MedicalXpress

Modified forms of bisphenol A found to alter hormone signaling in new, disturbing ways

July 17 2013

For years, scientists have been worried about bisphenol A. The chemical is known as an "endocrine disruptor," a substance that interferes with the body's hormone signaling system, and it's found in everything from plastic drink bottles to the linings of food and drink cans to the thermal paper used for cash register receipts—not to mention the urine of 92.6 percent of Americans over the age of six. BPA has been associated with the development of chronic diseases such as diabetes, asthma and ovarian dysfunction. In 2012, the FDA banned BPA from use in the production of baby bottles and drinking cups.

BPA's ubiquity in the environment led researchers to ask what it might be doing in publicly supplied drinking water, which is contaminated at its source by BPA-laden discarded plastic and later picks up more of the chemical when it passes through PVC plastic pipes. Most public water supplies are chlorinated to kill bacteria, and the BPA in the water also becomes chlorinated, acquiring one or more chlorine atoms from the water around it. The question was, how does this chlorinated BPA behave in the body?

The answer, generated from cell-culture experiments, was that it produced different but no less profound effects. "We found that when you modify the BPA it works just as dramatically but in different ways on the same systems," said University of Texas Medical Branch at Galveston professor Cheryl Watson, senior author of a paper on the study now online in *Endocrine Disruptors*.

Watson and graduate student René Viñas examined both chlorinated BPA and BPA that had undergone sulfonation and glucuronodation—two processes the body uses to make a compound easier to excrete. In all three cases the modified forms of BPA worked through membrane estrogen receptors to deactivate key signaling enzymes known as ERK and JNK kinases.

"These kinases are major control centers, gathering all the cell signals, making decisions and then expediting them," Watson said. "If you change the dynamic by inactivating kinases, you can mess up cell signaling."

Very low levels of modified BPA were sufficient to produce the results—a phenomenon commonly seen with membrane receptors. The responses followed what is known as a non-monotonic pattern, varying irregularly when different concentrations of modified BPA were tested. The large number of experimental procedures this made necessary were facilitated by a BIOMEK-FX robot, which Viñas programmed to considerably increase the efficiency and precision of the process.

"The robot cuts down on the experimenter time required, because it does so much of the mechanical work, and it makes results more replicable, because the robot does things exactly the same every time," Watson said. "It gives us hope that we can make an impact even with the sheer volume of chemicals that we have to study and the detail we have to study them in."

Provided by University of Texas Medical Branch at Galveston