Research links water disinfection byproducts to adverse health effects

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Michael Plewa, lead scientist and professor of genetics in the U of I Department of Crop Sciences, reports the first identification of a cellular mechanism linked to the toxicity of a major class of drinking water disinfection byproducts. This study, published in *Environmental Science & Technology*, suggests a possible connection to adverse health effects, including neurological diseases such as Alzheimer's. Credit: David Riecks, University of Illinois ITCS

University of Illinois scientists report the first identification of a cellular mechanism linked to the toxicity of a major class of drinking water disinfection byproducts. This study, published in *Environmental Science*

& Technology, suggests a possible connection to adverse health effects, including neurological diseases such as Alzheimer's.

"I'm not implying that drinking disinfected water will give you Alzheimer's," said Michael Plewa, lead scientist and professor of genetics in the U of I Department of Crop Sciences. "Certainly, the disinfection of drinking water was one of the most significant public health achievements of the 20th century. But the adverse effects of disinfection byproducts (DBPs) that are unintentionally formed during this process are causing concerns as researchers unveil their toxicity."

More than 600 DBPs have been discovered. Although researchers know some DBPs are toxic, little biological information is available on the majority of these water contaminants. The Environmental Protection Agency regulates only 11 of these DBPs, he said.

Plewa's laboratory investigated the biological mechanism, or the cellular target that leads to toxicity, in the second-most prevalent DBP class generated in disinfected water – haloacetic acids (HAAs).

"The EPA has regulated HAAs for nearly 15 years. However, we did not know how they caused toxicity before this study," he said. "Now that we've uncovered the mechanism for HAAs, we can make sense of past data that can lead to new studies relating to adverse pregnancy outcomes, different types of cancer, and neurological dysfunction."

Plewa believes this will assist the EPA in establishing regulations based on science. Their research will also help the water treatment community develop new methods to prevent the generation of the most toxic DBPs.

"It's fairly simple," Plewa said. "To increase the health benefits of disinfected water, we must reduce the most toxic DBPs. If we understand their biological mechanisms, we can come up with more

rational ways to disinfect drinking water without generating toxic DBPs."

In this study, researchers focused on three HAAs – iodoacetic acid, bromoacetic acid and chloroacetic acid. After they rejected their first hypothesis that the HAAs directly damaged DNA, they looked at research in a different area – neuroscience. Plewa's graduate student, Justin Pals, discovered an amazing connection, Plewa said.

In neurotoxicology, iodoacetic acid reduces the availability of nutrients or oxygen in neurons by inhibiting glyceraldehyde-3-phosphate dehydrogenase (GAPDH).

"Researchers are interested in understanding how to prevent damage after a stroke or other neurological damage," Plewa said. "Iodoacetic acid kills these cells. One of the targets they found was that iodoacetic acid inhibited GAPDH."

Plewa's lab conducted quantitative GAPDH enzyme kinetics and discovered that the data were highly correlated with a diversity of adverse health markers.

"All the pieces of the puzzle fell into place in an instant," Plewa said. "We had discovered our cellular target – GAPDH. Never before had this type of research been done with this level of precision and associated with a large body of adverse biological impacts."

They discovered that the HAA disinfection byproducts were toxic because the cells cannot make ATP, and this causes oxidative stress.

"Cells treated with HAAs experience DNA damage," Plewa said. "So they start expressing DNA repair systems. HAAs are not directly damaging DNA, rather they are inhibiting GAPDH, which is involved in

increasing the oxidative stress that we are observing."

A growing body of information has shown that GAPDH is associated with the onset of neurological diseases.

"If you carry a natural mutation for GAPDH and are exposed to high levels of these disinfection byproducts, you could be more susceptible to adverse health effects such as Alzheimer's," he said.

More research is needed to study iodinated disinfection byproducts because they are the most reactive in inhibiting GAPDH function and are currently not regulated by the EPA, Plewa said.

"We replaced the standard working model of direct DNA damage with a new working model based on a cellular target molecule," he said. "This discovery is a fundamental contribution to the field of drinking water science."

More information: This research, "Biological Mechanism for the Toxicity of Haloacetic Acid Drinking Water Disinfection Byproducts," was published in *Environmental Science & Technology*.

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