Investigation of Carbamazepine/Acetone Solvate Formation over a Range of Temperatures using Vapor Sorption Techniques

Daniel Burnett[1)] and Frank Thielmann[2)]
[1)] Surface Measurement Systems Ltd., 2222 South 12th Street, Suite D, Allentown, PA, USA
burnett@smsna.com
[2)] Surface Measurement Systems Ltd., 5 Warfside, Rosemont Road, Alperton, Middlesex, HA0 4PE, UK

PURPOSE

Physical and chemical stability of pharmaceutical solids is highly dependent on its polymorphic state. For example, the solvate state of crystalline substances is of particular concern. The ultimate solvated state can be dependent on both temperature and concentration of the solvate vapor. Also, different solvate forms can affect the material solubility, dissolution rate, flowability, and compressibility. For the above reasons, it is paramount to study the solvate behavior over a wide range of storage and processing conditions.

METHODS:

For many materials, phase transitions can be influenced by the amount of solvent vapor surrounding the sample. Dynamic Vapor Sorption (DVS) is a well-established technique for investigating the vapor sorption behavior for solid materials. In this study, acetone vapor isotherms were measured on carbamazepine to investigate its solvation behavior over a range of temperatures.

RESULTS:

Amorphous carbamazepine showed evidence of a stoichiometric solvated species when exposed to acetone vapor. The critical acetone vapor onset concentration to induce salvation was highly dependent on temperature. At 30 C, the carbamazepine solvate is not formed until 90% p/po. However, at 15 C, the solvated species is formed by 60% p/po. At several temperatures, the removal of acetone (desorption) was studied over different time scales to investigate kinetic limitations. These studies indicate that carbamazepine/acetone solvate formation is driven by thermodynamic factors.

CONCLUSIONS:

Amorphous carbamazepine formed a solvate at elevated acetone partial pressures over a range of temperatures. As the temperature is increased, the onset acetone vapor concentration necessary to form a solvate also increases. These gravimetric vapor sorption studies over a wide temperature range suggest solvate formation is driven by thermodynamic factors for carbamazepine.