Characterization of drugs substances by Thermal Analysis.

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In the Biopharmaceutical domain, the activity of the Research-Development department, Control Quality and Manufacturing Processes has rapidly increased. The aim is to be able to completely characterize the drug under development. Thermal Analysis, including a broad range of techniques gives the possibility to reach this goal in complement with others tools like chromatography, spectroscopy….

We are going to present different examples to demonstrate how thermal analysis could be useful:

- Xanthan gum is an anionic polyelectrolyte with a b-(1®4)-D-glucopyranose glucan (as cellulose) backbone with side chains of -(3®1)-a-linked D-mannopyranose-(2®1)-b-D-glucuronic acid-(4®1)-b-D-mannopyranose on alternating residues. It hydrates rapidly in cold water without lumping to give a reliable viscosity, encouraging its use as thickener, stabilizer, emulsifier and foaming agent. A study has been done to detect possible difference in hydration rate in pH 4.5 phosphate buffer using a specific calorimeter and its rotating reactor configuration.

- With a highly sensitive calorimeter, ongoing degradation of tablets could be observed reducing the time needed to evaluate pharmaceutical formulation stability. Experiments have been run on gabapentin at different temperature and different humidity.

- Detection of amorphous phase[1] thanks to the Thermally Simulated Currents (TSC) technique. This thermal analysis method which principle is to detect molecular mobility, appeared to have the capability of providing a clearer visualization of the presence of low levels of amorphous material which manifests as a glass transition event.

- Determination of heat of formation of two co-crystals : AB(I) and AB(II).
  With A : nicotinamide and B *:* α-*trans*-cinnamic acid.
  As it is not possible to interact directly A and B, we use the heat of dissolutions of A, B and AB in methanol and determine a cycle as follows (Hess's law):

ΔH_A^s

A + methanol → Solution of A

+ +

ΔH_B^s

B + methanol → Solution of B

↓ ΔH_{AB}^F ↓

ΔH_{AB}^s

AB + methanol → Solution of AB

$$\Delta H_{AB}^{F} = \Delta H_{A}^{s} + \Delta H_{B}^{s} - \Delta H_{AB}^{s}$$

With ΔH_{A}^{s} : heat of dissolution of A in methanol

ΔH_{B}^{s} : heat of dissolution of B in methanol

ΔH_{AB}^{s} : heat of dissolution of AB in methanol

ΔH_{AB}^{F} : heat of formation of AB

The experiments consists in measuring the heats of dissolution of A, B and AB and to calculate the heat of formation according to the here above equation.

References

1-Gopi M. Venkatesh, Maria E. Barnett, Charles Owusu-Fordjour and Marc Galop, Pharmaceutical Research, vol 18, N°1, 2001.