Molecular Dynamics Analysis of Interfacial Properties of Curcumin and Supercritical Fluids

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Many of the so-called active pharmaceutical ingredients (API) have different polymorphic forms, which can radically affect crystallization dynamics, co-crystallization abilities, solubilities and dissolution rates of the final products. Recent experimental results [1] suggest that interfacial properties could play significant role in polymorphic control. Specifically, distribution of conformations on the solid-melt interface can be a good predictor of the ratio of specific polymorphs after the melt is cooled.

The main objective of the present study is to obtain a theoretical description of the correlation between the changes in the local structure of an interface and changes in the conformational distribution / polymorphism of active pharmaceutical compounds. To this end, we have performed molecular dynamics simulations of bulk Curcumin crystals and Curcumin-scCO_2 interfaces. Curcumin is both culturally important and medically interesting due to the recent reports [2] of its biochemical activity. Supercritical CO_2 is one of the most accessible, environmentally friendly and widely used supercritical fluid solvents, allowing us to contrast computational results against some experimental or previous theoretical trends.

Throughout this project we have selected and developed both Curcumin and CO_2 force field models, developed a method of monitoring conformational changes, selected methods of identifying interfacial molecules (ITIM) and integrated it with many methods of local-structure description (such as radial distribution functions, angular distribution functions, Voronoi analysis, etc.).

References

[1] Oparin RD, Kurskaya MV, Krestyaninov MA, Idrissi A, Kiselev MG. *Eur J Pharm Sci*. 2020; 146: 105273.

[2] Maheshwari RK, Singh AK, Gaddipati J, Srimal RC. *Life Sci*. 2006; 78: 2081–2087.