Researchers worldwide have made tremendous strides in treating and managing all types of conditions from hypertension to diabetes, but life-saving solutions still elude many patients. Dr. Henry Daniell, Professor in Penn Dental Medicine’s Department of Biochemistry, has dedicated his career to tackling the oppressively high cost of medications, a devastating global health issue that prevents billions of people from managing what should be non-threatening conditions.

“One-third of the global population earns less than two dollars a day. This massive demographic faces the greatest risk of suffering from completely preventable or treatable diseases,” Dr. Daniell says. “My life’s goal, what I’ve been working toward for 20 years, is to break down this distressing health inequity.”

His unexpected solution? Lettuce. Dr. Daniell has developed a variety of shelf-stable biopharmaceuticals—drugs that combat protein deficiencies—that can be delivered through a capsule containing freeze-dried lettuce leaves infused with one of a myriad therapeutic proteins.

PLANT-POWERED INNOVATION
Dr. Daniell uses a “gene gun” to force cells from lettuce leaves to uptake a human gene, like insulin. The plant then produces the protein associated with the gene in its leaves, which can be grown, freeze-dried, and encapsulated for oral administration, rather than being administered by injection. Seeds from these plants produce drugs forever. This revolutionary method curbs the normally high cost of drug development and delivery.

“It is unacceptable that a medication like insulin, which was invented more than 50 years ago, is unobtainable for 90 percent of the world’s diabetics,” Dr. Daniell says. “Essential treatments are currently out of reach for so many patients, but this capsule delivery method has the potential to change all of that by breaking down the staggering cost barriers.”

While the modern production process for biopharmaceuticals depends on expensive fermenters that cost between $500 and $900 million, Dr. Daniell’s plant-based method requires significantly fewer resources. One growth chamber in an FDA-approved hydroponic facility, for example, is adequate to grow enough lettuce to treat the entire hemophilia population in the United States.

A VEHICLE FOR GLOBAL CHANGE
Unlike traditional injected drugs, capsules do not require refrigeration and thus can be shipped and administered anywhere in the world at a substantially lower cost. Breaking the “cold chain” of refrigeration that often prevents essential medications
from reaching corners of the world that do not have adequate electricity, let alone clinicians to properly deliver the injection, was one of Dr. Daniell’s primary goals.

In a recent polio outbreak, for instance, improper refrigeration of vaccines allowed the virus to mutate and spread from Southeast Asia to Africa. “Capsules make vaccinations more accessible on a global scale, but they also make them safer,” says Dr. Daniell, who is presently working on a plant-based polio booster vaccine.

Another property of plant cells makes them an ideal vehicle for protein drugs, Dr. Daniell discovered: their fibrous walls are made of cellulose, which protects the encased protein from being released prematurely before reaching the digestive system. Once there, bacteria in the gut can break down these cell walls and release the drug safely into the bloodstream. So, this simple approach takes advantage of a naturally available drug-delivery concept.

This ability to delay release opens up unprecedented possibilities for the oral delivery of a wide range of biopharmaceuticals. In preclinical trials, Dr. Daniell has demonstrated the successful treatment of major metabolic and genetic disorders using this platform, including Alzheimer’s (crossing the blood-brain barrier and degrading plaques), diabetes, pulmonary hypertension, hemophilia complications, and retinopathy. He has also worked on booster vaccines that could help to prevent global outbreaks of infectious diseases like tuberculosis, malaria, cholera, and polio. Several of these drugs are rapidly advancing toward FDA approval with support from the NIH SMARTT Program (Science Moving towArds Research Translation and Therapy) as well as major pharmaceutical companies.

**TOPICAL DRUG DELIVERY USING CHEWING GUM**

Dr. Daniell is also at the forefront of another new drug delivery method: chewing gum. Dental bacteria that cause gum disease hide underneath plaque, protecting them regardless of diligent oral care. Although dental hygienists can scrape away the plaque, it is difficult to remove all of the harmful bacteria. In collaboration with fellow Penn Dental Medicine researcher Dr. Hyun Koo, Dr. Daniell determined the biological composition of plaque and developed an enzyme that is capable of softening it in order to expose bacteria. He integrated this enzyme into a chewing gum, adding in an antibiotic that destroys weakened bacteria at the source.

By swapping injections for pills and an invasive procedure for chewing gum, Dr. Daniell is building a world where medical treatment is not only more pleasant, but more equitable, affordable, and effective.

**HOPE FOR HEMOPHILIACS**

Hemophilia, a genetic blood clotting disorder that can be severe, is among the diseases in which Dr. Daniell’s work has shown promise.

Patients with hemophilia regularly receive injections of a clotting factor to prevent excessive bleeding, but 20 to 30 percent of these patients develop antibodies against it. Dr. Daniell developed a therapy, encapsulated in plant cells, that prevents the formation of these harmful antibodies and aids in their reversal. Positive results in mice and dogs led to toxicology and pharmacokinetic studies funded by the NIH SMARTT Program, and now the therapy is progressing toward FDA approval.

“The results were quite dramatic,” Dr. Daniell says. “This drug could significantly improve outcomes for hemophilia patients who currently have very few treatment options.”

**MORE INFORMATION**

For more information on how to support the research of Dr. Daniell, contact Elizabeth Ketterlinus, Senior Associate Dean for Development & Alumni Relations, ekett@upenn.edu, 215-898-3328.