

References

- Ahangar, P., Mills, S. J., & Cowin, A. J. (2020). Mesenchymal stem cell secretome as an emerging cell-free alternative for improving wound repair. *International Journal of Molecular Sciences*, 21(19), 7038. doi: 10.3390/ijms21197038
- An, Y. H., Kim, D. H., Lee, E. J., Lee, D., Park, M. J., Ko, J., ... & Hwang, N. S. (2021). High-efficient production of adipose-derived stem cell (ADSC) secretome through maturation process and its non-scarring wound healing applications. *Frontiers in bioengineering and biotechnology*, 9, 681501.
- Arrigoni, C., D'Arrigo, D., Rossella, V., Candrian, C., Albertini, V., & Moretti, M. (2020). Umbilical cord MSCs and their secretome in the therapy of arthritic diseases: a research and industrial perspective. *Cells*, 9(6), 1343. <https://doi.org/10.3390%2Fcells9061343>
- Assegehegn, G., Brito-de la Fuente, E., Franco, J. M., & Gallegos, C. (2019). The importance of understanding the freezing step and its impact on freeze-drying process performance. *Journal of pharmaceutical sciences*, 108(4), 1378-1395. <https://doi.org/10.1016/j.xphs.2018.11.039>
- Bansal, R., Jha, S. K., & Jha, N. K. (2021). Size-based Degradation of Therapeutic Proteins-Mechanisms, Modelling and Control. *Biomolecular Concepts*, 12(1), 68-84. <https://doi.org/10.1515/bmc-2021-0008>
- Bari, E., Perteghella, S., Di Silvestre, D., Sorlini, M., Catenacci, L., Sorrenti, M., Marrubini, G., Rossi, R., Tripodo, G., Mauri, P., Marazzi, M., & Torre, M. L. (2018). Pilot Production of Mesenchymal Stem/Stromal Freeze-Dried Secretome for Cell-Free Regenerative Nanomedicine: A Validated GMP-Compliant Process. *Cells*, 7(11), 190. <https://doi.org/10.3390/cells7110190>
- Bari, E., Ferrarotti, I., Torre, M. L., Corsico, A. G., & Perteghella, S. (2019). Mesenchymal stem/stromal cell secretome for lung regeneration: The long way through “pharmaceuticalization” for the best formulation. *Journal of Controlled Release*, 309, 11-24.

Barril, P., & Nates, S. (2012). Introduction to Agarose and Polyacrylamide Gel Electrophoresis Matrices with Respect to Their Detection Sensitivities. In (Ed.), *Gel Electrophoresis - Principles and Basics*. IntechOpen. <https://doi.org/10.5772/38573>

Bhatnagar, B. S., Bogner, R. H., & Pikal, M. J. (2007). Protein stability during freezing: separation of stresses and mechanisms of protein stabilization. *Pharmaceutical development and technology*, 12(5), 505-523. doi: 10.1080/10837450701481157

Bio-Rad Laboratories, Inc. (n.d.). *Electrophoresis Guide, Interactive PDF, Rev C. Bulletin#6040*. Retrieved from https://www.bio-rad.com/sites/default/files/webroot/web/pdf/lsr/literature/Bulletin_6040.pdf

Brogna, R., Oldenhof, H., Sieme, H., Figueiredo, C., Kerrinnes, T., & Wolkers, W. F. (2020). Increasing storage stability of freeze-dried plasma using trehalose. *PLoS one*, 15(6), e0234502. <https://doi.org/10.1371/journal.pone.0234502>

Brom, J. A., Petrikis, R. G., & Pielak, G. J. (2023). How Sugars Protect Dry Protein Structure. *Biochemistry*, 62(5), 1044-1052. <https://doi.org/10.1021/acs.biochem.2c00692>

Bye, J. W., Platts, L., & Falconer, R. J. (2014). Biopharmaceutical liquid formulation: a review of the science of protein stability and solubility in aqueous environments. *Biotechnology letters*, 36, 869-875. <https://doi.org/10.1007/s10529-013-1445-6>

Chen, Y., Mutukuri, T. T., Wilson, N. E., & Zhou, Q. T. (2021). Pharmaceutical protein solids: Drying technology, solid-state characterization and stability. *Advanced drug delivery reviews*, 172, 211-233. doi:10.1016/j.addr.2021.02.016.

Chouw, A., Sartika, C. R., Milanda, T., & Faried, A. (2022). Interleukins profiling in umbilical cord mesenchymal stem cell-derived secretome. *Stem Cells and Cloning: Advances and Applications*, 1-9. <https://doi.org/10.2147%2FSCCAAS356763>

Dai Y, Tang H, & Pang S. (2021). The Crucial Roles of Phospholipids in Aging and Lifespan Regulation. *Front. Physiol.* 12:775648. doi: 10.3389/fphys.2021.775648

Damayanti, R. H., Rusdiana, T., & Wathoni, N. (2021). Mesenchymal stem cell secretome for dermatology application: a review. *Clinical, Cosmetic and Investigational Dermatology*, 14, 1401. <https://doi.org/10.2147/ccid.s331044>

Driscoll, J., Yan, I. K., & Patel, T. (2022). Development of a Lyophilized Off-the-Shelf Mesenchymal Stem Cell-Derived Acellular Therapeutic. *Pharmaceutics*, 14(4), 849. doi: 10.3390/pharmaceutics14040849

El Baradie, K. B. Y., Nouh, M., O'Brien III, F., Liu, Y., Fulzele, S., Eroglu, A., & Hamrick, M. W. (2020). Freeze-dried extracellular vesicles from adipose-derived stem cells prevent hypoxia-induced muscle cell injury. *Frontiers in cell and developmental biology*, 8, 181. <https://doi.org/10.3389/fcell.2020.00181>

Eleuteri, S., & Fierabracci, A. (2019). Insights into the secretome of mesenchymal stem cells and its potential applications. *International Journal of Molecular Sciences* (20)18. MDPI AG. <https://doi.org/10.3390/ijms20184597>

Falk, J. (2019). *Freeze-drying of protein pharmaceutical in vials with different character* (Dissertation). Uppsala Universitet. Retrieved from <https://ri.diva-portal.org/smash/get/diva2:1334697/FULLTEXT01>

Fonte, P., Soares, S., Costa, A., Andrade, J. C., Seabra, V., Reis, S., & Sarmento, B. (2012). Effect of cryoprotectants on the porosity and stability of insulin-loaded PLGA nanoparticles after freeze-drying. *Biomatter*, 2(4), 329–339. <https://doi.org/10.4161/biom.23246>

Gadda G. (2020). Choline oxidases. *The Enzymes*, 47, 137–166. <https://doi.org/10.1016/bs.enz.2020.05.004>

Gaidhani, K. A., Harwalkar, M., Bhambere, D., & Nirgude, P. S. (2015). Lyophilization/freeze drying—a review. *World journal of pharmaceutical research*, 4(8), 516-543.

García-Descalzo, L., García-López, E., Alcázar, A., Baquero, F., & Cid, C. (2012). Gel Electrophoresis of Proteins. In (Ed.), *Gel Electrophoresis - Principles and Basics*. IntechOpen. <https://doi.org/10.5772/37514>

- Hmadcha, A., Martin-Montalvo, A., Gauthier, B. R., Soria, B., & Capilla-Gonzalez, V. (2020). Therapeutic potential of mesenchymal stem cells for cancer therapy. *Frontiers in Bioengineering and Biotechnology*, 8, 43. <https://doi.org/10.3389/fbioe.2020.00043>
- Huang, T., Long, M., & Huo, B. (2010). Competitive binding to cuprous ions of protein and BCA in the bicinchoninic acid protein assay. *The open biomedical engineering journal*, 4, 271. doi: 10.2174/1874120701004010271
- Ibrahim, R., Mndlovu, H., Kumar, P., Adeyemi, S. A., & Choonara, Y. E. (2022). Cell Secretome Strategies for Controlled Drug Delivery and Wound-Healing Applications. *Polymers*, 14(14), 2929.
- Imamura, K., Ogawa, T., Sakiyama, T., & Nakanishi, K. (2003). Effects of types of sugar on the stabilization of protein in the dried state. *Journal of pharmaceutical sciences*, 92(2), 266-274. doi: 10.1002/jps.10305.
- Izutsu, K. I. (2018). Applications of freezing and freeze-drying in pharmaceutical formulations. In: Iwaya-Inoue, M., Sakurai, M., Uemura, M. (eds). Survival Strategies in Extreme Cold and Desiccation: Adaptation Mechanisms and Their Applications. *Advances in Experimental Medicine and Biology*, (1081), 371-383. Springer, Singapore. https://doi.org/10.1007/978-981-13-1244-1_20
- Kavoosi, G., & Ardestani, S. K. (2012). Gel Electrophoresis of Protein - From Basic Science to Practical Approach. In (Ed.), *Gel Electrophoresis - Principles and Basics*. IntechOpen. <https://doi.org/10.5772/38062>
- Kawasaki, H., Shimanouchi, T., & Kimura, Y. (2019). Recent development of optimization of lyophilization process. *Journal of chemistry*, 2019.
- Koganti, V. R., Shalaev, E. Y., Berry, M. R., Osterberg, T., Youssef, M., Hiebert, D. N., ... & Zhang, L. (2011). Investigation of design space for freeze-drying: use of modeling for primary drying segment of a freeze-drying cycle. *Aaps Pharmscitech*, 12(3), 854-861. DOI: <https://doi.org/10.1208%2Fs12249-011-9645-7>

Luo, C., Liu, Z., Mi, S., & Li, L. (2022). Quantitative investigation on the effects of ice crystal size on freeze-drying: The primary drying step. *Drying Technology*, 40(2), 446-458.
<http://dx.doi.org/10.1080/07373937.2020.1806865>

Meiliana, A., Dewi, N. M., & Wijaya, A. (2019). Mesenchymal stem cell secretome: Cell-free therapeutic strategy in regenerative medicine. *The Indonesian Biomedical Journal*, 11(2), 113-24. <https://doi.org/10.18585/inabj.v11i2.839>

Mensink, M. A., Frijlink, H. W., van Der Voort Maarschalk, K., & Hinrichs, W. L. (2017). How sugars protect proteins in the solid state and during drying (review): Mechanisms of stabilization in relation to stress conditions. *European Journal of Pharmaceutics and Biopharmaceutics*, 114, 288-295. doi: 10.1016/j.ejpb.2017.01.024.

Merivaara, A., Zini, J., Koivunotko, E., Valkonen, S., Korhonen, O., Fernandes, F. M., & Yliperttula, M. (2021). Preservation of biomaterials and cells by freeze-drying: Change of paradigm. *Journal of Controlled Release*, 336, 480-498. <http://dx.doi.org/10.1016/j.jconrel.2021.06.042>

Mitchell, R., Mellows, B., Sheard, J., Antonioli, M., Kretz, O., Chambers, D., ... & Patel, K. (2019). Secretome of adipose-derived mesenchymal stem cells promotes skeletal muscle regeneration through synergistic action of extracellular vesicle cargo and soluble proteins. *Stem Cell Research & Therapy*, 10(1), 1-19. <https://doi.org/10.1186/s13287-019-1213-1>

Mocchi, M., Bari, E., Marrubini, G., Bonda, A. F., Perteghella, S., Tartara, F., ... & Segale, L. (2021). Freeze-dried mesenchymal stem cell-secretome pharmaceuticalization: optimization of formulation and manufacturing process robustness. *Pharmaceutics*, 13(8), 1129. <https://doi.org/10.3390/pharmaceutics13081129>

Mocchi, M., Grolli, S., Dotti, S., Di Silvestre, D., Villa, R., Berni, P., ... & Perteghella, S. (2021). Equine mesenchymal stem/stromal cells freeze-dried secretome (Lyosecretome) for the treatment of musculoskeletal diseases: production process validation and batch release test for clinical use. *Pharmaceuticals*, 14(6), 553. doi: 10.3390/ph14060553

Munoz-Perez, E., Gonzalez-Pujana, A., Igartua, M., Santos-Vizcaino, E., & Hernandez, R. M. (2021).

Mesenchymal Stromal Cell Secretome for the Treatment of Immune-Mediated Inflammatory Diseases: Latest Trends in Isolation, Content Optimization and Delivery Avenues.

Pharmaceutics, 13(11), 1802. <https://doi.org/10.3390/pharmaceutics13111802>

Nadesh, R., Menon, K. N., Biswas, L., Mony, U., Subramania Iyer, K., Vijayaraghavan, S., ... & Nair, S.

(2021). Adipose derived mesenchymal stem cell secretome formulation as a biotherapeutic to inhibit growth of drug resistant triple negative breast cancer. *Scientific Reports*, 11(1), 23435.

doi: <https://doi.org/10.1038%2Fs41598-021-01878-z>

Nurhayati, R. W., Lubis, D. S. H., Pratama, G., Agustina, E., Khoiriyah, Z., Alawiyah, K., & Pawitan, J. A.

(2021). The Effects of Static and Dynamic Culture Systems on Cell Proliferation and Conditioned Media of Umbilical Cord-Derived Mesenchymal Stem Cells. *International Journal of Technology*, 12(6), 1187-1197. <https://doi.org/10.14716/ijtech.v12i6.5172>

Olsson, C., Jansson, H., & Swenson, J. (2016). The role of trehalose for the stabilization of proteins.

The Journal of Physical Chemistry B, 120(20), 4723-4731.
<https://doi.org/10.1021/acs.jpcb.6b02517>

Pittenger, M. F., Discher, D. E., Péault, B. M., Phinney, D. G., Hare, J. M., & Caplan, A. I. (2019).

Mesenchymal stem cell perspective: cell biology to clinical progress. *NPJ Regenerative medicine*, 4(1), 1-15. <https://doi.org/10.1038/s41536-019-0083-6>

Ratti, C. (2013). Freeze drying for food powder production. In *Handbook of food powders*, 57-84.

Woodhead Publishing. <http://dx.doi.org/10.1533/9780857098672.1.57>

Sandonà, M., Di Pietro, L., Esposito, F., Ventura, A., Silini, A. R., Parolini, O., & Saccone, V. (2021).

Mesenchymal stromal cells and their secretome: new therapeutic perspectives for skeletal muscle regeneration. *Frontiers in Bioengineering and Biotechnology*, 9, 652970.

<https://doi.org/10.3389/fbioe.2021.652970>

Schulman, I. H., & Hare, J. M. (2018). Mesenchymal stromal cells as a therapeutic intervention.

Stromal Cells-Structure, Function, and Therapeutic Implications. DOI:
10.5772/intechopen.78586

Shen, C. H. (2019). Quantification and analysis of proteins. *Diagnostic Molecular Biology*; Shen, C.-H., Ed.; Academic Press: Cambridge, MA, USA, 187-214.

<https://doi.org/10.1016/B978-0-12-802823-0.00008-0>

Singh, S. K., Kolhe, P., Wang, W., & Nema, S. (2009). Large-Scale Freezing of Biologics. *BioProcess International*.

Singh, R. P., & Heldman, D. R. (2008). Food Freezing. *Introduction to food engineering fourth edition*. Gulf Professional Publishing. eBook ISBN: 9780080919621

Tayebati, S. K., Marucci, G., Santinelli, C., Buccioni, M., & Amenta, F. (2015). Choline-containing phospholipids: structure-activity relationships versus therapeutic applications. *Current Medicinal Chemistry*, 22(38), 4328-4340.

<https://doi.org/10.2174/0929867322666151029104152>

Trenkenschuh, E., Richter, M., Heinrich, E., Koch, M., Fuhrmann, G., & Friess, W. (2022). Enhancing the stabilization potential of lyophilization for extracellular vesicles. *Advanced healthcare materials*, 11(5), 2100538. <https://doi.org/10.1002/adhm.202100538>

Ullrich, S. (2014). *Quantitative measurements of shrinkage and cracking during freeze-drying of amorphous cakes* (Doctoral dissertation, Friedrich-Alexander-Universität Erlangen-Nürnberg (FAU)).

Wang, B., Tchessalov, S., Cicerone, M. T., Warne, N. W., & Pikal, M. J. (2009). Impact of sucrose level on storage stability of proteins in freeze-dried solids: II. Correlation of aggregation rate with protein structure and molecular mobility. *Journal of pharmaceutical sciences*, 98(9), 3145-3166. <https://doi.org/10.1002/jps.21622>

Xia, J., Minamino, S., Kuwabara, K., & Arai, S. (2019). Stem cell secretome as a new booster for regenerative medicine. *BioScience Trends*, 13(4), 299-307. doi:
<https://doi.org/10.5582/bst.2019.01226>

Zhang, C. (2017). *Freeze-drying of engineered proteins using protein modelling tools and experimental validation* (Doctoral dissertation, UCL (University College London)).