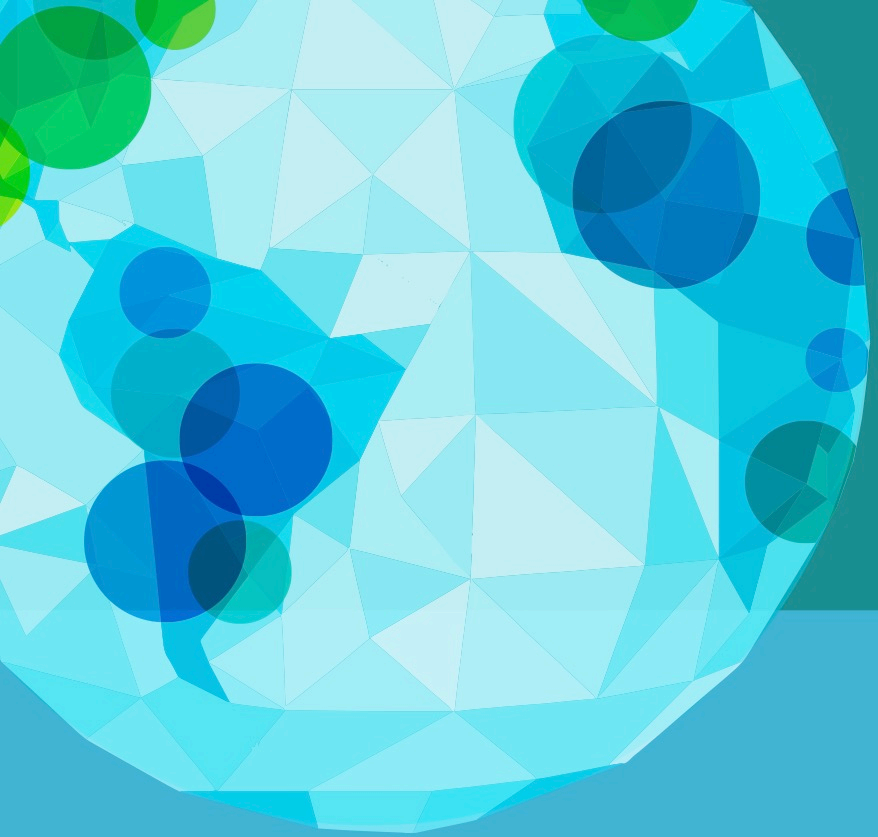


The Scientific Basis for Smokeless Tobacco Product Regulation:

Monitoring Product Types and Characteristics

Presented by: Mark Parascandola

Epidemiologist

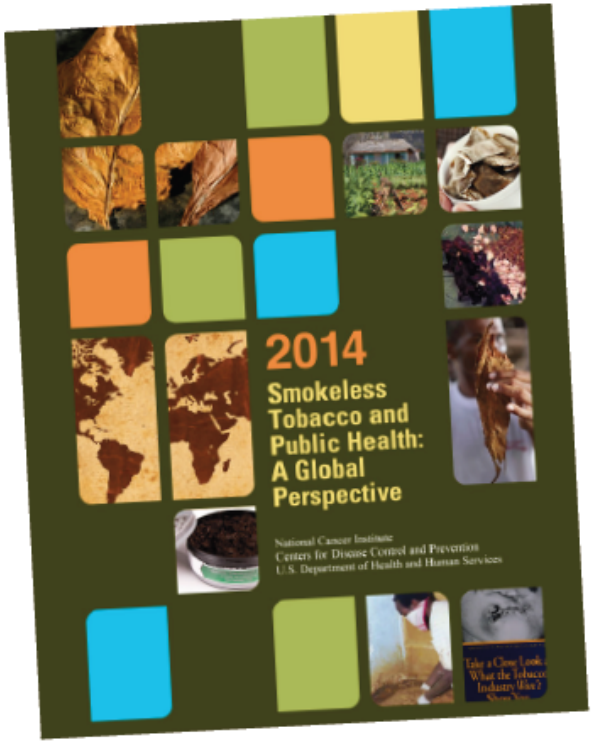
National Cancer Institute

NIH NATIONAL CANCER INSTITUTE

Center for Global Health

Smokeless Tobacco and Public Health: A Global Perspective (2014)

Editors: Dorothy Hatsukami, Mitch Zeller, Prakash Gupta, Mark Parascandola, Samira Asma



This report:

- Explores the current science on ST use, characteristics of ST products, and related intervention and policy efforts
- Discusses the international tobacco control efforts needed to best address this global challenge
- Is the work of 32 expert authors from around the world.

Published by the U.S. National Cancer Institute and the Centers for Disease Control and Prevention

Available at:

http://cancercontrol.cancer.gov/brp/tcrb

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What is ST?

- Unlike smoked tobacco, which is burned or heated and then inhaled, smokeless tobacco (ST) is predominantly used orally (chewed, sucked, dipped, held in the mouth, etc.) or nasally, which results in absorption of nicotine and other chemicals across mucus membranes
- ST products range widely in ingredients and complexity from simple cured tobacco to elaborate products
- Non-tobacco plant material that may affect the attractiveness, addictiveness, and toxicity of the products

Qiwam

Betel quid (paan)

Zarda

Gutka

Moist snuff

Dry snuff

Snus

Chimó

Moist snuff
(caffeinated)

Plug

Nasway

Toombak

Twist

Red tooth powder

Shammah

Orbs

Strips

Sticks

Tobacco-coated toothpicks

Mawa

Rapé


CAUSES CANCER
Peter Stuyvesant
SNUS 24
PREGNANT? BREAST-FEEDING? YOUR SMOKING CAN HARM YOUR BABY
Peter Stuyvesant
BLUE 20
TOBACCO IS ADDICTIVE
Peter Stuyvesant
RICH MINT BLEND snus
FLAVOURED TOBACCO POUCHES


LUCKY STRIKE
AN AMERICAN
LUCKY STRIKE
ORIGINAL WHITE PORTION


PALL MALL
ORIGINAL
PALL MALL
MADE IN SWEDEN
TRADITIONAL SNUS TASTE
PALL MALL
TOBACCO EXPERTISE
SINCE 1888


CAMEL
sticks
WARNING: This product is not a safe alternative to cigarettes.
CAMEL
orbs
WARNING: This product can cause mouth cancer.
CAMEL
strips
WARNING: This product can cause gum disease and tooth loss.
variety pack
WARNING: This product can cause gum disease and tooth loss.


CAMEL
snus
FROST
WARNING: This product is not a safe alternative to cigarettes.
Marlboro snus
RICH

Premade		Custom-made
Manufactured	**Cottage industry**	**Vendor/individual**
Product examples: • Chewing tobacco (plug/twist/loose leaf) • Creamy snuff • Dissolvables • Dry snuff • Gudahku/Gudahka • Khaini • Moist snuff • Kiwam • Rapé • Red toothpowder	Product examples: • Dohra • Gutka • Mainpuri • Nass/Naswar • Nasway • Betel quid (paan) • Rapé • Shammah • Toombak • Tuibur	Product examples: • Gudahku/Gudahka • Iqmik • Nass/Naswar • Nasway • Betel quid (paan) • Rapé • Shammah • Tapkeer • Tobacco leaf • Tombol • Toombak Some premade ingredients are used to make custom-made products: twist, zarda, toombak, gudahku/gudahka, and kiwam.

Tobacco
(IARC Group 1)
Nicotine/alkaloid
levels vary

Cultivated tobacco
(N. tabacum)

Aztec tobacco
(N. rustica)

Brazilian tree
tobacco
(N. glauca)

Air-cured | Flue-cured | Fire-cured | Sun-cured | Air-cured

Alkaline agents
boost pH and
percent free
nicotine

Slaked lime | Calcium carbonate | Sodium bicarbonate | Magnesium carbonate | Alkaline ashes

Areca nut
(IARC Group 1)
Mild stimulant

(Areca catechu)

Other plant-derived
materials

Tonka bean *(Dipteryx odorata)* | Camphor *(Cinnamomum camphora)* | Peruvian cocoa | Khat *(Catha edulis)* | Caffeine

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SEARO: ST Products

- Wide variety of products, usually custom made or cottage industry

Custom-made Products

Betel Quid

Mawa

Khaini

Mainpuri

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SEARO: ST Products

Categories are not mutually exclusive

Cottage Industry Products

Mishri

Gul

Zarda

Commercial Products

Kiwam

Gutka

Creamy Snuff

Table 1. Composition of the different types of chewing substances

	Areca nut[a]	Betel[b]			Catechu[d]	Tobacco[e]	Slaked lime
		Leaf	Inflo-rescence	Stem[c]			
Areca	X						
Betel quid without tobacco	X	X			(X)[f]		X
Betel quid with tobacco	X	X			(X)[f]	X	X
Gutka	X				X	X	X
Pan masala[g]	X				X		X
Khaini						X	X
Mawa	X					X	X
Mainpuri tobacco	X					X	X
Lao-hwa (Taiwan)	X[g]		X				X
Betel quid (Taiwan)	X[g]	X					X
Stem quid (Taiwan)	X[g]			X			X
Naswar						X	X
Zarda						X	X

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Tobacco Processing: Curing, Fermentation and Additives

- Fire curing causes chemical changes in the tobacco leaf -- PAHs, phenols, and volatile aldehyde levels tend to be higher in fire-cured tobacco than air-cured tobacco
- Tobacco fermentation induces chemical and biochemical changes. A portion of nitrate in fire-cured tobacco is converted to nitrite, which then reacts with alkaloids to produce TSNAs
- Additives include a variety of flavorants and alkaline modifiers (added to modify nicotine delivery)

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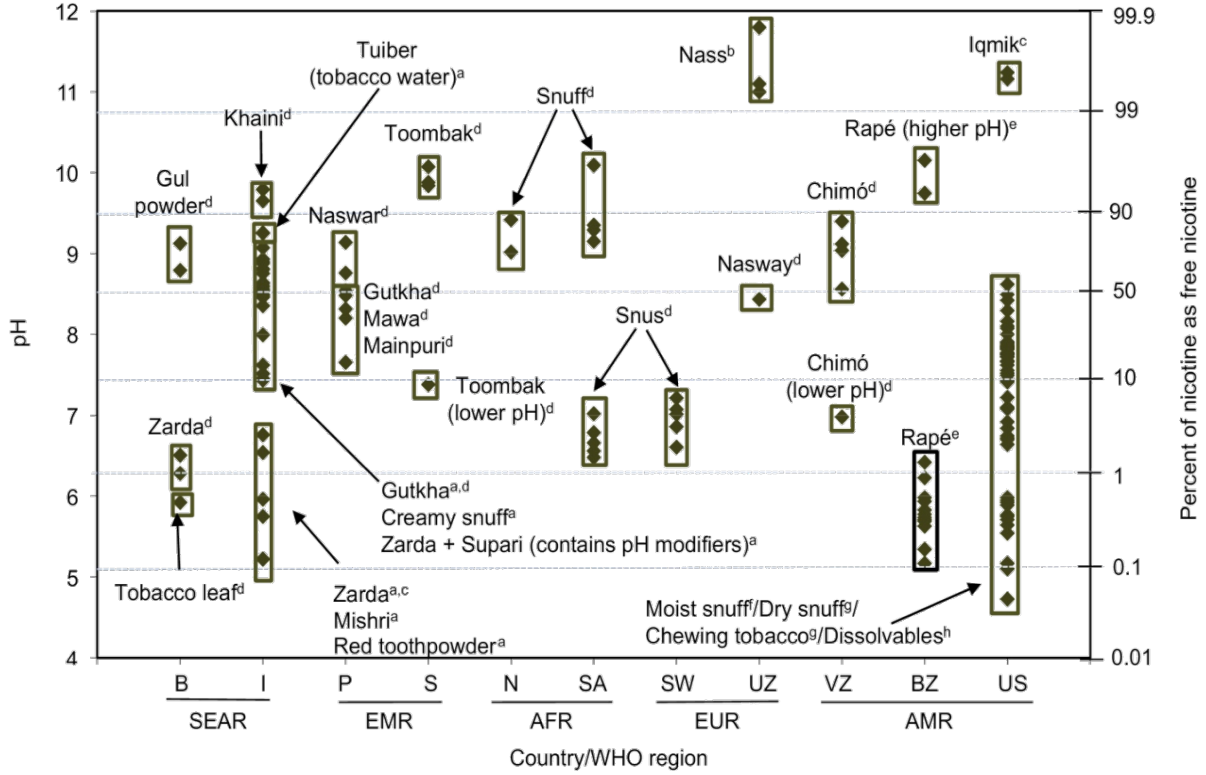
Variations in pH Level Determine Free Nicotine Levels



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TSNAs

- TSNAs are commonly considered among the most potent carcinogens in all tobacco products
- Five TSNAs have been identified in ST products: NNN, NNK, NNAL, NAT, NAB
- Use of different tobacco types, processing techniques, and tobacco blending approaches leads to wide variation of TSNA levels in various ST products

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Tobacco-specific Nitrosamine Content Varies By Almost 1000-fold

Ranges TSNAs in smokeless tobacco products

Constituent	Minimum value		Maximum value	
NNK (μg/g wet)	0.004	(Mawa)	516	(Toombak, sample 5)
NNN (μg/g wet)	0.045	(Gutka [handmade, Karachi])	368	(Toombak, sample 5)
Total TSNAs (μg/g wet)	0.084	(Gutka [handmade, Karachi])	992	(Toombak, sample 5)

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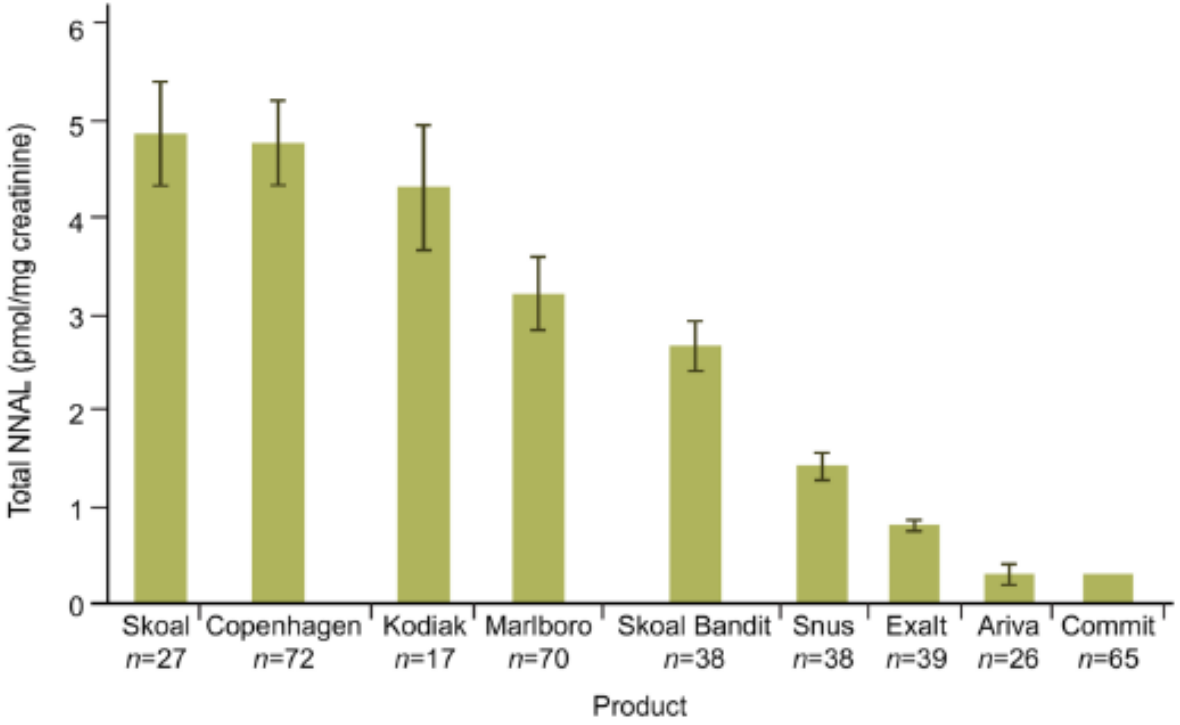
Total NNAL concentrations in urine of ST users varies across products

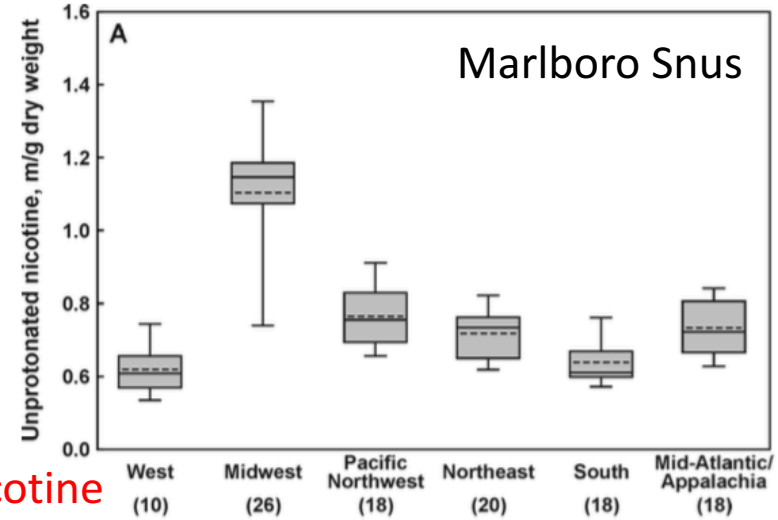


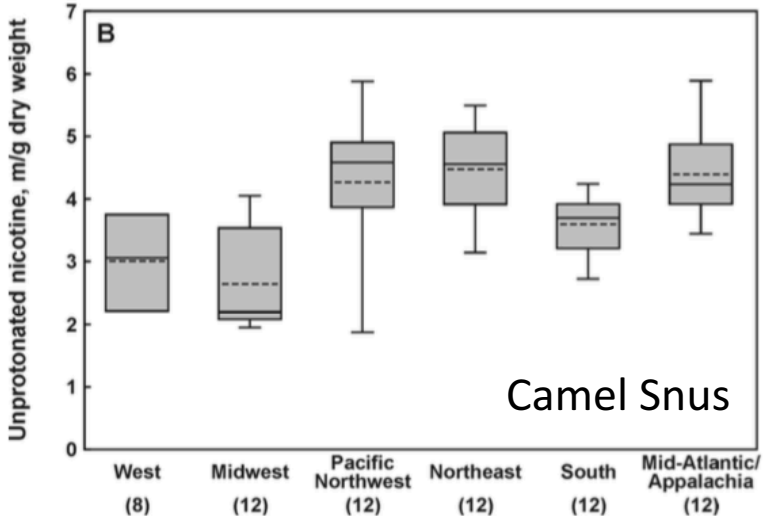
Monitoring Tobacco-Specific *N*-Nitrosamines and Nicotine in Novel Smokeless Tobacco Products: Findings From Round II of the New Product Watch

Irina Stepanov PhD[1], Lois Biener PhD[2], Katrina Yershova BS[3], Amy L. Nyman MA[2], Robin Bliss MS[3], Mark Parascandola PhD, MPH[4], Dorothy K. Hatsukami PhD[5]

- We analyzed tobacco-specific *N*-nitrosamines (TSNA) and nicotine in Marlboro and Camel snus tobacco products that were purchased in various regions of the country during the spring and summer of 2011.
- A total of 216 samples were received from different states representing 6 regions of the country.
- TSNA levels increased over time
- Unprotonated nicotine levels varied significantly by region

Nicotine





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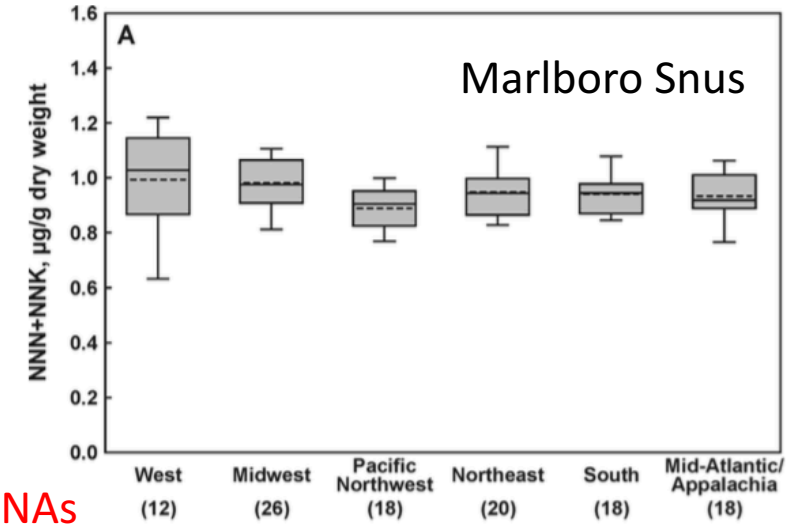
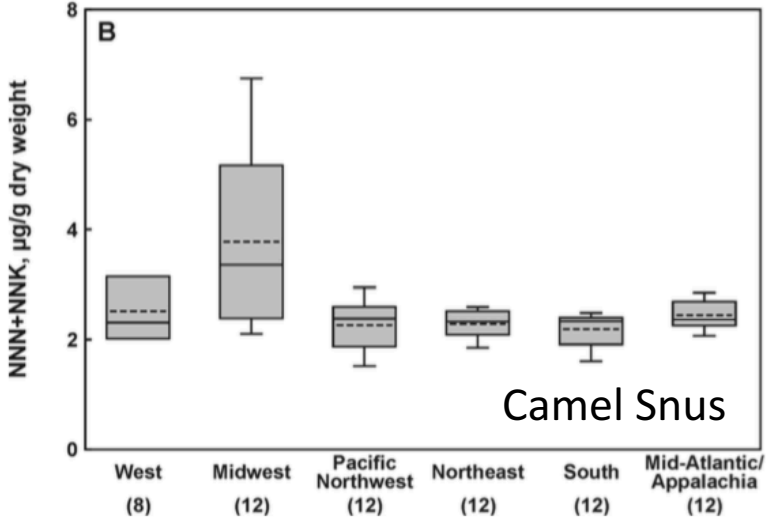
TSNAs



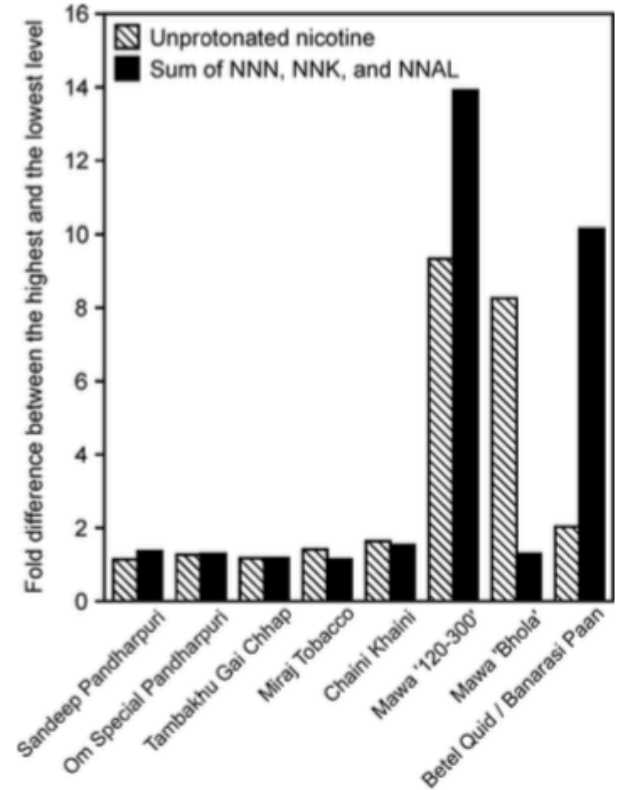


Constituent Variations in Smokeless Tobacco Purchased in Mumbai, India

Irina Stepanov, PhD
Prakash C. Gupta, PhD
Mark Parascandola, PhD, MPH
Katrina Yershova, BS
Vipin Jain, PhD
Gauri Dhumal, MSc
Dorothy K. Hatsukami, PhD

- Tobacco products were purchased at 3 markets in Mumbai, using a standardized protocol for sample collection, labeling, and storage.
- 39 samples representing 8 varieties of manufactured and vendor-made smokeless tobacco products.
- When expressed per wet weight of product, unprotonated nicotine varied more than 300-fold and TSNA content varied more than 650-fold across the products. Substantial vendor-to-vendor variations were also observed.

Figure 2
Variation of Unprotonated Nicotine and the Sum of Carcinogenic TSNA in Products Purchased from Various Vendors



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Analysis of Alkaloids in Areca Nut-Containing Products by Liquid Chromatography–Tandem Mass Spectrometry

Vipin Jain,[†] Apurva Garg,[‡] Mark Parascandola,[§] Pankaj Chaturvedi,[‡] Samir S. Khariwala,[#] and Irina Stepanov*[,†,⊥]

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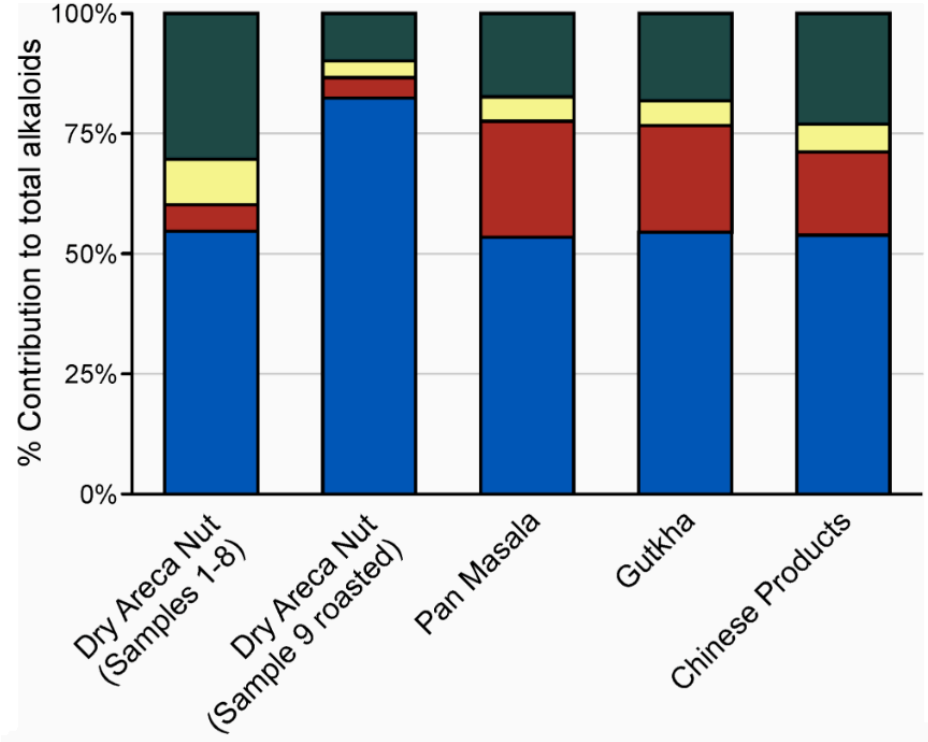
The results of the analyses revealed substantial variations in the levels of alkaloids across the tested products

Substantial differences in the relative contribution of individual alkaloids to the total alkaloid content were also observed among the different products.



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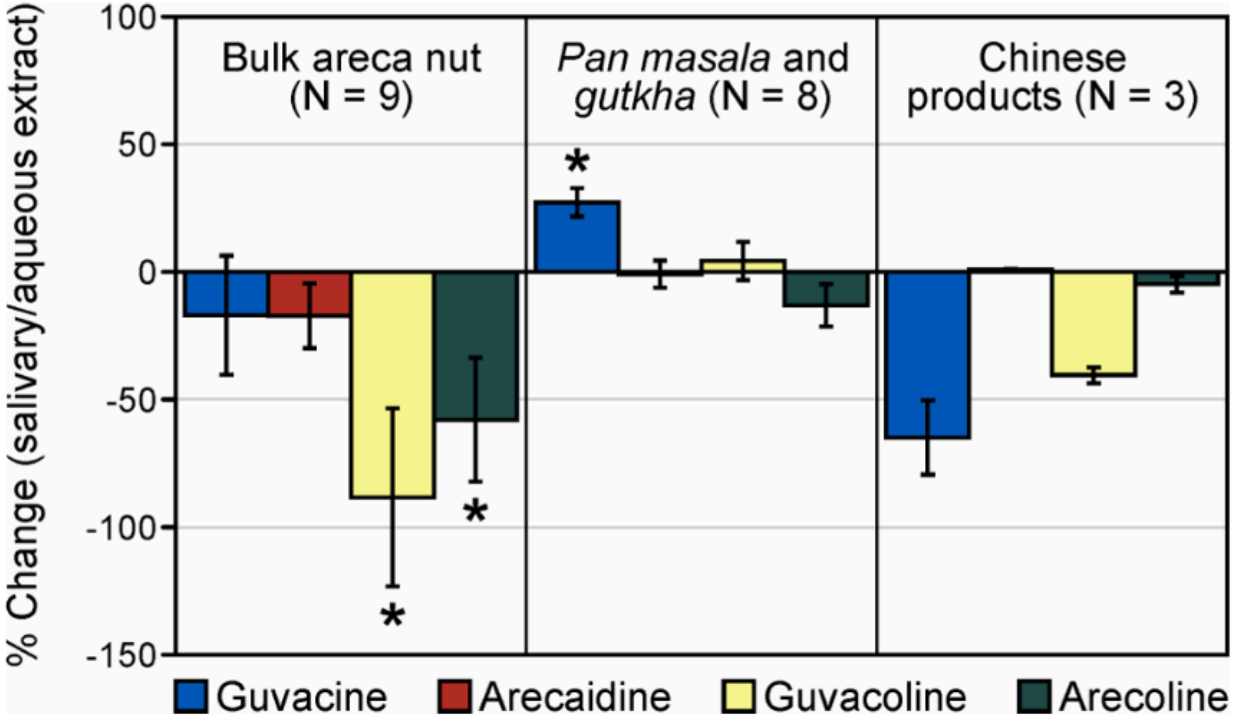

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Relative Risks associated with ST use vary between countries

Outcome	Country/region	Type of smokeless tobacco	Relative risk
Oral cancer	United States	Chew or snuff	2.6 (1.3–5.2)
	Scandinavia	Snus	1.0 (0.7–1.3)
	India	Smokeless tobacco†	5.1 (4.3–6.0)
Esophageal cancer	United States	Smokeless tobacco†	1.2 (0.1–2.3)
	Scandinavia	Snus	1.6 (1.1–2.4)
	India	Smokeless tobacco†	3.7 (1.6–8.4)
Pancreatic cancer	United States	Chew or snuff	1.4 (0.7–2.7)
	Scandinavia	Snus	1.8 (1.3–2.5)
	India	Mishri & other	2.0 (0.7–5.5)
Lung cancer	United States	Chew or snuff	1.8 (0.9–3.5)
	Scandinavia	Snus	0.8 (0.6–1.0)
	India	Mishri & other	1.6 (0.9–2.9)

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Annual Burden of Disease Attributable to Smokeless Tobacco Use in Two Countries: Sweden and India

Country/disease	Sex	Relative risk	Prevalence of smokeless tobacco use	Attributable fraction	Attributable burden of disease
Sweden					
Oral cancer	men	1.0	26%	0%	0
	women	1.0	7%	0%	0
Esophageal cancer	men	1.6	26%	13.5%	39
	women	1.6	7%	4.0%	4
India					
Oral cancer	men	5.1	33%	57.5%	26,131
	women	5.1	18%	42.5%	10,359
Esophageal cancer	men	3.7	33%	47.1%	13,569
	women	3.7	18%	32.7%	6,308

National Cancer Institute

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Oral cancer	men	1.0	26%	0%	0
	women	1.0	7%	0%	0
Esophageal cancer	men	1.6	26%	13.5%	39
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National Cancer Institute

Global Products Conclusion

- ST products should not be viewed as a single homogenous product category for assessing composition or health effects
- Because of these widely varying characteristics, along with different patterns of use, ST products are likely to differ across regions in their abuse liability, toxicity, carcinogenicity, and impact on health

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