Feb 24th, 5:00 PM - 6:00 PM

# Chiral Nanoparticles for Analysis Using Capillary Electrophoresis

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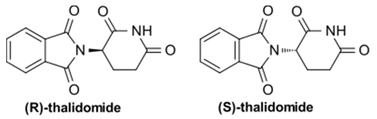
## 1. Abstract

Chiral separation of enantiomers is crucial in the area of drug development where two enantiomers of a compound can have varying effects as pharmaceuticals. For this reason, the Food and Drug Administration requires that each enantiomer of a chiral pharmaceutical be isolated and analyzed. Analytical and preparative scale chiral separations are thus critically important. Capillary electrophoresis (CE) and electrokinetic chromatographic (EKC) methods utilizing chiral additives have demonstrated significant advantages over conventional methods for analytical scale enantiomer separations. The use of chiral pseudostationary phases in EKC can allow for highly efficient and selective separations of chiral molecules due to the interaction of the pseudostationary phase (PSP) with one enantiomer over the other. Characterization of a polymer of N-Acetyl-Glucosamine will be used as the PSP in CE while utilizing reversible addition-fragmentation transfer (RAFT) polymerization techniques to produce polymers of a controlled assembly.

## 2. Background

**Chiral compounds have a single molecular formula but different three-dimensional structures (enantiomers) around an asymmetric carbon** (see figure of Thalidomide)

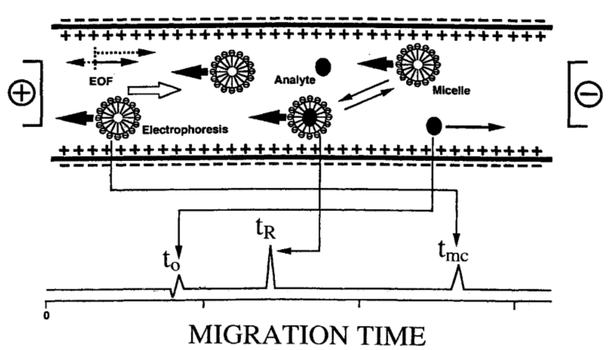



- *Many pharmaceuticals are chiral and must be produced and sold as pure enantiomers*
  - Human body has many homochiral functionalities within it, and will interact selectively or specifically with one enantiomer over another
  - The remaining enantiomer can be inactive or even toxic to the body
  - Thalidomide (figure above) is an example where one enantiomer is therapeutic and the other toxic
- Since 1992 the FDA has required the absolute chirality for all pharmaceuticals to be known and established early in drug discovery.
- *Separation and analysis of enantiomers is difficult*
  - Virtually identical chemical and physical properties
  - *Capillary electrophoresis and electrokinetic chromatography have previously been proven useful for separation and analysis of enantiomers*

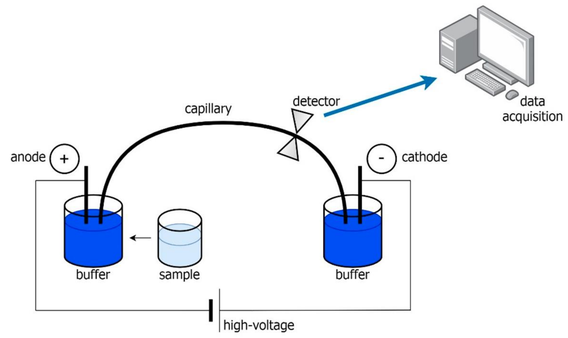
## 4. Pseudostationary Phase

- Pseudostationary phases PSPs are added to the buffer solution in capillary electrophoresis to interact differentially with sample mixture components and effect their separation.
- PSPs are typically micelles but may be ionic amphiphilic polymers
- Chiral PSPs have been previously shown to effect fast and efficient separations of enantiomers

**In this project we are developing novel chiral polymeric PSPs using RAFT polymerization**




## 3. Capillary Electrophoresis



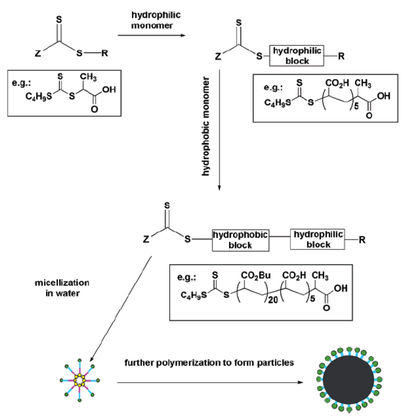

1. Capillary Column (fused silica, +/-50 µm ID, +/-40 cm long) is filled with buffer solution
2. Sample mixture is injected into capillary inlet
3. High strength electric field (+/-1000 V/cm) is applied, inducing migration of sample components by electrophoresis and electroosmotic flow
4. Ionic sample components electrophorese at unique velocities and reach the detector at different times to be read and analyzed.

- For nonionic components, or for ions with similar electrophoretic mobilities, an ionic **pseudostationary phase (PSP)** can be added to the buffer solution to interact with sample components and impart unique effective electrophoretic mobilities, thus allowing their separation.

## 5. Reversable Addition Fragment Transfer (RAFT) Polymerization

Chiral polymeric PSPs will be generated from chiral monomers using Reverse Addition-Fragmentation chain-Transfer (RAFT) polymerization

- RAFT controls the rate of polymerization and produces low dispersity in polymer structure and length
- RAFT produces living polymer chains that can be further polymerized with a second monomer to produce block co-polymer structures
- RAFT allows for the optimization of pseudostationary phase structure.

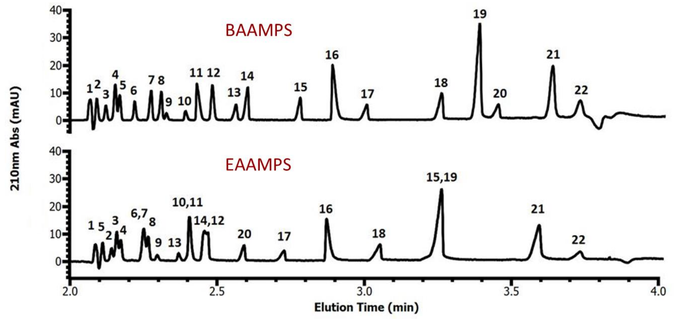



## Resources

1. https://oxbridgeapplications.com/blog/same-but-different-a-story-in-chirality/
2. https://www.mdpi.com/1420-3049/26/8/2135
3. Harvey, David. (2003). The Essence of Chromatography (Poole, Colin F.). Journal of Chemical Education - J CHEM EDUC. 80. 10.1021/ed080p883.1.
4. Christopher J. Ferguson, Robert J. Hughes, Duc Nguyen, Binh T. T. Pham, Robert G. Gilbert, Algirdas K. Serelis, Christopher H. Such, and Brian S. Hawkett, *Macromolecules* **2005,** 38, 2191-2204
5. Latex Nanoparticle Pseudo-Stationary Phases for Electrokinetic Chromatography: Versatile Chemistry Presents Opportunities for Improvements in Performance. Chris Palmer. MSU. [Accessed: April 17, 2022]

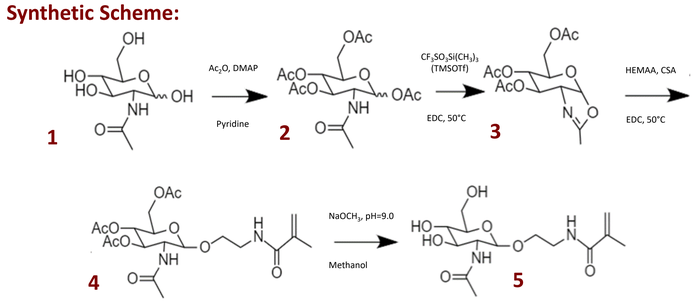
## 6. Selectivity in RAFT Co-Polymer Pseudostationary Phases

- **Co-Polymer PSP selectivity is affected by the chemistry and structure of the hydrophobic block**
- Achiral polymeric PSPs with butyl acrylate and ethyl acrylate hydrophobic blocks have been previously synthesized and utilized in the Palmer lab
- Butyl acrylate and ethyl acrylate copolymers showed different selectivity for the separation of 22 analytes (see below)
- *The chiral monomer produced in this work will constitute the hydrophobic block of the PSP, leading to separation selectivity between enantiomers.*

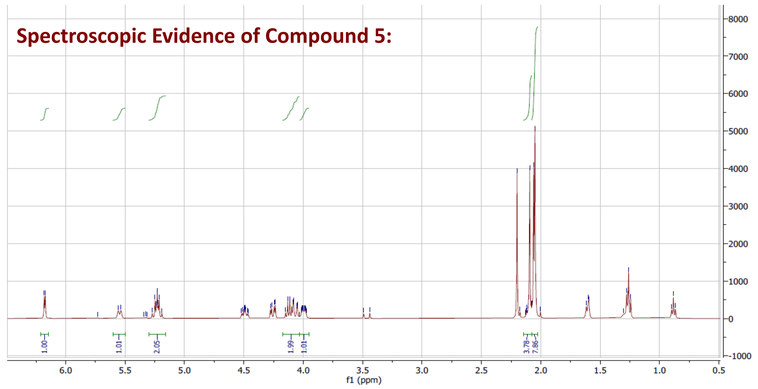



## 7. Chiral Monomer (N-Acetyl Glucosamine) Synthesis

**Synthetic Scheme:**




**Spectroscopic Evidence of Compound 5:**




## Future Work

- Complete diblock copolymer synthesis incorporating N-Acetyl Glucosamine Monomer
- Spectrophotometric and EKC characterization of N-Acetyl Glucosamine co-polymer
- Demonstration of enantiomer separations using N-Acetyl Glucosamine co-polymers