Exploring new drug treatment for addictions

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South Dakota State University researchers have demonstrated for the first time that a plant-derived compound used to treat nicotine addiction also has significant effects against alcohol addiction.

SDSU scientists are now investigating whether the compound may offer lasting treatment against alcohol relapse, craving, and perhaps alcohol-nicotine co-addiction as well.

“Alcohol and tobacco smoking are the top causes of preventable deaths in the U.S.,” associate professor Shafiqur Rahman in SDSU’s Department of Pharmaceutical Sciences said. “Total economic costs for alcoholism and tobacco-related diseases are about $900 billion per year in the U.S. Millions of Americans are at the heart of this crisis. So there are enormous medical, social and economic consequences for these kinds of addictive disorders.”

Rahman and his graduate student researcher, Ravi Sajja, a Ph.D. student in the SDSU College of Pharmacy, focused their initial work on looking at new applications for the compound, cytisine.

Cytisine is an alkaloid found in some plants such as the golden rain acacia, Cytisus laburnum. It is the key ingredient in a smoking cessation product sold in Europe. But until now, Rahman said, no one had looked at cytisine's potential in treating alcoholism or alcoholism-nicotine co-abuse.

The SDSU study examined what effect cytisine had on alcohol consumption in mice and in rats in separate trials. The rat model used animals that have a genetic predisposition toward alcoholism. These animal models are widely used for preclinical testing of drugs for addiction, Rahman said.

"We used the drug to determine if it had an effect on alcohol-seeking behavior, as well as on alcohol consumption," Rahman said. "Both actions are reduced by the drug. Based on these two animal models, we can conclude that cytisine reduced alcohol addiction in preclinical animal models. We also found that cytisine reduced alcohol addiction in a genetic model of alcoholism."

Common genes control the development of alcohol and nicotine addiction, Rahman said, though both genetic and environmental factors are at work as people form those addictions. Rahman wants to develop a medicinal compound that targets the brain receptor protein known as the nicotinic receptor, since it regulates the development of alcohol and nicotine addiction.

"Cytisine has some limitations. It works well for a short term, from one hour to four hours. After four hours, the action decreases. After 12 hours, the action is no longer there," Rahman said. "We need some new

drug that is long-acting, so that you could take, say, two pills in a day to cover for 24 hours."

Towards that goal Rahman and his collaborators have investigated lobeline, a naturally occurring alkaloid that is known to target a common brain receptor protein implicated in alcohol and nicotine dependence. The results obtained from preclinical models show promise in dealing with long-term management of alcoholism and alcohol-nicotine co-dependence. Rahman and collaborators at Indiana University School of Medicine at Indianapolis tested both compounds in a genetic model of alcoholism. The results show potential in combating alcohol addiction.

More information: The research was published in December 2009 in a prestigious peer-reviewed scientific journal, *Alcohol*. Rahman's laboratory published results of a separate study in July 2010 in the *International Journal of Experimental and Clinical Pharmacology* detailing how the compounds under consideration function in the brain's reward system, or how it affects neuronal system associated with drug addiction.

Provided by South Dakota State University