

From pasture to patient: Scientists distill cow's milk into drug delivery nano-capsules

Researchers led by Rob Gourdie developed a new, scalable method to purify exosomes, nano-sized drug delivery capsules harvested from cow's milk

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Exosomes are nano-sized biological capsules that cells produce to protect and courier delicate molecules throughout the body. The capsules are hardy enough to withstand enzymatic breakdown, as well as acidic and temperature fluctuations in the gut and bloodstream, making them a promising candidate for drug delivery.

Harvesting them to achieve clinical-grade levels of purity, however, is a complex process.

"Exosomes are abundant in cow's milk, yet they're difficult to isolate from other milk proteins and lipids," said Rob Gourdie, professor and director of the Center for Vascular and Heart Research at the Fralin Biomedical Research Institute at VTC.

Gourdie's laboratory developed a scalable method to harvest exosomes from unpasteurized cow's milk. Using this purification method, which was published this month in *Nanotheranostics*, the research team can extract roughly a cup of purified exosomes for every gallon of unpasteurized milk.

"For the first time, we've charted a path toward the industrial scalability of exosome purification for oral drug delivery," said Gourdie, who is also the Commonwealth Research Commercialization Fund Eminent Scholar in Heart Reparative Medicine Research and a professor of biomedical engineering and mechanics in Virginia Tech's College of Engineering.

The research team developed their multistep, cost-effective purification process, which optimizes filtration methods, and timing of temperature and chemical treatments affecting calcium levels, during the COVID-19 pandemic. Spencer Marsh and Kevin Pridham, both postdoctoral fellows in Gourdie's lab at the Fralin Biomedical Research Institute, and Jane Jourdan, Gourdie's lab manager, did the practical work to develop the proprietary procedure.

"Our team worked together effectively and safely on this project throughout the pandemic," Gourdie said. "It was a sight to see – their selfless teamwork, enthusiasm, and dedication to overcoming challenges is something that does not happen as often as you might think in science. There were many failures, but eventually, we figured out stepwise processes that worked."

Joy Wolfram, assistant professor of medicine at Mayo Clinic, who was not involved in the study, says the new protocol advances the pharmaceutical potential for exosomes.

“What’s remarkable is the quantity of extracellular vesicles they are able to produce. Isolating and manufacturing extracellular vesicles in a scalable manner has always prevented their translation into the clinic, but this paper shows a path to overcome those roadblocks,” Wolfram said. Wolfram previously published a protocol for using tangential flow filtration technology that Gourdie’s team adapted to isolate the milk exosomes.

Exosomes are secreted naturally by nearly all cell types in humans and other mammals and can be found abundantly in blood, lymph, urine, and milk. Lined with protective membranes, exosomes shuttle biomolecules, snippets of genetic material, and chemical signals between cells over long ranges.

Over the past decade, research into their pharmaceutical applications – particularly for the delivery of fragile drugs, such as peptides and microRNAs – has surged.

“Imagine instead of getting a vaccine shot, your nurse hands you a milkshake instead. Another milkshake may contain exosomes loaded with a therapeutic peptide designed to protect internal organs such as the heart from myocardial infarction,” Gourdie said.

Exosomes can also penetrate the blood-brain barrier, a collection of coupled cellular processes that protect the brain from unwanted pathogens and

chemicals, introducing a new way to deliver therapeutics to treat neurological diseases and brain cancer.

“Improving the viability of using exosomes opens up a wide range of drug delivery methods with unlimited clinical applications,” Gourdie said.

Gourdie partnered with Homestead Creamery, a local dairy processing plant, to obtain unpasteurized milk samples for the study.

“We have always built our business on relationships, and this is an exciting collaboration for us,” said Donnie Montgomery, co-founder and co-owner of Homestead Creamery.

Last year, Gourdie licensed the intellectual property to deliver heart medicine using exosomes through Virginia Tech’s LICENSE: Center for Technology Commercialization and formed The Tiny Cargo Co.

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