All you need is sound

Applications for acoustic resonance spectroscopy range from identifying chemical weapons to testing pharmaceutical tablets.

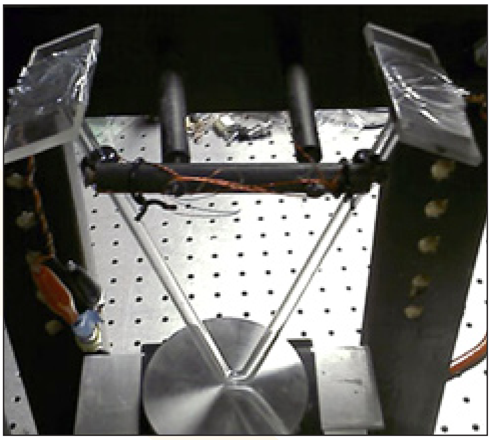
As consumers, how do we know that the medicines we buy really contain the ingredients we think they do? Most of the time, we rely on the packaging of the medicine and the reputation of the store or pharmacy where we purchased it. As an extra measure of protection, the pharmaceutical companies must test a few tablets from each batch to ensure that the products are labeled properly. If just one tablet is mislabeled, the U.S. Food and Drug Administration makes the company recall the entire quantity, and the company can lose millions of dollars.

HPLC is the most common analytical method used to identify drugs. However, with this technique, the tablet must be either ground or dissolved and the components extracted. "It is not unusual for an HPLC assay to run 10–20 minutes per tablet," says Robert A. Lodder of the University of Kentucky Medical Center.

Last year, Lodder described a method that he says could perform the same analysis in just seconds per tablet. His technique is a variant of acoustic resonance spectroscopy (ARS) (*AAPS PharmSciTech* **2006**, *7*, Article 59). The approach works with inexpensive, off-the-shelf components, such as an MP3 player and headphones, to quickly and accurately differentiate among pharmaceutical tablets of different sizes and shapes.

A military origin

Dipen Sinha of the Los Alamos National Laboratory developed ARS in 1989. He combined an old-style swept-frequency analyzer with two piezoelectric transducers. One transducer acted as the transmitter and the other as the receiver. As the transmitter vibrated the object to be examined, the receiver recorded the resonant vibrations and a frequency spectrum. Within minutes—or even seconds—a spectrum analyzer compared the frequency peaks with a library of known acoustic spectra and identified them with the aid of a laptop computer.


COURTESY OF ROBERT A. LODDER

In the ARS tablet-identification setup, the tablets are placed on the aluminum plate at the bottom and touch the vertex of the V-shaped quartz rod, which rings at resonant frequencies. At the top of the V are the transmitting and receiving piezoelectric transducers.

Sinha developed the technique for the detection of nuclear, chemical, and biological weapons. By 1996, he had perfected a portable ARS unit for use on the battlefield. It could noninvasively detect and identify the deadly chemicals held in any sealed artillery shell or similar container, and the entire analysis could be done within just a few minutes.

"The original tests were only for a few of the most important chemical weapons agents, such as GB, VX, mustard, and white phosphorous," Sinha explains. In 1997, the United Nations inspectors used ARS to look for chemical weapons in Iraq.

On to wood and medicines

Because ARS is nondestructive, Lodder became interested in using it to examine rare or old wood species for historical restoration projects. He demonstrated the technique's applicability by identifying 26 wood species (*Appl. Spectrosc.* **1993**, *47*, 1880–1886). His investigation showed that ARS outperformed NIR spectrometry by a wide margin, and he hoped to use the technique on historical structures damaged by fire. However, because of other commitments with his students, Lodder never completed these studies.

Nevertheless, Lodder and his team continued their exploration of ARS, and in 2005, they saw the technique's potential for rapidly identifying and differentiating tablets of different sizes and shapes. By making just a few electronic modifications, they converted an MP3 player and a set of headphones into a fully functional ARS unit. The system sends sound waves from one side of the headphones to interact with the sample; this creates resonances at certain frequencies. Those resonances are picked up by the other side of the headset, which has been modified to serve as a microphone.

"Commercial headphones play sound out of the speakers," Lodder explains. "We simply cut the line to one speaker and use the speaker leads as a microphone input. That microphone becomes the ARS detector. The other speaker in the headphones transmits the specially encoded excitation signal from the MP3 player into the sample."

Recently, Lodder has been combining ARS with integrated sensing and processing (ISP) to identify the solid-fuel premixes for a "pill safe" that can protect tablets that contain narcotics. If the safe is broken into, the fuel incinerates the pills. "The whole point of ISP–ARS is that the analysts do not need spectra at all," says Lodder. "Instantaneous results. . . . No lab people, no spectra, no computer interpretation required."

—Barry E. DiGregorio

