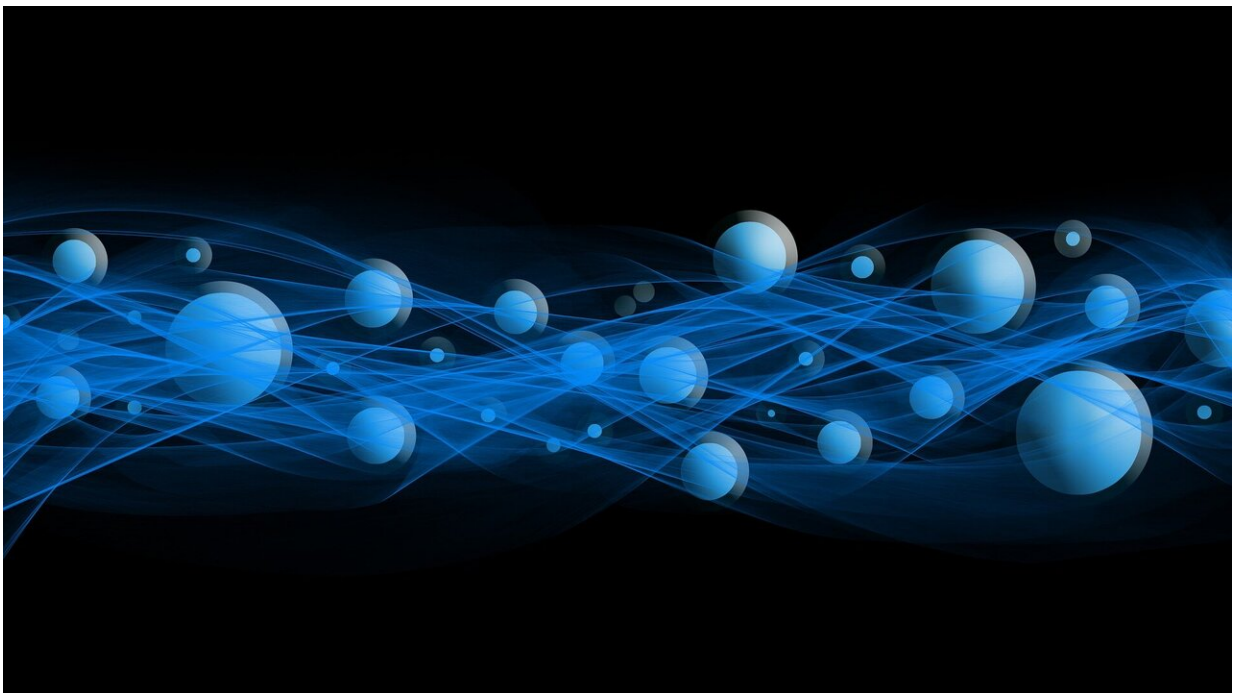


# Nanoparticle drug delivery provides pain relief and more effective opioid alternative in animal study

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An international team of researchers has used nanoparticles to deliver a drug—one that previously failed in clinical trials for pain—into specific compartments of nerve cells, dramatically increasing its ability to treat pain in mice and rats. The findings are published Nov. 4 in *Nature*

*Nanotechnology.*

"We have taken a drug—an FDA-approved anti-vomiting medication—and using a novel delivery method, improved its efficacy and duration of action in animal models of inflammatory [pain](#) and [neuropathic pain](#)," said Nigel Bunnett, Ph.D., chair of the Department of Basic Science and Craniofacial Biology at New York University (NYU) College of Dentistry and the study's senior author. "The discovery that nanoparticle encapsulation enhances and prolongs [pain relief](#) in laboratory animals provides opportunities for developing much-needed non-opioid therapies for pain."

Opioids, a class of drugs used to treat pain, carry a high risk for addiction and overdose. Moreover, their effectiveness diminishes over time, requiring growing doses to manage pain. Side effects of opioids, including constipation and suppressing breathing, only worsen as doses are increased.

"There are many reasons that opioids are not ideal for treating pain. Given the ongoing opioid crisis, which has taken hundreds of thousands of lives, we need safer, more effective alternatives," said Bunnett.

Bunnett and his colleagues study a family of proteins called G protein-coupled receptors, which are the target of one third of clinically used drugs. While it was thought that receptors function at the surface of nerve cells, they discovered that activated receptors move within the cell to a compartment called the endosome. In an endosome, receptors continue to function for prolonged periods. "The sustained activity of receptors in endosomes drives pain," said Bunnett.

In their study in *Nature Nanotechnology*, researchers at NYU College of Dentistry, Monash University, Columbia University, and the University of Santiago in Chile focused on a G protein-coupled receptor called the

neurokinin 1 receptor.

"Major pharmaceutical companies had programs to develop neurokinin receptor antagonists for chronic diseases, including pain and depression. However, in human trials, things fell apart," said Bunnett. "The neurokinin receptor is the poster child for failures in drug discovery to treat pain."

The researchers suspected that these drugs failed to work because they were designed to block receptors at the surface of cells rather than in endosomes.

To deliver drugs to endosomes, the researchers turned to nanoparticles—microscopic vehicles used for delivering drugs. Bunnett and his colleagues encapsulated into nanoparticles a neurokinin receptor blocker called aprepitant, an FDA-approved drug used to prevent nausea and vomiting that failed [clinical trials](#) as a [pain medication](#).

The nanoparticles were designed to enter nerves that transmit pain signals and release their aprepitant cargo in endosomes containing the neurokinin receptor. Nanoparticle-delivered aprepitant treated pain in mice and rats more completely and for longer periods than did conventional therapies, including opioids. Moreover, nanoparticle delivery minimized the dose of medication needed to treat the pain, which could be useful in avoiding side effects.

"The process we've developed is essentially like giving a drug infusion into the endosome of the cell," said Bunnett. "By delivering a previously ineffective pain drug to the right compartment within the cell, it became highly effective as a pain treatment."

The researchers are continuing to study the [use of nanoparticles](#) in delivering non-opioid pain medication, including developing ways to

target them only to nerve cells that sense pain, which would allow for even smaller doses of the [drug](#). They are also exploring encapsulating multiple drugs that block pain [receptors](#), which could further improve the efficacy of treatment. The researchers note that additional studies are needed before nanoparticle-delivered pain medication can be tested in humans.

**More information:** A pH-responsive nanoparticle targets the neurokinin 1 receptor in endosomes to prevent chronic pain, *Nature Nanotechnology* (2019). [DOI: 10.1038/s41565-019-0568-x](https://doi.org/10.1038/s41565-019-0568-x) , [nature.com/articles/s41565-019-0568-x](https://www.nature.com/articles/s41565-019-0568-x)

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