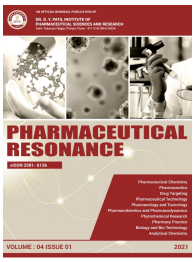
SHORT REVIEW

ENANTIOSELECTIVE SEPARATION OF DRUGS : ROLE OF POLYMERIC MEMBRANES



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Louis Pasteur studied wine diamonds (tartaric acid crystals) which rotate the plane-polarized light clockwise direction, while the crystals extracted from the bottle were optically inactive. When checked under the microscope, the optically inactive crystals have two types of non-superimposable mirror image crystals.[1] These crystals, when separated, rotate the plane polarize light in opposite directions. He called these enantiomers and coined the term "chirality."[2]

Though the human body looks symmetrical externally, the organs inside are placed asymmetrically.[3] The biomolecules like DNA, proteins, enzymes, sugars, and amino acids are exclusively asymmetric.[4] The handedness of these biomolecules greatly influences life on earth.[5] These biomolecules show exceptional specificity and selectivity towards metabolic processes.[6,7] Selectivity towards only one enantiomer of chiral drugs results in significant differences in their therapeutic efficacy and pharmacokinetic parameters, resulting in diversified pharmacological actions and pharmacodynamics having the same chemical structure.[8,9]

A classic example is thalidomide, a racemic drug used during the 1960s to treat nausea during pregnancy. Although the R-isomer of thalidomide is a safe sedative, unfortunately, the S-form causes severe congenital deformities.[10] Such well-known examples are listed below in table 1.

Much more emphasis is given on the enantiopurity of the drug moleculesto ensure their safety and potency. The requirement of an enantiopure therapeutic agent has resulted in the scientific quest for the development of robust, scalable, and efficient strategies. The approaches are subdivided into two parts: the chiral approach and the racemic approach.[11] Although the chiral method is more favored, it has several disadvantages, including expensive and hazardous hemochorial transition metal catalyst and highly enantiopure starting material. Little change in the ligand, solvent or even that of the protecting groups can severely skew the enantiopurity of products.[12] On the other hand, Both the enantiomers are synthesized in the racemic approach, followed by their separation using different chromatographic techniques.[13] Most of these chromatographic enantioselective separation techniques are tedious, time-consuming, and energy inefficient. At the same time, it needs skilled operators to handle these high-end instruments, subsequently resulting in a significant increase infinal product cost.[14]

Table 1: difference in the activity of enantiomer of chiral drugs.

Chiral Drugs	Enantiomers	
	(R)	(S)
Ibuprofen	Inactive	Analgesic
Citalopram	inactive	Antidepressant
Penicillamine	Highly Toxic	Antirheumatic

More emphasisis given to developing fast, easy-to-operate, cost-effective methodologies to produce enantiomers with high optical purity. The membranes -based simple filtration methods can be an attractive alternative concerning using all scales from laboratory to bulk chemical scale processes in the chemical industry.[15] The advantages of membranes are low energy consumption, high processing capacity, continuous operability, Low-cost, high efficiency, convenient for up-and / or down, simplicity, eco-friendly, and the possibility of integrating into other separation processes scale

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up.[16,17] Membrane-based chiral resolution can be achieved using either enantioselective or non-enantioselective membranes. The enantioselective membranes themselves can carry out chiral separation of stereoisomers as they contain chiral recognition sites.[18] On the other hand, non-enantioselective membrane-assisted processes, also called combinatorial methods, are generally combined with different chiral recognition approaches such as polymer-based resolution.[19]The chiral polymer coated on the achiral surface of the membrane makes the surface chiral and helps carry out the enantioselective separation of a racemic mixture.[20]

The separation mechanism involves forming a transition state complex of different energy between the chiral selector and enantiomers.[21] The difference in the complex strength is the basis for discrimination between the enantiomers, which is well explained with the help of a three-point interaction model.[22]

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