Drug loss during tablet crushing

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Abstract

This method describes the comparison of paracetamol quantification of a whole tablet vs a tablet that has been crushed in a proprietary tablet crusher. In this case we have used paracetamol as the model drug, but this basic approach can be applied to any solid dose form with appropriate adjustment of solvents (to ensure drug is completely dissolved for measurement) and UV wavelength. The use of HPLC can be substituted in place of simple UV if there is any indication of interference at the UV wavelength.

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Protocol

Standard curve

Step 1.

Standard solutions were prepared in the range 1 – 12 mcg/mL. This was prepared from a stock solution (1000 mcg/mL) containing 500 mg of paracetamol USP powder in 500 mL of 0.02 M NaOH, dissolved by 15 min sonication and mixed well, and a small volume filtered through 0.45 µm nylon filter. Aliquots of filtered stock in the range 0.1 to 1.2 mL were diluted to 100 mL with 0.01 M NaOH to prepare standard solutions with concentration of 1, 2, 4, 5, 6, 8, 10 and 12 mcg/mL at pH12. This method is based on the paracetamol assay in the British Pharmacopoeia as it ensures that the paracetamol is completely dissolved in this volume of liquid.

Control

Step 2.

1. Calculate average tablet weight from the individual weights of ten tablets: weigh 10 tablets individually, calculate the average.

2. Calculate average drug content from the individual contents of ten tablets. One tablet was transferred to a 500 mL volumetric flask. 100 mL 0.1 M NaOH was added to the flask and it was made up to volume with water. The paracetamol tablet was dissolved by sonication for 15 min, and a small volume was filtered through 0.45 µm nylon filter. Then 1 mL of filtrate was diluted to 100 mL in 0.01M NaOH and the absorbance measured at 255 nm. This was replicated for all 10 paracetamol tablets.

Crush tablets in a crusher

Step 3.

Select a crusher, crush one tablet.

Tablet crushing devices with disposable vessels (cups and bags) were used with the specific vessel supplied with or designed for use with the device (S2 Table, S2 Figure). Two empty cups (or a bag / a hand-twisted device / a syringe / mortar and pestle) were weighed, W1. One tablet was placed between the top and bottom cups (in the bag / hand-twisted device / syringe / mortar and pestle) and the weight was measured, W2. The tablet was crushed according to manufacturer instructions (where they existed).

The weight of the cups (or bag / device / syringe / mortar and pestle) with crushed tablet was measured, W3.

Powder retrieval by tapping out

Step 4.

The top cup (lid of hand-twisted device) was tapped to release the powder adhered to the bottom surface of the top cup (lid of hand-twisted device). The crushed tablet was poured or tapped out of the bottom cup (bag / bottom unit of hand-twisted device / syringe / mortar). The weight, W4, of the two cups (bag / device / syringe / mortar and pestle) was measured. The loss of tablet weight was calculated as weight of the individual tablet (W2-W1) minus the weight of crushed tablet recovered from tapping (W3-W4).

The crushed tablet was tapped out into a 500 mL volumetric flask via a funnel and prepared and measured as described for the control; this was assumed to be the recovered amount that could potentially be consumed by the patient. The powder that adhered to the bottom surface of the top cup (lid of hand-twisted device) and the powder remaining in the bottom cup (in the bag / in the bottom unit of hand-twisted device / in the syringe / on mortar and pestle) was transferred by exhaustively rinsing with water into a 100 mL volumetric flask. 20 mL 0.1 N NaOH was added to the flask and thereafter it was prepared and measured as described for the control. This was assumed to be the leftover that could not be taken by the patient.

Powder retrieval by rinsing with water

Step 5.

After crushing, approximately 30 mL of water was added to the crushed tablet in the bottom cup (bag / bottom unit of the device / withdrawn into the syringe), slight agitation given and the solution was poured out immediately into a 500 mL volumetric flask as the first rinse. This rinsing process was repeated with another 30 mL of water and poured into a separate 500 mL flask to study the amount of paracetamol in the second rinse. Both solutions were prepared and measured as described for the control. The leftover powder remaining in the top and bottom cups (bag / lid and bottom unit of hand-twisted device / syringe) was transferred by exhaustively rinsing with water into a 100 mL volumetric flask. 20 mL 0.1 N NaOH was added to the flask and thereafter it was prepared and measured as described for the control.

Powder retrieval by mixing with food

Step 6.

After crushing, 15 g of apple sauce (Threes Three, Lidcombe, NSW), honey (Capilano, Inala, QLD) or vanilla yoghurt (Yoplait, Melbourne, VIC) was mixed with the crushed tablet in the bottom cup with a spoon. The food and powder mixture was transferred by scraping out with the spoon into a 500 mL

volumetric flask via a funnel, and then prepared and diluted as described for the control. Leftover food and powder in the bottom cup and on the bottom surface of the top cup was transferred to a 100 mL flask and prepared and diluted as described for the leftover from tapping out. The absorbance measured for crushed paracetamol tablet mixed in foods was taken against a blank without crushed tablet that was otherwise prepared and diluted in the same way.

Data analysis

Step 7.

The amount (mg) of paracetamol recovered and leftover were calculated using the calibration curve.

The theoretical quantity of paracetamol contained in each tablet was calculated as actual tablet weight / average tablet weight x 500 mg.

The quantities of paracetamol recovered and leftover were converted into % recovery and % leftover by dividing the quantity recovered or leftover by the theoretical quantity of paracetamol in the tablet x 100. The % loss was calculated as 100 – % recovery.