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Spray Drying: A Review on Single Step Rapid Drying Technique.

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ABSTRACT

Spray drying is a method used to produce dry powder from a liquid or slurry by rapidly drying with a hot gas and it is mostly used in the food and pharmaceutical industries. This paper covers the parameters of spray dryer, principles of spray dryer, basics of spray drying, dryer configuration, collection of dried powder, and flow of drying gas, process design and control. Spray dryers can dry a product very quickly compared to other methods of drying. They also turn a solution or slurry into a dried powder in a single step, which can be advantageous for profit maximization and process simplification. Spray drying offers multiple opportunities that no other single drying technology can claim. Besides spray drying offers unique opportunities in particle size engineering. They can also turn a solution or slurry into a dried powder in a single step, which can be advantageous for profit maximization and process simplification. Spray dryers are also capable of handling a very wide range of feed materials and flow rates: a pharmaceutical company may use a lab scale system to dry a few kilograms of high value product whereas the mining industry might use a much larger drier to continuously process over 100 tons of material per hour.

Keywords: spray dryer, nozzle atomization, Solubilization,

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INTRODUCTION

A number of methodologies can be adapted to improve Solubilization of poor water soluble drug and further to improve its bioavailability. The techniques generally employed for solubilization of drug includes micronization, chemical modification, pH adjustment, solid dispersion, complexation, co-solvency, micellar Solubilization, hydrotropy etc. Solubilization of poorly soluble drugs is a frequently encountered challenge in screening studies of new chemical entities as well as in formulation design and development [1,2]. Any drug to be absorbed must be present in the form of an aqueous solution at the site of absorption [3-6]. As Solubility & permeability is the deciding factor for the in-vivo absorption of the drug, these can be altered or modified by enhancement techniques like [7]. The term 'solubility' is defined as maximum amount of solute that can be dissolved in a given amount of solvent. It can also be defined quantitatively as well as qualitatively.

Quantitatively it is defined as the concentration of the solute in a saturated solution at a certain temperature. In qualitative terms, solubility may be defined as the spontaneous interaction of two or more substances to form a homogenous molecular dispersion. A saturated solution is one in which the solute is in equilibrium with the solvent. The solubility of a drug is represented through various concentration expression such as parts, percentage, molarities, molality, volume fraction, mole fraction [8.9].

- PH Adjustment
- Co-Solvency
- Particle Size Reduction
- Microemulsions
- Micellar Solublization
- Complexation
- Supercritical Fluid (SCF) Process
- Solid Dispersions
- Spray Drying

PH ADJUSTMENT

Poorly water soluble drugs with parts of the molecule that can be protonated (base) or de protonated (acid) may potentially be dissolved in water by applying a pH change. pH adjustment can in principle be used for both oral and parenteral administration. Upon intravenous administration the poorly soluble drug may be precipitate because blood is a strong buffer with pH between 7.2 – 7.4. To assess the suitability of the approach, the buffer capacity and tolerability of the selected pH are important to consider. In the stomach the pH is around 1 to 2 and in the duodenum the pH is between 5-7.5, so upon oral administration the degree of solubility is also likely be influenced as the drug passes through the intestines. Ionizable compounds that are stable and soluble after pH adjustment are best suited [10,11].

CO-SOLVENCY

The solubility of a poorly water soluble drug can be increased frequently by the addition of a water miscible solvent in which the drug has good solubility known as co solvents [12]. Co-solvents are mixtures of water and one or more water miscible solvents used to create a solution with enhanced solubility for poorly soluble compounds. Historically, this is one of the most widely used techniques because it is simple to produce and evaluate. Examples of solvents used in co-solvent mixtures are PEG 300, propylene glycol or ethanol.

PARTICLE SIZE REDUCTION

The bioavailability intrinsically related to drug particle size. By reducing particle size, increased surface area improves the dissolution properties. Particle size reduction, it is done by milling techniques using jet mill, rotor stator colloid mills etc. Not suitable for drugs having a high dose number because it does not change the saturation solubility of the drug [13].

MICROEMULSIONS

Micro emulsions have been employed to increase the solubility of many drugs that are practically insoluble in water, along with incorporation of proteins for oral, parenteral, as well as percutaneous / Transdermal use [14,15]. A micro emulsion is an optically clear pre-concentrate containing a mixture of oil, hydrophilic surfactant and hydrophilic solvent which dissolves a poorly water soluble drug. Upon contact with water, the formulations spontaneously disperse (or 'self emulsifies') to form a very clear emulsion of exceedingly small and uniform oil droplets containing the solubilized poorly soluble drug. Micro emulsions are isotropic, thermodynamically stable transparent (or translucent) systems of oil, water and surfactant, frequently in combination with a co-surfactant with a droplet size usually in the range of 20-200 nm. These homogeneous systems, which can be prepared over a wide range of surfactant concentration and oil to water ratio, are all fluids of low viscosity.

MICELLAR SOLUBLIZATION

The use of surfactants to improve the dissolution performance of poorly soluble drug products has also been successfully employed. Surfactants can lower surface tension and improve the dissolution of lipophillic drugs in aqueous medium [16,17]. They can also be used to stabilize drug suspensions. When the concentration of surfactants exceeds their critical micelle concentration (CMC, which is in the range of 0.05-0.10% for most surfactants), micelle formation occurs, entrapping the drugs within the micelles [18]. This process is known as micellization and generally results in enhanced solubility of poorly soluble drugs. Commonly used non-ionic surfactants include polysorbates, polyoxy ethylated castor oil, polyoxyethylated glycerides, lauryl macroglycerides and mono- and di-fatty acid esters of low molecular weight polyethylene glycols.

COMPLEXATION

Complexation of drugs with cyclodextrins has been used to enhance aqueous solubility and drug stability. Cyclodextrins of pharmaceutical relevance contain 6, 7 or 8 dextrose molecules (α, β, γ-cyclodextrin) bound in a 1,4- configuration to form rings of various diameters. The ring has a hydrophilic exterior and lipophillic core in which appropriately sized organic molecules can form noncovalent inclusion complexes resulting in increased aqueous solubility and chemical stability.[19] Derivatives of β-cyclodextrins with increased water solubility (e.g. hydroxypropyl-β-cyclodextrins HP-β-CD) are most commonly used in pharmaceutical formulation. Cyclodextrin complexes have been shown to increase the stability, wettability and dissolution of the lipophilic insect repellent N, N-diethyl-m-polyamide (DEET) [20] and the stability and photo stability of sunscreens [21].

SUPERCRITICAL FLUID (SCF) PROCESS

The number of applications and technologies involving supercritical fluids has also grown explosively. It has been known for more than a century that supercritical fluids (SCFs) can dissolve nonvolatile solvents, with the critical point of carbon dioxide, the most widely used supercritical fluid. It is safe, environmentally friendly, and economical. The low operating conditions (temperature and pressure) make SCFs attractive for pharmaceutical research (Markku Rantakyla et al., 2004). A SCF exists as a single phase above its critical temperature (Tc) and pressure (Pc). SCFs have properties useful to product processing because they are intermediate between those of pure liquid and gas (i.e., liquid-like density, gas-like compressibility and viscosity and higher diffusivity than liquids). Moreover, the density, transport properties (such as viscosity and diffusivity), and other physical properties (such as dielectric constant and polarity) vary considerably with small changes in operating temperature, pressure, or both around the critical points [22,23]. Hence, it is possible to fine-tune a unique combination of properties necessary for a desired application.

SOLID DISPERSIONS

SCF techniques can be applied to the preparation of solvent-free solid dispersion dosage forms to enhance the solubility of poorly soluble compounds. Traditional methods suffer from the use of mechanical forces and excess organic solvents. In this technique, a poorly soluble drug is dispersed in a highly soluble solid hydrophilic matrix, which enhances the dissolution of the drug. Solid dispersion techniques can yield eutectic (non molecular level mixing) or solid solution (molecular level mixing) products [24,25]. A solid dispersion of carbamazepine in polyethylene glycol 4000 (PEG-4000) increased the rate and extent of dissolution of carbamazepine. In this method, a precipitation vessel was loaded with solution of carbamazepine and PEG4000 in acetone, which was expanded with supercritical CO2 from the bottom of the vessel to obtain solvent-free particles.

HYDROTROPHY

Hydrotropy is a Solubilization process whereby addition of a large amount of second solute results in an increase in the aqueous solubility of another solute. Solute consists of alkali metal salts of various organic acids. Hydrotropic agents are ionic organic salts.

Additives or salts that increase solubility in given solvent are said to “salt in” the solute and those salts that decrease solubility “salt out” the solute. Several salts with large anions or cations that are themselves very soluble in water result in “salting in” of non electrolytes called “hydrotropic salts” a phenomenon known as “hydrotropism”. Hydrotropic solutions do not show colloidal properties and involve a weak interaction between the hydrotropic agent and solute. Hydrotropy designate the increase in solubility in water due to the presence of large amount of additives. The mechanism by which it improves solubility is more closely related to complexation involving a weak interaction between the hydrotropic agents like sodium benzoate, sodium acetate, sodium alginate, urea and the poorly soluble drugs [26,27].

SPRAY DRYING

Spray drying is widely used in the industry for conversion of a suspension or solution into a dry powder product. In spray drying the suspension or solution feed is atomized and the droplet formed comes into contact with a hot gas. When the droplets and the heated gas come into contact, the solvent in the droplets evaporate, leaving a dry powdered product. Spray drying is presently one of the most exciting technologies for the pharmaceutical industry. It is an ideal process where the end products meet the precise quality standards regarding particle size distribution, residual moisture/solvent content, bulk density and morphology [28].

The development of spray drying equipment and techniques started in the 1870s. Spray drying has come of age ever since the technique was used during the World War II, because the idea to reduce the transport weight of foods and other materials became important2. The dried product from spray dryers can be in the form of powders, granules or agglomerates depending on the physical and chemical properties of the feed, the dryer design and final powder properties desired [29].

BENEFITS OF SPRAY DRYING [30,31]

It has a high precision control over:

- Particle size, bulk density, degree of crystalline and residual solvents
- Typical application in pre-formulated products
- Microencapsulation, solid solutions
- Improved bioavailability, improved product stability
- Products with unusual or difficult characteristics
- Sticky or hygroscopic products
- Slowly crystallizing products
- Difficult to isolate products
- Rapid drying for temperature sensitive materials

Spray dryers can dry a product very quickly compared to other methods of drying. They can also turn a solution or slurry into a dried powder in a single step, which can be advantageous for profit maximization and process simplification [33]. All spray dryers employ atomizer or spray nozzle to disperse the liquid or slurry into a controlled

drop size spray. The commonest of these are rotary disks and single-fluid high pressure swirl nozzles. Alternatively, for some applications two-fluid or ultrasonic nozzles are used. Depending on the process needs, drop sizes from 10 to 500 µm can be achieved with the appropriate choices. The most common applications are in the 100 to 200 µm diameter range .[33] The most common spray dryers are called single effect because there is only one drying air on the top of the drying chamber. In most cases the air is blown in co-current with the sprayed liquid. The powders obtained with such type of dryers are fine with a lot of dusts and poor flow ability [34].

Advantages

- Specific product properties can be achieved consistently throughout the dryer run.
- Operation is continuous and easily adaptable to automatic control.
- Unit can be designed for virtually any capacity required.
- Can control product density and porosity.
- Can handle heat sensitive and heat resistant materials.
- Can handle flammable, explosive, malodorous and toxic materials and those requiring hygienic conditions.
- Can dry feed stocks in solution, slurry, paste or melt form, including corrosive and abrasive feeds.

Disadvantages

- High fabrication and installation costs.
- Large size requires expensive supporting structures.

PRINCIPLES OF SPRAY DRYER

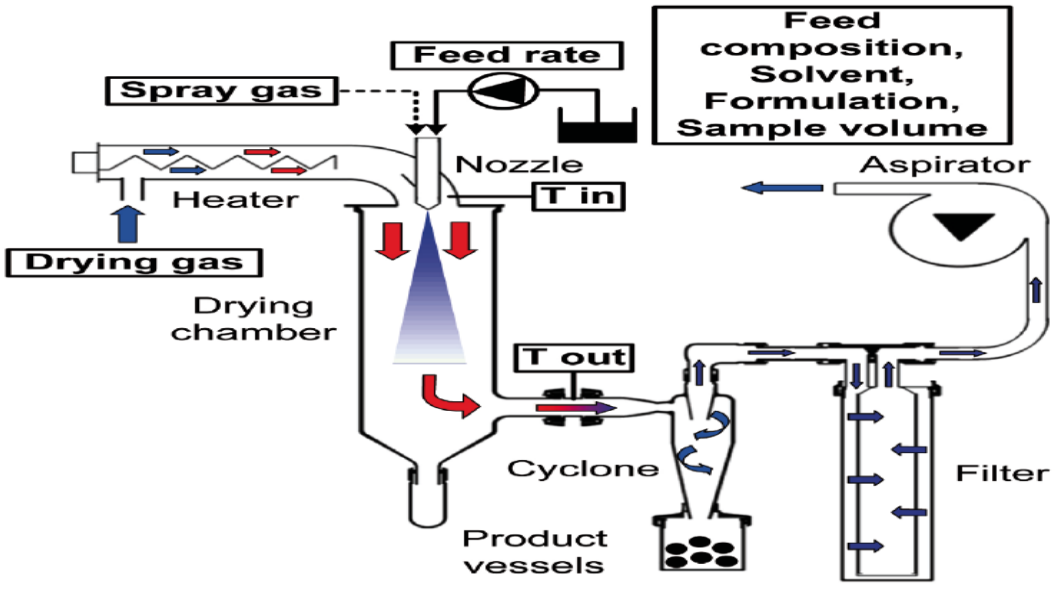

Figure 1: Process diagram of the Mini Spray Dryer B-190, B-191 and B-290 models with process parameters.

Atomization: The formation of sprays having the required droplet size distribution is vital to any successful spray dryer operation so that powder specifications can be met. Atomization is created by either a rotary atomizer or spray nozzle atomizer as shown in **Fig. 1.** The location of the fluid bed within the drying chamber achieves drying at lower temperature levels. It results in higher thermal efficiencies and cooler conditions for powder handling.

Co-current: Drying air and particles move through the drying chamber in the same direction. Product temperatures on discharge from the dryer are lower than the exhaust air temperature, and hence this is an ideal mode for drying heat sensitive products. When operating with rotary atomizer, the air disperser creates a high degree of air rotation, giving uniform temperatures throughout the drying chamber.

However, an alternative non-rotating airflow is often used in tower or FILTERMAT®-type spray dryers using nozzle atomizers with equal success.

Counter-current: Drying air and particles move through the drying chamber in opposite directions. This mode is suitable for products which require a degree of heat treatment during drying. The temperature of the powder leaving the dryer is usually higher than the exhaust air temperature [28].

Mixed flow: Particle movement through the drying chamber experiences both co-current and countercurrent phases. This mode is suitable for heat stable products where coarse powder requirements necessitate the use of nozzle atomizers, spraying upwards into an incoming airflow, or for heat sensitive products where the atomizer sprays droplets downwards towards an integrated fluid bed. The air inlet and outlet are located at the top of the drying chamber [28].

Atomization: Several types of atomization are available. They are centrifugal, nozzle, pneumatic and sonic atomization.

Centrifugal atomization: This uses a rotating disc or wheel to break the liquid stream into droplets. These devices normally operate in the range of 5,000 to 25,000 rpm with wheel diameters of 5 to 50 cm. The size of the droplets produced is nearly inversely proportional to the peripheral speed of the wheel1. The distribution of particle sizes about the mean is fairly constant for a given method of atomization. The mass flow of the liquid, its viscosity, solids content and surface tension influence particle size directly, but none to the degree of peripheral wheel velocity. Consequently, an increase in feed rate may slightly increase the particle size but use of a variable-speed drive on the centrifugal atomizer facilitates correction to the specified size [29]. One advantage of centrifugal atomization is that atomizing machines are available in many sizes. A small air-driven laboratory unit handles from 1 to 10 L/h of liquid feed, while the largest commercial units driven by 850-kW motors can handle in excess of 200,000 kg/h. [31].

Nozzle atomization: The second most common form of atomization is hydraulic pressure-nozzle atomization. Here the liquid is pressurized by a pump and forced through an orifice to break the liquid into fine droplets. Orifice sizes are usually in the range of 0.5 to 3.0 mm.

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As a result, a single nozzle is limited to somewhere in the order of 750 kg/h of feed, depending on pressure, viscosity, solids content and orifice size1. Greater pressure drop across the orifice produces smaller droplets. Therefore, to reduce the particle size for a given feed rate, the nozzle must be removed and a smaller orifice substituted. This in turn requires a higher pump pressure to achieve the same mass flow through the nozzle. Very large systems may have as many as 40 nozzles, making control of particle size difficult. Precise control, however, is not always required, and large, multiple-nozzle dryers are often used when the only requirement is that the mean particle size be quite large. Although nozzles are considerably less complicated than centrifugal atomizers, a high-pressure pump is required. During the drying of abrasive materials, the nozzles can pose special problems. The potential for plugging the relatively small orifices is another drawback for nozzle based atomization systems [28].

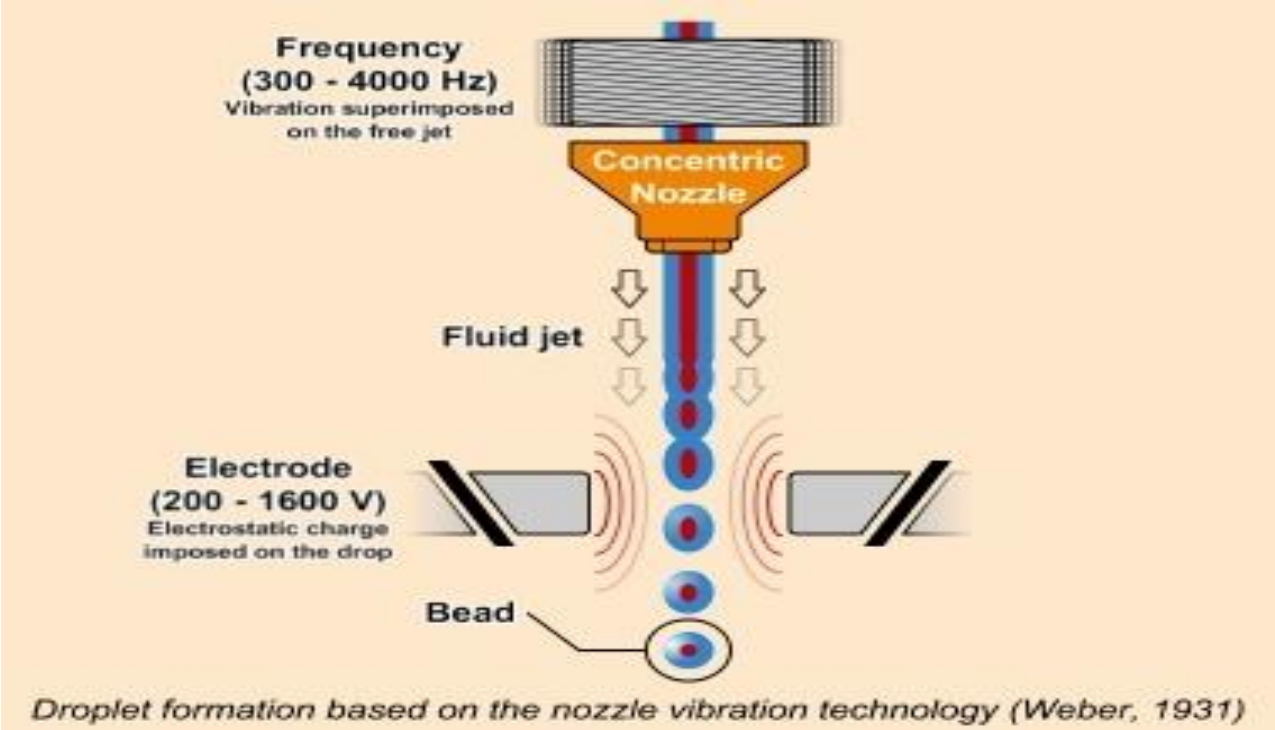

Fig 2: Droplet Formation Based On The Nozzle Vinration Technology

Pneumatic atomization: A third method used primarily in smaller drying systems is two-fluid pneumatic atomization. Here atomization is accomplished by the interaction of the liquid with a second fluid, usually compressed air. Neither the liquid nor the air requires very high pressure, with 200 kPa to 350 kPa being typical. Particle size is controlled by varying the ratio of the compressed air flow to that of the liquid. The main advantage of this form of atomization is that the liquid has a relatively low velocity as it exits the nozzle, and therefore, the droplets require a shorter flight path for drying. This makes two-fluid nozzles ideal for use in pilot- or laboratory-scale equipment [28].

Sonic atomization: this type of atomization employs the use of ultrasonic energy where the passing of liquid over the surface is vibrated at ultrasonic frequencies. These systems are suitable for producing very fine droplets at low flow rates. However, more development is needed if these atomizers are to find wider acceptance in industrial drying both in capacities handled and the range of different products to be atomized [28].

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Dryer configuration: The atomized droplets that are formed from the atomizing device have a velocity and direction initially established by the atomizer **(Fig. 3).** It is necessary for the heated gas to mix with the cloud of droplets, then begin evaporation, and influence the movement of the droplets inside the dryer, so that they can dry sufficiently and do not stick on contact with the dryer walls. This is accomplished by placing the atomizer in, or adjacent to, a properly designed air-disperser.

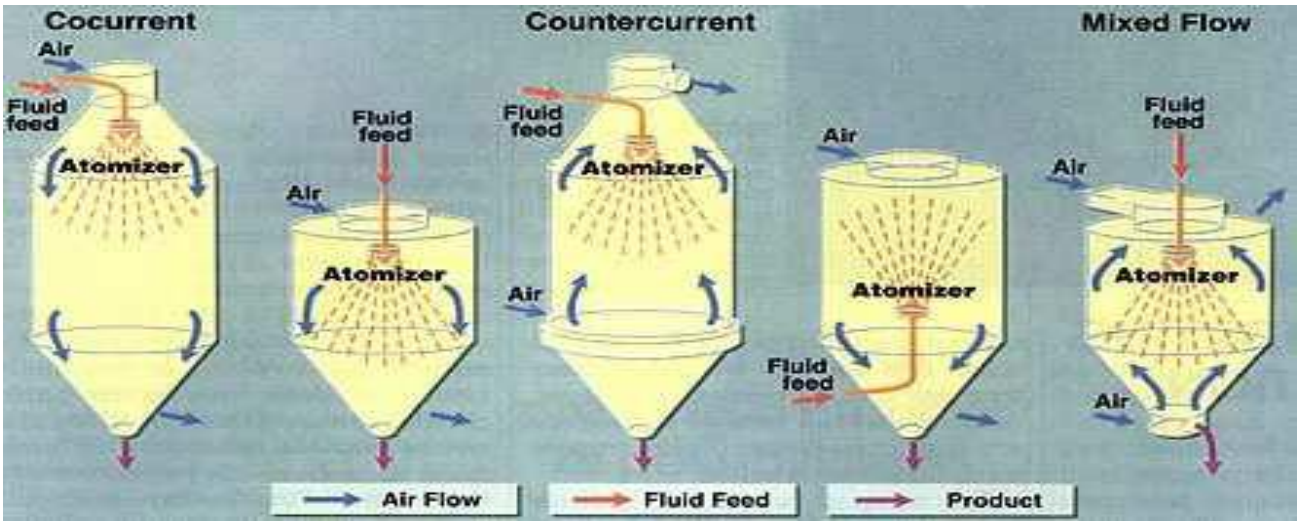

Fig.3: The atomized droplets that are formed from the atomizing device established by the atomizer

A concurrent configuration with nozzle atomizer is suited for commodity chemicals; a counter current design with a nozzle atomizer is best suited for products requiring heat treatment; a mixed-flow unit with a nozzle atomizer is ideal for coarse powders of heat-stable products [34].

The atomizer, disperser and drying chamber must all be properly configured to allow complete drying of all the droplets without deposits of wet material on the interior surfaces of the dryer. In addition, the total volume of the drying chamber and the flow patterns of the droplets and the air through the dryer must provide for sufficient contact time to allow evaporation of essentially all of the liquid. As a result, centrifugal atomizers are usually installed at the center of the roof of a relatively large-diameter spray dryer. The heated air is introduced through a roof-mounted air disperser around the atomizer, creating a concurrent flow of air and product. By coming in contact with the droplets as soon as they are formed, the heated air causes rapid surface evaporation, and keeps the solids relatively cool [34].

By the time evaporation slows down and becomes limited by diffusion of liquid from the center of the droplet to the surface, the particles have passed to a cooler region of the dryer. Therefore, heat-sensitive products can often be spray-dried using elevated temperatures in the inlet gas, even though those temperatures would damage the product in an oven or other processes that are not concurrent, or as fast as spray drying. The larger the particle size desired in the final powder, the larger must be the diameter of the drying chamber, regardless of the unit's total throughput.

When coarse powders are needed in small production rates, a pressure-nozzle spray, in fountain configuration, is often found to be a lot more practical. Here the spray travels upward until overcome by gravity and the downward flow of air. It then reverses direction and falls, finally landing in the bottom cone of the drying chamber. The big drawback in fountain-nozzle dryers is that the process is not concurrent. Rather, it is mixed flow, and drying actually begins in a cooler part of the dryer and continues into the hottest zone. Since each droplet is already partly dried, the evaporative cooling effect is lessened and the chance of thermal degradation becomes greater. Sometimes lower inlet temperatures solve this problem, but also reduce total evaporation capacity [34].

The third most commonly used configuration has pressure nozzles at the top of a dryer, spraying concurrently with the heated air. This takes advantage of evaporative cooling, but often requires the dryer to have a cylinder height of about 20 m. These "nozzle towers" are often used for foodstuffs, dyes, pesticides and other heat-sensitive products that must also be in a coarse, free-flowing powder form[34].

Collecting the dried powder: Once the product is dried to a free-flowing powder, it must be separated from the drying gas, which is now cooled and contains the evaporated liquid. Coarser powders are most easily collected directly from the bottom of the drying chamber cone. In this arrangement, the spent drying gas exits through an outlet duct in the center of the cone. The reversing of the gas flow allows the greatest fraction of the powder to settle in the cone, and slide to the bottom outlet often equipped with an air-lock [35].

Because the spent drying gas has some entrained powder, cyclones or fabric filters are often used to clean the gas. In some cases, the combination of cyclones followed by a wet scrubber proves more effective. If the powder is very fine, little is collected in the drying chamber. In this case, the cyclones or even the bag collector can become the primary collection point. Chamber collection is eliminated by using a U- bend at the outlet for both gas and powder from the chamber to the other collectors [36].

Process gas flow: The flow of drying gas through the system is much the same as for any gas suspension drying system. Heating by direct combustion of natural gas turns out to be the most efficient. Fuel oil or propane backup is often provided when gas curtailment is possible. If indirect heating is required, shelland- tube or finned-tube exchangers are used with steam or a heat-transfer fluid as a heat source. Electric heaters are used on small-scale dryers. In some instances, however, waste heat from another process is recovered either by direct injection into the drying gas stream or by heat exchanger. Industrial radial fans are used to move the gas through the system, employing a combination of forced and induced draft, or induced draft only. If ambient air is the drying gas, it may be filtered by coarse filters to remove leaves, dirt and so on. If a very clean process is required, high-efficiency particulate air filters can be used.

Ductwork with appropriate dampers, expansion joints, vibration isolators and noise-abatement devices is supplied with most dryers. All equipment is usually insulated and clad to minimize heat loss condensation, and personnel hazards [30].

Process design and control: Evaporation rate in a spray dryer is directly proportional to the product of the temperature difference from inlet to outlet and the mass flow of gas through the system. Outlet temperature is established by the desired moisture content in the product according to that product's equilibrium isotherm. Since true equilibrium is never reached, actual values are usually determined experimentally [30].

Inlet temperature is also determined by experience and should be as high as possible without product degradation. Then, for a given evaporation rate, the required process gas flow can be determined from the temperature difference. All system components can be sized based on gas flow. A gas residence time must be selected from experience, based on particle size desired and the product's known drying characteristics.

This permits direct calculation of a chamber volume. At this point, the method of atomization must be selected and matched with chamber dimensions to obtain the desired volume and configuration with respect to the atomized cloud. If nothing is known about the product, one needs to conduct pilot-scale experiments. Once designed and built, the drying system needs fairly simple controls. Although one should have a rough estimate of the actual gas flow through the dryer, it is usually best to fix the flow at the design rate. Since outlet temperature determines the moisture content in the final product, the temperature must be controlled and modulated with respect to other changes in the system. In the simplest case, the outlet temperature controls the heat input to the feed and thereby the inlet temperature, while holding the feed rate constant. In fact, dryers with a small nozzle atomizer do just that, using a single feedback control loop. One slightly more advanced approach is to use a "cascade control configuration" in which the outlet temperature controller can change the inlet controller's set point to achieve correct final moisture level in the product.[30] Pressure drops across filters and cyclones, and the pressure in the drying chamber are usually monitored, not controlled, to assure that the system is operating properly. Centrifugal atomizers require monitors for lube-oil flow, temperature, and vibration. On the other hand, nozzle systems require feed pressure monitoring [30].

Although a spray dryer can be operated with simple controllers, it is becoming normal practice to use programmable logic controllers (PLCs), which offer greater capability in monitoring alarming functions. In addition, these PLCs can initiate programmed start-ups and shutdowns. Inclusion of a personal computer offers data logging, trend analysis and other features used in statistical process control and other quality-assurance programs [30].

Applications of Spray Drying [37-40]

The range of spray drying technology in current usage reflects the diversity of the industries that dry their products in this way. The ubiquity of this drying technology results from a number of factors. The spray and drum dryers are the only two that can handle a pumpable fluid feed. Of these, the spray dryer is the only one which can produce powders of a specific particle size, porosity and moisture content. Spray dryers are also capable of handling a very wide range of feed materials and flow rates: a pharmaceutical company may use a lab scale system to dry a few kilograms of high value product whereas the mining industry might use a much larger drier to continuously process over 100 tons of material per

hour. The production of laundry detergents is one of the best known applications of spray drying and continues to be a large market.

Most detergents are formed in countercurrent towers with multilevel Nozzle atomization.

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