Novel trends in membrane contactor processes: Behavioral and structural studies of therapeutic activity of micelles of emerging green solvents

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Abstract

Hydrophobic deep eutectic solvents (DESs), a recent class of green solvents offer 100% atom economy, cost-effectiveness, potential biodegradability and negligible toxicity [1]. For augmenting biomedical applications wherein polar media is encountered, novel aroma-based therapeutic hydrophobic DESs were synthesised and dispersed in aqueous media to formulate nanoemulsions by newly introduced membrane-assisted nanoemulsification technique.

Microengineered reusable stainless-steel isoporous membranes (9 μm pores) were fabricated by low energy-intensive laser drilling technique [2]. Novel hydrophobic DES systems were successfully synthesized combining terpenes (menthol & thymol) and aroma-based compounds (vanillin & raspberry ketone). For membrane emulsification studies, a 2% (w/w) Tween 80 aqueous solution was the continuous phase. Among the various DESs-based dispersed phase concentrations tested, 4% (v/v) DES operated at optimized dispersion rate exhibited monomodal distribution with stable emulsion droplets of ~147 nm size and polydispersity index <0.2. Interestingly, even though **9 μm** pore-sized membrane was used, 60x smaller emulsion droplets were formulated.

Although, we previously attributed these effects to the self-assembly traits of DESs in emulsion systems [2], various characterization studies were explored for in-depth understanding of these dynamic systems. The behavioral studies constituting the static contact angle, interfacial tension and electrokinetic stability measurements depicted unique observations. Furthermore, the structural studies of these emulsion systems were investigated for the first-time by advanced NMR techniques like DOSY, NOESY and ROESY to substantiate the intermolecular and intramolecular interactions and orientations existing within the emulsions.

To harness the therapeutic effects of the starting components of hydrophobic DESs, first-ever studies on antifungal activities of these DESs-in-water nanoemulsions were explored. Four fungi

strains, namely, *Aspergillus fumigatus, Candida albicans, Candida krusei* and *Trichophyton mentagrophytes* were tested successfully against the individual compounds, synthesised DESs and optimised nanoemulsions to determine the minimum inhibitory and fungicidal concentrations. Interestingly, enhanced synergetic therapeutic effects of the individual components within the nanoemulsions were witnessed.

Acknowledgement

The presenter acknowledges financial support from Fundação para a Ciência e a Tecnologia (FCT), Portugal for PhD grant SFRH/BD/146967/2019. This research was supported by the Associate Laboratory for Green Chemistry - LAQV (UIDB/50006/2020 and UIDP/50006/2020), CIIMAR (UIDB/04423/2020 and UIDP/04423/2020), iNOVA4Health [UIDB/04462/2020 and UIDP/04462/2020] and LS4FUTURE [LA/P/0087/2020] which is financed by national funds from FCT/MCTES. Authors also acknowledge support grants PID2021-126132NB-I00, PID2021-127847OB-I00 and PDC2022-133866-I00 by MCIN/AEI (Spain).

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