

Setting the record straight - a reply to Goodpaster *et al.* - the real chemistry and toxicology of novel smokeless tobacco products

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Outline for presentation

- Background
- Objectives for presentation
- Press releases, quotations, and related information
- Results
- Conclusions
- Sponsorship and references

Background

- There has been continuing debate about the toxicology and possible impacts on public health associated with the use of dissolvable tobacco products and other novel smokeless tobacco products (STP)
- STPs with Gothiatek[®] analyte levels below those found in Swedish snus believed to have minimal health risks
- Little information on ingredients in dissolvable tobacco products until article by Goodpaster and coworkers
 - Chemical characterization of dissolvable tobacco products promoted to reduce harm
 - *J Agric. Food Chem. (JAFC)* 2011 Mar 23;59(6):2745-51
- Unfortunately, article contained serious errors

Objectives

- Show examples of press releases related to the article by Goodpaster and coworkers
- Review the analytical techniques used to characterize dissolvable tobacco products
- Show differences in product chemistries among different types of dissolvable tobacco products
- Compare our analytical approach and results with those recently published by Goodpaster and coworkers
- Discuss some compounds of particular interest reported by Goodpaster including their toxicological properties

Press releases and quotations on Goodpaster article

- "New 'dissolvable tobacco' products may increase risk of mouth disease." *Science Daily*, 16 Mar 2011
- "Study Findings from C.L. Rainey *et al.* Broaden Understanding of Smoking." *Health and Medicine Week*, 18 Apr 2011
- "Chemical Analysis: Understanding the ingredients in these new products could help to assess their impact on oral health." *C&E News*, 24 Feb 2011
- "Sorbitol's presence is alarming to dentists," says Goodpaster, "because it stimulates cavity-causing bacteria." *C&E News*, 24 Feb 2011

Indiana Tobacco Prevention and Cessation Commission

- “Dissolvable Tobacco Products: A New Threat”
 - “Dissolvable products may contain up to three times the amount of nicotine found in one cigarette”
 - “Smokers who use these products may get a higher dose of nicotine than they are used to, possibly resulting in nicotine poisoning ...adverse reactions such as tremors, nausea, vomiting, agitation, and in more extreme cases, seizures, coma, and death”
 - “Dissolvable tobacco is not a safe alternate to cigarettes. People who use spit tobacco are at risk of many health problems including cancers (lip, esophagus, pharynx, larynx, pancreas and stomach) and mouth diseases...”

(Quotations taken from http://www.in.gov/isdh/tpc/files/Dissolvable_tobacco_products_7_18_11.pdf)

Who is Goodpaster?



- **John Goodpaster Ph.D.**
 - ❑ Indiana U Purdue U at Indianapolis (IUPUI)
 - ❑ Assistant Professor
Director of Forensic and Investigative Sciences Program
 - ❑ Well funded with DoD grants on explosives detection
 - ❑ Formerly Forensic Chemist at BATF
 - ❑ Ph.D., Michigan State U

How did Goodpaster get into tobacco analyses?

- “We were approached by a member of the Tobacco Cessation and Biobehavioral Center with a request to assist in the analysis of a family of new tobacco products....”
- “Collaborative studies on the partitioning of tobacco components into biofilms, oral tissue and hair are planned. We are interested from a forensic standpoint in what could be termed ‘lifestyle markers’ that could be found in human hair.”

(Quotations taken from <http://chem.iupui.edu/people/john-goodpaster>)

Analytical strategies for dissolvable tobacco products

- Dissolvable tobacco products generally comprised of tobacco blend, sweeteners (can also serve as fillers), flavors, acidity regulators, and binding agents needed to hold the product together
- Reasonable to expect that dissolvable tobacco products would contain the volatile, semi-volatile, and nonvolatile components as found in cured tobaccos, tobacco products, including STP, and published ingredient lists
- Analytical strategies, to be complete, should cover
 - Polar compounds from ethanol through chlorogenic acid
 - Nonpolar compounds from 2-pentanone through Vitamin E

Goodpaster's analytical strategies and results

- Acetone extraction (ultrasonic) of ground dissolvable tobacco products (200 mg/2000 μ L)
 - Glycerol, menthol, nicotine, triethyl citrate, palmitic and stearic acids, two unknown compounds
 - GC/MS, split injection, 20°C/min, 20-min run time
- Tri-Sil extraction/derivatization of ground dissolvable tobacco products (5 mg/500 μ L)
 - Glycerol, xylitol (one style), sorbitol, unknown oligosaccharide
 - GC/MS, high-split ratio injection, 15°C/min, 20-min run time
- SPME of ground dissolvable tobacco products
 - Procedure of Clark & Bunch (*JAFCA* 1997, 45, 844-849)
 - Menthol, nicotine, triethyl citrate, carvone, vanillin, possible terpenoid, cinnamaldehyde and coumarin (only one style)

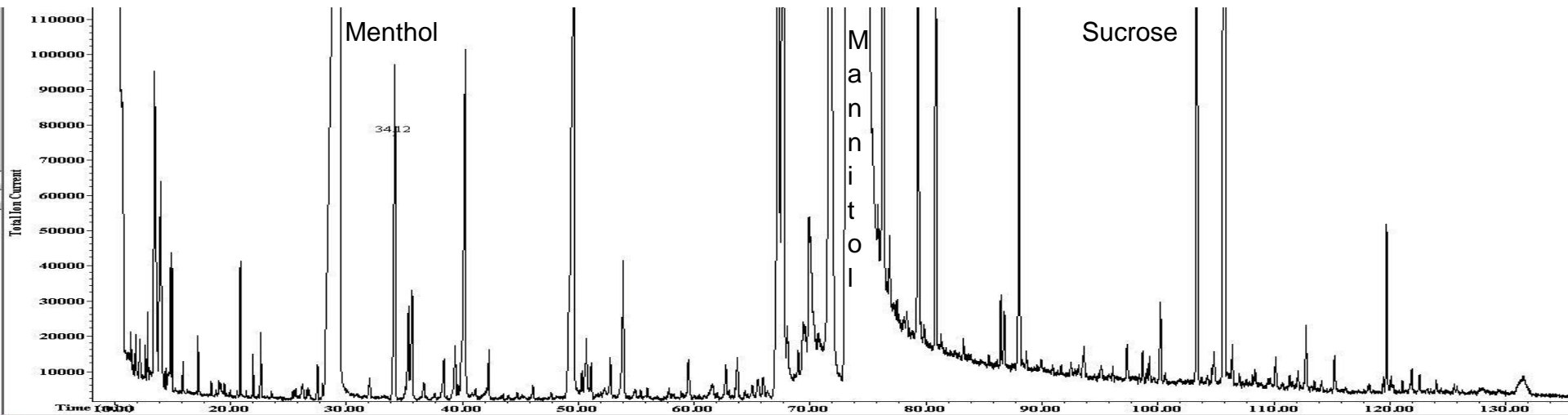
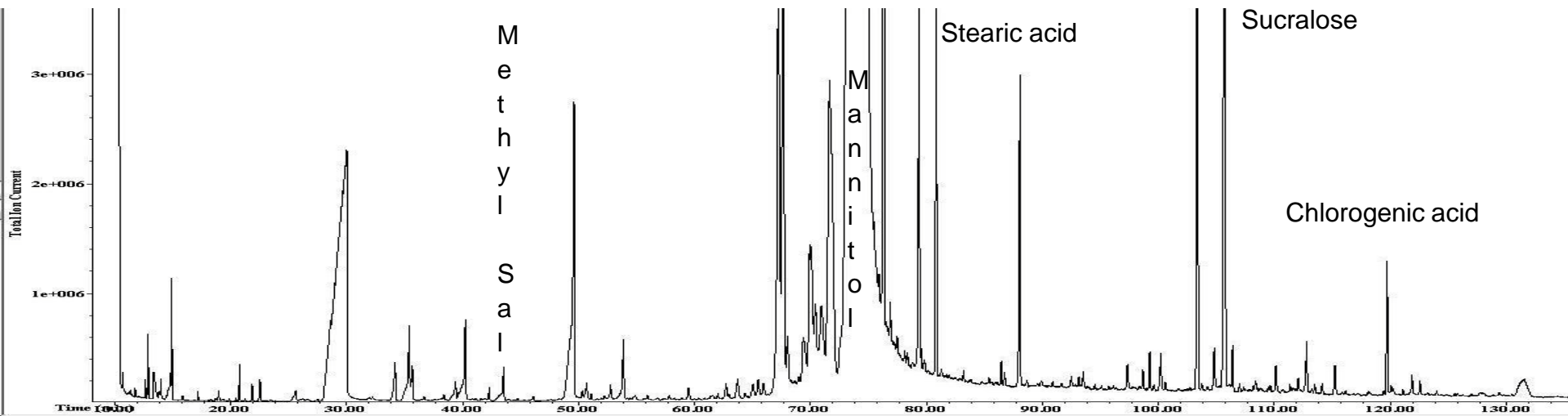
Our analytical strategies and overall results

- DS scan ground dissolvable tobacco products
 - 100 mg with 400 μ L DMF and 800 μ L BSTFA + ISTD
 - Found all silylated compounds reported by Goodpaster and many more not reported including sucralose
 - GC/MS, low-split injection (Jennings cup) at 50°C oven, 2°C/min to 300°C, 150-min run time, MS scan 40 – 700 amu, EI+
- Methanol (MeOH) scan ground dissolvable products
 - 250 mg with 1000 μ L methanol +ISTD (phenanthrene-d₁₀)
 - Found all compounds reported by Goodpaster for SPME and acetone scans except for cinnamaldehyde and coumarin, nothing else unexpected, just tobacco components
 - GC/MS, low-split ratio injection at 40°C oven, 2°C/min to 300°C, 150-minute run time, MS scan 40 – 700 amu, EI+

Results for tableted tobaccos

- DS Scan of tableted tobaccos
 - Total ion chromatograms (TICs) shown on next slide
 - Wintergreen flavored product shown in top TIC
 - Mint flavored product shown in bottom TIC
 - Both TICs are dominated by peak from mannitol-TMS which shows as a very broad peak at ~74 to 75 minutes
 - Both TICs show peaks for sucrose-TMS at ~103 minutes and sucralose ~106 minutes
 - The presence of the TMS derivative of chlorogenic acid at ~120 minutes indicates that these oral tobacco products are likely based on flue-cured, not the air-cured tobaccos used for most oral tobacco products

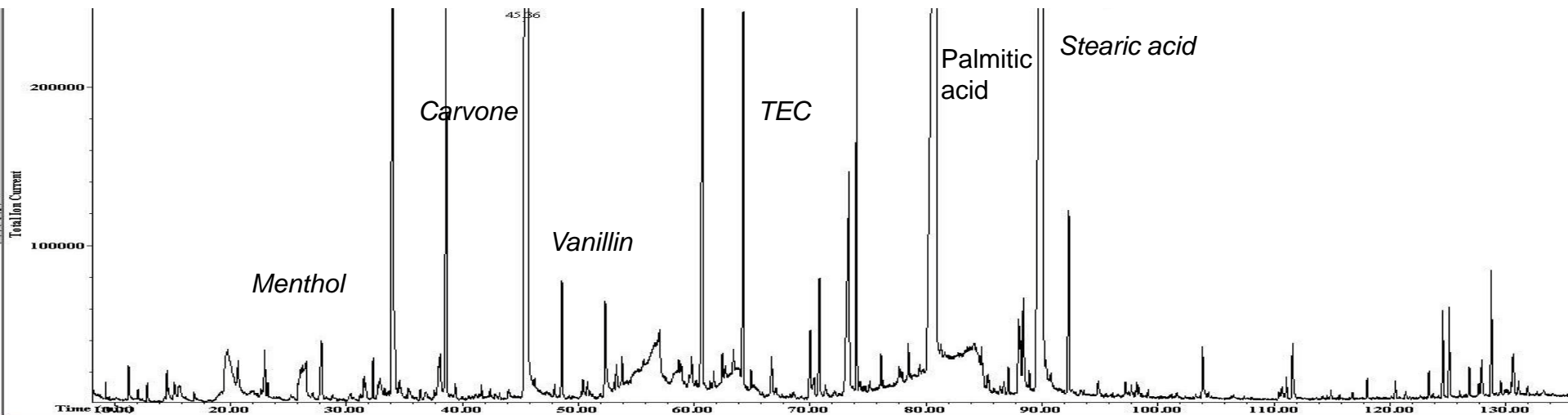
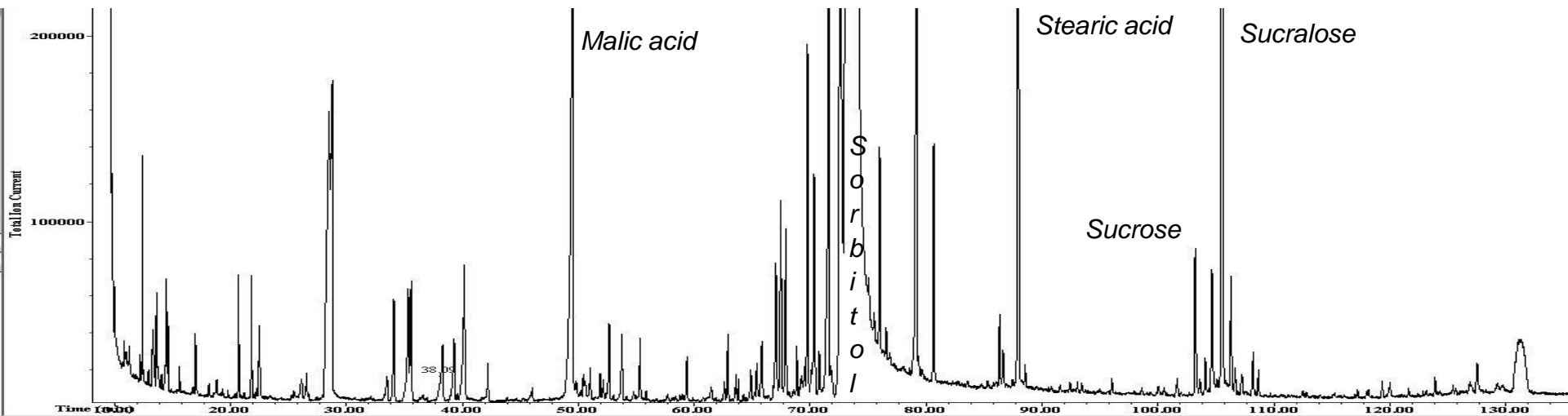
Results - Tableted tobaccos - Wintergreen (top), Mint (bottom)



Results for another tableted dissolvable tobacco product

- DS Scan (top) showed much more detail than reported by Goodpaster *et al.*, particularly the previously unreported sugar-like TMS derivative at ~106 minutes
- DS Scan also showed numerous organic acids such as malic acid, citric acid, and quinic acid; but no chlorogenic acid found so probably not flue-cured tobaccos
- MeOH scan (bottom) showed same compounds as reported by Goodpaster *et al.*, but numerous tobacco constituents found as well

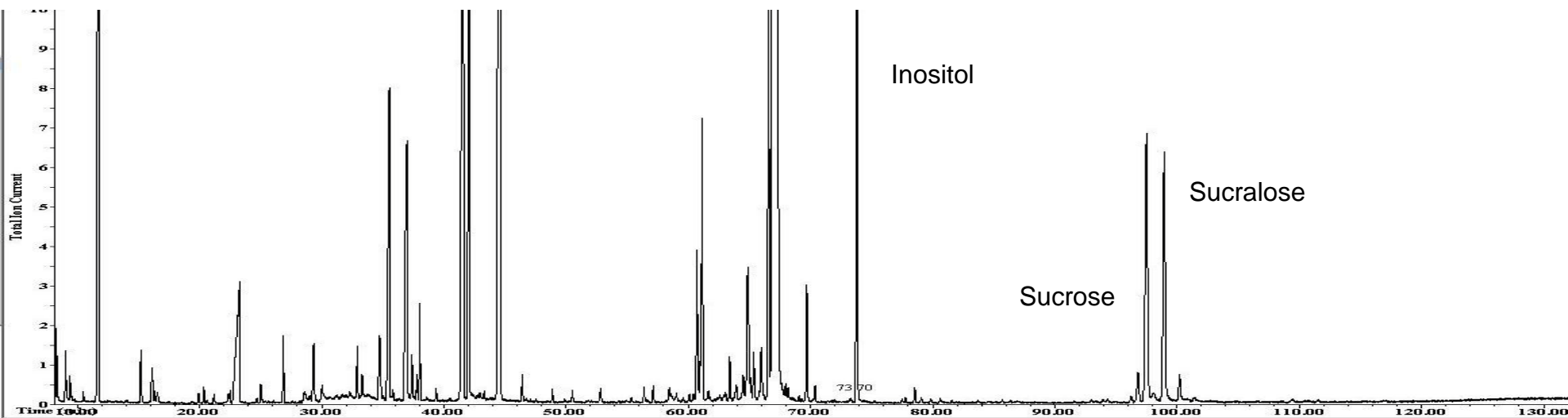
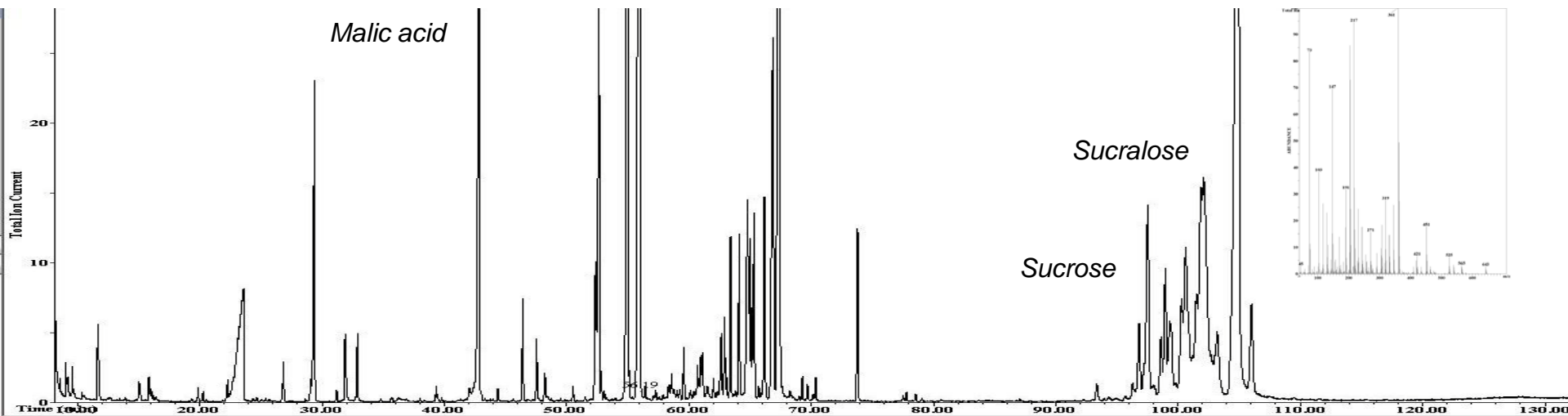
Results - Tableted tobacco - DS (top), MeOH (bottom)



Results for non-tableted dissolvable tobacco products

- Samples has to be cut into small pieces prior to silylation as too sticky to grind
- DS Scan (top) showed much more detail than reported by Goodpaster *et al.*, particularly the previously unreported sugar-like TMS derivative at ~105 minutes (see spectrum)
- DS Scan (bottom) for second type of non-tableted dissolvable tobacco products showed much different chemistry including apparent lack of malic acid, but had propylene glycol in addition to glycerol

Results - non-tableted dissolvable tobaccos - DS scans



Are Goodpaster's concerns on toxicology well founded?

- Toxicity associated with nicotine and smokeless tobacco
 - Dissolvable tobacco products well studied and have been on US-market since 2001 without significant adverse effects
 - No reported issues with regards to TSNAs, other toxicants
- Dental toxicity with sorbitol and to lesser extent xylitol
 - Sorbitol GRAS at 98% in candy, 75% in gum (21CFR184.1835)
 - Cited 1990 study by Kalfas *et al.* had only 23 subjects
 - FDA allows health claims on sorbitol and xylitol (21CFR101.80)
- Other toxicity concerns
 - Triethyl citrate – BIBRA misread; FEMA 3083, E1505, LD₅₀ >5g/kg
 - Cinnamaldehyde/coumarin – Cinnamaldehyde found in cassia bark oils, cinnamon; high variations in amounts of coumarin found in some samples (Woehrlin *et al.*, *JAFAC* 2010, 58, 10568-10575)

Conclusions

- The GC/MS techniques used by Goodpaster did not yield complete results
 - GC/MS scan of TMS derivatives missed many compounds
 - Sucralose and other disaccharides
 - Most monosaccharides and acids
 - Chlorogenic acid and other markers of product chemistry
 - GC/MS scans of volatile and semivolatile compounds
 - Showed major added compounds
 - Missed many tobacco compounds that could be useful in understanding product chemistry
- The toxicology reported was less than correct
 - Overstated potential adverse effects of dissolvable tobacco products
 - Toxicological properties given for some additives less than accurate

Sponsorship and references

■ Sponsorship

- This research was funded entirely by Lauterbach & Associates, LLC
- The travel and lodging expenses of the speaker were also funded entirely by Lauterbach & Associates, LLC

■ References – Copies of this presentation and related presentations on oral tobacco products along with abstracts of our journal articles can be found at <http://www.lauterbachandassociates.net/2101.html>