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A membrane bioreactor for biotransformations of hydrophobic molecules using organic solvent nanofiltration (OSN) membranes

Rogelio Valadez-Blanco[a], Frederico C. Ferreira[a], Ruben Ferreira Jorge[b], Andrew G. Livingston[a]*

[a]*Department of Chemical Engineering and Chemical Technology, Imperial College London, South Kensington Campus SW7 2AZ, UK*
email: a.livingston@imperial.ac.uk
[b]*Escola Superior de Biotecnologia, R. Dr. António Bernardino de Almeida, 4200 Porto, Portugal*

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1. Introduction

Biotransformations play an increasingly important role in organic synthesis processes, such as in the production of chiral precursors. However, two main constraints limit their wide application: (1) the hydrophobic nature of most biotransformation substrates and products prevents the use of high concentrations in the aqueous phase, in which biocatalysts have optimal performance; (2) substrates and products of biotransformation reactions are known to inhibit biocatalyst activity. Direct contact organic-aqueous bioreactors circumvent these limitations by allowing high substrate and product loads and reducing biocatalyst inhibition. Nevertheless, the strong mixing of the biomedium and organic phases causes irreversible emulsions that make downstream separation a practical constraint; moreover, the presence of the organic phase can inhibit or even stop the biocatalyst activity. To meet this challenge, membrane bioreactors separate the two phases allowing mass transfer through the membrane interface. Although these reactors avoid the emulsion and solvent toxicity problems, the mass transfer rate, the ability of the membrane to stabilise the interface and the membrane solvent resistance are the major technical challenges for their applicability. Two types of membranes have been used: porous [1] and non-porous [2]; the first are prone to aqueous-organic phase breakthrough [1], whereas the second may yield low mass transfer rates or the membrane materials lack solvent resistance [3]. In this work we study the feasibility of using organic solvent nanofiltration (OSN) membranes [3] as two-phase contactors for biotransformations of hydrophobic molecules. The production of *R*-citronellol from geraniol by baker's yeast was selected as our model biotransformation system [2] (Scheme 1). The results of our OSN system

*Corresponding author.

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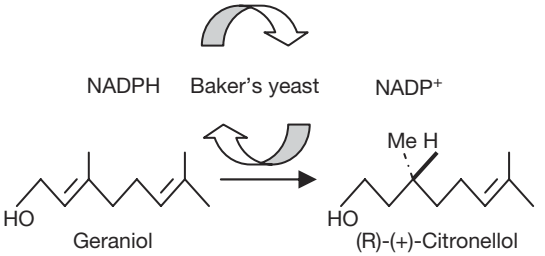
Table 1
Performance of different bioreactors and solvents tested for the model biotransformation system.

Reactor system	Organic solvent	Maximum volumetric productivity (mg L^{-1} h^{-1})	*R*-Citronellol % e.e.
Direct contact	Hexadecane	6.415	85.5
	Toluene	≈ 0	–
Membrane bioreactor	Hexadecane	2.114	82.1
	Toluene	2.836	32.7



Scheme 1. Model biotransformation: geraniol to citronellol by baker's yeast.

were compared with those of a direct contact two-phase bioreactor in terms of volumetric productivity, enantiomeric excess (e.e.) and product quality.

2. Experimental

We carried out two types of biotransformations using a direct contact two-phase bioreactor and an OSN membrane bioreactor for biotransformations (MBB) (Fig. 1). The volume ratio biomedium/organic was 10:1. A polyimide Starmem™ 122 membrane*[3], with an effective area of 0.015 m was used as the interface for the MBB. Two different organic solvents were used: hexadecane [2] and toluene.

*Starmem™ is a trademark of W.R. Grace and Co.

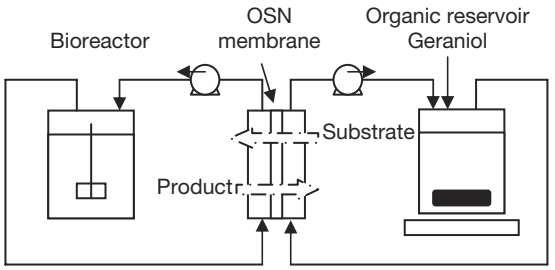


Fig. 1. Schematic of the membrane bioreactor for biotransformations (MBB).

3. Results and discussion

The highest volumetric poroductivity was achieved in the hexadecane direct-contact system (Table 1) which resulted about 3 times higher than those for the MBB; however, a strong emulsion was observed in the reactor (Fig. 2). On the other hand, considering that no citronellol production was obtained when toluene was used as the organic phase in the direct contact system, it was remarkable that the volumetric productivity of the toluene MBB was higher than that for the corresponding hexadecane run. This was due mainly the membrane preventing the solvent from direct contact with the biocatalyst, thus avoiding biocatalyst inactivation. However, the e.e. for the toluene-membrane system was much lower compared to that obtained in either of the

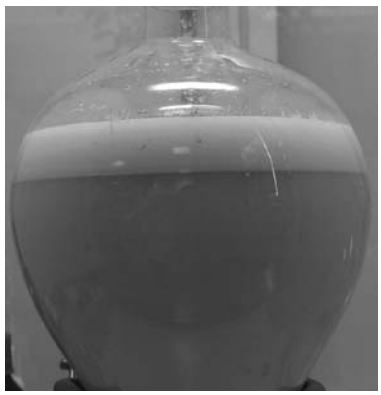


Fig. 2. Direct contact two phase emulsion after four days left in repose in a separation funnel.

hexadecane systems. The reason for this may be that, even though the organic-aqueous direct interface was avoided, the low concentrations of toluene in the aqueous phase caused the biocatalyst to lose its enantioselectivity. Finally, using a simple mathematical model we concluded that the MBB systems were mass transfer limited; to make the system kinetically-limited the membrane area should be doubled to 0.03 m^2.

4. Conclusions

A new approach was presented for a model biotransformation in a biphasic system using OSN membranes. This system not only prevented emulsion formation but also allowed the use of toluene as the organic phase, although with a reduction in stereoselectivity. The hexadecane direct contact two-phase biotransformation yielded the highest volumetric productivity; however, direct-contact reactors resulted in the formation of strong emulsions as well as biocatalyst inhibition by toluene.

Acknowledgment

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References

[1] W. Pronk, P. Kerkhof, C. Vanhelden and K. Vantriet, The hydrolysis of triglycerides by immobilized lipase in a hydrophilic membrane reactor, Biotechnology and Bioengineering, 32(4) (1988) 512–518.

[2] S. Doig, A. Boam, D. Leak, A. Livingston and D. Stuckey, A membrane bioreactor for biotransformations of hydrophobic molecules, Biotechnology and Bioengineering, 58 (1998) 587–594.

[3] L. White, W.R. Grace & Co., Polyimide membrane for separation of solvents from lube oil, US patent 5,264,166, 1993.