

Systematic study on the design of supramolecular deep eutectic solvents (SUPRADES) for the extraction of bioactive compounds.

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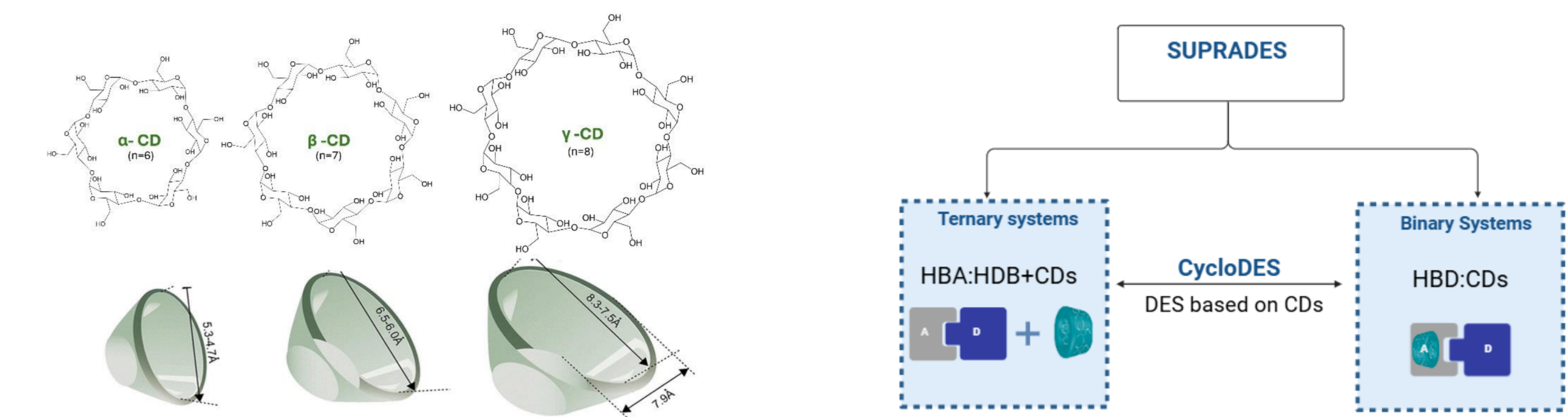
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BACKGROUND

Supramolecular deep eutectic solvents (SUPRADES) are a novel class of deep eutectic solvents (DES) capable of forming inclusion complexes. Cyclodextrins (CDs), cyclic oligosaccharides derived from enzymatic starch degradation, are characterized by their hydrophobic cavity and hydrophilic outer surface, enabling host-guest interactions. Native CDs typically contain six (α -CD), seven (β -CD), or eight (γ -CD) D-glucopyranose units, which determine their cavity size.

SUPRADES are developed using two main strategies: ternary systems, where a macrocycle is added to a pre-formed DES, and binary systems, where CDs or their derivatives act as hydrogen bond acceptors (HBA) with hydrogen bond donors (HBDs) such as alcohols, amides, or organic acids. In 2023, Balenzano et al. introduced the term CycloDES for SUPRADES incorporating CDs. These solvents are synthesized by magnetically stirring the precursor compounds in a sealed vial at a specific temperature, yielding a stable, transparent liquid at room temperature.



Scheme 1: Chemical formulas and 3D structures of α -CD, β -CD and γ -CD and SUPRADES synthesis strategies.

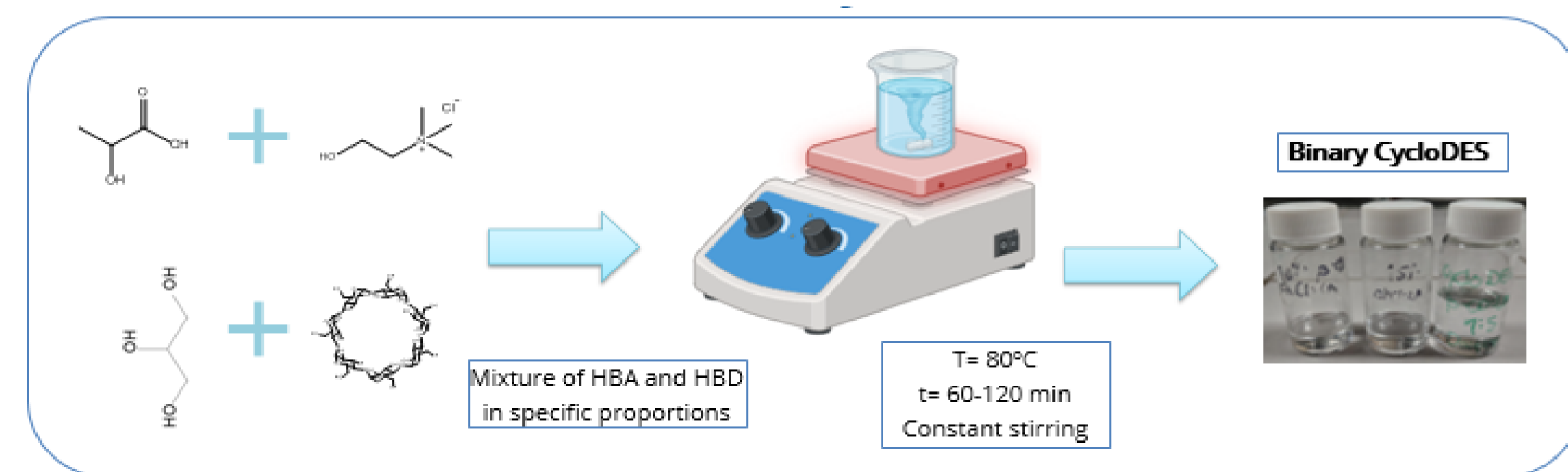


Figure 1. Binary CycloDES synthesis method

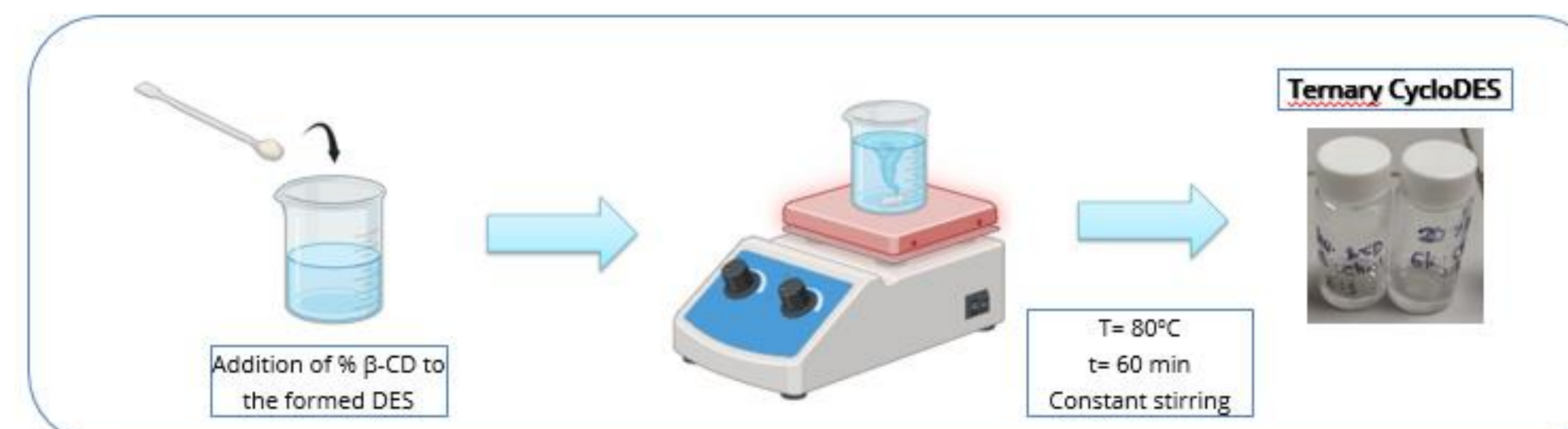


Figure 2. Ternary CycloDES synthesis method

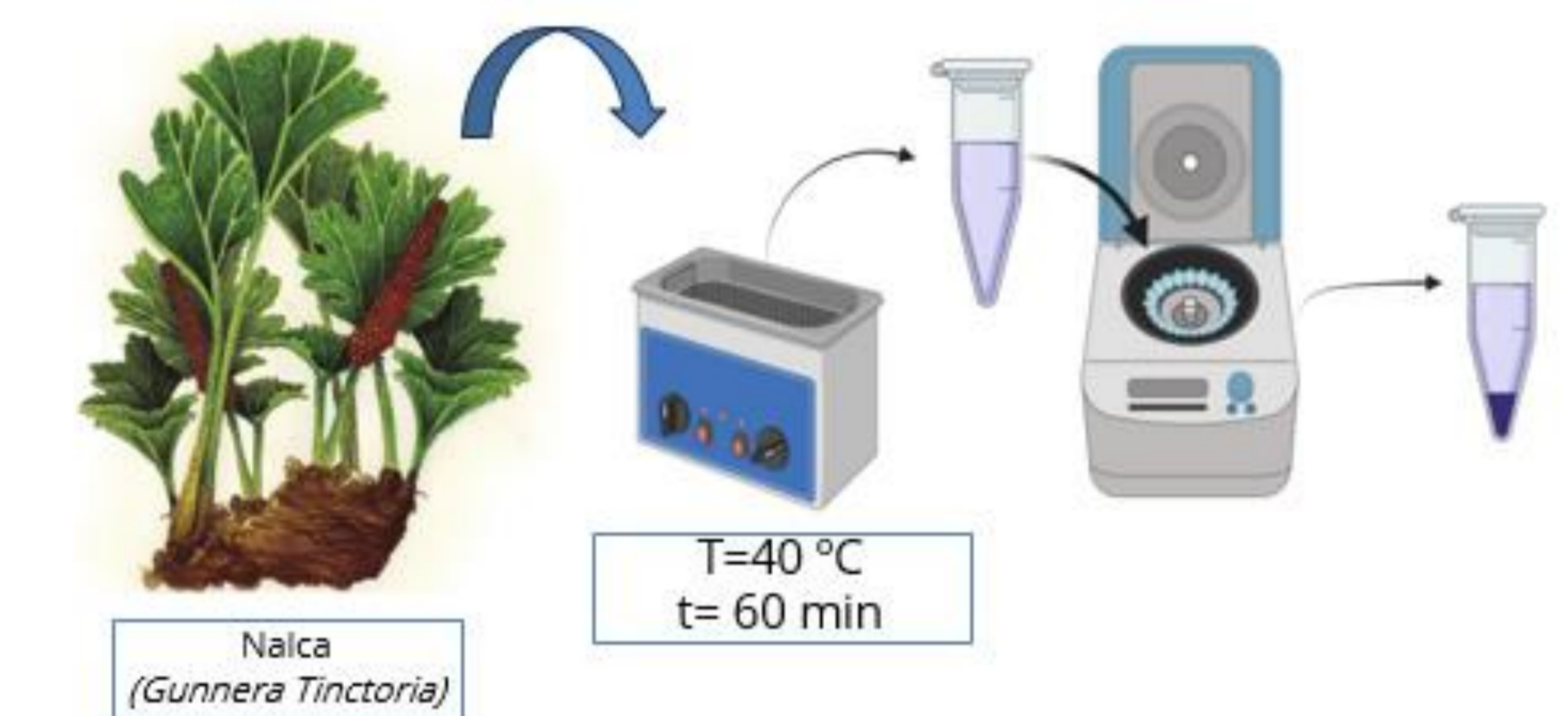


Figure 3. Ultrasound-assisted extraction methodology of polyphenols with CycloDES.

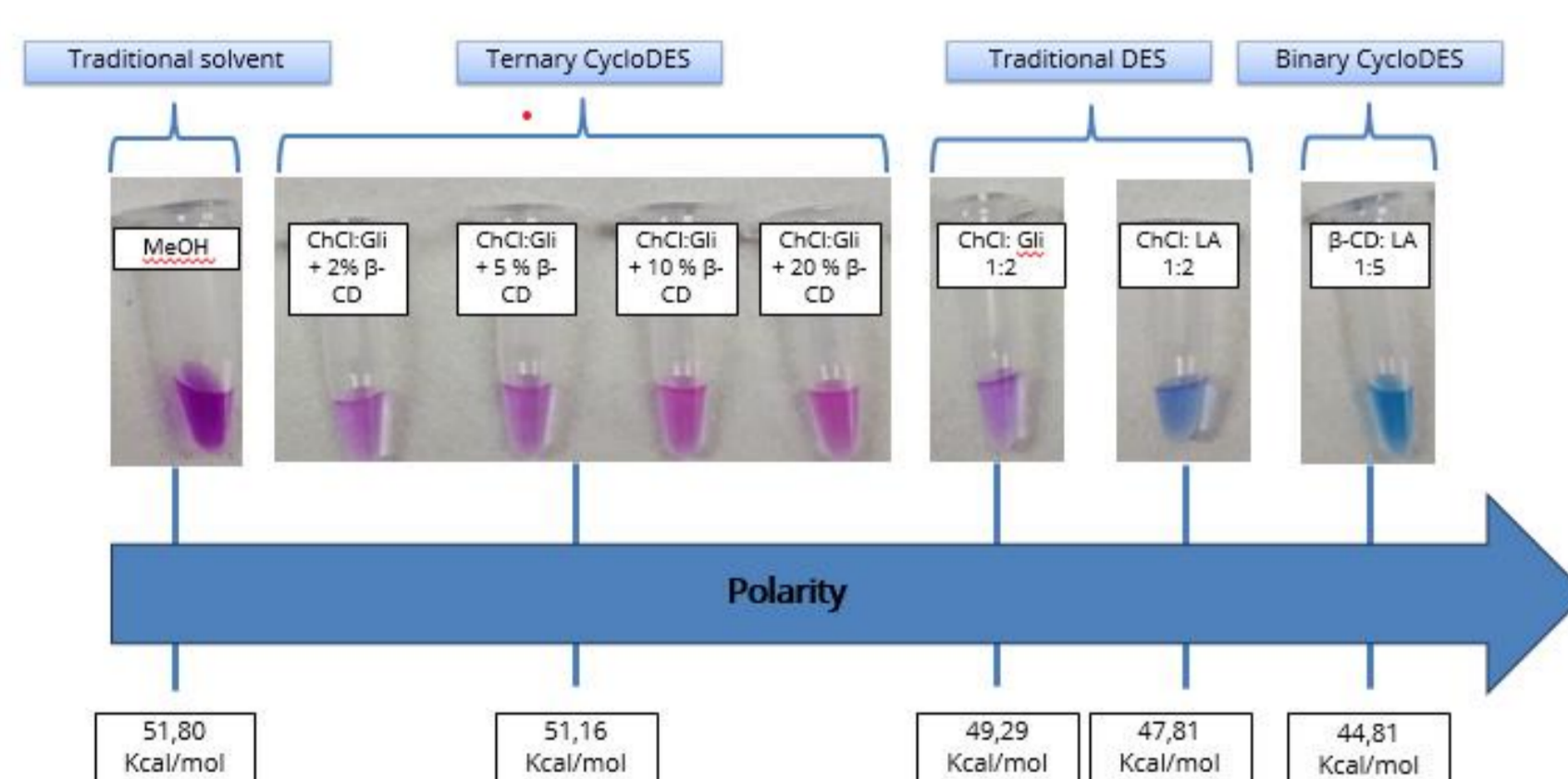


Figure 4. Polarity of CycloDES compared to traditional solvents and DES.

Table 1. Composition of DES studied

DES Type	Composition	Molar Ratio	Abbreviation
Conventional DES	Choline chloride: Glycerol	1:2	ChCl:Gli
	Choline chloride: Lactic acid	1:2	ChCl:LA
Ternary SUPRADES	Choline chloride: Glycerol + β -CD	1:2 + 2%	ChCl:Gli + 2% β -CD
	Choline chloride: Glycerol + β -CD	1:2 + 5%	ChCl:Gli + 5% β -CD
	Choline chloride: Glycerol + β -CD	1:2 + 10%	ChCl:Gli + 10% β -CD
Binary SUPRADES	Choline chloride: Glycerol + β -CD	1:2 + 20%	ChCl:Gli + 20% β -CD
Binary SUPRADES	β -cyclodextrin: Lactic acid	1:5	β -CD:LA

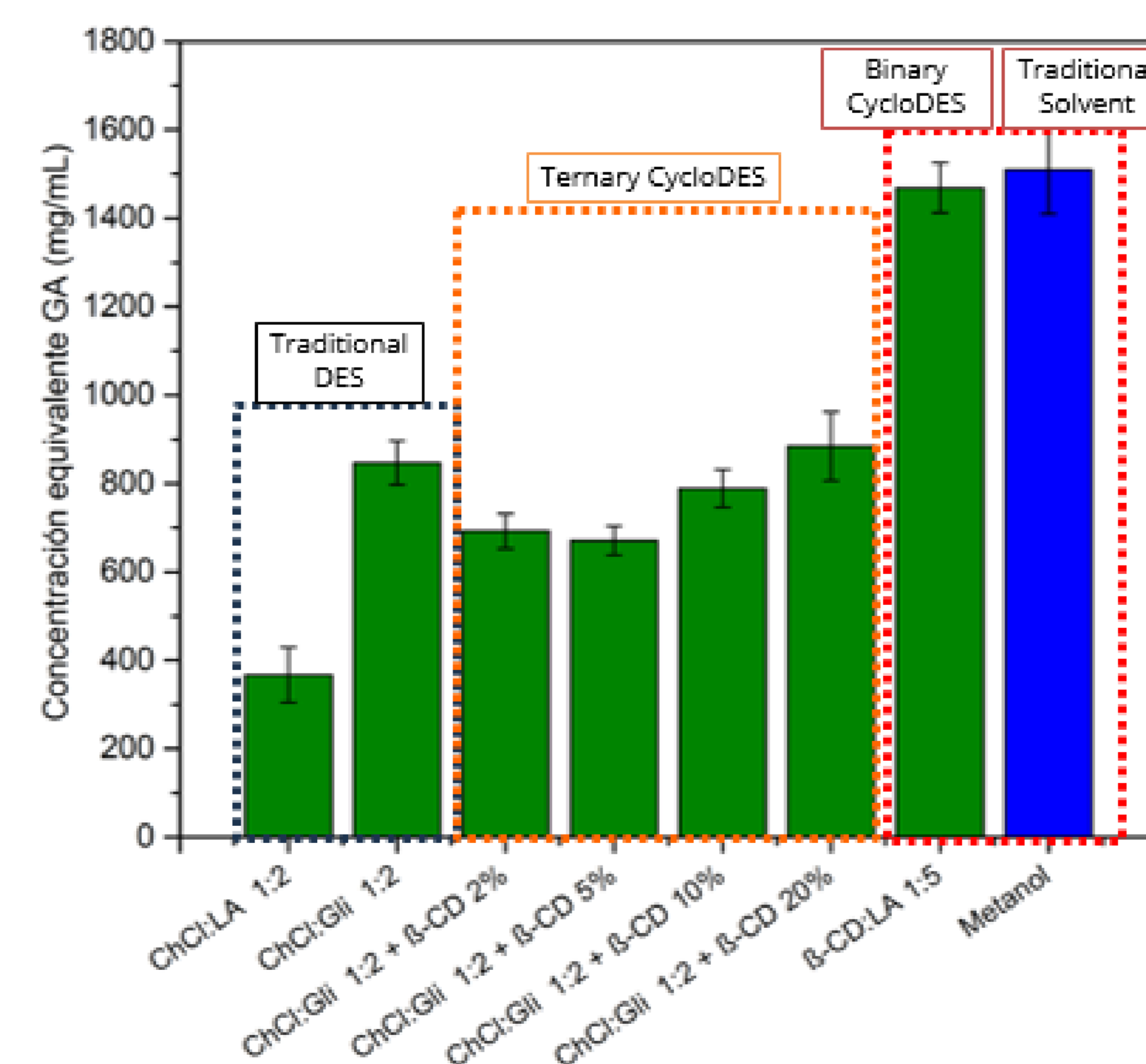
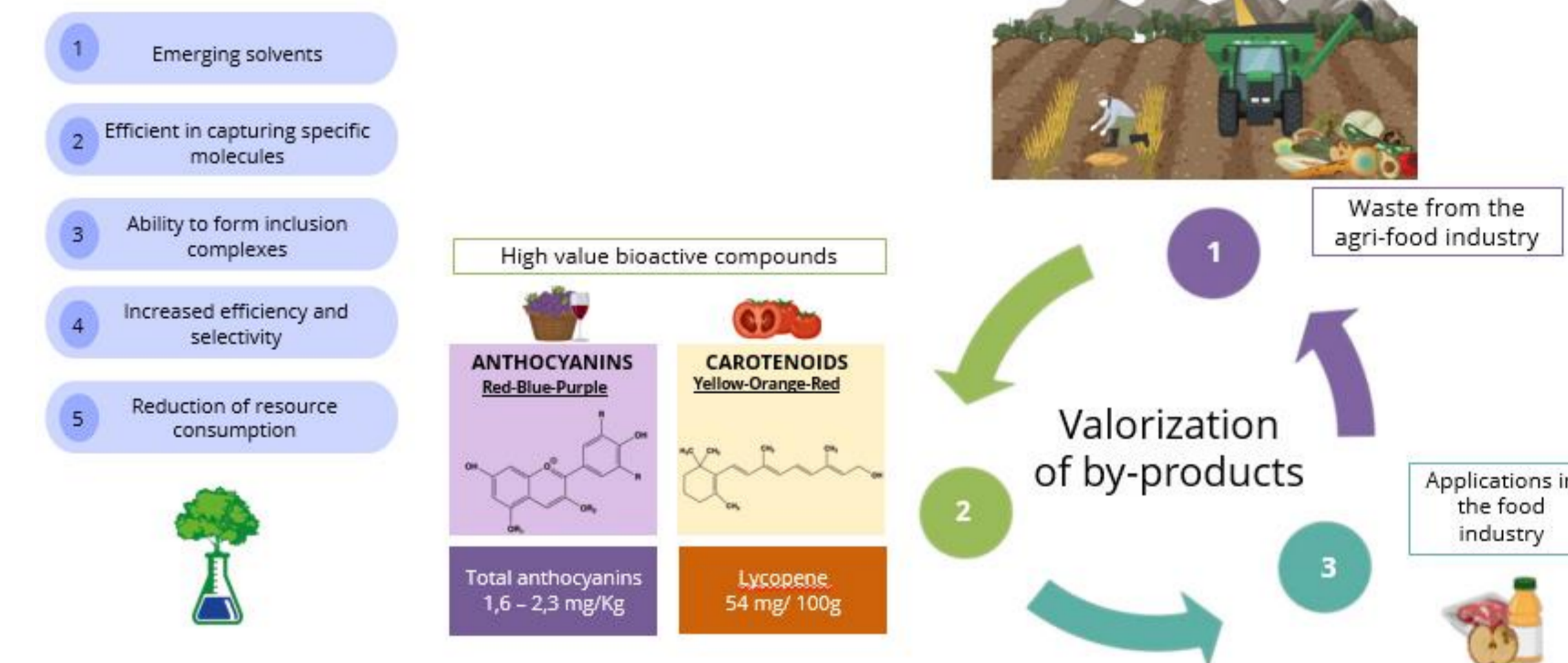


Figure 5. Determination of total phenols by the Folin-Ciocalteu method in Nalca leaf extract.

The extraction efficiency of polyphenols from Nalca (*Gunnera tinctoria*) leaves was assessed using the Folin-Ciocalteu method to determine total polyphenols. This efficiency was compared with two traditional DES and methanol as a conventional solvent.

SUPRADES for the extraction of bioactive compounds



CONCLUSION

The results highlighted significant differences in polyphenol extraction efficiency depending on the DES composition. The ChCl:Gli 1:2 system proved to be more efficient than ChCl:LA 1:2, emphasizing the importance of selecting the appropriate DES components to optimize performance in bioactive compound extraction applications. In the ternary SUPRADES, the addition of β -cyclodextrin (β -CD) did not improve extraction efficiency, possibly due to limited interaction between the solvent and polyphenol structures, highlighting the need for a more detailed analysis of molecular interactions. In contrast, binary SUPRADES achieved a significant increase in extractability, comparable to methanol, due to the ability to form inclusion complexes between β -CD and polyphenols. This not only allowed for selective extraction of desired compounds but also resulted in purer and higher-quality extracts. These findings underscore the potential of SUPRADES for sustainable and efficient polyphenol extraction applications.

References:

- [1] G. Balenzano et al., *Int J Pharm*, vol. 647 (2023).
- [2] M. Q. Farooq, V. R. Zeger, and J. L. Anderson., *J Chromatogr A*, vol. 1658 (2021).
- [3] R. Craveiro et al., *J Mol Liq*, vol. 215, pp. 534–540 (2016)