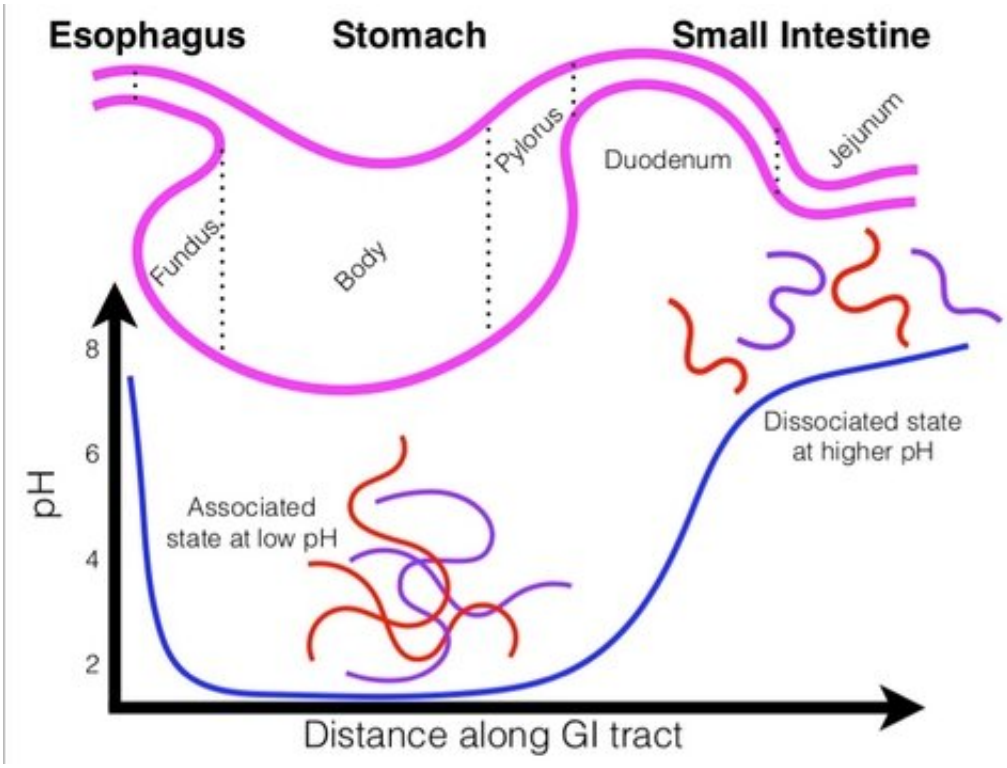
New polymer system may help revolutionize the next generation of medications

April 27 2022



Inside the acidic environment of the stomach, pZCs remain in their associated state, but disassociate as they move into the intestine. Credit: *Nature Communications* (2022). DOI: 10.1038/s41467-022-29851-y

Researchers at the University of Massachusetts Amherst recently announced that they have engineered a new class of material, called a "polyzwitterionic complex," or "pZC," which is able to both withstand the harsh acidic conditions of the stomach and then dissolve predictably

in the comparatively gentle environment of the small intestine. This property means that pZCs could help revolutionize the delivery of medicines of all sorts, from familiar oral antibiotics to new classes of delicate protein therapeutics.

"Despite the common experience of swallowing medications orally, there is a huge number of therapies that are not available orally," says Khatcher Margossian, the lead author of the study and a candidate for a dual M.D./Ph.D. from Rush Medical College and the UMass Amherst Department of Polymer Science and Engineering, respectively. This is because there are many drugs that can't withstand the stomach's harshly acidic environment. Two ways around this problem are to either inject or implant medications; but in both cases, the pain, fear and potential side effects can limit a patient's willingness to undergo treatment or to stick with the treatment plan through its full course. And even those drugs that are strong enough to withstand the stomach's acid and make it through to the small intestine, where they can be absorbed into the bloodstream, often do not make it through entirely intact.

"The doses of oral medications are usually larger than what our body really needs," explains Murugappan Muthukumar, the Wilmer D. Barrett Professor in Polymer Science and Engineering at UMass Amherst and the study's senior author. "This is because some of the medication decomposes in the stomach."

"If there were some way to protect this precious therapeutic cargo," says Margossian, "we could expand the library of medications that we can deliver orally." Figuring out how to protect the precious cargo is exactly what Margossian, Muthukumar, and their colleagues have done.

The study, recently published in *Nature Communications,* details a new class of material, called a pZC, which forms through a process known as "complex coacervation." In their system, two types of charged polymers,

a polyzwitterion and a polyelectrolyte, associate to form a protective droplet inside of which medications can travel. The trick that the pZC has to perform is that it not only needs to be tough enough to withstand the highly acidic stomach environment, it also has to disassemble in the much gentler, neutral conditions of the small intestine.

Paradoxically, the key to the group's success was not to strengthen the bonds between the polyzwitterion and polyelectrolyte but to weaken them. "Weakening the association between the two materials," says Muthukumar, "allows us to control precisely when they come apart. If the bonds are too strong, then there's no room to play."

The group's research is driven by the real-life needs of medical practitioners. Not only will these materials allow clinicians to more efficiently deliver the right dosages of drugs, but they will vastly increase the number of medications that can be taken orally. "This is a foundational technology that can alter how we treat disease," says Margossian. "We hope that our work will make its way into clinicians' hands and help them save lives."

More information: Khatcher O. Margossian et al, Coacervation in polyzwitterion-polyelectrolyte systems and their potential applications for gastrointestinal drug delivery platforms, *Nature Communications* (2022). DOI: 10.1038/s41467-022-29851-y

Provided by University of Massachusetts Amherst