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Manipulating tablets containing poorly soluble prednisolone to obtain paediatric doses

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Background

Manipulation of tablets is often necessary to achieve an appropriate dose in the paediatric ward[1]. Studies have shown a difference in dose accuracy obtained upon manipulation for different tablets, in particular for the slightly soluble drug substance aspirin[2]. Prednisolone is a very slightly soluble drug substance, and prednisolone tablets are frequently manipulated in paediatric care.

Aim

To investigate the dose accuracy and dose precision attained after manipulation of a commercially available prednisolone tablet, and to compare the results with those previously found for aspirin.

Materials and methods

- **Prednisolone tablets**: Prednisolon Alternova 5 mg “Alternova A/S”, Skælskør, Denmark
- **Dosing accuracy study**: Tablets were dissolved in 10 ml water. After 4 minutes of intermittent stirring, samples of 1 ml, a tenth of the tablet, were withdrawn (n=6).
- **Instrument**:
  - UHPLC-system from Shimadzu Corporation, Kyoto, Japan (Nexera, with Prominence DAD-detector).
  - Analytical column: ACE Excel 2 µm C18-AR, 2.1 x 100 mm, (Advanced Chromatography Technologies Ltd.)
  - The analytical method was validated for linearity, precision, and specificity.

Results

After manipulation of the prednisolone tablets by extraction of a tenth of a tablet, 92.2 % (85.3–95.1 %) of the intended dose (0.5 mg) was retrieved.

Table 1. Solubility of aspirin and prednisolone in water according to the European Pharmacopeia.

Drug substance	Solubility in water (15-25 °C)
Aspirin	Slightly soluble (1-10 mg/ml)
Prednisolone	Very slightly soluble (0.1-1 mg/ml)

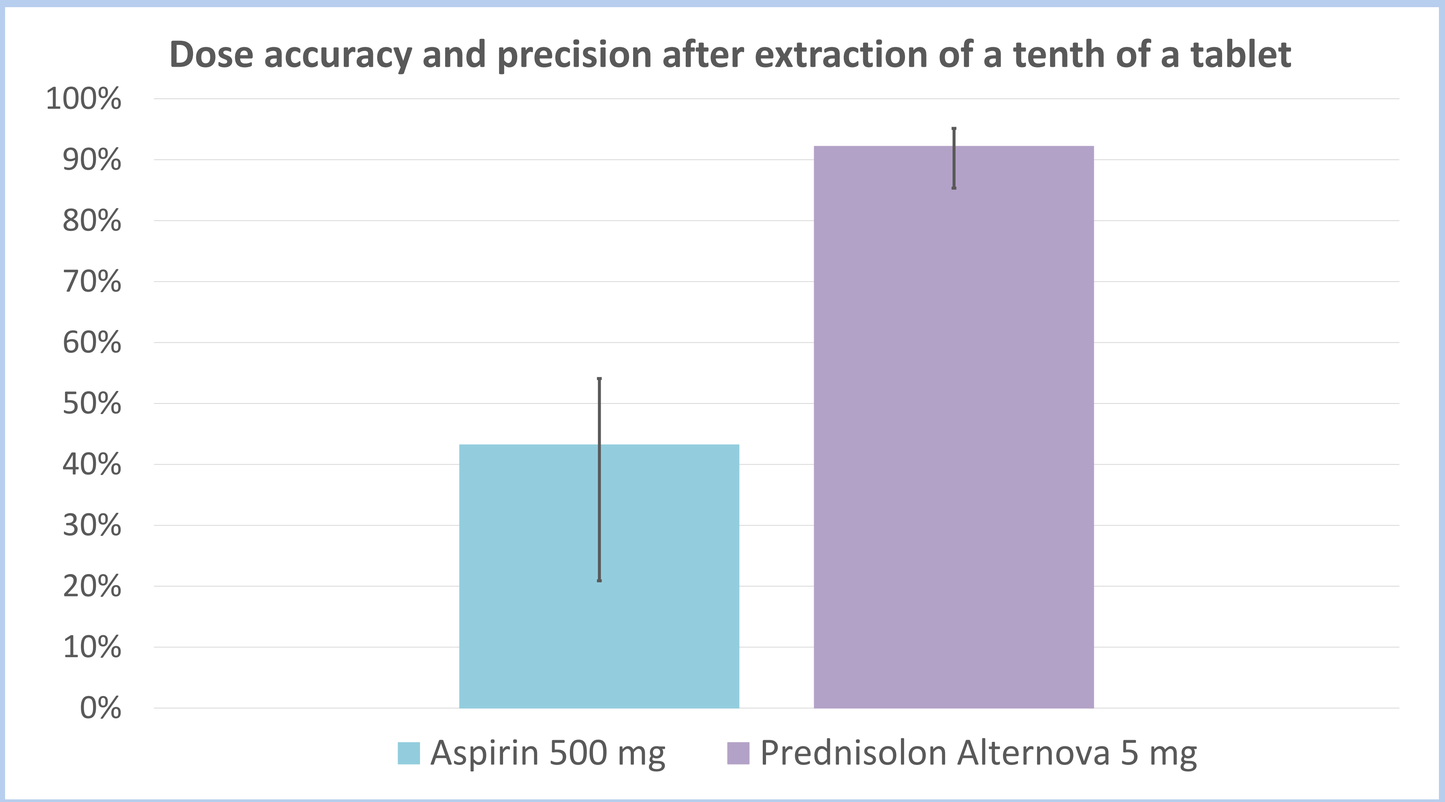

Fig 1. Dose accuracy and precision after extraction of a tenth of a tablet, given as per cent of intended dose. Results for Aspirin 500 mg “Bayer”, previously published [2], given for comparison. Error bars show low-high, n = 6.

Conclusion

- After manipulation by dispersion and dose extraction the prednisolone tablets were found to give doses within the limits of tablet fractions according to the European Pharmacopeia (85-115%).
- In contrast, conventional tablets containing aspirin (Aspirin 500 mg “Bayer”), has previously been shown not to exceeded 55% of the intended dose when a tenth of the tablet was extracted[2].
- This shows that knowledge about solubility is not always sufficient to judge the suitability for manipulation of tablets.

SYKEHUSAPOTEKENE

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References:
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2. Brustugun J., Notaker N., Paetz L.H., Tho I., Bjerknes K. Adjusting the dose in paediatric care: Dispersing four different aspirin tablets and taking a proportion. European Journal of Hospital Pharmacy. 2019. https://doi.org/10.1136/ejhpharm-2019-001903