

Capillary Electrophoresis and NMR studies of Enantioseparation Mechanism of Tolperisone

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Stereoisomers of chiral compounds commonly exhibit different pharmacodynamic, pharmacokinetic, metabolic, and toxicological properties. Consequently, there is a growing demand for efficient and cost-effective analytical methods capable of enantiomer separation with short analysis times. Capillary electrophoresis (CE) is a state-of-the-art separation technique that offers rapid analysis with high efficiency and resolution. Enantioselective analysis plays a crucial role not only in the quality control of chiral intermediates and final products but also holds fundamental importance in understanding molecular interactions in nature. Deeper insights into chirality can advance our knowledge of noncovalent intermolecular interactions - such as drug-receptor and substrate-catalyst interactions, as well as contribute to fields like supramolecular chemistry and materials science.

In the present study we aimed to investigate the noncovalent enantioselective interactions between the chiral cationic drug Tolperisone and various cyclodextrins (CDs) used as chiral selectors. Enantiomeric separations were performed using a fused-silica capillary (50 μm ID), with a 100 mM phosphate buffer at pH 2.95 serving as the background electrolyte. Notably, tolperisone enantiomers exhibited opposite affinity patterns toward several of the studied cyclodextrins. Following the CE experiments, selector-selectand interactions were further examined using nuclear magnetic resonance (NMR) spectroscopy, specifically ROESY (Rotating-frame Overhauser Effect Spectroscopy), to gain deeper insight into the spatial structure of the selector-selectand complexes.

The results showed that tolperisone forms inclusion complexes with each cyclodextrin, but the depth and orientation of inclusion varied. In some cases, enantiomers exhibited the same migration order in CE, yet the geometry of the resulting intermolecular complexes was different. Conversely, there were cases where different migration orders were observed, despite quite similar complex structures.

To better understand the underlying mechanisms for the observed phenomena, we plan to continue this research beyond the thesis by performing molecular modeling studies.