Supercritical fluid technology: Active Pharmaceutical ingredient processing

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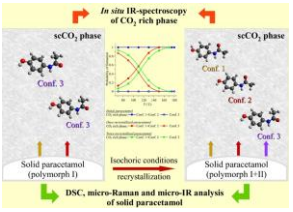
Abstract

Many of the new active pharmaceutical ingredient (API) candidates show a high activity in receptor studies, but are practically insoluble in any (hydrophilic) biological fluids. Therefore, such compounds will not reach the site of action *in vivo*, and never make useful API. Solubility of a compound on the one hand is determined by its solid state structure by the interaction between the molecules in the crystal lattice, and, respectively, by the solvation ability of the molecules in the solution on the other hand. More than half of the known API molecules show polymorphism, which is the existence of the chemically identical molecules in a variety of stechiometrically identical crystal forms. This means that different polymorphs, though of same chemical composition, are of different crystal structure, and they can exhibit widely different solubility and other physical and physico-chemical properties.[2-6] Therefore, understanding polymorphism, as well as determination of solvation mechanism and solubility, are strongly interrelated issues that are extremely relevant for biopharmaceutical evaluation and performance.

Many techniques are used for solubility enhancement such as salt formation, solubilization by co-solvent, use of pro drug, particle size reduction, lyophilization, melt agglomeration process, extruding method, spray drying technology[7], However these techniques have some limitations which are associated with the high energy process which cause the disruptions in the API crystal form, toxicity of the solvent, reproducibility. Recently there has been considerable interest to the use of supercritical fluids (SCF) technology for processing API molecules.

Indeed, in the pharmaceutical industry the use of SCF which is a promising alternative to replace processes such as extraction, drying and crystallization while more effectively controlling particle size and crystal polymorphism. Furthermore, SCF can replace environmentally toxic solvents that either require expensive purification procedures or remain in the final product in low but still toxic concentration. This presentation is divided in two parts. The first one is dealing with fundamental understanding of the supercritical states and in the second one I will show how the use of supercritical fluids technology may help to control solubility and polymorph for of an API these issues will be addressed by a combination of vibration spectroscopy and molecular modeling.



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Biography

Author has Abdenacer Idrissi received his M.Sc. in Physics from the University of Mohammed I (Oujda, Morocco), and his PhD in Physical Chemistry from the University of Lille (France), where he is a Professor of Chemistry and Physics at the present time. His research interest is focused on the understanding of the structure and dynamics of fluids including ionic liquids and supercritical fluids. The main problematics are the understanding of the cellulose dissolution, the control of the polymorphic forms of the bioactive molecules and the characterization of the short time dynamics of the dyes used in solar cells. These research are carried out using a combination of an array of spectroscopic technics (IR, Raman, neutron scattering, time resolved spectroscopy) with molecular dynamics simulation.

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