Drug – excipient compatibility

INTRODUCTION

Preformulation specialists are familiar with issues related to destabilizing interactions between stable active principle ingredients and excipients. Microcalorimetry used in step isothermal mode 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.

EXPERIMENT

Two samples were tested, that are blends of the same API with two different excipients (lactose and polyethylene glycol). The sample mass was 400mg and the amount of API was identical in both blends. The temperature was 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 was measured continuously.

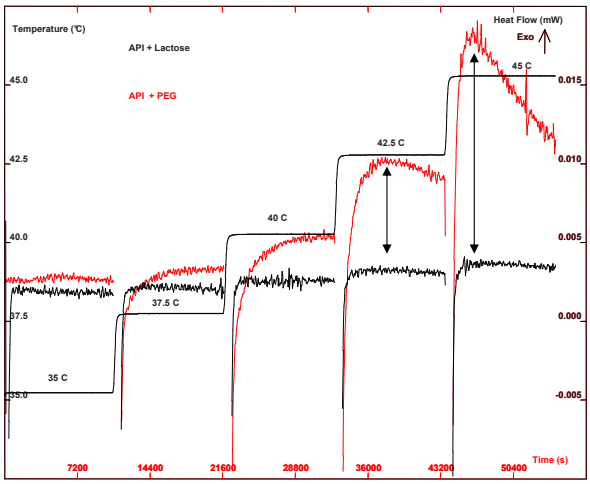


Figure 1 – Comparison of the heat released by two formulations of the same API at different temperatures. The arrows point out the increase of heat production from the sample containg PEG

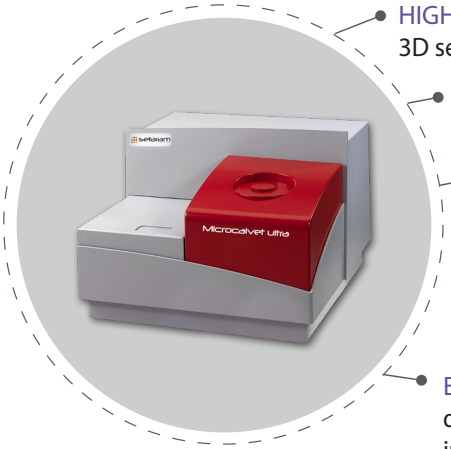
RESULTS AND CONCLUSION

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.

INSTRUMENT

MICROCALVET ULTRA

-20 to 170°C



HIGHEST HEAT MEASUREMENT ACCURACY
3D sensor based on Peltier elements with Joule effect calibration.

MODIFIABLE TEMPERATURE CONDITIONS
for increased flexibility and replication of real life conditions.

CONVENIENT INTERCHANGEABLE CRUCIBLES AND CELLS
to perform even the most demanding experiments using one instrument :
- high pressure (1000bar) and high vacuum
- pressure measurement and control
- mixing experiment

EXTERNAL COUPLING CAPABILITY
designed to increase your research options including manometry, BET instrumentation, gas analyzers, humidity controllers and gas panels

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