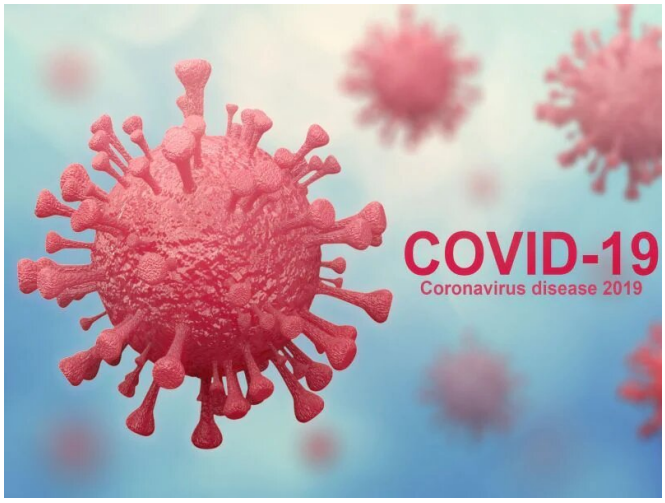
Nanotechnology might help fight deadly 'cytokine storm' of COVID-19

28 April 2020, by E.j. Mundell, Healthday Reporter



For many COVID-19 patients battling for their lives in the ICU, a runaway immune system response—known as a "cytokine storm"—is their primary foe.

Doctors have few tools to help tame this hyperinflammatory condition, but early research is suggesting that nanotechnology might safely deliver drugs to affected tissues, quieting the storm.

It's so far only been tested in mice, but researchers in Brazil and France said the approach could be "a new tool in the fight against the complex and multi-factorial phenomenon of uncontrolled inflammation." They reported their findings online April 27 in the journal *Science Advances*.

It's not clear why some young, robust patients experience life-threatening illness from COVID-19, while others have either mild or no symptoms.

But when severe illness does strike, it's often in the form of an out-of-control immune system response.

Inflammatory processes harm cells at multiple sites throughout the body and, if unchecked, this can lead to organ failure and death, noted a team led by Dr. Patrick Couvreur at the Institute Galien Paris-Sud, in France.

Key to the cytokine storm are connections "between inflammation and oxidative stress, both processes contributing to fuel one another, thereby establishing a vicious cycle," Couvreur's group explained.

Right now, there's no therapy that's able to interrupt this dangerous "crosstalk," they said. For example, anti-inflammatory drugs such as corticosteroids have not worked, because of their negative effects on tissue repair.

But the new findings may point the way to a successful treatment.

In their work, Couvreur's group focused on an extremely tiny "nanoparticle" formulation of adenosine, an anti-inflammatory compound already produced naturally by the body.

It's a powerful anti-inflammatory compound—maybe too powerful. If simply injected into the body, adenosine can trigger serious side effects, the research team said.

But the new nanotechnology approach appears to get around that, they added.

Couvreur's team created "multi-drug nanoparticles" by adding adenosine to squalene, a type of fat also found naturally in the body. Then they "encapsulated" both in the powerful antioxidant alpha-tocopherol, a type of vitamin E.

Using this nanotechnology approach, the researchers then delivered the compounds to the

tissues of mice who were in hyperinflammatory states such as sepsis (blood infection) or an immunological state resembling the typical "cytokine storm" of COVID-19.

The result: A notable decrease in tissues of a key pro-inflammatory cytokine called tumor necrosis factor alpha, along with a concurrent rise in levels of an *anti*-inflammatory cytokine called interleukin-10, the researchers reported.

These changes were observed in important organs such as the lungs and kidneys just four hours after treatment, Couvreur's group said.

The team added that the combo treatment—adenosine plus tocopherol—appeared more effective than the use of either drug alone.

Of course, this study was conducted in mice, and many therapies that appear promising in animals don't pan out in humans. But Dr. Matthew Heinz, an expert in the fight against infectious diseases, said the findings do "make sense."

"I'm surprised this was something they were able to do so quickly," said Heinz, an internist and hospitalist at Tucson Medical Center in Arizona. "It's pretty encouraging to have evidence that something like this might help some of our more critically ill COVID-19 patients survive the hyperimmune response known as a cytokine storm."

Heinz previously worked in the Obama administration's response to the Ebola crisis, and was the former director of provider outreach in the Office of Intergovernmental and External Affairs, at the U.S. Department of Health and Human Services.

Reading over the new findings, he said that "because the research is COVID-related, it's quite possible this could be moved into human trials a lot quicker than during normal times."

Heinz added that "this is still a relatively early stage—we have a little ways to go here—but it's good to see this kind of research already coming out with some very encouraging results on how to approach this tremendously heartbreaking situation that's killing tens of thousands of people in the United States."

More information: Flavio Dormont et al. Squalene-based multidrug nanoparticles for improved mitigation of uncontrolled inflammation, *Science Advances* (2020). DOI: 10.1126/sciadv.aaz5466