A NEW VOLATILES COLUMN FOR THE ANALYSIS OF VOLATILE COMPOUNDS IN PHARMACEUTICAL PREPARATIONS

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INTRODUCTION

There are a wide variety of solvents used in the processing of pharmaceutical preparations. The use of solvents is a necessity for the synthesis of many of the biologically active compounds but their removal from the finished drug is also important as many of the solvents used have undesirable health implications. Maintaining patient safety is of the utmost importance and the trend has been towards the use of less toxic solvents during the manufacture of pharmaceutical products. Low-level detection limits are however, still required for quality control and to ensure that the behavior of new drugs being trialed is not due to any residual solvent present. Existing guidelines as published by the International Conference on Harmonization (ICH) describe a list of specific solvents, along with daily exposure limits as part of the requirements for the registration of pharmaceuticals for human use. These solvents have been classified based on their toxicity as Class I-solvents to be avoided, Class II-solvents to be limited and Class III-solvents of low toxicity.

THE BPX-VOLATILES ADVANTAGE

Most of the commonly used solvents in pharmaceutical preparation are low molecular weight, volatile compounds that can be difficult to remove from the final target drug.

The new BPX-Volatiles capillary column from SGE has been specifically designed to analyze these types of compounds. The BPX-Volatiles column is one of highest temperature volatile capillary columns available. The maximum temperature limit of 300°C provides added flexibility to the chromatographer not previously available with other volatile columns. The thick film and excellent inertness combine to give excellent separation and peak shape of difficult-to-analyze components. Lower signal-to-noise ratios allow for lower detection limits at temperatures where most volatile capillary columns are reaching their maximum temperatures and highest bleed levels.

Phase:	**BPX-Volatiles, 1.4µm film**
Sample:	**200ppm in methanol**
Column:	**30m x 0.25mm ID**
Initial Temp:	40°C, 1min
Rate 1:	6°C/min to 80°C, 2min
Final Temp:	80°C
Detector Type:	Mass Spectrometer
Carrier Gas:	He, 6.7
Carrier Gas Flow:	0.9 mL/min
Constant Flow:	On
Average Linear Velocity:	35cm/sec at 50°C
Injection Mode:	Split
Split Ratio:	100:1
Injection Volume:	0.4µL
Injection Temperature:	250°C
Autosampler:	No
Liner Type:	4mm ID Single Taper Liner
Liner Part No:	**092017**
Column Part No:	**054980**
ms-NoVent™ Part no.:	113400
HP5973 restrictor:	113409
Full scan:	30-450

Components:
1. 1,1-Dichloroethene
2. 1,1,1-Trichloroethane
3. Carbon tetrachloride
4. Benzene
5. 1,2-Dichloroethane

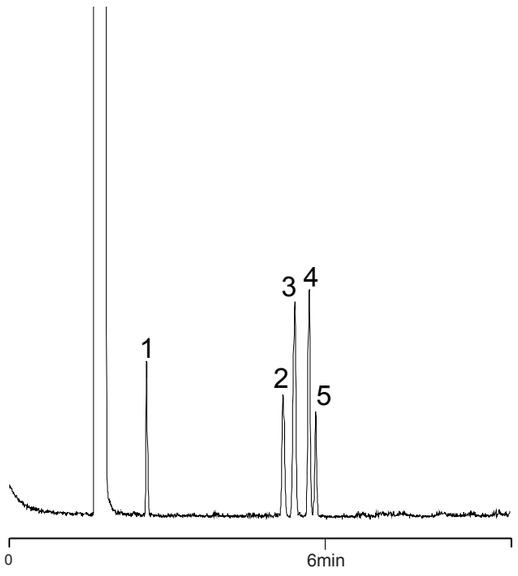

Figure 1. *Chromatogram of the Class I solvents on BPX-Volatiles. Note the excellent separation of the 1,2-Dichloroethane and Benzene.*

Components:
1. Pentane
2. Ethanol
3. Ethyl ether
4. Acetone
5. *iso*-Propyl alcohol
6. Ethyl formate
7. Methyl acetate
8. Dichloromethane
9. Methyl-t-butyl ether
10. *n*-Propanol
11. Ethyl acetate
12. 2-Butanone (MEK)
13. Tetrahydrofuran
14. *iso*-Butanol
15. *sec*-Butanol
16. *iso*-Propyl acetate
17. Heptane
18. Acetic acid
19. *n*-Butanol
20. Propyl acetate
21. 4-Methyl-2-pentanone
22. Isoamyl alcohol
23. *iso*-Butyl acetate
24. *n*-Amyl alcohol
25. Butyl acetate
26. Dimethyl sulfoxide

Phase:	**BPX-Volatiles, 1.4µm film**
Sample:	**200ppm**
Column:	**30m x 0.25mm ID**
Initial Temp:	50°C, 5 min
Rate 1:	10°C/min to 85°C, 1min
Rate 2:	15°C/min to 170°C
Final Temp:	170°C
Detector Type:	Mass Spectrometer
Carrier Gas:	He, 6.7
Carrier Gas Flow:	0.9mL/min
Constant Flow:	On
Average Linear Velocity:	35cm/sec at 50°C
Injection Mode:	Split
Split Ratio:	100:1
Injection Volume:	0.4µL
Injection Temperature:	250°C
Autosampler:	No
Liner Type:	4mm ID Single Taper Liner
Liner Part No:	**092017**
Column Part No:	**054980**

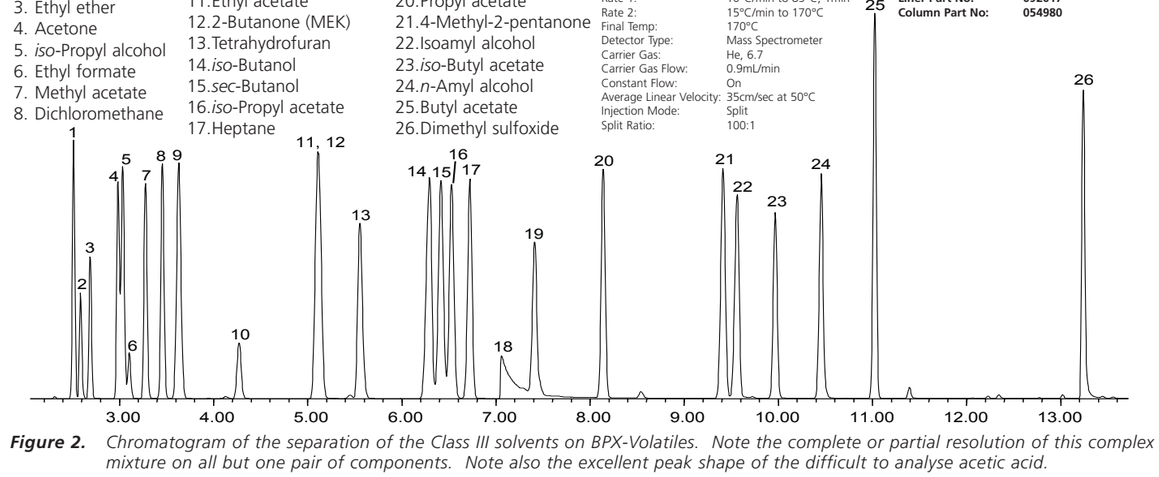

Figure 2. *Chromatogram of the separation of the Class III solvents on BPX-Volatiles. Note the complete or partial resolution of this complex mixture on all but one pair of components. Note also the excellent peak shape of the difficult to analyse acetic acid.*

THE ANALYSIS

The analysis of the Class I and Class III solvents can be clearly seen in **Figures 1** and **2** respectively. The Class I solvents are the most toxic of all of these solvents and are considered to be the least desirable solvents to use. The BPX-Volatiles column easily baseline resolves all compounds in the Class I mixture (Figure 1). Take particular note of the excellent baseline separation of the difficult-to-resolve 1,2-dichloroethane and benzene.

The more complex Class III solvent mixture is easily resolved when analyzed on BPX-Volatiles (Figure 2). The early eluting compounds such as pentane, ethanol and ethyl ether are extremely well resolved. Ethyl formate can easily be quantitated from acetone and iso-propyl alcohol and the difficult-to-resolve 2-butanone (MEK) and ethyl acetate are the only coeluting components. Baseline resolution is achieved on all of the 20 other components. The peak shape of the difficult to analyze acetic acid is excellent and the entire mixture is eluted in less than 14 minutes making it a time and cost effective analysis to perform on the BPX-Volatiles capillary columns.

SUMMARY

The BPX-Volatiles column has been specifically designed for the analysis of volatile mixtures. With a maximum temperature limit of 300°C the BPX-Volatiles column is among the highest temperature volatiles columns available. The high thermal stability of the phase results in a low bleed column ideal for low-level analyses. The BPX-Volatiles column is ideal for the analysis of pharmaceutical solvents such as Class I and Class III solvents. The separation of these components, coupled with the low detection limits and excellent inertness make the BPX-Volatiles the first choice for the analysis of pharmaceutical solvents.

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