EVALUATION OF THE IMPACT OF MACHINE-AIDED DEBLISTERING IN UNIT DOSE BLISTER PRODUCTION ON THE FUNCTIONALITY OF TABLET COATING

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Background and importance
Our Unit Dose blister production processes large quantities of drugs with deblistering machines (Fig.1). Damaged drugs are removed. However, it has not been studied if mechanical stress might cause unobservable damage and negative effects on functional coating.

Aim and objectives
We investigated the influence of machine-aided deblistering on the functionality of drug coating. Drugs were chosen for their high deblistering volume or critical active agent (worst case approach).

Materials and methods
Preparation:
- Thrombo ASS 100mg (TA) (Acetylsalicylic acid; enteric coating) and
- Quilonorm retard 450mg (QU) (Lithiumcarbonate; tablet film causing retardation of release)
were deblistered:
1. manually and then minimally damaged (positive control)
2. with deblistering machines Type RBP Bauer D1500\textsuperscript{1} (test sample)
3. manually (negative control)

Analysis: Ten tablets of each group were analysed:
1) TA+QU: Dissolution testing was performed following the methods of the European Pharmacopoeia\textsuperscript{2} (assembly with 37°C and motion of fluid). Requirements: two hours of acid stage duration in 0,1M HCl followed by fast (enteric coating) or delayed (retardation) disintegration in neutral buffer solution.
2) TA: Tablets were immersed into a methylene blue dye bath to visualise intactness of coating / damaged areas.

<table>
<thead>
<tr>
<th></th>
<th>minimally damaged TA</th>
<th>machine-deblistered TA</th>
<th>manually deblistered TA</th>
<th>minimally damaged QU</th>
<th>machine-deblistered QU</th>
<th>manually deblistered QU</th>
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| 0,1M HCl | disintegration starts within seconds, complete after 1h
(Fig.3) | no disintegration after 2h | no disintegration after 2h | no disintegration after 2h | no disintegration after 2h | no disintegration after 2h |
| phosphate buffer pH 7 | disintegration visible after 1h, complete after 2h
(Fig.3) | disintegration visible after 1h, complete after 2h | no disintegration after 1h, disintegration visible after 2h | no disintegration after 1h, disintegration visible after 2h | no disintegration after 1h, disintegration visible after 2h |
| dye bath (Fig.4) | cavities and grooves | even dying of surfaces | even dying of surfaces | | | |

Conclusion and relevance
Although minimal damage can lead to a loss of coating functionality, machine-aided deblistering showed no negative effects on coated tablets; Neither differences in disintegration tests nor in the dye bath were detected compared with manually deblistered tablets. These results support machine qualification and validation of this important step in our Unit Dose blister production and were examined upon a GMP inspection by the Austrian authority.

References
(1) https://www.rbp.de/produkte/rbp-d1500/
(2) Europäisches Arzneibuch, Verlag Österreich GmbH Band 1, 2.9.3 Wirkstofffreisetzung aus festen Arzneiformen (dissolution test for solid dosage forms)