Chemistry

Elizabeth Pennisi reports from Atlanta at a meeting of the American Chemical Society

Chemical disguises improve peptide drug

Some promising medications, if taken by mouth, get stopped by digestive juices or liver enzymes before they ever have a chance to do their work. Pharmacologists have now disguised one such drug, called a renin inhibitor, so that it can sneak into the bloodstream and pass through the liver intact.

Renin inhibitors block the production of a substance called angiotensin II, which can raise blood pressure. Clinical studies have shown that injections of renin inhibitors can lower high blood pressure, and recent findings suggest that high levels of renin may increase heart attack risk in people with moderate hypertension (SN: 4/20/91, p.245).

But daily injections are impractical as a routine treatment regimen, so researchers at Abbott Laboratories in North Chicago set out to develop an effective oral alternative. They now report successfully camouflaging renin inhibitors in two ways and testing several compounds using each strategy.

Standard renin inhibitors consist of peptides — amino acid chains linked by amide bonds, which are particularly vulnerable to disruption by enzymes. In one approach, the Abbott team made a "nonpeptide" that acts as a renin inhibitor but escapes recognition by peptide-degrading enzymes. "There are no naturally occurring amino acids as part of the structure," Abbott pharmacologist Hollis Kleinert says. "It's something that I think will be very useful for all sorts of medications."

In a second approach, the researchers made "dipeptides" — two amino acids linked by an amide bond — but they modified the bond so that enzymes wouldn't recognize it.

They then gave oral doses of these compounds to rats and tracked the drugs' survival in the body. About 20 percent of the renin inhibitor remained in active form after passing through the liver, they found. This "oral bioavailability" is double the amount considered necessary for the drug to work, Kleinert says, and four times greater than that achieved with oral administration of the standard form of the peptide.

Molecular octopi learn sticky tricks

Organic chemist Steven L. Regen has made a molecular octopus — sporting long arms lined with suckers that grab onto "prey" — and now he wants to train it to work for him. The body consists of six benzene rings that join to form a cylinder. The arms are polyether side chains, and the suckers are oxygen atoms that can bind to other substances.

When Regen and his colleagues at Lehigh University in Bethlehem, Pa., placed a layer of these molecules on water, the tiny octopi floated with their arms outspread. Knowing that side chains can sometimes be made to stick into water, the researchers then compressed this layer. As they shoved the molecules together, they discovered they could indeed force the octopi to tuck their arms temporarily under their bodies.

"We think of this as the octopus treading water at the air-water interface," says Regen.

He envisions "training" the octopi to separate ions from solutions. The sinking arms would encircle and latch onto the ions, so that octopi removed from the solution would bring the ions out with them. But first, Regen says, he needs to redesign his octopi to give their suckers enough strength to hold the ions securely as he moves them from one solution to another.

Spider toxins may take bite out of strokes

Think twice before squashing a spider. That eight-legged arachnid may one day save your life, or at least minimize damage caused by a stroke.

Many common spiders produce venom toxins that could inspire new treatments for stroke victims, says neurobiologist Hunter Jackson, president of Natural Product Sciences, Inc., in Salt Lake City. These poisons, which the spiders use to paralyze prey, inhibit the functioning of glutamate, a chemical that controls muscle movement in insects. In the human brain, glutamate serves as an important messenger, but it can also kill the brain's nerve cells under stress, exacerbating the damage done by a stroke. Consequently, researchers have sought to develop drugs that block its action.

With that goal in mind, Jackson searched the venoms of hundreds of common spider species. This painstaking task involved collecting, rearing and milking the creatures. It took about 10,000 milkings to get enough venom for experiments, he says, and each sample held dozens of toxins — including several arylamines, which attach to a cell's glutamate receptors, thus blocking glutamate's action. "It's really a gold mine of novel chemistries," he told SCIENCE NEWS.

Other types of glutamate blockers tend to cause serious side effects, but Jackson says at least 20 of those isolated from spider venoms show early promise in animal tests.

Enhancing that fresh-squeezed flavor

Processed orange juice might taste better now that chemists have deciphered Mother Nature's secret recipe for fresh flavor. Philip E. Shaw, a flavor chemist at the USDA's Citrus and Subtropical Products Laboratory in Winter Haven, Fla., used gas chromatography analysis to generate a profile of the gases that escape from juice and impart its fruity aroma. "The more this profile looks like the profile for fresh juice, the closer in taste [a concentrate will be] to fresh juice," says Shaw, who tested both fresh and processed juices.

To identify the right mixture, Shaw sampled the trace amounts of volatile gases that build up in the air space inside a container of orange juice. At first, he detected only 20 volatile substances; now he sees at least 40. "They were always there and your nose was picking them up, but our instruments weren't," he says. A recently developed technique enabled him to sweep these gases out of the air space, then cool and concentrate them prior to analysis.

The analyses offer juice manufacturers an indication of the flavors they need to add back after processing. "Each time we come up with a new technique for analyzing [the flavor], we're much better off," says Robert L. Wade, an analytical chemist at Procter & Gamble Research Laboratories in Cincinnati.

Swell idea for a chemical sensor

Many scientists want to perfect miniature chemical sensors to detect small quantities of drugs, pollutants, oxygen or other substances in the environment or the body. Yet after a decade's work, few such devices have reached the marketplace. Now, two chemists have patented their ideas for what they call a cheap technology with many applications. The secret of their device: a swellable polymer, says Marian F. McCurley of the National Institute of Standards and Technology in Gaithersburg, Md.

The new sensor contains two optical fibers, one to carry light down to the sensing tip and the other to carry the reflected light back out. The sensing tip consists of a polymer lens specially made to react to the substance being monitored. A reflective film coats one side of this lens.

When the polymer detects its target chemical, its cross-linkages change. Depending on the particular chemistry between the two materials, the polymer either expands to let water in or shrinks. As the lens changes shape, it pushes the reflective film closer to or farther from the optical fibers, thereby changing the amount of reflected light.

Unlike most biosensors, this one isolates the light from the chemical components, and that means the system should last longer, says Kenneth D. Legg, president of Polysense, Inc., in Wellesley, Mass., which plans to develop the technology.