Force field performance in recognition of solvent mediated polymorphism of 2, 6-dihydroxybenzoic acid from toluene and chloroform solution

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2, 6-Dihydroxybenzoic acid has been evaluated as an active pharmaceutical ingredient, for example in the treatment of tumors, and is employed, commonly, as a reagent in the synthesis of pharmaceutical materials especially antipyretic, analgesic and antirheumatism agents. In this molecular modelling study, two polymorphic forms of 2, 6-Dihydroxybenzoic acid were investigated in two different solvent environments to assess the effect of solvent type at same level of solution supersaturation, on the nature of the intermolecular hydrogen-bonding interactions. Experimentally it is found that, generally, Form I is crystallized from toluene while Form II is crystallized from chloroform solution[1]. Molecular dynamics (MD) techniques were applied to simulate the molecular recognition processes operating between solvent and solute molecules prior to nucleation and phase separation from solution. The MD simulations employed the computer program DLPOLY and the probabilities of finding specific intermolecular interactions in specific solvent environments were assessed by calculating radial distribution functions from the simulation trajectory files which initially equilibrated under NVE and followed by NPT ensembles. Dreiding[2] and OPLSAA performed well in simulating the liquid system such the pure solvent as the calculated densities, rdfs and diffusion in a good agreement to the theoretical values compared to COMPASS force field.

[1] R.J. Davey, N. Blagden, S., H. Alison, M. J. Quayle, S. Fuller, 2001, *Crystal Growth & Design*, **2001**, 1, 59-65
[2] F. Adam, R. B. Hammond, K. Pencheva, K. J. Roberts, R. J. Davey, *17th International Symposium on Industrial Crystallization Proceeding*, **2008**, Volume 1, 439-445.