

# Crushing enalapril tablets before dispersing in water provides accurate partial doses

## Background and Importance

- Manipulation of tablets (e.g. splitting, crushing and/or dispersing in water) to achieve partial doses is common in paediatric wards<sup>1</sup>.
- Studies on dose accuracy after manipulation have shown large variations depending on formulation and method of manipulation<sup>2</sup>.
- Previous observations on paediatric wards have shown enalapril tablets being crushed and dispersed in water as a common method of manipulation<sup>3</sup>.

## Aim and Objectives

To investigate dose accuracy obtained after manipulation of enalapril tablets using clinically relevant methods of manipulation.

## Materials and Methods

### Materials and analytical instrument

- Enalapril tablets: Enalapril Krka 5 mg, Krka Sverige AB.
- Instrument: HPLC-system from Shimadzu Corp (Nexera, with Prominence DAD-detector).
  - Analytical column: Supelcosil™ LC-8, 5 µm, 250x4.6 mm (Supelco®, Merck KGaA).
  - Analytical assay: Enalapril Maleate Tablets, USP.

### Disintegration time:

- Whole tablets were added to 10 ml water in a medicine cup. Time until full disintegration of the tablet while stirring intermittently was recorded.

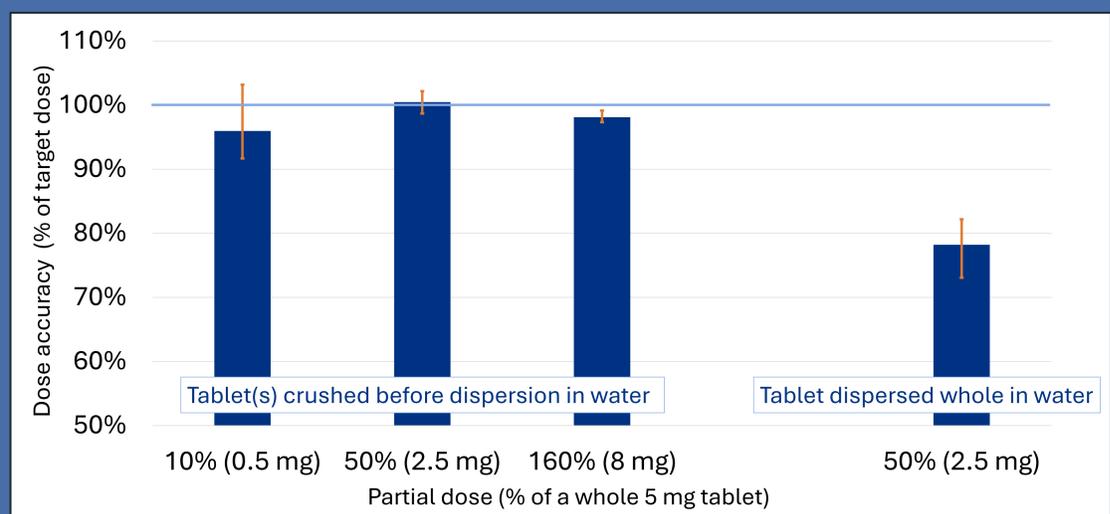
### Dose accuracy study:

- Tablets (one or two) were crushed and dispersed in 10 ml water in a medicine cup (n=6). After 30 seconds of stirring, samples of 1 ml, 5 ml or 8 ml were withdrawn with an oral syringe, extracting partial doses of 10 %, 50 % and 160 % of a tablet.
- Tablets were also dispersed whole in 10 ml water and 5 ml withdrawn (50 % of a tablet) after five minutes of intermittent stirring (n=6), regardless of full dispersal of the tablet.

## Results

Whole tablets had an average disintegration time of 13 minutes (12-14 minutes) while stirring

Crushing enalapril tablets before dispersion in water showed higher dose accuracy than dispersing the tablets whole. Dose accuracy after manipulation is summarized in Figure 1.



**Figure 1.** Dose accuracy after manipulation of *Enalapril Krka 5 mg* tablets to achieve partial doses. Tablets were either crushed before dispersion in water, or dispersed whole, before taking a partial dose. Average dose accuracy ± min-max values.

## Conclusion and Relevance



Long disintegration time confirmed why enalapril tablets consistently were crushed in the ward.



Crushing before dispersing tablets of enalapril provides accurate partial doses.



It's important to ensure that the whole tablet is dispersed in the liquid before extracting a dose.

## References

1. Bjerknes et al., *Acta Paediatrica* (2017) 106:503-508
2. Brustugun et al., *Eur J Hosp Pharm* (2021) 28:76-82
3. Hamre Svendsen et al. (under review)

# Manipulation of enalapril tablets for paediatric patients – to crush or not to crush?

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