Chemistry

Stefi Weisburd reports from New Orleans at the 194th national meeting of the American Chemical Society

Medicating through the nose

Scientists are producing a cornucopia of new peptides and proteins for treating ailments ranging from hypertension to diabetes. But for many of those who might reap the benefits, this biotechnology has been a hard pill to swallow. If the drugs are taken orally, they are decomposed by the digestive system before they can do much good. While injections are an option, scientists are searching for more palatable means of getting drugs into the body.

Researchers at California Biotechnology Inc. in Mountain View, Calif., are looking into the nasal membrane, a cell-layer-thick wall sitting next to a rich blood supply, as an alternative entry route for the new biotech products. According to William Lee, a nasal spray system for delivering insulin has passed the first part of clinical trials, and in animal studies the company has recently succeeded in getting human growth hormone (used for treating pituitary dwarfism) through the nasal cavity.

Insulin, growth hormone and other peptides and proteins are very large molecules which by themselves would not permeate the membrane. So Lee and his colleagues coat the hormone molecules with a small, detergent-like molecule that's a synthetic derivative of a compound produced by fungi. This "not only helps solubilize the drug and stabilize it in solution, but it increases the permeability of the nasal membrane to the drug," says Lee. "Our best guess at the moment is that the penetration enhancer [temporarily] loosens the binding of proteins between cells," letting the hormone slip past.

According to Vincent H.L. Lee at the University of Southern California in Los Angeles, researchers are investigating many natural and synthetic enhancers for getting other drugs, vitamins and contraceptives across vaginal, rectal and other areas and through the eye as well as through the nose. How the enhancers do their jobs is being actively studied at the moment, he says. In addition to weakening the binding of membrane cells, some enhancers appear to change the shape of enzymes – which normally prevent drugs from getting into the bloodstream – so that they cannot recognize the drug proteins.

A predator plant's chemical radar

One of the world's most devastating grain-crop parasites is *Striga asiatica*, a red-flowered plant that siphons nutrients from the roots of corn, sorghum and other plants. It is the second leading cause of cereal famine in Africa. In hopes of learning how to discourage the parasite, David Lynn, Gwendolyn Fate and Christopher Smith at the University of Chicago have unearthed a chemical system that enables *Striga* to seek out and attack its hosts.

Biologists have known that *Striga* seeds will germinate only if they are within 5 millimeters of a sorghum root. How does the seed "know" when it's at the proper distance? Lynn's group isolated a hydroquinone compound that is exuded by the sorghum root and that makes *Striga* seeds germinate. This compound reacts with oxygen to form a another quinone, which does not induce *Striga* germination. The researchers believe that the rate at which hydroquinones diffuse into the soil away from the sorghum root, along with the rate at which the oxygen-hydroquinone reaction takes place, defines a specific zone – around 5 mm from the sorghum root – that contains sufficient hydroquinone levels to germinate *Striga*.

Lynn's group also discovered that the newly germinated seedling roots use a kind of chemical radar to determine when they should launch their balloon-like haustoria, the specialized organs that attach to the host root. The researchers report that a *Striga* root tip releases an enzyme that they think diffuses through the soil and reacts with a sorghum root to form another quinone compound, which in turn diffuses back toward the *Striga* root, where it triggers haustoria formation.

Loosening bacteria's hold on implants

Polymers make it possible for physicians to replace a blocked artery, give a patient a new hip joint or deliver long-term intravenous therapies through catheters. However, the use of these synthetic implants is undermined by *Staphylococcus* bacteria, which are able to infect nearly all polymers, often necessitating their removal from the body. "Infection of medical devices and implants has become a major problem in prosthetic medicine," says Bernd Jansen of the University of Cologne in West Germany

Because adhesion of bacteria to polymers is thought to be the first step in infection, Jansen and his colleagues are exploring ways to discourage bacteria from settling on polymers – a process that is governed by electrostatic and other forces and also by poorly understood interactions between bacterial proteins and other proteins on the polymer. They have preliminary evidence that bacterial adhesion can be reduced if the blood protein albumin coats a polymer. And they have found that they can attract albumin rather than other proteins by modifying the polymer's surface properties. They also have some indication that surface modifications by themselves reduce bacterial adhesion.

Jansen's group is also developing ways to coat polymers with antibiotics and to incorporate antibiotics into the implants. Jansen says that by changing the polymer surface, they can extend the time an antibiotic coat clings to a polymer surface from 10 minutes to one day. Implants embedded with antibiotics continue to release them for more than five days.

Jansen says there is a close relationship between infection and blood clotting, the other major problem of synthetic vascular grafts, since bacteria can stick to clots and clot cells stick to infected surfaces. He says some of the surface techniques he is now using to combat infection were originally developed by him to prevent blood clotting.

A bizarre bezoar tale

Bezoars, or stomach stones, are clumps of fruit and vegetable matter, drugs, hair, carpet fibers or other substances that can accumulate in the gastrointestinal tract. Animal bezoars were once treasured for their supposed medicinal properties, and it is said that a gold-framed specimen was included in the 1622 inventory of Queen Elizabeth I's crown jewels.

While modern society has dropped the bezoar fad, it has contributed to the phenomenon in a unique way. Surgeons at the University of Missouri in Kansas City recently removed a 7-centimeter-long, tan, egg-shaped bezoar from the stomach of a 35-year-old man who admitted to nibbling and swallowing pieces of polystyrene (Styrofoam) cups.

This case of "polystyrenomania" is apparently a medical first, but it also presents something of a chemical mystery: How did the polystyrene foam get transformed into the hard, glassy state of the bezoar? When University of Missouri chemist Eckard W. Hellmuth soaked polystyrene foam in stomach acids, nothing much happened.

Hellmuth suspects that butter fats, in combination with the great pressures exerted by the stomach muscles, loosen the bonds between polystyrene molecules and gradually reorient them into a glass. This is a physical process, he says, which changes the material's surface area in much the same way soap bubbles are transformed into a liquid without undergoing significant changes in density. His hypothesis, which he plans to test soon in the laboratory, is based on work by others showing that dairy products can reduce the amount of stress needed to initiate small cracks in polystyrene containers.