

**APPLICATIONS OF SPRAY DRYER IN PHARMACEUTICAL INDUSTRY :
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ABSTRACT

The primary goal of the spray drying procedure is to provide dried particles with the appropriate physicochemical and morphological qualities which will be beneficial for pharmaceutical industry. The most recent research indicates that spray dryer technology is more important than any other drying method used in the pharmaceutical sector. The principle, construction, operation, and applications in the pharmaceutical industry are covered in this overview. Every year, the spray dryer apparatus is adjusted to improve the product's characteristics as required. The applications of the spray drying method include production of dry powders for inhalation (DPI), the encapsulation of medications, converts liquid formulations into free-flowing granules, ideal for drying heat-sensitive materials, enhancing the compatibility of different medications, boosting the aqueous solubility and bioavailability of the active ingredients, and creating taste-masking microspheres in oral disintegrating tablets. The present paper provides a comprehensive review about spray dryer technology and its applications in pharmaceutical industry.

Keywords: Spray dryer, aqueous solubility, bioavailability, modified release, Inhalation powder, heat-sensitive materials, pharmaceutical industry.

INTRODUCTION

A spray dryer is a device used to convert a liquid or slurry feed into a dry powder by rapidly drying it with a stream of hot gas. The process involves atomizing the feed into fine droplets, which are then introduced into a drying chamber where moisture evaporates almost instantly, leaving behind dry, solid particles¹. The capacity of this process to create free-flowing powders with regulated particle size and good stability makes it popular in the food, chemical, and pharmaceutical industries².

Spray drying is a widely established technique for the production of dry particles from fluid materials, utilizing a stream of hot gas as the drying medium^{1,3}. The process converts a liquid feed such as a solution, suspension, or emulsion—into fine, dry powder in a single, continuous step. First observed in

1860 and formally patented by Samuel Percy in the United States in 1872, the method has undergone significant evolution in terms of both design and industrial application³.

Spray drying's early development was constrained by problems with scalability, energy efficiency, and operational safety. But these issues were eventually resolved by technological developments, which resulted in improved performance and extensive industrial application. The introduction of spray drying in the food industry, especially in the creation of milk powder, which is still one of its most common applications today, marked a significant turning point in the technology's development in the 1920s⁴. During World War II, when it was vital to lighten the weight and bulk of food and other necessities for easier storage and transportation, the method's development was further pushed. This historical background contributed to the establishment of spray drying as a standard technology in a number of industries⁵.

Pharmaceuticals, chemicals, ceramics, and polymer manufacture are just a few of the industries that have used spray drying as a result of post-war developments. The increasing need for tailored particles with extremely particular physical and functional properties has kept spray drying at the forefront of research and development for over a century⁶.

The ability of spray drying to create free-flowing powders with regulated moisture content, morphology, and particle size distribution accounts for its long-lasting attractiveness. It is also a useful and effective tool in both research and large-scale production settings due to its high throughput capability and adaptability in handling a variety of input materials, from complex polymers to heat-sensitive biologics⁷.

Spray Drying Mechanism

The spray drying process can be broadly divided into three key stages:

1. Atomization
2. Droplet Drying (Droplet-to-Particle Conversion)
3. Particle Collection

Advantages of Spray Dryer⁸:

- Rapid drying converts liquid into dry powder within seconds.
- Suitable for heat-sensitive materials, preserving stability of proteins and enzymes.
- Produces powders with uniform and controlled particle size and shape.

- Continuous process ideal for large-scale industrial production.
- End product is dry, free-flowing, and usually doesn't require additional drying.
- Easily scalable from lab to industrial scale.
- Can handle various feed types including solutions, suspensions, and emulsions.
- Allows precise control over temperature, airflow, and droplet size.
- Enhances product stability and shelf life by reducing moisture.
- Inert gas drying can be used for oxygen-sensitive substances in closed systems.

Disadvantages of Spray Dryer ⁹:

- Consumes a large amount of energy due to the need for hot air.
- Equipment is bulky and expensive to install and maintain.
- Thermal efficiency is relatively low because of heat losses.
- Not suitable for very viscous feed materials, which are hard to atomize.
- Fine particles may be lost in the exhaust if not properly captured.
- Can generate dust, requiring additional dust handling and filtration.
- Exhaust air may require treatment, leading to environmental concerns.
- Requires skilled personnel for proper operation and control.
- Sticky materials may adhere to chamber walls, reducing product yield.
- Some sensitive components may degrade if temperature is not precisely controlled.

Pharmaceutical Applications:

1. Dry Powder for Inhalation (DPI) of Antibiotics

a) Tobramycin

High-pressure homogenization and spray-drying techniques were used to develop new dry powder inhalation formulations that combined micro- and nanoparticles to enhance lung deposition. Particle size was examined using laser diffraction. Spray-drying was employed to remove dried-powder nanoparticles from tobramycin nanosuspensions. A multi-stage liquid impinger was used to evaluate the different formulations' aerolization properties. Tobramycin nanoparticle suspensions comprising 2% (w/w) tobramycin and a mean particle size of about 200 nm were prepared using sodium

glycocholate. The spray-dried powders' results demonstrated that the formulations' better particle dispersion qualities during inhalation were a result of the nanoparticles. The most effective formulation had a fine particle fraction (percentage of particles below 5 μm) of roughly 61%, compared to 36% for the raw micronized tobramycin material. These novel tobramycin DPI formulations with nanoparticles, which are based on the use of very low levels of excipient and have strong lung deposition capabilities, present significant opportunities to enhance drug delivery to the pulmonary tract⁹.

b) Ciprofloxacin

For the most effective formulation, the fine particle fraction (percentage of particles below 5 μm) rose from 36% for the raw micronized tobramycin material to almost 61%. With their strong lung deposition capabilities and extremely low excipient levels, these novel tobramycin DPI formulations with nanoparticles have significant opportunities to enhance drug delivery to the pulmonary tract. The EE of the liposomes was found to vary between 44 and 87% w/w as the sucrose concentration was increased from 25 to 57% w/w. The powders contained partially crystalline particles with a volume median diameter of around 1 μm . The powders had modest water content (about 2% wt.) and remained stable at high relative humidity. Aerosol administration using the Osmohaler® inhaler at a flow rate of 100 L/min produced an aerosol fine particle fraction (% wt. < 5 μm) of 58–64%. The formulation with the highest sucrose concentration (2:1 w/w sucrose to lipid) demonstrated prolonged ciprofloxacin release from liposomes (80% released by 7 hours) in contrast to the initial liquid formulation, which shown ciprofloxacin released from liposomes in two hours¹⁰.

3) Aztreonam

A concentrated formulation of aztreonam lysinate was administered as an aerosol or dry powder formulation to treat pulmonary bacterial infections caused by gram-negative bacteria, including those caused by *Escherichia coli*, *Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Pseudomonas aeruginosa*, *Haemophilus influenzae*, *Proteus mirabilis*, *Enterobacter* species, *Serratia marcescens*, *Burkholderia cepacia*, *Stenotrophomonas maltophilia*, *Alcaligenes xylosoxidans*, and multidrug resistant *Pseudomonas aeruginosa*¹¹.

4) Clarithromycin

Clarithromycin (CLM), a member of the macrolide family, exhibits a broad spectrum of antibiotic activity. It is practically insoluble in water and has a poor solubility that depends on pH. In this work, a series of nanosuspensions including CLM and stabilizers like HPMC, NaCMC, polysorbate 80, poloxamer 188, and polyvinyl alcohol in varying ratios were made using the sonoprecipitation

method. To put it briefly, CLM was dissolved in an acidic solution, the pH of the solution was raised by sonication, and the effect of several stabilizers on the nanoparticles' size was evaluated. The nanoparticles were characterized using zeta potential, size, polydispersity index, differential scanning calorimetry, and dissolving studies. To compare the antibacterial activity of CLM nanosuspension with coarse powder, an agar well diffusion method was employed. The outcome demonstrated that HPMC was more successful in lowering particle size, and by adding HPMC E5 to the formulation at a ratio of 3:5 to CLM, a stable nanosuspension with a particle size of 340 nm was produced. Increased antibacterial activity and dissolution rate were successfully proven by the resultant nanosuspension¹².

5) Rifampicin

The purpose of this study was to examine a novel dry powder formulation of rifampicin (RF) that demonstrates an improved lung deposition profile by undergoing a polymorphic transition into a flake-like crystal hydrate. Rifampicin dihydrate (RFDH) was produced by recrystallizing RF in anhydrous ethanol. An amorphous RF (RFAM) control formulation was made by spray drying. The physicochemical properties of the RFDH and RFAM were described. The aerosol performances of RFDH and RFAM were examined using two dry powder inhalers (DPIs), an Aerolizer® and a Handihaler®, and a Next Generation Impactor (NGI). Slender, flimsy construction. This specific shape enhanced aerosolization properties while lowering the device's dependence on aerosolization. Because of its flaky look, RFDH has a reduced propensity to aggregate than spherical RFAM particles. The RFDH achieved a maximum fine particle fraction (FPFTD) of 68% with the aid of the Aerolizer® device³⁵. The RFAM showed significant chemical breakdown at nine months, but the RFDH showed no discernible chemical degradation. Delivering an antibiotic formulation with maximum power directly to the lung, the site of illness, is the benefit of the RFDH's excipient-free formulation¹³.

6) Norfloxacin

The objective of this study was to use norfloxacin (NFX) to create a novel hydrophilic matrix technology. Since extended-release pills are often intended to be taken once daily, the patient benefits and the likelihood of stopping medicine is decreased. Using hydrophilic hydrophilic polymers, such as poly(ethylene oxide) or hydroxypropylmethylcellulose, formulations with different molecular weights (MWs) and concentrations (20 and 30%) were made. The pills were found to remain stable after six months at $40 \pm 2^\circ\text{C}$ and $75 \pm 5\%$ relative humidity. The film-coating process is recommended to stop NFX photodegradation. The dissolution profiles demonstrated an

extended-release of NFX for each formulation that was developed. Drug diffusion and polymer relaxation or erosion mechanisms both regulated drug release, according to dissolution curves studied using the Korsmeyer exponential equation. A better erosion-controlled system was attained for formulations with lower MW and polymer quantities. As the MW and amount of polymer in the formulation increased, the gel layer got stronger and the dissolution became more dependent on drug diffusion. Formulations including intermediate MW polymers or a high concentration (30%) of low MW polymers demonstrated prolonged and thorough in vitro drug release. In this way, these formulations can potentially improve bioavailability in vivo¹⁴.

Used for: Treating lung infections, especially in diseases like cystic fibrosis, bronchiectasis or tuberculosis.

Spray drier converts liquid antibiotics into fine powder (1–5 µm) which are used to treat respiratory infection.

Antibiotics used:

- Tobramycin (e.g. TOBI® Podhaler)
- Ciprofloxacin
- Aztreonam
- **Benefits:** Targeted lung delivery, reduced systemic side effects, rapid action.

Companies using this:

- **Novartis:** TOBI Podhaler (spray-dried tobramycin powder)
- **Insmad Inc.:** Arikayce (spray-dried amikacin liposomal inhalation)
- **Pulmatrix:** Ciprofloxacin DPI using iSPERSE™ spray-drying platform

Table no.1: Marketed Dry Powder for Inhalation (DPI) of Antibiotics

Sr. No.	Drug name	Company name
1	Tobramycin	Novartis
2	Ciprofloxacin	Bayer AG
3	Aztreonam	Lexicare Pharma Pvt. Ltd.
4	Clarithromycin	Abbott
5	Rifampicin	Lupin Pharmaceuticals
6	Norfloxacin	Cipla, Jai Radhe Sales, China Chemical

2. Stabilizing Heat-Sensitive Antibiotics

Used for: Preserving antibiotics like erythromycin and ampicillin, which degrade in liquid form.

Spray drying role: Converts into amorphous or crystalline powders at controlled temperatures.

Result: Improves storage stability and shelf-life.

Common carriers used: Lactose, trehalose, mannitol.

Companies: GSK, Pfizer, Patheon (by Thermo Fisher)

a) Erythromycin

Many bacterial illnesses affecting the skin, respiratory system, intestines, bones, and other systems are being treated with erythromycin, a macrolide molecule with a wide variety of antibiotic properties. It was discovered in 1952 and immediately became famous because to its ability to treat illnesses that are resistant to other treatments. There are several drawbacks to erythromycin that pose serious clinical challenges. Their exceedingly low water solubility and instability in acidic settings result in reduced bioavailability and efficacy. Furthermore, higher dosages promote adverse effects and medication resistance. In an attempt to overcome these limitations, a variety of Erythromycin formulations, including nanoparticles, have been created throughout the last few decades¹⁵. Their physico-chemical characteristics, performances, and preparation/synthesis were also thoroughly examined. There is also discussion of the limitations of this research, including the measurement of Erythromycin.

b) Ampicillin:

Supercritical fluid expansion depressurization (SFED) is a novel technique for producing microparticles with a limited size distribution. Erythromycin microparticles were successfully precipitated from ethanol in this investigation using the SFED technique. The resultant particles were spherical or nearly spherical and less than 3 μm . The effects of the operation parameters on the size, distribution, and morphology of the particles were thoroughly examined. The concentration of the solution, the rate at which the solution was fed into the precipitator, the temperature in the precipitator, and the temperature and pressure in the mixing vessel were some of these variables. The results show that the solution feed rate and the mixing vessel pressure are the two most effective operational parameters, followed by the solution concentration. Although the temperatures in the mixing vessel and precipitator have little effect on the particles, they have a big impact on the yield of the final product. The SFED approach can manage the size, shape, and dispersion of erythromycin microparticles and create them with a tight size distribution by altering the operation parameters¹⁶. Using 10 MPa of pressure, 70 °C in the mixing vessel, 9 ml/min of solution feed rate, 15 mg/ml of

solution concentration, and 70 °C precipitator temperature were the optimal operating parameters for manufacturing erythromycin microparticles.

Table no.2: Marketed Heat-Sensitive Antibiotics

Sr.No	Drug Name	Company Name
1	Erythromycin	Divyajivan Healthcare Pvt. Ltd.
2	Ampicillin	Aurobindo Pharma Ltd.

3. Encapsulation of Antibiotics (Controlled Release)

Goal: To reduce dosing frequency and increase local effect.

Mechanism: Encapsulation in biodegradable polymers (e.g., PLGA) via spray drying.

Example: Spray-dried rifampicin microspheres for sustained release.

Applications: Tuberculosis, implant coatings, oral sustained-release systems.

Companies:

Evonik (RESOMER® polymers)

Lonza (Spray-dried multiparticulates for sustained release)

a) Cefotiofur

One of the largest threats to global public health today is diabetes. All throughout the world, the disease is becoming more common, and by 2030, 366 million people will be affected. Diabetes mellitus (DM) is quite prevalent in Saudi Arabia, with type 2 DM making up the majority of cases. Due to the poor tolerability of commercially available oral antidiabetic drugs during long-term therapy, a relatively significant number of patients with type 2 diabetes are still not receiving the correct care. Vildagliptin nanospheres were made with aminated gelatin by a spray-drying method; a restricted particle-size distribution was seen at 445 nm. The angle of repose was found to be $\theta < 33.5^\circ$. The drug content and percentage yield of the nanospheres were found to be $76.2\% \pm 4.6\%$ and $83\% \pm 2\%$, respectively. The nanosphere-swell profile was found to be $165\% \pm 7\%$. The nanosphere formulation took 12 hours to dissolve ($97.5\% \pm 2\%$), and the pure medication dissolved 100% in 30 minutes. In line with a Korsmeyer–Peppas kinetic model, its R^2 was 0.9838. Nanospheres displayed a remarkable

mucoadhesive property at 86.7% for eight hours in the wash-off test. The stability-study findings indicated that the nanospheres should be stored below room temperature because it exhibited no changes in their physicochemical features. Compared to the formulation of gelatin vildagliptin nanoparticles, 1.6% of the vildagliptin was retained after three hours, and after twelve hours, this percentage had increased to 98.2% ¹⁷.

4. Improving Solubility and Bioavailability of Poorly Soluble Antibiotics

Strategy: Convert crystalline antibiotics into amorphous solid dispersions.

Example antibiotics: Clarithromycin, rifampicin, norfloxacin.

Benefits: Increased dissolution rate, faster onset of action.

Companies involved:

Catalent Pharma Solutions

Hovione (specialist in spray-dried amorphous solid dispersions)

5. Combination Formulations of Antibiotics

Use case: Co-spray drying two or more antibiotics for synergistic action.

Example: Levofloxacin + metronidazole co-spray-dried powder.

Benefit: Improved pharmacokinetic harmony, single-dose therapy.

Companies:

Cipla, Aurobindo Pharma (generic formulation development)

Dr. Reddy's Labs (custom antibiotic blends)

a) Levofloxacin + metronidazole

Pseudomonas aeruginosa is typically the cause of the contaminated mucus plugs found in the respiratory systems of patients with cystic fibrosis. Nebulized levofloxacin is effective against *P. aeruginosa*, but cleaning and administering it takes a lot of effort. DPI can be a good alternative to get around this restriction if it is feasible to load a sizable required dose. The purpose of this work was to use a solvent-free spray drying process to produce and characterize a levofloxacin powder without an excipient. The resultant particles were small, spherical, and crystalline. Under pharmacopoeial impactor settings, high respirable fractions and fine particle emissions were produced even with high

drug loadings. Variations in the impactor pump's air flowrate have no effect on the aerodynamic performance. After a year of storage, most important traits remained unchanged. The fact that the novel technique requires only four capsules to deliver the same amount as the commercially available nebulization solution highlights its potential for treating cystic fibrosis¹⁸.

6. Spray Drying of Antibiotic-Loaded Nanoparticles

Function: Converts nanosuspensions into dry powders for ease of use.

Example: Colistin-loaded lipid nanoparticles spray-dried for pulmonary delivery.

Target: Multidrug-resistant (MDR) bacterial infections.

Key partners:

Skyepharma

Nanoform Finland

a) Colistin

Colistin is often the last antibiotic used to treat respiratory infections caused by multidrug-resistant Gram-negative bacteria, despite the fact that it is nephrotoxic when administered parenterally. Colistin inhalation therapy holds great potential for improving efficacy and reducing adverse effects. In this study, inhalable powder formulations of colistin (sulphate) were made by spray drying. The colistin granules had intact antibacterial activity against *Acinetobacter baumannii*, as demonstrated by broth microdilution. Both the spray-dried formulations and the amorphous raw material absorbed a significant quantity of water up to 30% (w/w) at a relative humidity (RH) of at least 70%. The high aerosol efficiency (emitted dose >86% and fine particle fraction total >83%) and physical stability in the amorphous state at 60% relative humidity and 25°C of the spray-dried formulations did not change after three months of storage¹⁹. The formulation particles fused together (but did not re-crystallize) at RH 90%, and the aerosolization performance was significantly diminished when stored at a higher RH of 75%. Although spray drying has been routinely utilized to make inhalable medication particles, this is the first publication that shows colistin powder can be physically stable in its amorphous state at ambient settings. This implies that the spray-drying method is suitable for developing a powdered version of colistin that may be inhaled²⁰.

II. OTHER MEDICINAL APPLICATIONS OF SPRAY DRYERS

7. Formulation of Biologics & Peptides

Use: Spray drying of insulin, interferons, and monoclonal antibodies.

Advantage: Mild drying conditions prevent protein denaturation.

Example: Insulin DPI (e.g., Afrezza by MannKind).

Companies:

MannKind Corp

Recipharm (Biologics spray drying CDMO)

Insulin DPI

"Quality by Design" (QBD) refers to a holistic approach to drug development. Understanding the formulation and process parameters and assessing the final product's performance are essential elements of QBD. For systemic distribution, protein inhalation requires specific product characteristics and a manufacturing process that produces the desired product. The purpose of this study was to better understand the spray drying process of insulin intended for pulmonary administration. In particular, the effects of formulation and process variables on insulin integrity and particle characteristics were investigated. Design of experiments (DOE) and multivariate data analysis were used to identify significant process parameters and correlations between particle properties. The process parameters of the nozzle, feed, drying air flow rate, and drying air temperature were the independent parameters in addition to the insulin concentration as a formulation parameter²¹. The dependent variables included droplet size, morphology, yield, density, tap density, moisture content, outlet temperature, geometric and aerodynamic particle sizes, and physical and chemical integrity. Principal component analysis was used to determine the correlation between the independent and dependent variables. There were prediction equations for every dependent variable, including interaction and quadratic terms. The insulin concentration was shown to be the most important factor overall, followed by the inlet drying air temperature and the nozzle gas flow rate. The insulin molecule's chemical and physical integrity remained unchanged.

8. Vaccines (Thermostable Powder)

Use: Spray-dried vaccines resist cold-chain failures.

Example: Spray-dried influenza vaccine, hepatitis B vaccines.

Key Companies:

Stabilitech (UK) (Now **Stablepharma**) – dry vaccine R&D

Serum Institute of India exploring thermostable vaccine formats

Influenza and hepatitis B vaccines.

It might be preferable to administer vaccinations using the pulmonary route rather than parenterally. Research on the best place for antigen deposition in the lungs to trigger the highest immune responses has produced conflicting results; these results may differ based on the type of vaccination and/or its physical state. Therefore, we examined in this study whether deep lung deposition matters for two different vaccines, the influenza and hepatitis B vaccines. Thus, the influenza subunit vaccine and the hepatitis B surface antigen were marked with a fluorescent dye and then spray-dried. Imaging results showed that when animals were injected pulmonary using a commercially available insufflator, powders were deposited in the trachea and central airways, while deep lung deposition was created by an in-house aerosol generator. Immunogenicity tests showed that formulations of dry influenza vaccines that targeted the deep lungs, central airways, or trachea elicited comparable immune responses. However, deep lung deposition produced an immunological response to the hepatitis B vaccine, while trachea/central airways deposition did not²². Thus, we conclude that whereas deep lung targeting is essential for the hepatitis B vaccine's efficacy, it is not for the influenza vaccine that is injected into the lungs.

9. Taste Masking of Bitter Drugs

Process: Co-spray drying APIs with polymers to mask bitter taste.

Example: Spray-dried metronidazole with Eudragit for pediatric use.

Industry users:

Dr. Reddy's, Zydus Cadila, Sun Pharmakh

Metronidazole

The metronidazole drug was encapsulated in this study by extracting hydroxypropyl methylcellulose and polyvinylpyrrolidone polymers from liquids using a nano spray drying process. We looked studied how formulation elements and process parameters affected manufacturing yield, product morphology and structure, and entrapment efficiency. The use of surface active admixtures, such as Pluronic F68, Tween-80, and polyvinyl alcohol, greatly increased the product yield. The entrapped metronidazole

was partially in both crystalline and amorphous phases in both amorphous polymers, as confirmed by DSC and powder X-ray diffraction studies. In relation to the drug content, the degree of crystallinity varied between 50.2 and 81.0% in the composites that contained hydroxypropyl methylcellulose and between 35.0 and 50.0% in the composites that contained polyvinylpyrrolidone²³. A melting point drop between spray-dried and bulk metronidazole products was found using differential scanning calorimetry. Peak broadening was seen in powder X-ray diffraction studies, which could be the result of the formation of microscopic drug crystallites. The TEM images showed a percentage of smaller crystals (20–50 nm in diameter) in addition to the larger crystals (200–400 nm). These smaller crystals are in line with the 19–87 nm coherent scattering domain sizes that were calculated using X-ray data. The drug-polymer composites created by the nano spray drying process were identified as crystalline-amorphous nanostructured micronized solid dispersions.

10. Sustained and Modified Release Formulations

Use: Spray-dried coated matrix particles for prolonged action.

API Examples: Propranolol, Diclofenac, Ibuprofen.

Matrix-forming excipients: HPMC, EC, chitosan.

Companies:

Colorcon (excipients for spray drying)

BASF Pharma Solutions

NSAIDS

This work investigates formulation methods for producing pharmaceutical powders from precipitated API (active pharmaceutical ingredient) nanoparticles. Composite granules were developed using two distinct formulation processes to address the difficulty of producing medicinal powders with enhanced bioavailability. Lactose granules were produced by embedding isolated ibuprofen nanoparticles (ibuprofen particle size: 100 nm) in a lactose matrix using spray drying. On the other hand, silica granules were produced by encasing ibuprofen nanoparticles in a nanoparticulate silica shell (principal silica particle size: 40 nm). Then, in order to assess different loading methods in terms of drug release, granules were analyzed utilizing dissolving tests. Additionally, differential scanning calorimetry (DSC) experiments were used to demonstrate the solid state, whether crystalline or amorphous, of APIs²⁴. Scanning electron microscopy (SEM) images also allowed for the description of the granules' form.

11. Pulmonary Delivery of Non-Antibiotic Drugs

Use case: COPD and asthma treatment (salbutamol, budesonide).

Spray dryer advantage: Uniform particle size, low residual solvent.

Examples:

Symbicort DPI (budesonide/formoterol)

Firms using:

AstraZeneca

Teva Pharmaceuticals

The purpose of this study was to ascertain the effects of varying spray drying parameters on the production of a 100:6 (w/w) composite of formoterol fumarate and budesonide. The systems were spray-dried as solutions consisting of 95% ethanol and 5% water (v/v) using a Büchi 191-Mini Spray Dryer. A 25–1 factorial design study was carried out to assess how altering spray drying processing parameters affected particle characteristics. The processing factors that were investigated included aspirator setting, pump rate, inlet temperature, spray drier airflow rate, and feed concentration. The thermal, micromeritic, and in vitro deposition properties of each batch of the resulting powder were characterized using twin impinger analysis. All things considered, the following parameters had the greatest impacts on every answer that was being examined: Carr's compressibility index – feed concentration (lower feed concentration giving smaller Carr's indices), median particle size – airflow (higher airflow giving smaller particle sizes), and production yield – airflow (higher airflow giving greater yields)²⁵. By altering the spray drying process parameters, the respirable percentage can vary by a factor of six to seven. When compared to the physical mix of micronized powders, the co-spray dried composite system demonstrated superior dosage uniformity, a 2.6-fold increase in respirable percentage in the twin impinger experiments, and the best in vitro deposition properties.

12. Orally Disintegrating Powders & Tablets

Goal: Fast-dissolving dosage forms.

Mechanism: Spray-dried matrix containing disintegrants + API.

Used in: Pediatrics, geriatrics.

Examples: Paracetamol, loratadine ODTs.

Companies:

Pfizer (Zydis® fast dissolve tech)

Aurobindo and **Strides Pharma** (generics)

Pediatrics and geriatrics

Oral disintegrating tablets (ODTs) are among the most widely used and frequently authorized dosage forms, especially for geriatric and pediatric patients. ODTs have garnered a lot of attention as desirable alternatives to conventional tablet and capsule formulations in an effort to improve patient compliance and prevent dysphagia. Many scientific techniques, such as mass extrusion, melt granulation, direct compression, sublimation, mold drying, spray drying, freeze drying, and the cotton candy process, have been employed to create ODTs. With these techniques, the pill dissolves in the mouth rapidly, negating the need for additional water or chewing²⁶. The current article focuses on ideal attributes, notable features, patented technologies, and formulation aspects, including the use of superdisintegrants. Additionally mentioned are the several commercially accessible preparations as well as the numerous scientific advancements in this subject to far²⁷.

13. Spray-Dried Liposomes and Micelles

Use: For targeted drug delivery (e.g., anticancer drugs like doxorubicin).

Drying purpose: Long-term storage, reconstitution stability.

Companies:

Hovione, Medispray, Medisca

Liposomes and Micelles

Objectives: Although solid lipid nanoparticles (SLNs), liposomes, and micelles are all appealing drug delivery vehicles, post-processing drying methods are required to maintain long-term stability due to their low aqueous stability. The ability of lipid-based micelles, liposomes, and SLNs to create stable, re-dispersible spray-dried powders with trehalose or a combination of trehalose and L-leucine was compared. This study provides fresh insights into the application of spray drying to enhance these lipid-based nanocarriers' long-term stability. **Methods:** Aqueous dispersions of SLNs loaded with liposomes, paclitaxel (PTX), and LDV-targeted micelles were converted into re-dispersible powders by spray drying²⁸. **Objectives:** Although solid lipid nanoparticles (SLNs), liposomes, and micelles are all appealing drug delivery vehicles, post-processing drying methods are required to maintain long-term

stability due to their low aqueous stability. The ability of lipid-based micelles, liposomes, and SLNs to create stable, re-dispersible spray-dried powders with trehalose or a combination of trehalose and L-leucine was compared. This study provides fresh insights into the application of spray drying to enhance these lipid-based nanocarriers' long-term stability. Methods: Aqueous dispersions of SLNs loaded with liposomes, paclitaxel (PTX), and LDV-targeted micelles were converted into re-dispersible powders by spray drying. Reconstituted spray-dried nanocarriers maintained their paclitaxel content and nanosize throughout a seven-day period at 4 °C. Conclusions The results of this investigation hold promise for the development of spray-dried, lipid-based, long-lasting nanocarriers²⁹.

14. Nutraceuticals and Herbal Medicines

Use: Spray drying of plant extracts (e.g., curcumin, ashwagandha, aloe vera).

Benefit: Stable, concentrated extract powders.

Examples: Green tea extract, gingerol, Boswellia serrata.

Companies:

Dabur, Himalaya, Patanjali, Avesthagen

Drying is one of the most common methods of food preservation, albeit consuming more energy. The global energy crisis has made alternatives to electric drying techniques vital. This study provides an overview of the many technologies that have been created and evaluated for the drying of ashwagandha (*Withania somnifera*) and liquorice (*Glycyrrhiza glabra*). There has been discussion of the various drying methods for ashwagandha and licorice. The possible uses of solar-powered drying devices for ashwagandha and licorice have been discussed. There is a substantial gap in the literature regarding solar drying techniques for ashwagandha and licorice³⁰.

15. Spray Drying for Clinical Trial Materials

Need: Small-batch, fast development of experimental drugs.

Use: Rapid feasibility for poorly soluble NCEs.

Providers: Lonza. Evonik

Capsugel (spray-dried dispersion development

In Experimental Pharmaceuticals

Spray drying is one of the most remarkable technologies now employed in the pharmaceutical industry. Because it converts a liquid feed into a powder in a single step, this continuous process is ideal when precise properties like particle size, morphology, and stability are required. This study covers the technology, current and prospective applications, and how current modeling and understanding tools enable a lean and risk-free process development stage³¹.

Table no.3: Pharmaceutical Industry Utilizing Spray Drying Technology

Company Name	Application Type	Specialization
Hovione	Antibiotics, inhalables, ASD, liposomes	Leader in spray-dried dispersions
Lonza	Antibiotics, biologics, inhalables	CDMO for complex APIs
Evonik	Controlled release, PLGA microspheres	RESOMER® polymer spray-drying tech
Catalent	Bioavailability enhancement, pediatrics	OptiForm®, Zydis® tech
Recipharm	Biologics, peptides	Biologic spray drying
Insmmed	Inhalable antibiotics	Arikayce spray-dried liposome
Patheon (Thermo)	Oral solid dose, antibiotics	Clinical trial material & tech transfer
MannKind Corp.	Dry powder insulin	Clinical trial material & tech transfer
Novartis	Clinical trial material & tech transfer	TOBI Podhaler
AstraZeneca	Respiratory medicines	DPI formats using spray drying

- Facilitates the development of needle-free nasal or oral vaccines by creating powder forms suitable for mucosal administration.
- Assists in tissue engineering by drying materials like collagen and hydrogel into powder form for scaffold production³⁰.
- Supports development of implantable drug delivery systems by preparing spray-dried drugs for incorporation into biodegradable matrices or beads.

Medical Applications:

- Enables formulation of inhalable therapeutics, including biologics, antibiotics, and anticancer agents for respiratory delivery.
- Used in the preparation of spray-dried diagnostic agents such as contrast media or radiopharmaceutical powders.
- Produces wound healing powders containing antimicrobial agents or growth factors for direct application on wounds³².

Innovation in Spray dryer^{33,34}:

1. Closed-Loop Spray Drying Systems

- Traditionally, spray drying was done in open-loop systems using hot air.
- Closed-loop spray dryers use inert gases (like nitrogen or CO₂) instead of air, allowing safe drying of solvents and oxygen-sensitive materials.
- Widely used in pharmaceutical and nutraceutical industries for drying APIs and biologics.

2. Low-Temperature Spray Drying

- Conventional spray drying operates at high inlet temperatures (150–300 °C), which is unsuitable for proteins, peptides, enzymes, and probiotics.
- Innovations include:
 - Vacuum spray drying → lower boiling points achieved under vacuum.
 - Supercritical CO₂-assisted spray drying → allows particle formation at mild conditions.
- Result: Increased stability of heat-sensitive biomolecules.

3. Nano- and Micro-Encapsulation via Spray Drying

- Modified techniques allow entrapment of drugs, probiotics, enzymes, flavors, and essential oils in protective matrices.
- Innovations:
 - Spray drying with polymer carriers (HPMC, PVP, PLGA) for controlled release.
 - Lipid-based spray drying (spray congealing + drying hybrid).
- Outcome: Improved stability, taste masking, and controlled release.

4. Spray Drying for Inhalable Therapeutics

- Precision engineering of particles for Dry Powder Inhalers (DPIs) and Pulmonary delivery.
- Innovations:
 - Particle engineering for aerodynamic size (1–5 μm).
 - Amorphous solid dispersions (ASDs) to improve solubility of poorly soluble APIs.
 - Companies like Novartis, AstraZeneca, and Lonza use spray drying for pulmonary drugs.

5. Continuous Spray Drying

- Replaces traditional batch drying with continuous manufacturing, aligning with FDA's push for continuous processing.
- Provides consistent particle size, better process control, and easier scale-up.
- Example: GEA and Buchi have developed continuous spray dryers for pharma R&D and production.

6. Hybrid Drying Technologies

- Combination of spray drying + freeze drying or spray drying + microwave drying to enhance stability and drying speed.
- Used for biologics, vaccines, and antibody formulations.

7. Spray Drying with Smart Materials

- Use of stimuli-responsive polymers (pH, temperature, enzyme-sensitive).
- Enables targeted drug delivery systems (colon-specific, tumor-targeting).

- Example: Eudragit-coated spray-dried microparticles for colon delivery.

8. Energy-Efficient & Green Spray Drying

- Traditional spray drying consumes huge amounts of energy.
- Innovations:
 - Heat-recovery systems.
 - Use of renewable energy-assisted drying.
 - Eco-friendly solvents (ethanol/water systems).
- Trend toward green pharmaceutical manufacturing.

9. Spray Drying for Biologics & Vaccines

- Advances in stabilization of proteins, mRNA, and vaccines in spray-dried powders for room-temperature storage.
- Especially important for COVID-19 vaccines, where cold-chain was a major issue.
- Companies are developing thermostable vaccine powders via spray drying.

10. Digitalization and Process Analytical Technology (PAT)

- Integration of sensors, AI, and real-time monitoring.
- Allows online particle size monitoring, moisture detection, and morphology control.
- Digital twins being developed for predictive optimization of spray drying.

Conclusion: Spray drying is considered a powerful technological process since it brings feasibility to the production of free-flowing particles with well-defined particle size. This manufacturing method may produce dry particles in the submicron to micron range, and it is in fact cost-effective. Furthermore, this technique's versatility, high productivity, and wide range of applications make it increasingly appealing to the scientific community. Since the final product must meet exact quality standards for particle size distribution, residual moisture content, bulk density, and shape, spray drying is currently one of the most interesting technologies for the pharmaceutical sector. Overall, spray drying has a bright future for Pharmaceutical Industry due to its versatility, efficiency and the driving force of poorly soluble drugs.

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