Drug – excipient compatibility

Introduction:

Preformulation specialists are familiar with issues related to destabilizing interactions between potentially stable active principle ingredients and excipients. Step isothermal microcalorimetry provides comparative data allowing the selection of the most stable formulation [1] and the identification of the elements which are at the source of the interaction.

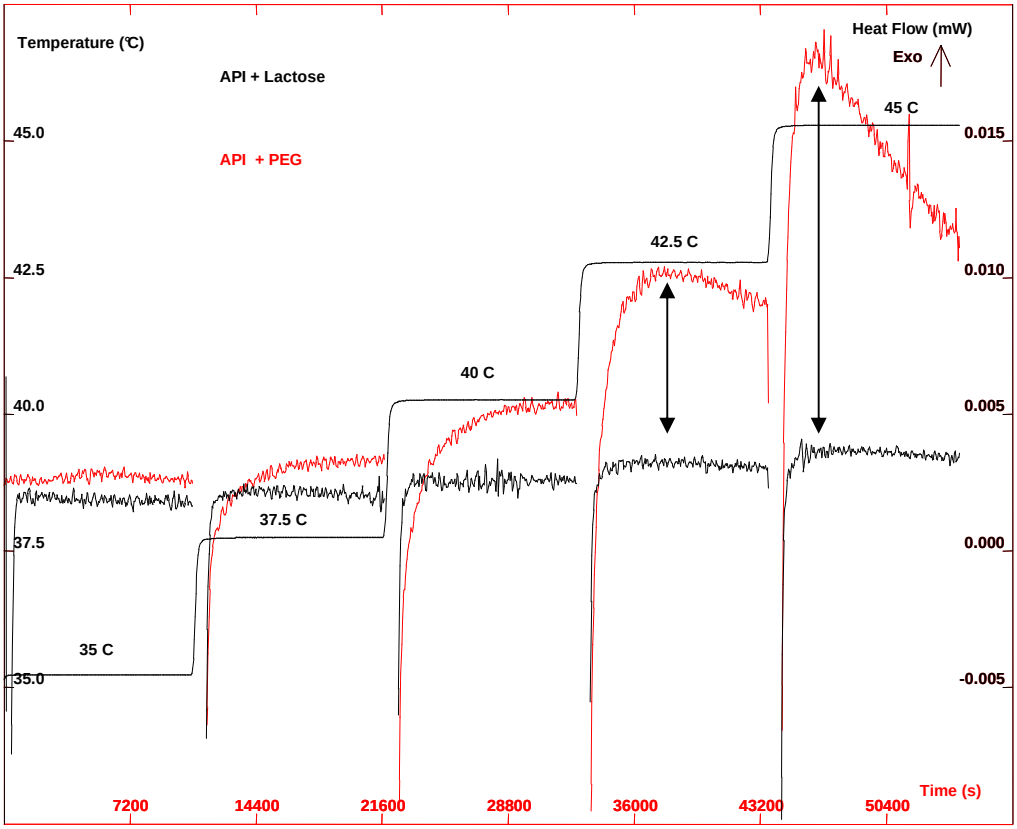

Figure 1 – Comparison of the heat release of two formulation of the same API at different temperatures. The arrows point out the increase of heat production from the smaple containg PEG

Experimental

Two samples are tested, that are blends of the same API with two different excipients (lactose and polyethylene glycol). The sample mass is 400mg and the amount of API is identical in both blends. The temperature is maintained during 3 hours successively at 35°C, 37.5°C, 40°C, 42.5°C and 45°C, and the heat flow coming from the sample is measured continuously.

Results and Discussions

At 35°C, both samples lead to a signal very close to 0µW, meaning that they are thermally stable. At 37.5°C and 40°C, the signal corresponding to the API + PEG blend starts raising, meaning that an exothermic effect takes place in the sample and is accelerated with temperature. At 42.5°C and 45°C, the signal differences become obvious. From these two tests it is possible to state that API + Lactose is more thermally stable than API + PEG. Extra tests of pure PEG and API would be requested in order to check if the exothermic effect comes from an interaction between API and PEG, or if it comes from a self reaction of PEG or API.

[1] International Journal of Pharmaceutics 342 (2007) 145–151

µDSC3 Evo
-20°C to 120°C

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