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SPRAY DRYING: INNOVATIVE PHARMACEUTICAL TECHNOLOGY

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Abstract:

The main purpose of spray drying method in pharmaceutical technology is to get dried particles in desired characteristics like their physicochemical and morphological properties. In these recent studies, there is identifying the important of spray dryer technology compare to all other drying method used in food and pharmaceutical industry. In this review there is basic construction of spray dryer machine and their process and how the construction part of machine affects the characteristic of product (dried particles). The further year there is modification in spray dryer machine to improve a characterization of product as per required. Types of spray dryer are done based on direction air and feed flow, depend upon number of passes before the dried product is separated, based on aspect ratio, fluidize spray dryer, multistage spray dryer, compact spray dryer, integrated filter dryer, FILTERMAT® dryer.

In this present review is focus on spray dryer has critical parameter which will be affect the properties of the final dried product, this parameter taken under consideration. Innovation in spray drying technology improve efficiency in food and pharmaceutical products. In this there are advantages of spray dryer technique compare to other drying method. Spray drying method is mainly used in encapsulation of drugs, co-processed excipients and drugs, improve the compatibility of various drugs, increasing the aqueous solubility and bioavailability of the active substances and taste masking microsphere in oral disintegrating tablets. Aim of the present review is to give all possible information and brief usefulness of spray dryer technology.

Keywords: *Spray dryer, atomizer, pharmaceutical, co-processed excipients, aqueous solubility, bioavailability, modified release, Inhalation powder.*

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INTRODUCTION:

The idea of spray drying is conversion of feedstock from a fluid state into dried powder form due to spraying feedstock into hot gaseous drying chember. This technique overcome the problems of continuous process performance, efficacy and safety.the first industrial application of this technique its use for milk powder production. [1] Spray dryer is introduce during World war, this time need to be of transportation of huge amount of foods in emergency at this time due to this technique there is reduce the weight and volume of foods having better conservation technique.After world war, are finespray dryer is use for pharmaceutical industries.In recent year research is done for various construction in spray dryer which gives the desired characteristics of product.This method is mainly used for the powder has poor flowability,also problems associate with chemical materials than other drying technique. [2,3]

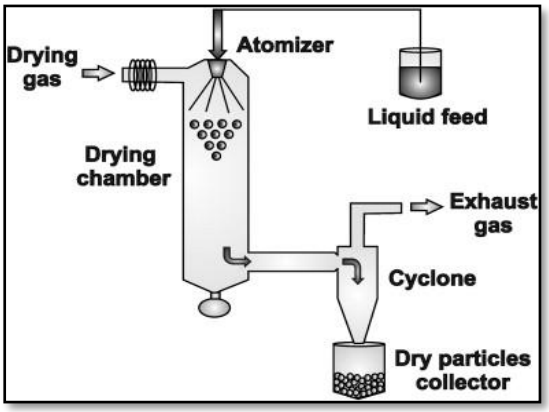

Figure 1: Spray dryer

Spray drying involves the stages:

1) Feedstock: This are liquid must be concentrated products prior to administration into drying medium, the feedstock include solution, emulsion, suspension.

2) Atomization: It is process create the optimum condition for evaporation of solvent and get dried particles at desired size. The atomization occurs by different device called as atomizer. This formation of very large surface areas that are exposed to the drying gas. [1,2] This large surface area facilitates the heat transfer from the heated drying gas to the atomized fluid particles that results in evaporation of the solvent in seconds and mass transfer back into gas phase. An only method of drying allowing for the formation of particles with the desired physiological and morphological properties. [4]

a. Rotary atomizer: Driven by high velocity discharge of liquids from edge of wheels or disc. The outward flowing liquid with respect to rotating wheel surface accelerates to the periphery and then disintegrate into a spray of droplets.

Atomization Energy: Centrifugal energy

Atomization parameter: Wheel speed in rotation per minute (RPM)

Types of spray: fine, coarse or medium
Mean droplet size: 30-120 µm
Advantages: mainly they do not clog and they tend to produce more uniformly sized droplets. The liquid feed supply under the low pressure than other nozzles.
Disadvantage: Rotary atomizer present difficulties in handling viscous feed.

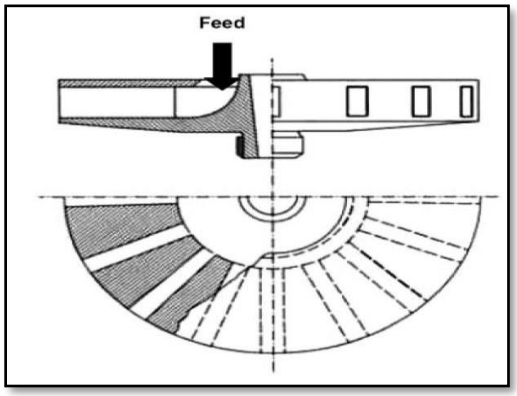

Figure 2: Rotary atomizer

b. Pressure nozzle (or hydraulic) atomizer: This facilitated by discharge of liquid under pressure through an orifice. This nozzle is also called one-fluid nozzles. Pressure energy is converted to kinetic energy, and feed emerging from the nozzle orifice as a high speed film readily breaks into a spray of droplets.
Atomization energy: Pressure energy.
Atomization parameters: Nozzle pressure.
Operating pressure range: 250–10,000 PSI.
Type of spray: Coarse and less homogeneous.
Mean droplet size: 120–250 µm.
Advantage: This nozzle is give higher density (greater size particles) of powdered product and with good flow characteristics.
Limitations: At high feed rates, sprays are generally less homogeneous and coarser than rotary atomizers.

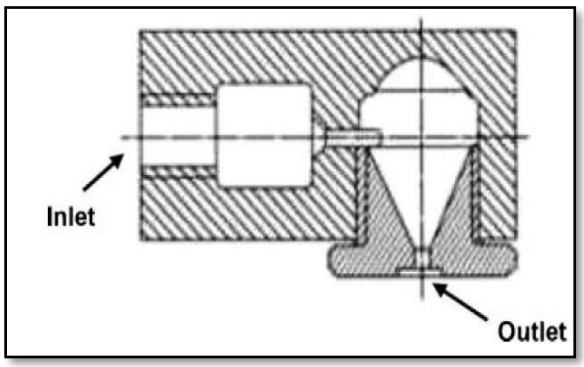

Figure 1: Pressure atomizer

c. Two- fluid nozzle atomizer: Two-fluid atomizers feature the break of liquid on impact with high velocity air or other gaseous flow. Compressed air creates a shear field, which atomizes the liquid and produces a wide range of droplet sizes. If such a construction provides the ability to atomize one kind of feed, it is called a three-fluid construction. The four-fluid nozzle may be used to develop polymeric particles with prolonged or controlled release. [1,5] It allows the production of particles smaller than 1 mm in diameter and with a significantly narrower size distribution than the two-flow nozzle. [1,6] The use of four-fluid nozzles allows the production of nanoparticles with enhanced pulmonary and oral absorptions of materials that are insoluble in water. [1,7]

Atomization energy: Kinetic energy.
Atomization parameters: Nozzle pressure.
Operating pressure range: 250–10,000 PSI
Type of spray: Medium coarseness but poor homogeneity
Mean droplet size: 30–150 μm.
Advantage: This nozzle handling highly viscous feed, finer and more homogeneous spray compared to pressure nozzles and have better control over the droplet size.
Limitation: ineffective heat transfer, chances of clogging of nozzle, expensive clean up and tedious maintance procedure.

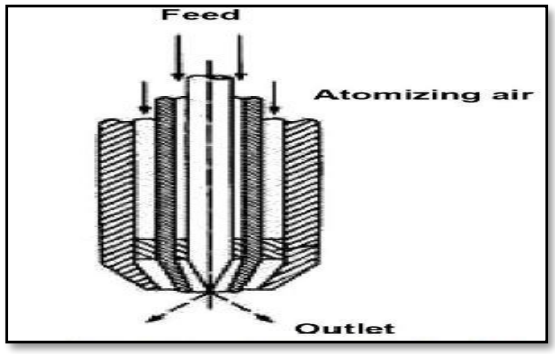

Figure 4: Two fluid atomizer

d. Ultrasonic atomizer: In such nozzles, a high-frequency electric signal is applied to two electrodes placed between two piezoelectric transducers, causing vibrations that are further transferred and amplified by a titanium nozzle tip. The nozzle outlet in the atomization spot vibrates at the ultrasonic frequency and causes the feed to be atomized. The low-voltage electro-hydrodynamic nozzle has been developed for the atomization of very labile particles (e.g., DNA particles) and for when a small size (<5 mm) and high homogeneity of the product is required.

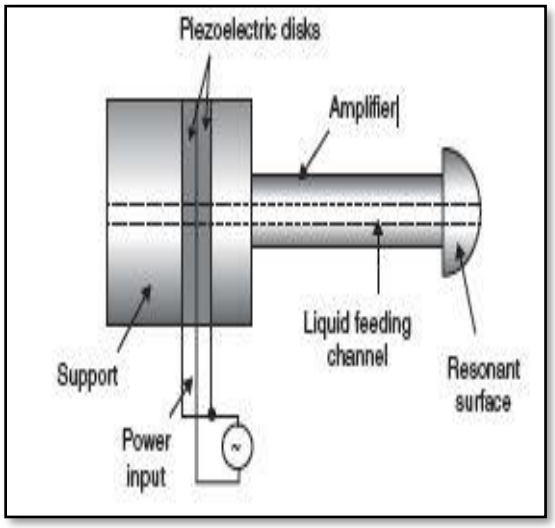

Figure 2: Ultrasonic atomizer

3) Air–Droplets Contact Systems:

The term ‘‘air–droplets contact’’ refers due to in drying chamber spray droplets contact with hot gas and inert gas such as nitrogen maximum amount of solvent will be evaporating.

A. Co-current flow: In this both atomizing discs and nozzle-based constructions are used. The co-current dryer is the most universal and the most often used type of drying chamber. [1,9] This results in advantages of low temperature and low residence time of particles, it is suitable for heat sensitive product. This is highly undesirable, especially in expensive pharmaceutical formulations, because its occurrence strongly affects the process efficiency. [1,8] This allows the product moisture content to be brought to the desired values relatively slowly. [1,11]

B. Counter-current flow:
In this method, the agglomeration of dried particles (porous powder) is quite common, which can be useful for some pharmaceutical applications. [1,8] This type of arrangement is used only for heat-resistant products.

C.Mixed flow: The air enters into top and atomizer located at bottom. This operator must be managed the problem of mixing the moist product already dried and product descending down to chamber. For thermo stable substances, this most economical. [1,8]

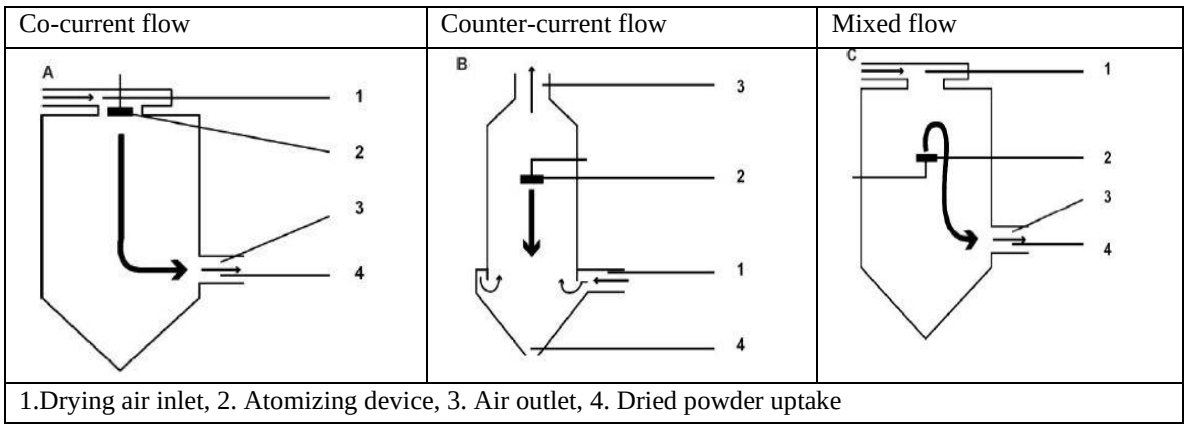

Figure 3: A. co-current flow, B. counter -current flow, C. mixed flow

4) Droplet Drying: Moisture evaporation takes place in two stages-

1. During the first stage, in a drying chamber droplet of liquid due to contact with hot drying air results continuous evaporation of moisture in droplet. [12,13]
2. The second stage, due to constant rate of evaporation is occur no longer moisture is present at surface of droplet, this causing a dried shell to form at the surface. There is diffusion occurs at the droplet surface results increasing in thickness of the shell.

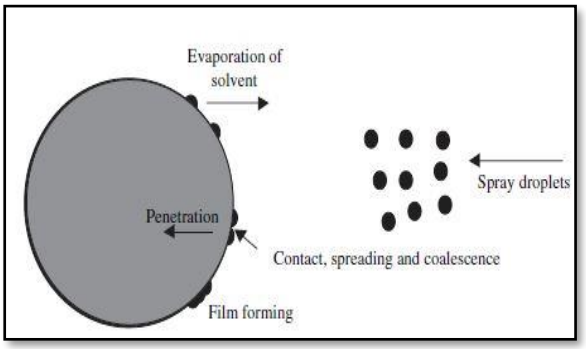

Figure 4: Approach of film formation with fluid bed coating device

5) Separation: Cyclones, bag filters, and electrostatic precipitators may be used for the final separation stage. Wet Scrubbers are often used to purify and cool the air so that it can be released to atmosphere.

Types of spray dryer:

1) Based on the direction of air and feed flow:

a. Open cycle: - This is the standard layout of spray dryer, with wide usage. It involves drawing the drying air from the atmosphere, heating and conveying it through the chamber once, and then exhausting it back to the atmosphere. The variations in this layout could be with respect to the type of separation equipment used (i.e. use of cyclone separator, bag filter or electrostatic precipitator).

b. Closed cycle: -Closed cycle dryers work on the principle of recycling and reusing the gaseous medium, which is usually a relatively inert gas such as nitrogen, or air in special cases. A closed cycle dryer is used when the feedstock is prepared by dissolving the solids in flammable solvents, in order to reduce the explosion risk and to obtain a complete recovery of the solvent. This have advantage when toxic feed is used.

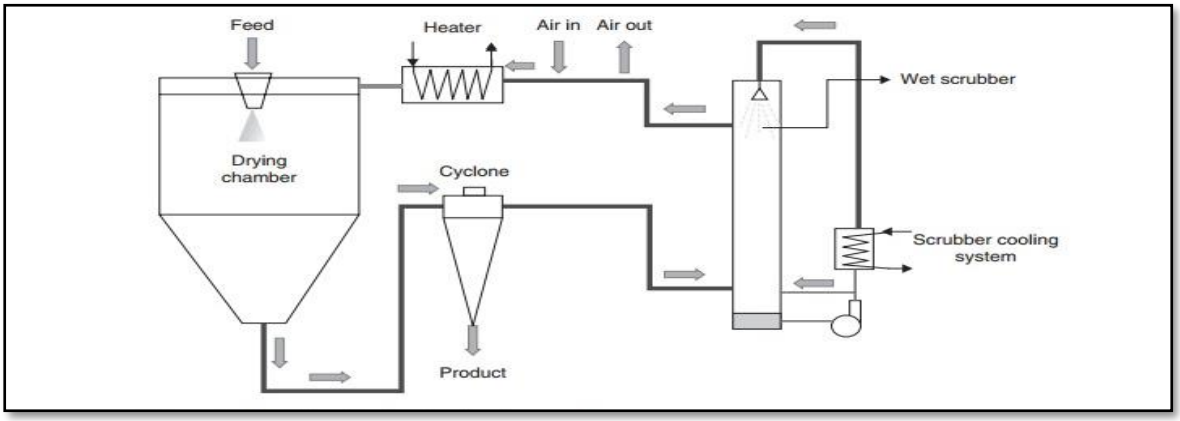

Figure 5: Closed cycle spray dryer

c. Semi closed cycle: - This dryer design is cross between open and closed cycle dryer. An amount of air equal to combustion air bled from system at the other end of the process. The gas mainly (products of combustion) is recycled through the dryer. The recycled gas has very low oxygen content, making it suitable for materials that cannot be exposed to oxygen due to explosive hazard or product degradation.

2) Depend upon number of passes before the dried product is separated:

a. Single stage spray dryer: In this dryer, the moisture is reduced to the target level in a single pass through the spray chamber. This is operate at an inlet temperature of 150–200°C and an outlet temperature of around 95°C.the outlet temperature should be higher due to that get final product with low moisture content but it's not suitable for heat sensitive material.

b. Two stage spray dryers: In a two-stage spray dryer, the required moisture content is attained two stages. After leaving the spray chamber, the moisture content of the particles from the first stage, which is typically at the level of 5–10%, is further reduced during a second stage, accomplished in a fluidized bed dryer. The recycled gas has very low oxygen content, making it suitable for materials that cannot be exposed to oxygen due to explosive hazard or product degradation.

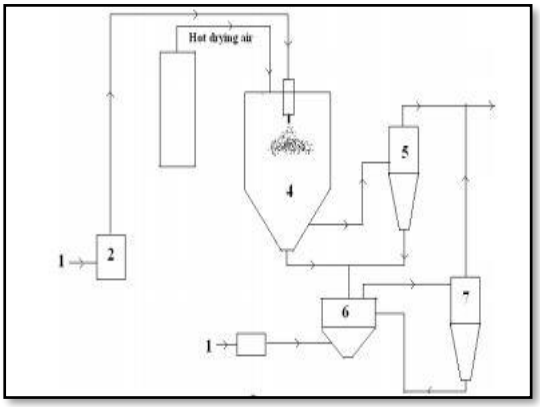

Figure 6: two stage spray dryers (1-air; 2- feedstock; 3- dried product; 4- drying chember;5- cyclone ; 6- stationary fluid bed; 7- bed cyclone)

3) Based on aspect ratio:

a. Short form: Short form dryers have height to diameter ratios (aspect ratio) of around 2: 1. The short form dryer are the most widely used, as they accommodate the comparatively flat spray disk from a rotary atomizer. A short form dryer with a bottom outlet is more suitable for drying of heat sensitive materials, such as proteins, due to the low amounts of recirculated gas and, hence, shorter residence time of the particle. Small chambers are more frequently used, mainly because they allow the usage of both atomizing discs and nozzles. [1,10]

b. Tall form: Tall form designs are characterized by height to diameter aspect ratios of greater than 5: 1. The greater aspect ratio also contributes to the longer residence time of the particles in the drying chamber.

4) Fluidized spray dryer: The Fluidized Spray Dryer combines spray drying and fluid bed drying technologies and offer excellent product flexibility and excellent thermal efficiency. Sticky products can be dried successfully, and the concept is ideal for drying heat sensitive products, and improved aroma retention is accomplished. [12,14]

5) Multi stage dryer: The process produces non-dusty, free flowing agglomerated powders with high flavor retention. It operates with low outlet-temperatures, achieving high thermal efficiency. This design concept is successful for drying high fats, hygroscopic, and sticky products that are difficult to handle in more conventional designs.

6) Compact spray dryer: Atomization is created by either a rotary atomizer or spray nozzle atomizer. 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.

7) Integrated filter dryer: Integrated Filter Dryer - Combines an integrated fluid bed and filter arrangement. It is an adaptable and flexible spray dryer for the food ingredients, food, dairy, chemical, and pharmaceutical industries. The Integrated Filter Dryer (IFD™): features and benefits include: improves powder quality, no handling of product outside drying chamber, reduced noise level and lower energy consumption.

8) Filtermat® dryer: The FILTERMAT® Spray Dryer is frequently used in food and dairy applications. It operates at a low outlet temperature, achieving high thermal efficiency. It is recommended system for drying high fat, sugar-based, hydrolyzed, and fermented products.

The operator of a spray dryer has direct influence on:

– The inlet temperature of the drying air;
– The drying air flow rate;
– The supply rate of the liquid stream; and
– The pressure (and amount) of atomizing air (for the pneumatic nozzle, for other atomizing devices—other appropriate parameters related to atomization).

Other process parameters, such as:

– The outlet temperature of the drying air;
– The droplet size;
– The drying efficiency (product mass); and

– The physical properties of the dried product (e.g., the particle size, moisture content, and hygroscopicity); are dependent on the mutual relationships of the parameters adjusted by the operator, on drying air humidity (most often drawn from the atmosphere), and on the properties of a given feed.

Innovations in spray drying:

A. Sterile spray drying for stable injectable liquid formulation: Soluble glass microspheres forming a monodisperse suspension in anhydrous fluorocarbon liquid because the microspheres are solid, their density can be precisely controlled to match that of the surrounding liquid. Such suspensions are physically stable and the particles neither settle nor float in the liquid phase. [12,15]

B. Foam spray drying: In this method liquid food is foamed, such as milk or coffee, before spraying it into the drier. The result is faster drying rate from the expanded foamed droplet surface area, and lighter density dried product. This is known as foam-spray drying. [12,16]

C. Spray drying for the production of crystalline products: Spray drying is known to produce predominately amorphous material due to the almost instantaneous transition between liquid and solid phases. However, spray drying can also be used to obtain crystalline products. [12,18] To achieve such a goal, the product is fed in a crystalline suspension, instead of a solution, to the drying chamber. Feeding the crystals in the right form allows spray drying to fine tune crystal size distribution and final content of residual solvents. [12,17]

Advantages:

1) Spray dryer is widely used in Pharmaceutical, Chemical, Material, and Cosmetic and Food industries. [20, 21, 22, 23]
2) Used both lab and industrial, it is rapid, continuous, reproducible and single step. [20, 24, 25, 26]
3) Final drying requires in other common technique use to produce particles but is not required in spray-drying. [20, 27, 28]
4) Spray dryer is scalability and cost effectiveness, so it is commonly used in industry.
5) Fast solvent evaporation method and it is accompanied more quickly than lyophilization, that's why this technique has great potential alternative for lyophilization. [20, 31, 32, 33]
6) Possibility to dry a broad spectrum of compounds due to innovation in spray dryer technique there is also drying of heat-sensitive substances without major detrimental effect. [20,29]
7) This technique was conceived as dehydration process used to prolong the life span of the products.
8) Remarkable advantage is that the powders obtained by spray drying have better flow properties than conventional formulations. Example: microparticles poly (D, L-lactic acid) both by spray drying and solvent evaporation with angle of response of 29.7 and 42.2 respectively including excellent flow property in the first case and poor in second case. [20, 29]
9) In spray dryer separator (filter system) are effective under industrial setting to increase the yield.

Limitation:

1) Aseptic process maintains is more challenging than it is for lyophilization.
2) Problem during handling of protein materials because material exposed to significant shear stress during atomization and large surface mass ratio in droplets result in significant air-water interfaces at which protein can be denature.
3) Spray drying with some unique caveats as well.
4) There may be difficulties associate with handling of hygroscopic powder.
5) The fact that material recovery is less than 100 % is also an issue when considering it is implementation for high cost therapeutics.

Applications:

1) Modified release from spray dried particles:

Microencapsulation is a technique where liquid droplets, solid particles or gas compounds are entrapped in an encapsulating agent. The compound to be encapsulated usually stays in the core of the capsule surrounded by the encapsulating agent or dispersed in one matrix containing the encapsulating agent. [35,36]

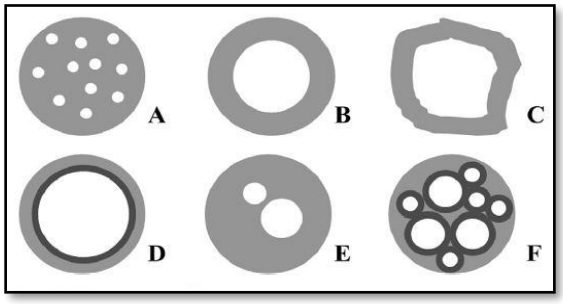

Figure 10: Morphology of different types of microcapsules: A: matrix, B: simple Microcapsule, C: irregular microcapsule, D: multiwall microcapsule, E: multi-core microcapsule and F: aggregate of microcapsules.

Encapsulating agents: The criteria for selecting a wall material are based on the physicochemical properties of the substance to encapsulate (porosity, solubility) and of the encapsulating agent (viscosity, mechanical properties), the compatibility between the two (the wall material should be insoluble and should not react with the core) and processing. [35,37,38,39] this are mainly solution of polymers like chitosan [35,39,41,42] , Modified chitosan [35,43,44,45] , Crosslinking agents [35,46] trying for drugs like Ampicillin, Acetaminophen, acyclovir and Exotoxin .Microencapsulation using spray dryer use for food industry. There is also done encapsulation of food pigment such as lycopene was successfully microencapsulation by spray drying using a wall system consisting of gelatin and sucrose. Spray drying has been considered as an excellent means of preservation of nutritive value of vitamins and this technique could consequently be suitable to encapsulate all vitamin groups. [47]

2) Co-processed excipients through spray dryer:

This is novel technique by combine two excipients and excipients with drug.

Particle property	Excipient functionality
Enlargement of particle size	Flowability, compressibility
Particle size distribution	Segregation potency
Enlargement of particle porosity	Compressibility, solubility
Surface roughness	Flowability, segregation potency

Table 1: Various particle properties influencing excipient functionality

Example of Co-processed excipients prepared from spray dryer are Ludipress, [49] Fujicalin, [49] Advantose 100, [49] Starlac[49].

a) Ludipress : - It is combination of lactose, PVP and Crosspovidone. It is use in chewable tablets and lozenges, for effervescent tablets and as bulking agent for modified release formulations.
b) Fujicalin : - fujicalin is spherically granulated dicalcium phosphate anhydrous prepared by spray-drying. It has lower particle size, high porosity and high specific surface area. It is gives significantly stronger tablets than Di-cafos.
c) Advantose 100 : - It is a spray-dried maltose having spherical particles with optimal combination of fine and coarse particles that contributes superior flow. Compared to microcrystalline cellulose, spray dried maltose can tolerate significantly greater compression force without capping upon ejection from the tablet die; it has low hygroscopicity and low reactivity than microcrystalline cellulose.
d) Starlac : - Starlac is co-processed excipient consists of lactose monohydrate and maize starch produced by spray- drying, it has good flowability depending on the spray-drying process, an acceptable crushing force due to lactose content and its rapid disintegration depending on starch.

3) Increasing the aqueous solubility and bioavailability of active substances:

There are many drugs they have problem regarding solubility in the water, due to overcome this various method are involve to increase solubility. [50, 51] Spray drying to produce particles with reduced size and to control the characteristics of final particle such as size, shape, morphology, surface properties and electrostatic charge.

Spray dryer improve the aqueous solubility [52] of drug like Artemisinin, Griseofulvin [52], Itraconazole, Flurbiprofen, Curcumin and Piroxicam. Artemisinin that has been spray dried with different ratios of maltodextrin and under different process parameters. The aqueous solubility of cospray-dried material was related process parameter influence the particle characteristics that responsible for solubility. [50]

4) Inhalation powders:

Spray-drying has ability to produce homogeneous particles within the desired small particle size range (< 5 μm), [53] low moisture content, and high drug purity. In the case of an IgG1 antibody formulation spray-dried with mannitol, trehalose, saccharose, and isoleucine and subsequently vacuum dried, it was demonstrated that these substances increase the stability of the stored protein powders and enhance their intrinsic properties spray drying to create a stable dry protein powder for pulmonary delivery.

5) Improve the compatibility of various drugs:

Improving the compatibility of drugs via co-spray drying is an interesting manufacturing technique for the pharmaceutical industry since it uses a one-step process to dry and agglomerate powder, thus obtaining homogenous powder which can become free-flowing through process optimization. Example; Powder mixtures containing Acetaminophen (drug conc. 70% w/w) and ibuprofen (drug conc. 75%) were successfully manufactured on production scale spray dryer. [54] Direct compression of powder is done without granulation, milling and blending steps.

6) Taste masking microsphere in oral disintegrating tablet:

In recent year, microencapsulation and microspheres has been developed taste masking by creating physical baarier to protect the bitter drugs from coming in contact with the patients taste bud.

Jianchen Xua et al. done Famotidine microsphere by using spray dyer than directly compressed into tablet (ODT). [55] The microsphere neither decrease the bioavailability and nor delay release of famotidine significantly. Based on the result spray-dried microspheres provide an effective method for taste masking and can be incorporated in ODT.

CONCLUSION:

Spray drying is presently one of the most exciting technologies for the pharmaceutical and food industries. It is ideal process where the end product complies with precise quality standards regarding particle size distribution, solvent content, bulk density and morphology. One of the advantages of spray drying technology is that multiple application and the wide range of products that can be obtained. Due to novel modification of spray dryer machine give satisfactory result of end product compared to other drying process. spray drying offer unique opportunities in particle size engineering.

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