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Reply to the Letter to the Editor

Dear Sir,

We want to comment the "Letter to the Editor" from Dr. Changquan Calvin Sun.

Dry granulation often results in tablets with inferior tensile strength compared to direct compression. In literature the partial loss of compactability after roll compaction and dry granulation was first described as work hardening by Malkowska and Khan (1983). It was explained with a limited binding potential which is partially consumed in the first compression step. Materials with plastic deformation properties are particularly sensitive to this phenomenon.

In a more recent paper by Sun and Himmelspach (2006), the effect of reduced tensile strength of dry granulated granules of MCC was related primarily to a particle size increase during granulation rather than work hardening. In absence of extensive fracture the particle size increase resulted in a lower surface area available for bonding. The authors used sieve cuts (44–106 μm and 250–500 μm) prepared from different types of microcrystalline cellulose (MCC). Non-compacted and compacted materials were compared. The authors showed that there was a negative correlation between particle size of granules and tensile strength of tablets. The tabletability of granules with similar size distribution was stated to be similar and independent of primary particle size.

In the study of Sun and Himmelspach (2006), the roll compaction was only performed at one compaction force level. It is well known, that the effect of roll compaction on compactability is highly dependent on the compaction force used during roll compaction. A careful inspection of Fig. 4 reveals that same sieve cuts of granules made from different particle sizes of raw MCC resulted in different tablet tensile strengths. The sieve fraction made from granules of MCC of smaller particle size resulted in tablets with higher tensile strength compared to those made of MCC with a higher original particle size (cf. Fig. 4). The authors state the differences in tensile strength as similar and being caused by different particle size distributions within the sieve fractions. The particle size distributions are not shown but a calculated specific surface area is given.

The same amount of magnesium stearate (0.5%) was added indepentendtly of the particle size of the original MCC or the granule size fraction. Since the outer specific surface area of the powder particles or the granules is different, the addition of the same amount of magnesium stearate results in a different thickness of the layer of magnesium stearate on the powders and granules. The large size fraction of granules having a smaller outer surface area has a higher thickness of magnesium stearate layer compared to the smaller size fraction. This might explain partly the lower tensile strength of larger granules with a smaller surface area. It is difficult to attribute the partial loss in compactability unambiguously to the particle size of the granules, if different magnesium stearate layers were present. Two mechanisms may be confounded.

In our recent study (Herting and Kleinebudde, 2007) tablets were prepared from dry granules by using an external lubrication. This method avoids the presence of magnesium stearate layers of different thickness on the granules. We have not investigated, whether the intergranular bonding strength is lower than the intergranular bonding strength. However, at least for the dry granules prepared from low porosity ribbons (i.e. high specific compaction force) this assumption seems to be valid when looking at the fracture plain of the tablets.

It could be shown that the granule particle size increased by using MCC types of smaller primary particle sizes. Nevertheless, the tablets made from the coarser granules showed a higher tensile strength. This indicates that the tablet tensile strength is not solely dependent on the granule size.

We agree with Sun and Himmelspach that the particle size of the granules made from plastically deforming materials is important for the compactability of the granules. However, we disagree that this is the primary mechanism explaining the partial loss in compactability. The particle size of the starting materials is also of importance and the work-hardening phenomenon cannot be completely neglected. In fact the two studies are consistent, but the interpretation of the significance of the particle size enlargement differs.

References

Herting, M.G., Kleinebudde, P., 2007. Roll compaction/dry granulation: effect of raw material particle size on granule and tablet properties. Int. J. Pharm. 338, 110–118.

Malkowska, S., Khan, K.A., 1983. Effect of recompression on the properties of tablets prepared by dry granulation. Drug Dev. Ind. Pharm. 9, 331–347.

Sun, C.C., Himmelspach, M.W., 2006. Reduced tabletability of roller compacted granules as a result of granule size enlargement. J. Pharm. Sci. 95, 200–206.

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