Can liquid-chromatography scan techniques be as useful a tool for e-liquids as gas-chromatography scan techniques have been for cigarette tobaccos?

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Gas chromatography (GC) scan techniques

- Applicable to volatile, semivolatile, and nonvolatile compounds found in tobacco and tobacco products
- Nonvolatile compounds such as sugars can be made volatile with derivatization
- GC scan techniques have been useful for detecting product contamination, sources of odd-taste, etc.
- Scan techniques applied to unsmoked product to avoid variation that occurs with machine smoking

E-liquids and tobacco constituents

- In a broad sense, most e-liquids contain a subset of compounds found in tobacco, but in different proportions (some trace flavors in tobacco are major flavor components of e-liquids)
- On the other hand, glycerin (VG), propylene glycol (PG) and often nicotine are major components as in American-style cigarettes; simple sugars also found in some e-liquids

Liquid chromatography (LC) scan techniques

- Applicable for most compounds from volatile to nonvolatile; little need for high temperatures
- Do not have to worry about thermal degradation
- Generally no need for compressed gas systems
- However, LC has some problems for scan work
  - Lack of positive peak identification without expensive instrumentation [e.g., mass spectrometry (MS)]
  - Lower chromatographic resolution than GC
- Fortunately, these problems are not insurmountable

LC approaches for scan techniques

- Use several different chromatographic conditions
  - Use columns with different stationary phases
  - Use different mobile phases and/or use columns in normal-phase (NP), reverse-phase (RP), or aqueous-normal- phase (ANP) modes
  - Generally 3 distinctly different conditions will allow for separation of compounds in a mixture
- Use selective detection
  - Use variable wavelength UV-VIS detectors under conditions that favor compound-selective detection
  - Use less-sensitive detection for major components

Goals for e-liquid scan techniques

- Confirm that we made what we intended to make
- Confirm that product is within regulations for allowed ingredients and amounts used
- Spot changes in products due to aging or other post-production events
- Spot products that contain ingredients that should not be used under any circumstances
- To achieve these goals, must know what is in “good” products and concentration ranges for the ingredients in “good” products

Identifying the “good” in “good” products

- Known “good” e-liquids and flavor concentrates used
  - Mixture of 17 high-VG, low-nic, highly-flavored products from one manufacturer that we used in our prior studies
  - Mixture of 76 flavor concentrates reportedly from well-known flavor house that was diluted 20/80 with 50/50/2.5 VG/PG/nic base e-liquid; also used in our prior studies
  - Mixture of commercial e-liquids including some claiming to be nicotine salt formulations
- In addition, test mixtures were spiked with adulterants reported in the literature as well as nonvolatile sweeteners such as sucralose

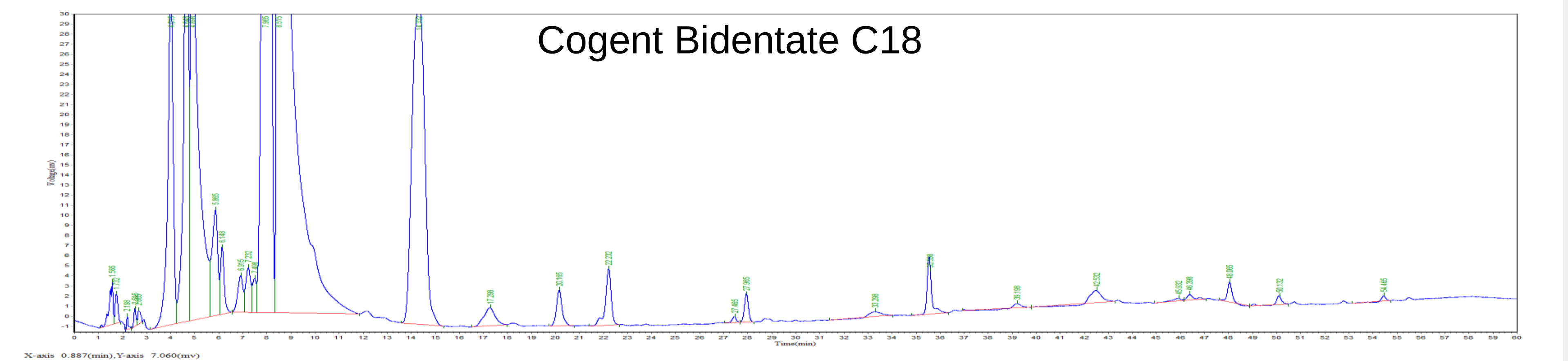
Instrumentation

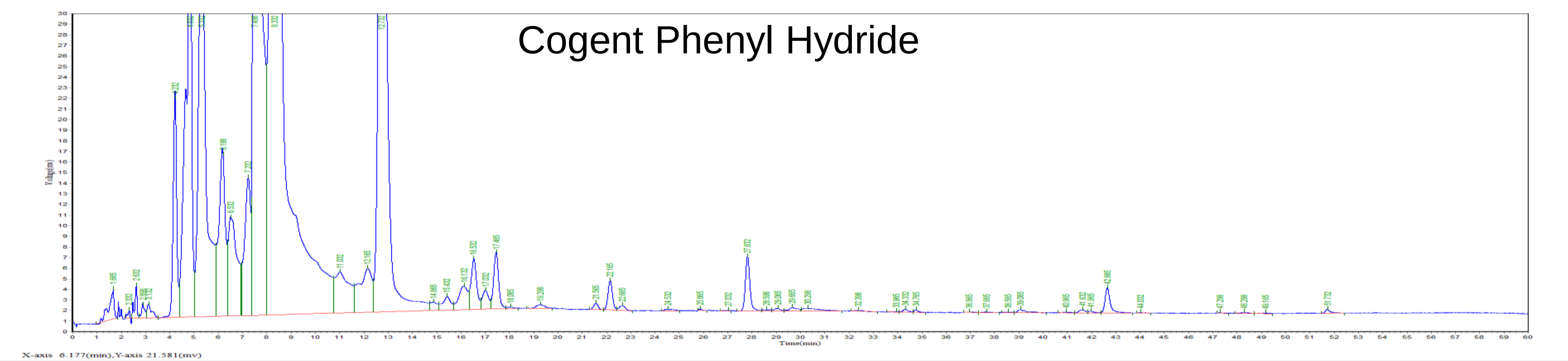
- Fluidics
  - Waters 510 pumps, 680 gradient controller
  - Rheodyne 7725 (20 µL), 9825 (10 µL) injectors
- Detectors
  - Waters 410 Differential Refractometer and Column Heater
  - Waters 486 Tunable Absorbance Detectors using following wavelengths (nm) for selective detection: 280 (ArCO-), 260 (nicotine, other Ar-), 242 (menthol), 232 (RCOOR'), 212 (RCOOH), 195 (ROH)
- Chromatography data systems
  - N2000 chromatography data systems [Science Technology (Hangzhou, China) Inc.]

Chromatography

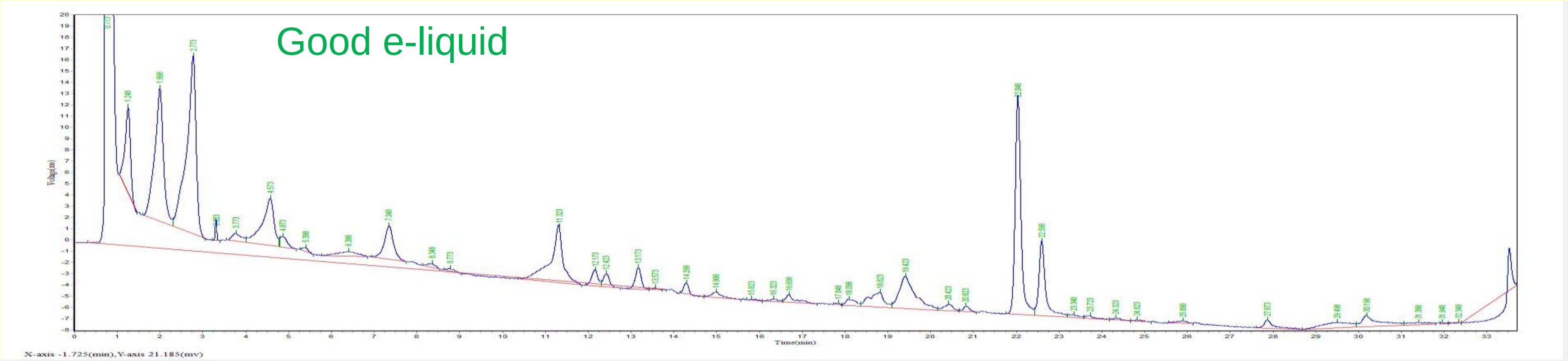
- Columns
  - Cogent Bidentate C-18, Phenyl Hydride, Diol, and Amide (all 250 x 4.6 mm)
  - ZORBAX SB-C3 column (150 x 2.1 mm)
- Operating conditions
  - RP LC with Cogent columns (Bidentate C-18, Phenyl Hydride): Pump A: 17/83 ACN/H2O; Pump B: 83/17 ACN/H2O; 1 mL/min; time (min)/% B: 0/0, 5/10, 54/90
  - RP LC with ZORBAX SB-C3 column: Pump A: 17/83 ACN/H2O; Pump B: 83/17 ACN/H2O; 0.5 mL/min; time (min)/% B: 0/0, 2/10, 30/100
  - Isocratic elution for Cogent Diol and Amide: 1 mL/min with 50/50 mixture Mobile Phases A and B (ANP conditions)

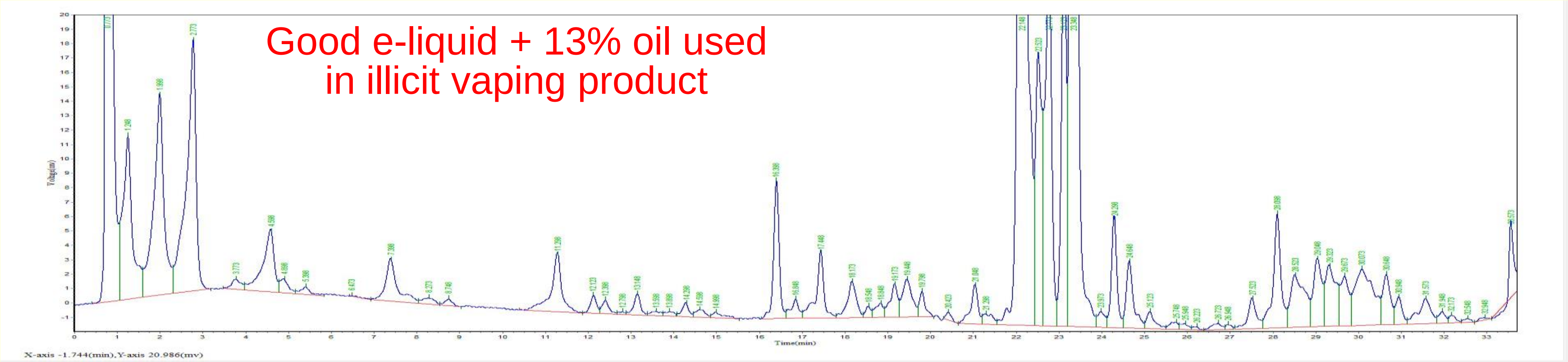
Same sample, but different column





“Good” vs. “Bad” same column





Conclusions

- LC scan techniques are an easy, effective tool for characterizing e-liquids
  - Can tell the “good” from the “bad”
  - Can be applied using simple, low-cost instrumentation
  - Sample preparation is easy; just weigh and dilute
  - No need to collect the aerosol from machine vaping of the e-liquid to tell “good” from ‘bad”
- There are drawbacks to this technique
  - Requires known “good” e-liquids and/or ingredients
  - Time-consuming unless one has UV detector that can simultaneously record signals at multiple wavelengths
  - In most cases, cannot positively identify the constituents that make an e-liquid bad