First identification of a strong oral carcinogen in smokeless tobacco

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Scientists today reported identification of the first substance in smokeless tobacco that is a strong oral carcinogen ? a health risk for the 9 million users of chewing tobacco, snuff and related products in the U.S. ? and called upon the federal government to regulate or ban the substance.

The researchers reported here at the 244th National Meeting & Exposition of the American Chemical Society, the world's largest scientific society. The meeting, which continues through Thursday, features more than 8,600 reports on new developments in science, with an anticipated attendance of 14,000 scientists and others.

"This is the first example of a strong oral cavity carcinogen that's in smokeless tobacco," said Stephen Hecht, Ph.D., who led the study. "Our results are very important in regard to the growing use of smokeless tobacco in the world, especially among younger people who think it is a safer form of tobacco than cigarettes. We now have the identity of the only known strong oral carcinogen in these products."

Evidence has been accumulating for years that people who use smokeless tobacco have an increased risk of cancer of the mouth, esophagus and pancreas. Scientists also knew that smokeless tobacco users are exposed to a variety of carcinogens and experience some damage to their genetic material impairing its normal function. But until now, no substance in these products was clearly implicated as a cause of mouth cancer, explained Hecht, who is at the University of Minnesota.

Hecht's team identified the culprit as (*S*)-NNN, one of a family of hundreds of compounds called nitrosamines, most of which are carcinogenic, capable of causing cancer. Nitrosamines occur in a variety of foods, ranging from beer to bacon, and also form naturally in the stomach when people eat foods containing high levels of nitrite. But nitrosamine levels in smokeless tobacco are far higher than in food.

To do it, they gave laboratory rats a low dose of two forms of NNN, suspected carcinogens in smokeless tobacco, for 17 months in doses roughly equivalent to a person consuming half of a tin of smokeless tobacco every day for 30 years. One substance, (*S*)-NNN, induced large numbers of oral and esophageal tumors in the rats.

"The most popular brands of smokeless tobacco that are sold in the U.S. have unacceptably high levels of this particular carcinogen," explained Hecht. "And smokeless tobacco is a known cause of oral cancer. Obviously, we need to decrease the levels of this material in all smokeless tobacco products — or eliminate it altogether." Hecht adds that removing (*S*)-NNN from these products is feasible. In fact, some products on store shelves today have reduced levels of the carcinogen.

Hecht explained that the U.S. Food and Drug Administration has the authority to regulate tobacco products, but no regulations on the levels of specific carcinogens exist yet. "My suggestion is that levels of (*S*)-NNN in smokeless tobacco be decreased to below 10 parts per billion. That would make it more consistent with the levels of nitrosamines in food products," he said. (*S*)-NNN also is in cigarettes and other smoked tobacco items, and he suggested that the substance be regulated in these products, as well.

More information:

Abstract

Smokeless tobacco products, with a growing market share, contain NNN, an established esophageal carcinogen in the F-344 rat. (S)-NNN is the predominant form of NNN in tobacco. We previously demonstrated that (S)-NNN, administered in the drinking water to rats, is

metabolized locally producing pyridyloxobutyl DNA adducts in the oral cavity and esophagus, with levels higher than from (R)-NNN, thus raising the possibility that orally administered (S)-NNN might be an oral cavity carcinogen. This study demonstrated the powerful carcinogenicity of (S)-NNN in the rat oral cavity. All 20 rats treated with 15 ppm (S)-NNN in the drinking water for 17 months had multiple oral tumors including malignant squamous cell carcinomas. A total of 91 oral tumors were observed, along with esophageal tumors. (R)-NNN was considerably less active. (S)-NNN is thus the only known strong oral cavity carcinogen in smokeless tobacco and should be removed from these preducts without delay.

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