Pills give patients a shot inside the stomach

Capsules that internally inject insulin and other medicines could do away with daily jabs

By Robert F. Service

In 1922, a 14-year-old boy in Toronto, Canada, received the first injection of insulin to treat life-threatening diabetes. The same year, researchers began to test oral insulin formulations, hoping to relieve people with diabetes of daily shots. That effort failed, as have dozens of similar attempts. But realistic hope for oral insulin may finally be here. Researchers report in this issue of Science that they’ve engineered a capsule that, once ingested, pokes a tiny hole in the lining of the stomach to deliver insulin or other so-called biologic medicines that can’t be taken by mouth.

Other research groups and companies have also made recent progress in delivering once-injected medicines orally, raising hopes that for many patients, painful injections may become a thing of the past. “This field is really at an exciting stage,” says Samir Mitragotri, a biomedical engineer at Harvard University. “I think it’s going to completely transform how patients take drugs.”

Optimism has surged before. But the harsh environment of the stomach and intestine has thwarted many attempts to deliver complex, delicate drugs by mouth. “There are a lot of dead bodies in this space,” says Mir Imran, CEO of Rani Therapeutics, a San Jose, California, company working to commercialize oral biologics. “People keep trying because it’s such an important area.”

Unlike traditional pharmaceuticals, which are small molecules that the digestive tract easily absorbs, biologics are typically proteins: large, unwieldy molecules produced by microbes or other living cells. Biologics, which include seven of the 10 top selling medicines, are small molecules that the digestive tract can’t wiggle their way in. Moreover, the gastrointestinal tract’s “aggressive defenses” are intended to work with existing drugs, they could spread rapidly if approved, realizing a century-old goal—and the hopes of countless patients.

In rats and pigs, the pill could deliver essentially the same insulin levels into the bloodstream as a subcutaneous injection. And histology studies showed no signs of lasting damage from daily internal needle punctures. “It’s a very smart design,” says Edith Mathiowitz, a biomedical engineer at Brown University. However, she adds, the team needs to ensure that creating even tiny perforations in the stomach doesn’t pose long-term health problems for patients, and that undesirable proteins or bacteria can’t wiggle their way in alongside the insulin.

Rani Therapeutics is banking on similar ingenuity. Instead of a spring, Rani’s pills use a chemical reaction set off by the small intestine’s pH to generate carbon dioxide that inflates a tiny balloon. The balloon presses a needle packed with the drug through the intestinal lining. Although it has not published papers on its pills, Rani has completed more than 100 animal studies. In an initial safety study of pills without needles or drugs, people reported no awareness of the device’s balloon as it inflated, Imran says. This year, he adds, the company plans its first clinical trials of pills loaded with octreotide, a biologic that treats acromegaly, a dangerous enlargement of the face, hands, and feet.

It could take years for any of these technologies to complete safety and efficacy studies. But because the engineered pills are intended to work with existing drugs, they could spread rapidly if approved, realizing a century-old goal—and the hopes of countless patients.
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