VALIDATION OF A LIMIT TEST METHOD FOR ANALYSIS OF PRIMARY AROMATIC AMINES (PAA) IN ELECTRONIC CIGARETTE LIQUID AND AEROSOL

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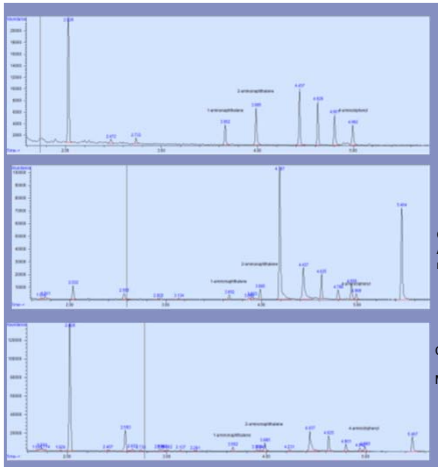
ABSTRACT

Primary aromatic amines (PAAs) are compounds of interest that are routinely found in mainstream tobacco smoke. With the increasing interest in e-cigarette aerosol and liquid products, there is need for sensitive methods of measurement for PAAs when evaluating these matrices. The method described here is a modification of a method routinely used in a high-sample throughput laboratory for PAA analysis in e-liquid and aerosol.

This method is a limit test, and it utilizes a low level standard and a matrix spike (FMCS) to demonstrate realistic low level responses for comparison against samples. The standard is used as a clean matrix reference while the matrix spike represents a true representation of the responses of each analyte in various formulations of electronic cigarette e-liquid and aerosol. The target PAAs analyzed are 1-aminonaphthalene, 2-aminonaphthalene and 4-aminobiphenyl.

Electronic cigarette aerosol is collected using a 44-mm Cambridge filter pad (CFP) which is then extracted with 5% HCL through both an MCX and HLB cartridges. The final fraction is collected in toluene and derivatized with heptafluorobutyric anhydride. The final sample is analyzed by GCMS using negative chemical ionization (NICI).

The method has been validated as a limit test in concordance with the ICH guidelines.



Level 1 Standard

Cigalike Electronic Cigarette Aerosol Mint Chromatogram matrix spike (FMCS)

Cigalike Electronic Cigarette Liquid Mint Chromatogram Matrix spike (FMCS)

RESULTS

Specificity and adequate recovery in matrix are critical to a good limit test. The table below shows reproducible and ample signal in both matrices for this method.
This method was validated for specificity, limit of detection (LOD), and sample and standard stability. Results for S/N for the standard, samples and FMCS are shown below

Eliquid	Level 1 Nominal Concentration ng/ml	Level 1 Standard S/N	Eliquid 1 unspiked S/N	Eliquid 2 unspiked S/N	Eliquid 3 unspiked S/N	Eliquid 1 FMCS S/N	Eliquid 2 FMCS S/N	Eliquid 3 FMCS S/N
1-AM	0.5	38.9:1	<3	<3	<3	51.8:1	37.3:1	75.2:1
2-AM	0.5	69.5:1	<3	3.6	<3	97.6:1	71.3:1	123.2:1
4-BPH	0.4	16.0:1	<3	<3	<3	17.4:1	15.8:1	23.0:1

Aerosol	Level 1 Nominal Concentration ng/ml	Level 1 Standard S/N	Aerosol 1 unspiked S/N	Aerosol 2 unspiked S/N	Aerosol 3 unspiked S/N	Aerosol 1 FMCS S/N	Aerosol 2 FMCS S/N	Aerosol 3 FMCS S/N
1-AM	0.5	40.3:1	<3	<3	<3	32.7:1	36.0:1	21.2:1
2-AM	0.5	155.9:1	<3	3.7	3.2	27.5:1	58.6:1	39.9:1
4-BPH	0.4	98.3:1	<3	ND	ND	13.2:1	16.0:1	14.6:1

EVALUATING ELECTRONIC CIGARETTE AEROSOL AND LIQUID

A standard at the limit is prepared and extracted for a clean matrix reference. A sample matrix is also spiked at the limit and extracted (FMCS). Responses for each analyte in matrix are somewhat different from the responses in the clean matrix, and therefore give a more accurate assessment when comparing samples to the expected limit.

Method Parameters
Agilent 5977A/7890B
DB-5MS 30x.25x.25
1 ul injection
10:1 split

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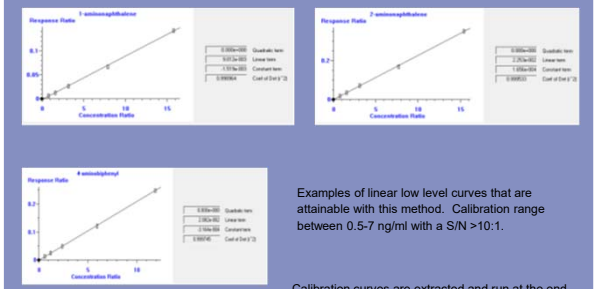
	°C/min	°C	Hold time (min)	Run time (min)
Initial	N/A	130	0	0
Ramp 1	20	235	0	5.5
Ramp 2	40	325	0	7.5

Calibration Curves



Examples of linear low level curves that are attainable with this method. Calibration range between 0.5-7 ng/ml with a S/N >10:1.

Calibration curves are extracted and run at the end of the sequence to give a quantitated value should any analyte yield a response greater than the level 1 matrix spike (FMCS). Each analyte has shown to have acceptable linearity and sensitivity.

CONCLUSIONS

We have developed and validated a limit test for the specific determination of the PAA method. The trace level evaluation of various matrices has been successfully completed with this version of the PAA method. The sensitivity achieved at low levels for 1-aminonaphthalene, 2-aminonaphthalene and 4-aminobiphenyl in a clean but challenging matrix has led the way to developing this limit test. Evaluating the responses of target analytes against the level 1 matrix spike gives an accurate assessment of responses for sample comparison.

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