Diabetes treatments get sweet help from nature

Mexican shamans have a wealth of experience in treating 'sweet blood', a disease that affects the indigenous population in the highlands of Mexico at record rates. Their wisdom is now helping researchers develop diabetes drugs from natural remedies.

According to a new report released at the Eighteenth World Congress of the International Diabetes Federation in Paris, 194 million people worldwide are diabetic. The numbers are expected to rise to 333 million by 2025. The prevalence of diabetes is particularly high among some native communities.

Nearly one in three Native Americans aged 55 or older has diabetes, according to new data from the US Centers for Disease Control and Prevention. The data also indicate that the prevalence of type 2 diabetes among native communities is growing faster than in the overall US population.

The prevalence of type 2 diabetes has traditionally been high in the highlands of Mexico. Helmut Wiedenfeld, a pharmacologist at the University of Bonn, and his colleagues investigated the plant extracts shamans give their diabetic patients.

"We have now finished the phytochemical analysis of four plants, and we know their active ingredients," says Wiedenfeld. The researchers presented the latest findings—the discovery of new pyron-glycosides derived from the plant *Acosmium panamense*—in early September at the annual meeting of the Society for Medicinal Plant Research in Kiel, Germany.

Preliminary experiments in rat models of diabetes confirm that the plant extracts, as well as mixtures of their active ingredients, have a hypoglycemic effect. Small clinical trials are now under way in Mexico City. Wiedenfeld is also trying to get a pharmaceutical company to develop herbal prescription drugs for type 2 diabetes.

Because the studies are preliminary, cautions Edmond Ryan at the University of Alberta in Canada, it is too early to predict the fate of these treatment candidates. "I think there are a lot of good chemicals out there in nature that will be beneficial," Ryan says. "But proving that they are beneficial in good clinical trials is the most critical thing."

A second, more promising, approach is based on Western medicine and uses a compound from the saliva and venom of the lizard *Heloderma suspectum*, which lives in the Gila river valley in Arizona. The valley is home to Pima Indians, who have the highest prevalence of diabetes in the world.

Courtesy of Helmut Wiedenfeld

Some new diabetes treatments are being derived from plants in the Mexican highlands.

When the Gila monster lizard bites down on its prey, it secretes the chemical exendin-4, which is homologous to, and acts like human glucagon-like peptide-1 (GLP-1). Exendin-4 increases insulin secretion in a glucose-dependent fashion, which means that the risk for hypoglycemia is low. "It is like a self-regulated smart drug," says Alain Baron, senior vice-president of clinical research at Amylin Pharmaceuticals, which is developing the drug.

The compound has many other properties that make it attractive for the treatment of diabetes. For example, new research suggests that it may be capable of correcting the β-cell deficit in diabetes. But unlike its cousin, GLP-1, exendin-4 has a long half-life and is therefore about 100 to 1,000 times more potent.

Exendin-4 is currently being tested in three randomized, placebo-controlled phase 3 trials in type 2 diabetes patients who are taking metformin, a sulfonylurea, or both, but are not achieving glucose control. Results are expected later this year. At the Paris meeting, Baron presented preliminary results suggesting that after 24 weeks of treatment, 44% of patients achieved glucose levels that were within the American Diabetes Association's target range.

"These human results are very encouraging," says Timothy Kieffer at the University of British Columbia in Canada. "They continue to support the notion that so-called GLP-1 mimetics will offer patients with diabetes fantastic new treatment options."

The company aims to gain approval from the US Food and Drug Administration by 2005, but questions remain. For example, nausea may lower treatment compliance. It is also intriguing that lizard venom would treat diabetes, notes Kieffer. "One wonders what the function of this peptide is in the Gila monster venom," he says. "Clearly its bite is not designed to treat diabetes."

Martina Habeck, London

Canada considering a 'CDC North'

A new national public health center might be in Canada's future, says Federal Health Minister Anne McLellan. The center, which would be similar to the US Centers for Disease Control and Prevention, would be "a nerve center of expertise and research," McLellan announced in her 18 August speech at the Canadian Medical Association's annual meeting.

Canada's health-care system was left reeling after the epidemic of severe acute respiratory syndrome (SARS) there earlier this year. It became obvious then that Canada lacks expertise in dealing with public health crises, says Alison McGeer, a leading SARS researcher and director of infection control at Mount Sinai Hospital in Toronto. "What we most missed was a team to collect and analyze data more quickly as the outbreak was going on," McGeer says. In the case of another outbreak, the proposed national agency would coordinate epidemiology, laboratory investigation and public health experts across the country.

The center is just one part of a pledge by Canada's federal, provincial and territorial health ministers to make public health their top priority. The ministers are also working to increase public health human resources, form a national health council to monitor health-care reform and spending, enhance existing national disease surveillance and information infrastructure and make the case for an additional C$2 billion for health care.

The details of the center's structure and location are still being worked out by health ministers. But it won't come cheap—costs for the multisite agency are estimated to approach C$1 billion. "Getting money for public health is always a problem," says McGeer. "[But] I hope we've learned enough from SARS in Canada that we'll spend the money."

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