

# WHEN ENZYMES MET IONIC LIQUIDS: A JOURNEY TO "DREAM" CHEMISTRY.

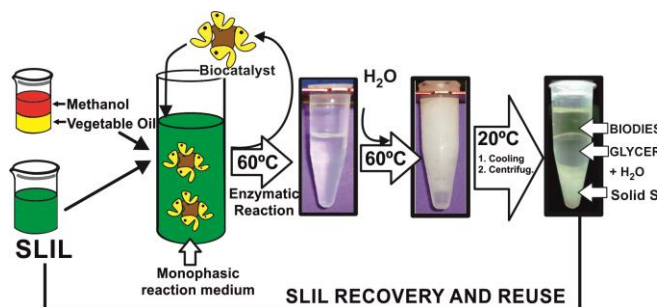
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Enzymes clearly constitute the most powerful green tools for catalyzing chemical processes, since their activity and selectivity (stereo-, chemo- and regioselectivity) are far ranging. Although enzymes are designed by living systems to work in aqueous solutions, there are numerous potential advantages in employing enzymes in non-aqueous environments (e.g. new chemical transformations, higher solubility of hydrophobic substrates, easy reuse, etc). However, the "Achilles heel" of enzymes in non-aqueous system is deactivation, usually related with irreversible structural and conformational changes on its native structure. Water is the key component for all non-conventional media, because of the importance that enzyme–water interactions have in maintaining the active conformation of enzymes.<sup>[1]</sup>

Since 2000, ionic liquids (ILs) have emerged as exceptionally non-aqueous green reaction media because of their unique solvent properties, headed by their negligible vapour pressure, and their exceptional ability to over-stabilize enzymes, even under extremely harsh conditions (e.g. scCO<sub>2</sub> at 120 bar and at 150 °C). ILs are able to preserve the essential hydration layer around enzymes, maintaining all the excellences of its catalytic behaviour. Another interesting feature for biocatalysis in ILs is the possibility to design two-phase multicatalytic reaction systems (e.g. IL-scCO<sub>2</sub> biphasic systems), which allow straightforward and clean processes for product recovery and biocatalyst reuse (e.g. continuous DKR of sec-alcohols).<sup>[2]</sup> The discovery of the sponge-like character of hydrophobic ILs (Sponge-Like Ionic Liquids, SILs) was key for designing straightforward and green biocatalytic processes, involving both biotransformation and separation steps for producing nearly pure compounds of high added value (e.g. flavour esters, biodiesel, monoglycerides, etc.).<sup>[3]</sup>



**Fig 1.** Clean biocatalytic production of biodiesel using SLILs.<sup>[3]</sup>

Alternatively, biocatalysis in solvent-free systems, based on Deep Eutectic Solvent (DESs) technology, constitutes another successfully approach for developing clean and green processes of industrial interest (e.g. xylityl laurate, panthenyl monoesters, etc). Multi-enzymatic and/or multi-chemoenzymatic chemical transformations in these non-conventional systems, mimicking the metabolic pathways found in nature, is "dream" chemistry that is getting closer.<sup>[4]</sup>

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## References.

- [1] *Biocatalysis in Green Solvents*, Ed. P. Lozano, Academic Press-Elsevier London, **2022**.
- [2] R. Villa *et al.* Ionic liquids as an enabling tool to integrate reaction and separation processes. *Green Chem.* **2019**, *21*, 6527-6544.
- [3] P. Lozano *et al.* Sponge-like ionic liquids: a new platform for green biocatalytic chemical processes. *Green Chem.* **2015**, *17*, 3706-3717.
- [4] P. Lozano *et al.* From green to circular chemistry paved by biocatalysis. *Green Chem.* **2023**, *25*, 7041-7057.