Kepler Universitätsklinikum

PP-002

COMPOUNDING FOR PAEDIATRIC PATIENTS - INCREASING QUALITY THROUGH MECHANISATION?

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Background and Purpose

In order to assess the quality of extemporaneously prepared capsules for paediatric patients we conducted a series of uniformity tests[1] in 2012. Results showed considerable fluctuations in quality of mixing being recognised as most critical and dependent on personal skills.

Previous results:

> Over 50% failed to comply with pharmacopoeial standards

Based on the results of our previous study we chose to test mechanisation by using a blender in the preparation process. Aim of our study was to ensure sufficient mixing capacity of the tested device in real life conditions and consequently to improve the uniformity of content in our capsules.

Our objectives were to:

> Increase uniformity of content

> Meet pharmacopoeial criteria

> Establish reproducibility

Material and Methods

To mimic a realistic setting we compounded manually grinded acetylsalicylic acid and maize starch using a v-blender[2]. The loading and mixing process was conducted by one person corresponding to the manufacturer's instructions. From each mixture samples were taken at representative points of the blender (figure 1), quantified by high performance liquid chromatography and analysed according to European Pharmacopoeia 8.

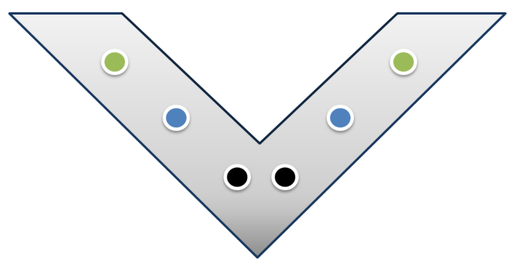

Figure 1: v-cone blender with sample locations (two samples per location)

Quantification via high performance liquid chromatography[3]:

> Column: LiChrospher 100 RP 18 (5 µm)

> Solvent: H_2O/Methanol/Phosphate buffer (pH 3,5) (mixing ratio 70/20/10)

> Injection volume: 5 µl

> Flow-rate: 1,0 ml/min

> UV-VIS Detection: 254 nm

> Retention time: 9.5 min

Results

As a first step seven mixtures were analysed, which all complied with pharmacopoeial requirements by meeting the criteria "uniformity of content of single-dose preparations", i.e. acceptance values below 15 (Ph. Eur. 2.9.40, figure 3). Nevertheless, deviations from the expected value were high (up to 41.7%) with an average deviation of 11.3% (figure 2).

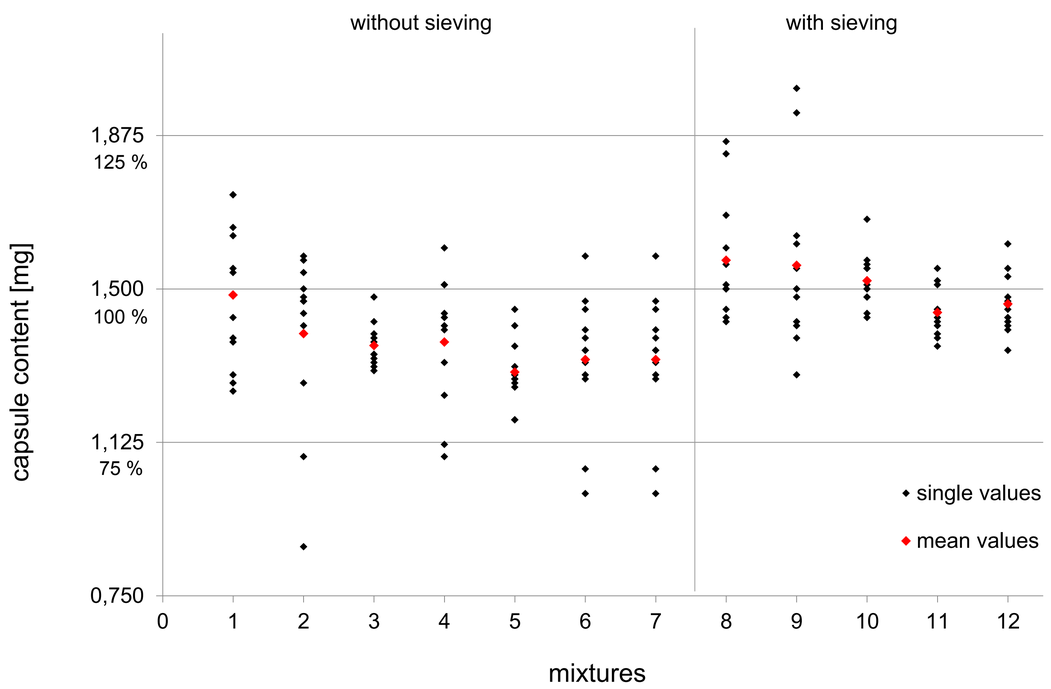

Figure 2: content of active ingredient measured in the samples

A review of the process revealed an unsatisfactory grinding process and showed the necessity to ensure homogeneous particle size. Addressing this issue by introducing a sieving step, another five mixtures were analysed, all of which fulfilled the pharmacopoeial directive (Ph. Eur. 2.9.40, figure 3) with distinct improvement of both maximum and average deviations (≤ 24.2% and ≤ 5.9%, figure 2).

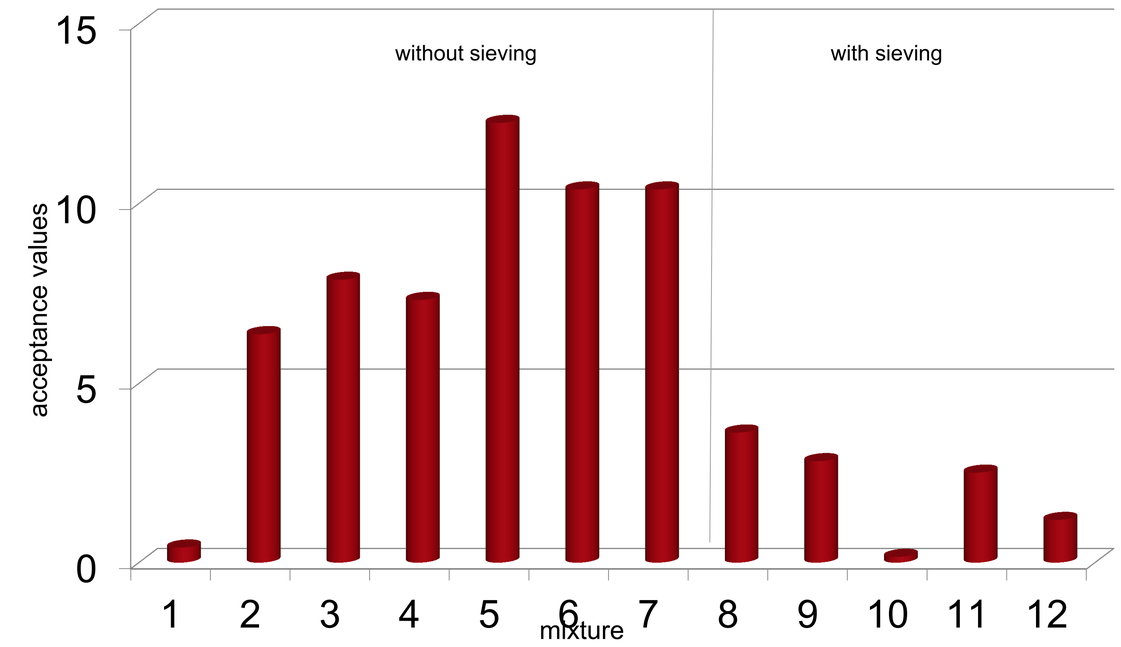

Figure 3: acceptance values (max. 15; Ph. Eur. 8.8, 2.9.40) of the measured mixtures

Conclusions and Discussion

Our study indicates that the use of a blender improves uniformity of content significantly compared to manually blended capsules, but homogenous particle size is needed for optimal results. Thus a sieving step should be introduced. Further testing with capsules composed of crushed tablets will be carried out before implementation into practice.

References

1. "Quality in pharmaceutical compounding" by M. Raffl, A. Pointinger; Poster at the EAHP Congress in Milan 2012
2. Manual of the "ProMixer V-Blender" by Torpac Inc.
3. Hager's Handbook, 5th Edition, Volume 7