

# Can we continue to ignore chemical constituents of novel smokeless tobacco products other than the GothiaTek® analytes?

**John H. Lauterbach, PhD, DABT  
Lauterbach & Associates, LLC  
Macon, GA 31210-4708 USA**

**Deborah A. Grimm, Ph.D.  
Tulane University Coordinated Instrumentation Facility  
New Orleans, LA 70118-5698**

# Outline for presentation

- Background
- Objectives for presentation
- Press releases and quotations
- Analytical strategies for dissolvable tobacco
  - Strategies reported by others
  - Our analytical strategies
- Results
- Conclusions
- Sponsorship and references

# Background – 1

- 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<sup>®</sup> analyte levels below those found in Swedish snus believed to have minimal health risks
- Main focus of critique on dissolvable tobacco products
  - Has not been on levels of harmful constituents
  - But on issues related to attractiveness of products to special populations, alleged candy-like properties, and other aspects of abuse liability – products too effective?
- Minor focus on pediatric poisonings (packaging)

## Background – 2

- US FDA list of 96 harmful & potentially harmful constituents (“HPHC”) in tobacco products and tobacco smoke
  - Harmful constituents (“HC”)
    - Human carcinogens (known, likely, probably, possibly)
    - Respiratory toxicants and cardiovascular toxicants
    - California EPA reproductive and developmental toxicants
  - Potentially harmful constituents (“PHC”) have at least two of the following measures of abuse liability (addiction):
    - Central nervous system activity
    - Animal drug discrimination
    - Conditioned place preference
    - Animal self-administration
    - Human self-administration
    - Drug liking
    - Signs of withdrawal

## Background – 3

- Testimony presented at meetings of FDA Tobacco Products Scientific Advisory Committee (“TPSAC”) has brought forth additional definitions of PHC
  - Intentional additives – not constituents – that are believed to
    - Mask tobacco taste or bitterness
    - Reduce or ameliorate smoke harshness
    - Give products candy-like taste or aroma or sweet taste
    - Allow higher consumption rates
  - Definitions first applied in discussions on menthol and now being used in discussions on dissolvable tobacco products
- State-based anti-tobacco agencies trying to minimize or prohibit use of dissolvable tobacco products based on non-FDA definitions of potentially harmful constituents

# Objectives

- Show some examples of US state-based initiatives against dissolvable tobacco products
- Review the analytical techniques used to characterize dissolvable tobacco products
- Show differences in product chemistries among different types of dissolvable tobacco products
- Focus on tobacco constituents and additives that may be of concern in terms of current proposed and possible future lists of harmful and potentially harmful constituents – Note: apparently some regulators think it is bad if we formulate products that are well accepted by consumers – sweeteners as potentially harmful

## Press releases and quotations on dissolvable tobacco products

- "New 'dissolvable tobacco' products may increase risk of mouth disease." *Science Daily*, 16 Mar 2011
- "Sorbitol's presence is alarming to dentists," says Goodpaster, "because it stimulates cavity-causing bacteria." *Chemical & Engineering News*, 24 Feb 2011
- "In passing today's resolution, the board made an important statement – that dissolvable tobacco products are a risk to the public's health." Dr. C. Urbina, Colorado Dept. of Pub. Health and Environ., 22 Sep 2011
- "Smokers ... may get a higher dose of nicotine than they are used to, ... and in more extreme cases, seizures, coma, and death." Indiana Tob. Prev. Cessation Comm.

# 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

# Analytical strategies reported for dissolvable tobacco products

- Goodpaster *et al.*, *JAFAC* 2011 59, 2745-2751
  - Acetone extraction (ultrasonic) of ground dissolvable tobacco products (200 mg/2000  $\mu$ 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  $\mu$ 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 (*JAFAC* 1997, 45, 844-849)
    - Menthol, nicotine, triethyl citrate, carvone, vanillin, possible terpenoid, cinnamaldehyde and coumarin (only one style)

# Our analytical strategies

- DS scan ground dissolvable tobacco products
  - 100 mg with 400  $\mu$ L DMF and 800  $\mu$ 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  $\mu$ L methanol +ISTD (phenanthrene-d<sub>10</sub>)
  - 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+

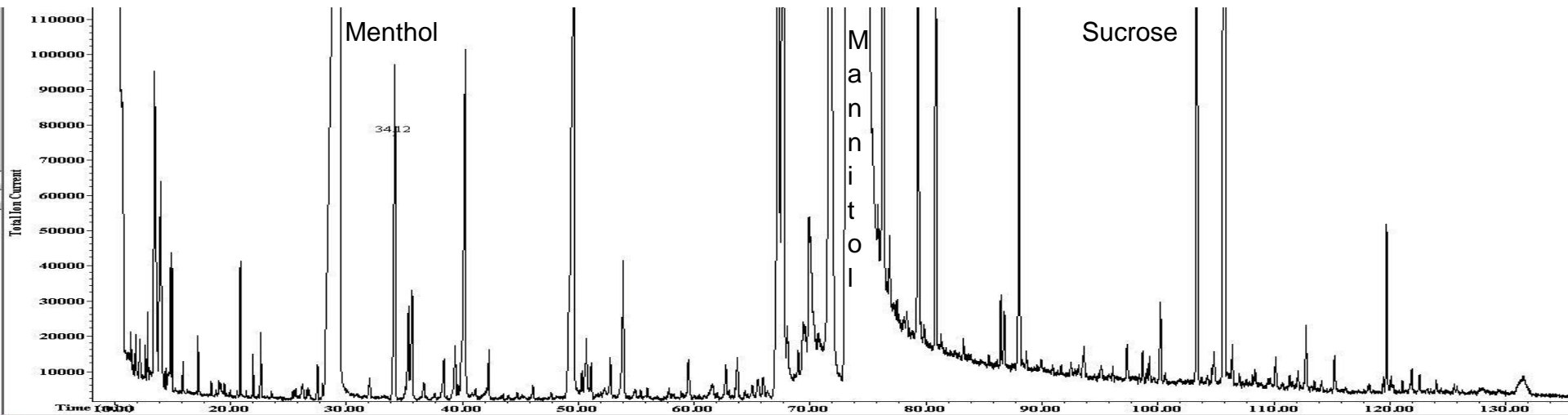
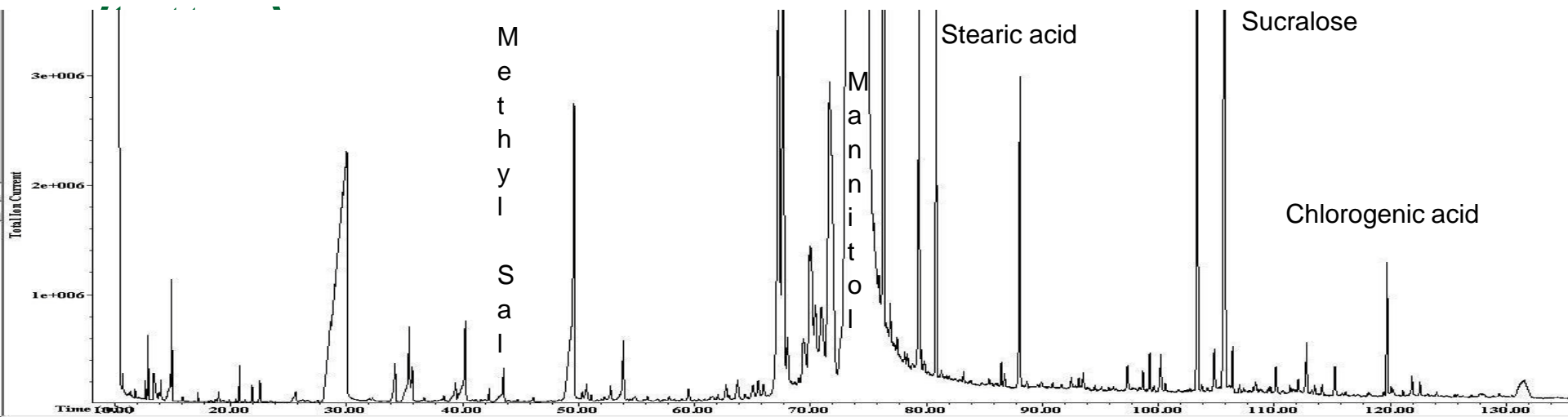
## Cautionary note on the samples we analyzed

- The samples we analyzed were from one-time samplings at several retail stores in Georgia, Florida, and North Carolina
- In one case, we obtained product from another research group that may have been test market product
- Since we may have analyzed test market product and/or brand-styles with limited distribution, our analyses should be viewed with caution as products may have changed after we obtained our samples
- Analyses of products sampled in a systematic matter should be done before conclusions are drawn as to the compositions of current product

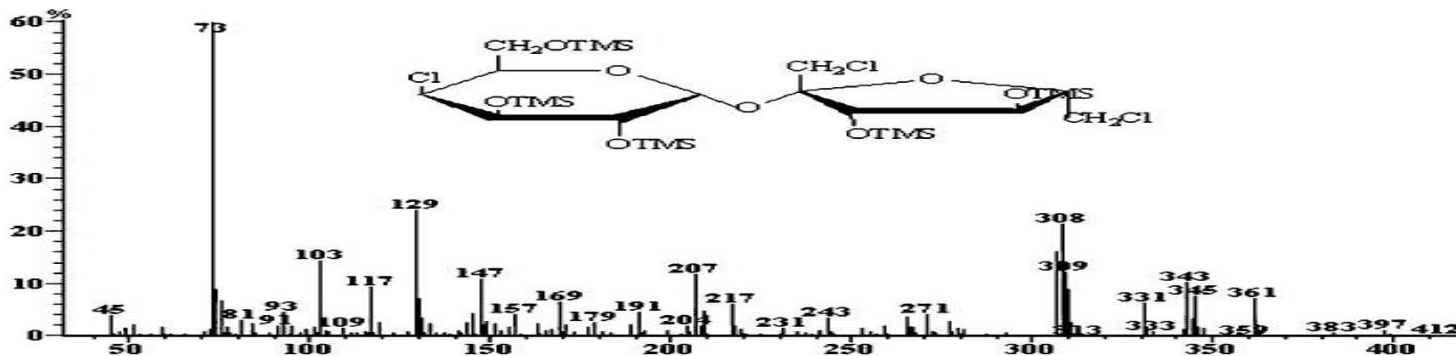
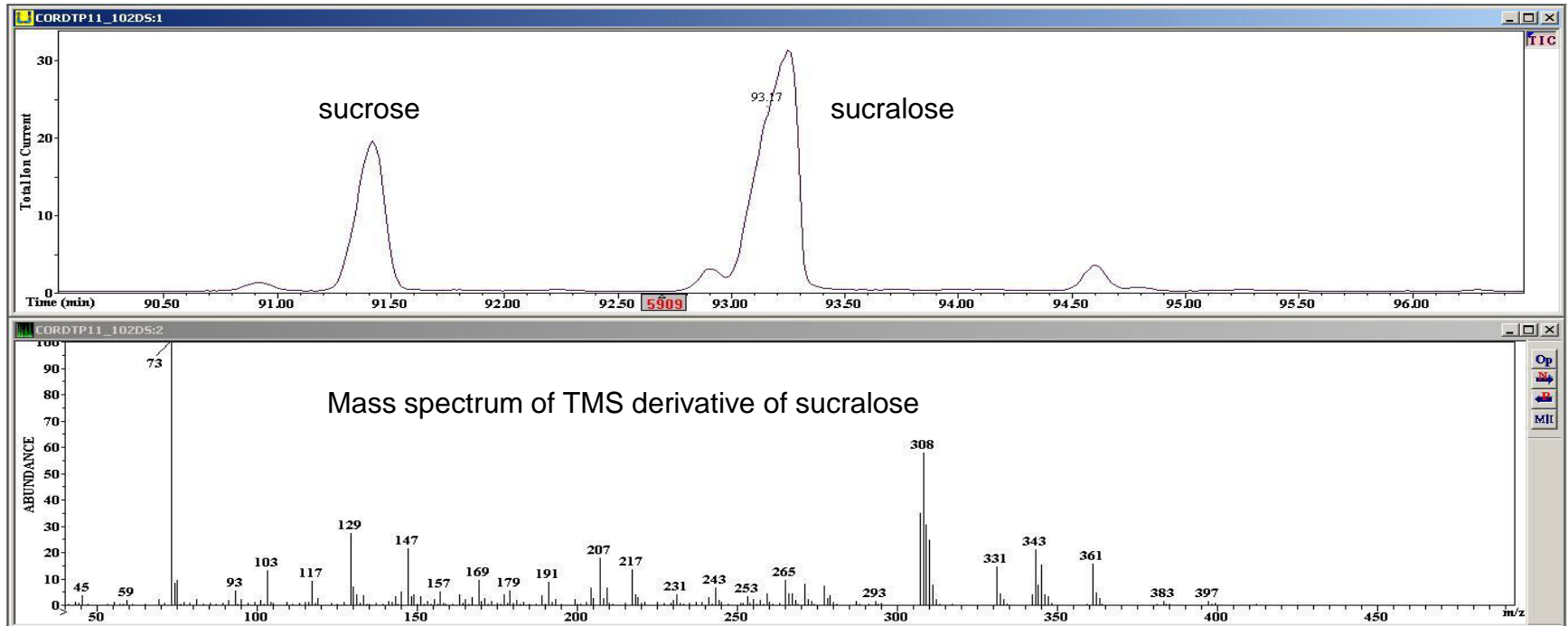
# Some results for two dissolvable tobacco products

- DS scan results for two dissolvable tobacco products
  - 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 - Dissolvable tobaccos - Wintergreen (top), Mint

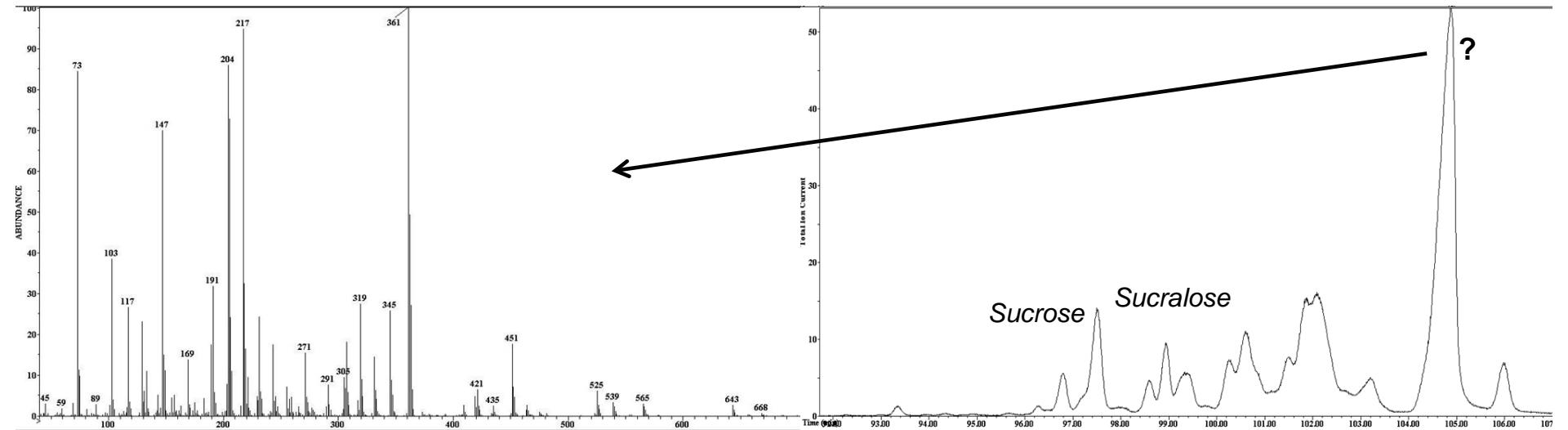
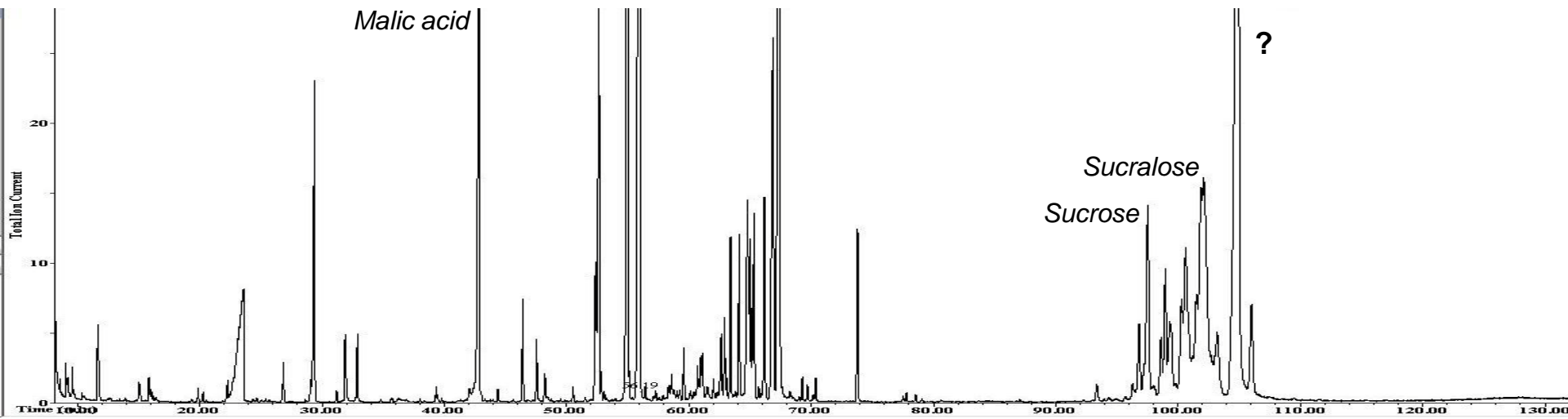


# Sucralose in a dissolvable tobacco product



Mass spectrum of TMS derivative of sucralose reported by Qiu *et al.*, **Chromatographia** 2007, 66, 935-939

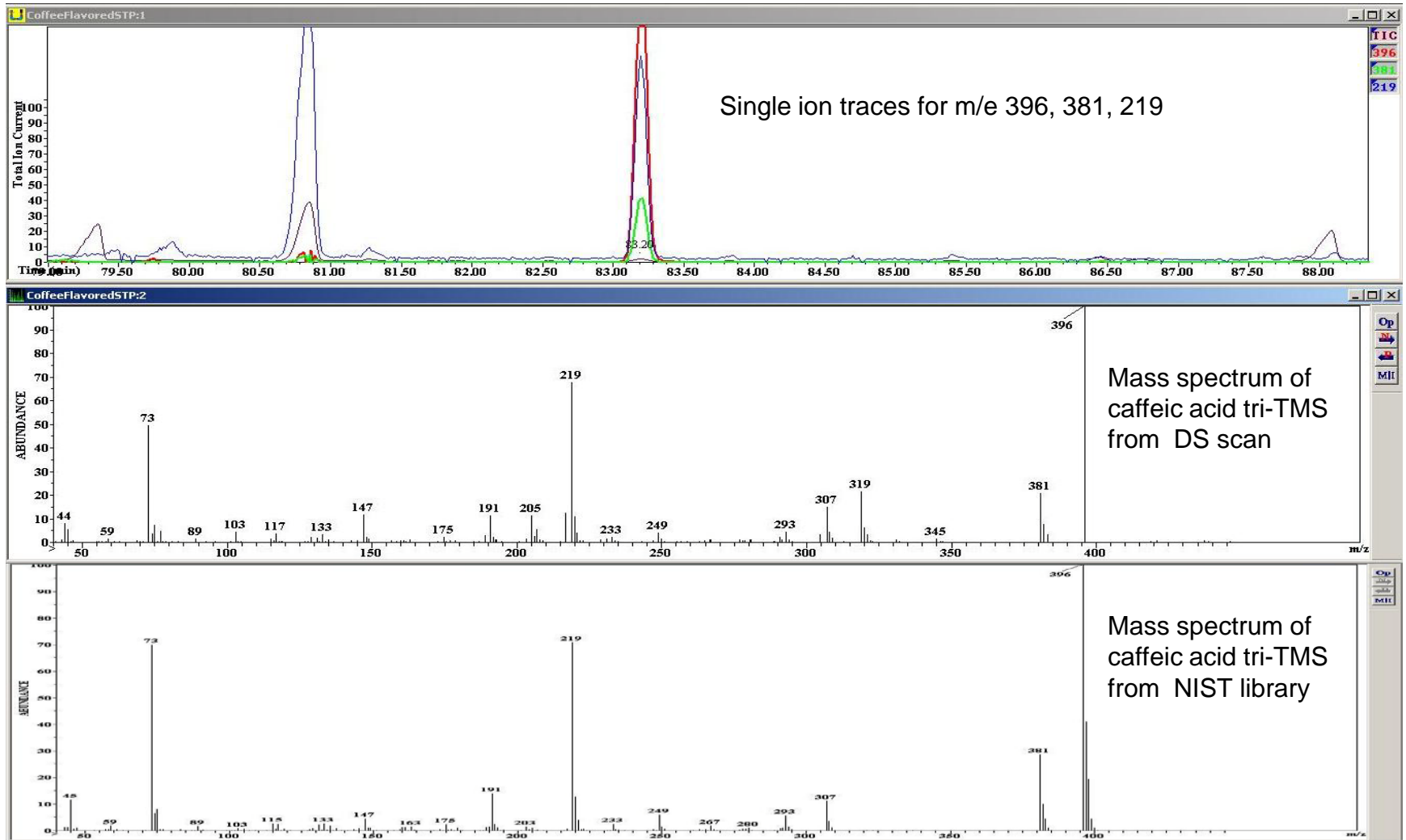
# DS scan of another type of dissolvable tobacco product



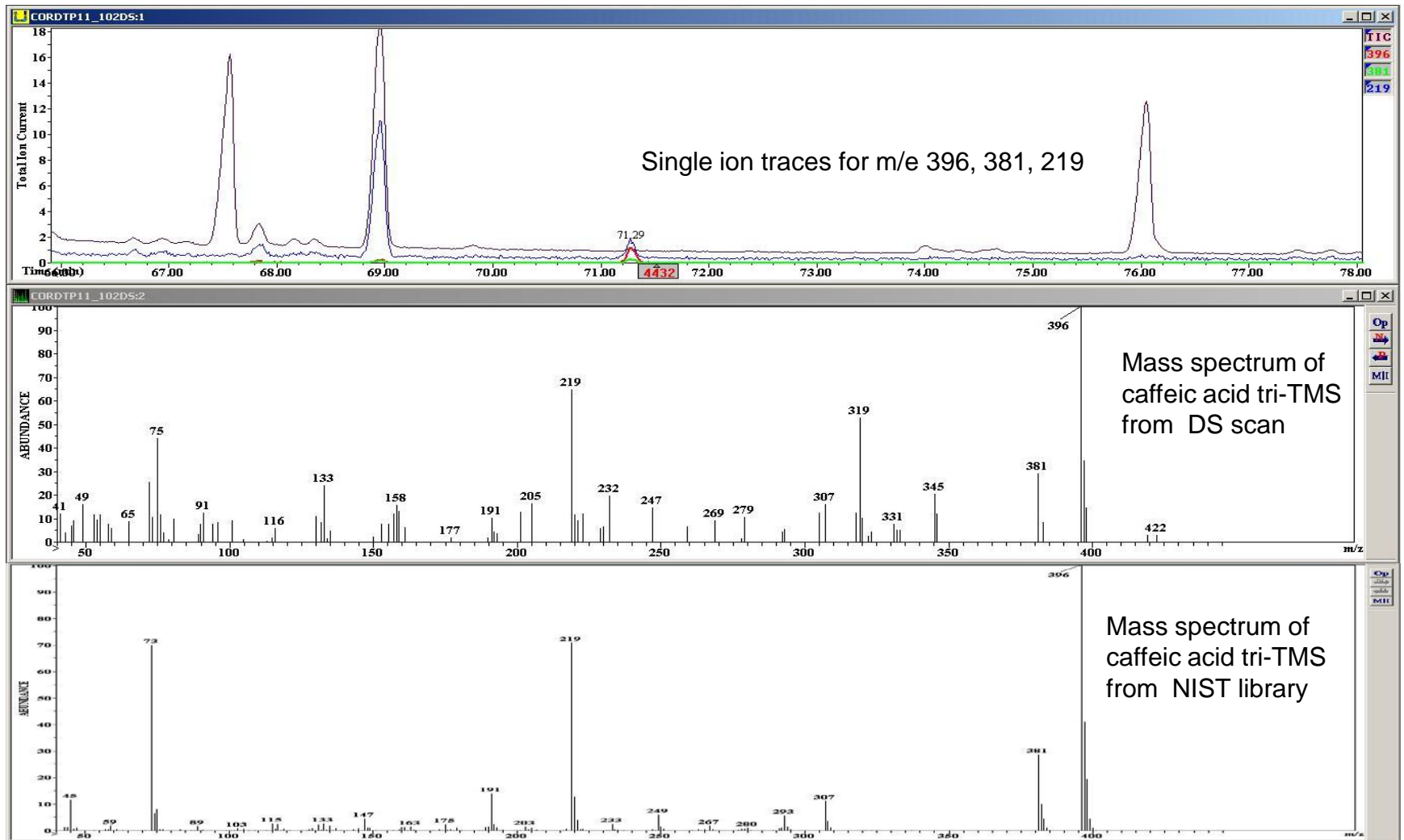
# Caffeic acid in smokeless tobacco products

- Caffeic acid is on FDA's proposed list of harmful and potentially harmful constituents ("HPHC") in tobacco products and tobacco smoke
  - Everyone was surprised, common constituent of coffee
  - Known rodent carcinogen (<http://potency.berkeley.edu>)
    - Kidney, stomach tumors in rats – TD<sub>50</sub> 297 mg/kg/day
    - Lung, kidney, stomach tumors in mice -- TD<sub>50</sub> 4900 mg/kg/day
  - TPSAC decision based on presence in tobacco smoke
- Caffeic acid ("CA") found in flue-cured tobaccos – Court and Hendel, *Tob. Sci.* 1986, 30, 56-59
  - CA can be found in tobacco from KY3R4F cigarettes
  - CA can be found in tobacco from chocolate-flavored filtered cigar
- Can caffeic acid be found in STP?

# DS scan showing caffeic acid in coffee-flavored STP



# Caffeic acid in a dissolvable tobacco product



# Conclusions

- Novel STP such as dissolvable tobacco products are easily analyzed with GC-MS equipment in most college undergraduate chemistry laboratories
- Novel STP make an attractive target for analytical chemists outside the tobacco industry to do tobacco analyses and get support from the anti-tobacco forces
- Use of very intense sweeteners in STP may raise issues of potential harm by making products overly attractive
- Caffeic acid, a compound on the FDA's HPHC list, appears to be present in some STP brand-styles
- Analytes other than the GothiaTek<sup>®</sup> analytes should be considered when evaluating novel STP products

# 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>