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A QBD APPROACH IN SPRAY DRIED SOLID DISPERSION TECHNOLOGY

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ABSTRACT

Most of the New Chemical Entities (NCEs) discovered are poorly soluble or lipophilic in nature which can cause poor bioavailability after oral administration. Poor solubility and bioavailability posechallenge in the development of efficient pharmaceutical formulation. The application of solid dispersions is a useful method to increase the dissolution rate of these drugs and thereby improve their bioavailability. Numerous technologies canbe used for development of solid dispersion, among them spray dryingtechnology can be successfully useful for development of product from lab scale to commercial scale dueto rapid solvent evaporation during the process, cost effectiveness,possibility of continuous manufacturing and ease of scalability. In recent time, there is an increased demand from regulatory authorities to implement Quality by Design (QbD) approach in product development stage. Objective behind this is to understand the manufacturing process together to achieve final product within predefined excellence. This review covers the theoretical framework for QbD approach in spray dryingtechnology, the effect of process parameters such as feed flow rate, inlet temperature, outlet temperatureand formulation parameters such as feed composition and feed concentration on critical quality attributes.

KEYWORDS: Spray drying, solid dispersion, Quality by design (QbD), solubility enhancement, selection of polymer and solvent.

INTRODUCTION

It is estimated that most compounds undergoing development at the present time are poorly water-soluble which limit formulation approaches, clinical application and marketability because of their low dissolution and bioavailability. According to the Biopharmaceutical ClassificationSystem (BCS), a drug compound is poorly soluble if the highest dose strength is not soluble in 250 ml aqueous media over the pH ranges at 37°C. These compounds mostly belong to ClassII, which are poorly soluble and highly permeable according to the pH of the gastrointestinal fluid and tend to present solubility or dissolution rate-limited absorption. [2]

Various approaches to overcome the poor aqueous solubility ofdrug candidates have been investigated in drug research and development such as salt formation, prodrug formation, particle size reduction, complexation, microemulsions, nanoemulsions, nanosuspensions, solid–lipid nanoparticle and solid dispersion which is considered one of the most successful strategies to improve the dissolution profile of poorly soluble drugs (Table 1).

Table 1: Solubility enhancing technologies for poorly soluble drugs.

Physical methods	Chemical modification
Particle size reduction (micronization or nanosuspensions)	Salt formation
Polymorphism	Prodrug approach
Change in crystal habit	
Complexation/ solubilisation	
Solid dispersion	

SOLID DISPERSION TECHNOLOGY

Solid dispersion consists of two or more than two components, generally a carrier polymer and drug along with stabilizingagent (and/or surfactant or other additives). Historically, the term “solid dispersion” was defined as a dispersion of drug in a solid matrix where the matrix was either a small molecule or polymer. The dispersed state has included many forms such as eutectic mixtures, crystalline/glass solutions, and amorphous/crystalline suspensions. Taking account of its currently most-used form, a solid dispersion can now be more narrowly defined as dispersion of drug in an amorphous polymer matrix where the drug is preferably in the molecularly dispersed state. In solid dispersion when the drug is molecularly dispersed within a suitablecarrier, mostly polymers, it exhibits a higher apparent solubility and/or a higher dissolution rate compared to crystalline state of thedrug. [9] The most important role of the added polymer in solid dispersion is toreduce the molecular mobility of the drug to avoid the phaseseparation and re-crystallization of drug during storage. The increase in solubility of the

drug in solid dispersion is mainlybecause drug remains in amorphous form which is associatedwith a higher energy state as compared to crystalline counterpartand due to that it required very less external energy to dissolve. Additionally, formation of smallparticle size with better porosity, wettability and surface areaare the main reasons for the improvement in bioavailability.

There are basically two types of solid dispersions depending upon the physical state of the carrier: crystalline and amorphous solid dispersions.Former system contains the crystalline drug dispersed within a crystalline or semi-crystalline carrier. Later system contains a carrier which is amorphous rather than crystalline, and it can be additionally classified into solid crystalline suspension, solid glassy suspension, and solid glassy solution.

The solid dispersions can also be classified into four generations based on their composition as following (Table 2): First generation solid dispersions are prepared usingcrystalline carriers such as urea and sugar, which were the firstcarriers to be employed in solid dispersion. They have thedisadvantage of forming crystalline solid dispersion, which arethermodynamically more stable and did not release the drug asquickly as amorphous ones. Second generation solid dispersions include amorphouscarriers instead of crystalline carriers which are usuallypolymers. These polymers include synthetic polymers such as povidone (PVP), polyethyleneglycols (PEG) and polymethacrylates as well as natural product based polymers such as hydroxylpropylmethyl-cellulose (HPMC), ethyl cellulose, and hydroxypropoylcellulose or starch derivates like cyclodextrins. In the third generation solid dispersions,the surface active agents or self-emulsifiers are introducedas carriers or additives and showed significant improvement inovercoming the problems such as precipitation and recrystallization. The surfactants used as carriers include poloxamer, compritol 888 ATO, gelucire 44/14, inutec SP1 and soluplus. [2] The fourth generation solid dispersion is a controlled release soliddispersion (CRSD) containing poorly water-soluble drugs with ashort biological half-life. CRSD of poorly water-soluble drugs oftenrequires two targets: solubility enhancement and extended releasein a controlled manner. In CRSD, the molecular dispersion of poorly water-soluble drugs in carriers will improve the drug solubility while water insoluble polymers or swellable polymers can be used to retard the drug release in the dissolution medium .The conventional polymers used for retarding the release of poorly water-soluble drugs in CRSD include ethyl cellulose (EC), HPC, Eudragit RS, RL, poly (ethylene oxide) (PEO) and carboxyvinyl polymer (Carbopol).[2]

Table 2: Classification of solid dispersion based on composition.

First generation	Second generation	Third generation	Fourth generation
-Contains crystalline carrier	-Contains amorphous polymer	-Contains surfactant polymer	-Contains water insoluble polymer or swellable polymer
-Low dissolution rate due to crystalline carrier - Low stability	- Increase dissolution rate - Precipitation under supersaturation - Low stability	-Highest dissolution rate -Decrease precipitation under supersaturation - Increase stability	- Increase dissolution rate - Controlled release

There are two main mechanisms of drug release from immediate release solid dispersions: drug-controlled release and carriercontrolledrelease. When solid dispersions are dispersed in water, the carriers often dissolve or absorb water rapidly due to their hydrophilic property and form concentrated carrier layer or gel layer in some cases. If the drug dissolves in this layer and the viscosity of this layer is high enough to prevent the diffusion of the drug through it, the rate limiting step will be the diffusion of the carrier into the bulk phase and this mechanism is carrier-controlled release. If the drug is insoluble or sparingly soluble in the concentrated layer, it can be released intact to contact with water and the dissolution profile will depend on the properties of drug particles (polymorphic state, particle size, drug solubility). Infact, these two mechanisms often occur simultaneously becausethe drug may be partly soluble or entrapped in the concentratedcarrier layer. [2]

Table 3: Preparation methods of solid dispersion.

Melting method Ice bath agitation Thin film cooling Liquid nitrogen Spray congealing Hot-melt extrusion MeltrexTM Melt agglomeration **Melting solvent method**	**Solvent evaporation** Rotary evaporation Heating on hot plate Spray drying Freeze drying Supercritical anti-solvent Co-precipitation Electrostatic spinning Spray freeze drying Ultra-rapid freezing Fluid-bed coating

SPRAY DRYING TECHNOLOGY

Spray drying is a unit operation capable of transforming solutionsor suspensions into a solid product.[1] Spray drying technology can be defined as a unit operation in which a liquid stream (solution, suspension or emulsion) is constantly divided into very fine droplet (by a

process known as atomization) into a glass compartment where they come in contact with hot gas and get dried into fine particles, which are further separated from the drying gas using a cyclone or a bag-filter. It's a moderate drying technique where gentle temperatures and little exposure times are used (as compared to other solid dispersion technology like melt extrusion) that yields powder with reasonable particle. Moreover, the fast drying process within few seconds or milliseconds is also important to prevent phase separation between the drug and polymer components.

The spray drying process consists of four basic stages: atomizationof the liquid, mixing of the liquid with the drying gas, evaporation of the liquid and separation of the dried particles fromthe gas. The liquid solution or suspension is transported from thecontainer to the nozzle entrance via a pump system.[1]

To fully understand the characteristics of spray-dried powders, one needs to examine the mechanism for drying within a single droplet (Figure 1). Typically, there are many very small particles suspended in a sphere of liquid. When the droplet is first exposed to hot gas, rapid evaporation takes place. Material dissolved in the liquid will tend to form a thin shell at the surface of the sphere. Although the evaporation has kept the particle itself quite cool, as the liquid concentration decreases, the particle will begin to heat. Evaporation then takes only as quickly as the liquid can diffuse to the surface of the sphere. This phase of the drying process is called first-order drying or is said to be diffusion-rate-limited.

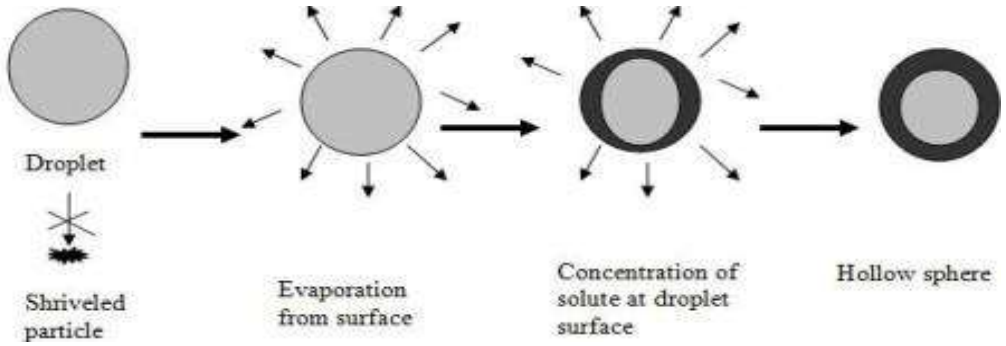

Fig. 1: Mechanism of drying of SDD

Spray driers can operate in open cycle mode for aqueous based or in closed-loop mode for organic based system.The solvent ismostly aqueous, but in case of solid dispersion preparation, organicsolvents are mainly used. In case of using organic solvents in the feed, inert drying gases are used (e.g. dry nitrogen) in combination with a closed-cycle setup.[1]

Selection of polymerfor spray dried dispersion (SDD)

With the aim to accomplish the desired solubility and stability ofamorphous form of drugs, selection of right polymer(s) or carrier(s) is required in the initial stage of formulation development.The ideal polymer to formulate as SDDs are identified by their physicochemical properties like glass transition temperature (Tg) of polymer, nature of polymer (anionic/cationic) and presence of functional group, hygroscopicity of polymer, solubility in common organic solvent, thermal stability, etc.Some polymers work as a wetting agent tosolubilize the released drug, where as others will also help to stabilize the supersaturated drug solution. The existence of useful moieties like hydrogen donors or acceptors is a surplus advantage which helps to inhibit crystallization of a drug from a glass solution. Generally physical instability or nucleation occurs below Tg of polymer due to higher molecular mobility, so polymer with higher Tg value is usually preferred in solid dispersion to improve shelf life of final formulation. Polymers can boost the physical stability of system by increasing the Tg of miscible mixtures and for that it should be also molecularly miscible with drug. There are numerous carriers like enteric polymers, hydrophilic polymers, amphiphilic polymers and surfactants are used in spray drying technology.

Table 4: List of carriers used for SDD.

Carriers	Example
Enteric polymers	Methylacrylate polymers, hydroxypropyl methyl cellulose phthalate (HPMCP), Cellulose acetyate phthalate(CAP)
Hydrophilic polymers	Starch, Sodium carboxy methyl cellulose, sodium alginate, polyethylene glycol(PEG), polyvinyl pyrollidone(PVP), β-cyclodextrin
Surfactants	Lecithin, polyethylene-polypropylene glycol, bile salt
Amphiphilic polymers	PEG modified starches, polyethylene oxides/polypropylene glycol copolymer, polyacrylic acids and polyacrylates

Solvent systems for SDD preparation

Selection of an acceptable solvent system is an equally important prerequisite for the formation of amorphous SDD. The first indispensablecondition is indeed to find out a common solvent(s)system to solubilize all feed components viz., API, carrier and otheradditives.[1]

The basic criteria for the selection of spray drying solventsystem include-

- high solubility of drug and carrier in theselected solvent (>50 mg/ml),

- the generation of a feed solutionwith acceptable viscosity,
- low toxicity
- high volatility for the ease of solvent evaporation during droplet drying,
- appreciable chemical stability offeed components in the selected solvent and
- non-combustive in spray drying environment

In general, lower boiling solvents are very easy to evaporate and it results in higher solid production yield. The addition of a co-solvent can increase the solubilityof hydrophobic molecules by reducing the dielectricconstant of the solvent.

Table 5: List of commonly used solvents for SDD.

Solvents	Boiling point(°c)	Density(g/ml)	Dielectric constant	Solubility in water(g/100g)
Methanol	64.6	0.791	32.6	Miscible
Ethanol	78.5		24.6	Miscible
Acetone	56.2	1.049	20.7	Miscible
Chloroform	61.7	1.498	4.81	0.795
Methylene chloride	39.8	1.326	9.08	1.32
Dimethylsulfoxide	189	1.092	47	25.3
Water	100	0.998	78.54	-
Ethyl acetate	77	0.895	6	8.7

QUALITY BY DESIGN (QBD) APPROACH IN SPRAY DRYING

The modern concept of the pharmaceutical quality systems focuses on the pharmaceutical development based on the concept of Quality by design (QbD). ICH Q8 defines quality as "The suitability of either a drug substance or drug product for its intended use. This term includes such attributes as the identity, strength, and purity." ICH Q6A[15] emphasizes the role of specifications stating that "Specifications are critical quality standards that are proposed and justified by the manufacturer and approved by regulatory authorities."

Pharmaceutical QbD is a systematic, scientific, risk-based, holistic and proactive approach to pharmaceutical developmentthat begins with predefined objectives and emphases product and processes understanding and process control. [5] It means designing and developing formulations and manufacturing processes to ensure predefined product quality objectives. QbD identifies characteristics that are critical to quality from the perspective of patients, translates them into the attributes that the drug product should possess, and establishes how the critical process parameters can be varied to consistently produce a drug product with the desired characteristics. In order to do this the relationships between formulation and

manufacturing process variables (including drug substance and excipient attributes and process parameters) and product characteristics are established and sourcesof variability identified. This knowledge is then used to implement a flexible and robust manufacturing process that can adapt and produce a consistent product over time. [16]

Following are the key steps involved in QbD:

- Defining the quality target product profile(QTPP).
- Identifying potential critical quality attributes(CQAs).
- Risk assessment: Linking Material Attributes and Process Parametersto Drug Product CQAs.
- Defining design space.
- Define control strategy.
- Product Lifecycle Management and Continual Improvement.

Quality target product profile (QTPP)

The QTPP forms the basis of design for the development of the product, which may include: intended use in clinical setting, route of administration, dosage form, delivery systems, dosage strength(s), container closure system, dissolution or drug product quality criteria (e.g., sterility, purity, stability and drug release) appropriate for the intended marketed product.

As per the ICH guidance Q8 R2, QTPP is defined as a prospective summary of the quality characteristics of a drug product that ideally will be achieved to ensure the desired quality, taking into account safety and efficacy of the drug product. [5]

Critical Quality Attribute (CQA)

It is defined as a physical, chemical, biological or microbiological property or characteristic that should be within an appropriate limit, range, or distribution to ensure the desired product quality. [5] Identification of CQAs is done through risk assessment as per the ICH guidance Q9. [4] Risk assessment is a valuable science-based process used in quality risk management that can aid in identifying which material attributes and processparameters potentially have an effect on product CQAs. Risk assessment tools can be used to identify and rank parameters (e.g., process, equipment, input materials) with potential to have an impact on product quality,based on prior knowledge and initial experimental data. The risk assessment and process development experiments can lead to an understanding of the linkage and effect of process parameters andmaterial attributes on product CQAs, and also help identify the

variables and their ranges within which consistent quality can be achieved. These process parameters and material attributes can thus be selected for inclusion in the design space.

Use of a risk assessment tool

Ishikawa (fishbone) diagram identifies potential variables which can have animpact on the desired quality attribute. Here the variables are ranked based on probability, severity, and detectability using failure mode effects analysis(FMEA) or similar tools based on prior knowledge and initial experimental data.Design of experiments or other experimental approaches could then be used toevaluate the impact of the higher ranked variables, to gain greater understanding ofthe process, and to develop a proper control strategy.[5]

Following is an example of Ishikawa diagram for spray drying operation: [8]

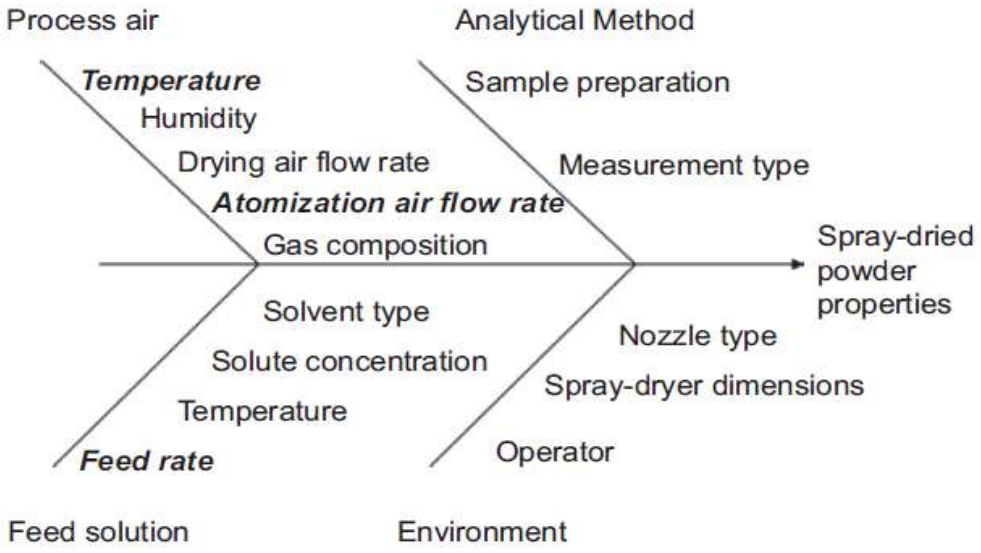

Fig 2: Ishikawa diagram for spray drying operation.

Design Space

The relationship between the processes inputs (material attributes and process parameters) and the critical quality attributes can be described in the design space. Design space can be defined as the multidimensional combination and interaction of input variables (e.g., material attributes) and process parameters that have been demonstrated to provide assurance of quality. [5]A design space can be described in terms of ranges of material attributes and process parameters, or through more complex mathematical relationships. It is possible to describe a design space as a time dependent function (e.g., temperature and pressure cycle of a lyophilisation cycle), or as a combination of variables such as components of a multivariate model. Design space is proposed by the applicant and is subject to regulatory assessment and

approval. Working within the design space is not considered as a change. Movement out of the design space is considered to be a change and would normally initiate a regulatory post approval change process.[5]

Control Strategy

A control strategy is designed to ensure that a product of required quality will be produced consistently. It is defined as a planned set of controls, derived from current product and process understanding that ensures process performance and product quality. The controls can include parameters and attributes related to drug substance and drug product materials and components, facility and equipment operating conditions, in-process controls, finished product specifications, and the associated methods and frequency of monitoring and control.

Product Lifecycle Management and Continual Improvement

Throughout the product lifecycle, companies have opportunities to evaluate innovative approaches to improve product quality. Process performance can be monitored to ensure that it is working as anticipated todeliver product quality attributes as predicted by the design space. This monitoring could include trend analysis of the manufacturing process as additional experience isgained during routine manufacture.

Case studies

Maltesen M.J. et al[6] have investigated the effects of processand formulation parameters on particle characteristics and insulin integrity.Design of experiments (DOE) and multivariate data analysis were used by them to identify important processparameters and correlations between particle characteristics. The independent parameters includedthe process parameters nozzle, feed, and drying air flow rate and drying air temperature along withthe insulin concentration as a formulation parameter. The dependent variables included droplet size, geometricparticle size, aerodynamic particle size, yield, density, tap density, moisture content, outlet temperature,morphology, and physical and chemical integrity. Principal component analysis was performed by them to find correlations between dependent and independent variables. Prediction equations were obtainedfor all dependent variables including both interaction and quadratic terms. Overall, they have concluded that the insulin concentration was the most important parameter, followed by inlet drying air temperature and the nozzle gas flow rate. The insulin concentration mainly affected the particle size, yield and tap density, while the inlet drying air temperature mainly affected the moisture content. No change was observed inphysical and chemical integrity of the insulin molecule.

Kumar S. et al [8] have applied the Quality by Design (QbD) approach in spray drying process for the conversion of liquid nanosuspensions into solid nano-crystalline dry powders using indomethacin as a model drug. The effects of critical process variables: inlet temperature, flow and aspiration rates on critical qualityattributes (CQAs): particle size, moisture content, percent yield and crystallinity were investigated employing a full factorial design. A central cubic design was employed to generate the response surfacefor particle size and percent yield. Multiple linear regression analysis and ANOVA were employed to identifyand estimate the effect of critical parameters, establish their relationship with CQAs, create designspace and model the spray drying process. Inlet temperature was identified as the only significant factor(p value <0.05) to affect dry powder particle size. Higher inlet temperatures caused drug surface meltingand hence aggregation of the dried nano-crystalline powders. Aspiration and flow rates were identifiedas significant factors affecting yield (p value <0.05). Higher yields were obtained at higher aspiration andlower flow rates. All formulations had less than 3% (w/w) moisture content. Formulations dried at higherinlet temperatures had lower moisture compared to those dried at lower inlet temperatures.

CQAs IN SPRAY DRIED SOLID DISPERSION

Spray drying is a complicated process and understanding the relationship between process parameters and formulation parameters is essential for the reproducible production of high quality material. Process parameters to consider during a spray drying process are: inlet temperature, drying gas properties (humidity, flow rate), feed rate, compressed air flow rate etc. On the other hand, formulation parameters to consider are feed composition (API, carrier, solvent), feed concentration, solvent type etc.[1]

Feed composition

The solubility difference among drug, carrier and other additives in a feed solution (solvent) leads to a different degree of saturation/supersaturation of these components. This would expectedly influence several underlying phenomenaduring droplet drying. Moreover, the excessive gapin temperature dependent solubility between solute componentscan potentially induce radial demixing during particle formation asan insoluble component starts precipitating earlier at the shrinking droplet surface. [1] According to Raoult's law, the partial vapour pressure of the solvent in the feed solution is directly influenced by the solute content which has direct impact on the solvent evaporation rate. More specifically, the polymer content in the feed solution greatly modulates the vapour pressure as polymers are reported to

show an immense composition dependent intermolecular interaction with solvents. The outer skin formation during droplet drying and hencethe retardation of evaporation rate is highly dependent on the solution concentration of carrier having film forming properties like PVP. The other latent feed solution properties that can be altered with the variation in drug to polymer ratio are viscosity, surface tension, specific gravity, pH, etc. This would impact the droplet size (distribution) during spray drying and inturn the rate of solvent removal.[1] The rate of core to surface transportof solvent and then evaporation from a droplet surface decrease with the increase in feed viscosity due to higher fraction and/ormolecular weight of polymer present in solution. [1] Also, breakup length of liquid jet during atomization increases with increasing feed viscosity resulting into larger droplets. The shift in rheological regime of feed solution from Newtonian to non-Newtonian can drastically change the spray rate, droplet size (distribution) and density. Paudel and Van den Mooter observed the marked difference in overall solvent evaporation rate from naproxen-PVPsolutions containing same total solute content but different drugto polymer ratio. [13]The solution state properties such as polymer diffusion coefficient and solute–solvent supramolecular interactions are drastically altered with the different drug to polymerratio. Besides, it is well known, especially from polymer literature, that the influence of composition on non-covalent interactions (dispersive, polar, H-bonding) in metastable solutions is governed by specific ternary interaction attributes among two solutes and solvent rather than binary parameters Therefore, polymer folding/unfolding and dispersed state of drug in solution (monomer or multimer) as a function of composition are key attributes for the unique solid state structure in SDD. [13] These facts imply the utmost importance of composition dependent solution dynamics in predictingthe phase behaviour of the resulting SDD.

Feed concentration

Typical feed concentration used for the preparationof amorphous pharmaceutical solid dispersion preparation ranges from 10 to 20% (w/v).[1] With increasing feed concentration, higher drop in evaporation rate and hence drying is expected compared to pure solventor dilute solution. At particle level, lower solute content in feed solution typicallygenerates spherical and smaller particles. The increased hygroscopicity due to the higher effective surface area (smaller particle size) of amorphous solid dispersions prepared from dilute feed solutions led to the decrease in physical stability despite of their slower relaxation behaviour. In contrast, larger particles are generated from concentrated and hence viscous solutions due to the formation of larger droplets. It is well known that the geometric mean diameter of

spray dried particles is directly proportionalto the feed concentration. Additionally, it is reported that a concentrated feed solution may also lead to the formation of hollow spray dried particles with rough surface, higher porosity andbulk density. The feed concentration effecton the surface morphology depends upon the chemical nature offeed solution components.

The process yield increases when the feed concentration increases, but starts to decrease at higher (above the experimental range) feed concentrations. These phenomena can be explained by the fact that, at higher feed concentrations there could be an increase in tendency of droplets to coalesce on collision with each other or the wall, which might result in a lower yield. On the other hand according to Raoult's law the evaporation rate is inversely proportional to the feed concentration, owing to a decrease in the evaporation rate at high feed concentrations. These could increase the adhering tendency of particles at higher feed concentrations due to insufficient drying and could result in a loweryield. A lower process yield from a dilute solution is generallydue to the formation of smaller particles which are highly electrostatic and have increased wall adhering tendencies and thuscould be difficult to collect using a cyclone.

Feed flow rate

The feed rate is the foremost parameter to start with for attaining the balance between throughput and proper drying considering the drying capacity of a particular spray drier set up. Apart from the atomization pattern and droplet size (distribution), feed rate primarily governs the time period a particle remains in the drying chamber, conveyer, cyclone and bag filters during the spray drying operation. As feed rate directly affects the saturation degree of exiting gas, it influences the outlet temperature at the given drying set up. Therefore the upper limit of flow ratefor a given feed solution is set to attain sufficient drying of the particles before they hit the spray dryer wall.

Inlet and outlet temperature

The temperature of the drying gas encountering the droplets of the atomized feed is considered as the most important determinantof the internal structure of the resulting spray dried particles. Next to feed solution development and feed rate setting, optimizationof inlet temperature is crucial to attain the targeted outlet temperature. Having directimpact on solvent evaporation kinetics from the drying droplet,it is a primary process variable

responsible for the development of the unique phase structure and controlling the level of residual content and bulk/particulate level properties of the final product.

Outlet air temperature is one of the most critical parameters which exclusively affect the product morphology like particlesize, surface roughness, density, stickiness of particles, residual solvent or moisture levels, product yield, etc. Outlet temperature of drying gas is the derived process parameter dependent upon inlet temperature, drying gas flow rate and enthalpy of evaporation of solvent in feed. After performingspray drying process, secondary drying of powder is generallyrequired to remove the excess residual solvent because, presence of solvents may plasticize the solid dispersion by increasing molecular mobility and it results in the development ofcrystal growth. Spray drying process carried out at a loweroutlet temperature gives a product with high residual solventlevels and poor flow property. The overall process efficiency of spray drying is highly dependent on the ratio of inlet to outlet temperature.

CONCLUSION

Spray drying is a time-tested manufacturing process for amorphous solid dispersion of poorly water soluble drugs. The understanding on the influence of various formulation and process parameters on the molecular to particulate/bulk level properties of spray dried dispersions is the current need in this field. Spray drying process involves interactions between various formulation variables (like feed concentration, solvent type, type of polymer) and process conditions (drying gas flow rate, feed rate, outlet temperature, atomization rate) which can significantly influence the particle characteristics (yield, particle size, residual solvent content, flow property, surface area and release profile) of the solid dispersion. Thus the implementation of QbD approach in the drying of feed solution containing poorly water soluble API, polymer and additives can result in the robust process development and subsequent scale up with the desired product properties as per predefined objectives.

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