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REVIEW ARTICLE

Rising Horizon of Pharmaceutical Industry: Spray Drying a Review

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ABSTRACT

Spray drying is one of the most frequently employed technique adopted by pharmaceutical industry including manufacturing of powder with desired properties. It is an incessant process wherein any pump able liquid might be transformed in a free flowing powder. Spray drying is appropriate technique in the drug delivery systems owing to the uniformity of particles and its size. The technique is proved to be very potential for systematic delivery of therapeutic peptides, antibiotics and proteins. In current study, the process and use of spray drying were reviewed and the consequences of diverse affecting parameter were explicated. It is also used for dry heat labile products for instance enzymes and proteins with least possible effect on action and generate drugs with better solubility and drying of nanoparticles, granulation, microencapsulation and coating ahead of its renowned application on drying of liquids, aerosols and vaccines. Numerous researches endorsed the application of spray drying in pharmaceutical industry however many aspects required for future development.

Keywords: Spray drying, applications, review, pharmaceuticals.

INTRODUCTION

In modern era, particle manufacturing has been employed to intend complex particles fulfilling the demands; for instance particle void, particles having controlled surface morphology with less density, well-designed layer particle, or smaller subunit encompassed by particles for instance nanoparticles or we can say defined voids [1]. A strong perceptive of the particle design process is obligatory; owing to the complexity of these particles for flourishing particle production. This stimulates advance investigation into the physical and chemical means that manage the drying and particle development method in the aerosol phase [2].

Spray drying being a continuous single-step unit operation works on mechanism in which free flowing liquid is utilized to generated droplets that ultimately dry to individual particle as pass from hot gaseous drying medium. The techniques develop over an era of numerous decades knowingly from 1870s to early 1900s. An earliest technology was introduced in 1933 and the first spray dryer was manufactured in the USA [3]. Since then, an incredible progress of spray drying technique with the sophistication in the equipment and hardware design and better considerate of fluid dynamics has made the process a multipurpose operational technique in various manufacturing fields that range from ceramics, paints, food and dairy products, detergents, fertilizers and

pharmaceutical manufacturing. In addition, the technique is also use for the development of essential nutrients like protein and its polymers and vitamins. Distinctiveness of drying technique takes account on paid evaporation of solvent which make it useful for generation of amorphous solid dispersions. This equipment's have been useful in numerous fields include pharmaceutical products, plastic industries, food and ceramic, *etc*. It is employed since a long period however it is always be an dynamic field of novelty, determined by the ever escalating stipulation for new urbane particles [4]. In pharmaceuticals world, spray drying is employed for the drying of various ingredients including APIs and excipients as it is single-unit process [5]. The technique is used in the pharmaceutical industry to make particles that outline the base for development of dry dosage forms for parenteral use, pulmonary delivery, and are used as aerosols, powders, suspensions, *etc*. These particles must be capable to stabilize the API and give physical stability for the dosage form on storage. The powder must have sufficient flow ability and suitable aerodynamic properties in respiratory delivery.

The process of spray drying is among the top drying technique used to switch, free flowing materials into semi-solid and to convert solid subdivision in a sole stride as the evaporation takes places when fluid feed make contact with hot air. Quick evaporation being a cooling process maintains the droplets' temperature fairly low, so considerably or pessimistically nor affecting the products' features [6]. Conversely, spray drying has often been depicted as an unsuitable drying technique owing to its frequent elevated temperature of process. Some thermo labile substances for instance enzymes and vitamins can be inactivated or damage under high temperatures, in the process of spray drying [7].

Spray drying process engage multifaceted connections of method, apparatus and feed considerations; these entire have an effect on the excellence of an ultimate product [8]. The process can manufacture high-quality product with little influence of water action and weight reduction resultant with easy transport and storage. The physical and chemical properties of product primarily based on particle size, viscosity, speed of feed flow, pressure and kind of atomizer, spray dryer inlet and exit temperatures [9]. The technique is frequently selected since it can develop material very swiftly whilst provide relative control in the distribution of particle dimension [10].

The merits of the process are:

- It is capable to work in various functions that vary from aseptic pharmaceutical processing to production of ceramic powder.
- To assemble various product qualifications wide range of differently designed spray dryers are available.
- It is use equally with heat-resistant and heat labile products.
- Competence needed as rates of feeding material from few pound/hour to more than 100 tons/hour.
- The excellence of powder doesn't get affected throughout the process.
- The process has feature of being incessant and flexible to complete usual control.
- They are capable of pumping the feed that can be caustic, inflammable, volatile, abrasive, or lethal.
- Feedstock can be in form of suspension, gel, paste, slurry, solution or melted form.
- The density of the product is under control.
- Almost sphere-shaped particles can be formed.
- Material does not get in touch with metal surfaces until dried, reducing corrosion problems.

However, the de-merits of the process are:

- Granules with particle size >200 mm are not manufactured by this process.
- Sophisticated heat exchange tool is frequently needed for exclusion because of reduces thermal capability at less inlet temperature and the exhausted air stream encloses heat.

METHODOLOGY

Spray Drying Process Mainly Involves Five Steps

Spray drying process consists of five main stages:

(i) Concentration: Proceeding to prologue into the spray dryer, concentrated fluid is fed.

(ii) Atomization: The stage of atomization generates the optimal prerequisite needed for evaporation resulting in dried product comprising the needed properties.

(iii) Droplet-air contact: In the chamber, hot gas came in contact with previously atomized liquid and loss 95% H_2O in jus few seconds in form of droplets.

(iv) Droplet drying: Two stages involve in moisture evaporation;

1) The evaporation occurs at fairly constant rate in first step, because enough moisture is present in droplet to substitute the liquid at surface.

2) The next stage started when a dehydrated shell appears at the surface because no sufficient moisture is left to maintain saturated conditions. Thus, the rate of evaporations is governed by moisture diffusion through the shell.

(v) Separation: Electrostatic precipitators, bag filters and cyclones are employed for concluding this stage. Wet Scrubbers chill the air with the intention that it can be released to air and are employed frequently.

These stages along with their considerations of operations have key impact on properties of dried product and its competence. The final product such as granules, powder, agglomerates can be obtained by using either gel, suspension, concentrated feed or any paste [11]. Figure **1** illustrates the major spray dryer sections.

Design and Essentials of Spray Drying Atomizers

In general, the process of atomization is supposed to create fine particles or in other case liquids suspensions can be made in gas on order to reduce particle size. Throughout the drying process, the atomization process continuously converts fluid in desired dried particle by consistent heat and mass transfer. Exterior area of the particles amplifies exponentially, due to continuous decrease in size of particles and their dispersal in drying gas. Without disturbing the integrity substance, the moisture exclude from the system by means of small sized droplets while the division of fluid feed occurs constantly. Atomizers like pneumatic nozzles, rotary atomizers, pressure nozzles and sonic nozzles are attained to perform atomization [12]. On the basis of types of their energies, atomizers are classified for instance in pressure atomizer pressure buildup is used or in rotary atomizers centrifugal energy acts on fluid to atomize [13]. Along with their mode of work the properties of feed and the need of desired dried product with suitable particles are also considered while selecting the atomizer. Numerous imperative functions should be present in atomizer which is summed up underneath:

i. For achieving the subsequent distribution of material in chamber and their mixing with hot gas, dryer should spread out the material.
ii. Particles should be of medium size. Not enough big to dry at some extent or not small to become complicated as smaller units may also get scorched by the hot gas.
iii. Metering tool should be another aspect of Atomizer, as it should adjust the feed rate in dryer;
    a) Two fluid nozzles or air atomization
    b) Rotary nozzles or disk nozzles
    c) Airless atomization nozzles
    d) Ultrasonic nozzles, and
    e) Pressure nozzles

Air Flow

a) Co-current flow: The co-current flow works with co-current dryers, Spray along with air are intended for inflowing the dryer and together pass through the chamber in the same way.

b) Counter-current flow: From opposite ends of the dryers the air and the spray enter that is air inflow from the base and the atomizer situated at the top.

c) Mixed flow: Both counter and co-current are mixed (atomizer at base and dryer situated at top) are generated mixed flow [14].

Spray Drying Chamber

A flow model is sustained by the air inside the chamber, which prevents the aggregation of dried product on wall/atomizer. The final product is controlled by temperature and movement of inlet air. Figures **2** and **3** exemplify the category of spray drier like single stage dryer and two stage dryer, respectively.

The 2 stage dryers permit the lower temperatures in the dryer and making it satisfactory option for heat labile materials [15].

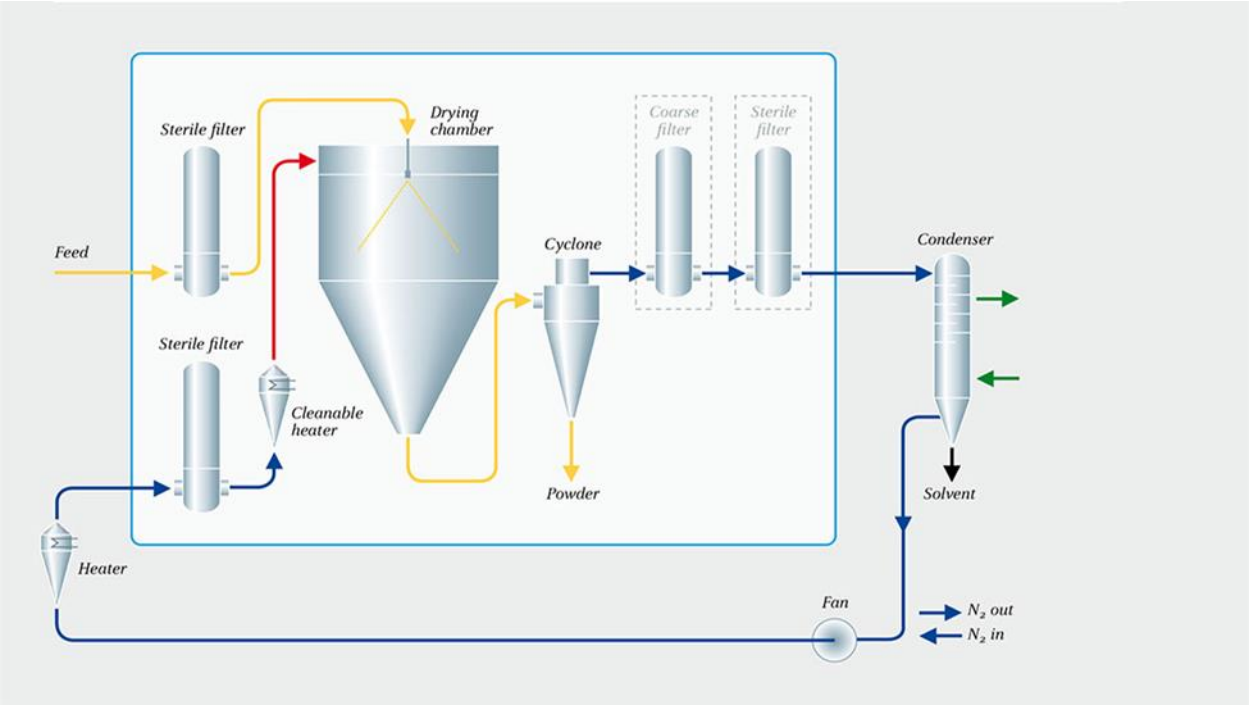

Figure 1. Major components of a spray dryer.

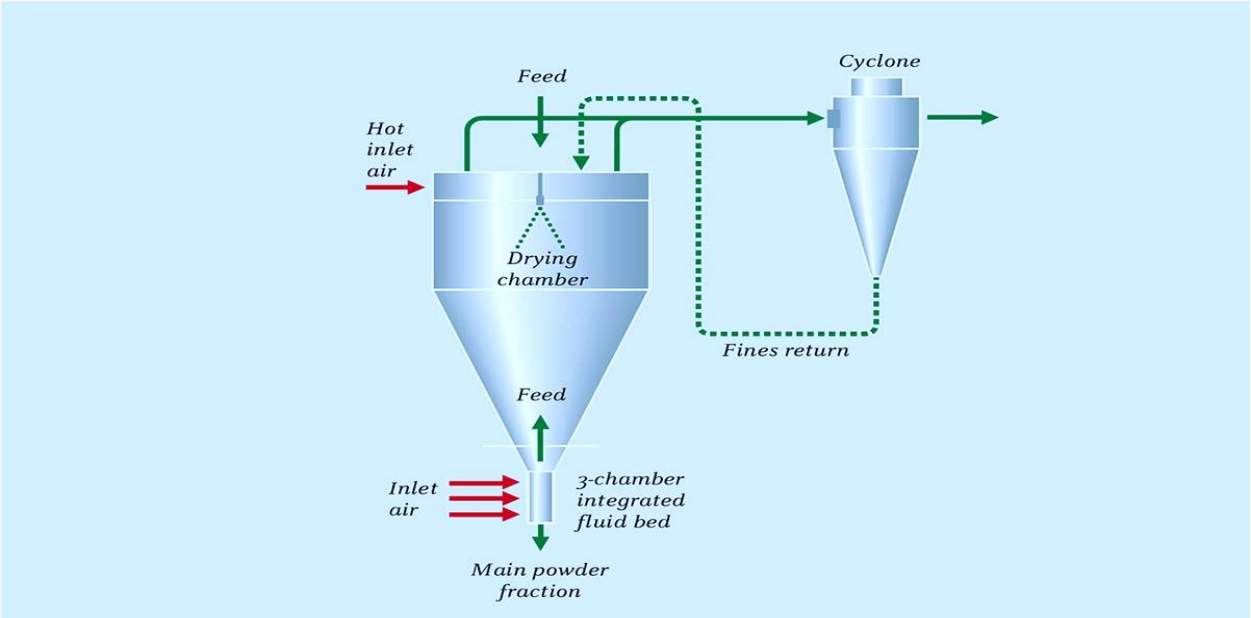

Figure 2. Single stage dryer.

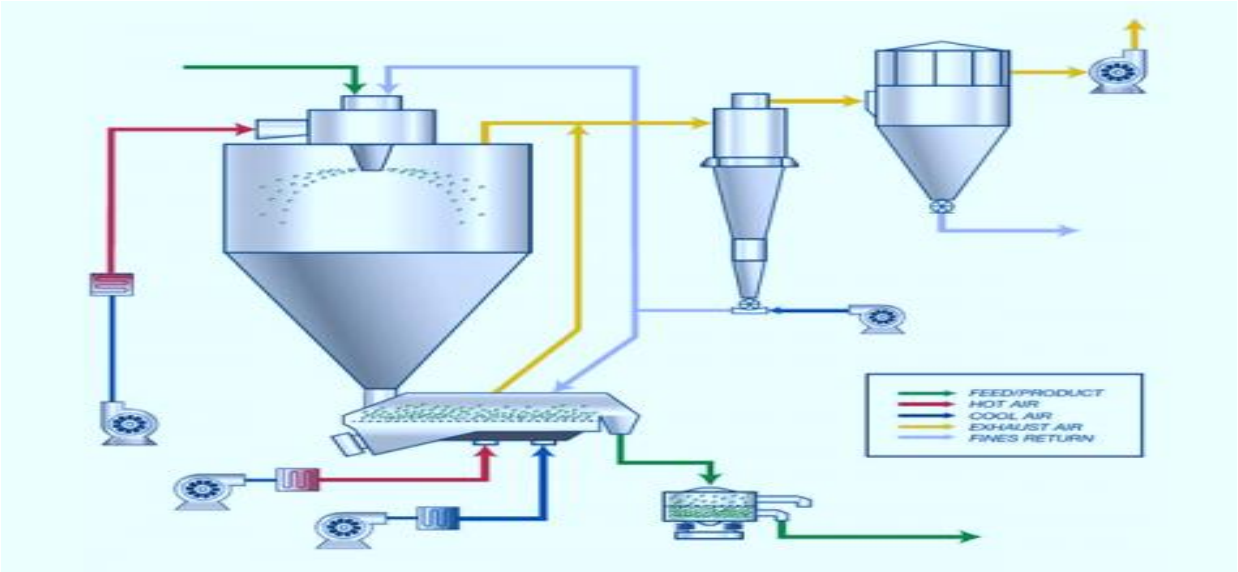

Figure 3. Two stage dryer.

Multi Stage Dryer

The procedure of this dryer is successful in drying sticky product, products with high affinity toward water (hygroscopic) and high fat which gives hard times in handling in other conservative design. Agglomerated powders are obtained with features of free flowing and non-dusty. The elevated flavors are retained and so elevated thermal effectiveness as low outlet temperature is maintained.

Compact Spray Dryer

Spray nozzle or rotary atomizers are used to produce atomization, resulting in great thermal efficiency and surrounding remain cooler from surrounding because the fluid bed is position in such a way that drying occur at lesser temperature levels, providing ease in powder handling [16].

Considerable Considerations for Spray Drying

a) Inlet temperature of air: The moisture loss occurs quickly at higher temperature but this may alter physicochemical properties of heat liable material.

b) Outlet temperature of air: It leads the sizing of powder resurgence equipment's, larger will be the powder recovery equipment size if outlet air temperature rises. It also manages powders' ultimate moisture component.

c) Viscosity: Smaller amount of pressure or energy is required for the formation of specific spray if viscosity is lower. Otherwise higher the viscosity, delayed will be the achieving of pattern of spraying.

d) Solid content: To retain the accurate droplet pattern high solid feed that are over 30% should be handled with care.

e) Surface tension: Small amount of surfactant can lower the surface tension considerably which can signify in a wider spray pattern including small droplets with highly developed viscosity.

f) Feed temperature: Higher temperature of the sprayed solution brings more energy in the system so drying the solution more effortlessly.

g) Volatility of solvent: In drying method increased volatility is preferred but choices are inadequate nowadays. In various cases the solvent option is limited to water.

h) Nozzle material: Stainless steel inserts are usually used in pharmaceuticals. The nozzles, which are resistant to abrasion and fine resistant corrosion to some feed materials and are easily accessible, are preferred to be used in spray drying such as tungsten carbide nozzles [17].

RESULTS

Considering all the major aspects required and fulfilled in pharmaceutical product manufacturing such as distribution of particle size, bulk density, residual moisture content and morphology, spray drying is currently the most preferred electrifying technique used for drying [18]. Multistage methods, temperature gradient systems, novel spray techniques and other like these have got much consideration in manufacturing.

The exposure of the heat can be minimized by concurrent drying and product is recovered at 15°C (below the outlet temperature) [19]. This process can be applied on capsules, vaccines, antibiotics, protein, peptides and inhalation [20].

Microencapsulation is a technique which is frequently using for food materials. The process is cheap, economical and equipment are readily available for production as compare to other methods for example the process of freeze-drying is expensive 30-50 times as compare to encapsulation [20, 21] as discussed by Quinn 1965 [22]. It is also considered that the spray drying is also waste some amount of energy as all energy consumption is impossible to utilize.

DISCUSSION

Spray drying is widely used in many pharmaceutical applications including powder preparations. With the help of this spherical and non-spherical particles can be made with the characteristics of solid or hollow. The pressure spray nozzles can produce particles with the range of 20 to 600 microns [21-24]. Rotary atomizers can also have made more uniform size of particles as compare to pressure atomizers.

Generally, The spray drying process has better distribution of drug , color and improved flow properties with less lubricant and wet mass [25, 26]. By the result of this, the concentrated binder gives strong tablets with help of binder and granular materials than it combines with active pharmaceutical ingredient (API) with polymer. It makes the dissolutions rate more improved as compare to others like other drugs including indomethacin, ibuprofen, cyclodextrin, paracetamol, diazepam, *etc*. [27].

During the days of advancement, biotechnology has emerged with the new method of spray drying which seems to be the most appropriate and shielding method of drying. Some researchers have proved that due to low efficacy it's been discouraged to use the laboratory spray dryer. In experimental purpose, the mentioned efficacy where not exceed from 50% which is not needed a breakthrough in economical point of view but further processes in research and analyses is needed [28].

Spray drying technology is meant for powder designed for inhalation *via* a respiratory track. For achieving the purpose, the particles should be appropriate in size and shape for homogeneous dispersion for examples vaccines and aerosols [29]. It contained live attenuated Newcastle virus [30]. The formation of spray dried saccharose, trehalose, mannitol and iso-leucine for IgG, enhance the stability of the stored powder with enhancing the intrinsic properties [31]. Further *in vivo* studies have shown advancement in vaccine and immunologically [32]. In a laboratory scale, the vaccines of tuberculosis has manufactured successfully with 60% sustained CFUs (colony-forming unit) and remain stables up to 56 days under accelerated test conditions having different excipients properties [33, 34].

For manufacturing of these type of viable organism the use of HEPA (High Efficiency Particulate Air) filters is mandatory for drying and sterilization, atomizing of air with fast product collection. Due to its high quality materials, sterilization with superheated steam with lot of high cost engineering with separate spray dried where necessary [35, 36].

CONCLUSION

Spray drying is latest utmost pharmaceutical and food industries techniques with good quality standards, suitable particle size distribution, dissolution, bulk and tap densities, morphology along with better residual content. It is currently gaining attention for manufacturers and investors due to conveniences in many aspects including storages and less inventory. For future application, the new spray systems with temperature gradient promisingly change the arena of research and development [22, 23, 37-40]. Various designs of machine with latest equipment's are widely used throughout the world with better operations, output capacity and desirable features for manufacturing of capsule filling, vaccines and areoles. Researches showed great improvement in different dosage form with the technique of spray drying but still further analysis is required.

REFERENCES

1. Vehring R, Foss WR, Lechuga-Ballesteros D. Particle formation in spray drying. J Aerosol Sci. 2007; 38(7):728-46.
2. Trandafir DL, Turcu RV, Simon S. Structural study of spray dried silica–germanate nanoparticles. Mater Sci Eng B. 2010; 172(1):68-71.
3. Hayashi H. Drying technologies of foods-their history and future. Drying Technol. 1989; 7(2):315-69.

4. Nandiyanto AB, Okuyama K. Progress in developing spray-drying methods for the production of controlled morphology particles: From the nanometer to submicrometer size ranges. Adv Powder Technol. 2011; 22(1):1-9.
5. Vehring R. Pharmaceutical particle engineering via spray drying. Pharm Res. 2008; 25(5):999-1022.
6. Roustapour OR, Hosseinalipour M, Ghobadian B, Mohaghegh F, Azad NM. A proposed numerical–experimental method for drying kinetics in a spray dryer. J Food Eng. 2009; 90(1):20-6.
7. Yoshii H, Buche F, Takeuchi N, Terrol C, Ohgawara M, Furuta T. Effects of protein on retention of ADH enzyme activity encapsulated in trehalose matrices by spray drying. J Food Eng. 2008; 87(1):34-9.
8. Chegini GR, Khazaei J, Ghobadian B, Goudarzi AM. Prediction of process and product parameters in an orange juice spray dryer using artificial neural networks. J Food Eng. 2008; 84(4):534-43.
9. Tonon RV, Brabet C, Hubinger MD. Influence of process conditions on the physicochemical properties of açai (Euterpe oleraceae Mart.) powder produced by spray drying. J Food Eng. 2008; 88(3):411-8.
10. Obón JM, Castellar MR, Alacid M, Fernández-López JA. Production of a red–purple food colorant from Opuntia stricta fruits by spray drying and its application in food model systems. J Food Eng. 2009; 90(4):471-9.
11. Cal K, Sollohub K. Spray drying technique. I: Hardware and process parameters. J Pharm Sci. 2010; 99(2):575-86.
12. Sollohub K, Cal K. Spray drying technique: II. Current applications in pharmaceutical technology. J Pharm Sci. 2010; 99(2):587-97.
13. Murugesan R, Orsat V. Spray drying for the production of nutraceutical ingredients—a review. Food Bioproc Tech. 2012; 5(1):3-14.
14. Gabites JR, Abrahamson J, Winchester JA. Air flow patterns in an industrial milk powder spray dryer. Chem Eng Res Des. 2010; 88(7):899-910.
15. Sherwood B, Zeleznik J, Schaible D, Barkulin W, Theissing KH, inventors; Zeleznik Joseph A, assignee. Process for co-spray drying liquid herbal extracts with dry silicified MCC. United States patent application US 11/593,760. 2007.
16. Araújo RR, Teixeira CC, Freitas LA. The preparation of ternary solid dispersions of an herbal drug via spray drying of liquid feed. Drying Technol. 2010; 28(3):412-21.
17. Jafari SM, Assadpoor E, He Y, Bhandari B. Encapsulation efficiency of food flavours and oils during spray drying. Drying Technol. 2008; 26(7):816-35.
18. Fávaro-Trindade CS, Santana AD, Monterrey-Quintero ES, Trindade MA, Netto FM. The use of spray drying technology to reduce bitter taste of casein hydrolysate. Food Hydrocoll. 2010; 24(4):336-40.
19. Wan LS, Heng PW, Chia CG. Spray drying as a process for microencapsulation and the effect of different coating polymers. Drug Dev Ind Pharm. 1992; 18(9):997-1011.
20. Seville PC, Li H-Y, Learoyd TP. Spray-dried powders for pulmonary drug delivery. Crit Rev Ther Drug Carrier Syst. 2007; 24(4):307-60.
21. Gauvin WH, Katta S. Basic concepts of spray dryer design. AICHE J. 1976; 22(4):713-24.
22. K MS, MP W. Review on spray drying technology. Int J Pharm Chem Biol Sci. 2014; 4(2):219-25.
23. Patel RP, Patel MP, Suthar AM. Spray drying technology: an overview. Indian J Sci Technol. 2009; 2(10):44-7.
24. Meghwal M, Goyal MR, editors. Food Process Engineering: Emerging Trends in Research and Their Applications. CRC Press; 2016.
25. Michael JK. Spray drying and spray congealing of pharmaceuticals. In: Encyclopedia of pharmaceutical technology. Marcel Dekker INC, NY. 1993; 14:207-21.
26. Michaud J. Starch based excipients for pharmaceutical tablets. Pharm Chem. 2002; 42-4.
27. Gonnissen Y, Verhoeven E, Peeters E, Remon JP, Vervaet C. Coprocessing via spray drying as a formulation platform to improve the compactability of various drugs. Eur J Pharm Biopharm. 2008; 69(1):320-34.
28. Maury M, Murphy K, Kumar S, Shi L, Lee G. Effects of process variables on the powder yield of spray-dried trehalose on a laboratory spray-dryer. Eur J Pharm Biopharm. 2005; 59(3):565-73.
29. Colonna C, Conti B, Genta I, Alpar OH. Non-viral dried powders for respiratory gene delivery prepared by cationic and chitosan loaded liposomes. Int J Pharm. 2008; 364(1):108-18.
30. Corbanie EA, Remon JP, Van Reeth K, Landman WJ, Van Eck JH, Vervaet C. Spray drying of an attenuated live Newcastle disease vaccine virus intended for respiratory mass vaccination of poultry. Vaccine. 2007; 25(49):8306-17.
31. Schüle S, Schulz-Fademrecht T, Garidel P, Bechtold-Peters K, Frieß W. Stabilization of IgG1 in spray-dried powders for inhalation. Eur J Pharm Biopharm. 2008; 69(3):793-807.

32. Corbanie EA, Vervaet C, Van Eck JH, Remon JP, Landman WJ. Vaccination of broiler chickens with dispersed dry powder vaccines as an alternative for liquid spray and aerosol vaccination. Vaccine. 2008; 26(35):4469-76.
33. Wong YL, Sampson S, Germishuizen WA, Goonesekera S, Caponetti G, Sadoff J, *et al*. Drying a tuberculosis vaccine without freezing. Proc Natl Acad Sci. 2007; 104(8):2591-5.
34. Costantino HR, Andya JD, Nguyen PA, Dasovich N, Sweeney TD, Shire SJ, *et al*. Effect of mannitol crystallization on the stability and aerosol performance of a spray-dried pharmaceutical protein, recombinant humanized anti-IgE monoclonal antibody. J Pharm Sci. 1998; 87(11):1406-11.
35. Cai T. Cultivation of Nannochloropsis salina and Synechocystis sp. PCC6803 in Anaerobic Digestion Effluent for Nutrient Removal and Lipid Production. MS Thesis. The Ohio State University 2012.
36. Comba S, Arabolaza A, Gramajo H. Emerging engineering principles for yield improvement in microbial cell design. Comput Struct Biotechnol J. 2012; 3(4):e201210016.
37. Schwarzkopf JD, Sommerfeld M, Crowe CT, Tsuji Y. Multiphase flows with droplets and particles. CRC Press; 2011.
38. Hickey JA, Ganderton D. Pharmaceutical process engineering. CRC Press. 2016.
39. Filkova´ I, Huang LX, Mujumdar AS. Industrial Spray Drying Systems. In: Handbook of Industrial Drying; Mujumdar AS, Ed. CRC Press/Taylor & Francis Group, Boca Raton, FL 2006; pp. 215-54.
40. Maroulis ZB, Saravacos GD, Mujumdar AS. Spreadsheet-Aided Dryer Design. In: Handbook of Industrial Drying; Mujumdar AS, Ed. CRC Press/Taylor & Francis Group, Boca Raton, FL 2006; pp. 121-34.