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A Mechanistic Review and Comparison of Achiral Helical Polymers to Conventional Chiral Stationary Phases for Enantioselective Separation

Enantiomers are pairs of molecules with the same chemical formula and structure, but are not superimposable on each other – mirroring the opposing molecule, a property known as chirality. Chirality has played a critical role in pharmaceuticals, as enantiomers often exhibit drastically different biological activities. Traditional chiral stationary phases (CSPs) in high-performance liquid chromatography remain the standard for separating enantiomers, but limited by their high cost, structural rigidity, inaccessibility, and design constraints. There is constant research in seeking alternatives to traditional CSPs, such as proteins and natural polymers. Research has led to focus on achiral polymers with induced helicity, which utilize geometric interactions to mimic CSP-like behavior and show comparable performance in separating and recognizing separate racemic mixtures of enantiomer molecules. These achiral helical polymers have shown a variety of complex mechanisms that increase their versatility, being adjustable and flexible to fit the needs of biochemical contexts. This review assesses the mechanisms of helicity induction, structural adaptability, and pendant-based tuning in these polymers, comparing their qualitative strengths with those of conventional CSPs. Achiral helical polymers are cost-effective and extremely adaptable; however, due to the lack of a universal polymer and the requirement for intensive understanding in polymer synthesis, they prove to be very difficult to replace current traditional CSPs in the market. There are many applications of achiral helical polymers in analytical and pharmaceutical chemistry, such as live biosensing and targeted separation. However, research is still underway to discover more mechanisms for synthesizing more complex and powerful helical polymers.