

SMALL-SCALE COMPOUNDING USING A POWDER DISPENSING TOOL FOR INDIVIDUALISED SOLID DOSAGE FORM DRUG DELIVERY

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Background

Pharmacy compounding is a valuable tool for personalised medicine (e.g. dose and excipients) to children where suitable doses/dosage forms are not available. In many cases, liquid-based dosage forms are available allowing for a mL-based, individualised therapy. However, there are cases where e.g. capsules are the preferred form.

Solid dosage forms allows for a child to easily self administer the medication e.g. during times away from home such as during school. For many years there have been methods for reformulating tablets in the pharmacy by crushing and reformulate to fill batches of capsules (e.g. 50 capsules) including also novel capsule filling techniques [1].

It would be valuable to find a flexible method that readily (within an hour) would provide bespoke capsules with the aim of providing higher patient safety, compared to the manipulation that otherwise would take place in the ward.



Fig 1. Ready to use (RTU) products from the pharmaceutical industry based on e.g. PDCO/PIP regulations [2] are preferably used. However, in many cases the licensed product needs to be reformulated (if API is not available) by the pharmacy or manipulated [3] in the ward or home before being given to the patient. The EDQM has provided a document for parenteral use that can be useful for support in decision making [4]. Photo by Johan Alp, Creative Commons license.

Results and discussion

HPD Quantos can be part of a method for preparing individual solid dosage forms, the equivalence that of one-fifth of a tablet. Capsules were made with the mean filling weight of 19,0 mg (target dose 20 mg) and a relative standard deviation of 12% for allopurinol (see Fig 3).

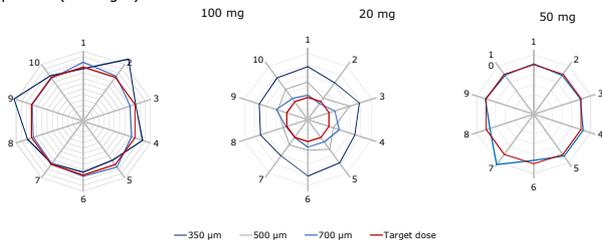


Fig 4. Filling volumes of capsules with content of Cellets pellets as a model product with quality of 350, 500 or 700 Sieve fraction manually filled with Quantos HPD with 2,5 mm diameter head. Scale unit equals 10 mg in all diagrams.

Data presented in Fig. 4 suggest that higher sieve fractions give a more uniform and accurate dosing. Dosing with a handheld device is dependent of user skills and environmental factors such as air humidity (risk of static electricity).

References

1. Evaluation of the Quantos® powder dosing system for capsule manufacturing in a hospital pharmacy. Will et al., 21st EAHP Congress, Vienna, Austria, 16-18 March 2016 (VIE15-0795).
2. http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/general/general_content_000265.jsp
3. Modric: <http://www.alderhey.nhs.uk/wp-content/uploads/MODRIC-GUIDELINES-April-2017.pdf>
4. https://www.edqm.eu/sites/default/files/resolution_cm_res_2016_2_good_reconstitution_practices_in_health_care_establishments_for_medicinal_products_for_parenteral_use.pdf

Purpose

The purpose of this study was to evaluate powder dispensing equipment as a means for filling of single capsules and suggest a suitable work flow.

Material and methods

Capsules were filled as part of a master thesis project at the Department of Pharmacy, Uppsala University, Sweden. To dispense powder the microbalance MT5 (Mettler Toledo), "Quantos handheld powder dosing system", model HPD (Mettler Toledo, orifice size 2,5/4 mm) was used. Model substances: Allopurinol Teva 100 mg tablet (Teva, Sweden) and Cellets microcrystalline cellulose pellets (Harke Pharma GmbH). Capsule "Coni-snap" of various sizes (Capsugel) were screened.

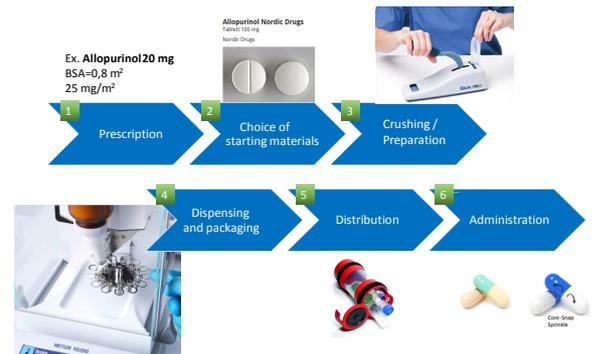


Fig 2. Suggested work flow for small scale pharmacy compounding as an alternative to the less controlled manipulation done in hospital wards. Photos courtesy of Medicalexpo, Mettler Toledo, Swislog, Capsugel and fss.se.

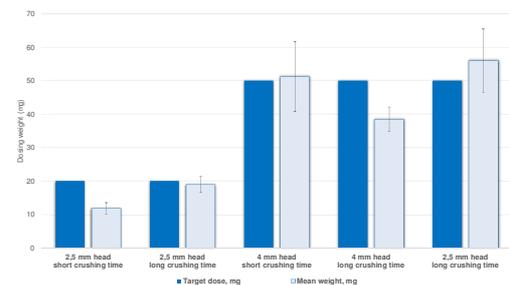


Fig 3. Capsule weight after filling with two different Quantos Dosing heads (2,5 mm or 4 mm diameter) of manually crushed (short time 30 sec, long time 45 sec) Allopurinol tablets.

Conclusion

We present a method for producing capsules that allows for individualised dosing. An advantage is that single capsules can be produced with the possibility of daily dosage regimen change, tapering schemes etc.

The handheld version of Quantos is not accurate enough for small capsule sizes. If this equipment is to be used, the capsules must be individually weighed and out-of-specification capsules rejected. There are automated systems with integrated scales on the market that can be used also for potential toxic substances that enable filling of smaller doses. With that in place the method would be well-functioning in a hospital pharmacy setting as an alternative, offering increased patient safety, to manipulation in ward.

Acknowledgements

Mettler Toledo is acknowledged for providing the Quantos handheld dispenser free of charge. Dr Lucia Lazorova, Dep of Pharmacy, Uppsala University for providing material and weighing equipment.