Membrane processes for the production of pure enantiomers

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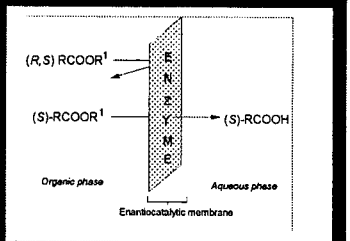
Enantiomers are molecules that have non-superimposable mirror image of each other.

The reason of the interest in developing membrane technology to produce pure enantiomers is in the importance of using optically pure isomers as: 1) pharmaceuticals; 2) food additives; 3) feeds; 4) flavours; fragrances; 5) agrochemicals.
In general, only one of the two enantiomers has a beneficial effect, whilst the other can be inactive or have serious undesired side-effects.

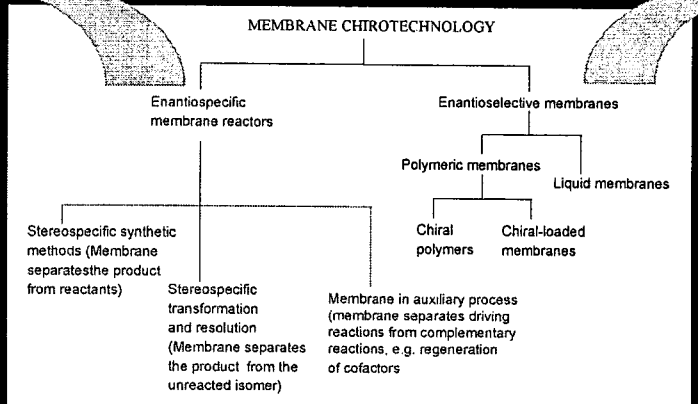
The present work concerned the study of membrane systems for the production of pure enantiomers. In particular, the final aim is to develop methodologies that would allow the possibility of resolving racemic mixtures of enantiomers by i) enantiocatalytic membrane reactors (by combining chemical conversion and separation) or by ii) enantioselective membranes (with no chemical conversion).

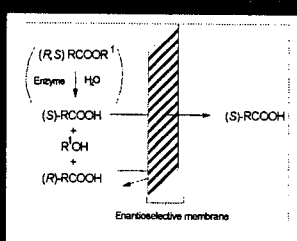
In the first case, the stereoselective properties of a biocatalyst, which preferentially converts only one of the two enantiomers, were combined with membrane separation operations. The chiral system is therefore the catalyst, while the membrane forms the reaction microenvironment and guides the separation of the produced enantiomer from the racemic reagents. (This activity is mainly guided by the Italian Partner, ITM-CNR).

In the second case, the membrane itself is the chiral system and it is able to resolve racemic mixtures by promoting stereoselective mass transport. In other words, the membrane is able to distinguish between two enantiomers and selectively permit the transport of only one of them, which will be separated and recovered in the permeate stream. (This activity is mainly guided by the Korean Partner, KRICT).



Enantiocatalytic membrane reactor (kinetic resolution)

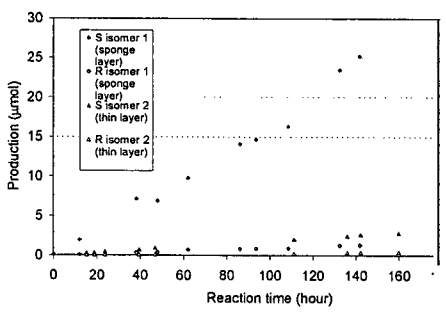




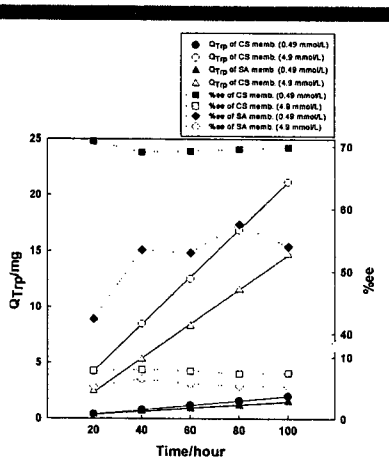
Intrinsically enantioselective membrane
(Chiral separation)

The multiphasic enantiocatalytic enzyme membrane reactor consisted of an organic phase (iso-octane) which dissolved the naproxen methyl ester, a lipase-loaded membrane, and an aqueous phase (phosphate buffer pH 7.00) which extracted the reaction product. Lipase preferentially converted the (S)-naproxen methyl ester to (S)-naproxen acid that was simultaneously separated by membrane.
Capillary polyamide membrane with 10 kDa NMWCO and polysulfone membrane with 30 kDa NMWCO were applied, with lipase loaded in the sponge layer or on the thin layer of membranes.

SA and chitosan membranes were prepared by casting and drying the solutions of SA and chitosan, followed by crosslinking with GA.
Optical resolution of tryptophan and tyrosine (α-amino acids) through the SA and chitosan membranes was carried out by employing a pressure driven process. The applied pressures for the optical resolution were 1 and 2 kgf/cm^2.



Production of (S)-Naproxen and (R)-Naproxen by lipase immobilized in the sponge layer or on the thin layer of PA 10 kDa membrane as function of reaction time.



Q_{trp} and flux in the optical resolution of tryptophan racemates through both SA and chitosan (CS) membranes (SI = 80 %) at 1 kgf/cm^2 of operating pressure. The concentrations of the feed solution were 0.49 mmol/L and 4.9 mmol/L.

The lipase-immobilized membrane reactor showed much higher stability as a function of time compared to the free enzyme in stirred tank reactor. Polyamide gave better performance compared to polysulfone membrane.

Both SA and chitosan membranes crosslinked with GA are possible for the optical resolution of α-amino acids, especially tryptophan and tyrosine, by a pressure driven process.

References

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Na Li, Lidietta Giorno, Enrico Drioli. (2003). Effect of immobilization site and membrane materials on multiphasic enantiocatalytic enzyme membrane reactors, Annals of the New York Academy of Sciences, 984:436-452.