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ANALYSIS OF DIFFERENT SET-UPS FOR SCALING-UP THE BIOCATALYTIC SYNTHESIS OF PANTHENYL MONOESTERS

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PURPOSE OF THE ABSTRACT

The incorporation of bioactive molecules to commodities is under increasing demand because of their benefits to health. Nonetheless, the use of solely active ingredients has some hints derived from their structure, which determines a previous step of modification to improve their miscibility with different formulas, their performance, stability, or duration effects. In the field of cosmeceuticals the acylation of bioactive molecules is the predominant modification, which improves the dermal absorption of hydrophilic biomolecules and stabilizes the antioxidant activity of the aromatic ones.

However, the concerns about the impact of chemical modifications on health and the environmental burden demand the design of more sustainable approaches (1). At this point, solvent-free reactions catalyzed by enzymes stand out as the more promising strategies from the sustainable point of view. When working in the absence of solvent is not always possible due to substrates' non-miscibility, the formation of a eutectic mixture between substrates is a smart strategy to achieve their coexistence in the same phase (2). In addition, the enzymes show outstanding biodegradability, efficiency, and selectivity which permits on-demand customization of the substrates leading to innovative compounds. For example, polyalcohol panthenol is the pro-vitamin B5, which acylated derivative is highly demanded in the cosmetic and pharmacological fields because of its bioactive properties (humectant, wound-healing, etc.) (3,4). However, it has been reported how the selective single esterification of panthenol, achieves the same result but also provides an additional surfactant activity which is also very convenient for the aforementioned sectors (2).

This work shows the optimization and validation of a gradual scaling-up process for the solvent-free biocatalytic synthesis of panthenol monoesters, based on eutectic mixtures with different free fatty acids (FFAs), and different size set-ups (ultrasounds, orbital shaking, rotary evaporator, and mechanically stirred reactor) to reach a final 500 g reaction size (Figure 1) (5). The intensification of the process at higher scales has been assessed by kinetic studies and the productivity (monoester (g) / reaction time (h) x biocatalyst (g)) achieved. The results point to 3 key parameters to shift the equilibria towards the synthesis: (1) the longer alkyl chain in the FFA (i.e. the yield increases from 63 % yield for panthenyl butyrate to 83 % yield for panthenyl myristate), (2) an efficient agitation and (3) high-performing water removal (i.e. systems coupled to vacuum). The last two parameters, dependent on the set-up, are improved at higher scale systems (rotary evaporator, and mechanically stirred reactor) affording not only

the best results (87 %-95 % monoester yield), but also a significant five-fold reduction of the amount of biocatalyst which in addition can be recovered and reuse for 5 cycles.

In addition, different Green Metrics Parameters (ϵ , AE, 1/S, MRP, RME, PMI, TCR, E-factor, EcoScale) have guided the scaling process from the benchmark scale to the 500 g size, highlighting the higher sustainability of this strategy respect to others previously reported.

These results demonstrate the process of scaling-up this solvent-free reaction, based on eutectic mixtures and biocatalysis, from the benchmark to a relevant environment, is feasible and provides an intensification of the performance with economical and sustainable up-gradings.

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FIGURES

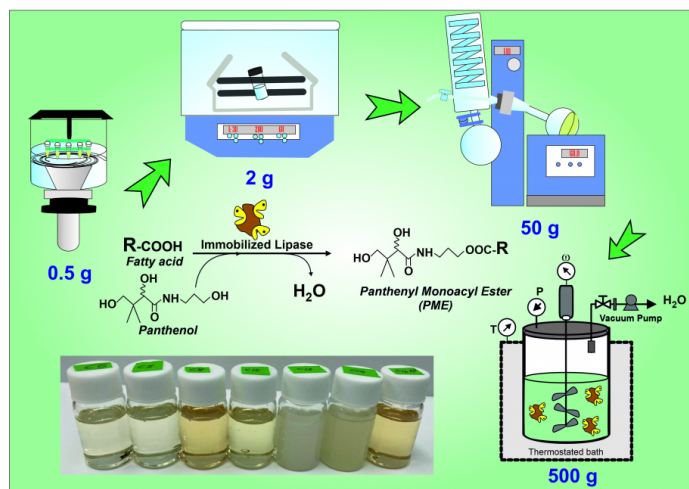


FIGURE 1

Figure 1.

Scheme of biocatalytic esterification of FFAs with panthenol and set-ups for scaling-up. Bottom left: picture of panthenyl monoesters with different alkyl-chain lengths

FIGURE 2

KEYWORDS

sustainable | biocatalysis | scaling-up | green metrics

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