Study: How to freeze-dry a potential COVID-19 vaccine

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The freeze-dried ingredients of a liposome-based vaccine that could be developed for COVID-19. Credit: Douglas Levere / University at Buffalo

Things that are freeze-dried: Astronaut food. Emergency rations. And, just maybe, some future COVID-19 vaccines.

Freeze-drying is a method for removing water from a product. First, you freeze the item you're trying to dehydrate, causing any water in it to become ice. Then, you remove the ice through a process called sublimation, in which ice turns directly into vapor under low pressure.

In a new study, scientists report that they have successfully freeze-dried a liposome-based liquid vaccine formula that could be developed for potential use in COVID-19 vaccines.

A vaccine that employs the freeze-dried liposomes is still a long way off. But if developed successfully, dehydrated doses could be shipped and stored at room temperature, eliminating logistical problems associated with some of the most popular existing vaccines for the disease.

The findings will be published in *Science Advances* on Dec. 1, with University at Buffalo biomedical engineering researchers Jonathan Lovell and Moustafa Mabrouk as the senior and first authors, respectively.

"At the time we started this project, the first COVID-19 vaccines were just getting rolled out, and there was a lot of news about how they needed ultra-cold storage, and how that was a huge logistical challenge. Especially in low- and middle-income countries, it may not always be feasible to have that type of refrigeration infrastructure. So we started to look at whether we could make a thermostable COVID-19 vaccine using a liposome-based vaccine platform that we worked on previously," says Lovell, Ph.D., SUNY Empire Innovation Associate Professor in the Department of Biomedical Engineering in the UB School of Engineering and Applied Sciences and the Jacobs School of Medicine and Biomedical Sciences at UB.

The freeze-dried ingredients of a liposome-based vaccine that could be developed for COVID-19. Credit: Douglas Levere / University at Buffalo

The new study focuses on a liquid injection that consists of ingredients including water; specialized liposomes carrying a synthetically produced version of the spike protein of the COVID-19 virus; and a small amount of sugar, which helps to protect the formula during the freeze-drying process.

The freeze-dried product looks a bit like cotton candy, mint green in color.

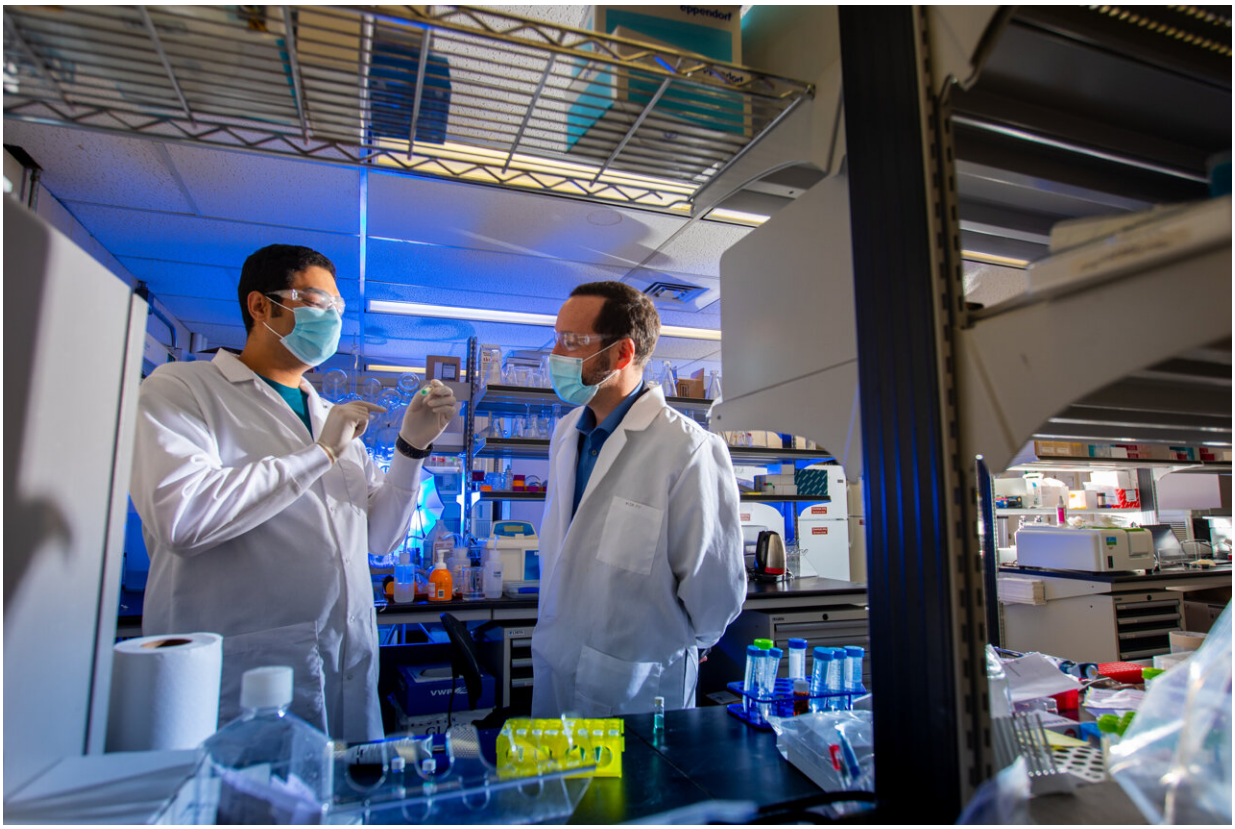
"Upon dehydration, the formula was stable at elevated temperatures, and we showed that it can withstand room temperatures and even higher

temperatures for at least a week," says Mabrouk, a UB biomedical engineering Ph.D. student. "After that, we reconstituted the formula by adding water. When we tested this in mice, it induced effective antibody responses and offered protection against the COVID-19 virus."

Co-authors also include Wei-Chiao Huang and Breandan Quinn at UB; Kevin Chiem and Luis Martinez-Sobrido at the Texas Biomedical Research Institute in the U.S.; Edurne Rujas at The Hospital for Sick Children Research Institute in Canada and University of the Basque Country in Spain; Dushyant Jahagirdar and Joaquin Ortega at McGill University in Canada; Meera Surendran Nair, Ruth H. Nissly, Victoria S. Cavener, Nina R. Boyle, Ty A. Sornberger and Suresh V. Kuchipudi at Pennsylvania State University in the U.S.; and Jean-Philippe Julien at The Hospital for Sick Children Research Institute and University of Toronto in Canada.

Moustafa Mabrouk, University at Buffalo biomedical engineering PhD student, holds a vial containing ingredients of a liposome-based liquid vaccine that could be developed for COVID-19. Credit: Douglas Levere / University at Buffalo

A vacuum chamber holds ingredients of a liposome-based vaccine that could be developed for COVID-19. The chamber is used for freeze-drying products. Credit: Douglas Levere / University at Buffalo



University at Buffalo biomedical engineering PhD student Moustafa Mabrouk (left) and Jonathan Lovell, SUNY Empire Innovation Associate Professor in the UB Department of Biomedical Engineering. In the journal *Science Advances*, Lovell, Mabrouk and colleagues report successfully freeze-drying specialized liposomes that could be developed for use in future COVID-19 vaccines. Credit: Douglas Levere / University at Buffalo

Moustafa Mabrouk, University at Buffalo biomedical engineering PhD student, works in the lab. Credit: Douglas Levere / University at Buffalo

The specialized liposomes examined in the *Science Advances* study are being researched for potential use in vaccines against multiple diseases. The liposomes were originally developed in Lovell's UB lab and have been licensed by the university to POP Biotechnologies, a startup company that Lovell co-founded. (Huang is also a POP Biotechnologies employee.)

A COVID-19 vaccine candidate that relies on POP Biotechnologies' liposome-based vaccine delivery system is in human trials in South Korea. That vaccine candidate, called EuCorVac-19, is under development by POP Biotechnologies and South Korean biotech

company EuBiologics. EuCorVac-19 has slightly different ingredients from the vaccine formula studied in the Science Advances paper.

"We have not tested freeze-drying on the EuCorVac-19 vaccine," Lovell says. "However, I think the data in this new study suggest that, in theory, the EuCorVac-19 formula may be amenable to this type of treatment to make it very thermostable, which would benefit any global deployment."

More information: Moustafa T. Mabrouk et al, Lyophilized, thermostable Spike or RBD immunogenic liposomes induce protective immunity against SARS-CoV-2 in mice, *Science Advances* (2021). DOI: 10.1126/sciadv.abj1476. www.science.org/doi/10.1126/sciadv.abj1476

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