IJPSR (2017), Vol. 8, Issue 4 **(Review Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 20 September, 2016; received in revised form, 23 December, 2016; accepted, 08 January, 2017; published 01 April, 2017

APPLICATION OF SPRAY DRYING TECHNIQUE FOR PREPARATION AMORPHOUS SOLID DISPERSION

Bhushan N. Phapale [*1] and Aniket P. Patil [2]

Macleods Pharmaceuticals Ltd [1], G2 Saket Bldg, Mahakali Caves Rd, Shantinagar, Andheri (E), Maharashtra - 400093, India.
Indoco Remedies Ltd [2], R92/93, TTC MIDC, Thane-Belapur Rd, Rabale, Navi Mumbai, Maharashtra - 400701, India.

Keywords:

Amorphous Solid Dispersion, Spray Drying, Process Parameters, Poorly Water Soluble Drugs

Correspondence to Author:
Bhushan N. Phapale

Macleods Pharmaceuticals Ltd,
G2 Saket Bldg, Mahakali Caves Rd,
Shantinagar, Andheri (E),
Maharashtra - 400093, India.

E-mail: bhushan.phapale17@gmail.com

ABSTRACT: As time passes more and more poorly water soluble drug are being discovered. Formulating these drugs in to amorphous solid dispersion is an effective strategy to deliver poorly water soluble drugs. Spray drying is one of common and a well-established manufacturing technique which can be used to formulate amorphous solid dispersions (ASDs). However, the spray drying is complex phenomenon and the spray drying process parameters yield the ASD with specific characteristics. Various diverse factors interact in an inter-dependent manner to determine the final product properties. This review discusses the basic background of spray drying, and various aspects of spray drying such as instrumentation, thermodynamics, drying kinetics, particle formation process and scale-up challenges are included. Recent advances in the spray-based drying techniques are mentioned along with some future avenues where major research is needed.

INTRODUCTION: Due to the recent advancement in drug discovery more and more drug molecules, which can be categorized under Biopharmaceutics classification system (BCS) class 2 or 4 [1], **Fig. 1**. The use of non-aqueous (or solvent mixture) based media for screening and purification purposes in high throughput screening tend to give hits with higher molecular weight and lipophilicity [2, 3]. The goal for identification and targeting of kinase pathways, ion channels, nuclear receptors and protein–protein interactions with potent and selective agents is also motivating the choice towards lipophilic compounds [4, 5].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.8(4).1541-49

Article can be accessed online on: www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.8 (4).1541-49

Apart from chemistry based strategies to improve solubility, responsibility is on formulation scientists to provide enabling drug delivery strategies for such candidates. For a compound to reach to its target site, it should first be dissolved in the gastrointestinal (GI) fluid [6]. The dissolution rate at which this happens is given by the Nernst Brunner equation [7].

$$\frac{dC}{dt} = \frac{SD(Cs - Ct)}{Vh}$$

Where,
dC/dt is dissolution rate of the drug,
S is surface area of the dissolving surface,
D is diffusion coefficient of the drug,
Cs is saturation solubility,
Ct is concentration at time t,
V is volume of dissolution medium and
h is the thickness of the diffusion layer surrounding the dissolving particle.

In vivo drug release, the two factors cannot be modified; they are diffusion coefficients of the drug and dissolution medium volume. Thus, the strategies focus on altering solubility and/or surface area. Solubility and surface area can be modified by converting poorly soluble drugs in amorphous form. In the amorphous form, the crystalline form of the drug is converted to amorphous state which has higher solubility compared to crystalline form due to excess thermodynamic properties. In amorphous state, there is no energy requirement to break the crystal lattice structure so that the drug molecules can interact with solvent molecules through intermolecular interactions and become solubilized. But the amorphous form has tendency to crystallize thereby negating the solubility advantage due to excess thermodynamic properties. This issue can be resolved by formulating them in amorphous solid dispersion (ASD).

ASDs consist of drug molecules dispersed in polymeric carriers. The drug stabilization is a consequence of factors such as intermolecular interactions, physical barriers to the crystallization process (local viscosity), anti-plasticization effect exerted by the polymer and the reduction in chemical potential of the drug [8]. ASD can be prepared by various methods such as milling, hot melt extrusion and spray drying [9]. This review focuses on use of spray drying for preparation of ASD's.

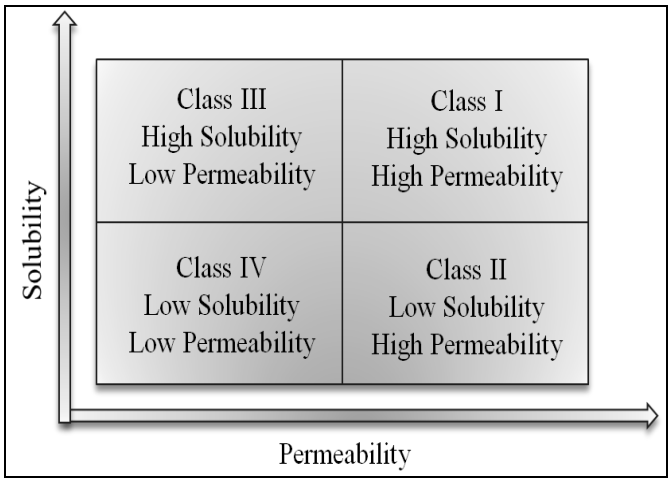

FIG. 1: BIOPHARMACEUTICAL CLASSIFICATION SYSTEM

Spray drying process: Spray drying is an continuous, energy intensive and scalable drying process [10, 11]. The process can generate micron to nano size particles that have a narrow distribution in a very short time-frame. For the context of this review, spray dryer equipment is a solid state transforming reactors where the crystalline starting material is converted into amorphous product. The first patent of spray drying process is more than 140 years old, wherein it was described as a process for simultaneously atomizing and desiccating fluid and solid substances. The process was meant for exhausting moisture and to prevent destructive chemical change.

Historically, the spray drying process has been most extensively used in food and chemical industry. However, its use quickly expanded to other industries such as cosmetics, fabrics and electronics. The first use of this technique in the pharmaceutical field was for the manufacture of pure API. From there on it has been used ever increasingly for various specialized applications such as microcapsules, composite microparticles, nanoparticles, controlled release particles, and liposomes [12]. The spray drying process sequentially involves several steps as shown in **Fig. 2**. Firstly, the feed solution/suspension is pumped into the drying chamber through a nozzle. The solution from the nozzle tip the droplets are atomized and come in contact with the drying fluid i.e., hot gas (often air) inside the drying chamber. The residence time inside the drying chamber depends on the process parameters and the equipment dimensions and may normally last for a few milliseconds. During the transit through the drying chamber energy-mass transfer takes place at the dynamic droplet surface. Finally, the dried material is separated from the drying medium using a cyclone and is collected in a collection device. The exhaust gases are filtered via HEPA filters. To accomplish the abovementioned steps, various parameters are used as described below.

The choice of the feed pump used depends on the viscosity of the feed material and the type of atomizer system used [13]. Rotary atomizers or bi-fluid nozzles uses low pressure pumps. Pressure nozzles necessitate the use of high pressure pumps. Various atomizer designs are available in market and use different kinds of forces input to obtain fine droplets [14]. Atomizers can be either rotary, pneumatic hydraulic (pressure), or ultrasonic nozzles.

In rotary atomizers, centrifugal force is responsible for breaking down of the liquid stream into small droplets. Modification in the rotary atomizers such as straight or curved grooves provides opportunities for particle engineering [13, 15]. When using this atomization set-up care should be taken to use drying chamber of sufficient length. For expensive drugs, material adhesion to the drying chamber walls can be a limiting factor. Bi-fluid or multi-fluid nozzles utilize the pressure energy and can be used with narrow chambers. In pneumatic nozzles kinetic energy of the compressed carrier gas is transferred to the liquid surface at a central collision point causing droplet formation. Ultrasonic nozzles use vibrational energy for atomization but still find limited use in industrial settings due to their low throughput [16].

The atomized droplets encounter the drying air in the drying chamber. The air-droplet contact system can be of counter-current, concurrent or mixed flow type. Cocurrent contact system is most widely employed for pharmaceutical purposes [17]. The residence time needed in the chamber and its dimensions is determined by the droplet size distribution generated by the atomization set-up[18].

The particle collection can take place at the bottom of the drying chamber from where it needs to be scrapped. Scrapping devices such as vibratory devices, mechanical brushes and/or compressed air might be used [14]. It has been shown for lab-scale spray dryers that drug–polymer miscibility varies with location from which the product is collected [19]. Although in large scale spray dryers there are no reports of such variability, such a scenario is not impossible. Therefore, caution should be exercised while using scrapping devices for ASD as it might induce mixing of the product with different degrees of phase behavior. Likewise, mechanical brushes employing ‘stress’ might possibly result, in the change of phase behavior of binary solid dispersions [20-23].

Such issues can be avoided by an additional design feature in the drying chamber i.e., a cone shaped bottom part which assists in flow of the product. Bag filters and cyclones are widely used as a separation device. Typical cyclones used in pharmaceutical settings are reverse-flow; gas–solid separators wherein the centrifugal force drives the separation of two phases with different mass. The centrifugal flow is generated because of the tangential entry of the gas–solid mix into the cyclone body. As the gas moves down in the swirling flow the particles experience centrifugal force and get deposited on the cyclone walls as a result of particle inertia. Particles further settle down due to gravitational force and motion of the boundary layer. Finally, the direction of the glass flow reverses as the gas phase hits the cyclone bottom. The gas now moves via a reverse vortex through the central axis of the cyclone to the gas outlet at the top of the cyclone [24]. All of the abovementioned steps have a crucial impact on the drying efficiency of the process and therefore can majorly impact the solid state properties of ASD.

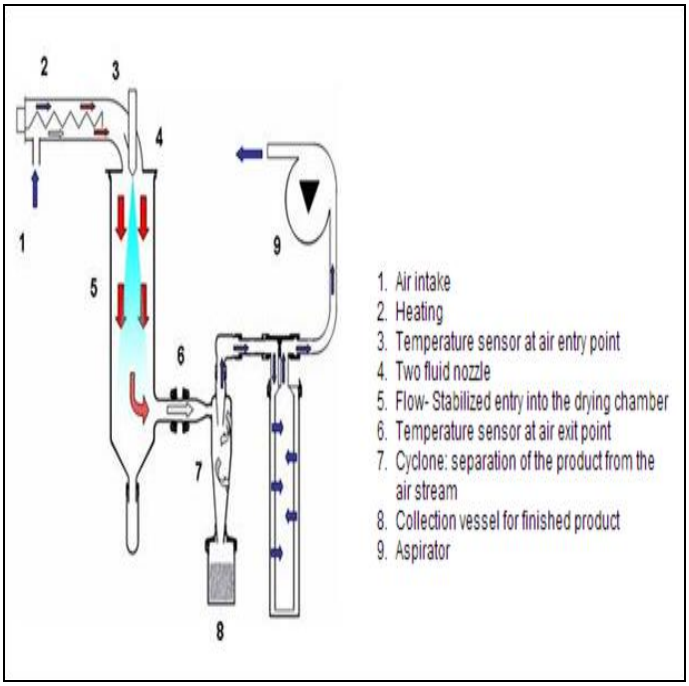

FIG. 2: GENERAL SPRAY DRYING INSTRUMENT

Thermodynamics of spray drying: In the spray drying process, both mass transfer and the heat along with their temporal and spatial aspects determine the final product features. The atomization has the crucial impact since, it involves the generation of a large surface area over which heat and mass transfer takes place.

Drying kinetics: Initially, the mass transfer from the atomized feed suspension/solution is similar to that of a pure solvent droplet [25, 26]. The migration of the solvent to the droplet/ solid particle surface can be mediated through molecular diffusion from high concentration in the central droplet region to the

lower concentration at the surface, convection of moisture within the droplet, via evaporation within a solid and subsequent gas transport out of the solid by diffusion and/or convection and capillary flow [27]. Upon reaching critical moisture content the 'falling rate period' commences. During the switch from constant to falling drying rate period over time, the droplet temperature shifts from close to the thermodynamic wet-bulb temperature to the dry-bulb temperature. Hence, for some initial part of the drying period the droplet and its content are safe from the high drying temperatures. In the constant drying rate regime, the solvent evaporation rate is driven by the heat transfer to the droplet.

This is accompanied by an increase in the humidity of the carrier gas which slows down particle formation rate. As more and more solvent evaporates, the evaporation rate into the gas medium is dominated by the solid content in the droplet. The reason for the shift from constant to falling drying period is because throughout the droplet journey in the drying chamber, its viscosity increases. At a certain point the solidification at the droplet surface takes place hindering the solvent escape from the droplet. From the stand-point of the amorphization of the dissolved drug, the drying rate can be a critical factor in determining whether the substance is completely crystallized or not, especially in the case of poor glass formers. Also, the time-period for which the drying mass is exposed to dry-bulb temperature can be critical for the stability of the amorphous form which is susceptible to high temperature. Therefore, adequate care should be taken to control the drying kinetics for generating amorphous product.

The effect of the process parameters and particle formation: The formation of smooth spherical particles is just one of the various kinds possibly formed using spray drying. The millisecond time scale between the droplets to particle transition is anxious with competitive dynamic events, all of which impact the final morphology of the particle. The particle attributes embraced by the term 'particle morphology' include size, shape, and structure and surface properties. The theoretical framework behind the empirical evidence is based on equations describing the link between process parameters, product attributes and material characteristics [28].

A generalized view-point on the particle formation process involves three stages. Before stage 1 is initiated, the droplet undergoes rapid heating with no mass change [29-31]. In stage 1, solvent evaporation starts and results in a decreasing droplet surface. The concentration gradient between the droplet surface and core also drives solute movement inside from the surface [32]. Nevertheless, the solute diffusion is often not able to follow the reduction in droplet diameter and shell formation takes place in stage 2. The solvent evaporation continues from the surface and further from the interior of the droplet [29]. This added droplet surface enhancement thickens the crust thus resisting mass transfer. Any heat transfer to the droplet at this stage increases the particle temperature. The reduction in moisture level only takes up to a certain minimum level identified as bound solvent which cannot be removed by drying or equilibrium moisture content [30].

Since the shell resists the solvent evaporation after a certain stage, there is internal pressure build-up inside the particle. Depending on the strength, thickness of the shell and internal pressure build up it can burst, inflate or crack [33]. In the final stage 3, the droplet experiences drying where there is no mass change. Various spray drying process parameters significantly impact the particle formation process [34]. The process variables include inlet temperature, feed rate, atomization parameters and drying gas flow rate. Feed solution variables such as solution dynamics of the feed and drug/polymer ratio and feed concentration, also significantly impact the quality attributes of the product.

The critical physical parameters which lie at the core of the process and feed variable induced changes are vapor pressure, evaporation rate, drying time, crystallization rate, film formation rate, droplet size/distribution, heat/mass transfer and outlet temperature. At a particulate/bulk level, the basic properties affected are particle shape, particle size, surface smoothness, and breaking strength. Related derived properties affected are bulk density, compressibility and flowability.

The flowability can be an issue if commercialization is desired. The flowability can be improved by further granulation of the powder [35].

Feed variables: Modulating feed parameters is an important influencing factor in a successful spray drying operation. Spray drying feed for preparing ASD typically contains three important components: the pure API(s), carrier(s) and the solvent(s) and other additives. Under appropriate assumptions, some scientist have identified critical factors of this multi-component system in the Stokes–Einstein equation [36].

$$D = \frac{K_B T}{6\pi\eta r}$$

where,
D is the diffusion coefficient,
KB is the Boltzmann constant (1.38 × 10−23 m2 kg s−2 K−1),
T is the absolute temperature,
η is the viscosity of the solution and
r is the globular radius. Various aspects of the spray drying feed is discussed below.

Solvent system: Various solvents, together or in combination, have been employed to prepare feed solutions for spray drying. These solvents are aqueous, alcohols (methanol, ethanol or isopropanol) or other organic solvents such as dichloromethane (DCM), acetone, methyl ethyl ketone, dioxane, tetrahydrofuran (THF), chloroform, ethyl acetate, and acetonitrile. Amongst these, DCM is the most commonly utilized for preparation solvent system despite its toxicity potential [34]. DCM has low boiling point (39.8 °C), high volatility and excellent solubilizing power for various drug and polymers. Common solubility of feed components in a solvent is critical to obtain molecularly dispersed solid dispersions.

Incomplete solubility, precipitation or inhomogeneous mixing in the blend may be frozen due to high viscosity as a result of fast drying and eventually produce inhomogeneous component distribution in solid dispersions. Some solid dispersion carriers are hydrophilic in nature and not completely soluble in organic solvents. Often, solvent mixtures such as alcohol–water [37], alcohol–DCM [38], and acetone–methanol [39] are used to overcome this issue. A water–ethanol–DCM mixture was used to solubilize itraconazole and polyvinyl alcohol–polyethylene glycol graft copolymer (Kollicoat IR) having different solubility spectra and ASD was obtained [40]. Choice of the mixture components and their ratio is critical as some combinations can result in reduction the drug release and different morphology [41]. Naproxen–PVP solid dispersions were found to have better miscibility when DCM–acetone solvent mixture was used followed by methanol–acetone and DCM–methanol [42]. This study showed that spray drying from solvent/anti-solvent mixture resulted in solid dispersions with greater drug–polymer miscibility, higher physical stability and lesser crystallinity than when using a mixture of good solvents [43].

Influence of solute components in feed solution: Solvent evaporation is an energy intensive process. One of the obivious consequences of the addition of a solute is that thermal efficiency increases with solid content as less solvent has to be evaporated [26]. Solute properties are equally important as a lot of feed solution properties such as viscosity, evaporation rate, pH, depend on the solute and its concentration in the feed. Physical properties of a solvent such as its boiling point, vapor pressure and freezing point are affected upon addition of solute [44]. This process is entropy driven, lowering of vapor pressure of the solvent in the feed solution due to the presence of solute particles. It follows that this colligative phenomenon will be affected by the presence of the carrier and the drug. Boiling point of the solvent which is directly related to the evaporation rate is elevated by addition of solute. It has been demonstrated that addition of PVP in solvent systems consisting of various volumetric combinations of methanol, DCM and acetone showed concentration dependent deviation in evaporation rate of feed solution compared with that of the pure solvent mix owing to interaction of solvents with PVP [42, 45].

Such changes in concentration are also reflected in the tap density, morphology and relaxation behavior of the final particles. The atomization of concentrated feed often leads to large diameter droplets resulting in coarser particle size and high particle density [46, 47].

Interestingly, Littringer et al. found that influence of feed concentration on the droplet size at high atomizer revolution rates is less [48]. This is also an example of possible complex interaction between various process parameters (in this case between feed concentration and atomizer revolution rate). The changes upon varying process parameters are not limited to bulk level changes only but are also reflected at the molecular level.

Process parameters: Various spray drying variables such as feed flow rate, inlet and outlet temperatures, drying and atomization gas type, and the atomization nozzle type and flow rate influence the CQA of the spray dried ASD. For instance, process parameter alterations can vary the crystallinity of the spray dried material thereby affecting porosity, flowability, solubility, sorption characteristics, dissolution rate and bioavailability [49]. In the following sub-sections, the influence of varying process variables is described in detail. However, all these paramters have an interactive and complex relationship on the influence on spray dried material. If there are two interacting factors, then the value of one factor on the target value can be dependent on the set-value of the other factoralso. More than two factors can also be involved. For instance, particle size is result of feed concentration, droplet size, drying air temperature and feed rate [48].

Feed flow rate: The rate at which the feed is injected influences the droplet size, droplet velocity and its distribution [50]. Thermodynamically, feed injection can be viewed as mass transfer into a particular drying gas volume which will have a direct effect on the outlet temperature. As the feed rate is increased, the outlet temperature decreases. Feed rate also determines the duration of the process for which particles are exposed to high temperatures. This is particularly relevant in the lab-scale equipment of non-continuous nature. Feed rate can impact the particle surface topography [48]. An increase in feed flow rate caused a reduction in particle size and crystallinity of the artemisinin–maltodextrin microparticles [51]. The smaller droplets were direct consequence of higher energy supplied for breaking the droplets. Increase in feed flow rate and pressure also resulted in a reduced heat of fusion[52].

Inlet and outlet temperatures: The inlet/drying temperature directly affects the heat and mass transfer phenomenon in the spray drying droplet. The mass and heat transfer does not remain purely convective–diffusive and convective– conductive, when the drying temperature is changed from low to higher than solvent boiling point [53]. The temperature and the moisture gradients generated inside the droplet due to higher temperatures can influence the particle formation process, which in turns create moisture gradients inside the droplet [47]. This can affect the morphology of the dried particle. Temperature variation results in different surface properties and shape such as particle roughness [48, 54]. Higher inlet temperature results in enlarged particle diameter [51]. Skin formation at the droplet surface can take place due to high inlet temperatures leading to solvent entrapment. The outer skin can be destroyed by solvent evaporation. Increased agglomeration at higher inlet temperature has also been hypothesized to cause an increase in particle size. A higher drying temperature leads to a quicker drying due to more heat transfer into the drying droplet [55]. This has two effects on the fate of the droplet. From a solid state viewpoint, for glass-forming materials faster drying (/cooling) rate results in enhanced conversion of the equilibrium fluid state into the non-equilibrium solid state.

Atomization and drying gas type and flow rate: Atomization and drying gas type are very crucial in the spray drying process, it can potentially influence the droplet size, number density, and velocity, ultimately affecting the characteristics of the final product [56, 57]. Various kinds of atomization gases such as air, N_2, CO_2 and Ar have different physical properties which are important for the atomization process. Atomization gas property such as specific heat capacity and density are critical for the atomization process. The sorption behavior of the samples atomized and dried by different gases also varies due to changes in particle size and/ or shape and crystallinity variation. When considering a gas as a drying medium, mass transfer and heat becomes an important factor. The mass flow rate, specific heat and temperature differential of the drying gas determine the energy lost in the evaporation process [58]. Some scientist proved that CO_2 provides better heat and mass transfer than air and N_2 [59].

To avoid product oxidation, inert atmosphere can be obtained by using N_2 as the drying gas [60]. Also process yield can vary significantly with different drying mediums for spray drying. Closed loop drying mediums such as N_2 and CO_2 gases resulted in a lower yield of 40% of lactose powder as compared with 70% when air was used as a drying medium due to lower absolute humidity in the latter [61]. The drying gases such as CO_2 can act as a plasticizer can potentially alter solid state behavior. The plasticization function depends on the solubility of the gas in the polymer which will be different for different gases and this may affect the properties of spray dried material.

CONCLUSION: Spray drying is a versatile technique which has been employed extensively for generating amorphous forms of drugs, as an efficient drying technique and particle engineering. This process has certain weaknesses such as poor flowability of the resulting powder making downstream processing challenging, and the need for a secondary drying step to remove residual solvent. The microstructure of ASD is extremely critical for their performance. Since formulation component and process parameters have a significant effect on stability and release profile, a series of experiment will be required establish which conditions are most useful for generating a homogeneous solid dispersion. The use of experimental design strategy is an enormous respite. But future research needs to establish a well-defined link between ASD microstructure along with its performance and the formulation and process parameters. One important avenue which needs to be explored further is the role of solution state drug carrier interactions, factors affecting them and how they are related to the strength of the solid state interactions between components at molecular level. It is a well-known fact that drug-carrier H-bonding is very important for ASD stability.

However, not much research have been conducted regarding the impact of various nozzle types, atomization rate and drying temperature on the interactions in the liquid state and whether it can be translated into differences in solid-state interactions. Some research has been done relating the transition of solution state interactions to solid state during spray drying but further knowledge would aid in alteration the process to enhance the stabilizing intermolecular interactions.

Additionally, there is an increasing attention to the effect of downstream processing on ASD stability. However, not much is known about the exposure of the ASD to the compressive stress and the role of drug–polymer interactions. Such information would aid in better informed downstream processing decisions for susceptible systems. Obtaining ASD product which requires minimum downstream processing is an ideal scenario and can be investigated further.

REFERENCES:

1. Amidon GL, Lennernäs H, Shah VP, Crison JR: A theoretical basis for a biopharmaceutic drug classification: the correlation of in vitro drug product dissolution and in vivo bioavailability. Pharmaceutical research 1995; 12(3):413-20.
2. Lipinski CA, Lombardo F, Dominy BW, Feeney PJ: Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. Advanced drug delivery reviews 2012; 64:4-17.
3. Lipinski CA: Drug-like properties and the causes of poor solubility and poor permeability. Journal of pharmacological and toxicological methods 2000; 44(1):235-49.
4. Keserű GM, Makara GM: Hit discovery and hit-to-lead approaches. Drug discovery today 2006; 11(15):741-8.
5. Wells JA, McClendon CL: Reaching for high-hanging fruit in drug discovery at protein–protein interfaces. Nature 2007; 450(7172):1001-9.
6. Williams HD, Trevaskis NL, Charman SA, et al.: Strategies to address low drug solubility in discovery and development. Pharmacological reviews 2013; 65(1):315-499.
7. Dokoumetzidis A, Macheras P: A century of dissolution research: from Noyes and Whitney to the biopharmaceutics classification system. International journal of pharmaceutics 2006; 321(1):1-11.
8. Surikutchi BT, Patil SP, Shete G, Patel S, Bansal AK: Drug-excipient behavior in polymeric amorphous solid dispersions. Journal of Excipients and Food Chemicals 2013; 4(3):70-94.
9. Chaudhari SP, Dave RH: Evaluating the Effects of Different Molecular Weights of Polymers in Stabilizing Supersaturated Drug Solutions and Formulations Using Various Methodologies of the Model Drug: Fenofibrate. Journal of Pharmaceutical Sciences and Pharmacology 2015; 2(3):259-76.
10. Kemp IC: Fundamentals of energy analysis of dryers. Modern Drying Technology 2011; 4:1-46.
11. Mujumdar AS: Handbook of industrial drying: Crc Press; 2014.
12. Parikh DM: Handbook of pharmaceutical granulation technology: CRC Press; 2016.
13. Drying YI: Improvement in drying and concentrating liquid substances by atomizing: Google Patents; 1872.

14. Cal K, Sollohub K: Spray drying technique. I: Hardware and process parameters. Journal of pharmaceutical sciences 2010; 99(2):575-86.
15. Baker C: Industrial drying of foods: Springer Science & Business Media; 1997.
16. Shah N, Sandhu H, Choi DS, Chokshi H, Malick AW:Amorphous Solid Dispersions. Theory and Practice: Springer; 2014.
17. Zbicinski I, Strumillo C, Delag A: Drying kinetics and particle residence time in spray drying. Drying Technology 2002; 20(9):1751-68.
18. Oakley DE: Spray dryer modeling in theory and practice. Drying Technology 2004; 22(6):1371-402.
19. Worku ZA, Aarts J, Singh A, Van den Mooter G: Drug–polymer miscibility across a spray dryer: A case study of naproxen and miconazole solid dispersions. Molecular pharmaceutics 2014; 11(4):1094-101.
20. Singh A, Van Humbeeck J, Van den Mooter G: A new twist in the old story-can compression induce mixing of phase separated solid dispersions? A case study of spray-dried miconazole-PVP VA64 solid dispersions. Pharmaceutical research 2014; 31(11):3191-200.
21. Singh A, De Bisschop C, Schut H, Van Humbeeck J, Van Den Mooter G: Compression Effects on the Phase Behaviour of Miconazole–Poly (1-Vinyl pyrrolidone -Co-Vinyl Acetate) Solid Dispersions—Role of Pressure, Dwell Time, and Preparation Method. Journal of pharmaceutical sciences 2015; 104(10):3366-76.
22. Ayenew Z, Paudel A, Rombaut P, Van den Mooter G: Effect of compression on non-isothermal crystallization behaviour of amorphous indomethacin. Pharmaceutical research 2012; 29(9):2489-98.
23. Ayenew Z, Paudel A, Van den Mooter G: Can compression induce demixing in amorphous solid dispersions? A case study of naproxen–PVP K25. European Journal of Pharmaceutics and Biopharmaceutics 2012; 81(1):207-13.
24. Hoekstra AJ:Gas flow field and collection efficiency of cyclone separators, TU Delft, Delft University of Technology; 2000.
25. Snyder HE: Pharmaceutical spray drying: solid-dose process technology platform for the 21st century. Therapeutic delivery 2012; 3(7):901-12.
26. Masters K: Spray drying handbook. Spray drying handbook 1979; (Ed. 3).
27. Perry RH, Green DW: Perry's chemical engineers' handbook: McGraw-Hill Professional; 1999.
28. Akter F, Saha M, Ansary J, Debnath A, Shams T: Study of dissolution characteristics of ibuprofen by different polymers and solid dispersion techniques. International Journal of Pharmaceutical Sciences and Research 2015; 6(4):1528.
29. Farid M: A new approach to modelling of single droplet drying. Chemical Engineering Science 2003; 58(13):2985-93.
30. Mezhericher M, Levy A, Borde I: Spray drying modelling based on advanced droplet drying kinetics. Chemical Engineering and Processing: Process Intensification 2010; 49(11):1205-13.
31. Chaudhari SP, Dave RH: Investigating the Effect of Molecular Weight of Polyvinylpyrrolidone and Hydroxypropyl Methyl Cellulose as Potential Antiprecipitants on Supersaturated Drug Solutions and Formulations using Weakly Acidic Drug: Indomethacin. International Journal of Pharmaceutical Sciences and Research 2016; 7(10):3931-48.
32. Kim EH-J, Dong Chen X, Pearce D: On the mechanisms of surface formation and the surface compositions of industrial milk powders. Drying Technology 2003; 21(2):265-78.
33. Nešić S, Vodnik J: Kinetics of droplet evaporation. Chemical Engineering Science 1991; 46(2):527-37.
34. Paudel A, Worku ZA, Meeus J, Guns S, Van den Mooter G: Manufacturing of solid dispersions of poorly water soluble drugs by spray drying: formulation and process considerations. International journal of pharmaceutics 2013; 453(1):253-84.
35. Chaudhari SP, Dave RH: To prepare and characterize microcrystalline cellulose granules using water and isopropyl alcohol as granulating agents and determine its end-point by thermal and rheological tools. Drug development and industrial pharmacy 2015/05/04 2015; 41(5):744-52.
36. Edward JT: Molecular volumes and the Stokes-Einstein equation. J chem Educ 1970; 47(4):261.
37. Lee E-J, Lee S-W, Choi H-G, Kim C-K: Bioavailability of cyclosporin A dispersed in sodium lauryl sulfate–dextrin based solid microspheres. International journal of pharmaceutics 2001; 218(1):125-31.
38. Tung NT, Park CW, Oh To, et al.: Formulation of solid dispersion of rebamipide evaluated in a rat model for improved bioavailability and efficacy. Journal of pharmacy and pharmacology 2011; 63(12):1539-47.
39. Wu JX, Yang M, van den Berg F, Pajander J, Rades T, Rantanen J: Influence of solvent evaporation rate and formulation factors on solid dispersion physical stability. European journal of pharmaceutical sciences 2011; 44(5):610-20.
40. Janssens S, Anné M, Rombaut P, Van den Mooter G: Spray drying from complex solvent systems broadens the applicability of Kollicoat IR as a carrier in the formulation of solid dispersions. European journal of pharmaceutical sciences 2009; 37(3):241-8.
41. Rizi K, Green RJ, Donaldson M, Williams AC: Production of pH-responsive microparticles by spray drying: Investigation of experimental parameter effects on morphological and release properties. Journal of pharmaceutical sciences 2011; 100(2):566-79.
42. Paudel A, Van den Mooter G: Influence of solvent composition on the miscibility and physical stability of naproxen/PVP K 25 solid dispersions prepared by cosolvent spray-drying. Pharmaceutical research 2012; 29(1):251-70.
43. Pahwa R, Kataria U, Rana A, Rao R, Nanda S: solid dispersion technology: recent advancements in the delivery of various phytoconstituents. International Journal of Pharmaceutical Sciences and Research 2015; 6(2):510.
44. Sinko PJ, Allen Jr LV, Popovich NG, Ansel HC: 1: 1. Martin's Physical Pharmacy and Pharmaceutical Sciences. 2006.
45. Bercea M, Eckelt J, Wolf BA: Vapor pressures of polymer solutions and the modeling of their composition dependence. Industrial & Engineering Chemistry Research 2009; 48(9):4603-6.
46. Al-Obaidi H, Brocchini S, Buckton G: Anomalous properties of spray dried solid dispersions. Journal of pharmaceutical sciences 2009; 98(12):4724-37.
47. Abiad MG, Campanella OH, Carvajal MT: Effect of Spray Drying Conditions on the Physicochemical Properties and Enthalpy Relaxation of α-Lactose. International Journal of Food Properties 2014; 17(6):1303-16.
48. Littringer EM, Mescher A, Eckhard S, et al.: Spray drying of mannitol as a drug carrier—the impact of process

parameters on product properties. Drying Technology 2012; 30(1):114-24.
49. Langrish T: Assessing the rate of solid-phase crystallization for lactose: the effect of the difference between material and glass-transition temperatures. Food Research International 2008; 41(6):630-6.
50. Williams III RO, Watts AB, Miller DA: Formulating poorly water soluble drugs. Vol 3: Springer Science & Business Media; 2011.
51. Sahoo NG, Abbas A, Judeh Z, Li CM, Yuen KH: Solubility enhancement of a poorly water-soluble anti-malarial drug: Experimental design and use of a modified multifluid nozzle pilot spray drier. Journal of pharmaceutical sciences 2009; 98(1):281-96.
52. Ståhl K, Claesson M, Lilliehorn P, Lindén H, Bäckström K: The effect of process variables on the degradation and physical properties of spray dried insulin intended for inhalation. International journal of pharmaceutics 2002; 233(1):227-37.
53. Adhikari B, Howes T, Bhandari B, Troung V: Surface stickiness of drops of carbohydrate and organic acid solutions during convective drying: experiments and modeling. Drying Technology 2003; 21(5):839-73.
54. Littringer EM, Noisternig MF, Mescher A, et al.: The morphology and various densities of spray dried mannitol. Powder technology 2013; 246:193-200.
55. Martins RM, Siqueira S, Tacon LA, Freitas LA: Microstructured ternary solid dispersions to improve carbamazepine solubility. Powder technology 2012; 215:156-65.
56. Aftel R, Gupta AK, Cook C, Presser C:Gas property effects on droplet atomiation and combustion in an air-assist atomier. Paper presented at: Symposium (International) on Combustion, 1996.
57. Ozbilen S: Influence of atomising gas on particle characteristics of Al, Al-1 wt-% Li, Mg, and Sn powders. Powder metallurgy 2000; 43(2):173-80.
58. Dobry DE, Settell DM, Baumann JM: Spray Drying and Scale-Up. Pharmaceutical Sciences Encyclopedia 2015.
59. Kudra T, Poirier M: Gaseous carbon dioxide as the heat and mass transfer medium in drying. Drying Technology 2007; 25(2):327-34.
60. Dobry DE, Settell DM, Baumann JM, Ray RJ, Graham LJ, Beyerinck RA: A model-based methodology for spray-drying process development. Journal of pharmaceutical innovation 2009; 4(3):133-42.
61. Islam M, Langrish T: The effect of different atomizing gases and drying media on the crystallization behavior of spray-dried powders. Drying Technology 2010; 28(9):1035-43.

How to cite this article:
Phapale BN and Patil AP: Application of spray drying technique for preparation amorphous solid dispersion. Int J Pharm Sci Res 2017; 8(4): 1541-49.doi: 10.13040/IJPSR.0975-8232.8(4).1541-49.