How a Novel Polymer Can Bring Long-Acting Therapeutics to Patients

Stephanie Reed, PhD, is the Director of Translational Product Development at Secant Group, a textiles and biomaterials company. At Secant Group, Dr Reed leads a team of scientists whose goal is to launch new biomaterial polymers for commercial use in controlled release drug products, biomedical devices, and tissue engineering applications.

What is Hydralese?

Secant Group has been developing Hydralese as a new biomaterial platform for a few different applications, but most notably controlled delivery of active pharmaceuticals. We also have partnerships in the medical device space.

Secant has been developing a new polymer called poly(glycerol sebacate) (PGS). It originally was pioneered for tissue engineering and regenerative medicine at the Langer lab at MIT by Dr Yadong Wang. We've built upon that foundational research and brought it in-house, developing our own IP-protected commercial process for synthesizing this polymer. We've really optimized it and honed it specifically for controlled release and medical device applications.

We have a particular crosslinking chemistry that we apply to PGS, and we make this polymer PGS urethane (PGSU), which is our Hydralese platform. We are looking to bring it to the market as a new alternative that goes above and beyond the existing polymers that are currently serving the pharmaceutical industry.

What is new or novel about this polymer?

This polymer has kind of a unique blend of properties. It's a soft and flexible elastomer, but it's also biodegradable. And there is no polymer that's currently commercially available that has these two properties combined. That in itself is very unique. But on top of it, it's also a very biocompatible polymer. Because PGS is heavily researched in the tissue engineering field, PGSU has pro-healing, anti-inflammatory, anti-microbial, anti-adhesive, and hemocompatible properties when you use it inside the body, such as in an implantable or injectable form.

When Hydralese degrades through contact with water, it biodegrades back into starting components – glycerol and sebacate – that can be metabolized by cells and actually feed the cells as nutrients. But it also is very bio-inert, so you don't have chronic inflammation or fibrous encapsulation, or other issues that the other polymers on the market may cause.

The most commonly used biodegradable polymers can produce a very acidic local micro environment in the tissue, which poses challenges. Non-degradable polymers require removal at the end of drug treatment, so you can't use them for injectable microsphere suspensions, because you can't retrieve those microspheres back after distribution within the tissue.

The way that our polymer degrades is through erosion, like an ice cube. The outer layers are slowly getting sloughed off, getting smaller and smaller over time.

That's how we can achieve linear, zero-order controlled release of various drugs. And so because we rely on erosion rather than diffusion of the drug out of the polymer matrix, we can deliver very hydrophilic and hydrophobic payloads. That contributes to the versatility.

What does zero-order controlled release mean for delivery or patient experience?

With the release kinetics that we can achieve using Hydralese, the benefits are very multifaceted. First of all, you get a very low burst release immediately upon implantation or introduction into the body. That's huge, because a lot of other polymers release a substantial portion of their payload just over the first few days, especially at high loadings.

That can be problematic, especially if you have a drug that has a very narrow therapeutic window. You don't want excessively high concentrations because the drug could be toxic or could have side effects. You also don't want sub-therapeutic concentrations, because then you're not actually delivering an effective dose to the patient.

So, starting with a very low amount of burst release, and then following it with a very reliable daily release rate is incredibly important. We can sustain this linearity at very high drug loadings, which is unprecedented across biodegradable and non-degradable polymers alike.

Historically, long-acting implants or injectables had to be formulated with highly potent APIs, because you could only load maybe 10-20% drug by weight into your dosage form. But now that we can load 50, 60, even up to 80% drug by weight into the Hydralese polymer, you can pack in a lot more payload and realize more efficient delivery.

That opens up numerous opportunities: we work on HIV prevention and dual delivery alongside contraceptives; we target many different neurological diseases as well; oncology is an area with very specific needs; animal health is a field that would benefit from better options. We do a lot of work in ophthalmology as well, where smaller dimensions and longer-lasting treatments mean an enormous quality of life improvement for patients. With Hydralese you can less frequently inject or implant in the eye while delivering a large amount of payload into a very small footprint.

We can formulate Hydralese with those high payloads and still sustain release for six months or 12 months of therapeutic delivery. So, it unlocks the market from what was before limited to highly potent APIs to now the entire space of all APIs. With our platform, it really broadens the portfolio of APIs that can be delivered and accordingly diseases that can be treated.

What does this potential technology mean for patients?

Everything that we do at Secant Group is very patient-centric. And what we really want to emphasize with Hydralese, specifically in the pharmaceutical world for things like controlled release, is that when you have a biodegradable implant, injectable, or oral formulation, you don't have to be concerned about safety. So, from the patient's perspective, they're not going to have long-term complications, they're going to have convenience, they're going to have options, and they're going to have control. From a clinician's perspective, long-acting formulations improve adherence to medication, reduce health care costs, and improve overall global wellness.

Patients also don't have to go back to the clinic to get their implant removed at the end of treatment. And this is particularly impactful, especially when you look at low- and middle-income countries. If you're going to dose a contraceptive or an HIV prophylactic implant, it's a huge logistical and societal challenge to even complete the initial appointment. Often, people in these countries don't have access to clinics, they don't have access to their physician on a regular basis, and there can be social stigma associated. It may be prohibitively burdensome for them to even make that trip. For the patient, using a bioerodible implant, which can still be retrieved in the event of an adverse drug reaction, it's one less thing they have to worry about. It's empowerment; it's safety; it's access.

What does the collaboration process look like for your work?

This is our company's biomaterial platform, and we have strong intellectual property protection around our platform, but we are not looking to commercialize on our own.

We are instead really seeking, establishing and fostering good partnerships and collaborations with others who are experts in their respective fields. We work with industry and academic partners who develop the drug, design the medical device, or vet the end-use application. What we bring to the table is this polymer platform, which is novel and very versatile. Using Hydralese offers our partners competitive advantage and opportunities for patent lifecycle extension.

Typically, we start out with some initial feasibility studies. Usually someone will approach us with some requirements in mind: maybe they have a target product profile that they're seeking, and they'll send us their drug of interest. Then we do formulation and characterization and fabricate dosage forms of different shapes.

We have years of experience manufacturing implants, microspheres, gastro-retention devices, coatings, thin films, and fibers. We make all of these prototypes in-house, and then we test and analyze them very thoroughly. We provide this data package back to our collaborators along with hundreds of samples for them to further evaluate internally on their own.

We frequently will start at the bench level performing in-vitro characterization. And then we move into in-vivo evaluation, such as small animal studies or large animal studies. All of this is with the intention of gathering datasets that become increasingly complex, translatable, and convincing as we progress. We aim to show promise at every step of the way, and we work with our customers to move through tech transfer and scale up towards first time in humans and through clinical trials, and ultimately through commercial launch.

Where do you see Hydralese making the biggest impact?

There are three main controlled release therapy areas that we're really focused on. One of them is HIV and infectious diseases, one is ophthalmology, and the last is central nervous system disorders. On the medical device side, cardiovascular products play a key role in our textile business and represent a chance to leverage our expertise, in the form of standalone, composite, or combination devices.

These are the areas where we're really making significant strides and where we feel Hydralese has the opportunity to revolutionize the standard of care, and we're moving very quickly with some different partners in these spaces. It's quite an exciting journey to lead – whether it's implants, coatings, microspheres, or gastric retention – we're working diligently to make our Hydralese vision a reality and soon bring better solutions for patients. ◆

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