73rd Tobacco Science Research Conference

Analysis of e-liquids of electronic cigarettes containing nicotine salts

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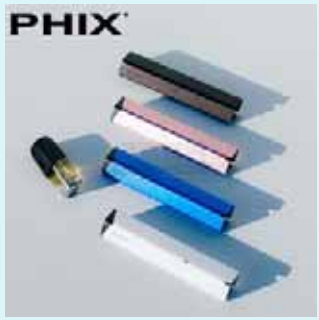
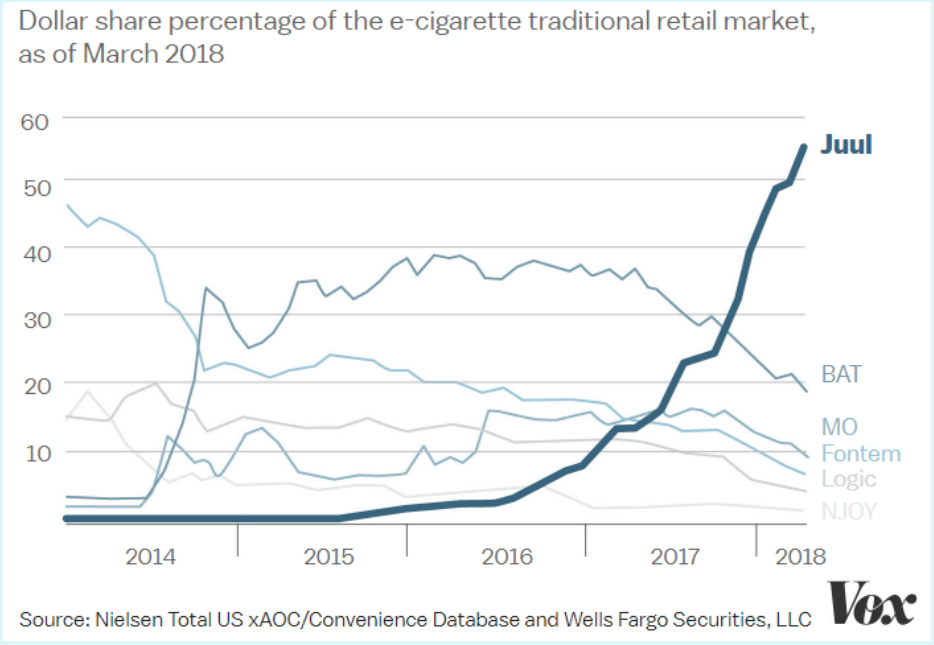
September 16th, 2019

Sales of Juul are booming, especially in US market.





https://www.vox.com/science-and-health/2018/5/1/17286638/juul-vaping-e-cigarette

Juul delivers a hit of nicotine like a cigarette smoothly. That's because of its "nicotine salts."

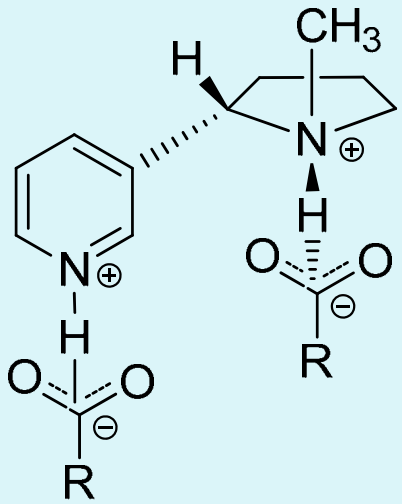
Generation	E-liquids	Power	Nicotine type	Nicotine content(%)
1th	pre-filled	low	free base	Normally < 3%
2th	refillable	Mid	free base	Normally < 3%
3th	refillable	High (adjustable)	free base	Normally < 1%
4th	pre-filled	low	**Salts**	**Normally > 5%**

Different generations of electronic cigarettes

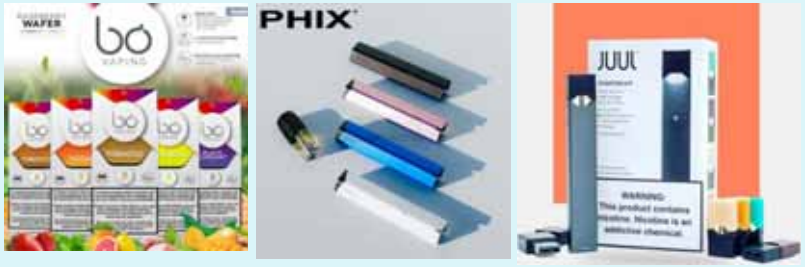
Mathur A, Dempsey O. The journal of the Royal College of Physicians of Edinburgh, 2018,48(4):346-351.
https://www.vox.com/science-and-health/2018/5/1/17286638/juul-vaping-e-cigarette

Analysis of e-liquids of electronic cigarettes containing nicotine salts

- I. Type of nicotine salts
- II. Nicotine concentrations
- III. pH
- IV. Enantiomeric composition of nicotine



Sample information
(Products that may use nicotine salts)

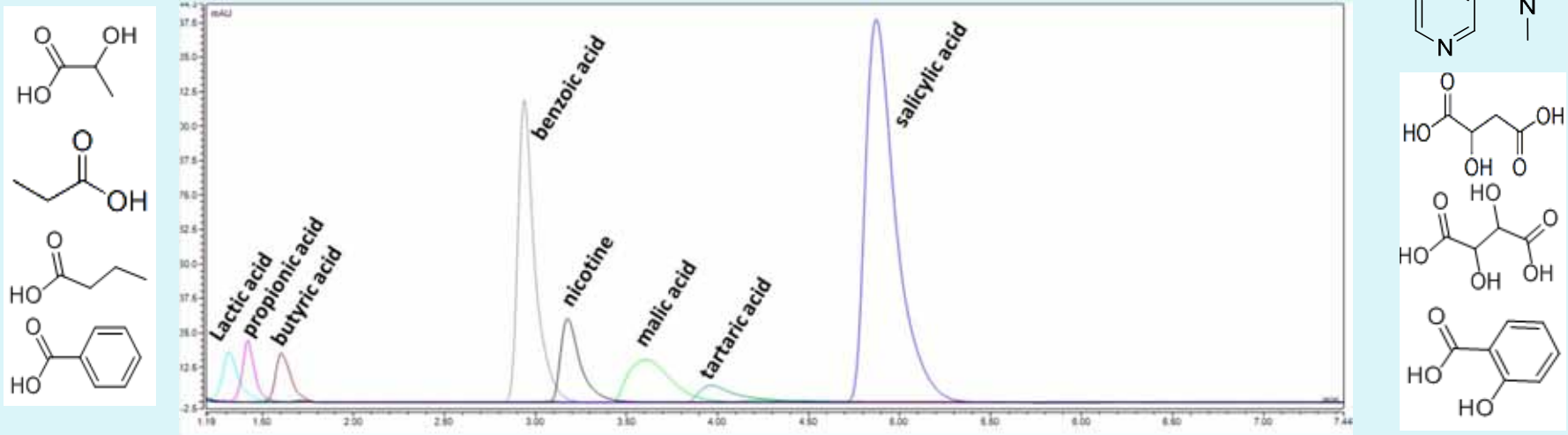


◆ **171 Ordinary samples: e-liquids that NOT labelled containing nicotine salts.**

No	Sample	Company	Nicotine content (labeled)
1	Nut tobacco	UPON, China	50 mg
2	Liquid nicotine salts	HFNO, China	100 mg/mL
3	Solid nicotine salts	HFNO, China	100 mg/mL
4	bo/ice menthol	JWELL	4.00%
5	bo/gold tobacco	JWELL	5.00%
6	bo/Icy mint	JWELL	5.00%
7	bo/kiwi berries	JWELL	3.50%
8	VUSE solo/melon	R.J. Reynolds	/
9	VUSE solo/original	R.J. Reynolds	/
10	VUSE solo/nectar	R.J. Reynolds	/
11	VUSE solo/berry	R.J. Reynolds	/
12	VUSE solo/mint	R.J. Reynolds	/
13	VUSE ciro/melon	R.J. Reynolds	/
14	VUSE ciro/nectar	R.J. Reynolds	/
15	VUSE ciro/tropical	R.J. Reynolds	/
16	VUSE ciro/mint	R.J. Reynolds	/
17	VUSE ciro/menthol	R.J. Reynolds	/
18	Vype pro/wild berries	R.J. Reynolds	18mg/ml
19	Vype pro/master blend	R.J. Reynolds	18mg/ml
20	Vype pro/crushed mint	R.J. Reynolds	18mg/ml
21	PHIX/butters cotch	MLV	5.00%
22	PHIX/hard starwberry	MLV	5.00%
23	PHIX/original	MLV	5.00%
24	Myblu Intense/Neon dream	Fontem Ventures	4.00%
25	Myblu Intense/honey moon	Fontem Ventures	4.00%
26	Myblu Intense/citra zing	Fontem Ventures	4.00%
27	Myblu Intense/tobacco chill	Fontem Ventures	4.00%
28	JUUL/classic menthol	Juul Labs Inc	5.00%
29	JUUL/creme brulee	Juul Labs Inc	5.00%
30	JUUL/mango	Juul Labs Inc	5.00%
31	JUUL/cool cucumber	Juul Labs Inc	5.00%
32	JUUL/classic tobacco	Juul Labs Inc	5.00%

Simultaneously determination of nicotine and seven organic acids

Method (HPLC-UV)



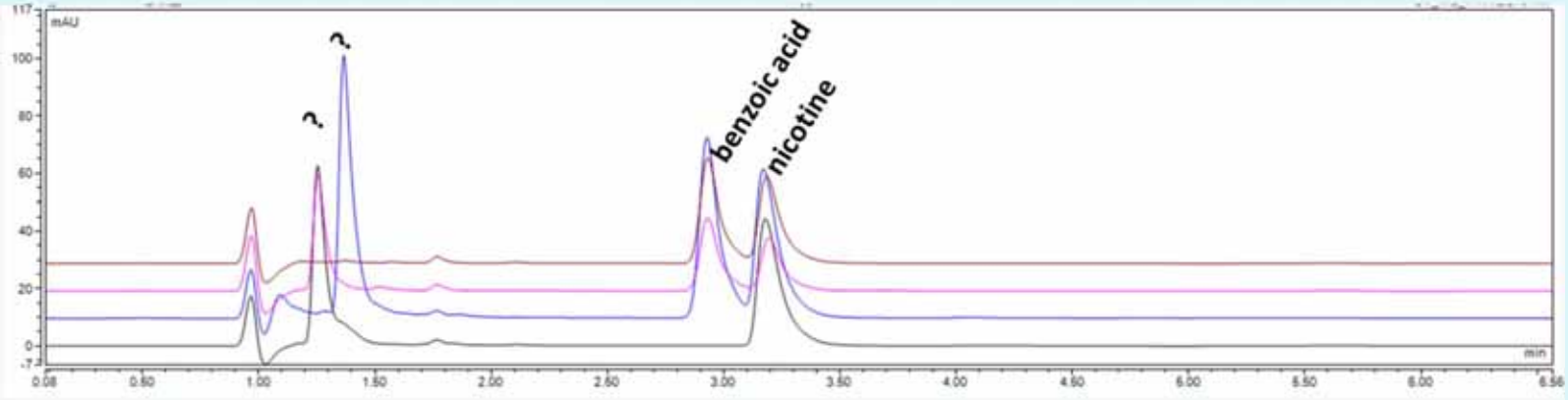
—Column: Acclaim Trinity P1 (simultaneous cation exchange (CEX), anion exchange (AEX), and reversed-phase (RP))

— Mobile phase: 1.07 g dibasic sodium phosphate dodecahydrate (3 mmol) + 1.80 g monobasic sodium phosphate (15 mmol) + 27 mg tetrasodium pyrophosphate decahydrate (60 µmol) + 750 g water (750 mL), pH 6.3 + 196 g acetonitrile (250 mL).

— Flow rate: 0.60 mL/min. Temperature: 30 °C. Detection: UV at 210 nm.

Simultaneously determination of nicotine and seven organic acids

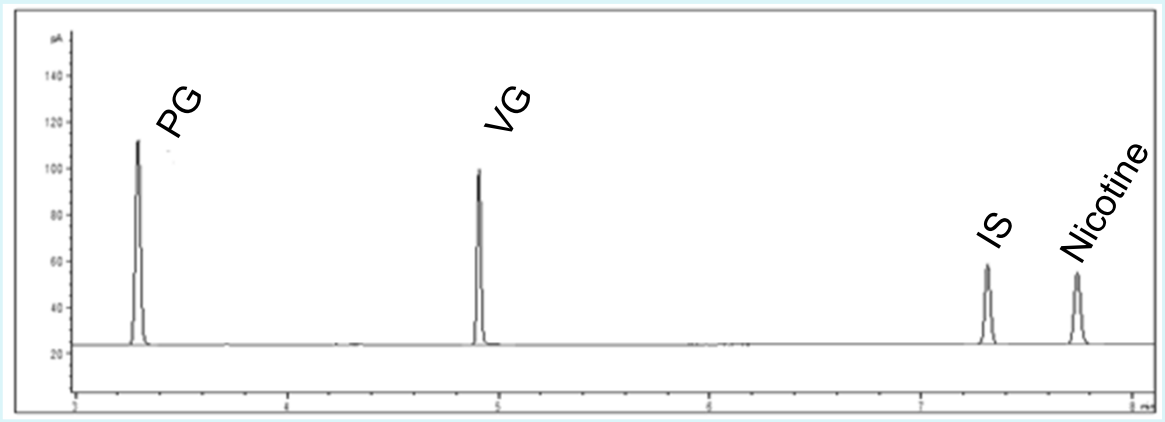
Result & discussion



- **Benzoic acid nicotine salt was detected in about one third samples** (such as 1#， Vype pro， PHIX，JUUL), **nicotine ditartrate was detected in one samples** (3#), but the type of nicotine salts could not be qualified in other samples.
- **Mixed nicotine salts may be used in some samples**. For example, two organic acids may be used in some e-liquids, such as PHIX/original and Vype pro/wild berries, but neither of the other two organic acids can be identified besides benzoic acid.
- **Same brand with different tastes may use different nicotine salts**. For example, for bo (4 #~7 #), 6 # was benzoate, 5 # was benzoate and another organic salt (unidentified), but 4 # and 7 # were unidentified.

Nicotine concentrations

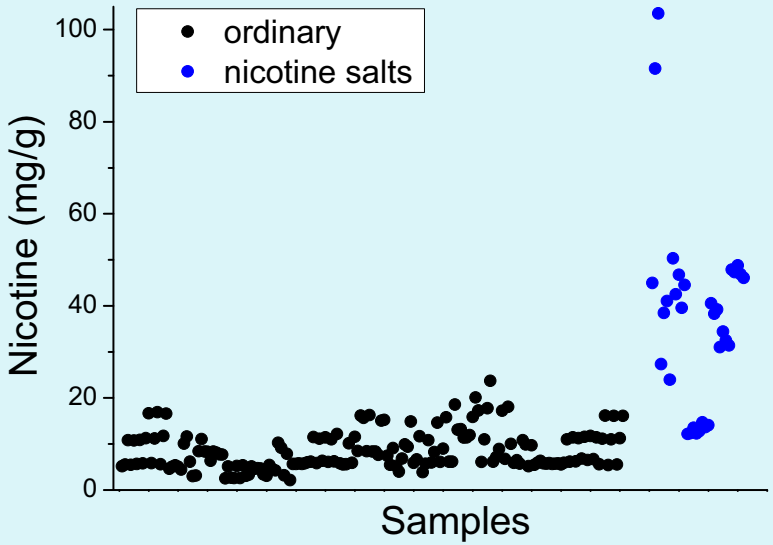
Method (GC-FID)

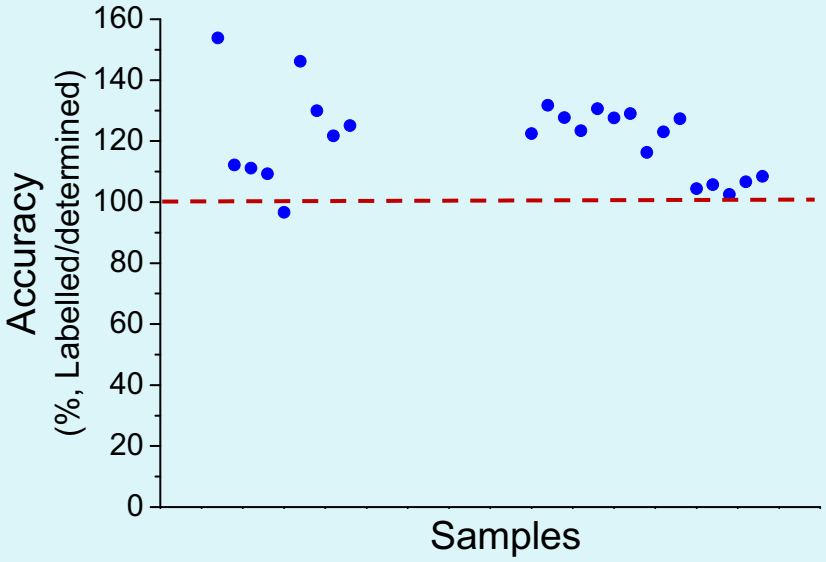


— Column: DB-ALC1 capillary column (30 m × 0.32 mm × 1.80 μm)
— Temperature program: 100 °C (1 min) to 130 °C at 15 °C/min, then to 220 °C (10 min) at 40 °C/min
Flow rate: 0.60 mL/min. Temperature: 30 °C. Detection: UV at 210 nm.
— Inlet temperature: 250 °C
— Detector temperature: 275 °C
— Injection volume: 1.0 μL, split ratio 50:1

Nicotine concentrations

Result & discussion

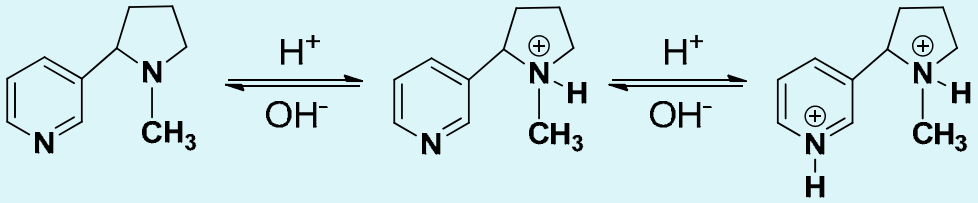


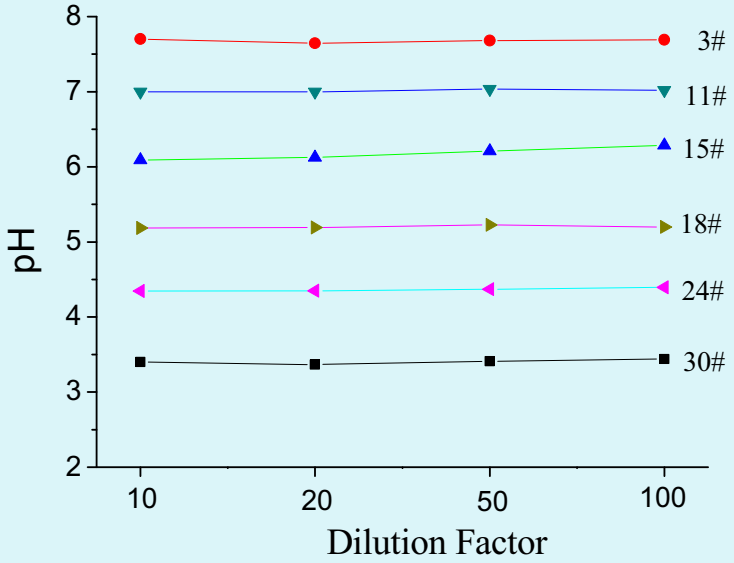


- Nicotine content of e-liquids containing nicotine salts was significantly higher than that of ordinary e-liquids
- Labeled nicotine contents were 96.6%~146.2% of determined nicotine content.

Determination of pH of e-liquids

Method



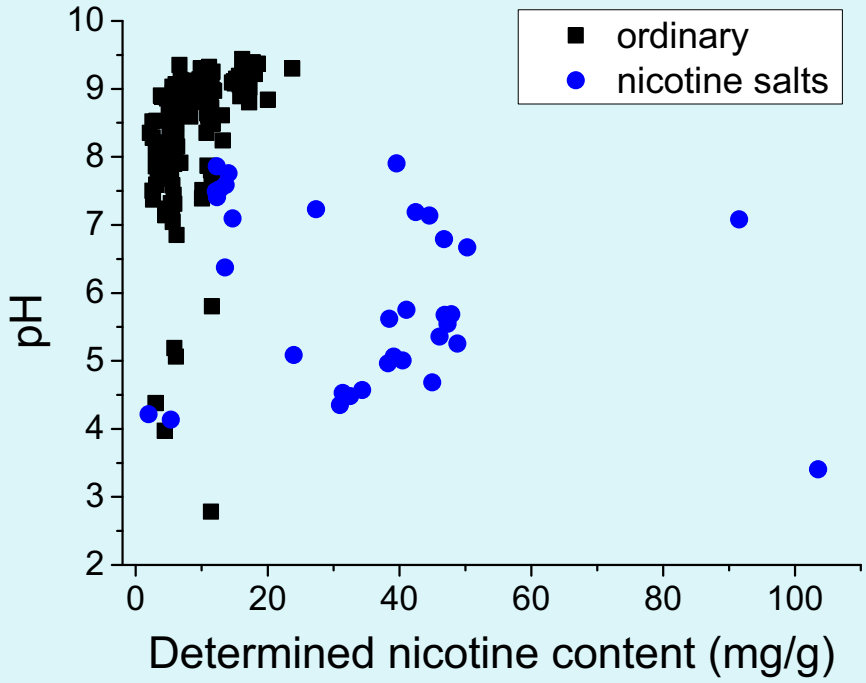


— E-liquids were diluted 10 times with ultrapure water (adjusted to 7.00±0.05) before determination of pH with acidometer.

*Nicotine and Tobacco Research, 17, 1270–1278.**2015**.*

Determination of pH of e-liquids

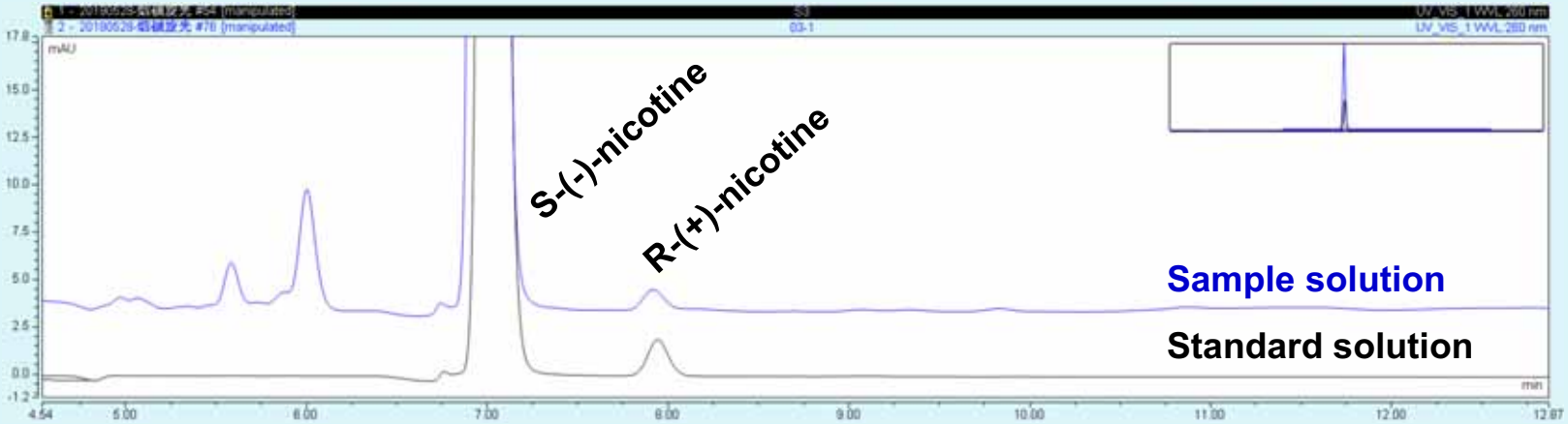
Result & discussion



- pH of e-liquids containing nicotine salts was significantly lower than that of ordinary e-liquids.

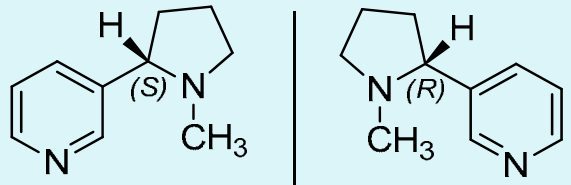
Determination of enantiomeric composition of nicotine

Method



—Column: Chiralcel OD-H (250 mm*0.46 mm*5μm)
— Mobile phase: Hexane: methanol = 98:2 (V/V)
— Flow rate: 0.60 mL/min
— Temperature: 30 °C
— Detection: UV at 252 nm.

*Chirality, 30, 923-931.**2018**.*

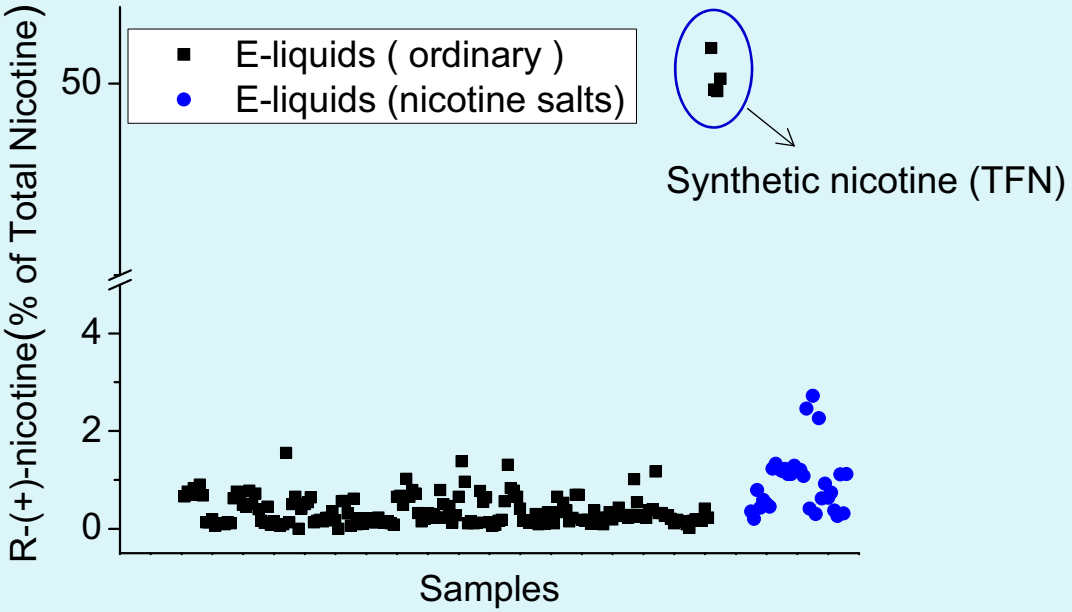


(S)-(-)-Nicotine **(R)-(+)-Nicotine**

From tobacco: ≈ 99 : 1
From synthesis: ≈ 50 : 50

Determination of Enantiomeric composition of nicotine

Result & discussion



- Ratios of R-(+)-nicotine e-liquids containing nicotine salts ranged from 0.2 to 2.5, similar with that of majority of ordinary e-liquids (0.1~1.2), except those using synthetic nicotine (49.8~50.9)
- Nicotine in the e-liquids with nicotine salts originated from tobacco, rather than from artificial synthesis.

Conclusion

- I. Nicotine benzoate and ditartrate were detected in about one third samples. Mixed nicotine salts may be used in some samples. The same brand with different tastes may use different nicotine salts.
- II. Nicotine content of e-liquids containing nicotine salts was significantly higher than that of ordinary e-liquids. Labeled nicotine content was generally higher than determined nicotine content.
- III. pH of e-liquids containing nicotine salts was remarkable lower than that of ordinary e-liquids.
- IV. Nicotine in the e-liquids originated from tobacco, rather than from artificial synthesis.

Limitations

- More efficient and high throughput method should be developed for simultaneously determination of organic acids and nicotine in e–liquids, including target and non-target analysis, such as HPLC-MS/MS or HPLC-TOFMS.

Thank you for your attention!