

## ABSTRACT

Microbial natural products are well known for their role in antibiotic development history and their potential for new drugs development [1]. However, it is estimated that only a minor part of the bacterial secondary metabolite chemical space is known [2]. In this sense, we aim to explore and wider the microbial metabolites known by using supercritical fluid chromatography and extraction approaches. The use of supercritical fluid chromatography (SFC) and UltraPerformance Convergence Chromatography (UPC<sup>2</sup>) can act as facilitators for the fractionation and isolation of compounds that could not be resolved by traditional chromatography approaches [3], while supercritical fluid extraction (SFE) can have the capacity to recover compounds that are inaccessible by ultrasound-facilitated extraction [4]. Finally yet importantly, both supercritical fluid approaches are regarded as greener techniques. We present here a workflow for facilitating the isolation and characterization of new microbial natural products using supercritical fluid approaches.

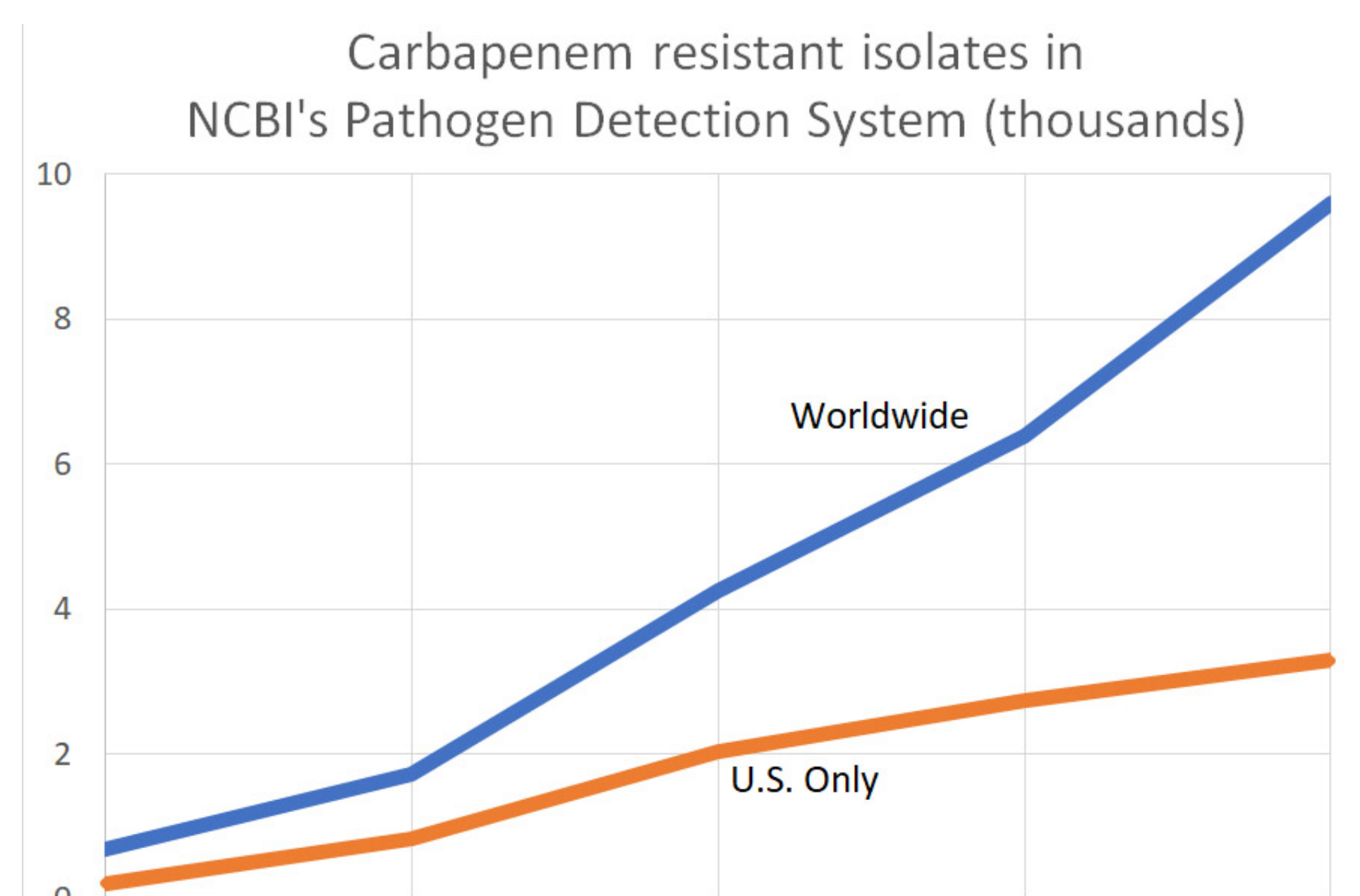
## OBJECTIVE



**New antibiotic discovery**  
with a greener process!

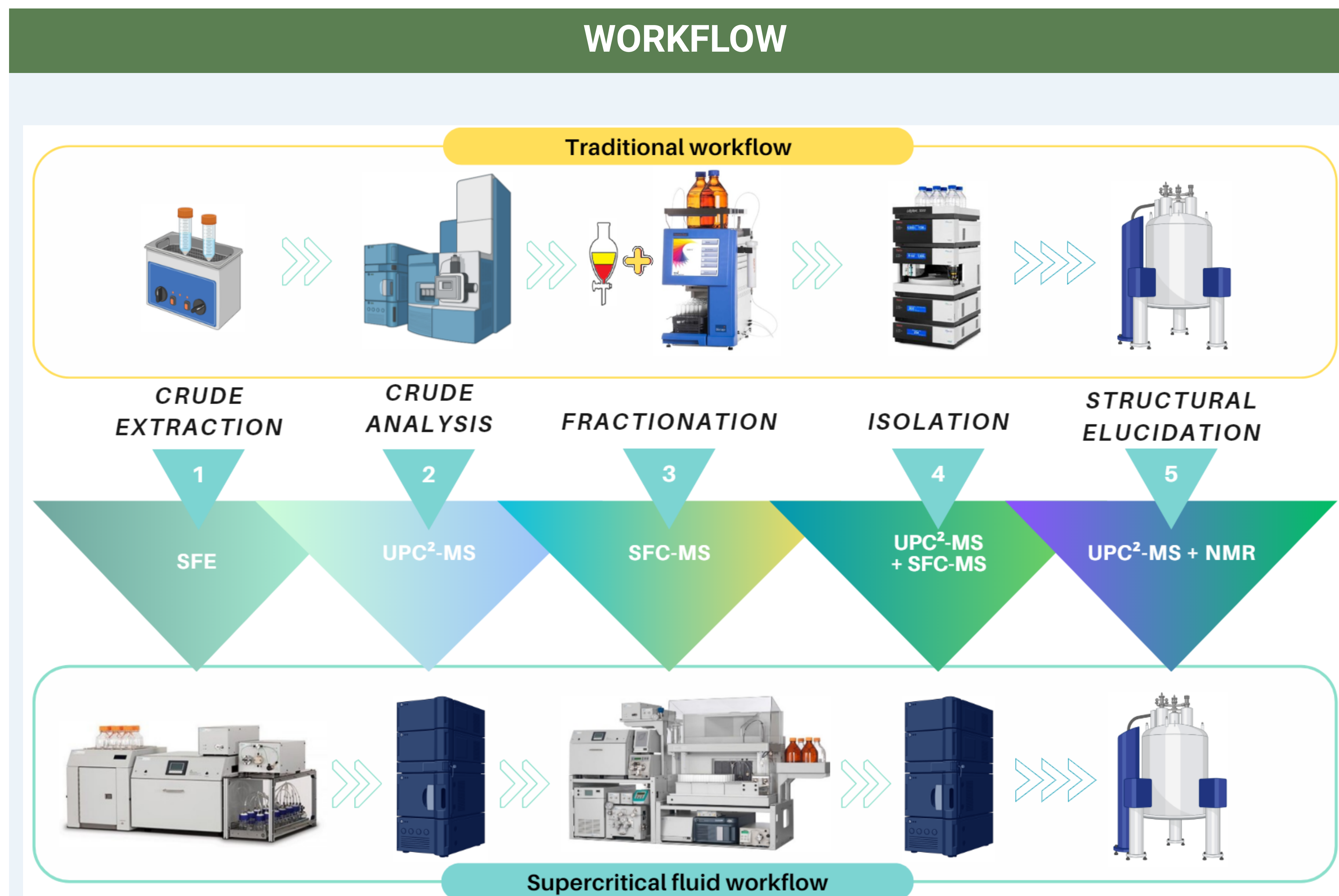
## WHY

### Continuous rise in antimicrobial resistance

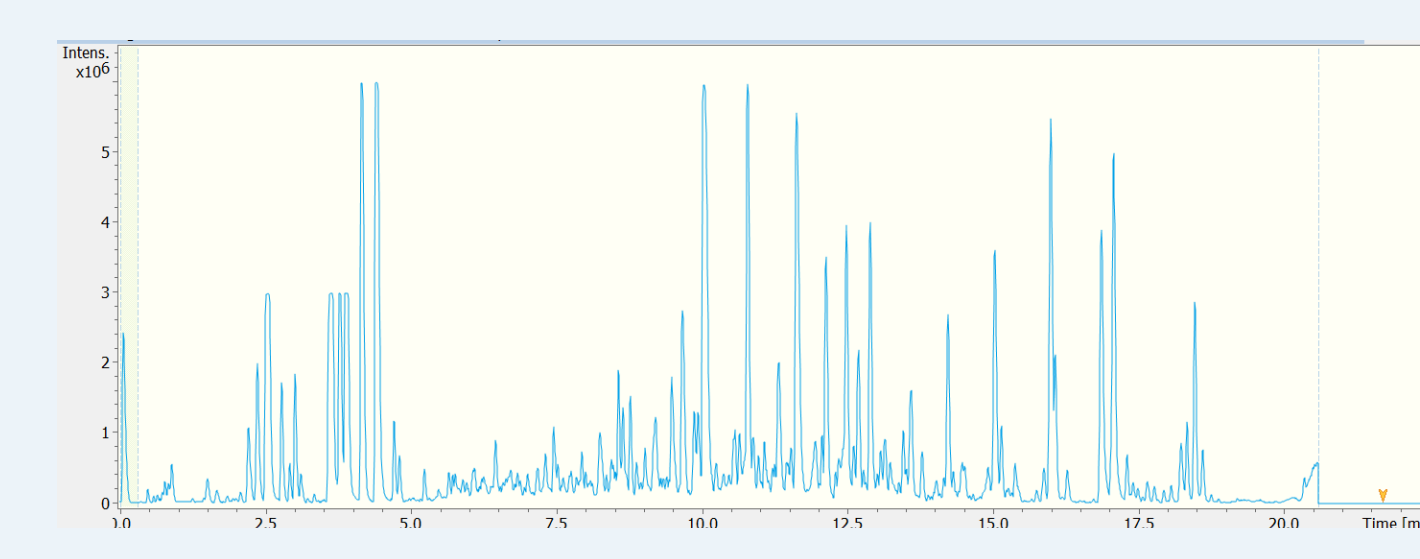


Carbapenem resistance, an example of antimicrobial resistance (AMR) growth between 2014 and 2018 [5].

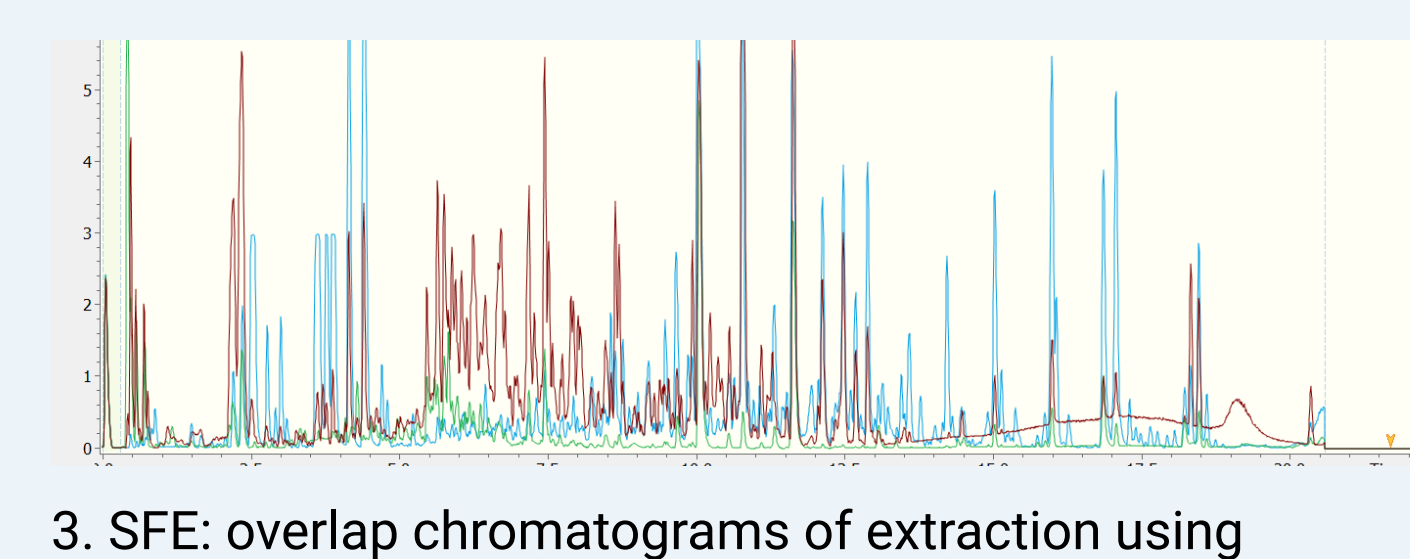
## WORKFLOW



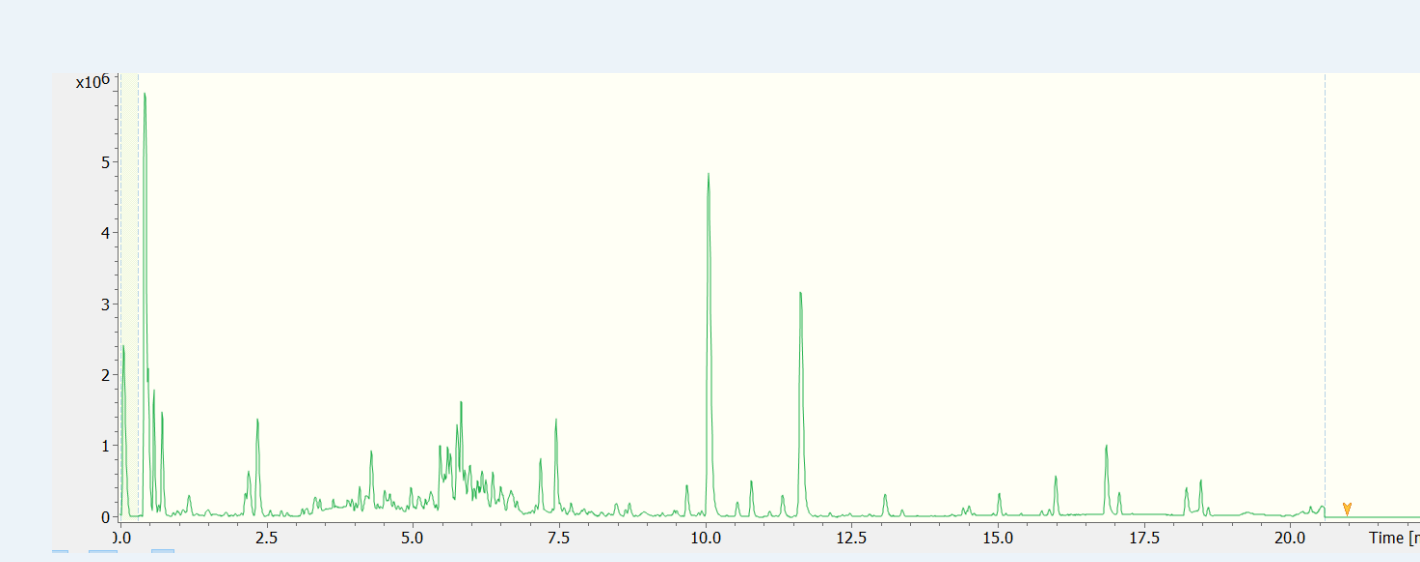
### EXAMPLE: SFE EXTRACTION VS TRADITIONAL METHANOL EXTRACTION



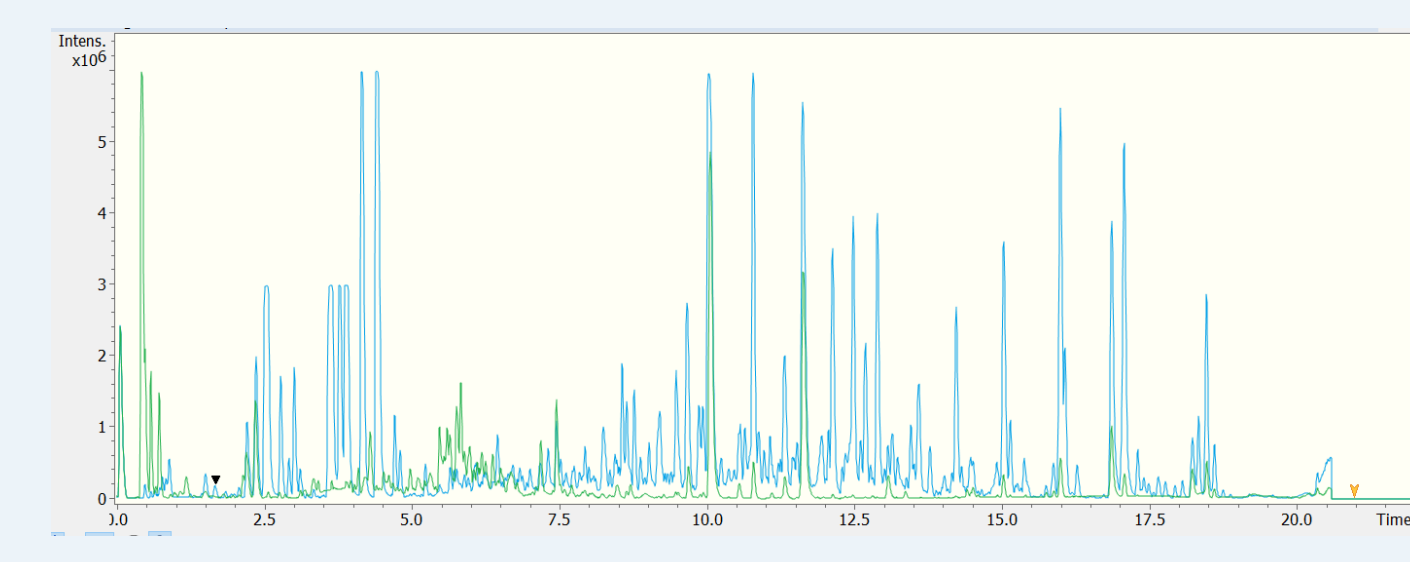
1. Extraction with SFE: 20% Ethyl Acetate and 80% CO<sub>2</sub>.



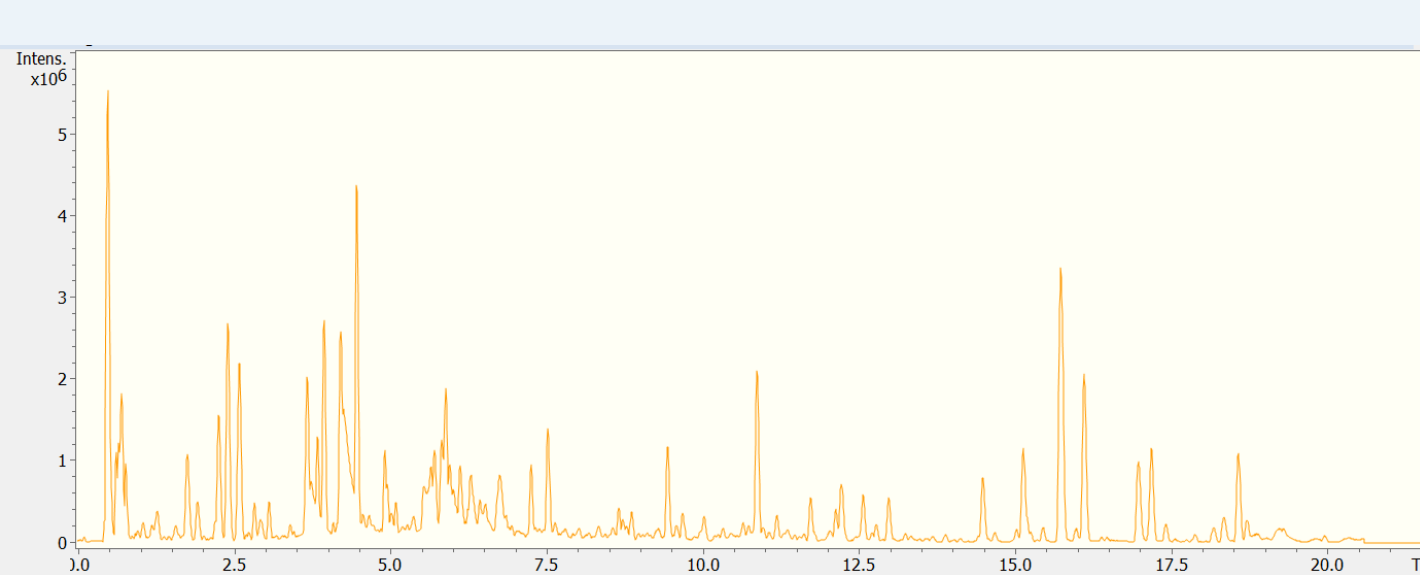
3. SFE: overlap chromatograms of extraction using 20% organic solvent (MeOH, EtAc, i-Pro) and 80% CO<sub>2</sub>.



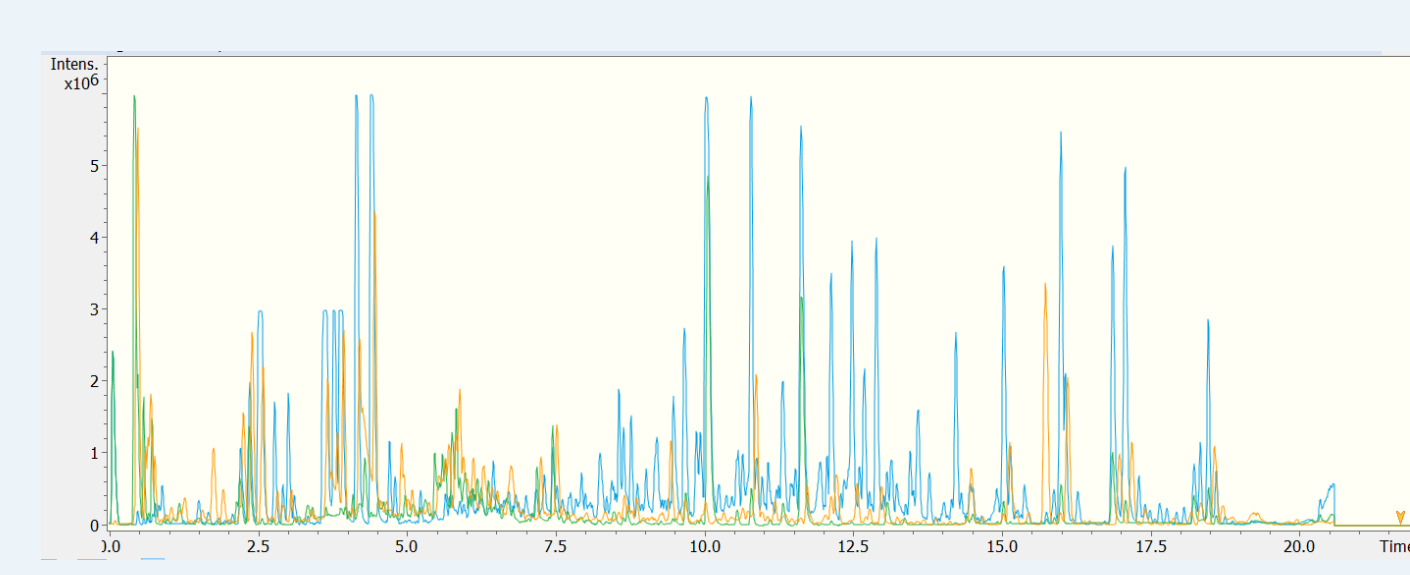
2. Extraction with SFE: 20% Methanol and 80% CO<sub>2</sub>.



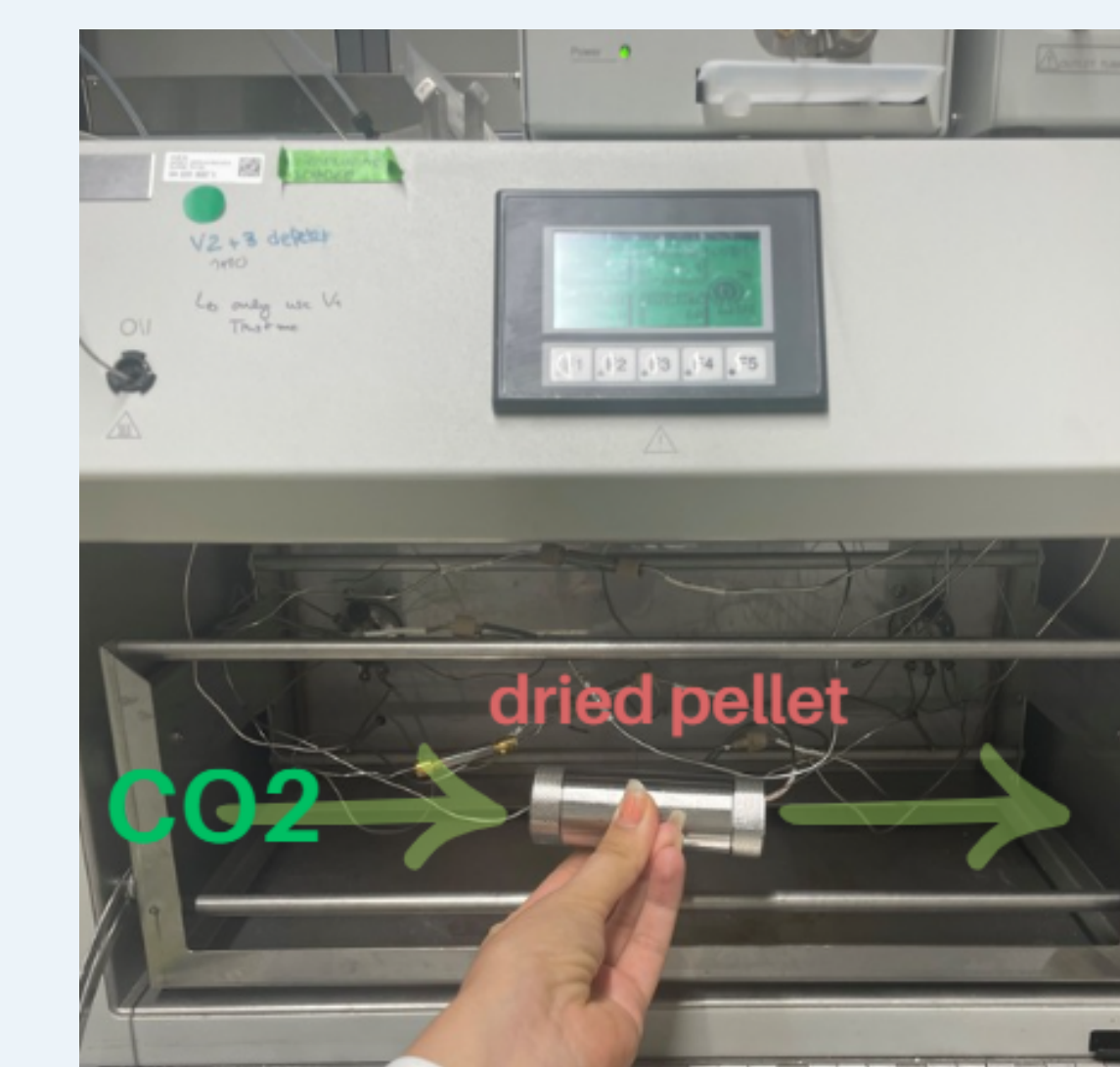
4. SFE: overlap chromatograms 1 and 2.



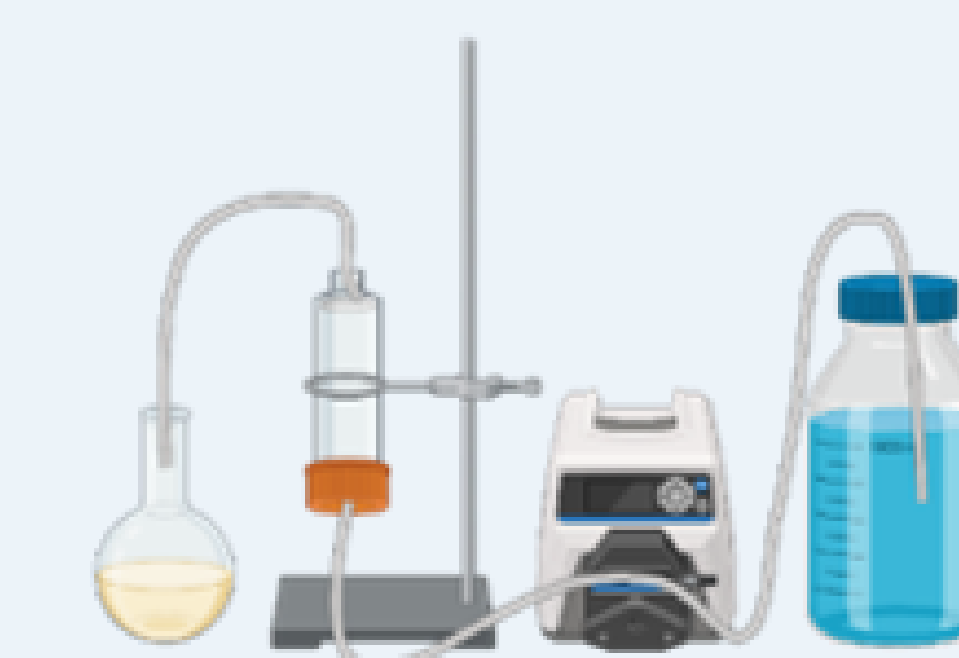
5. Extraction using traditional methanol cartridge system.



6. Overlap of chromatograms 1, 2 (SFE) and 5 (traditional methanol cartridge extraction).



SFE system

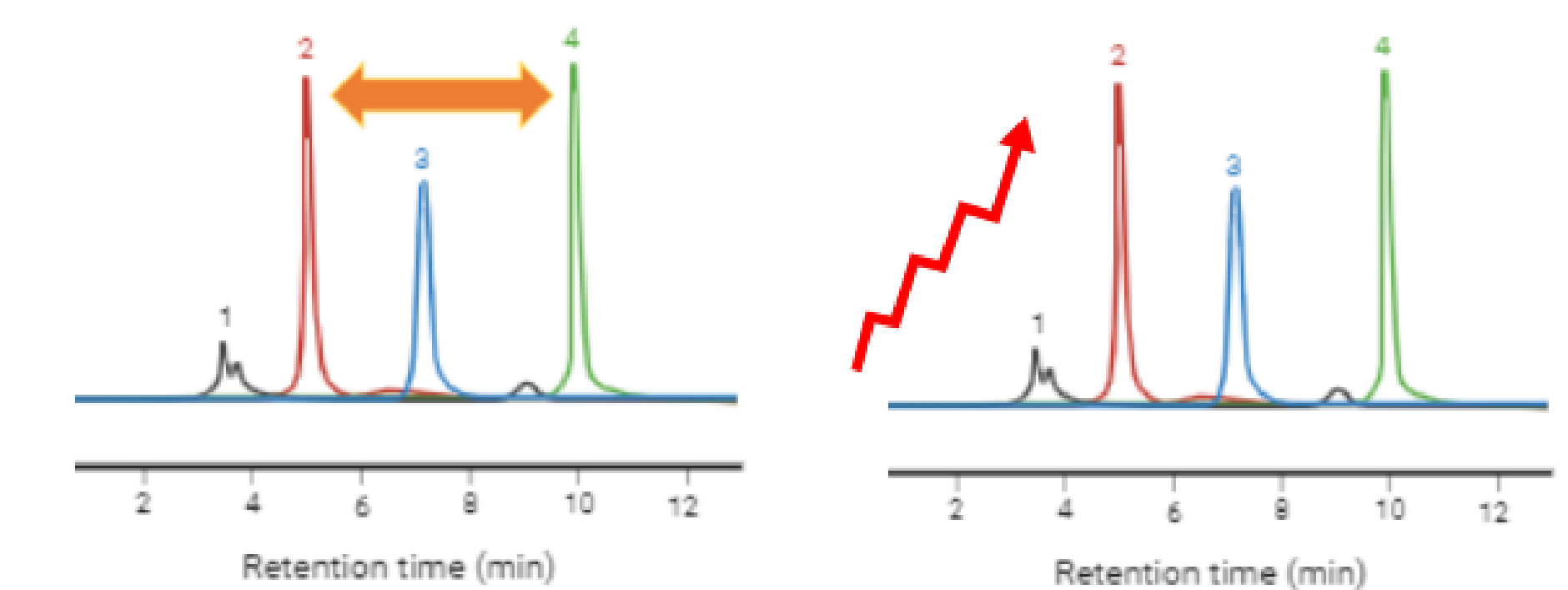


Extraction with methanol in a cartridge system

## ADVANTAGES



GREENER PROCESS



DIFFERENT SEPARATION

LOWER LOSS & HIGHER CAPACITY



INCREASING THE CHANCE OF NEW COMPOUND DISCOVERY!

## REFERENCES

- [1] Hutchings MI, Truman AW, Wilkinson B. Antibiotics: Past, present and future. *Current Opinion in Microbiology*. 2019;51:2–80.
- [2] Alam K, Abbasi M, Hao J, Zhang Y, Li A. Strategies for natural products discovery from uncultured microorganisms. *Molecules*. 2021;26(10):2977.
- [3] Jones MD, Yu K, Potts W. Comparing Orthogonality of Convergence Chromatography to Reversed-Phase LC. *Waters Application Note* 2013.
- [4] Bader CD, Neuber M, Panter F, Krug D, Müller R. Supercritical fluid extraction enhances discovery of secondary metabolites from myxobacteria. *Analytical Chemistry*. 2020;92(23):15403–15411.
- [5] National database of antibiotic resistant organisms (NDARO) - pathogen detection - NCBI (no date) National Center for Biotechnology Information. Available at: <https://www.ncbi.nlm.nih.gov/pathogens/antimicrobial-resistance/> (Accessed: 20 September 2024).

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