Characterization of Extractables from Corning® and Competitor PET and PETG Bottles

Application Note

CORNING

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Introduction

Extractables are chemical entities that migrate from a contact surface after exposure to a solvent under exaggerated conditions of time, temperature, and/or pressure[1]. The results of extractable studies help identify potential leachables that can migrate from a contact surface during real process conditions. Many regulatory agencies recommend assessing the extractable and leachable profiles of containers used for the production, storage, and packaging of biopharmaceuticals.

In this study, Ultra Performance Liquid Chromatography (UPLC) was used to evaluate the extractables profile for numerous commercially available polyethylene terephthalate (PET) and polyethylene terephthalate glycol (PETG) bottles using a range of solvents recommended by the BioPhorum Operations Group (BPOG)[2]. The results demonstrate that Corning square and octagonal PET bottles have low levels of extractables that are comparable with Competitor PET and PETG bottles, as well as the glass control.

Materials and Methods

Bottle Samples (PET and PETG)

- Corning octagonal PET bottle, 500 mL (Corning Cat. No. 431733)
- Corning square PET bottle, 500 mL (Corning Cat. No. 431532)
- Competitor 1 square PET bottle, 500 mL
- Competitor 1 square PETG bottle, 500 mL
- Competitor 2 square PETG bottle, 500 mL

Glass Control Sample

- PYREX® glass bottle, 500 mL (Corning Cat. No. 1395-500)

Sample Extraction

BPOG-recommended solvents were added at 400 mL/bottle and incubated at 40°C for 0, 1, and 7 days with 90 rpm agitation. The solvents used were: HPLC-grade water (polar solvent); 50% ethanol (EtOH, organic solvent); 5M sodium chloride (NaCl, salt solution); 0.5N sodium hydroxide (NaOH, high-pH solvent); and 0.1M phosphoric acid (low-pH solvent). The ethanol extraction was conducted with no agitation due to safety concerns with solution flammability. The extracts were analyzed by UPLC.

UPLC Analysis

A 5 µL aliquot of each extract was run on an ACQUITY® UPLC® H-Cass system (Waters) using a CORTECS® C18 column (Waters) in reverse phase with a flow rate of 0.7 mL/min. Bisphenol A (BPA) and bis(2,4-di-tert-butylphenyl)phosphate (bDtBPP) standards were run together with the extracts from the bottles to help identify the presence of these undesired extractables in the bottle extracts.

Two independent experiments were conducted to ensure data reproducibility.

Results

Figures 1 to 5 show representative UPLC chromatograms of the 7-day extractions performed with 5 different solvents. Each peak represents a single extractable. As expected, no BPA nor bDtBPP were detected in the extracts from any of the tested PET or PETG bottle samples.

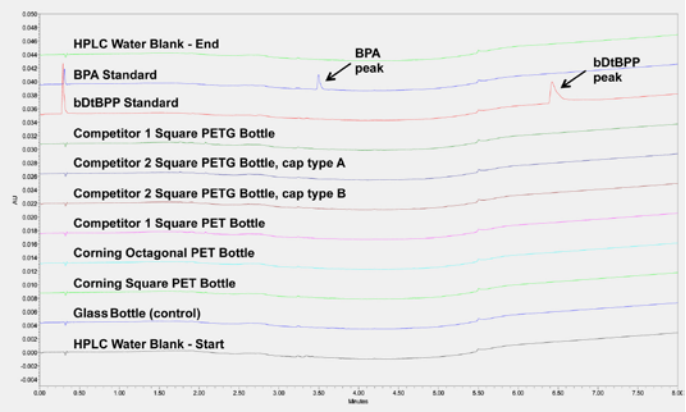

Figure 1. UPLC chromatograms of water extracts at day 7.

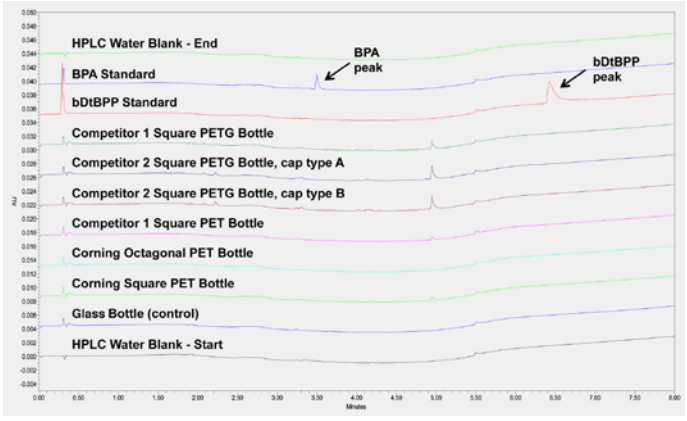

Figure 2. UPLC chromatograms of 50% ethanol extracts at day 7. The unknown peak around 4.9 min. retention time was more pronounced for extracts from PETG than PET bottles.

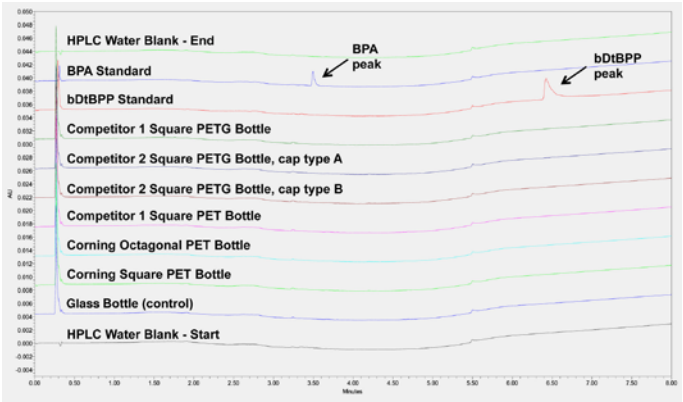

Figure 3. UPLC chromatograms of 5M sodium chloride extracts at day 7.

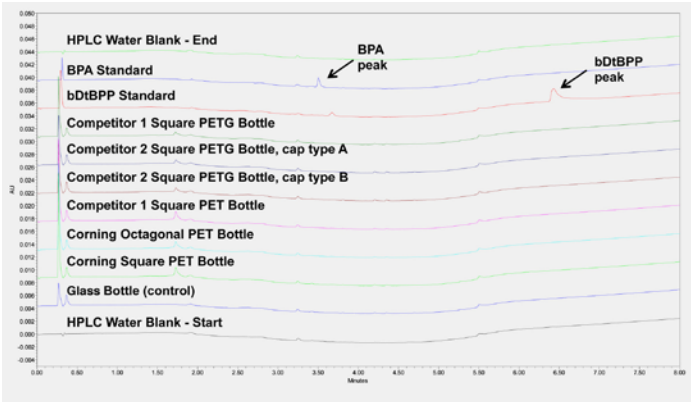

Figure 4A. UPLC chromatograms of 0.5N sodium hydroxide extracts at 0-hour.

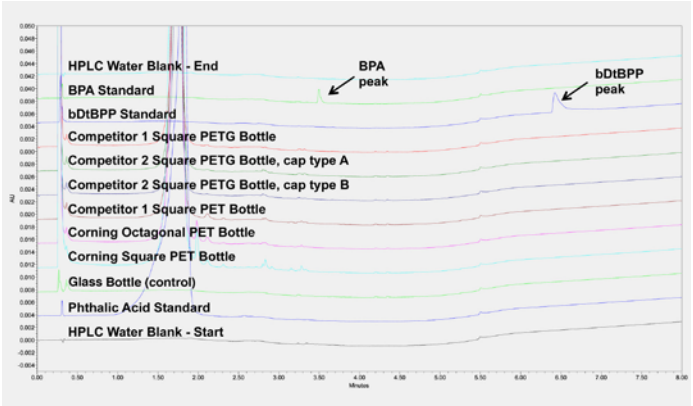

Figure 4B. UPLC chromatograms of 0.5N sodium hydroxide extracts at day 7. The big peak around 1.7 min. corresponds to the phthalic acid and indicates a breakdown of PET and PETG material under the harsh 0.5N NaOH solvent extraction conditions.

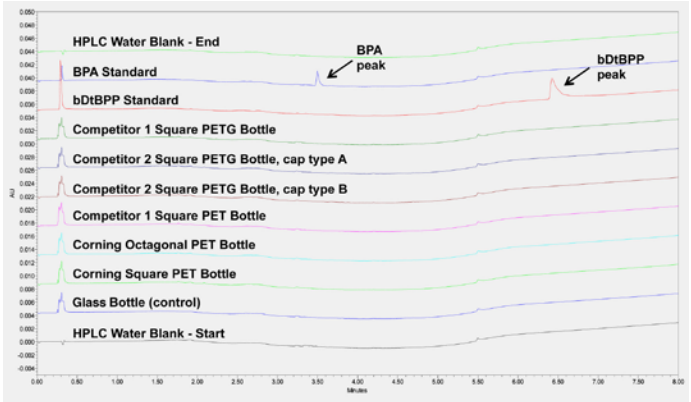

Figure 5. UPLC chromatograms of 0.1M phosphoric acid extracts at day 7.

Summary and Conclusions

- Low levels of extractables were observed in extracts from Corning® square and octagonal PET bottles using BPOG-recommended solvents (polar, organic, salt solution, and low pH) for 0, 1, and 7-day extraction time points.
- The extractable levels were comparable with those of Competitor square PET and PETG bottles, as well as the glass control.
- The breakdown of PET and PETG material under the harsh 0.5M sodium hydroxide (high-pH solvent) condition was evident by the presence of phthalic acid in the extracts from all bottle samples tested.

References

1. BPOG best practices guide for evaluating leachables risk from polymeric single-use systems used in biopharmaceutical manufacturing. 2017.
2. Weibing Ding, Gary Madsen, Ekta Mahajan, Seamus O'Connor, and Ken Wong. Standardized extractables testing protocol for single-use systems in biomanufacturing. Pharmaceut. Eng. 34 (6), 2014.

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