ABSTRACT

The foundational knowledge required to comprehend chiral medicines is covered in this section. For a more in-depth explanation of chirality and enantiomers, chemistry undergraduate textbooks are excellent resources. The most crucial fact is that chiral medicines come in two structurally similar forms, but because of their distinct shapes in three dimensions, they can function significantly differently in biological systems. The two potential forms are referred to as enantiomers, and a given chiral drug's two enantiomers ought to be regarded as distinct medications. The following section goes into further detail on this subject. Formally speaking, chirality is the geometric quality of a hard item (such as a medication or molecule) that prevents it from being superimposed on its mirror copy. **Achiral molecules** are those that are able to be superimposed on their mirror images.

From the fundamental components of life, such as lipids, carbohydrates, and amino acids, to the structure of the human body, chirality is a feature of matter that permeates biological systems. Being left- or right-handed—that is, having mirror representations of one's own hand but not being able to superimpose them—is a common way to illustrate chirality. Enantiomers are chiral molecules that have two mirror reflections of each other. Enantiomers occur in pairs, just like hands do. The two molecules in an enantiomer pair may behave differently in chiral settings like the body's receptors and enzymes, but they have the same chemical makeup and can be represented in the same way in two dimensions (such as a drug structure on a package insert).

A mixture of equal parts of both enantiomers of a chiral medication is known as a racemate (sometimes termed a racemic mixture). While a carbon atom connected to four distinct groups is the most common source of chirality in pharmaceuticals, chirality can also come from other sources. Stereoisomers or solitary isomers are other terms used to describe single enantiomers. These phrases do not necessarily indicate the presence of a single enantiomer and can also be used to describe achiral medications and compounds. Isomer molecules, for instance, have drastically diverse structures even though they have the same stoichiometric molecular formula. However, the terms enantiomer, single isomer, and/or single stereoisomer are sometimes used interchangeably in talks about chiral medicines.

INTRODUCTION

Enantiomers of a chiral drug exhibit indistinguishable physical and chemical characteristics within an achiral setting. However, when within a chiral environment, one enantiomer may manifest varied chemical and pharmacological attributes compared to its counterpart. Due to the inherent chirality of living systems, each enantiomer of a chiral drug can elicit distinct responses in vivo. Thus, the behavior of the **R-enantiomer** of a drug can differ significantly from that of the **S-enantiomer** within a patient's body. In the case of a chiral drug, it is advisable to regard the two enantiomers as distinct substances with differing properties unless evidence suggests otherwise.

Many commonly prescribed medications are available in the form of two distinct chiral isomers (enantiomers), each exhibiting its own unique chemistry, receptor affinity, and pharmacokinetic profile. The clinical utility of these individual enantiomers remains largely uncertain.

Separation of racemates into their component enantiomers is a process called resolution. Since enantiomers have identical physical properties, such as solubility and melting point, resolution is extremely difficult.

The asymmetric atom is called a chirality centre,[13][14] a type of stereocenter. A chirality center is also called a **chiral center [**15][16][17] or an asymmetric center.[18] Some sources use the terms stereocenter, stereogenic center, stereogenic atom or stereogen to refer exclusively to a chirality center,[15][17][19] while others use the terms more broadly to refer also to centers that result in diastereomers (stereoisomers that are not enantiomers).[14][20][21]

Compounds that contain exactly one (or any odd number) of asymmetric atoms are always chiral. However, compounds that contain an even number of asymmetric atoms sometimes lack chirality because they are arranged in mirror-symmetric pairs, and are known as meso compounds. For instance, meso tartaric acid (shown on the right) has two asymmetric carbon atoms, but it does not exhibit enantiomerism because there is a mirror symmetry plane. Conversely, there exist forms of chirality that do not require asymmetric atoms, such as axial, planar, and helical chirality.[15]

Even though a chiral molecule lacks reflection (Cs) and rotoreflection symmetries (S2n), it can have other molecular symmetries, and its symmetry is described by one of the chiral point groups: Cn, Dn, T, O, or I. For example, hydrogen peroxide is chiral and has C_2 (two-fold

rotational) symmetry. A common chiral case is the point group C_1, meaning no symmetries, which is the case for lactic acid.

It is most effective to distinguish between a chiral drug's two enantiomers based on its optical rotation or absolute configuration. Other classifications, such D and L (notice the capitalization), are used for sugars and amino acids, but they are unique to these molecules and don't apply to other substances in general. It is best to avoid using the terms "d," which stands for "dextro," and "l," which stands for "levo." For absolute configuration, the R/S system and the +/− method for optical rotation should be utilised instead. To clearly represent the three-dimensional structure of the molecule, the absolute configuration at a chiral centre is denoted by R or S.

In his pioneering work, **Louis Pasteur** was able to isolate the isomers of sodium ammonium tartrate because the individual enantiomers crystallize separately from solution. To be sure, equal amounts of the enantiomorphic crystals are produced, but the two kinds of crystals can be separated with tweezers. This behavior is unusual. A less common method is by enantiomer self-disproportionation.

The second strategy is asymmetric synthesis: the use of various techniques to prepare the desired compound in high enantiomeric excess. Techniques encompassed include the use of chiral starting materials (chiral pool synthesis), the use of chiral auxiliaries and chiral catalysts, and the application of asymmetric induction. The use of enzymes (biocatalysis) may also produce the desired compound.

A third strategy is **Enantioconvergent synthesis,** the synthesis of one enantiomer from a racemic precursor, utilizing both enantiomers. By making use of a chiral catalyist, both enantiomers of the reactant result in a single enantiomer of product.[30]

Enantiomers may not be isolable if there is an accessible pathway for racemization (interconversion between enantiomorphs to yield a racemic mixture) at a given temperature and timescale. For example, amines with three distinct substituents are chiral, but with few exceptions (e.g. substituted N-chloroaziridines), they rapidly undergo "umbrella inversion" at room temperature, leading to racemization. If the racemization is fast enough, the molecule can often be treated as an achiral, averaged structure.

IMPORTANCE OF ENANTIOMERS

Of the chiral medications that are marketed, about half are enantiomer mixtures rather than single enantiomers.1 In this section, specific examples of single-enantiomer drugs that are presently available on the market are provided along with a discussion of the possible benefits of using chiral drugs alone. Practice-based physicians will have greater access to single-enantiomer medications in the future. In addition, certain drugs may be offered in both their single-enantiomer form and simultaneous mixture of enantiomers. In certain situations, it is imperative to differentiate between the racemic and single enantiomers as they may have different recommended uses, dosages, and efficacies.

The chemistry of many essential biological (metabolic and regulatory) processes is directly regulated by chiral compounds, which include proteins, amino acids, nucleosides, sugars, and several hormones. These compounds are the fundamental building blocks of life. [3, 4] Enantiomers are essentially mirror images of chiral compounds, such as drugs, herbicides, and pesticides. These compounds can have very different metabolic, pharmacological, therapeutic, and/or toxicological properties. [5] Interestingly, many important biological compounds, such as proteins, amino acids, nucleosides, sugars, and several hormones—the building blocks of life—are chiral, and as a result, the chemistry of many basic biological (metabolic and regulatory) processes is directly controlled.

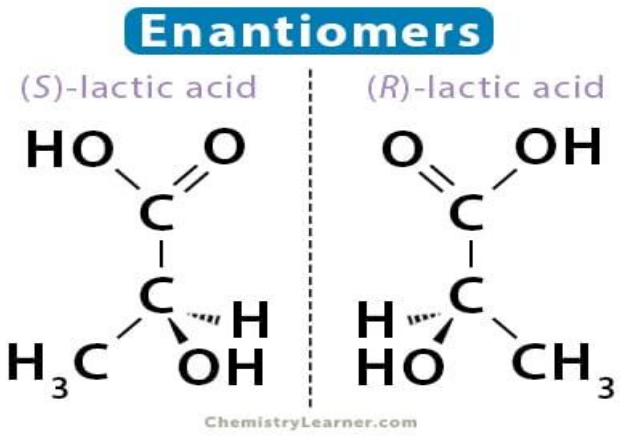
As a result, the two enantiomers of a chiral substance react differently with the complementary receptor or enzyme molecule in a biological milieu that is highly stereoselective or enantioselective. [6] This issue is especially critical in the pharmaceutical business, as many medications in use are known to be chiral (approximately 56%) [4], with just around 25% being pure enantiomers. Furthermore, chirality is significant in other industries such as agrochemicals, food, and petroleum. [7, 8, 9] For example, about 30-40% of currently approved pesticides, insecticides, and herbicides are chiral. [6,8,10]

Naproxen is an anti-inflammatory/pain killer that it briefly took to deal with a sport injury. Interestingly, the S-enantiomer is what causes the desired effects of the painkiller while the R-enantiomer is chemically inert. Both enantiomers are actually toxic to your liver and if you are prescribed naproxen, the enantiomer that you are taking is S-Naproxen. It would be silly to take R-Naproxen because it does not work as a painkiller. In chemistry, sometimes it can be expensive, laborious, and unpractical to completely purify an enantiomer. An optimal naproxen

racemic mixture is one that has a very high S to R enantiomer ratio or 99.99% S-Naproxen is what you want.

Enantiomers are important because the response of an organism to a particular compound often depends on how that enantiomer fits a specific site on a receptor molecule from the organism. In chemistry, the scientist is concerned about which enantiomer is the active one—the enantiomer that is meant to target the receptor. Ideally, the pharmaceutical drug should consist of the pure active isomer.

Antibiotics possess many chiral centers and different functionalities which are beneficial for molecular interactions with enantiomers, and are suited for the chiral separation of a broad range of compounds. Since their solubility is structure dependent, antibiotics are applicable as chiral selectors to both aqueous as well as nonaqueous approaches. The first usage of macrocyclic antibiotics as chiral selector molecules was introduced by **Armstrong et al.** in 1994 prior to which the majority of chiral CE separations relied on CDs. Five classes of antibiotics are now commonly used for enantioseparation, including macrocyclic antibiotics, more simple interconnected structures, and noncyclic selectors. Some antibiotic classes are more suited for the separation of compounds that possess specific physicochemical properties, for example, glycopeptides are often used for the separation of acidic analytes, while basic compounds are best recognized by ansamycins. The exact chiral recognition mechanism has, however, not been fully elucidated.



Different types of antibiotics used in chiral analysis:

Antibiotic class	**Structural characteristics**	**Antibiotic**
Glycopeptides	Multiples macrocycles, each cycle containing two aromatic rings	1.Avoparcin 2.Balhimcyin 3.Bromobalhimcyin 4.Eremomycin 5.Ristocetin 6.Teicoplanin 7.Vancomycine
Ansamycines	Single macrocycle with naphthahydroquinone ring	1.Rifampicin 2.Rifamycin
Macrolides	Single macrocyclic lactone with sugar monomer side chains	1.Azithromycin 2.Boromycin 3.Clarithromycin 4.Erythromycin
Lincosamides	No macrocycle, consecutively contains a amine, an amide, and a sugar moiety	1.Clindamycin
Aminoglycosides	No macrocycle, multiple interconnected glycosidic rings, functionalized with nitrogen atoms	1.Fradiomycin 2.Kanamycin 3.Streptomycin

OBJECTIVES

Enantiomers are pairs of molecules that are mirror images of each other but cannot be superimposed onto one another. They are important in fields like chemistry and pharmacology. Some objectives for studying enantiomers might include:

1. **Understanding Stereochemistry:** Enantiomers provide a platform for studying stereochemistry, which involves the three-dimensional arrangement of atoms within molecules.
2. **Chiral Recognition:** Exploring methods to distinguish between enantiomers, which is crucial in analytical chemistry and drug development.
3. **Pharmacological Effects:** Investigating how enantiomers can have different pharmacological effects, even though they have the same chemical formula and structure.
4. **Biological Significance:** Studying the biological significance of enantiomers, especially in how they interact with biological systems like enzymes and receptors.
5. **Synthetic Challenges:** Exploring the synthesis of specific enantiomers, which can be challenging but is essential for pharmaceuticals and other applications where purity is critical.
6. **Regulatory Considerations:** Understanding the regulatory considerations surrounding enantiomers, particularly in drug development where different enantiomers may have varying efficacy and safety profiles.

DISCUSSION

Enantiomers are pairs of molecules that are non-superimposable mirror images of each other. They have identical physical properties, but they interact differently with polarized light and other chiral molecules. They are important in fields like pharmacology and biochemistry due to their different effects on biological systems. Enantiomeric separation is the process of separating enantiomers, which are molecules that are non-superimposable mirror images of each other. These molecules have the same chemical formula but differ in their spatial arrangement of atoms. Since enantiomers often exhibit different biological activities, it's important to separate them for various applications such as pharmaceuticals, agriculture, and flavor and fragrance industries. The separation techniques rely on exploiting the differences in the interactions between the enantiomers and a chiral environment.

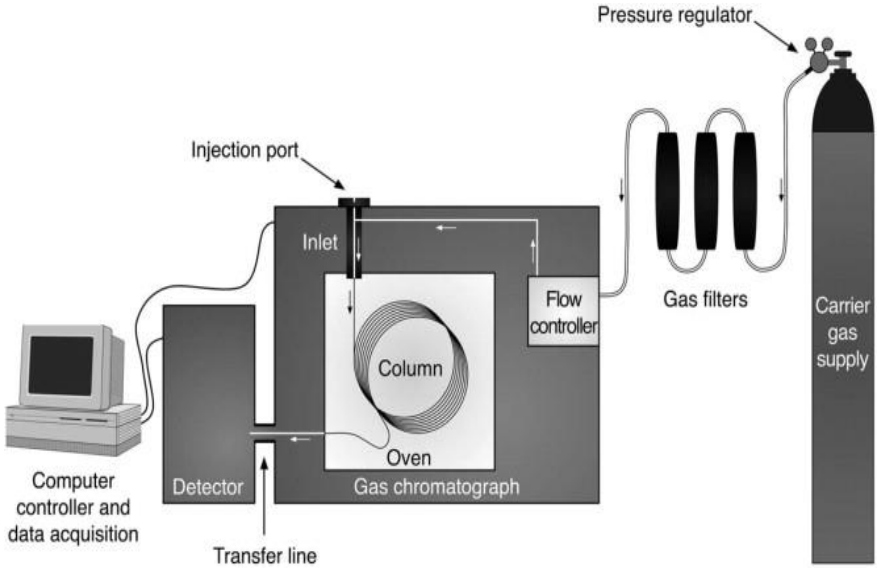
Enantiomers often exhibit different biological activities. One enantiomer might have a desired therapeutic effect while the other could be inactive or even exhibit undesirable effects. Separating them ensures that only the desired enantiomer is used, reducing potential side effects and maximizing therapeutic efficacy. Regulatory agencies often require pharmaceutical companies to produce enantiomerically pure drugs to ensure safety and efficacy. This is particularly important for chiral drugs where the activity can vary significantly between enantiomers. In chemical synthesis, producing enantiomerically pure compounds can be challenging. Separating enantiomers allows chemists to work with specific stereochemical forms, enabling more efficient synthesis and avoiding costly purification steps.

Enantiomers are important because they are molecules that are mirror images of each other but cannot be superimposed onto one another. This property leads to different interactions with other molecules, such as enzymes or receptors in our bodies, which can have profound effects on biological processes, drug efficacy, and chemical reactions. Understanding enantiomers is crucial in fields like pharmacology, organic chemistry, and biochemistry. Enantiomeric separations are essential because it allows us to separate and analyze enantiomers, which are molecules that have identical physical properties but exhibit different biological activities. This separation is crucial in fields like pharmaceuticals, where one enantiomer may have the desired therapeutic effect while the other could cause side effects or be inactive. Techniques for enantiomeric separation, such as chiral chromatography or asymmetric synthesis, enable the production of pure enantiomers, ensuring the safety and efficacy of drugs and other compounds.

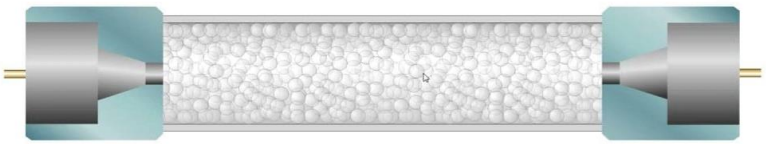
SEPERATION TECNIQUES OF ENANTIOMERS

For the purpose of separating enantiomers, resolution techniques are essential. Several goals for study centred on these methods are as follows:

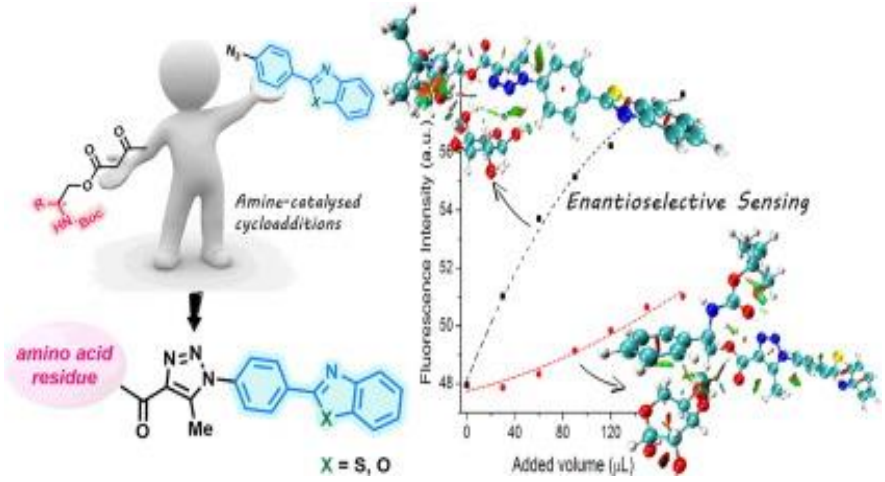
1. **Development and Optimisation of Methods:** Examine and improve chromatographic techniques, such as gas chromatography (GC) and high-performance liquid chromatography (HPLC), to achieve effective enantiomer separation. To attain good resolution and selectivity, this entails optimising variables such stationary phase composition, mobile phase conditions, and column temperature.



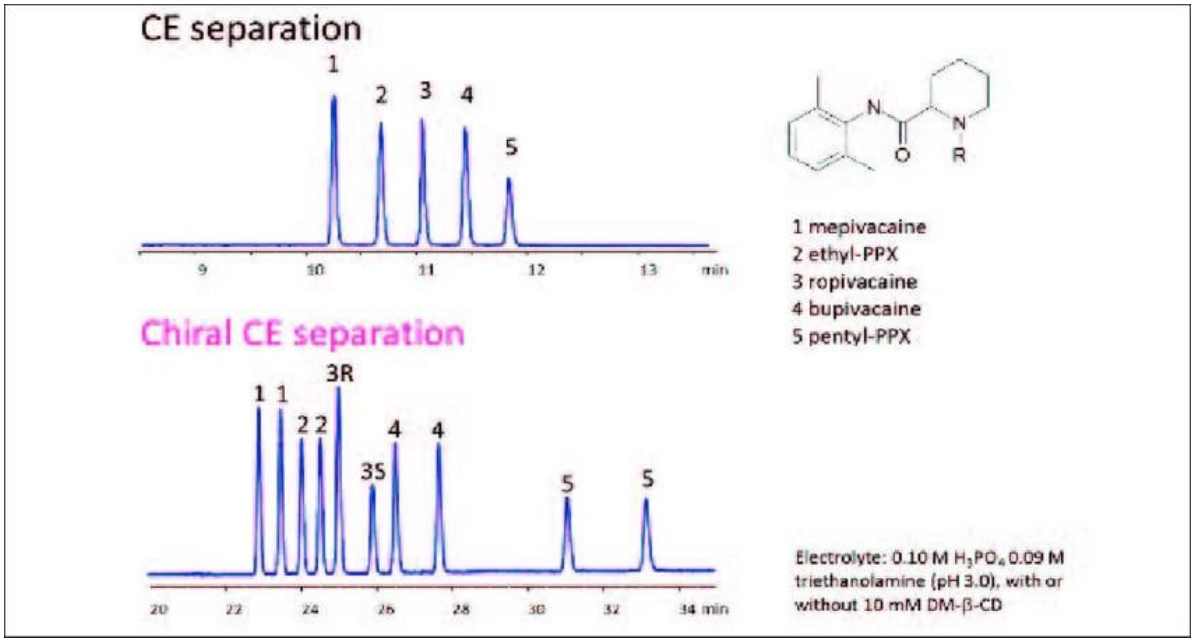
2. **Stationary Phase Design of Chiral Domain:** Provide chiral stationary phases (CSPs) that are more stable and enantioselective than before. For usage in HPLC or GC columns, this may entail the synthesis, characterisation, and immobilisation of novel chiral selectors, such as chiral ligands or polysaccharides, onto solid supports.



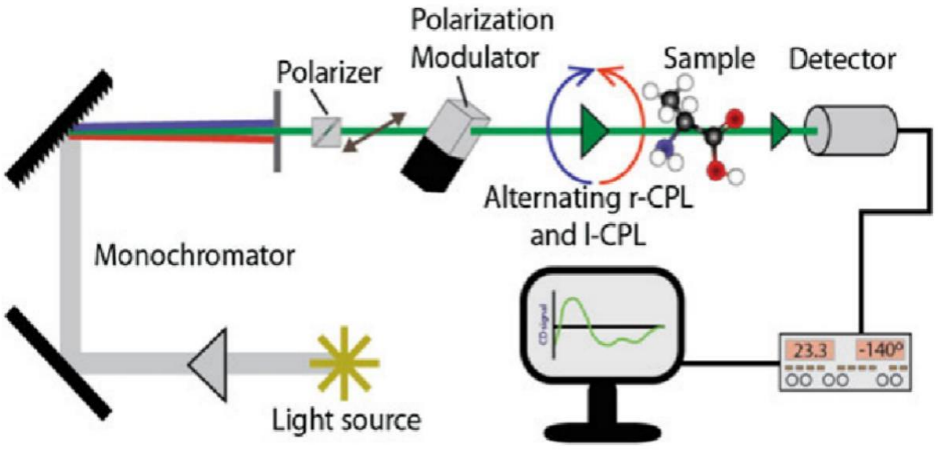
3. **Enantioselective Detection:** In order to perform enantiomeric analysis, investigate novel detection techniques, such as Polarimetry, mass spectrometry (MS), or circular dichroism (CD). Provide highly accurate and precise methods for the sensitive and selective detection of chiral compounds.



4. **Automation and Miniaturization:** The objective is to create chromatographic systems that are both automated and small in size for the purpose of high-throughput enantiomeric analysis. This covers the development of capillary electrophoresis technologies, integrated chromatography platforms, and microfluidic devices that can quickly and efficiently execute chiral separations with little sample consumption. The purpose of this study is to assess the effectiveness of chiral chromatography techniques in the analysis of enantiomers found in complex samples, including biological fluids, pharmaceutical formulations, and environmental samples. To reduce interferences and increase the sensitivity and robustness of the process, develop sample preparation and cleanup strategies.
5. **CE foe chiral analysis:** For chiral analysis, CE is ideal because of several advantages. The good removal efficiency allows for baseline separation even at relatively low selectivities. Furthermore, several hundred thousand plates of CE efficiency enable the baseline resolution of enantiomer pairings with apparent selectivity values smaller than 1.01. The remarkable efficiency is also due to the flat U-profile of the flow and the incredibly low resistance of the mass-transfer operations. Shorter columns, faster mass transfer, and quicker flow allow for speedier analysis.



6. **Circular Dichroism Spectroscopy:** A Chirascan spectrometer, manufactured by Applied Photo Physics in England, equipped with a thermoelectrically driven single cell holder, was used to make the CD spectroscopy measurements. One nm step size, one s time interval per point, and one nm bandwidth were used for the experiments. The quartz cuvette that was employed has an optical path of 0.5 cm. Trifluoroethanol (TFE) was used to measure the CD spectra of both the dipeptide and pure oligopeptide molecules. Using aliquots of pure chemicals, a stock racemic solution with a concentration of 0.1 mM was created.



7. **Partial-filling technique:** In the PFT, a small plug of the PSP is introduced into the capillary instead of being incorporated in the bulk buffer solution. The analytes first interact with the PSP in the selector plug prior to their migration toward the detector, while

the PSP stays within the capillary and does not enter the ion source. An apparent mobility higher than the mobility of the EOF is required for the analytes to pass the selector plug . If this cannot be achieved, a stationary selector plug can be employed, where the EOF is suppressed by using coated capillaries or by using a BGE at low pH. Longer migration times are observed for the latter strategy; however, for both approaches, an optimized concentration and zone length result in an increased separation efficiency and sensitivity. Usually, slightly lower resolutions are obtained with the PFT compared with the CMT due the shorter zone length and possible zone broadening at the PSP-buffer boundary.

CONCLUSION

In conclusion, enantiomer separation plays a crucial role in various scientific disciplines, particularly in chemistry, pharmacology, and biotechnology. By understanding the properties and behaviors of enantiomers, researchers can delve into intricate aspects of stereochemistry, chiral recognition, pharmacological effects, and biological interactions. Additionally, the synthesis and purification of specific enantiomers pose significant challenges yet offer promising avenues for drug development and other applications where chirality is paramount. Regulatory considerations further underscore the importance of accurately separating and characterizing enantiomers to ensure the efficacy and safety of pharmaceuticals and other products. Overall, advancements in enantiomer separation techniques continue to drive innovation and enhance our understanding of molecular structure and function in diverse fields.

FUTURE SCOPE

The future scope of enantiomer separation looks promising, especially with advancements in analytical techniques like chromatography, electrophoresis, and molecular modelling. There's potential for improved resolution, efficiency, and scalability, which could benefit industries like pharmaceuticals, agrochemicals, and materials science. Additionally, there's growing interest in green and sustainable separation methods, which could drive innovation in this field further. Advances in chiral technology are allowing the commercial synthesis of single-isomer compounds hitherto of academic interest only. By understanding the role of these stereoisomers in biological systems, the next logical step is the application of this knowledge to human physiology and pharmacology.

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