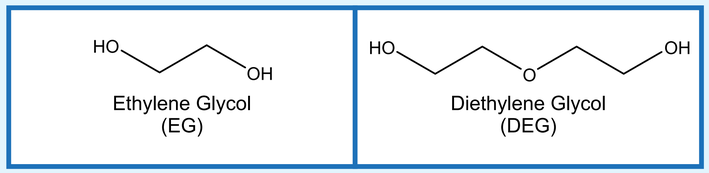
Quantitative Screening of Potential Contaminants in E-cigarette Formulations: Ethylene Glycol and Diethylene Glycol

Niti H. Shah, Christopher McFarlane, Jason W. Flora, and Karl A. Wagner
Altria Client Services, 601 East Jackson Street, Richmond, VA 23219

INTRODUCTION

- E-liquid and aerosols typically contain propylene glycol (PG), glycerin, water, nicotine, and flavors
- Ethylene glycol (EG) and diethylene glycol (DEG) were included in the evaluation by FDA as potential impurities in e-cigarette formulations[1]



- EG and DEG are potential contaminants of glycerin

OBJECTIVE

- Develop a sensitive and selective method for quantitative analysis of EG and DEG in e-liquids by gas chromatography-mass spectrometry (GC-MS)
- Analyze commercially available e-liquids (refill products) for the presence of EG and DEG in order to determine if the method is fit for purpose

METHOD

Parameter	Description
GC Column	DB WAX (30 m x 0.25 mm ID x 0.25 µm)
Oven Temperature Program	Initial 90 °C hold for 2 min Ramp 5 °C/min to 180 °C Ramp 30 °C/min to 240 °C hold for 3 min
Column Flow Rate	1.15 mL/min
Injector Temperature	240 °C
Selected Ion Monitoring (SIM)	Ethylene glycol (EG): m/z 31 and 62 Diethylene glycol (DEG): m/z 45 and 75 1,3-Propanediol (1,3-PD): m/z 57 and 58 (ISTD)
Ion Source Temperature	240 °C
Interface Temperature	250 °C
Method Run Time	25 min
Sample Requirement	0.5 g/10 mL extraction solution (methanol)

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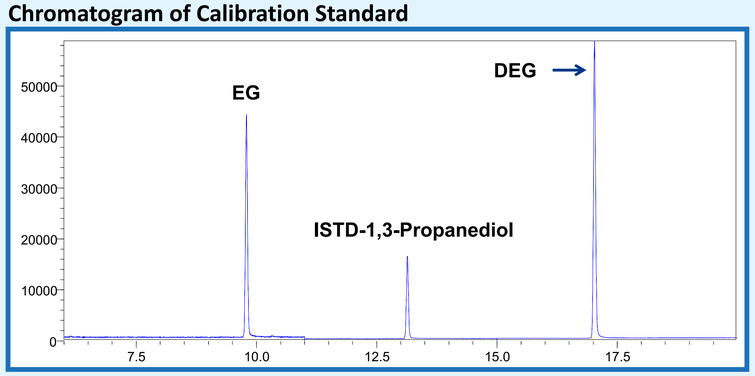
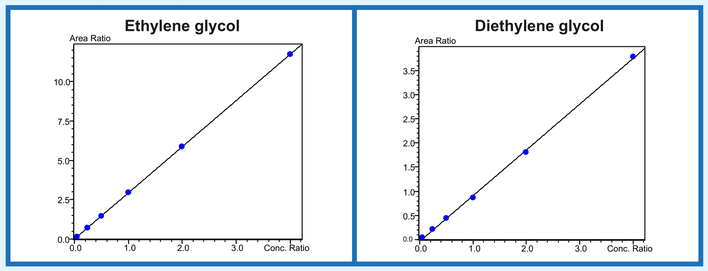
ABSTRACT

The US Food and Drug Administration (FDA) evaluated two commercial e-cigarettes and a nicotine replacement therapy inhaler in 2009 (DPATR-FY-09-23).[1] Ethylene glycol (EG) and diethylene glycol (DEG) were included in this evaluation as potential impurities in e-cigarette formulations.[1] DEG was found in one e-cigarette cartridge in the study; however, quantities were not included. The US Pharmacopeia (USP) discusses permissible levels of EG and DEG in USP grade polyethylene glycol and glycerin (< 0.1%), the major components of most e-vapor product formulations.[3] The USP only provides non-selective methods for the analysis of these potential contaminants in propylene glycol and glycerin. These methods are subject to potential interferences caused by flavor systems found in e-liquids. Therefore, the purpose of this work was to develop and validate a sensitive and selective method specifically for the quantitative screening of e-liquids for EG and DEG. The method developed and validated uses gas chromatography-mass spectrometry (GC-MS). All requirements for method validation were met such as linearity, accuracy, precision, limits of detection (LOD), and limits of quantitation (LOQ). The linearity was demonstrated with a coefficient of determination of >0.999 for the calibration range of 10 to 800 µg/g of e-liquid.

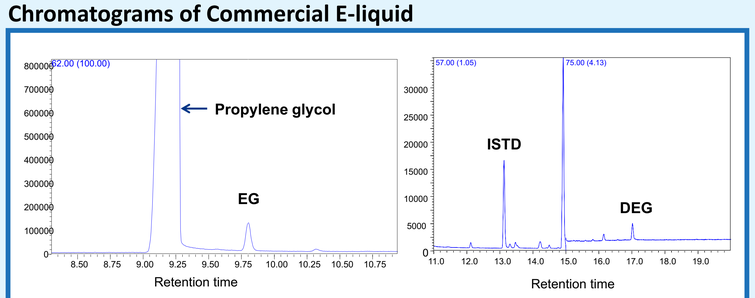
Chromatogram of Calibration Standard



Calibration Curves



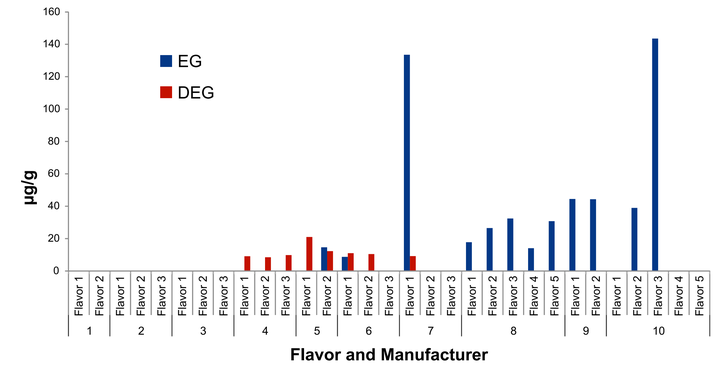
Chromatograms of Commercial E-liquid



EG and DEG are well separated from major components of e-liquids

RESULTS

EG and DEG in Commercial E-liquids



Of the 31 commercial e-liquids (refill products from 10 manufacturers) tested, measurable amounts of EG were detected in 12 products and DEG in 8

Validation Summary

Parameter	Result
Calibration Range	10 µg/g – 800 µg/g
Linearity	R^2 > 0.999
Accuracy	98.5 % – 102.4 % (3 levels)
Precision	< 8.2 % RSD
Limit of Detection	1.0 µg/g

SUMMARY

- A selective and sensitive method was developed for the analysis of EG and DEG in e-liquids
- Measurable amounts of EG or DEG were in 67% of the 31 e-liquids tested
- Concentrations ranged from 10-143 µg/g for EG and 10-20 µg/g for DEG

REFERENCES

1. Westenberger BJ, Deputy Director, CDER/OPS/OTR, Division of Pharmaceutical Analysis, FDA Archived document, Evaluation of e-cigarettes, May 4, 2009, DPATR-FY-09-23
2. FDA, Guidance for Industry: Testing of Glycerin for Diethylene Glycol, May 2007
3. USP, USP 31-NF 26, Glycerin, USP, Rockville, MD, USA, 2008, pp. 2286–2287