
ENANTIOMERIC SEPARATION OF DRUGS BY HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY (HPLC)

Tawfeeq Ramzan^{1*}, Dr. Tanya Sharma²

¹Research Scholar, Department of Pharmacy, Faculty of Pharmaceutical Sciences Mewar University, Chittorgarh, 312901, Rajasthan, India

²HOD and Assistant Professor, Department of Pharmacy, Faculty of Pharmaceutical Sciences Mewar University, Chittorgarh 312901, Rajasthan India.

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*Corresponding Author: Tawfeeq Ramzan

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Research Scholar, Department of Pharmacy, Faculty of Pharmaceutical Sciences

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ABSTRACT

Chirality plays a fundamental role in pharmaceutical sciences. Many drugs exist as enantiomers that exhibit different pharmacological and toxicological properties. High-performance liquid chromatography (HPLC) has emerged as a reliable technique for separating these enantiomers due to its precision, reproducibility, and adaptability. This review discusses principles, methods, stationary phases, applications, and future perspectives of chiral HPLC separations.

INTRODUCTION

Chirality refers to molecules that are not superimposable on their mirror images. Enantiomers often show different biological effects because biological systems are chiral. Regulatory authorities require enantiomeric purity testing. HPLC has become the most widely used method due to high resolution and flexibility.

IMPORTANCE OF ENANTIOMERIC SEPARATION

Enantiomers differ in pharmacokinetics, pharmacodynamics, and toxicity. One enantiomer may be active while the other may be inactive or harmful. Therefore, separation ensures safety, efficacy, and regulatory compliance in pharmaceuticals.

PRINCIPLES OF CHIRAL SEPARATION

Chiral separation is based on interactions such as hydrogen bonding, π - π interactions, steric effects, and dipole interactions. These lead to temporary diastereomeric complexes that result in different retention times.

METHODS

Direct methods use chiral stationary phases (CSPs), while indirect methods use derivatization to form diastereomers. Direct methods are more common due to simplicity and efficiency.

CHIRAL STATIONARY PHASES

CSPs include polysaccharide-based, protein-based, cyclodextrin-based, and macrocyclic antibiotic phases. Polysaccharide CSPs are most widely used due to broad applicability and high resolution.

MOBILE PHASE CONSIDERATIONS

Mobile phase composition, pH, temperature, and additives significantly affect resolution. Normal phase, reverse phase, and polar organic modes are commonly used.

APPLICATIONS

HPLC is used in drug development, quality control, and bioanalysis. It helps in determining enantiomeric purity and studying pharmacokinetics.

RECENT ADVANCES

Recent advances include UHPLC, LC-MS coupling, and development of hybrid CSPs. These improve sensitivity, speed, and selectivity.

CHALLENGES AND FUTURE PERSPECTIVES

Challenges include high cost of CSPs and complex method development. Future work focuses on greener methods and universal CSPs.

Additional discussion on method optimization, resolution factors, and analytical validation enhances understanding of enantiomeric separations in HPLC systems.

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