

# Molecular simulation of the separation of isoleucine enantiomers by $\beta$ -cyclodextrin with polar solvents

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**1. Introduction** – Cyclodextrins (CDs) are macrocyclic molecules composed of glucose units (6 for  $\alpha$ -CD, 7 for  $\beta$ -CD, 8 for  $\gamma$ -CD, etc) forming truncated cone-shaped compounds. These have cavities of different internal diameters capable of including molecules of different structure, size and composition [1, 2]. Isoleucine (Ile) is an  $\alpha$ -amino acid used in the biosynthesis of proteins. It is essential in human liver and adipose and muscle tissue, but the body cannot synthesize it and then must be obtained from the diet. Inclusion complex formation and chiral separation of amino acids and amino acid derivatives by CDs has been studied with different experimental techniques such as electrospray mass spectrometry, capillary electrophoresis and gas chromatography [3, 4]. These processes have been carried out in vacuo or with solvents like water. Previously, we analyzed the enantiodiscrimination and inclusion complex formation of some amino acids with  $\beta$ -CD, by means of a molecular mechanics (MM) and dynamics (MD) simulation [5]. The aim of the present study is to theoretically examine the interaction between Ile and  $\beta$ -CD in the presence of polar solvents.

**2. Simulation Method** - The interaction energy is modelled by the AMBER force field in which the polarity of organic modifiers is represented by different values of dielectric constant  $\epsilon$  in the electrostatic contribution to energy, and also by the configuration of Ile (zwitterion). In some pH conditions or with polar solvents, amino acids appear as zwitterions with the  $NH_3^+$  and  $COO^-$  groups instead of  $NH_2$  and  $COOH$ , and this implies not only different electric charge distribution, but also a different molecular configuration [5]. Molecular dynamics is based on the resolution of classical equations of motion to determine the trajectories of the particles, depending on the initial conditions of Ile enantiomers.

**3. Results and Discussion** - Molecular dynamics simulations show that the most probable configuration of Ile enantiomers is located near the centre of  $\beta$ -CD, in solvents such as benzene, acetone, ethanol or water. The regions where the enantiomers remain more time in the simulation correspond to locations with greater chiral discrimination.

**4. Conclusions** – The model presented in this study reproduces the capacity of Ile to form inclusion complexes with  $\beta$ -CD, in agreement with experimental findings.

## References

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## Acknowledgements

We are grateful to the Ministerio de Economía y Competitividad (FIS2016-79596-P, AEI/FEDER, UE) for their generous financial support.