to deposit droplets onto a hydrophobic target surface that provides retention of the spherical shape. This retention of shape minimizes the difference in drying behavior between a sessile droplet and a free falling droplet. The stationary drying droplet can be monitored very well by camera as it is always in the focus plane. The approach offers also opportunities for drying multiple droplets simultaneously.

A drawback of the technique is that the presence of the surface affects the air temperature and flow pattern of the drying air close the droplet. Heat conduction via the contact area between droplet and surface has been found to contribute only about 5% to the total amount of heat transferred.[34]

During acoustic levitation, a single droplet is fixated in air during drying due to a counterbalancing acoustic force. Acoustic levitation uses a quasi-steady sound-pressure distribution in a confined space enabling suspended droplets to be levitated by the balance between the body force of the droplet and the acoustic radiation force on its surface.[35,36] Standing sound waves are generated by the levitator that consists of (1) a transducer that is attached to a piezo-electric crystal that vibrates at an ultrasonic frequency, and (2) a reflector.[37] Cameras are used to monitor the evolution in morphology.[38] The drying rate can be derived from the particle diameter and the vertical positioning of the droplet in the field[35] or by continuously measuring the moisture content by means of a dew point hygrometer.[39] The initial positioning of liquid droplets in the acoustic field requires some exercise. Furthermore, the acoustic field has some effect on the shape of the droplet and the heat and mass transfer rates, where the transfer coefficients are larger compared to those of free falling droplets.[40]

Free flight SDD

Free flight drying methods consist of a single droplet or a stream of uniform droplets generated at the top of a column dryer by means of a monodisperse

Table 2. An overview of research on morphology development during SDD.

Influencing factor	Author	Studied component	Set-up	Parameter range	Effect on morphology
Composition	Both et al. [1]	Whey protein and maltodextrin	Sessile droplet	Different component ratios	More whey protein: vacuole, more MD: wrinkled
	Sadek et al. [3]	Micellar casein and whey protein	Sessile pendant droplet	Different protein ratios	Casein: wrinkled, whey: vacuole
	Tran et al. [4]	Lactose, whey protein, skim milk	Suspended droplet	Different protein/lactose ratios	More rigid crust with high protein
Initial dry matter content (DM)	Bouman et al. [5]	Whey protein	Sessile droplet	5–30% (w/w)	Lower DM wrinkled, higher DM vacuole
	Wu et al. [6]	Skim milk	Free-flying droplet	33–54% (w/w)	Lower DM wrinkled, higher DM vacuole
	Rogers et al. [7]	Skim milk	Free-flying droplet	4–40%	More extensive buckling at low DM
Air temperature	Bouman et al. [5]	Whey protein	Sessile droplet	20 °C, 40 °C, 60 °C, and 80 °C	No effect on morphology
	Rogers et al. [7]	Fresh skim milk	Free-flying droplet	120–140 °C	Low T wrinkled, high T vacuole
	Tran et al. [4]	Lactose	Suspended droplet	60–180 °C	Low T, shriveled with small cavities High T, larger single cavity
Air humidity	Sadek et al. [8]	Micellar casein	Sessile pendant droplet	2 and 40%	No effect on morphology
	Griesing et al. [9]	Mannitol	Acoustic levitation	1, 5, 10, and 15%	Increasing air humidity led to a decrease in porosity

(piezoelectric) nozzle, micro-syringe, pulsed-orifice, or an electrostatic drop generator.[2,7,26,41] This methodology most closely resembles the drying conditions in an industrial spray dryer. The droplet formation often relies on induced Rayleigh instability causing the periodic breakup of a liquid jet.[42] The generated droplets fall freely through the drying column as a consequence of gravitational force and they will eventually experience the same drying history. The technique imposes difficulties for observing and recording the morphology evolution and monitoring the drying kinetics. During free flight droplet drying the drying rate of the droplets is indirectly measured. For example Vehring et al.[32] determined this by monitoring the droplet diameter at different distances from the point of injection by means of light scattering. Furthermore, during free flight droplet drying there is no option to directly monitor the temperature changes or mass loss of individual droplets.[26] Morphology development of particles may be studied by sampling at different points in the dryer as done in the work of El-Sayed et al.[43]

SDD related to physical particle properties

Morphology development

Single droplet drying has been frequently used to assess drying kinetics of drying droplets, which has been extensively reviewed before.[2,22] More recently studies address the development of particle morphology (Table 2). Understanding the particle morphology development during drying creates prospects to control particle morphology, and with that the properties of a powder. Different stages during droplet drying in relation to morphology can be distinguished: (1) the constant drying rate period, where phase separation of components might occur, (2) the locking point which is the moment of first visual skin formation, and (3) the development of the final particle morphology. For example, the effect of droplet composition on the morphology development was studied following this approach (Figure 1), where droplets of whey protein form a smooth surface with a large vacuole and maltodextrin droplets form a wrinkled surface.[1]

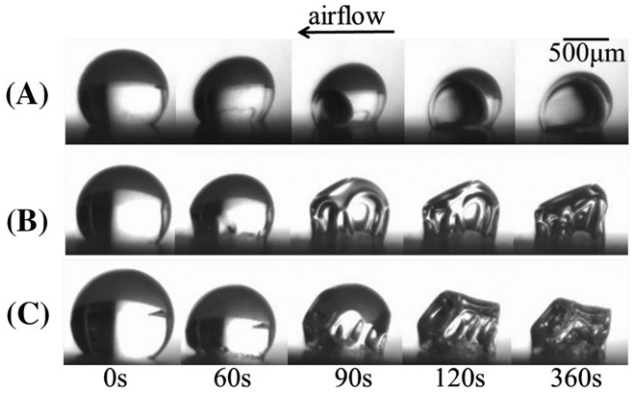

Figure 1. Morphology development in time for three droplets with different composition; (A) 0:100, (B) 50:50, (C) 90:10 (Maltodextrin DE12:Whey protein isolate). Droplets with an initial radius of 500 μm were dried in a sessile single droplet dryer at 70 °C. The air flow enters from the right side as indicated by an arrow (adapted from Both *et al.* [1]).

Besides droplet composition other process parameters can be varied to understand particle morphology

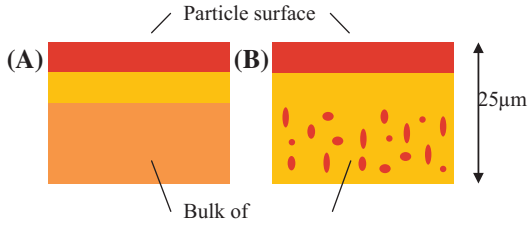

Figure 2. Schematic representation of phase separation near the surface of a dried lactose-macromolecule mixture, with two possible scenarios: (A) the bulk matrix is homogeneous, (B) the bulk of the particle is phase separated into macromolecule enriched zones in a lactose matrix. With yellow: lactose, red: macromolecule (BSA, HPMC, or poloxamer), and orange: mixture of both. The image was adapted from Nuzzo *et al.* [45].

development, e.g. the feed initial solids content, the air temperature and the air humidity (Table 2). Generally speaking, during slower drying, e.g. at lower initial dry matter content, lower air temperatures, or higher air humidity, droplets are more likely to be wrinkled/buckled, whereas the opposite will lead to particles with a large vacuole and a smooth surface.

Component migration and phase separation

The surface composition of a powdered particle is often not similar to its bulk composition, which can drastically alter the rehydration properties.[44] Components diffuse from the surface towards the centre because of the development of a concentration gradient due to evaporation of water from the surface. Components with a higher molecular weight will have a lower relative diffusivity and are therefore more likely to have an increased concentration at the surface [45]. Furthermore, it was shown that the atomization process could induce phase separation in model whole milk, where directly after dispensing the surface of the droplets contained more than 90% fat, whereas the bulk composition contained 44% fat.[46] Lastly, surface active components such as proteins in food products may also migrate to the surface, as these have a preference to be at the air/water interface.[47] For example, in drying model skim milk droplets there was, besides fat enrichment, protein enrichment at the surface: from 50% protein at the surface after dispensing to 70% at the surface of the dried particle.[46] The surface composition of these powders was measured by X-ray Photoelectron Spectroscopy (XPS), which is a method that measures the elemental composition of the surface.

Ideally, internal composition of the drying particles can be characterized as well. An interesting method to measure this is Confocal Raman microscopy (CRM), which has a penetration depth of ~25 µm, whereas

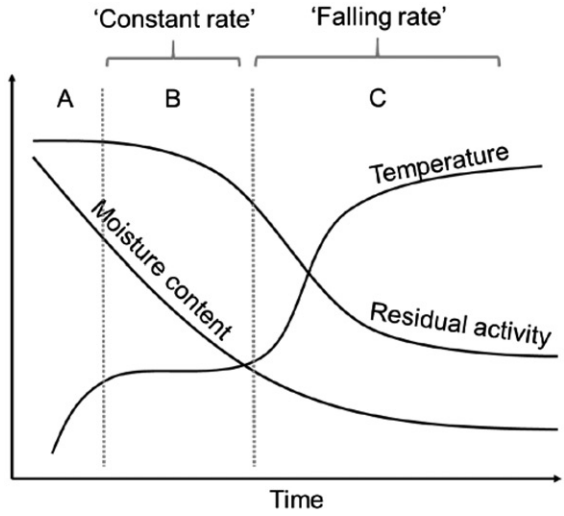

Figure 3. Schematic drawing of the temperature and moisture content profiles during single droplet drying and the corresponding inactivation of an enzyme: (A) heating-up period; (B) constant rate period; and (C) falling rate period (adapted from Perdana *et al.*, and Sloth *et al.* [49, 50]).

this is only ~10 nm for XPS. CRM can visualize the internal structure of a dried particle without the necessity of staining or cutting of the sample.[48] The working principle of CRM relies on the photon response upon laser illumination of a sample. A laser beam is focussed on the sample by a microscopic lens, and the Raman scattered photons are collected. In this way a picture can be reconstructed of the chemical composition or the physical properties of the sample. Using this technique the phase segregation in dried droplets of lactose-biopolymer mixtures was visualised, with the studied biopolymers being BSA, HPMC, and poloxamer.[49] In agreement with previous XPS measurements, an enrichment of the biopolymers at the surface was found. Additionally, it was shown that the zone below the top layer was depleted from the biopolymer (Figure 2). The bulk matrix below this depletion zone appeared to be either macroscopically mixed (Figure 2a), or phase separated into macromolecule enriched zones in a lactose matrix (Figure 2b) The occurrence of phase separation could be influenced by the component ratio and drying time.[49] Similar observations were done for mixtures of two biopolymers.[50] Furthermore, using CRM, it was shown that phase segregation is related to particle morphology formation.[1] Droplets containing maltodextrin DE12 and whey protein (95:5 on a dry matter basis), showed different morphology depending on the drying temperature. Particles with more phase segregation of maltodextrin DE12 and whey protein, showed that the morphology will be dominated by the whey protein.

Therefore, mapping the internal structure of dried droplets can improve the knowledge of morphology development.

Single droplet drying of bioactive ingredients

Conditions during SDD such as initial droplet size, the drying air temperature, the initial water content, and the formulation are known to have profound effect on the inactivation behavior of bioactive ingredients. Single droplet drying studies have characterized inactivation kinetics of enzymes and living bacteria to better control retention of enzyme activity or bacterial viability during spray drying processes.

Inactivation of enzymes

As an example Figure 3 illustrates the temperature and moisture history during SDD and its influence on enzyme inactivation. Initially, the droplet temperature approaches the wet-bulb temperature (period A) after which the temperature and the drying rate remain constant (period B). In the constant rate period only slight inactivation of enzyme occurs. After a critical moisture content is reached, the drying rate decreases due to internal diffusion limitation. As a consequence of the reduced drying rate, the droplet temperature increases to the dry-bulb temperature (period C). During the falling rate period the droplet temperature may be assumed homogeneous inside small droplets, while an internal moisture gradient develops with a relative wet core and a nearly dry surface.[51]

The residual activity of enzyme after SDD depends on the applied drying conditions (i.e., drying temperature, air humidity, initial droplet size) and formulation. Yamamoto and Sano[52] investigated retention of activity of three enzymes (i.e. β-galactosidase, glucose oxidase and alkaline phosphatase) during glass filament SDD. Residual enzyme activity was increased when lowering drying air temperature, reducing the droplet size and/or using sugar carriers with lower molecular weight. Similarly, residual activity of alkaline phosphatase during droplet drying is increased when decreasing air temperature and droplet size.[53] Usually, first-order kinetics are assumed to describe the dependence of the inactivation rate constant on temperature and moisture content and this inactivation rate constant decreases with decreasing moisture content at a specified temperature.[54,55] Sessile droplet drying of β-galactosidase at temperatures of 80–110 °C indicated that the enzyme activity is better retained near the surface of the particle due to the lower moisture content in that region.[34] In another study, during levitated SDD rapid inactivation of the L-Glutamate dehydrogenase (GDH) was observed after the critical moisture content was reached, which was explained by the increasing droplet temperature in this falling rate period.[56]

A commonly applied strategy to preserve enzyme activity during drying is to add a carrier, e.g. sugars/polyols, where the stabilization mechanism has been explained by two hypotheses.[57] The vitrification hypothesis assumes that the carriers increase the free energy barrier for enzyme unfolding by providing a rigid, inert solid matrix with low molecular mobility in the glassy state. The water replacement hypothesis assumes that the hydroxyl groups in the carrier matrix interact via hydrogen bonds to the surface of the proteins and thus 'replaces' the hydrogen bonding interaction with water.[58] For example, both addition of trehalose and sorbitol stabilized the enzyme GHD during levitated SDD. Given that the anhydrous glass transition temperature of sorbitol (T_g -7 °C) is much lower than that of trehalose (T_g 115 °C) the results were explained via the water replacement hypothesis.[59] In a spray drying study, the enzyme alkaline phosphatase was incorporated into inulin or trehalose.[60] Here, it was discussed that enzyme stabilization may be explained via the vitrification hypothesis when the T_g is below the storage temperature and via the water replacement hypothesis when the T_g is higher than the storage temperature of the powder.

Survival of living bacteria

During spray drying both dehydration and thermal stresses can lead to inactivation of living bacteria. Via SDD experimentation viability loss could be quantitatively described by the sum of dehydration and thermal inactivation.[61] Perdana et al. also found that at drying temperatures below 45 °C inactivation of *L. plantarum* WCFS1 was mainly due to dehydration.[61] At temperatures above 45 °C thermal inactivation was the main influencing factor affecting the survival of *L. plantarum* WCFS1. Similar results were found by Ghandi et al. who showed that at temperatures below 55 °C dehydration stresses primarily affected the survival of *Lactococcus lactis* spp. *cremonis*, while at temperatures of 65 °C and higher inactivation was caused by the sum of thermal and dehydration stresses.[62] Similarly, Fu et al. observed at temperatures above 50–65 °C that the inactivation rate of *L. cremonis* increased rapidly and temperature was the main factor influencing the inactivation rate.[63] Conclusions in this study were drawn from analysing the morphology of the dried cells, where cells dried at

higher temperatures (90–110 °C) had more holes in the cell wall than cells dried at lower drying temperature (70 °C).

Spray drying studies, and thus also SDD experiments, are often carried out to evaluate the effect of different drying matrices on the survival of bacteria. The advantage of SDD is that using well–defined drying conditions can generate more in depth insight in the mechanisms of protection by the different matrices. As discussed before, there are two types of stresses; thermal and dehydration stresses. Single droplet drying at a low temperature (25 °C) was used to investigate how carbohydrates or proteins protect *L. plantarum* WCFS1 against the combination of dehydration and thermal stresses.[64] Here, survival after drying decreased with increasing molecular weight of the carbohydrates, while the effect of the T_g was limited. This may be explained by the water replacement hypothesis where small carbohydrates interact more closely with phospholipids in the bacterial membrane compared to large molecules. For proteins or amino acids, there was no relation between molecular weight and survival or T_g and survival. In the same study, additional laboratory spray drying experiments were carried out to study the effect of formulation on thermal inactivation only. During fast drying of small (~10 µm) droplets that are too challenging to study during SDD, the inactivation was explained due to thermal stresses only as the bacteria are rapidly fixated in a glassy matrix.[61]

Besides the composition of the drying matrix, survival has also been correlated to the evolving morphology of a drying droplet. Wang et al., for example demonstrated that by calcium-induced thermal protein aggregated milk formulations led to increased survival of *L. rhamnosus* compared to bacteria in regular skim milk.[65] This was explained by the more porous particle structure and thus faster drying kinetics for the calcium-aggregated milk. A study by Khem et al.[66] reported higher survival of *L. plantarum* A17 during SDD of whey protein solutions in which early skin formation was observed. Due to skin formation the droplet temperature increased earlier but more gradual to the bulk air temperature compared to droplets with lactose and trehalose for which a later but sudden rise in temperature was observed. The sudden increase in temperature was hypothesized to explain the higher inactivation for the non-skin forming formulations. Similarly, in a study of Zheng *et al.*[67] SDD studies with reconstituted skim milk showed increased survival for *L. rhamnosus* GG and *L. cremonis* compared to lactose and growth medium as carriers. It was also hypothesized that calcium ions and whey protein play a crucial role in the survival. In contrary, for reconstituted whole milk no enhancement of survival was monitored despite the slow gradual increase in droplet temperature. Possibly, other factors such as the presence of fat could play a role here.

Overall the main benefit of using SDD experiments for studying survival of probiotics is the ability of doing accurate measurements during the transformation from droplet to particle. In this way it is possible to link the survival to temperature, moisture levels and morphology during different stages of drying. Furthermore, this is very helpful in unravelling protective effects of different types of drying matrices.

Scientific challenges

Although new insights are gained via SDD studies, still challenges are ahead to develop mechanism-based guidelines for spray drying of functional food powders. Below we formulate four main scientific challenges for SDD studies:

1. SDD methods have restrictions with respect to handling of realistically sized droplets and high solids feed solutions. Because both droplet size and initial solids have profound effect on the drying rate and morphology development, development of droplet-on-demand dispensers that can make smaller droplets of high viscous liquids is desired. Alternatively, SDD experiments may be complemented with other experiments (e.g. drying of ultrathin films) that facilitate measurements on complex system with similar length scale.
2. SDD studies on morphology development require more in-depth analyses of skin formation. It is extremely difficult to assess mechanical properties of the droplet skin in situ. Therefore, rheological characterization of bulk materials could for example be combined with numerical modelling approaches to connect heat and mass transfer to skin formation and thus morphology development.
3. Mapping of intra particle component distribution is crucial for validation of numerical models and challenging hypotheses. One may use XPS and CRM as discussed, but also other analytical techniques could be explored in combination with SDD. Methods such as Laser Speckle Imaging[68] or NMR/MRI[69] have been applied to monitor internal dynamics or water distribution during drying of paint and vegetables, respectively. Application of such analytical methods to small and fast drying droplets is however only feasible if

the spatial and temporal resolution of these techniques are sufficient.

4. Recent SDD studies suggest that stabilization of bioactive ingredients is function of both chemical composition and drying kinetics as influenced via the particle structure.[65] Future research should elucidate the contribution and mechanism of both factors in the stabilization in a systematic way.

Conclusions

Multiple SDD methods have been developed throughout the years that approach the conditions of drying droplets in spray dryers. Although single droplet approaches have their disadvantages, still SDD studies provided valuable insight into the complex spray drying process by especially addressing how heat and mass transfer and formulation affect the conversion of a droplet into dried powder particles. Especially, it is found that the rate of the conversion processes greatly influences the physical properties of powder particles such as morphology and component distribution via phase separation and diffusive transport phenomena. Understanding on how formulation and drying conditions influence primary particle properties will support development of powders with for instance improved flowability and reconstitution behavior. Other studies revealed better insight on how the drying trajectory influences the retention of specific bioactivity, i.e. residual enzyme activity or viable bacteria and supported the development of protective formulations and kinetics models to describe inactivation behavior of enzymes and living bacteria during drying of droplets. Having said this, although SDD approaches are a powerful tool to study the drying process, different scientific challenges are ahead to improve SDD methods and/or to combine these with advanced analytical techniques or modelling approaches. Finally, to make use of the knowledge gained from SDD methods, validation of hypotheses and optimization of drying conditions using lab-scale or pilot-scale spray dryers are pivotal.

Disclosure statement

No potential conflict of interest was reported by the authors.

References

[1] Both, E. M.; Karlina, A. M.; Boom, R. M.; Schutyser, M. A. I. Morphology Development during Sessile Single Droplet Drying of Mixed Maltodextrin and Whey Protein Solutions. *Food Hydrocolloids* **2018**, *75*, 202–210.

[2] Sadek, C.; Schuck, P.; Fallourd, Y.; Pradeau, N.; Le Floch-Fouéré, C.; Jeantet, R. Drying of a Single Droplet to Investigate Process–Structure–Function Relationships: A Review. *Dairy Sci. Technol.* **2015**, *95*, 771–794.

[3] Sadek, C.; Li, H.; Schuck, P.; Fallourd, Y.; Pradeau, N.; Le Floch-Fouéré, C.; Jeantet, R. To What Extent Do Whey and Casein Micelle Proteins Influence the Morphology and Properties of the Resulting Powder?. *Drying Technol.* **2014**, *32*, 1540–1551.

[4] Tran, T. T. H.; Jaskulski, M.; Avila-Acevedo, J. G.; Tsotsas, E. Model Parameters for Single-Droplet Drying of Skim Milk and Its Constituents at Moderate and Elevated Temperatures. *Drying Technol.* **2017**, *35*, 444–464.

[5] Bouman, J.; Venema, P.; de Vries, R. J.; van der Linden, E.; Schutyser, M. A. I. Formation during Drying of Sessile Whey Protein Droplets. *Food Res. Int.* **2016**, *84*, 128.

[6] Wu, W. D.; Liu, W.; Gengenbach, T.; Woo, M. W.; Selomulya, C.; Chen, X. D.; Weeks, M. Towards Spray Drying of High Solids Dairy Liquid: Effects of Feed Solid Content on Particle Structure and Functionality. *J. Food Eng.* **2014**, *123*, 130–135.

[7] Rogers, S.; Duo, W.; Xu, S.; Lin, Q.; Dong, X. Particle Shrinkage and Morphology of Milk Powder Made with a Monodisperse. *Biochem. Eng. J.* **2012**, *62*, 92–100.

[8] Sadek, C.; Schuck, P.; Fallourd, Y.; Pradeau, N.; Jeantet, R.; Le Floch-Fouéré, C. Buckling and Collapse during Drying of a Single Aqueous Dispersion of Casein Micelle Droplet. *Food Hydrocolloids* **2016**, *52*, 161–166.

[9] Griesing, M.; Grosshans, H.; Hellwig, T.; Sedelmayer, R.; Gopireddy, S. R.; Pauer, W.; Gutheil, E.; Moritz, H.-U. Influence of Air Humidity on the Particle Formation of Single Mannitol-Water Droplets during Drying. *Chemie-Ingenieur-Technik* **2016**, *88*, 929–936.

[10] Bhandari, B. R.; Bansal, N.; Zhang, M.; Schuck, P. *Handbook of Food Powders: Processes and Properties*. Elsevier: New York, NY, 2013.

[11] Valdek, M.; Helmo, K.; Pritt, K.; Besterci, M. Characterization of Powder Particle Morphology. *Proc. Estonian Acad. Sci. Eng.* **2001**, *7*, 22–34. In

[12] Fu, X.; Huck, D.; Makein, L.; Armstrong, B.; Willen, U.; Freeman, T. Particuology Effect of Particle Shape and Size on Flow Properties of Lactose Powders. *Particuology* **2012**, *10*, 203–208.

[13] Takeiti, C. Y.; Kieckbusch, T. G.; Collares-Queiroz, F. P. Morphological and Physicochemical Characterization of Commercial Maltodextrins with Different Degrees of Dext Rose-Equivalent. *Int. J. Food Prop.* **2010**, *13*, 411–425.

[14] Bumiller, M.; Carson, J.; Prescott, J. A Preliminary Investigation Concerning The Effect Of Particle Shape On a Powder's Flow Properties. In *World Congress on Particle Technology*, Sydney, Australia, 2002.

[15] Gharsallaoui, A.; Roudaut, G.; Chambin, O.; Voilley, A.; Saurel, R. Applications of Spray-Drying in Microencapsulation of Food Ingredients: An Overview. *Food Res. Int.* **2007**, *40*, 1107–1121.

[16] Huang, S.; Vignolles, M.-L.; Chen, X. D.; Le Loir, Y.; Jan, G.; Schuck, P.; Jeantet, R. Spray Drying of Probiotics and Other Food-Grade Bacteria: A Review. *Trends Food Sci. Technol.* **2017**, *63*, 1–17.
[17] Peighambardoust, S. H.; Golshan Tafti, A.; Hesari, J. Application of Spray Drying for Preservation of Lactic Acid Starter Cultures: A Review. *Trends Food Sci. Technol.* **2011**, *22*, 215–224.
[18] Knorr, D. Technology Aspects Related to Microorganisms in Functional Foods. *Trends Food Sci. Technol.* **1998**, *9*, 295–306.
[19] Costa-Silva, T. A.; Nogueira, M. A.; Souza, C. R. F.; Oliveira, W. P.; Said, S. Lipase Production by Endophytic Fungus Cercospora Kikuchii: Stability of Enzymatic Activity after Spray Drying in the Presence of Carbohydrates. *Drying Technol.* **2011**, *29*, 1112–1119.
[20] Broeckx, G.; Vandenheuvel, D.; Claes, I. J. J.; Lebeer, S.; Kiekens, F. Drying Techniques of Probiotic Bacteria as an Important Step towards the Development of Novel Pharmabiotics. *Int. J. Pharm.* **2016**, *505*, 303–318.
[21] Charlesworth, D. H.; Marshall, W. R. Evaporation from Drops Containing Dissolved Solids. *AIChE J.* **1960**, *6*, 9–23.
[22] Fu, N.; Woo, M. W.; Chen, X. D. Single Droplet Drying Technique to Study Drying Kinetics Measurement and Particle Functionality: A Review. *Drying Technol.* **2012**, *30*, 1771–1785. (February 2015).
[23] Tian, Y.; Fu, N.; Wu, W. D.; Zhu, D.; Huang, J.; Yun, S.; Chen, X. D. Effects of Co-Spray Drying of Surfactants with High Solids Milk on Milk Powder Wettability. *Food Bioprocess. Technol.* **2014**, *7*, 3121–3135.
[24] Walton, D. E. The Evaporation of Water Droplets. A Single Droplet Drying Experiment. *Drying Technol.* **2004**, *22*, 431–456.
[25] Sunkel, J. M.; King, C. J. Influence of the Development of Particle Morphology upon Rates of Loss of Volatile Solutes during Drying of Drops. *Ind. Eng. Chem. Res.* **1993**, *32*, 2357–2364.
[26] Adhikari, B.; Howes, T.; Bhandari, B. R.; Truong, V. Experimental Studies and Kinetics of Single Drop Drying and Their Relevance in Drying of Sugar-Rich Foods: A Review. *Int. J. Food Prop.* **2000**, *3*, 323–351.
[27] Tran, T. T. H.; Avila-Acevedo, J. G.; Tsotsas, E. Enhanced Methods for Experimental Investigation of Single Droplet Drying Kinetics and Application to Lactose/Water. *Drying Technol.* **2016**, *34*, 1185–1195.
[28] Lin, J. C.; Gentry, J. W. Spray Drying Drop Morphology: Experimental Study. *Aerosol Sci. Technol.* **2003**, *37*, 15–32.
[29] Walton, D. E.; Mumford, C. J. The Morphology of Spray-Dried Particles. *Chem. Eng. Res. Design.* **1999**, *77*, 442–460.
[30] Walton, D. E.; Mumford, C. J. Spray Dried Products - Characterization of Particle Morphology. *Trans IChemE* **1999**, *77*, 21–38.
[31] Wallack, D. A.; El-Sayed, T. M.; King, C. J. Changes in Particle Morphology during Drying of Drops. II. Effects on Drying Rate. *Ind. Eng. Chem. Res.* **1990**, *29*, 2354–2357.
[32] Vehring, R.; Foss, W. R.; Lechuga-Ballesteros, D. Particle Formation in Spray Drying. *J. Aerosol Sci.* **2007**, *38*, 728–746.
[33] Perdana, J.; Fox, M. B.; Schutyser, M. A. I.; Boom, R. M. Single-droplet experimentation on spray drying: Evaporation of a sessile droplet. *Chem. Eng. Technol.* **2011**, *34*, 1151–1158.
[34] Perdana, J.; Fox, M.; Schutyser, M. A. I.; Boom, R. Mimicking Spray Drying by Drying of Single Droplets Deposited on a Flat Surface. *Food Bioprocess. Technol.* **2013**, *6*, 964–977.
[35] Brenn, G.; Deviprasath, L. J.; Durst, F.; Fink, C. Evaporation of Acoustically Levitated Multi-Component Liquid Droplets. *Int. J. Heat Mass Transf.* **2007**, *50*, 5073–5086.
[36] Shitanishi, K.; Hasegawa, K.; Kaneko, A.; Abe, Y. Study on Heat Transfer and Flow Characteristic under Phase-Change Process of an Acoustically Levitated Droplet. *Microgravity Sci. Technol.* **2014**, *26*, 305–312.
[37] Zaitone, B. Drying of Multiphase Single Droplets in Ultrasonic Levitator. 2009.
[38] Schiffter, H.; Lee, G. Single-Droplet Evaporation Kinetics and Particle Formation in an Acoustic Levitator. Part 1: Evaporation of Water Microdroplets Assessed Using Boundary-Layer and Acoustic Levitation Theories. *J. Pharm. Sci.* **2007**, *96*, 2274–2283.
[39] Groenewold, C.; Möser, C.; Groenewold, H.; Tsotsas, E. Determination of Single-Particle Drying Kinetics in an Acoustic Levitator. *Chem. Eng. J.* **2002**, *86*, 217–222.
[40] Yarin, A. L.; Brenn, G.; Kastner, O.; Rensink, D.; Tropea, C. Evaporation of Acoustically Levitated Droplets. *J. Fluid Mech.* **1999**, *399*, 151–204.
[41] van Deventer, H.; Houben, R.; Koldeweij, R. New Atomization Nozzle for Spray Drying. *Drying Technol.* **2013**, *31*, 891–897.
[42] Wu, W. D.; Patel, K. C.; Rogers, S.; Chen, X. D. Monodisperse Droplet Generators as Potential Atomizers for Spray Drying Technology. *Drying Technol.* **2007**, *25*, 1907–1916.
[43] El-Sayed, T. M.; Wallack, D. A.; King, C. J. Changes in Particle Morphology during Drying of Drops of Carbohydrate Solutions and Food Liquids. 1. Effect of Composition and Drying Conditions. *Ind. Eng. Chem. Res.* **1990**, *29*, 2346–2354.
[44] Gaiani, C.; Ehrhardt, J. J.; Scher, J.; Hardy, J.; Desobry, S.; Banon, S. Surface Composition of Dairy Powders Observed by X-Ray Photoelectron Spectroscopy and Effects on Their Rehydration Properties. *Colloids Surf. B Biointerf.* **2006**, *49*, 71–78.
[45] Meerdink, G.; van't Riet, K. Modeling Segregation of Solute Material during Drying of Liquid Foods. *AIChE J.* **1995**, *41*, 732–736.
[46] Foerster, M.; Gengenbach, T.; Woo, M. W.; Selomulya, C. The Influence of the Chemical Surface Composition on the Drying Process of Milk Droplets. *Adv. Powder Technol.* **2016**, *27*, 2324–2334.

[47] Fäldt, P.; Bergenståhl, B.; Carlsson, G. The Surface Coverage of Fat on Food Powders Analyzed by ESCA (Electron Spectroscopy for Chemical Analysis.). *Food Struct.* **1993**, *12*, 225–234.
[48] Everall, N. J. Confocal Raman Microscopy: common Errors and Artefacts. *Analyst* **2010**, *135*, 2512–2522.
[49] Nuzzo, M.; Sloth, J.; Brandner, B.; Bergenstahl, B.; Millqvist-Fureby, A. Confocal Raman Microscopy for Mapping Phase Segregation in Individually Dried Particles Composed of Lactose and Macromolecules. *Colloids Surf. A Physicochem. Eng. Aspects* **2015**, *481*, 229–236.
[50] Nuzzo, M.; Sloth, J.; Bergenstahl, B.; Millqvist-Fureby, A. Phase Segregation in Individually Dried Particles Composed of Biopolymers. *Langmuir* **2015**, *31*, 10946–10954.
[51] Perdana, J.; Fox, M. B.; Boom, R. M.; Schutyser, M. A. I. Establishing Guidelines to Retain Viability of Probiotics during Spray Drying. *Drying Technol.* **2015**, *3937*, (February): 150211124521004.
[52] Yamamoto, S.; Sano, Y. Drying of Enzymes: enzyme Retention during Drying of a Single Droplet. *Chem. Eng. Sci.* **1992**, *47*, 177–183.
[53] Etzel, M. R.; Suen, S. Y.; Halverson, S. L.; Budijono, S. Enzyme Inactivation in a Droplet Forming a Bubble during Drying. *J. Food Eng.* **1996**, *27*, 17–34.
[54] Perdana, J.; Fox, M. B.; Schutyser, M. A. I.; Boom, R. M. Enzyme Inactivation Kinetics: Coupled Effects of Temperature and Moisture Content. *Food Chem.* **2012**, *133*, 116–123.
[55] Sloth, J.; Jorgensen, K.; Bach, P.; Jensen, A. D.; Kiil, S.; Dam-Johansen, K. Spray Drying of Suspensions for Pharma and Bio Products: Drying Kinetics and Morphology. *Ind. Eng. Chem. Res.* **2009**, *48*, 3657–3664.
[56] Lorenzen, E.; Lee, G. Slow Motion Picture of Protein Inactivation during Single-Droplet Drying: A Study of Inactivation Kinetics of L -Glutamate Dehydrogenase Dried in an Acoustic Levitator. *J. Pharm. Sci.* **2012**, *101*, 2239–2249.
[57] Chang, L. Q.; Pikal, M. J. Mechanisms of Protein Stabilization in the Solid State. *J. Pharm. Sci.* **2009**, *98*, 2886–2908.
[58] Liao, Y.; Brown, M. B.; Nazir, T.; Quader, A.; Martin, G. P.; Effects Of, S.; Trehalose On The, P.; Of The, N. S.; Of, S.-D. *Lysozyme. Pharm. Res.* **2002**, *19*, 1847–1853.
[59] Lorenzen, E.; Lee, G. Trehalose and Sorbitol Alter the Kinetic Pattern of Inactivation of Glutamate Dehydrogenase during Drying in Levitated Microdroplets. *J. Pharm. Sci.* **2013**, *102*, 4268–4273.
[60] Grasmeijer, N.; Stankovic, M.; Waard, H. D.; Frijlink, H. W.; Hinrichs, W. L. J. Unraveling Protein Stabilization Mechanisms: Vitrification and Water Replacement in a Glass Transition Temperature Controlled System. *Biochimica Et Biophysica Acta (BBA) - Proteins Proteomics* **2013**, *1834*, 763–769.
[61] Perdana, J.; Bereschenko, L.; Fox, M. B.; Kuperus, J. H.; Kleerebezem, M.; Boom, R. M.; Schutyser, M. A. I. Dehydration and Thermal Inactivation of Lactobacillus plantarum WCFS1: Comparing Single Droplet Drying to Spray and Freeze Drying. *Food Res. Int.* **2013**, *54*, 1351–1359.
[62] Ghandi, A.; Powell, I.; Chen, X. D.; Adhikari, B. Drying Kinetics and Survival Studies of Dairy Fermentation Bacteria in Convective Air Drying Environment Using Single Droplet Drying. *J. Food Eng.* **2012**, *110*, 405–417.
[63] Fu, N.; Woo, M. W.; Selomulya, C.; Chen, X. D. Inactivation of *Lactococcus lactis* Ssp. cremoris Cells in a Droplet during Convective Drying. *Biochem. Eng. J.* **2013**, *79*, 46–56.
[64] Perdana, J.; Fox, M. B.; Siwei, C.; Boom, R. M.; Schutyser, M. A. I. Interactions between Formulation and Spray Drying Conditions Related to Survival of *Lactobacillus plantarum* WCFS1. *Food Research International* **2014**, *56*, 9–17.
[65] Wang, J.; Huang, S.; Fu, N.; Jeantet, R.; Chen, X. D. Thermal Aggregation of Calcium-Fortified Skim Milk Enhances Probiotic Protection during Convective Droplet Drying. *J. Agric. Food Chem.* **2016**, *64*, 6003–6010.
[66] Khem, S.; Woo, M. W.; Small, D. M.; Chen, X. D.; May, B. K. Agent Selection and Protective Effects during Single Droplet Drying of Bacteria. *Food Chem.* **2015**, *166*, 206–214.
[67] Zheng, X.; Fu, N.; Duan, M.; Woo, M. W.; Selomulya, C.; Chen, X. D. The Mechanisms of the Protective Effects of Reconstituted Skim Milk during Convective Droplet Drying of Lactic Acid Bacteria. *Food Res. Int.* **2015**, *76*, 478–488.
[68] van der Kooij, H. M.; Fokkink, R.; van der Gucht, J.; Sprakel, J. Quantitative Imaging of Heterogeneous Dynamics in Drying and Aging Paints. *Sci. Rep.* **2016**, *6*, 34383
[69] Xu, F.; Jin, X.; Zhang, L.; Chen, X. D. Investigation on Water Status and Distribution in Broccoli and the Effects of Drying on Water Status Using NMR and MRI Methods. *Food Res. Int.* **2017**, *96*, 191–197.