# Recent Trends in the Separation of Chiral Drugs

**Sudha T**

Adhiparasakthi College of Pharmacy, India

## Abstract

Many of the currently used drugs in practice are mixtures of enantiomers. Although they have the same chemical structure, the enantiomeric forms of a drug can differ in potency, selectivity for receptors, transporters and / or enzymes, rate of metabolism, metabolites, excretion and toxicity, behavior in biological systems (like pharmacokinetics, bioavailability, efficacy and biopharmaceutical parameters). Therefore, it is important to promote the chiral separation and analysis racemic drugs in pharmaceutical industry, in order to eliminate the unwanted isomer from the preparation. The use of single enantiomer drugs can potentially lead to simpler and more selective pharmacologic profiles included therapeutic indices, simpler pharmacokinetics due to different rate of metabolism and decreased drugs interactions. For example, Levorotary–isomer of all β-blockers is more potent in blocking β - adrenoceptors than their dextrorotary-isomer, such as S (-) -propranolol is 100 times more active than its R (+)-antipode.

In the early period analytical chiral separation was a rather difficult task and separation methods were not as advanced as today. Nevertheless, it was clear that chiral drugs should be enantiomer separated and each isomer should be used separately. Enantiomers are separated by using the modern techniques like HPLC and Chiral HPLC has proven the best methods for the direct separation and analysis of enantiomers. The physical method and enantioselective immunoassays are used for characterization of chiral or racemic drugs. The chiral separation of racemic drugs is a necessary operation in pharmaceutical industry. Therefore the development of new chiral separation techniques and will be a topic subject in academic research as well as in industrial advance. It is also important to give more information about chiral drugs especially racemic form to health care professionals in order to help them to finding an optimal treatment and a right therapeutic control.

Chirality can be defined as the potential of a molecule to occur in two asymmetric forms that are non-superimposable mirror images of each other without changing the atomic composition, atom-atom connections, or bond orders. This phenomenon generally occurs due to a difference in the three-dimensional orientation of four different substituents attached to a single central atom, creating what can be considered left-hand and right-hand versions of the same molecule. These two versions of the molecule are referred to as enantiomers. When attempting to superimpose these versions, there will always be at least one substituent attached to the chiral atom that cannot be superimposed. In order to differentiate the two enantiomers, the Cahn-Ingold-Prelog system, or simply the R / S notation is employed, as recommended by the International Union of Pure and Applied Chemistry (IUPAC). The D / L notation used for amino acids and sugars is restricted to those two molecular types with the D / L notation standing for dextrorotatory (clockwise) and levorotatory (counter-clockwise) optical rotation of polarized light. This convention is not in general use now, having been replaced by the R / S notation for chirality and + / - notation for optical rotation [5]. Enantiomers are usually described as having identical physical properties in achiral environments with the exception of the rotation of plane polarized light. In fact, plane polarized light is comprised of left- and right-handed components of circularly polarized light which is chiral and the phenomenon of optical rotation is due to slight differences in the way in which chiral molecules interact with these components. For a thorough presentation on chirality notations and examples, we refer the reader to the IUPAC home page (http://goldbook.iupac.org/) and the article by Caldwell & Wainer [5]. Molecules that are super-imposable on their mirror images are referred to as achiral.

An external file that holds a picture, illustration, etc.

a) Basic chirality. These two molecules have the same atoms and the same atom-atom connections but they cannot be fully superimposed. They are therefore referred to as enantiomers and appear as mirror images in three-dimensional depictions. The central atom (*) is therefore considered to be a chiral center. (Note that bond lengths and atomic diameters have been simplified in order to focus on the basic concepts in these depictions.) (b) R / S conformations. In order to differentiate enantiomer pairs, R (rectus) and S (sinister) are used. To determine the R or S notation for the chiral molecules of the substituent atoms attached to the chiral atom are prioritized based on their atomic number with the higher number being the higher priority (therefore, F>N>C>H). The molecule is rotated until the lowest priority substituent, in this case H, is behind the chiral center. The chiral center is R if the three remaining substituents go clockwise from highest (F) to lowest priority (C). The chiral center is S if the three remaining stituents go counter-clockwise from highest to lowest priority.

When both enantiomers of a compound are present at equal concentrations in a sample, it is referred to as a racemate or a racemic

mixture. Kinetic and thermodynamic resolution can be employed to separate enantiomers as can chiral chromatographic methods. Stereoselective chemical processes like asymmetric synthesis (sometimes referred to as chiral synthesis) or stereoselective enzymes can favor one enantiomer over the other. As more complex molecules are considered, chirality can still occur, with more complex substituents attached to a chiral center or multiple chiral centers. These molecules, when not enantiomers of each other, are referred to as diastereoisomers. Likewise, such molecules can have different physical properties like boiling points, melting points, etc. When a potential chiral center has two identical atoms attached to it, the next "level" of atoms needs to be considered in order to establish priority and therefore nomenclature. For example, if two carbons are attached to the chiral center and one of those carbons has only hydrogens attached while the other carbon has an oxygen atom attached, then the carbon-oxygen substituent has the higher priority over the carbon-hydrogens in determining the R or S orientation.

## Properties of Chiral Compounds

Enantiomeric pairs will have the same mass, atomic composition, melting points, boiling points, and other physical characteristics will be the same (except for the rotation of polarized light) but, as a left-hand glove does not properly fit the right hand, chiral molecules can induce stereoselectivity into the reactions and interactions in which they participate. While physically, and chemically, enantiomers may behave essentially identical, in a chiral environment (such as biomolecular constituents in a living organism) the outcomes of their reactivities can be dramatically different.