

An 18-month e-liquid stability study

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Outline for presentation

- Basis for the research
 - Change in color of e-liquids in pods and tanks during use
 - Change in taste of aerosol with changes in power
 - Prior research showed that even moderate temperatures caused changes
- Protocol for determining chemical changes over aging
 - Sampling
 - Chromatographic analyses
- Example chromatograms showing differences – frozen versus aged
 - Chromatography of samples diluted prior to injection
 - Injection of undiluted e-liquids
 - Injection of undiluted e-liquids containing menthol
- Conclusions

Sampling protocol for the aging study

- Products for the study – all 120 mL bottles -- received early October
 1. “CHRUNCHY COOKIE” and “COCONUT”
 2. “CHERRY PIE” and “CUSTARD”
 3. “BLUE RASPBERRIES” and “CANDY”
 4. “CHOCO CHIP COOKIE” and “VANILLA ICE CREAM”
- Weekly sampling beginning on 31 OCT 2019
 - Two samples were squeezed from each bottle into 4 mL screwcap glass vials
 - One set was kept at ambient conditions, the other placed in chest-type freezer
 - 120 mL bottles kept at ambient conditions
 - Both ambient and frozen samples of Products 1 and 4 were taken on 6 Feb. 2020 and sent to Labstat International for Neutral Red Uptake cytotoxicity assays
 - Lab operations suspended on 6 Mar. 2020 on account Covid-19. All frozen samples kept frozen; all ambient samples kept on laboratory desk
 - Final sample analyses begun on 8 May 2021

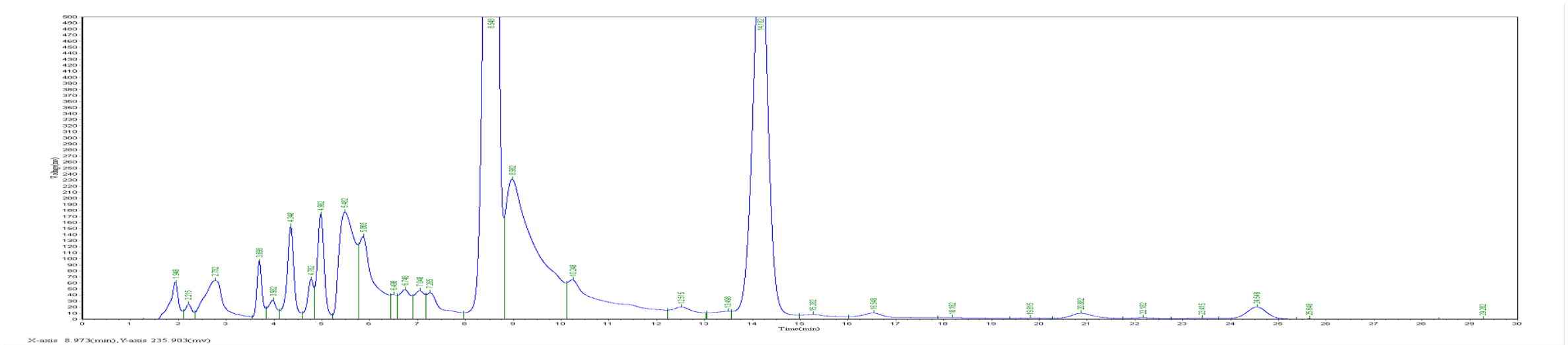
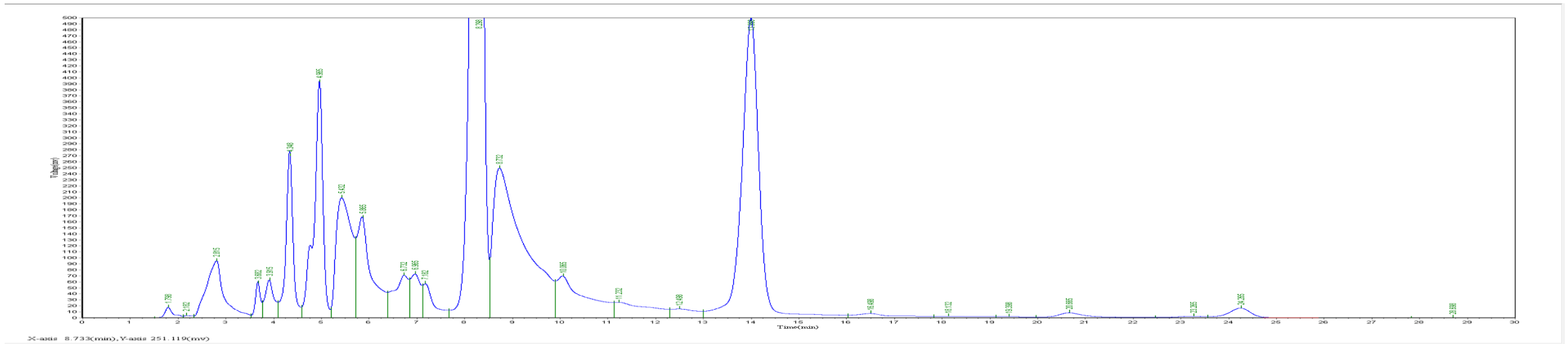
Chromatography protocol for the aging study

- Samples analyzed after dilution with methanol to 1 % and 10 %
 - Isocratic system with loop injection valve and variable wavelength UV detector
 - Acetonitrile /water mobile phase at 75/25, 50/50, or 25/50 mixtures (1 ml/min)
 - Cogent Bidentate C18 and Phenyl Hydride columns (250 x 4.6 mm)
 - 10 µL injection volume
 - Use 195 nm and 280 nm for UV detection (separate injections each wavelength)
 - 1 µL injection volume as described below with Bidentate C18 column
- Samples analyzed without dilution
 - Isocratic system with loop injection valve and differential refractometer detector
 - Acetonitrile /water mobile phase at 75/25 mixture at 1 mL/min
 - YMC Triart C18 column (250 x 4.6 mm)
 - 1 µL injection volume
 - Both column oven and detector thermostatted at 35 °C
 - Final sample analyses begun on 8 May 2021
 - Mobile-phase (10 µL) injected between runs to clean system

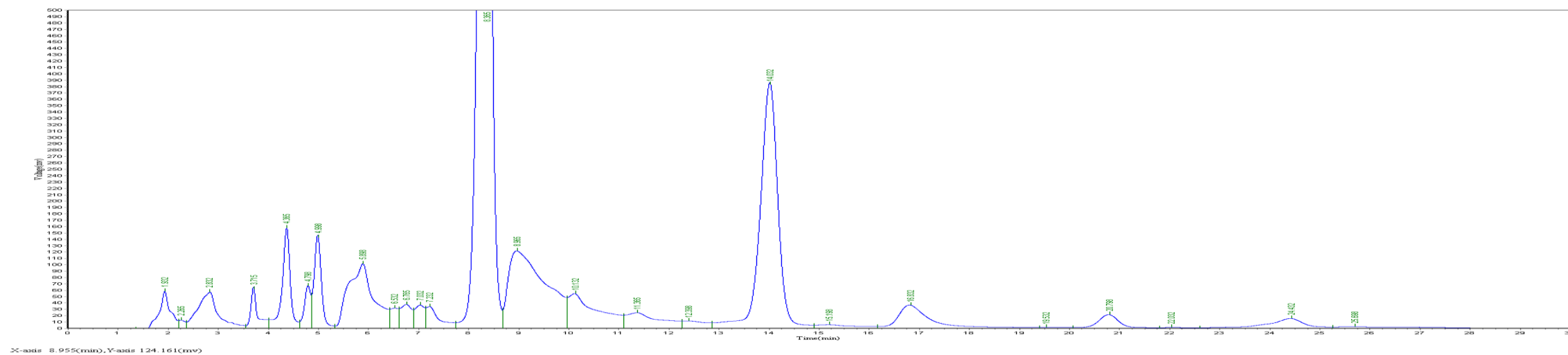
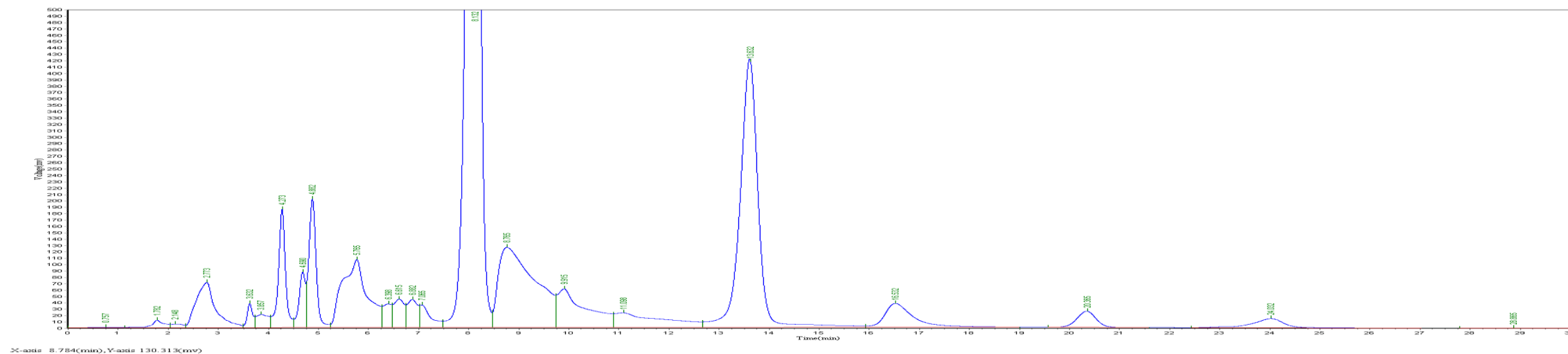
Index of chromatograms

Slide Number	Product Number or Name	Chromatographic conditions	Important differences frozen (or new) versus aged
6	2	Bidentate C18, UV 280 nm 25 acetonitrile 75 water	Increased height of peak at 14 minutes in aged, likely PG acetal of aromatic aldehyde
7	4	Bidentate C18, UV 280 nm 25 acetonitrile 75 water	Only clear difference is increase in height of peak just before 2 minutes in aged product
8	1	Bidentate C18, UV 280 nm 25 acetonitrile 75 water	Aging eliminated peak at 9 minutes and deceased peak at 13 minutes
9	3	Bidentate C18, UV 195 nm 75 acetonitrile 25 water	Aging eliminated broad peak at 15 minutes
10	4	Triart C18, RID 75 acetonitrile 25 water	Aging reduced height of peak just after 6 minutes
11	V2 Menthol 2.4	Triart C18, RID 75 acetonitrile 25 water	Aging reduced height of menthol peak (just before 6 minutes but others increased)

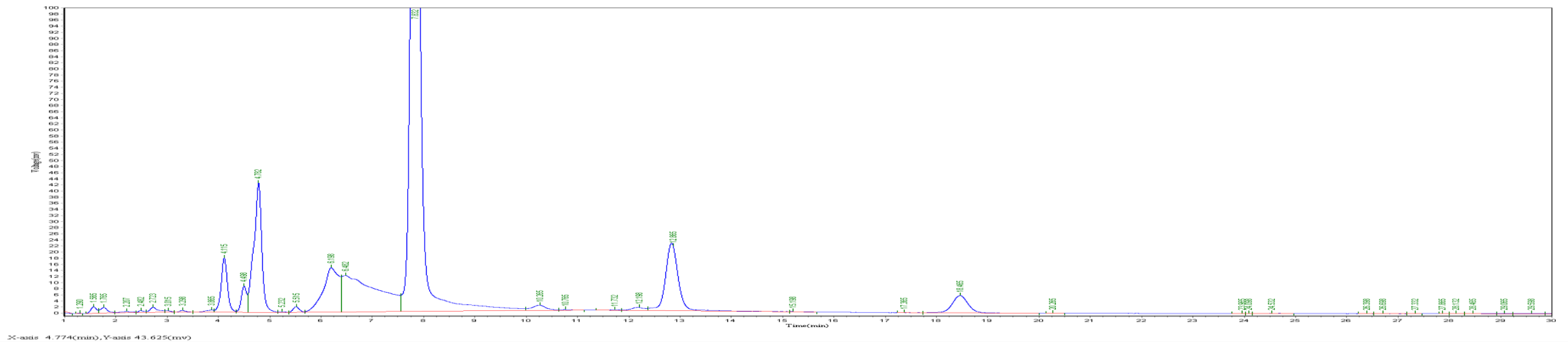
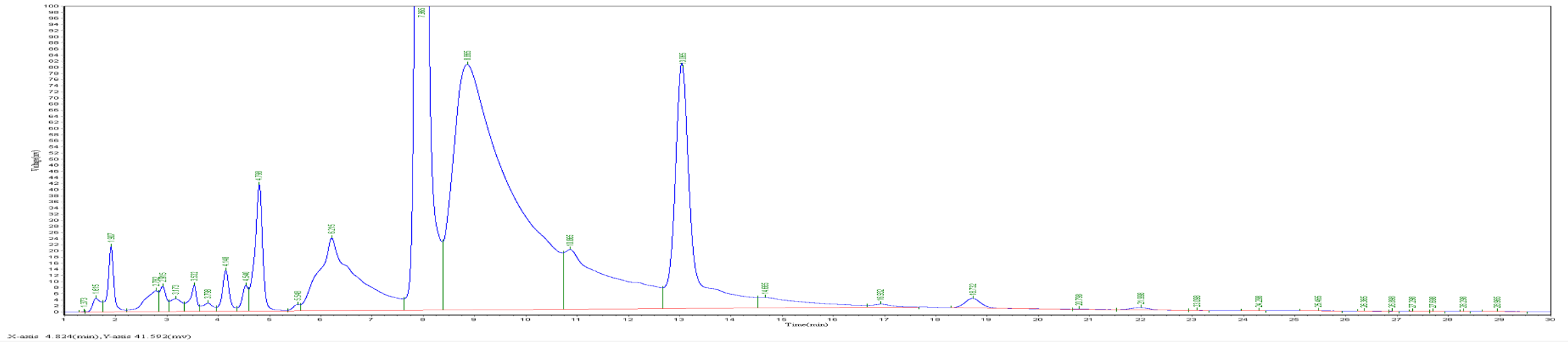
Frozen versus aged – Product 2 280 nm BiDC18



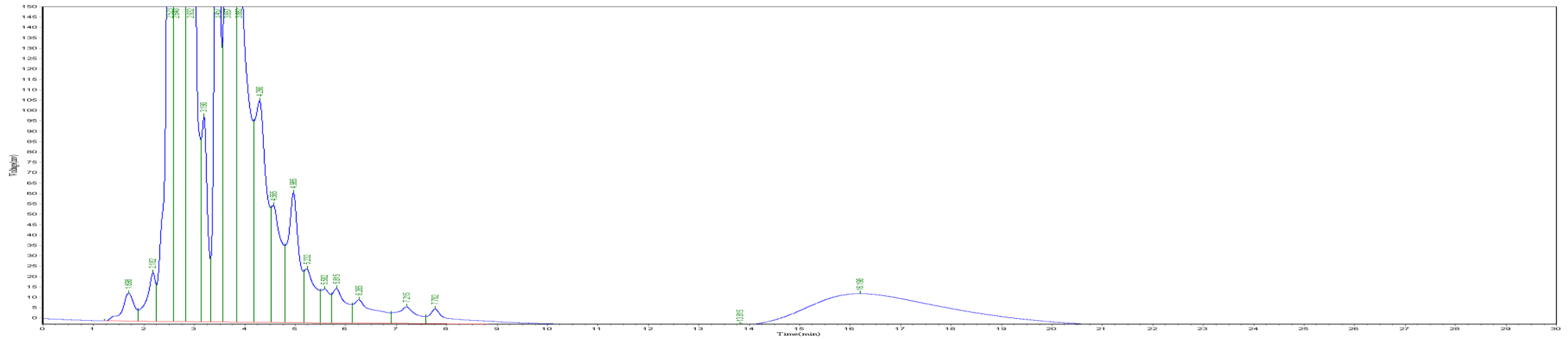
Frozen versus aged – Product 4 280 nm BiDC18



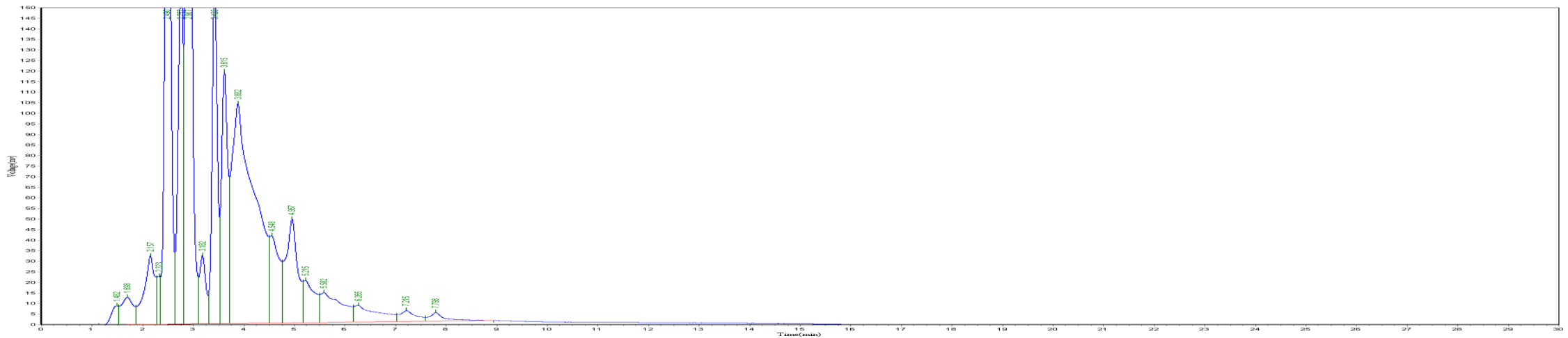
Frozen versus aged – Product 1 280 nm BiDC18



Frozen versus aged – Product 3 195 nm BiDC18

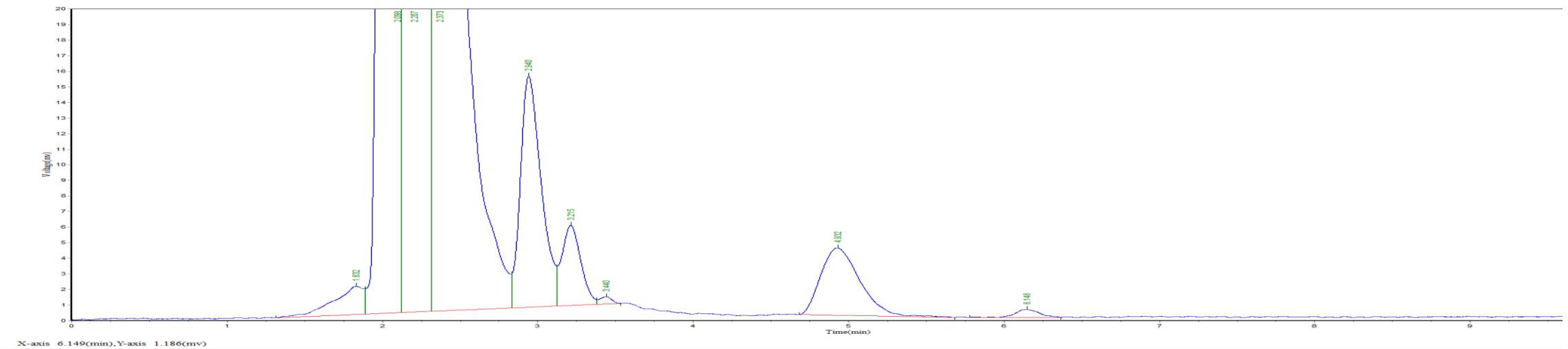
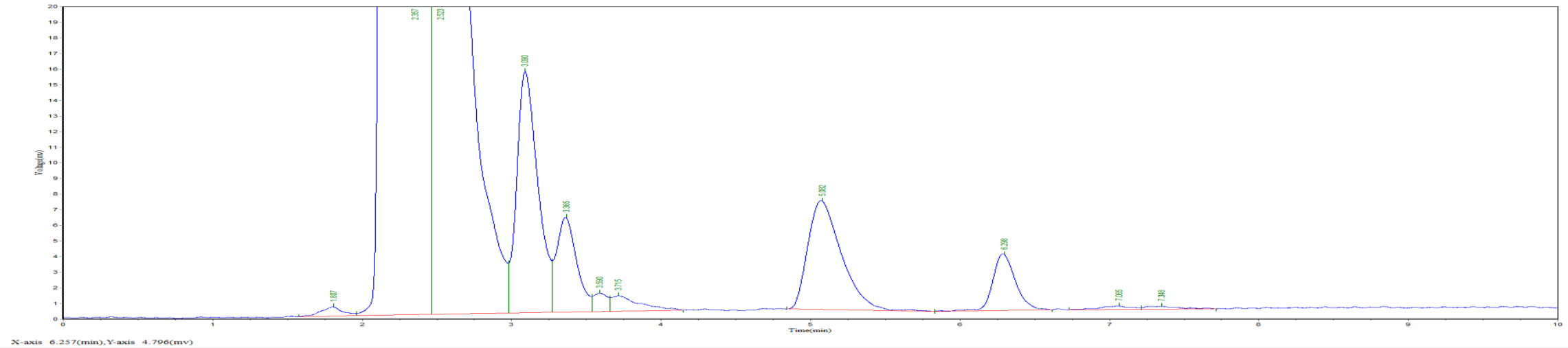


X-axis: 4.966(min), Y-axis: 61.007(mv)

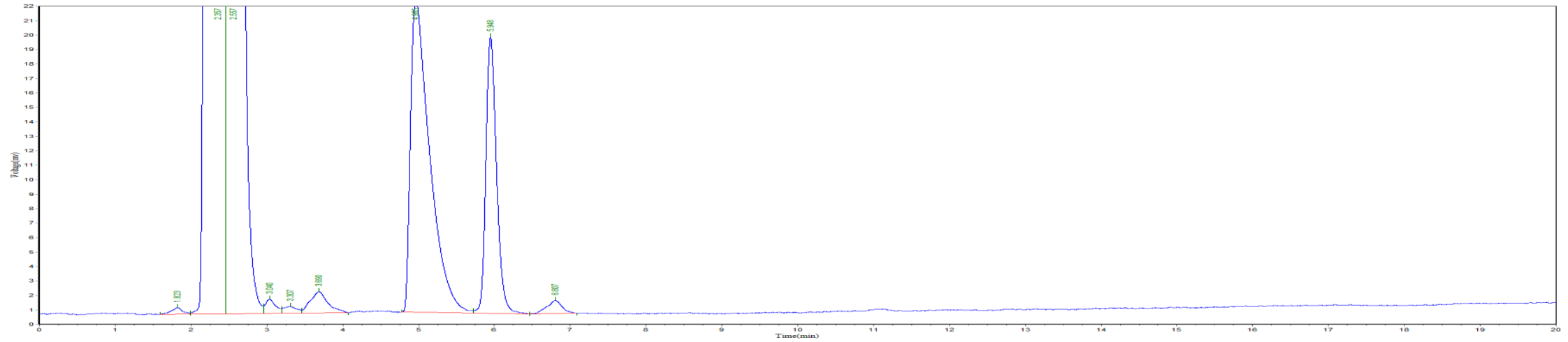


X-axis: 4.983(min), Y-axis: 50.336(mv)

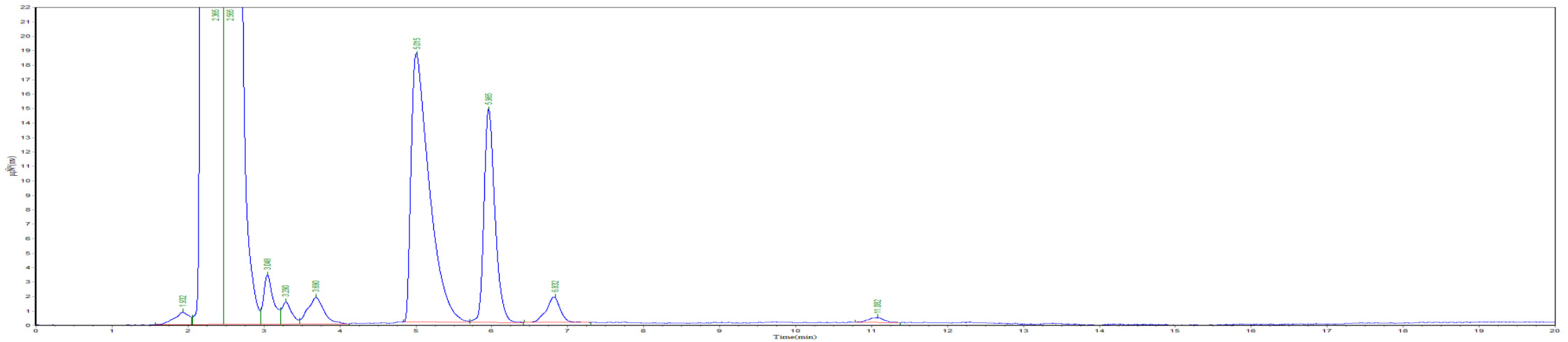
Frozen versus aged – Product 4 RID Triart C18



New versus old – V2 Menthol 2.4 RID Triart C18



X-axis 5.939(min), Y-axis 20.232(mv)



X-axis 5.961(min), Y-axis 15.333(mv)

Conclusions

- Most e-liquids will change with time when kept at room temperature
- Apparent changes may include
 - Loss of volatiles
 - Reaction of propylene glycol and possibly glycerol with aromatic aldehydes
- E-liquid product changes can be found with simple LC instrumentation and conventional 250 x 4.6 mm columns
- Samples can be analyzed without dilution with 1 μ L injection
 - Saves sample preparation time
 - Permits use of refractive index detectors
- The cytotoxicity assays on frozen product and product aged for six months under ambient conditions did not show any differences
- It is helpful to have multiple batches of each brand-style to be investigated along with samples of flavors commonly used in e-liquids