Evolution of critical tablet attributes with temperature

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Goal

Determine the impact of the temperature on tablet attributes: appearance and hardness.

Materials and Methods

MATERIAL	2 batches of customer formulation with Poloxane and PEG6000
PRESS MODEL	STYL'One Evo (MEDELPHARM, Beynost, France)
SOFTWARE	Analis software 2.08.10
TOOLING	Heated die Concave punches
TABLET TESTER	Sotax ST-50

TARGET TABLET WEIGHT	150 mg
METHODOLOGY	Tabletability equation from USP Monograph <1062> current edition 4-point compression profiles at 20°C and 50°C

$$TS = \frac{10 \times Ha}{\pi.DI\,(2.84.\frac{Th}{Di} - 0.126.\frac{Th}{W} + 3.15.\frac{W}{Di} + 0.01)} \qquad \text{Log(TS)} = \alpha.\text{Log(P)} + \beta$$

Results

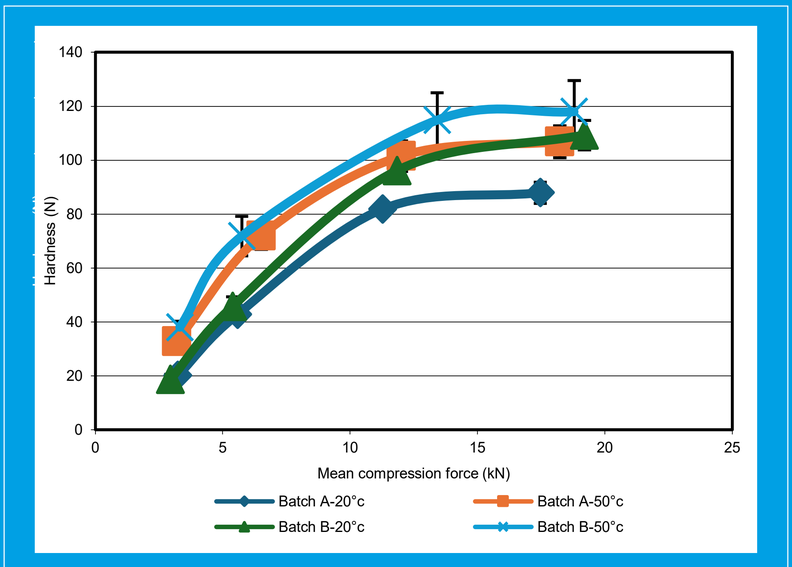

Figure 1: Hardness as the function of the compression force and the temperature

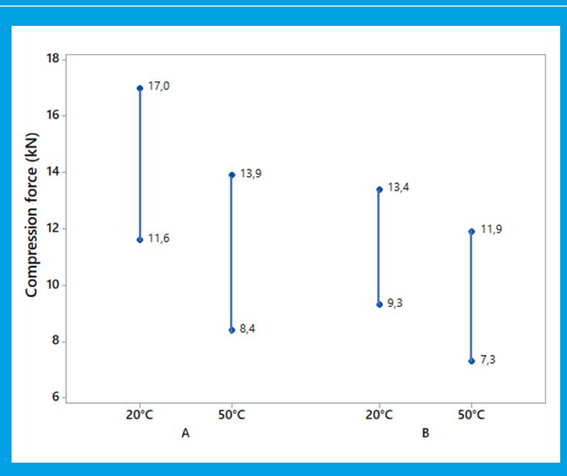

Figure 2: Design space of the compression forces to achieve suitable tensile strength as a function of the batch and the temperature

Discussion

The range of compression forces to achieve acceptable tablets differs from Batch A to Batch B, and also changes with temperature. As the temperature rises during the manufacturing, the main compression force must be adapted.

TABLET ASPECT

Sticking was observed after manufacturing 30 tablets at 50°C, which led to tablet defects. No sticking was observed at 20°C.

Figure 3: Punch surface after manufacturing of tablets at 20°C (left) and 50°C (right)

The tablet sticking continued to worsen with an increase in production time. Based on the customer's target production speed (58 RPM), this defect would require the tablet press to be stopped every 2 minutes. This production delay is not acceptable in respect of the target price of this product. External lubrication was also tested but couldn't delay sticking.

Conclusion

The heated die developed by MEDELPHARM for the STYL'One Evo brought to light differences on a critical process parameter due to the rise of the temperature as observed on high output rotary presses. This rise in temperature also led to intense sticking on punch faces. The customer considered changing the formulation to avoid tablet defects and poor industrial performance. Some other industrial solutions for rotary presses are available, such as cooled turrets.

The use of the heated die to simulate the higher temperature often seen during the production of batches can help test the viability of different formulation candidates. Predicting temperature sensitivity at the start of the development stage is a way to speed up the time to market of candidate drugs.

References

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