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Static vs. dynamic extraction – Comparing best practice for Single Use Technology

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Static vs. Dynamic Extraction – Comparing Best Practice for Single Use Technology

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Introduction

The objective of this study is to compare the extractables profile generated from filters when using either (i) Dynamic – Recirculation extraction, (ii) Dynamic – Orbital Shaker extraction, or (iii) Static Soak extraction.

Study Design

This study used Opticap® XLT 10 Capsules, with Gamma Durapore® 0.22 µm media (catalog number KVGLG1TTT1). The filters had an effective filtration surface area (SA) of 0.73 m^2 (7300 cm^2).

- All filters were from the same lot.
- Capsules were gamma irradiated ~45 kGy and extracted within 5 weeks of irradiation.
- Capsules were extracted with Milli-Q® water at 40ºC
- Samples were collected at: 30 min, 4 hrs, 8 hrs, 24 hrs, 48 hrs, and 168 hrs.
- The extracts were analyzed for: pH, small organic acids by ion chromatography, total organic carbon (TOC), volatile organic compounds (VOC) by GC/MS, organic compounds by RP-HPLC-UV, and metals by ICP.
- Triplicate samples were prepared per time point.

(i) Dynamic – Recirculation

- Capsules and reservoir contained ~2000 mL of water. A flow rate of 250 mL/minute was used to recirculate the water through the filter.
  SA/V ratio = 3.7 cm^2 to 1 mL
- At each sampling point, 170 mL was removed from the system and replaced with 170 mL of fresh water.
- The same three filters were used for all time points.
- Control: An all perfluoroalkoxy (PFA) pump and polytetrafluoroethylene (PTFE) tubing were used to limit system extractables. A system control sample was generated by circulating water through all the same components (except the filter) and aliquots were removed at each time point.

(ii) Dynamic – Orbital Shaker

- Capsules were filled with ~1710 mL of water and extracted horizontally on an orbital shaker (50 rpm).
  SA/V ratio = 4.3 cm^2 to 1 mL
- At each sampling point capsules were drained into a PFA container, homogenized, and aliquots transferred to sample jars for each assay.
- Control: A solvent blank was stored in a PFA container, and aliquots were removed at each sampling time point.

(iii) Static Soak

- The Capsules were filled with ~1650 mL of water and stored vertically in the incubator.
  SA/V ratio = 4.4 cm^2 to 1 mL
- At each sampling point capsules were drained into a PFA container, homogenized, and aliquots transferred to sample jars for each assay.
- Control: A solvent blank was stored in a PFA container, and aliquots were removed at each sampling time point.

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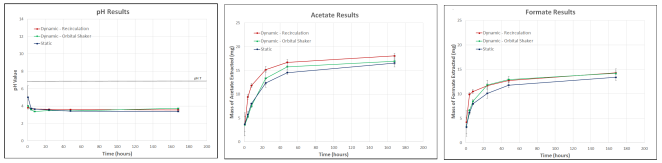
Results

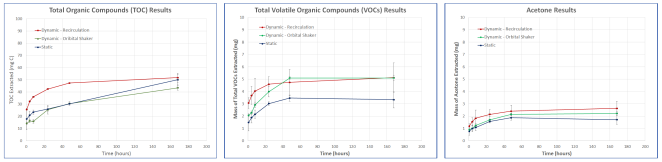
All graphs show the mass of extracted vs time. (*Except for pH and RP-HPLC*)
All graphs show the average of the three replicate samples. (*Except for RP-HPLC)*
The error bars are the standard deviation between the three replicates.

pH, Acetate, and Formate



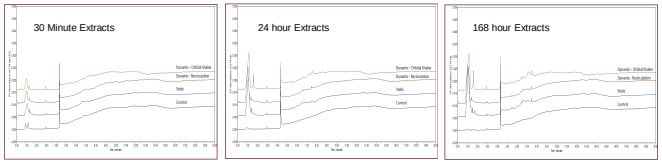
- In all samples the pH dropped to about pH 4 due to the generation of acetate and formate, formed as a result of the gamma irradiation.
- Both acetate and formate results have a similar pattern – increasing quickly in the first 24 hours, then only slightly more over the next six days.

TOC, Total VOC, and Acetone



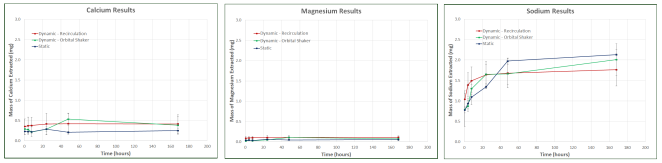
- All three graphs show a similar pattern – increasing quickly in the first 24 hours, then only slightly more over the next six days.
- Acetone was the most prominent VOC detected, accounting for half of the Total VOC concentration. Others compounds (not shown) include acetaldehyde, 2-pentanone, and methyl isobutyl ketone.

Organic Compounds by RP-HPLC



- The chromatographs show only one of the three replicates at each time point.
- All three extraction techniques generate a similar profile, all increasing with time. (The peaks of interest are from 5-9 minutes.)
- The recirculation chromatograph peaks are the smallest due to dilution from the higher extraction volume and the addition of fresh solvent at each sampling time point.

Metals



- Only three metals (calcium, magnesium, and sodium) were detected in the extracts.
- All three metals were present at the same concentrations, regardless of the extraction technique.

Comparison of the Different Extraction Techniques

The following tables summarize the advantages and disadvantages or each of the three extraction techniques.

Parameter	Dynamic – Recirculation	Dynamic – Orbital Shaker	Static Soak
Extraction Kinetics	**Best** Most efficient kinetics	**Better**	**Good** Least efficient kinetics for the early sample time points.
Sample Throughput	**Fair** Capable of testing 2 filters per incubator	**Better** Capable of testing 18 filters per incubator	**Best** Capable of testing 36 filters per incubator
Data Variability	**Best** The same three filters were used for all time points	**Good** Data variable due to individual filters used at each sampling time point.	**Good** Data variable due to individual filters used at each sampling time point.
Test Samples	**Best** 3 filters needed for this study	**Good** 18 filters needed for this study (3 per sample time point)	**Good** 18 filters needed for this study (3 per sample time point)
Complexity	**Fair** (i) Most complex to execute. (ii) Least robust procedure with a greater risk of contamination. (iii) Need more controls (solvent and system). (iv) More complex calculations needed to account for mass removed at the earlier sample time points.	**Best** (i) Easy to execute (ii) Easy to calculate results	**Best** (i) Easy to execute (ii) Easy to calculate results

Summary

- Recirculation extraction had the most efficient extraction kinetics, followed by orbital shaker, and lastly static soak. This was most evident in the results from the early sample time points. However, by day 7 all three extraction techniques demonstrated similar concentrations of all compounds detected in the study.
- The profile of extractable compounds was identical for each technique.
  i. All the same compounds were detected in the extracts regardless of the extraction technique.
  ii. The order of prominence (compound with the highest concentration) was the same regardless of the extraction technique.
- All compounds had a similar extraction profile; increasing quickly over the first 24 hours, then only slightly more over the next 6 days.
- Each extraction technique has advantages and disadvantages compared to the others.