Take-off sensor as a tool for sticking assessment during tablet development

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INTRODUCTION

More than 70% of candidate drugs have low solubility (BCS Class II and IV) (Nikolakakis et al. 2017). Making tablets with low solid fraction improves the dissolution rate (Van der Ban et al. 2017), but increase the risk of sticking (Capece, 2019).

The take - off sensor developed by MEDELPHARM, France allows to give an attribute to sticking.

Linear ejection equipped with the take off sensor

Illustration of sticking

MATERIAL AND METHOD

Material

The results displayed here are based on a customer's blend. No further information can be disclosed. Magnesium stearate (MF-3V, Peter Greven) was used for external lubrication purpose.

True density

True density was mesured with a helium pycnometer, AccuPyc II 1340 (Micromeritics). Materials were placed in the measurement cell (11.75 cm^3) and purged with helium at 19.5 psig 10 times before measurement of the true density.

Tableting and sticking assessment

The final blend was compacted into tablets using a single punch compaction simulator (STYL'One Evo, MEDELPHARM) equipped with capsule shaped tooling. A six-point compression profile was performed mimicking a KORSCH XL 100 Euro D at 30RPM and 30 tablets were manufactured per point. A strain gage is attached to the linear ejection system and measure the detachment force of the tablet from the lower punch with an acquisition frequency of 4000Hz.

The external lubrication system was connected to the STYL'One Evo forced feed shoe.

The weights, dimensions and hardness of the tablets were measured using a semi-automatic tablet tester Sotax ST-50 (Sotax, Switzerland).

RESULTS AND DISCUSSION

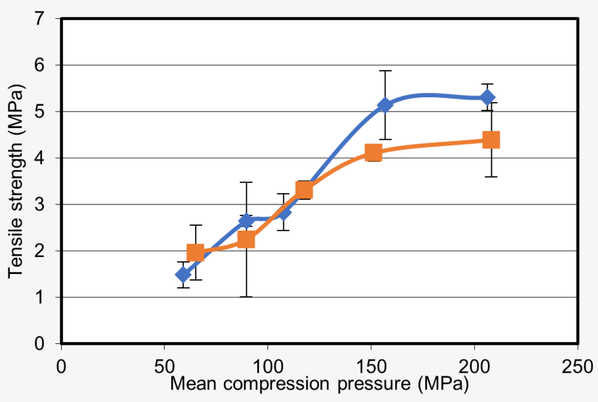

Figure 1 Tensile strength as a function of compression pressure without external lubrication (in blue) and with external lubrication (in orange)

Our customer was aiming a minimum tensile strength of 2MPa to comply with its tabletability standards. Here, a tensile strength above 2MPa can be achieved for a compression pressure above 75MPa.

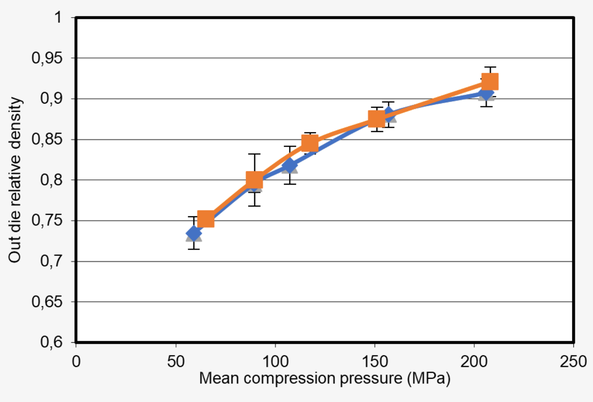

Figure 2 Solid fraction as a function of compression pressure without external lubrication (in blue) and with external lubrication (in orange)

As this product had a low solubility, our customer was aiming a solid fraction below 0.80.

A maximum pressure of 100MPa should be applied to comply with the customer requirements.

Figure 3 Take-off force as a function of compression pressure without external lubrication (in blue) and with external lubrication (in orange)

The take-off forces are high for compression pressures below 100MPa and intense sticking could be observed.

The use of external lubrication allowed to lower the take-off forces and cancel the appearance of sticking.

CONCLUSION

During those trials, the take-off sensor was able to put a figure on the sticking and to help the customer to find the best settings to get a balance between manufacturability attributes (tensile strength), dissolution profile assessment (solid fraction) and risk of sticking (take-off force). Here, the use of external lubrication allowed to widen the manufacturing space for this product.

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