# Evaluating Extractables and Leachables from Purification Resins in Biopharmaceutical Manufacturing

RESOLIAN
ANALYTICAL SCIENCES

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## Introduction

In the production of biopharmaceuticals, purification resins are widely used during downstream processing to ensure the drug product is free from undesired impurities. Purification resins risk releasing process-equipment related leachables (PERLS) into drug products, impacting efficacy and safety of the drug product by:

- Binding to active sites
- Protein denaturation
- Direct patient exposure

**Aim: Develop a protocol for the detection and quantification of extractables from purification**

## Materials and Method

Four purification resins extracted, in solvents listed figure 1, these bracketed the polarities and pH of media used in purification stages. See table 1 for conditions, techniques and interpretation information of method.

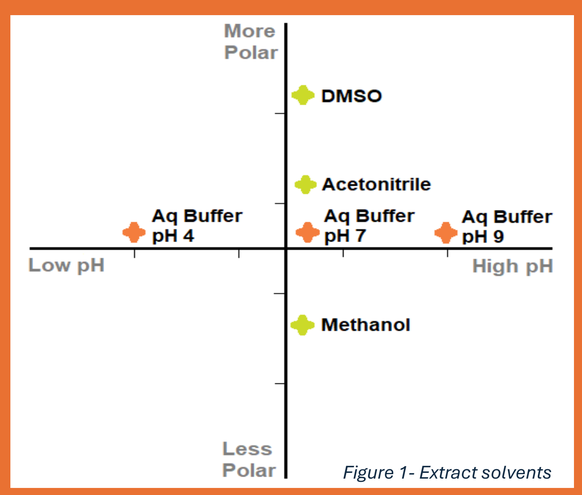


*Figure 1- Extract solvents*

***Table 1 - Methodology***

| | |
|---|---|
| **Extraction Conditions** *(as per ISO10993-12, 2021)* | 72 hours (±2h) at 50°C (±2°C) |
| | Solvents listed figure 1 |
| **Analytical Techniques** | HR-LC-MS |
| | GC-MS |
| | ICP-MS |
| **Data Review Interpretation** | Organics identified against matched standards and NIST/in-house libraries |
| | Semi quantification against surrogate reference materials |
| | Inorganics identified and quantified against target elements |

## Results

- Range of organic and inorganic extractables were detected.
- Majority of PERLs were observed in organic solvents. extracts, representing worst-case conditions.
- Key organic species are listed in figure 2, example chromatograms in figure 3.
- Inorganic analysis showed presence of Fe and Al in one resin sample.

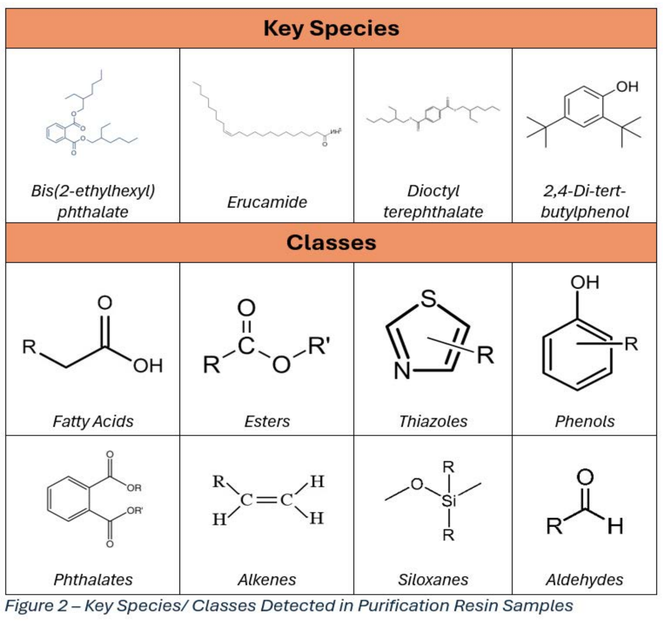


*Figure 2 – Key Species/ Classes Detected in Purification Resin Samples*

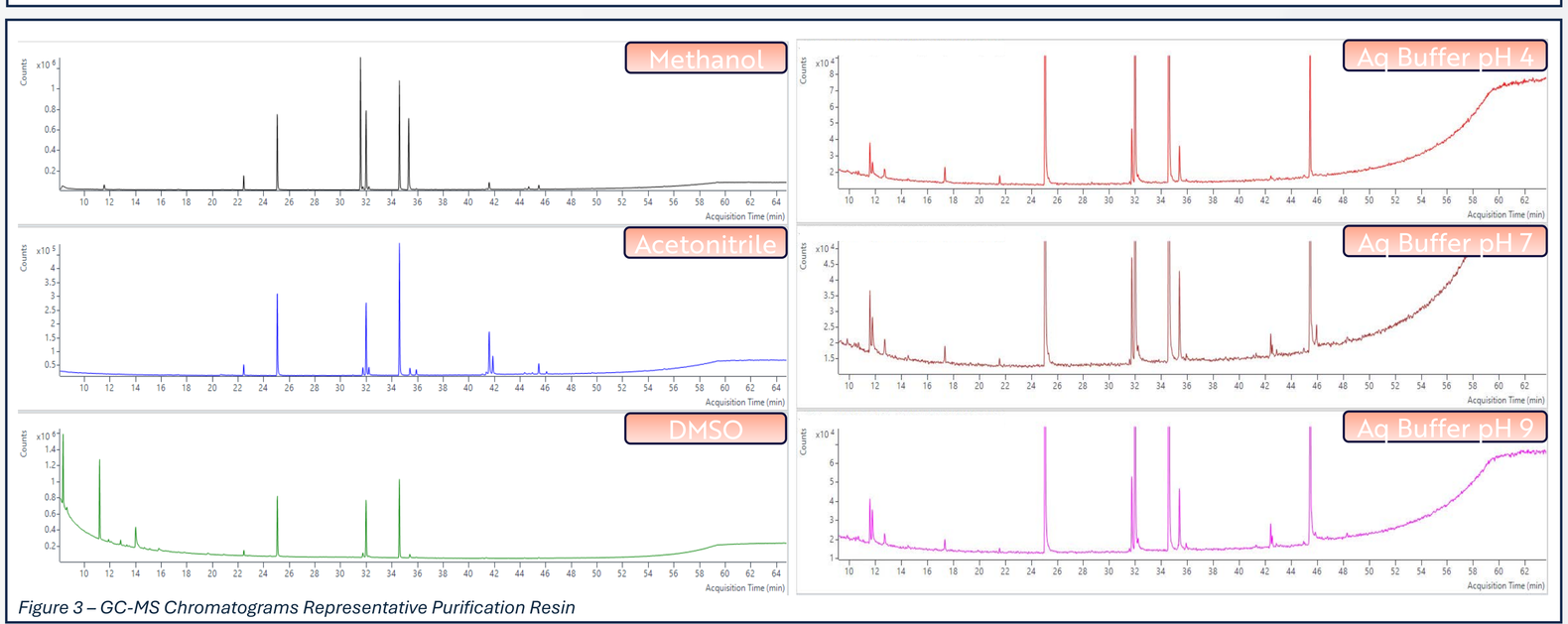


*Figure 3 – GC-MS Chromatograms Representative Purification Resin*

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- ✓ Extractables and Leachables (E&L) profile impurities from pharmaceutical and healthcare applications.
- ✓ E&L assessments are in accordance with latest regulations and utilise organic and inorganic screening alongside diverse sample preparation techniques

## Conclusions

- ✓ Analytical protocol for assessment of PERLs from purification resins was successfully developed.
- ✓ Number of organic and inorganic PERLs were detected in four commercially available resins.
- ✓ The protocol can be used to assess compatibility of resins to downstream manufacturing processes and to evaluate risk to final drug product integrity.

**Further work**

- Monitor target PERLs in a drug product.
- Investigate impact on the efficacy of drug product due to interaction of PERLs with biopharmaceuticals.

**References**
International Organization for Standardization. (2021). *ISO 10993-12:2021 - Biological evaluation of medical devices – Part 12: Sample preparation and reference materials.* ISO. https://www.iso.org/standard/79576.html