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Editorial

Applications of Spray Freeze-drying for Formulating Bioactive Wound Powders

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Chronic wounds do not heal in an expected timeline. The complications of chronic wounds make them an important issue for public health. The quality of life of patients with chronic wounds is negatively affected because of heavy exudates and unpleasant odor, infections, and organ disabilities.[1] Therefore, wound care and promoting wound repair by using appropriate wound dressings should be considered. Modern wound dressings are designed to prevent infection, provide moist condition, exchange gases and water vapor, and uptake excess fluids.[2] A more recent innovation is bioactive wound dressings that are modern dressings containing functional components with therapeutic effects.[3] These dressing deliver active components like biopolymers, growth factors, antioxidants, and antimicrobial agents to wound.

Several marketed bioactive wound dressings have been formulated as powders or particulate solids, bioactive wound powders (BWPs), such as Altrazeal,[4] Cartix,[5] DermFactor,[6] and XCelliStem.[7] From manufacturing point of view, BWPs have simple formulation and high physicochemical and microbial stability.[8] From application point of view, they can be applied to deep and irregular shaped wounds, show high residence time at wound bed, and provide rapid therapeutic effects because of their higher contact with wound micro-environment.[9,10] Furthermore, BWPs do not cause pain or tissue damage in the process of dressing change.[11]

In situ hydrogel forming BWPs transform from a solid to hydrogel after absorbing wound exudates.[12] The formed hydrogel adheres to wound surface, provides a moist condition, promotes cellular growth, delivers therapeutic agents, has permeability to gases and water vapor, and is easily removed by washing.[13,14] In situ hydrogel forming BWPs preserve features of both BWPs and hydrogels and overcome drawbacks of semisolid hydrogels including their long term physicochemical and microbial stability.[14] To ensure rapid formation of a hydrogel, the particles of the formulated BWP should have small size, high porosity, and sufficient surface hydrophilicity.

Compounds from different sources have been developed as BWPs, including medicinal plants,[15] animal-derived compounds,[5,16] and biopolymers.[17] These BWPs can be produced by various techniques. The selected method should preserve the stability of the compound, provide

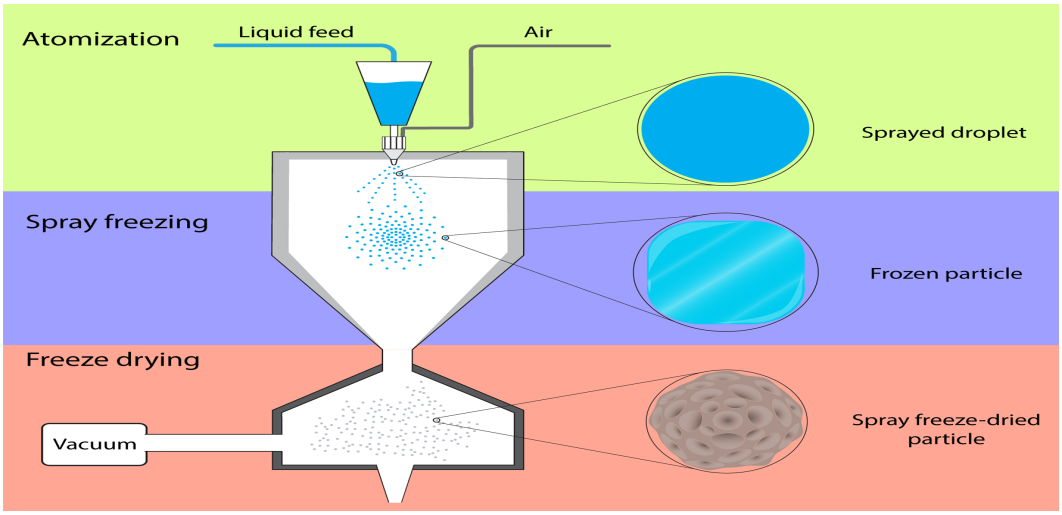

Figure 1. Schematic representation of spray freeze drying process.

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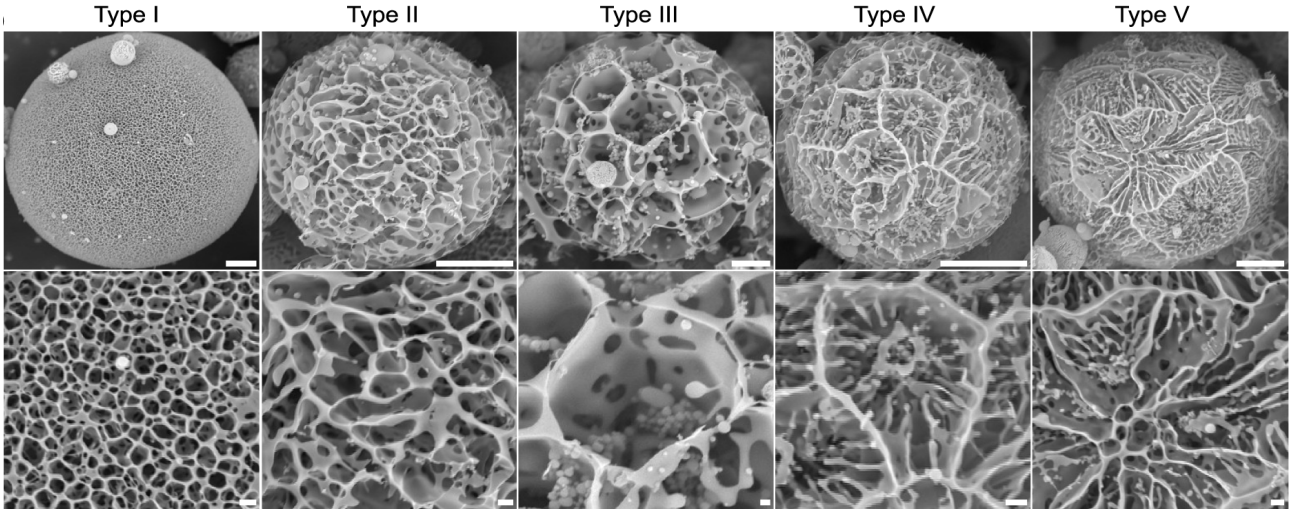

Figure 2. Scanning electron microscopy images of porous microparticles of dextran prepared by spray freeze-drying. As the molecular weight and concentration of dextran solutions is varied, morphology and porosity of formed particles is changed. Scale bars correspond to 10 μm (top row) and 1 μm (bottom row). Adopted with permission from ref. 24. Copyright 2022 American Chemical Society.

particles with narrow size distribution, have low waste of materials, be used for large scale production. Furthermore, the produced particles should exhibit optimum flowability, rapid fluid uptake, and can control the release of loaded therapeutic agent. Until now, the most used methods are spray drying,[13] freeze-drying,[18] and milling.[16] However, these methods face some limitations. Spray drying and milling can compromise stability of sensitive molecules such as proteins and peptides.[19,20] On the other hand, freeze-drying needs a long drying time and produces a solid cake that needs further steps of milling and sieving to provide a powder form with appropriate properties.[21]

Recently, spray freeze-drying (SFD) has attracted significant attraction as a particle engineering method. This method has been used for preparing powders intended for nasal, pulmonary, transdermal, and oral drug delivery.[22] As Figure 1 shows, the SFD process consists of three consecutive steps of liquid atomization, droplet freezing, and lyophilization.[23] First, the liquid feed (solution, suspension, or emulsion) is atomized as fine droplets. Then the atomized liquid droplets are frozen by means of liquid nitrogen. Finally, the dried particles are formed by solvent sublimation from these frozen droplets under reduced pressures. The SFD process produces spherical and porous particles with good control over their particle size distribution.[22] Furthermore, it is possible to prepare porous particles with distinct structures by changing the concentration and components of feed liquid or modifying processing parameters such as lyophilization pressure and temperature (Figure 2).[24] The advantages of preparing BWPs by SFD include preserving stability of sensitive molecules, good flowability, and rapid fluid uptake due to their porous structure. Considering these, we propose SFD as a promising method for preparing in situ gel forming BWPs, BWPs containing nanoparticles, and BWPs based on proteins and peptides such as growth factors. Application of SPD in this field can provide new opportunities to address challenges of spray drying and freeze-drying and develop effective multifunctional BWPs.

Author Contributions

Shahram Emami: Conceptualization, Writing - Original Draft. Sepehr Mehdizadeh: Investigation, Writing - Review & Editing. Ehsan Manafzadeh: Investigation, Writing - Review & Editing.

Conflict of Interest

The authors report no conflicts of interest.

References

1. Koehler J, Brandl FP, Goepferich AM. Hydrogel wound dressings for bioactive treatment of acute and chronic wounds. Eur Polym J. 2018;100:1-11. doi:10.1016/j.eurpolymj.2017.12.046
2. Boateng JS, Matthews KH, Stevens HNE, Eccleston GM. Wound healing dressings and drug delivery systems: A review. J Pharm Sci. 2008;97(8):2892-923. doi:10.1002/jps.21210
3. Dhivya S, Padma VV, Santhini E. Wound dressings – a review. Biomedicine. 2015;5(4):22. doi:10.7603/s40681-015-0022-9
4. Fitzgerald RH, Bharara M, Mills JL, Armstrong DG. Use of a nanoflex powder dressing for wound management following debridement for necrotising fasciitis in the diabetic foot. Int Wound J. 2009;6(2):133-9. doi:10.1111/j.1742-481X.2009.00596.x
5. Benito-Martinez S, Perez-Kohler B, Rodriguez M, Izco JM, Recalde JI, Pascual G. Wound healing modulation through the local application of powder collagen-derived treatments in an excisional cutaneous murine model. Biomedicines. 2022;10(5):960. doi:10.3390/biomedicines10050960
6. Chen S, Huan Z, Zhang L, Chang J. The clinical application of a silicate-based wound dressing

(dermfactor®) for wound healing after anal surgery: A randomized study. Int J Surg. 2018;52:229-32. doi:10.1016/j.ijsu.2018.02.036
7. Thakar H, Sebastian SM, Mandal S, Pople A, Agarwal G, Srivastava A. Biomolecule-conjugated macroporous hydrogels for biomedical applications. ACS Biomater Sci Eng. 2019;5(12):6320-41. doi:10.1021/acsbiomaterials.9b00778
8. Tiozzo Fasiolo L, Manniello MD, Tratta E, Buttini F, Rossi A, Sonvico F, et al. Opportunity and challenges of nasal powders: Drug formulation and delivery. Eur J Pharm Sci. 2018;113:2-17. doi:10.1016/j.ejps.2017.09.027
9. Romić MD, Klarić M, Lovrić J, Pepić I, Cetina-Čižmek B, Filipović-Grčić J, et al. Melatonin-loaded chitosan/pluronic® f127 microspheres as in situ forming hydrogel: An innovative antimicrobial wound dressing. Eur J Pharm Biopharm. 2016;107:67-79. doi:10.1016/j.ejpb.2016.06.013
10. Chen Y-W, Lu C-H, Shen M-H, Lin S-Y, Chen C-H, Chuang C-K, et al. In vitro evaluation of the hyaluronic acid/alginate composite powder for topical haemostasis and wound healing. Int Wound J. 2020;17(2):394-404. doi:10.1111/iwj.13285
11. Chalimidi KR, Kumar Y, Kini UA. Efficacy of collagen particles in chronic non healing ulcers. J Clin Diagn Res. 2015;9(6):PC01-3. doi:10.7860/JCDR/2015/11782.6001
12. Del Gaudio P, Amante C, Civale R, Bizzarro V, Petrella A, Pepe G, et al. In situ gelling alginate-pectin blend particles loaded with ac2-26: A new weapon to improve wound care armamentarium. Carbohydr Polym. 2020;227:115305. doi:10.1016/j.carbpol.2019.115305
13. De Cicco F, Reverchon E, Adami R, Auriemma G, Russo P, Calabrese EC, et al. In situ forming antibacterial dextran blend hydrogel for wound dressing: Saa technology vs. Spray drying. Carbohydr Polym. 2014;101:1216-24. doi:10.1016/j.carbpol.2013.10.067
14. Pagano C, Calarco P, Di Michele A, Ceccarini MR, Beccari T, Primavilla S, et al. Development of sodium carboxymethyl cellulose based polymeric microparticles for in situ hydrogel wound dressing formation. Int J Pharm. 2021;602:120606. doi:10.1016/j.ijpharm.2021.120606
15. Salhi N, Bouyahya A, Fettach S, Zellou A, Cherrah Y. Ethnopharmacological study of medicinal plants used in the treatment of skin burns in occidental morocco (area of rabat). S Afr J Bot. 2019;121:128-42. doi:10.1016/j.sajb.2018.10.038
16. Ahmed TAE, Suso HP, Maqbool A, Hincke MT. Processed eggshell membrane powder: Bioinspiration for an innovative wound healing product. Mater Sci Eng C Mater Biol Appl. 2019;95:192-203. doi:10.1016/j.msec.2018.10.054
17. Yu SY, Ullrich PJ, Weissman JP, Joshi CJ, Taylor R, Patel A, et al. Evaluation of altrazeal transforming powder dressing on stage 2-4 pressure ulcers: A clinical case series. J Wound Care. 2022;31(Sup5):S6-S12. doi:10.12968/jowc.2022.31.Sup5.S6
18. Hall TJ, Azoidis I, Barroso IA, Hughes EAB, Grover LM, Cox SC. Formulation of an antimicrobial superabsorbent powder that gels in situ to produce reactive oxygen. Mater Sci Eng C Mater Biol Appl. 2021;118:111479. doi:10.1016/j.msec.2020.111479
19. Kumar S, Burgess DJ. Wet milling induced physical and chemical instabilities of naproxen nano-crystalline suspensions. Int J Pharm. 2014;466(1):223-32. doi:10.1016/j.ijpharm.2014.03.021
20. Ziaee A, Albadarin AB, Padrela L, Ung M-T, Femmer T, Walker G, et al. A rational approach towards spray drying of biopharmaceuticals: The case of lysozyme. Powder Technol. 2020;366:206-15. doi:10.1016/j.powtec.2020.02.057
21. Zhang X, Jiang L, Li X, Zheng L, Dang R, Liu X, et al. A bioinspired hemostatic powder derived from the skin secretion of andrias davidianus for rapid hemostasis and intraoral wound healing. Small. 2022;18(3):2101699. doi:10.1002/smll.202101699
22. Vishali DA, Monisha J, Sivakamasundari SK, Moses JA, Anandharamakrishnan C. Spray freeze drying: Emerging applications in drug delivery. J Controlled Release. 2019;300:93-101. doi:10.1016/j.jconrel.2019.02.044
23. Ishwarya SP, Anandharamakrishnan C, Stapley AGF. Spray-freeze-drying: A novel process for the drying of foods and bioproducts. Trends Food Sci Technol. 2015;41(2):161-81. doi:10.1016/j.tifs.2014.10.008
24. Kämäräinen T, Kadota K, Tse JY, Uchiyama H, Yamanaka S, Tozuka Y. Modulating the pore architecture of ice-templated dextran microparticles using molecular weight and concentration. Langmuir 2022;38(21):6741-51. doi:10.1021/acs.langmuir.2c00721