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New enzyme therapy shows proof of concept as treatment for cocaine overdose

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A long-acting enzyme that rapidly and safely metabolizes cocaine in the blood stream is currently being investigated in animal models as a possible treatment for cocaine overdose. This research is being presented Oct. 29 at the 2015 American Association of Pharmaceutical Scientists (AAPS) Annual Meeting and Exposition, the world's largest pharmaceutical sciences meeting in Orlando, Fla. Oct. 25-29.

The National Survey on Drug Use and Health has reported that approximately 1.9 million Americans were using cocaine in 2008. A 2008 Drug Abuse Warning Network report also showed that cocaine was involved in 482,188 of the nearly two million visits to emergency departments for drug misuse or abuse. Taking cocaine can result in severe health issues, including cardiovascular issues (disturbances in heart rhythm and heart attacks) neurological effects (strokes, seizures, headaches, and coma) and gastrointestinal complications (abdominal pain and nausea). Currently, there are no marketed treatments for individuals who overdose on cocaine.

Chang-Guo Zhan, Ph.D., a professor, and Fang Zheng, Ph.D., an associate professor at the College of Pharmacy at the University of Kentucky, along with their research team previously designed and tested CocH1, an enzyme that specifically breaks down cocaine without producing harmful byproducts in the body as a result. The researchers are currently evaluating a novel enzyme, E12-7Fc-M3 for its ability to neutralize cocaine in the blood stream using molecular modeling technology. E12-7Fc-M3 was tested in vivo to examine its activity

against cocaine. Following injection of cocaine into mice and rats, scientists gave the cocaine-metabolizing enzyme to the animals intravenously.

E12-7Fc-M3 not only demonstrated a significantly improved efficiency against cocaine, but also had a considerably prolonged biological half-life in mice and rats of roughly 110 hours, compared to the half-life of CocH1-HSA (a pharmaceutical formulation of CocH1), which was only about eight hours. A single administration of 0.25 mg/kg E12-7Fc-M3 followed by multiple doses of 5 mg/kg E12-7Fc-M3 was shown to accelerate cocaine hydrolysis in mice and rats for at least 20 days. A single dose of 2.5 mg/kg E12-7Fc-M3 was also found to completely eliminate 25 mg/kg of cocaine in mice and rats for at least seven days.

"This next stage of our research is promising, showing that the enzyme has extended function in small animal models and potentially even longer in humans," said Zhan. "We envision that this therapy could eventually become a viable treatment option in emergency rooms for people who overdose on cocaine."

More information: R6236 - Long-Acting Cocaine Hydrolase as Enzyme Therapy for Cocaine Addiction will be presented during the Thursday Morning Poster Session from 8:30 - 11:30 a.m. on Oct. 29 in OCCC - Exhibit Hall WA3.

Provided by American Association of Pharmaceutical Scientists