

A Candy That's Good for Your Teeth? Researchers at UCLA Say Yes!

Imagine going to your dentist and, along with the toothbrush and dental floss you receive at the end of your teeth cleaning, you're handed a lollipop. And then you are told that sucking on this candy will help prevent tooth decay, not cause it. In response to your quizzical look, the dentist replies, "that's right, it's a 'candy' that's good for your teeth!" This could be happening soon thanks to research performed at the UCLA School of Dentistry under a UC Discovery Grant.

Dr. Wenyuan Shi, partnering with C3 Jian, a research company, has determined that an extract of licorice root (*Glycyrrhiza uralensis*) targets and kills the primary bacteria (*Streptococcus mutans* or *S. mutans*) responsible for tooth decay, which scientists call dental caries. And, importantly, it does it without killing all of the hundreds of other bacteria in your mouth that are helpful, not harmful, to your oral health. In fact, Shi has determined that dental plaque per se is not bad for your teeth, as long as the decay-causing bacteria are not present in it. He found that plaque can actually act as protection from the re-colonization of the bad bacteria.

The results were first reported in February 2006 in the *Journal of Natural Products* published monthly by the American Chemical Society and the American Society of Pharmacognosy. Shi says his study provides a scientific basis for a practice – chewing licorice root – that has been a common in Chinese and other cultures for thousands of years.

The U.S. Surgeon General has identified two major diseases of the mouth – tooth decay and periodontal disease. Both are caused by bacteria that are killed by the licorice root extract. According to Health Care Financing Administration estimates, in 1998, \$53.8 billion was spent for dental services in the U.S., representing 4.5% of total health care expenditures. Spending on dentistry in 2006 is expected to be about \$80 billion, of which 45 percent will be spent on the treatment of cavities and tooth decay.

Shi, a microbiologist by training who did post doctoral work at UC Berkeley and is now Chairman of the Oral Biology Department at the UCLA School of Dentistry, was interested in developing a new therapeutic approach to dentistry, which traditionally focuses on plaque removal and hygiene. He was keenly aware of the challenge ahead -- new pharmaceutical drugs often require tens of millions of dollars for research and many years of clinical trials before they reach the market.

Shi, who calls dentistry "an amazing playground for microbiologists," therefore decided to pursue a different approach. He started looking at Chinese herbal medicines. He says, "After 3,000 years of empirical clinical trials these herbs have generally been shown to be safe." His hope was that these herbs could potentially lead to something safe, effective, easy to develop and inexpensive to produce that, as a non-pharmaceutical, could be brought to market faster. (Nutritional supplements -- so-called "nutriceuticals" -

- do not require the same FDA approval as new drugs.) Shi was also hoping that a less expensive herbal medicine would more greatly benefit underserved populations.

Delta Dental Insurance, the original grant sponsor, was very interested in the project – an herbal medicine that could reduce tooth decay obviously had the potential to reduce dental insurance claims costs.

Shi collaborated on the project with various colleges and hospitals of Traditional Chinese Medicine in China. Over the years more than 5,000 Chinese herbs have been used to create and refine more than 100,000 formulas to fight various types of infections, illnesses and diseases. Using the clinical files from China, Shi began by using statistical analysis to determine the top 400 most commonly prescribed and effective herbs and then tested each using the latest anti-cavity biological assays developed at UCLA to see which, if any, had anti-microbial effectiveness, or efficacy, against *S. mutans*.

Shi says that normally when randomly testing the effectiveness of compounds in a chemical library, a researcher might have a hit rate of less than 1 in 1,000 or even 1 in 10,000. His study achieved a remarkable 10 – 15% hit rate in finding efficacy. The screening led him to licorice root extract as one of the most effective of the herbs tested. “This was particularly charming because in both Chinese and in Western cultures, people have been chewing it maybe for the taste, but it also has a lot of good health reasons. It stimulates saliva flows, has anti-bacterial properties and keeps bacteria from adhering to your teeth.”

Shi eventually looked at more than 800 herbs and has now established an herbal library that is useful to researchers studying a host of other diseases. He has already given samples of the licorice extract to other groups at UCLA that are studying the immune system, cancer and aging. Shi eventually discovered a number of other antimicrobial herbs. When combined into a mixture with the laboratory name of F101, three of these herbal extracts have great bioactivity against oral pathogens which he says is strong, fast and effective at selectively killing oral pathogens including *S. mutans* and others.

Another specific herbal formula will first be commercialized in the form of the sugar-free lollipop. Dr. Maxwell Anderson, President of C3 Jian and a dentist himself, is working with a candy manufacturer to produce the lollipops and says, “We’ve turned an old fashioned candy into a high technology delivery device.”

The lollipop makes an ideal delivery vehicle for the extract, he says, because it can be used with patients of all ages and can’t be choked on or swallowed too quickly. The latter is important because it has the pharmaceutical property of “substantivity.” This means it keeps the active ingredients in contact with the organisms in your mouth long enough for them to work. Anderson says, “As the lollipop dissolves in your saliva, we end up with the right concentration of the herbs to kill the cavity causing bacteria in the oral cavity.”

Anderson notes that the new herbal lollipop may have additional uses; the same bacterial genus, streptococci, also causes strep throat and the licorice root extract is effective against *Helicobacter*, the bacteria scientists have shown are associated with stomach ulcers. As the saliva that dissolves the lollipop is swallowed, of course, it passes through the throat and stomach as well.

Anderson says the collaboration with UC has enabled the testing of a much greater number of herbs than his company could have achieved on its own without the UC-developed high throughput screening assay.

Shi warns that not all licorice or licorice-flavored candies work against tooth decay. Many do not have the required chemical extract and have a lot of refined sugar that, of course, is bad for your teeth not good for them.

Through this study, Shi says, UCLA's dental school has become one of the leading promoters of minimally invasive dentistry. As a result of his work on this grant, Shi has been invited to lecture all over the country and the world and is working with health organizations including the California Department of Health Services and the U.S. Indian Health Service.

He says his dream for dentistry in the future is that a patient goes to the dentist, gets a saliva test to determine if the risk of disease is present. If at risk, they receive an appropriate prescription drug yet to be developed, and the problem is cured without any form of surgical intervention. Through early detection, risk assessment and preventive measures, someday babies may never suffer from tooth decay, Shi says. And that would be "candy" for everyone!

As for the near term, C3 Jian is working with a candy manufacturer on the lollipop and other products that will eventually be available through your dentist as samples and at retail outlets.

The UC Discovery Grant-funded research has profoundly affected the careers of two of the post-doctoral students who worked on the project. One is now working with an industry company (not C3 Jian) on developing the technology for the consumer market. The other went back to China to become a professor at one of the country's traditional medicine schools.