Addictive nut's derivatives could help smokers break the nicotine habit

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Compounds derived from areca nuts could help cigarette smokers quit. Credit: Roger Papke, Ph.D.

As many as 600 million people in Southeast Asia chew areca nuts with betel leaves, sometimes adding tobacco leaves. Many users are addicted to this harmful "betel quid" preparation, which can create a sense of

euphoria and alertness. Yet researchers have now discovered that compounds derived from the nut could help cigarette smokers—as well as betel quid chewers—kick their habits.

The researchers will present their work today at the 253rd National Meeting & Exposition of the American Chemical Society (ACS).

"There's a commonality to the two addictions, so we thought we could develop drugs that target both," says Roger L. Papke, Ph.D., one of the lead researchers on the project. Fellow lead researcher Nicole A. Horenstein, Ph.D., and Papke, along with Clare Stokes and Marta Quadri, Ph.D., are studying compounds from the areca nut to make new molecules that might work better than existing smoking cessation drugs such as Chantix (varenicline).

More than 480,000 people die each year in the U.S. from the effects of cigarette smoking, according to the U.S. Centers for Disease Control and Prevention. Prescription smoking cessation drugs currently on the market can work well but can also cause harmful side effects. For example, some patients taking the drug varenicline report having suicidal thoughts, sleepwalking and having cardiovascular problems.

Because of varenicline's side effects, researchers such as Papke and Horenstein are working on alternatives at the University of Florida. Varenicline reduces nicotine cravings by binding to the same receptors that attach nicotine molecules to brain cells, but it activates those receptors to a lesser degree. Undesirable effects occur because the drug also binds to other nicotine receptors that aren't involved in addiction, Papke explains. "The molecules that we're developing are more specific—they do not target those other receptors at all, so our compounds should be safer," he says.

The idea to study the areca nut came when Papke obtained a

headhunter's sword from Borneo. He learned that the peculiar carvings on its hilt might have been made by someone using betel quid. Quids are prepared by mixing sliced areca nuts with slaked lime (calcium hydroxide), spices or sweets, and in some cases tobacco, and wrapping the concoction in leaves from the betel vine. Quid chewing turns users' teeth bright red and forces them to spit out a lot of red saliva, which discolors local sidewalks and buildings. Worse, quid use is addictive and leads to serious health effects including oral cancer and cardiovascular issues.

In prior work (see below for a video), Papke and Horenstein studied arecoline, one of the psychoactive alkaloids in the areca nut. They discovered that arecoline stimulates the same brain cell receptors responsible for nicotine addiction but doesn't stimulate the other types of nicotine receptors.

Now, Horenstein is synthesizing a range of compounds with structures that are slightly different from arecoline. The researchers have found that some of these new compounds also bind to the addiction-related receptors, while leaving the other receptors alone. That means these arecoline analogs may be able to treat addiction to cigarettes or to betel quids without side effects. The next step for Horenstein and Papke is to seek funding so they can test these potential new drugs in animal trials.

  More information: Selective nicotinic acetylcholine receptor activities from the areca nut, the 253rd National Meeting & Exposition of the American Chemical Society (ACS), 2017.

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