Poster Reprint

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# Up in Vape: What is in my E-Juice Other than Nicotine, Propylene Glycol, and Glycerin

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## Introduction

In 2017, 2.8% of adults in the United States use e-cigarettes or vaporizers. It is estimated that by 2025 vaping will be a $47.11 billion market. Initially, these were designated as e-cigarettes, to aid a person to stop smoking tobacco cigarettes. With the different ratios of propylene glycol to glycerin; creating a large cloud, the number of flavors available, and removal of nicotine and the addition of cannabis components many more people are turning to vaping. The analysis of these e-liquids consists of diverse flavoring agents. This work will present an optimized chromatography and workflow to find features, identify compounds, create a personal library, and easily create a MRM method for low level detection of significant targets.

## Methods

A variety of E-liquids were purchased from a local vape store in Sunnyvale, Ca. Due to the high viscosity of the sample, a 2:1 dilution in acetone was required. A one microliter injection was made into a split/splitless inlet at 240ºC, with a split injection of 25:1 using the Agilent UI low pressure drop liner. Separation was performed on a DB-Wax UI 30 m x 250 µm x 0.25 µm with a He carrier gas flow of 1.2 mL min-1. The GC was coupled to the Agilent 7000D with an ion source temperature of 300 ºC and 150ºC for the two quadrupoles. Data analysis was performed using Agilent MassHunter Data Analysis Software.

## Preliminary Data

The mixture of e-liquids included fruity, sweet desserts, and traditiona lysis of a variety of flavoring agents. The DB-Wax UI column was an optimal phase for this analysis due to the reduced activity for acids and high polarity for the polar components in the e-liquid. This phase also allowed for the retention of small alcohols, methanol, isopropanol, and ethanol to elute around 2 mins with good peak shapes. The first step in the process was a full scan acquisition, followed by chromatographic deconvolution to provide cleaned spectra for library searching. The NIST17 library was used for tentative identifications and correlation to the Harmful and Potentially Harmful Constituents (HPHCs) list for tobacco products from the FDA. Table 1*

## Experimental

| | | |
|---|---|---|
| Acetaldehyde | Coumarin | Nitrobenzene |
| Acetamide | Cresols | Nitromethane |
| Acetone | Crotonaldehyde | 2-Nitropropane |
| Acrolein | Cyclopenta[c,d]pyrene | N-Nitrosodiethanolamine |
| Acrylamide | Dibenz[a,h]anthracene | N-Nitrosodiethylamine |
| Acrylonitrile | Dibenzo[a,e]pyrene | N-Nitrosodimethylamine |
| 4-Aminobiphenyl | Dibenzo[a,h]pyrene | N-Nitrosomethylethylamine |
| 1-Aminonaphthalene | Dibenzo[a,i]pyrene | N-Nitrosomorpholine |
| 2-Aminonaphthalene | Dibenzo[a,l]pyrene | N-Nitrosonornicotine |
| Anabasine | 2,6-Dimethylaniline | N-Nitrosopiperidine |
| o-Anisidine | Ethyl carbamate (urethane) | N-Nitrosopyrrolidine |
| Benz[a]anthracene | Ethylbenzene | N-Nitrososarcosine |
| Benz[j]aceanthrylene | Ethylene oxide | Nornicotine |
| Benzene | Formaldehyde | Phenol |
| Benzo[b]fluoranthene | Furan | Propionaldehyde |
| Benzo[k]fluoranthene | Indeno[1,2,3-cd]pyrene | Propylene oxide |
| Benzo[b]furan | Isoprene | Quinoline |
| Benzo[a]pyrene | Methyl ethyl ketone | Styrene |
| Benzo[c]phenanthrene | 5-Methylchrysene | o-Toluidine |
| 1,3-Butadiene | (NNK) | Toluene |
| Caffeic acid | Naphthalene | Vinyl acetate |
| Catechol | Nicotine | Vinyl chloride |
| Chrysene | | |

Table 1. Harmful and Potentially Harmful Constituents (HPHCs) list for tobacco products from the FDA..

Using the analytes that matched the HPHCs list, a simplified workflow for creating MRM transitions was utilized, and saved in a database for future methods. This new MRM method provided low level detection of the analytes, which allowed for a larger sample dilution to reduce the amount of sample injected into the instrument. One of the e-liquids contained diacetyl, a compound known to cause “popcorn lung,” a type of lung disease. Most of the e-liquids included the expected vanillin, but also several other isomers like ethyl vanillin and a propylene glycol acetal species even though their flavor profiles were bubble gum, tobacco and cotton candy. One of the e-liquids had a trace amount of coumarin, which is a banned compound for the use in food products.

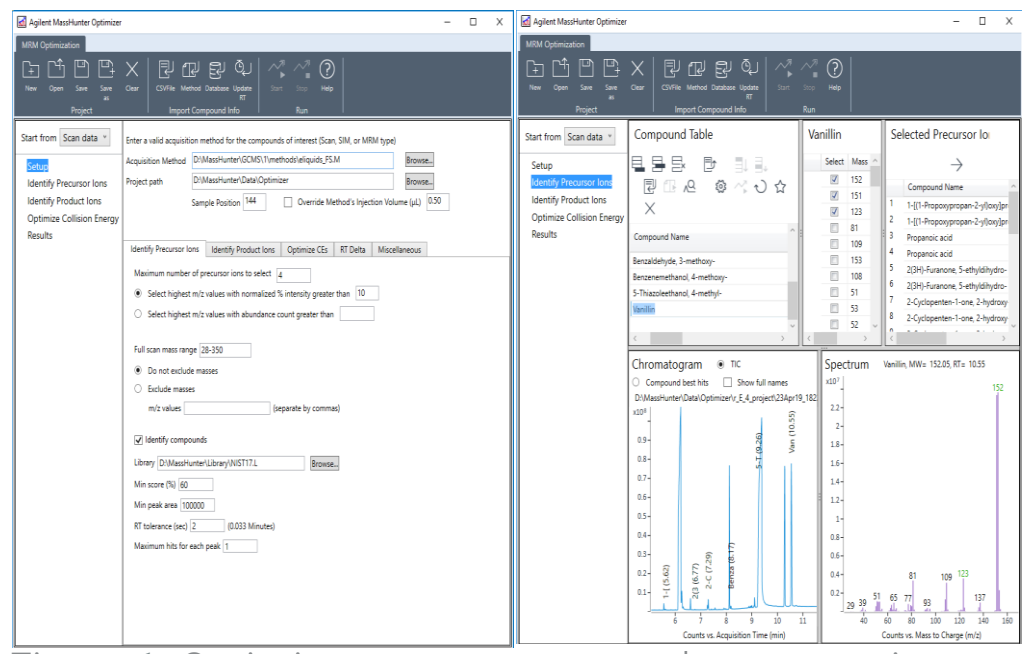


Figure 1. Optimizer setup screen and precursor ion analysis view. Precursor ions are found using deconvolution to produce cleaned spectra for accurate ion assignment.

## Optimizer Workflow Overview

**Precursor Ions Known?**

Accurate RTs are known

1. Import *.csv (names, RTs) or manually add compounds (names, RTs)
2. Acquire and analyze scan data

Library available

1. Acquire or import scan data
2. Identify compounds (built-in Unknowns Analysis

Precursor ions are suggested

1. Review suggested precursor ions, make edits
2. Send to product ion scan
3. Selected product ions – Optimize collision energy

Confident Automatic MRM Optimization

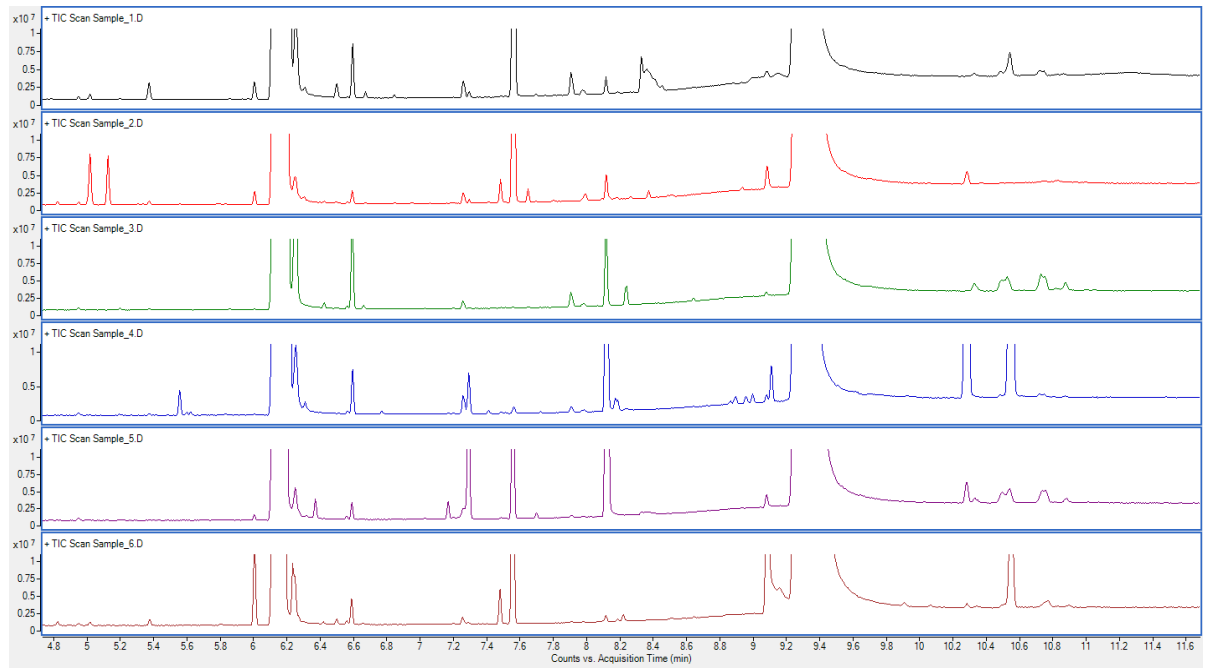


Figure 2. Full scan chromatograms from MS1 to use for compound identifications and initiating MRM Optimizer.

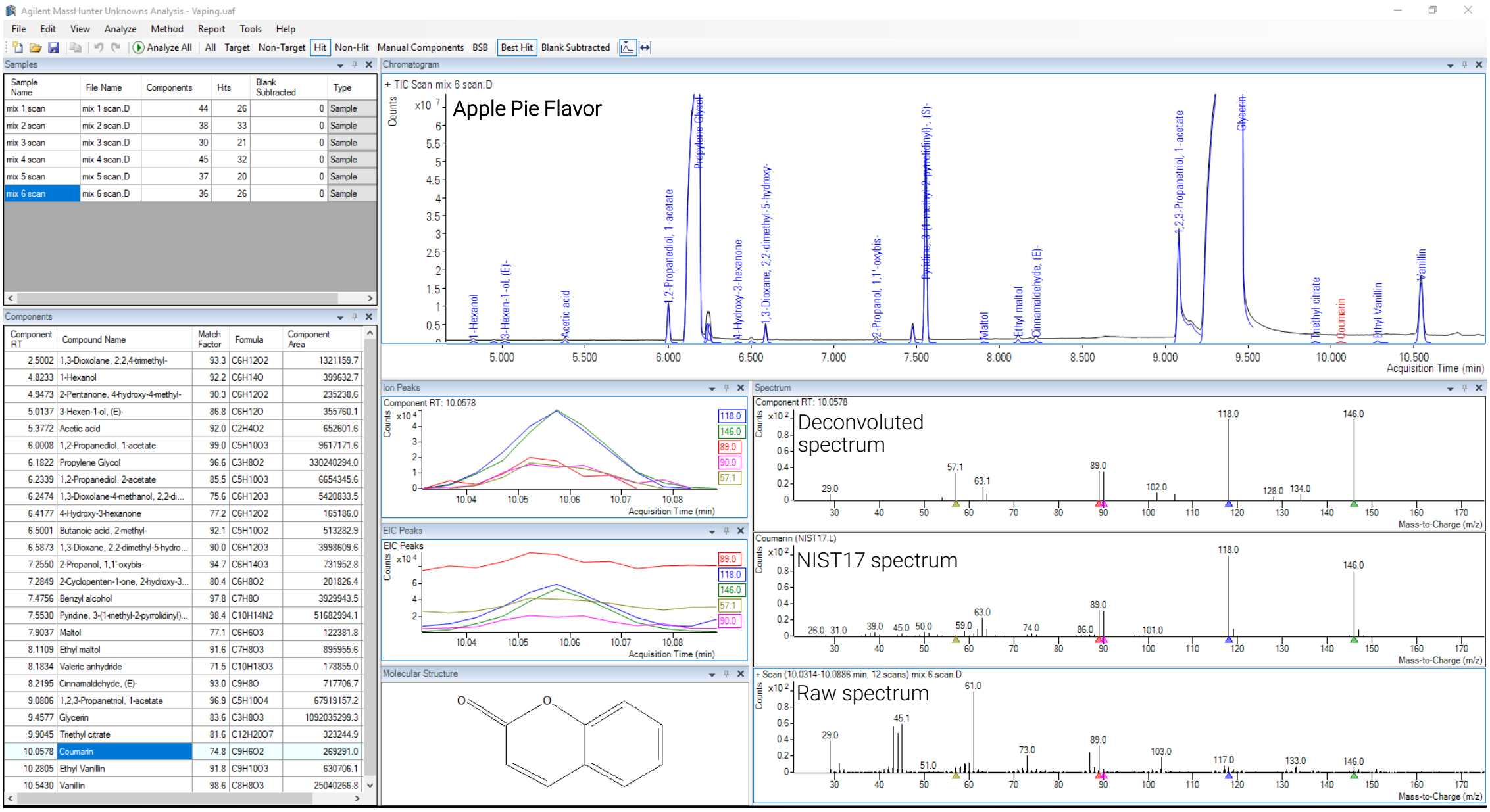


Figure 5. Compound annotation using the NIST17 library from deconvoluted spectra from the apple pie e-liquid. Library minimum match factor was 70. Greater than 70% of the components detected were annotated by the library search.

## Results and Discussion

# Building a screener MRM database of transitions from scan data, individual compounds can be easily identified at trace levels

| Component RT | Compound Name |
|---|---|
| 2.49 | 1,3-Dioxolane, 2,2,4-trimethyl- |
| 3.96 | 1-Butanol, 3-methyl- |
| 4.49 | Acetoin |
| 4.83 | 1-Hexanol |
| 5.02 | 3-Hexen-1-ol, (E)- |
| 5.13 | 2-Hexen-1-ol, (Z)- |
| 5.20 | Silane, ethyltrimethyl- |
| 5.37 | Acetic acid |
| 5.56 | 1,3-Dioxolane, 2,2,4-trimethyl- |
| 5.60 | 1-[(1-Propoxypropan-2-yl)oxy]propan-2-yl acetate |
| 5.63 | 1,3-Dioxolane, 2,2,4-trimethyl- |
| 5.79 | Formic acid |
| 5.83 | Propanoic acid |
| 6.00 | 1,2-Propanediol, 1-acetate |
| 6.20 | Propylene Glycol |
| 6.24 | 1,2-Propanediol, 2-acetate |
| 6.26 | 1,3-Dioxolane-4-methanol, 2,2-dimethyl- |
| 6.30 | Butanoic acid |
| 6.37 | Acetylpyrazine |
| 6.42 | 2-Butanol, 1-methoxy- |
| 6.42 | Benzeneacetaldehyde, .alpha.-methyl- |
| 6.43 | 2-Butanol, 1-methoxy- |
| 6.50 | Butanoic acid, 2-methyl- |
| 6.60 | 1,3-Dioxane, 2,2-dimethyl-5-hydroxy- |
| 6.66 | 3-Hexanol, 2-methyl- |
| 6.67 | 1,2-Propanediol Butyrate Ester |
| 6.77 | 2(3H)-Furanone, 5-ethyldihydro- |
| 6.85 | 1,2-propanediol butyrate |
| 7.17 | 1,2-Propanediol, 3-methoxy- |
| 7.26 | 2-Propanol, 1,1'-oxybis- |
| 7.29 | Hexanoic acid |
| 7.41 | Phenol, 2-methoxy- |
| 7.48 | Benzyl alcohol |
| 7.56 | Pyridine, 3-(1-methyl-2-pyrrolidinyl)-, (S)- |
| 7.65 | Phenylethyl Alcohol |
| 7.70 | Glycolaldehyde dimethyl acetal |
| 7.80 | Isophthalic acid, ethyl tridec-2-ynyl ester |
| 7.91 | Maltol |
| 7.98 | 2-Thio-2,4-oxazolidinedione |
| 7.99 | 3-(1-Methyl-2-pyrrolidinyl)pyridine |
| 8.12 | Ethyl maltol |
| 8.17 | Benzaldehyde, 3-methoxy- |
| 8.19 | 2(3H)-Furanone, 5-butyldihydro- |
| 8.22 | Cinnamaldehyde, (E)- |
| 8.24 | Glycerol 1,2-diacetate |
| 8.26 | 1-Propanol, 2-(2-hydroxypropoxy)- |
| 8.33 | Lacthydrazide |
| 8.37 | Oxiranecarboxylic acid, 3-methyl-3-phenyl-, ethyl ester, trans- |
| 8.64 | 2(3H)-Furanone, 5-hexyldihydro- |
| 8.93 | Pyridine, 3-(3,4-dihydro-2H-pyrrol-5-yl)- |
| 9.11 | Benzenemethanol, 4-methoxy- |
| 9.16 | Acetic acid ethenyl ester |
| 9.26 | 5-Thiazoleethanol, 4-methyl- |
| 9.38 | Formaldehyde |
| 9.42 | Glycerin |
| 9.91 | Triethyl citrate |
| 10.28 | Ethyl Vanillin |
| 10.33 | 1,4-Dioxane-2,6-dimethanol |
| 10.52 | Propanoic acid, propyl ester |
| 10.55 | Vanillin |
| 10.73 | 2,3-Butanediol, 1,4-dimethoxy- |
| 10.88 | 1,4-Dioxane-2,6-dimethanol |

Table 2. List of annotated components from the 6 samples with confidence of 80% or higher using the NIST17 library.

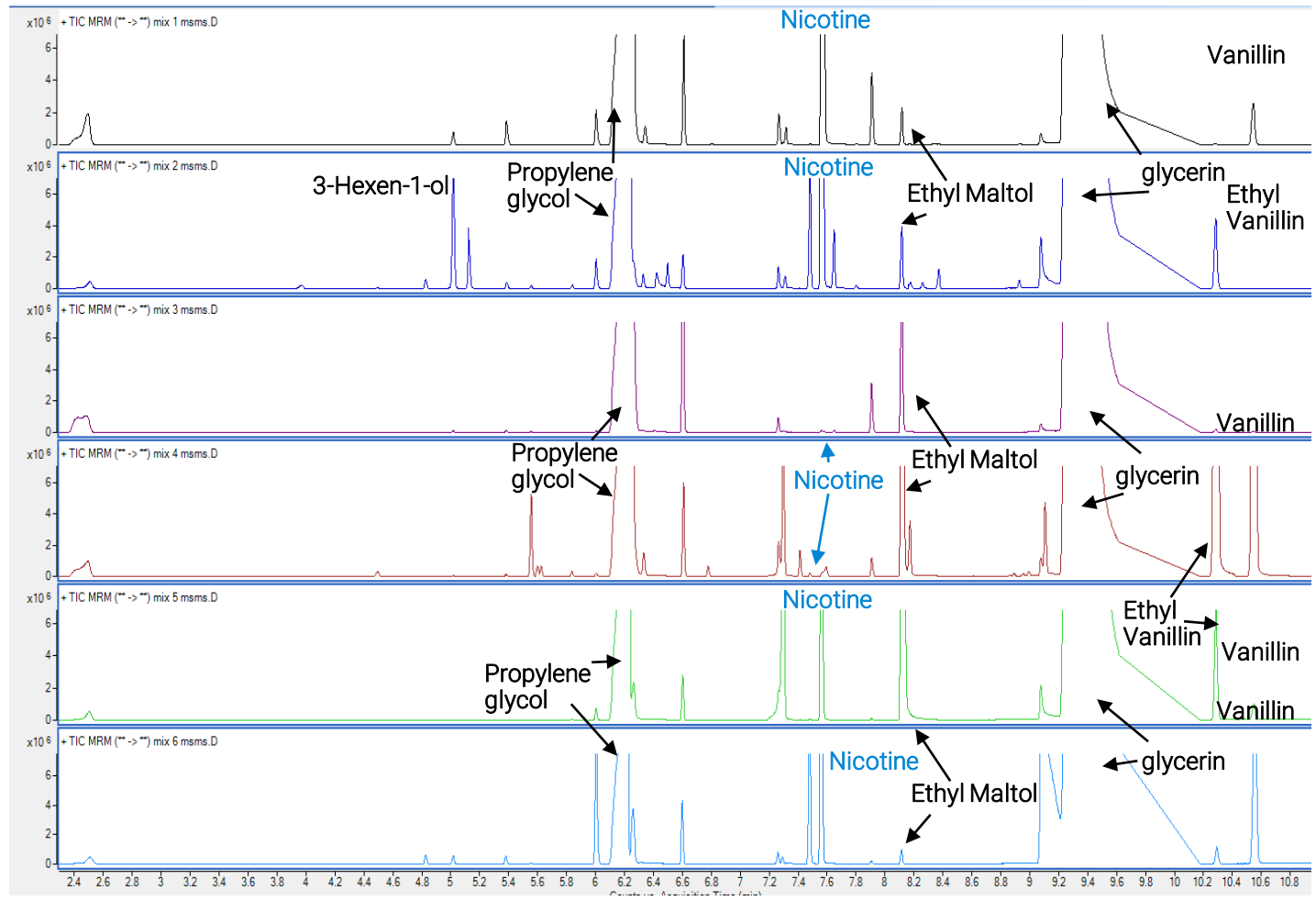


Figure 5. Comparison of MRM results of Sample 1- 6 diluted 200x for the MRM analysis. Only 3 samples were labelled to contain nicotine but all had an observable amount.

## Conclusions

A benchtop GC/MS system is an ideal analytical tool for the analysis of e-cigarette liquids since it can be used to both quantify major components (such as nicotine) and screen for minor components whose presence may be considered a health risk.

Components can be tentatively identified by library searching their electron impact (EI) mass spectra against large, commercially available, data bases such as NIST17.

By using a MRM database the identification of HPHCs and flavor compounds allows for trace identification of all compounds.
Additional compounds can easily be added to the MRM database using scan data and the MRM Optimizer.


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