

he says. And his consumer retail background makes him acutely alert to the needs of the public. He supports the creation by his predecessor, John Battle, of a new panel to coordinate public consultation on developments in the biosciences, as providing a model for involving the public in science policy-making. "Public confidence in some areas of policy has become quite low," he says.

But the government's changes in the administration of science have not satisfied everyone. Oxford University neurobiologist Colin Blakemore, president of the British Association for the Advancement of Science, told the group's annual science festival last week that he thought the OST is inappropriately located within the DTI. "It makes sense to place science in its own department with

a minister at Cabinet level," he says. Sainsbury rejects such a move: He told a press conference at the meeting that merely making the OST independent would make little difference to the administration of science, while taking research away from other departments into a single ministry would "create a worse set of problems than the one you are trying to cure." —NIGEL WILLIAMS

BIOCHEMISTRY

A Sweet Way to Keep Proteins Safe

A strategy used by plants and insects to wrap proteins in a protective sugar cocoon is poised to move from lab bench to marketplace

To Carl Leopold, the secret to life is rock candy. In 1987 the plant physiologist at the Boyce Thompson Institute in Ithaca, New York, set out to probe how corn seeds can survive dry storage for as much as half a century, then, after being sprinkled with water, revive suddenly and send up shoots. Leopold found that a dried seed's delicate enzymes and membranes are protected by a kind of glass armor—hardened sugars that melt in water, releasing the seed's protein machinery to crank up the process of germination.

Now, drug developers are wielding these same glassy shields to protect fragile protein drugs from the harsh world until they are absorbed by the bloodstream. Inhale Therapeutic Systems, a biotech company in San Carlos, California, has licensed the approach and begun clinical tests of an inhalable insulin encapsulated in sugar. The company is now exploring the same strategy for other therapeutic proteins, from calcitonin for osteoporosis to α -1-antitrypsin for emphysema. And other researchers hope to develop sugar-encased drugs and nutritional supplements for countries that have scant means for refrigerating and transporting fragile proteins. Leopold says he's amazed at how this basic plant survival mechanism, called vitrification, is blossoming into a practical tool. Adds John Baust, director of the Center for Cryobiological Research at the State University of New York, Binghamton, "We're going to see more applications of vitrification emerge in the coming years."

When Leopold struck out on his sugar-coated path, he says, his team members "certainly weren't thinking of drug delivery systems at all." After finding that corn's glass is made from sucrose and raffinose in a 3:1 ratio, Leopold's group set out to reproduce the sugar shield in the test tube. The researchers dissolved the sugars and mixed them with the enzymes isocitrate dehydrogenase, glucose-6-dehydrogenase, or luciferase, all of which are easily damaged when dried. They used a

vacuum pump to dry the solutions and put the residue on a shelf. When liberated from the sugars several weeks later, the enzymes worked fine. The vitrified sugars, the researchers found, protect proteins from denaturation—much like insects stuck in tree sap can be preserved for millions of years if the sap hardens to amber.

Leopold wasn't the only researcher to discover this life-preserving mechanism. In the late 1980s, Felix Franks, a physical chemist and water expert at the University of Cambridge in England, found that certain insects also tolerate freezing by forming glassy sugars. When temperatures drop be-



Rock solid. Corn seeds are protected by glassy sugars akin to rock candy.

low about -20 degrees Celsius, insects such as *Eurosta solidaginis* and *Epiblema scudderiana*—bugs that trigger tumor formation in plants—convert their reserves of glycogen, a glucose polymer, into an array of simple sugars and sugar-based alcohols. The sugars then vitrify, preventing bodily fluids from forming damaging ice crystals. In spring, the glass melts, vital proteins regain activity, and the insects revive.

Unknown to each other, Leopold and Franks applied for U.S. patents on their glass-stabilization methods in the early 1990s. "It's fascinating that two scientists came to fairly simultaneous inventions from

totally different backgrounds," says Stephen Hurst, Inhale Therapeutic's vice president of licensing and intellectual property.

Inhale is now developing the idea into an inhalable insulin, a product that has eluded scientists for decades. Researchers coat insulin with sugars, then shoot the mixture through nozzles that disperse it into particles, less than 3 micrometers in diameter, that dry immediately. In the lungs, the tiny spheres dissolve and are absorbed. In a clinical trial completed last June, 60 diabetics on inhaled insulin for 3 months maintained blood sugar levels as stable as those of diabetics on injected insulin. Inhale plans to launch a larger trial in November before seeking federal approval to market the insulin.

The approach does have drawbacks: For instance, the inhalable insulin is effective for only a few hours at a time, so most patients would need a nightly injection to control insulin levels while they sleep. Still, many needle-shy patients "would be better off if they could get more insulin," says diabetes specialist Carl Grunfeld of the University of California, San Francisco. They might benefit from the inhalable version, he adds. Inhale's other inhalable drugs are further up the pipeline.

Animal-feed supplements could also benefit from sugar-coating. Leopold and Cornell University animal nutritionist Xingen Lei are trying to improve commercial corn and soybean pellets by spiking them with a sugar-encapsulated enzyme called phytase. The enzyme should enable livestock to exploit more of the phosphorus in the pellets because it breaks down phytic acid, which is attached to much of the phosphorus and limits the element's absorption.

Such work could have "tremendous application" to people too, Lei says, because phytic acid contributes to malnutrition by locking up calcium, zinc, and iron in grains that are staples in many developing countries. Says Cornell nutritionist Gerry Combs, who studies mineral deficiencies in Bangladesh, "It would be a wonderful thing if we had an economical, heat-stable phytase supplement made available to all people in the developing world." A little sugar, it seems, is the best way to make the nutrients go down.

—CAROL POTERA

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CARL LEOPOLD