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Nano spray-dried drugs for oral administration

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Abstract
Many pharmaceuticals such as pills, capsules, or tablets are prepared in a dried and powdered form. In this field, spray drying plays a critical role to convert liquid pharmaceutical formulations into powders. Spray drying is an important technology that is fast, simple, reproducible, and scalable. It has a wide application range, in food, chemicals, and encapsulation of pharmaceuticals. The technology can be divided into conventional spray drying and nano spray drying. This review focuses on nanosized drug delivery systems intended for oral administration produced by nano spray drying. Finally, topics such as morphology, particle size, size distribution, surface analysis, bioavailability, drug release, release kinetics, and solid-state characterization (by differential scanning calorimetry, X-ray diffraction, Fourier transform infrared spectroscopy, nuclear magnetic resonance) of oral drug delivery systems produced by nano spray drying are discussed. The review attempts to provide a comprehensive knowledge base with current literature and foresight to researchers working in the field of pharmaceutical technology and nanotechnology and especially in the field of nano spray drying.

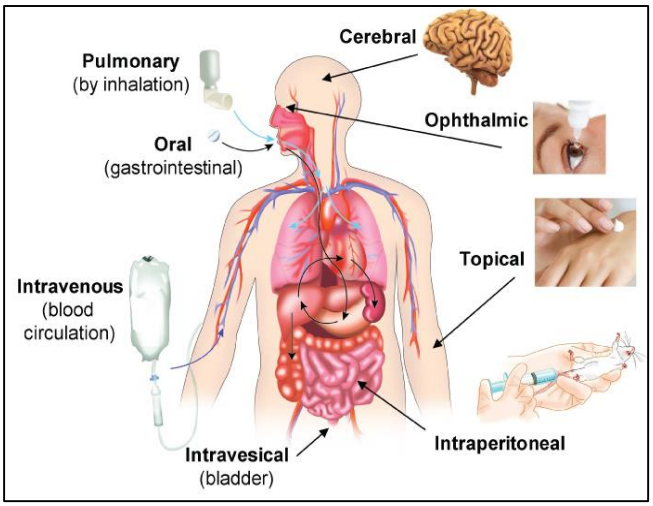
Keywords: Nano spray drying, drug delivery system, pharmaceuticals, oral administration, encapsulation

Introduction

The pharmaceutical industry, a new drug's active ingredient that exhibits strong biological activity but has poor water solubility or very short circulation half-life will likely face significant development challenges or will be considered as failed. Another view is that less active but pharmaceutically optimal compounds may be more suitable candidates for development. In both cases, it may result in less ideal medicines being produced [1]. Today, one of the most important ways to use drugs more effectively is nanotechnology. This is especially prominent in nanomedicine/-carrier/-pharmaceutical, and nano-based drug delivery systems, where nanotechnology-based particles are of great interest [2]. There are many examples in the literature and clinic regarding the use of multifunctional nano pharmaceuticals such as polymeric nanoparticles (NPs), liposomes, solid lipid nanoparticles (SLNs), quantum dots (Qdots), iron oxide NPs, gold NPs, dendrimers, micelles, and carbon nanotubes [3].
Important advantages of nanocarriers as drug carriers include high stability (i.e., long shelf life), high encapsulation capacity, incorporation of both hydrophilic and hydrophobic substances, and feasibility of variable administration routes. These nanocarriers can also be designed to control (continuous) drug release from the matrix [4]. There are different routes of administration to the body for nanodrug delivery systems, such as oral, nasal, ophthalmic, parenteral, dermal, transdermal, pulmonary, and others [5]. One of the most preferred methods of administration in both conventional and nanodrug delivery systems is oral administration. Oral drug administration is simple, non-invasive, and painless, and therefore often has high patient compliance. Advances in nanomedicine and nanotherapeutics require spray dryers with a high yield of nanoscale particles with narrow size distribution. Several comprehensive reviews on nano spray drying technology have already been published [6-8].

First, the concept of nano spray drying is explained by understanding the key elements of the equipment and influences of the process parameters on the final powder properties, such as particle size, morphology, encapsulation efficiency, drug loading, and release kinetics. In addition, solid-state characterizations of nano spray-dried products are considered.

Examples of administration routes of Nano spray dried pharmaceuticals



Components of Nano spray dryer

The main components of B-90 nanospray dryer developed by BUCHI Labortechnik AG are discussed as below [18, 19].

a) Spray head: The spray head is very important component of the nano spray dryer. It incorporates the nebulizer and provides electrical connections well as bypass for spraying solution. It receives the solution from the peristaltic pump and passes it to nebulizer.

b) Nebulizer: It produces well-controlled micro droplets from emulsion, which are ejected into the spray cylinder. It composed of a piezoelectric actuator with a thin stainless-steel membrane. The centre of the membrane contains an array of micron-sized holes and vibrates at ultrasonic frequencies, allowing the ejection of precisely sized droplets at high speed.

c) Electrostatic particle collector: It consists of high voltage (HV) electrode and collecting electrode. It is tubular in shape and consists of a stack of smooth cylindrical colleting electrode and a star shaped discharge electrode. HV electrode seats at the bottom plate of the particle collector and it provided with protective for its easy removal and cleaning. A very high voltage in the range 15–20 kV is applied to the metallic cylinder to produce an electrical field between the discharge and the collecting electrodes. Solid particles are accumulated at the surface of the cylindrical particle collecting electrode by a strong electrical field generated via high voltage by HV-Electrode.

d) Peristaltic pump: A peristaltic pump with variable speed control provided to circulate the feed uniformly from the reservoir through the spray head to the spray mesh and back to the reservoir.

e) Drying chamber: The drying process takes place inside the drying chamber wherein the submicron size droplets of emulsion ejected from nebulizer come in contact with laminar stream of hot drying gas. Length of chamber decides the residence time. The modular glass assembly permits modification of the length of the drying chamber and is easy to clean. High temperature resistance and high transparency borosilicate glass are used for chamber. The vertical configuration guides the submicron particles toward the electrostatic particle collector while minimizing particle adhesion to the sidewalls of the drying chamber, thus resulting in high collection efficiency. Drying gas follows laminar stream in the chamber and its velocity is in the range of 0.05–0.1 m/s. The air residence time in the drying chamber is about 12–20 s.

f) Heater: The heater provides optimal energy required to raise inlet drying gas temperature to desired/selected temperature (generally 120 °C). The heater assembly comprised of porous structure which is embedded with an electrical heating coil. The porous structure also ensures a laminar flow of drying gas in the chamber.

g) Outlet Filter: The outlet filter recovers small fines of powder particles from exist air in order to avoid their entrainment into the surrounding atmosphere.

h) Aspirator: It works as pump and ensure constant supply of drying gas in laminar pattern. The heated air flow rate into the nanospray dryer can be adjusted to a value between 80 and 160 L/min by setting the aspirator speed. In open loop mode, aspirator is connected directly to the inlet of the nanospray dryer without a pressure regulating valve. If the air humidity is too high, the current in the particle collector could be too low. In that case, ambient humidity can be reduced by the use of the dehumidifier. In “closed loop” mode, the gas stream is built up using the aspirator. The drying gas outlet is then connected via the dehumidifier, inert loop and aspirator to the drying gas inlet of nanospray dryer.

Oral administration of drugs

Challenges of the Oral Drug Administration Route

The oral route is a preferred drug administration route, but it is often difficult to achieve effective drug delivery and minimize side effects with conventional drug delivery systems However, compared with other drug delivery routes, the absorption mechanism of orally administered drugs is quite complicated. Oral drugs need to be soluble in the gastric fluid so they can be absorbed in the stomach, the small intestine, or the colon. Orally administered drugs can be absorbed in four types of pathways: Transcellular, paracellular, carrier-mediated transcellular, and facilitated transport. Among these pathways, the transcellular pathway is the main mechanism. Significant improvements in oral administration have been seen with nano pharmaceuticals, which can be listed as follows [9-14].

- Improved oral bioavailability of not only hydrophobic drugs but also hydrophilic and biological drugs through various mechanisms,
- Protection of biologically unstable drugs from the harsh environment of the gastrointestinal system (GIS),
- Prolonged duration of the drug in the GIS with strong mucoadhesive properties,
- Improved design as specific nanocarriers for receptor mediated transport,
- Targeted design according to the desired region (e.g., stomach, small intestine, intestinal lymphatic system, colon) in the GIS, and
- Targeted design to the GIS-specific disease areas (e.g., gastric ulcers, Helicobacter pylori infections, ulcerative colitis) or cells in the GIS

HPMC: Hydroxypropyl Methylcellulose; HPMCAS: Hydroxypropyl Methylcellulose Acetate Succinate; DSPC: Distearoylphosphatidylcholine [19-26].

Table 1: Examples of FDA-approved medicaments that use spray drying technology as preparation method

Trade name	Drug	Application	Polymer, Excipient	Maximum drug dose	Company	FDA approval
Prograf	Tacrolimus	Immunosuppressant (prevents organ rejection)	HPMC	5 mg per capsule	Astellas Pharma	1994
Exhubera	Insulin	Diabetes	Mannitol, glycine, sodium citrate	1 or 3 mg per capsule	Pfizer/Nektar	2006
Intelence	Etravirine	HIV medicine	HPMC	100 or 200 mg per tablet	Janssen	2008
Zortress	Everolimus	Immunosuppressant (prevents organ rejection)	HPMC	0.75 mg per tablet	Novartis	2010
Aridol/Osmohale, Bronchitol	-	Asthma/Cystic fibrosis	Mannitol	5 to 40 mg per capsule	Pharmaxis	2010
Incivek	Telaprevir	Hepatitis C	HPMCAS	375 mg per tablet	Vertex	2011
Kalydeco	Ivacaftor	Cystic fibrosis	HPMCAS	150 mg per tablet	Vertex	2012
TOBI Podhaler	Tobramycin	Inhalation therapy	DSPC, calcium chloride, sulfuric acid	28 mg per capsule	Novartis	2013
Raplixa	-	Bleeding control during surgery	Fibrinogen/Thrombin	79 mg/726 IU per gram powder	Nova Laboratories	2016

Application examples of Nano spray-dried drugs for oral administration

Direct Transformation of Pure Poorly Water-Soluble Drugs

Nano spray drying is particularly suitable for the direct transformation of pure, poorly water-soluble drugs into submicron powders, such as:

- Dexamethasone/anti-inflammatory,58
- furosemide/diuretic,33
- Indomethacin/anti-inflammatory,85
- Mecigestone/steroidal hormone,153
- Nicergoline/vasodilator,154 or
- Nimesulide/analgesic.155

Encapsulation of Drugs

The wall materials for the encapsulation of pharmaceuticals by nano spray drying for oral administration are mainly water-soluble polymers, such as gum arabic, alginate, gelatin, carboxymethyl cellulose, chitosan, Compritol, sodium caseinate, pectin, Carbopol, Kollidon, and Eudragi. The criteria for the selection of the wall material are as varied as for microencapsulation, including water solubility and edibility, compatibility with the encapsulated active ingredient, easy emulsification, high encapsulation efficiency, mechanical strength, storage stability, and suitable release properties [15].

Formation of solid dispersions

Valdecoxib is a selective cyclooxygenase-2 inhibitor, administered orally as an analgesic and anti-inflammatory drug. It is relatively insoluble in water.[16] developed solid dispersions of valdecoxib and a hydrophilic polymer by co-spray drying. The selected hydrophilic carriers were polyvinylpyrrolidone K30 (PVP) and hydroxypropyl cellulose (HPC). The saturation solubility, dissolution rate and stability of the spray dried drug, the solid dispersions and their corresponding physical mixtures were compared with the pure drug substance. All spray dried samples as well as the physical mixtures suggested increased saturation solubility and dissolution rate immediately after processing. Additionally, DSC and XRPD experiments of the spray dried valdecoxib and the solid dispersions showed the generation of an amorphous form of the drug.

Increased bioavailability

Spray drying can be used to enhance the solubility and dissolution rate of poorly soluble drugs. This usually occurs via the formation of pharmaceutical complexes or via the development of solid dispersions [17]. Dried Pharmaceutical.

Reference

1. Shi J, Votruba AR, Farokhzad OC. Nanotechnology in drug delivery and tissue engineering: from discovery to applications. Nano Letters 2010;10(9):3223-3230.
2. Patra JK, Das G, Fraceto LF. Nano based drug delivery systems: recent developments and future prospects. Journal of Nanobiotechnology. 2018;16:71.
3. Babu A, Templeton AK, Munshi A, Ramesh R. Nanodrug delivery systems: A promising technology for detection, diagnosis, and treatment of cancer. AAPS PharmSciTech. 2014;15:709-721.
4. Gelperina S, Kisich K, Iseman MD. The potential advantages of nanoparticle drug delivery systems in chemotherapy of tuberculosis. American Journal of Respiratory and Critical Care Medicine. 2005;172(12):1487-1490.
5. Nikolić V, Ilić-Stojanović S, Petrović S. Chapter 21—Administration routes for nano drugs and characterization of nano drug loading. In: Characterization and Biology of Nanomaterials for Drug Delivery. editors. Elsevier, Netherlands; c2019. p. 587-625.
6. Wang B, Zhang W, Zhang W, Mujumdar AS, Huang L. Progress in drying technology for nanomaterials. Drying Technology. 2005;23(1-2):7-32.
7. Okuyama K, Abdullah M, Lenggoro IW. Preparation of functional nanostructured particles by spray drying. Advanced Powder Technology. 2006;17(6):587-611.
8. Heng D, Lee SH, Ng WK, Tan RBH. The Nano Spray Dryer B-90. Expert Opinion on Drug Delivery. 2011;8(7):965-972.
9. Date AA, Hanes J, Ensign LM. Nanoparticles for oral delivery: design, evaluation and state-of-the-art. Journal of Controlled Release. 2016;240:504-526.
10. Wang B, Zhang W, Zhang W. Progress in drying technology for nanomaterials. Drying Technology. 2005;23(1-2):7-32.
11. Lee SH, Heng D, Ng WK. Nano spray drying: A novel method for preparing protein nanoparticles for protein therapy. International Journal of Pharmaceutics. 2011;403(1-2):192-200.
12. Nandiyanto AB, Okuyama K. Progress in developing

spray-drying methods for the production of controlled morphology particles: From the nanometer to submicrometer size ranges. Advanced Powder Technology. 2011;22(1):1-9.
13. Sosnik A, Seremeta KP. Advantages and challenges of the spray-drying technology for the production of pure drug particles and drug-loaded polymeric carriers. Advances in Colloid and Interface Science. 2015;223:40-54.
14. Gharsallaoui A, Roudaut G, Chambin O. Applications of spray-drying in microencapsulation of food ingredients: An overview. Food Research International. 2007;40(9):1107-1121.
15. Ambike AA, Mahadik KR, Paradkar A. Stability study of amorphous valdecoxib. International Journal of Pharmaceutics. 2004;282(1-2):151-162.
16. Broadhead J, Rouan SKE, Rhodes CT. The spray drying of pharmaceuticals. Drug Development and Industrial Pharmacy. 1992;18(11&12):1169-1206.
17. BUCHI AG. Labor technik Nano Spray Dryer B-90 Brochure Flawil. Switzerland. 2010;11592236:1012.
18. Kawabata Y, Wada K, Nakatani M, Yamada S, Onoue S. Formulation design for poorly water-soluble drugs based on biopharmaceutics classification system: Basic approaches and practical applications. International Journal of Pharmaceutics. 2011;420(1):1-10.
19. Huang Y, Dai WG. Fundamental aspects of solid dispersion technology for poorly soluble drugs. Acta Pharmaceutica Sinica B. 2014;4(1):18-25.
20. Brough C, Williams RO 3rd. Amorphous solid dispersions and nano-crystal technologies for poorly water-soluble drug delivery. International Journal of Pharmaceutics. 2013;453(1):157-166.
21. Lam J, Vaughan S, Parkins MD. Tobramycin Inhalation Powder (TIP): An efficient treatment strategy for the management of chronic *Pseudomonas aeruginosa* infection in cystic fibrosis. Clinical Medicine Insights: Circulatory, Respiratory and Pulmonary Medicine. 2013;7:61-77.
22. Konstan MW, Geller DE, Minić P, Brockhaus F, Zhang J. Tobramycin inhalation powder for *P. aeruginosa* infection in cystic fibrosis: The EVOLVE trial. Pediatric Pulmonology. 2011;46(3):230-238.
23. Anderson SD, Daviskas E, Brannan JD, Chan HK. Repurposing excipients as active inhalation agents: The mannitol story. Advanced Drug Delivery Reviews. 2018;133:45-56.
24. Guntur VP, Dhand R. Inhaled insulin: Extending the horizons of inhalation therapy. Respiratory Care. 2007;52(7):911-922.