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A REVIEW ON INFLUENCE OF SYSTEM PARAMETER ON SPRAY DRIED MICROSPHERE

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ABSTRACT

Spray drying is a closed, one-phase process that allows us to convert a liquid input product into a solid output product. (Solution, suspension, and rarely emulsion). It is widely employed technique for the production of microsphere, which are extensively used in industries such as pharmaceuticals, cosmetics etc. The process involves atomizing a liquid feed into small droplets, which are subsequently dried to form solid microsphere. The successful application of spray drying relies on optimizing various system parameters to achieve desire product characteristics. This review article provides a comprehensive overview of the influence of system parameters, including feed rate, feed concentration, inlet temperature, drug polymer ratio etc. on the spray drying process of microsphere. It has been demonstrated that a higher nozzle air pressure boosts manufacturing yield without any prior justification The air-drying temperature is crucial for particle size and recovery. The size, dispersion, and velocity of the droplets are affected by the feed injection rate. The feed concentration has a fairly small impact on droplet size. When the air flow rate was decreased, it appeared that the particle size increased. Increasing the drug to polymer ratio was also observed to marginally enhance the size of the microspheres.

KEYWORDS: Spray drying, parameters, Input temperature, nozzle shape, Air aspirator capacity.

INTRODUCTION

Microspheres, which range in size from 1 to 1000 nm, are free-flowing powders made of biodegradable synthetic polymers or proteins. Some of the drawbacks of traditional therapy can be avoided, and the therapeutic effectiveness of a specific drug can be improved, with the help of a well-designed controlled drug delivery system. In order to deliver a medicinal chemical to the target region with a continuous regulated release, there are several different methods. The vast range of applications of the microsphere drug delivery system, which includes directing the medicine to a specific region and assisting with imaging and diagnostic characteristics, has drawn a lot of attention. Microspheres attracted a lot of interest for their sustained release as well as their ability to direct anti-cancer medications to the tumor. Spherical microparticles called microspheres are employed in applications where a consistent and predictable particle surface area is crucial. A medication is enclosed inside a special polymeric membrane that is positioned centrally within a microsphere.

By spraying the feed into a hot drying medium, feed is continuously transformed from a fluid condition into dried particulate form. The feed can be a solution, slurry, emulsion, gel, or paste as long as it can be pumped and atomized. A highly dispersed liquid combined with a enough amount of heated air to cause the evaporation and drying of liquid droplets. The heat for evaporation is provided by the air, which also transports the dried product to the collector before it is removed together with the moisture. The feed droplets remain at temperatures much below the hot air temperature for a very brief period of time while losing moisture to the hot air. As a result, spray drying is also referred to as "Low Temperature Drying". Depending on the physical and chemical characteristics of the feed, the drier design, and the intended final product property, the dried product may be in the form of powders, granules, or agglomerates.[1]

In order to obtain the end product with required properties, the parameters of the process must be carefully selected. Almost each parameter, which is modified during the spray drying process, has a smaller or bigger effect on the obtained end product. The size of dried particles depends on the nozzle shape, on the indicator of feedstock, and conditions of the process. The humidity content is an indicator of the end product quality in a process of spray drying. The efficiency is very important for the progress of a total spray drying process, and it is determined as a proportion of the mass of a substance being dried to the end product mass.[2]

SPRAY DRYING TECHNIQUE

In recent years, there has been a lot of attention paid to the particles that are produced during the spraying process. Through these endeavours, spray technology has been used to create particles for a variety of products, including microencapsulated flavours and pharmaceutical direct compression excipients and/or granulations. Spray congealing and spray drying are the two primary spraying techniques. The action in spray drying is primarily that of evaporation, whereas in spray congealing it is that of a phase change from a liquid to a solid. The two processes are similar, except for energy flow. In the case of spray drying, energy is applied to the droplet, forcing evaporation of the medium resulting in both energy and mass transfer through the droplet. In spray congealing, energy only is removed from the droplet, forcing the melted to solidify. Spray drying is the most widely used industrial process involving particle formation and drying. It is highly suited for the continuous production of dry solids in either powder, granulate or agglomerate form from liquid feedstocks as solutions, emulsions and pumpable suspensions. Therefore, spray drying is an ideal process where the end-product must comply with precise quality standards regarding particle size distribution, residual moisture content, bulk density, and particle shape.[3]

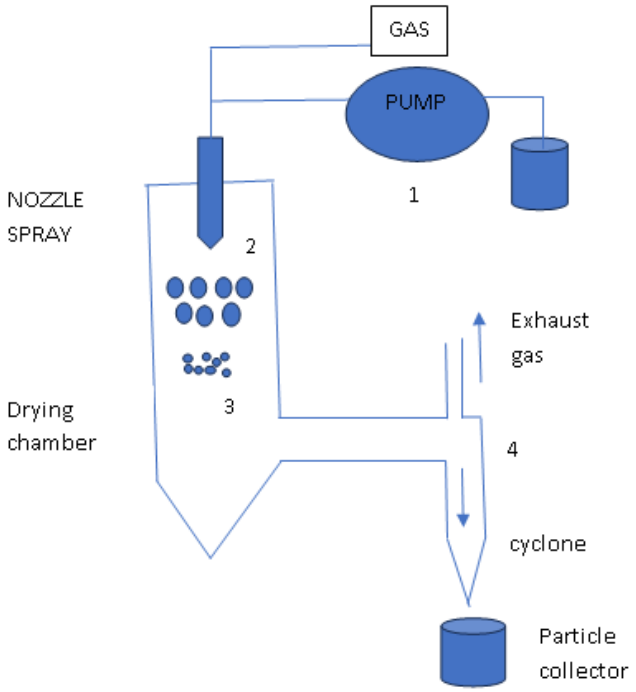

Fig:1 Spray dryer.

The spray-drying procedure consists of four phases.

1. The solution feed is atomized with the gas through a nozzle and pumped into the drying chamber in accordance with the pump speed.
2. Droplets are dried once they are atomized.
3. The drying chamber produces dry powder.
4. A cyclone at the bottom of the apparatus induces the separation of powder and air, and the finished powder is collected in a receiver

Operating conditions and dryer design are selected based on the product's drying characteristics.[4-5]

SPRAY-DRYING PROCESS PARAMETERS

Spray drying technique involves atomizing a feed solution with a hot drying air stream to create a dry powder.[6]

Spray drying allows for the adjustment of a variety of parameters, which makes it an appealing method for designing particles with certain size or form properties. The process yield is crucial and also depends on the other process variables. Indeed, a sticky powder will stick to the device's walls, producing a low yield. The residual water content in the finished product is subsequently determined by the production process since it is based on the atomization and evaporation of the solvent.

Some factors are specified to primarily affect the characteristics of the particle powder, such as the input temperature (T-In), airflow rate, and pump speed. Only the outlet temperature (T -Out) can be detected in addition to these programmable parameters, however it provides information on the powder's characteristics. The T-Out, which is the temperature recorded at the drying chamber's bottom, is a function of the formulation's excipient and API content as well as other process variables including the feed solution rate and the T In. The production of powder with little remaining moisture is encouraged by a high T-Out.[7]

AIR ASPIRATOR CAPACITY

An aspirator transports the air needed to dry the nebulized droplets inside the instrument. Because it has a big impact on how droplets become solid particles, this parameter has been determined to be especially crucial. The amount of time it took for air to circulate inside the instrument was reduced as the aspirator rate increased. This process decreases the amount of time that nebulized droplets spend in contact with drying air, which is advantageous for thermolabile chemicals because they spend less time in contact with hot air.

However, if solvent evaporation and solid particle transformation take longer than expected relative to the instrument's air persistence time, then an increase in aspirator may not be advantageous.[8-9]

Although there are other nozzle types, including rotating and ultrasonic nozzles, bi-fluid nozzles—through which a liquid and a gas flow—are most frequently utilised in the manufacture of pharmaceutical powders.[8] It's interesting to note that the airflow rate has the biggest impact on particle size distribution. In fact, the energy available to scatter the liquid feed and subsequently break liquid droplets during atomization grows as the air pressure into the bi-fluid nozzle increases. As a result, both the final powder particles and the droplets are smaller. Additionally, it has been demonstrated that a higher nozzle air pressure boosts manufacturing yield without any prior justification.[10-11]

AIR-DRYING TEMPERATURE

The air-drying temperature is crucial for particle size and recovery.[12] The temperature used in spray-drying preparations must be appropriate for the item to be dried and, in particular, the solvent utilised.[13]

The rate of solvent volatilization (evaporation) depends on the inlet temperatures. The boiling point of the solvent and the glass transition temperature of the intended use polymeric materials should also be taken into consideration when choosing inlet temperatures. Spray drying input temperatures are typically greater than the solvent's boiling point to guarantee prompt volatilization.[14]

According to Singh *et al.*, the T_o – In, has a direct effect on the phenomenon of heat and mass transmission in the spray-drying droplet. A greater drying temperature results in a faster drying process because more heat is delivered into the drying droplet. Depending on the API and excipients used, the fast development of an outer layer on the droplet could produce porous particles or particles with corrugated surfaces.[15]

T- In, mostly influences particle shape, according to Mockedieck *et al*. The T In-controlled evaporation rate itself has an impact on the Pe number. In reality, a high T-In (> 120 °C) results in the solvent evaporating quickly, which raises the Pe number and creates corrugated surfaces on the particles. Additionally, it makes sense that a high T-In would lead to the production of dry powder with minimal water in it.[16]

Tonon et al., claim that drying at higher temperatures causes faster drying rates, which promote early structure creation and permit the particles to contract during drying. Low intake temperature results in less shrinkage and a greater diameter for the particle. The creation of microspheres is decreased as a result of the inlet air temperature, which can also result from powder melting and adhering to the chamber wall. If the inlet temperature is low (140^oC), there won't be enough heat to dry the product, which means there will be some water in the product and the wet powders will be more likely to stick to the chamber wall, lowering the yield. Low yields were detected and a lot of particles formed on the chamber wall when the inlet temperature was too high (reaching 180°C).[17]

PERISTALTIC PUMP PERFORMANCE

Significant volumes of nebulized fluid are dried during the spray drying process as a result of high pumping rates. The outcome is the development of large, irregular particles that are not completely dry after exiting the desiccating chamber because heated air may take some time to quickly transform liquid droplets into solid microparticles.[18]

The size, dispersion, and velocity of the droplets are affected by the feed injection rate.[19]

A specific volume of drying gas can be thought of as receiving mass through feed injection in terms of thermodynamics, and this mass transfer will directly impact the outlet temperature. As the feed rate increases, the outlet temperature decreases. Feed rate has an impact on how long particles are exposed to high temperatures during the process. This is crucial for non-continuous lab-scale machinery. The feed rate may have an impact on the particle surface topography.[20]

Smaller droplets were produced when the droplets were broken with more energy. Higher feed flow rates and pressure resulted in less heat of fusion.[21]

The droplet size rises when the feed flow rate is increased while the atomization pressure stays constant. This is plainly obvious given that the nozzle would have the same amount of energy for the atomization process with increased feeding volumes. The droplet's size is somewhat decreased as a result of the modest reduction in droplet fissions.[22]

According to Ogunjimi A.T. *et al*.'s analysis, the powder yield decreased as the feed flow rate rose. This could be due to a rise in feed load at higher feed flow rates, which slows down heat and mass transfer, insufficiently dries the product, and causes it to adhere to the chamber walls, all of which reduce yield.[23]

LIQUID FEED CONCENTRATION

The feed concentration, representing the solid particle fraction in the solution.

Feed concentration can impact the particle size: A high feed concentration (>5% m/v) leads to the formation of droplets with smaller solvent amounts, which accelerates the solvent's evaporation rate and causes the creation of wrinkled particles (correlated to a high Pe number), which can affect particle size.[24]

The feed concentration has a fairly small impact on droplet size. The mean droplet size is rarely impacted by the feed concentration, despite the fact that the breakup length of the liquid jets somewhat rises with increasing mannitol concentration due to a little increased viscosity.[25]

AIR FLOW RATE

The spray dryer's aspirator is linked to the aspirator motor, which pushes pressurised drying air into the spray chamber. By changing the aspirator flow rate, the amount of hot drying air entering the spray chamber may be managed.[26]

When the air flow rate was decreased, it appeared that the particle size increased. Liquid was disturbed into smaller droplets at higher air flow rates. So, at higher air flow rates, microspheres with smaller particle sizes were formed.[27]

DRUG TO POLYMER RATIO

Maximum value was attained at a mass ratio of 1:3. Drug loading and yield rose as the drug to chitosan ratio increased. The encapsulation rate, however, showed a negative trend as the mass ratio grew.[28]

It has been reported that, an increase in the drug-to-polymer ratio leads to an increase in particle size, which may be brought on by an increase in the viscosity of the feed solution, which affects how the disperse phase interacts with the dispersion medium and, consequently, the particle size distribution.[29]

Increasing the drug to polymer ratio was also observed to marginally enhance the size of the microspheres.[30]

POLYMER CONCENTRATION

Large amounts of solvent are used to produce the dilute polymer solution, which yields microspheres with a lower bulk density than those made at greater concentrations following solvent evaporation. A decreased yield results from the reduced density since the cyclone can precipitate fewer microparticles and vacuum can remove more particles. The yield is always higher because raising the polymer concentration can also increase the particle density and probably the proportion of big particles.[31]

The morphology and size of microparticles were both impacted by the polymer concentration.[32]

According to the results, microparticles made using a 12.5, 15, and 17.5% w/w polymer solution had similar morphologies, whereas using a higher polymer concentration produced microparticles with an irregular surface, hemispherical protrusions, and some agglomeration phenomena Additionally demonstrated that increasing the polymer concentration from 12.5 to 20% w/w led to a modest increase in the mean particle sizes.[33]

Table no. 1: Shows The Network of Mutual Interactions Between The Spray Drying Factors.[34]

Process Parameters	Particle powder properties
Liquid Feed concentration	Particle size
Feed rate	Particle size Particle shape Water content
Nozzle air pressure	Particle size Production yield
Inlet temperature	Particle shape Water content

SOLVENT USED IN SPRAY DRYING

Various solvents, together or in combination, have been employed to prepare feed solutions. These solvents are either aqueous, alcohols (methanol, ethanol or isopropanol) or other organic solvents such as dichloromethane (DCM), acetone, methyl ethyl ketone, dioxane, tetrahy drofuran (THF), ethyl acetate, chloroform and acetonitrile. Amongst these, DCM is the most commonly utilized system despite its toxicity potential.

According to the International Council for Harmonization (ICH), The procedure of spray drying is applicable for all class II and class III solvents. To achieve a satisfactory yield and reduce residual solvent in the finished powder, relative solvent volatility should be the main requirement. During the spray drying process, droplet viscosity and surface tension are essential components for efficient feed atomization.[35]

Table no. 2: Various solvent and their paramters.

SOLVENT	INLET TEMPRATURE	FEED RATE	ASPIRATOR CAPACITY	Compressed air flow
Water[36]	170^{O}C	2.5 ml/min	100%	440 Nl/hr
Acetonitrile[37]	80^{o}c	0.5 ml/min	100%	600Nl/hr

DCM[38]	50^{O}C	4 ml/min	100%	700 Nl/h
Deionized water[39]	122^{O}C	6 ml/min	100	500 Nl/h
DCM-Ethanol[40]	55^{0}C	4 ml/min	100%	700 Nl/h
Ethanol-water[41]	130^{O}C	3ml/min	100%	670 Nl/h
Acetone[42]	60^{O}C	7.5 ml/min	100 %	347 Nl/h
Ethanol[43]	140^{O}C	5ml/min	50%	450 Nl/h
Isopropyl alcohol[44]	160^{O}C	3ml/min	55%	600 Nl/h

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