

Implications of crushing paracetamol tablets prior to administration in yoghurt to elderly patients: Is there a dilemma?

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Introduction

- What is the dilemma?
 - Aged population
 - Medication load in the elderly
 - Increase in swallowing difficulties
 - Dysphagia
 - CVA
 - Parkinson's Disease
 - Dementia
 - Decreased Consciousness
 - Majority of medications are tablets or capsules
 - Most oral medications are crushed
 - Trans-dermal products, rectal administration

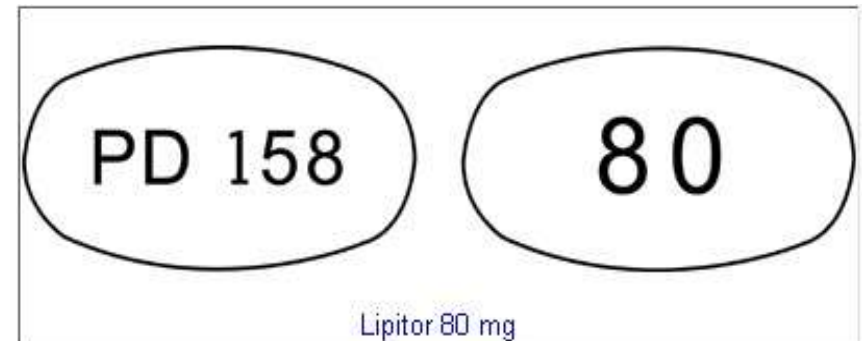
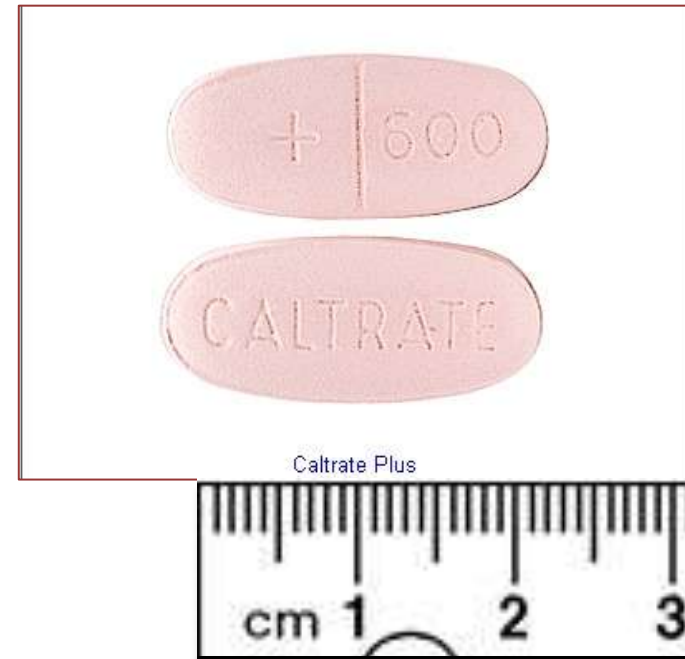
Introduction

- Crushing of medication
 - enables easier administration to the elderly with dysphagia
 - enables ‘covert’ administration
 - is necessary as limited availability of liquid formulations



Introduction

- Lipitor[®] (*Atorvastatin*)
 - Size of a cashew nut or more than 2cm
- Caltrate[®] (*Calcium Carbonate*)
- *Fish Oil*



Introduction

WHY NO ORAL LIQUIDS?

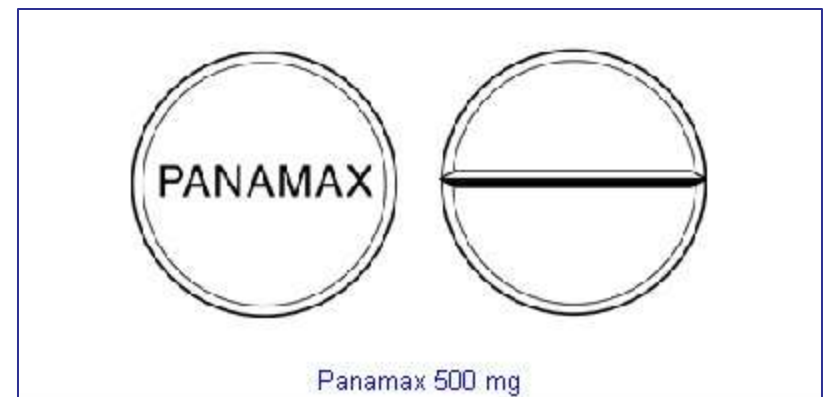
- Limited market size – but need is increasing
- Stability of liquid formulations
- Often paediatric formulations
 - Expense
 - Paracetamol 1000mg qid = 20ml qid (48mg/ml)
- Available liquid preparations:
 - Digoxin
 - Frusemide
 - Haloperidol
 - Risperidone
 - Some Opioids

Objective

- To determine whether crushing paracetamol tablets and mixing the powder in a vehicle (yoghurt) had implications on:

- Stability
- Dissolution profile
- Bioavailability

of this simple analgesic



Why paracetamol in vanilla yogurt?

- Registered nurses in aged care facility in Townsville were surveyed:
 - Vehicle for administering crushed medications.
 - Chocolate syrup
 - Jam
 - Custard
 - Mashed banana
- Audit of medication charts for crushed medications

Medication being crushed	Number of patients
Coloxyl and Senna tablets	20
Paracetamol 500mg tablets	19
Aspirin 100mg tablets	10
Frusemide 40mg tables	7

Unlicensed Use

- Crushing / opening capsule alters the dosage form resulting in:
 - Unlicensed use of medication
 - Manufacturer is released of liability
- Liability moves to
 - Person crushing / administering medicines
 - Doctor (if ordering medicine to be crushed)
- Pharmacist can give advice on altering dosage form
 - Expert on dosage forms – design and excipients

Altering a dosage form

- Potential to cause a primary loss of dose:
 - By the process of crushing, transferring and administration
 - Important in medications with low therapeutic index
 - Warfarin
- Potential for secondary loss of dose by:
 - Altered absorption
 - Stability changes
 - Local (gastrointestinal) irritation
 - Altered taste/texture
 - Change to intended site of action



Paracetamol - Stability

METHOD

- Pure paracetamol powder mixed with yoghurt
- Mixture dissolved in methanol
- Solution diluted and filtered
- Concentration of paracetamol measured by UV spectrophotometry

RESULT

- Yoghurt demonstrated not to interfere with analysis
 - Analytical method validation
 - Specificity
- Measured paracetamol concentration agreed with amount added → method of analysis valid

Paracetamol - Stability

METHOD

- Paracetamol (Panamax[®]) 500mg tablet crushed in a mortar and pestle
- Crushed drug (plus excipients) mixed with vanilla yoghurt and let stand for time periods up to 60 minutes
- Mixture dissolved in methanol and analysed by UV spectrophotometry as previous testing.

RESULT

- No significant difference observed in paracetamol levels measured immediately after mixing and those allowed to stand for 60 minutes
- Stability of paracetamol + excipients (Panamax[®]) in yoghurt is acceptable

Method - Dissolution

- Paracetamol (Panamax[®]) 500mg tablet crushed in a mortar and pestle
- Crushed drug (plus excipients) mixed with different quantities of vanilla yoghurt and spread across a watch glass
- The paste was spread to increase surface area
- The watch glass was placed in a dissolution apparatus



Method - Dissolution

- USP has guidelines for dissolution of paracetamol
 - Minimum of 80% of the drug must be dissolved following 30 minutes at 50rpm in 900ml of pH 5.8 phosphate buffer
- Vankel VK 7000 Dissolution Testing Station
 - Simulated motion of stomach with rotating paddle
 - Containing phosphate buffer
 - pH 5.8 (USP)
 - 50 rpm (USP)

Method- Dissolution

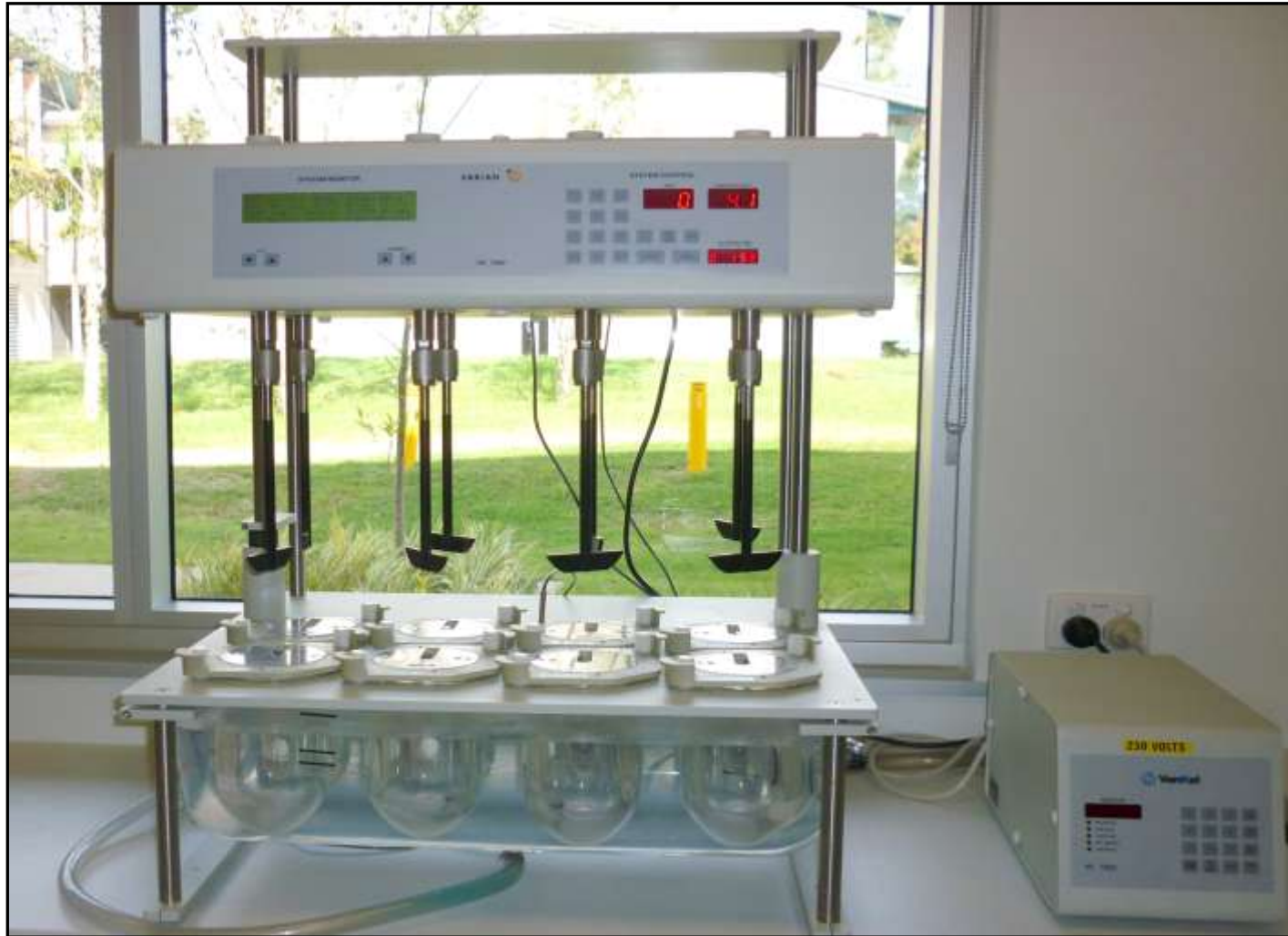


Figure 1. Photograph of Dissolution Apparatus - Vankel VK7000

Method - Dissolution

- Comparative dissolution studies were conducted to determine the difference in dissolution between:
 - one whole tablet
 - one whole crushed tablet
 - one whole crushed tablet mixed with varying amounts of yoghurt
- At timed intervals, samples removed, filtered, diluted and analysed by UV spectrophotometry
- All studies performed in triplicate

Results- Dissolution

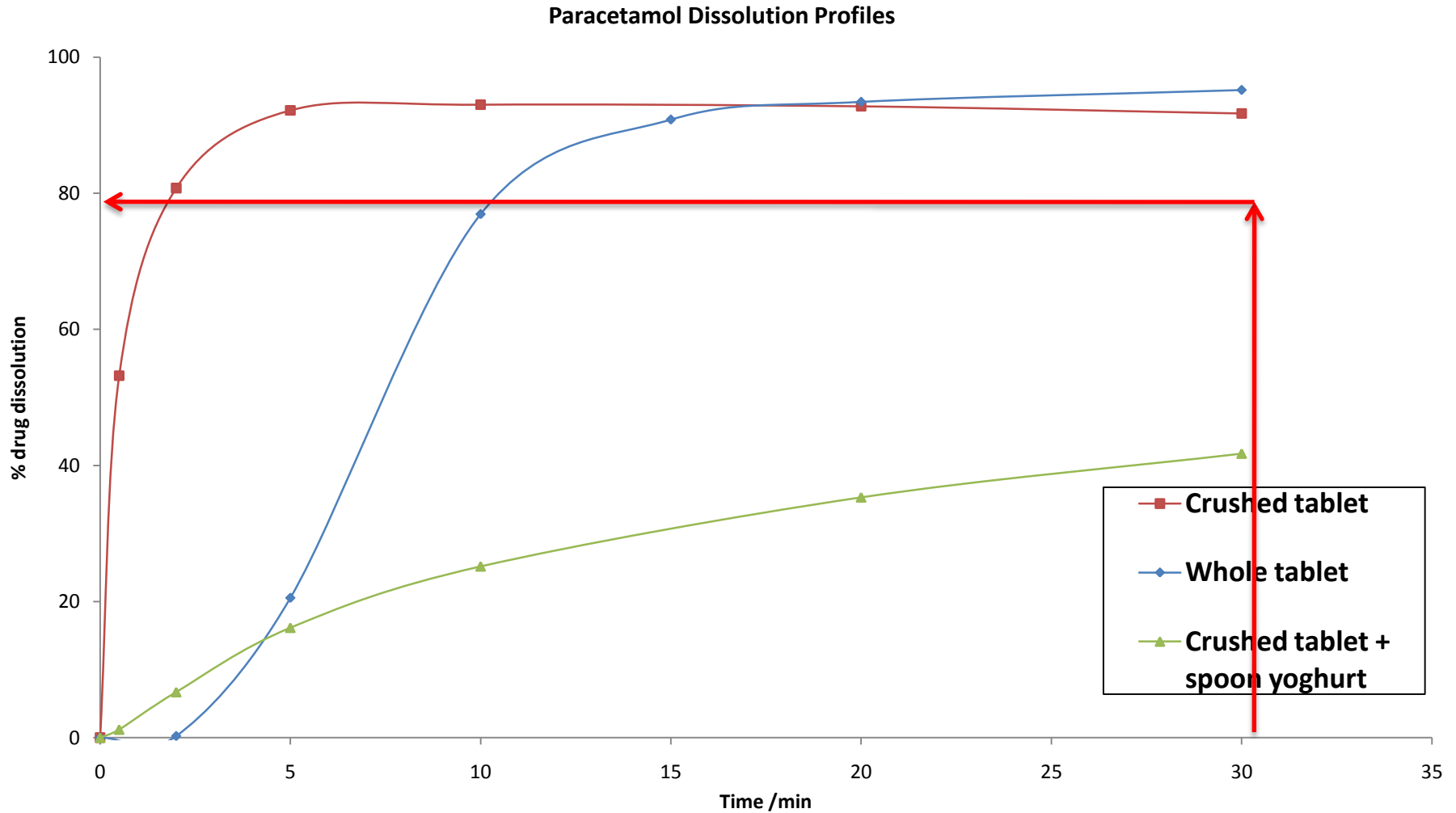


Figure 2. Dissolution profiles of crushed , whole tablet and crushed tablet in yogurt

Discussion

- Disintegration precedes dissolution
- Difference in the crushed and whole tablet reflects the step of manual disintegration by crushing the tablet (Figure 2)
 - Results comply with the USP Standard
- Dissolution is altered by addition of yoghurt
- Medium retards dissolution
 - Does not comply with USP Standard (80% / 30 min)
 - Less than 40% of drug dissolved after 30 minutes

Results- Dissolution

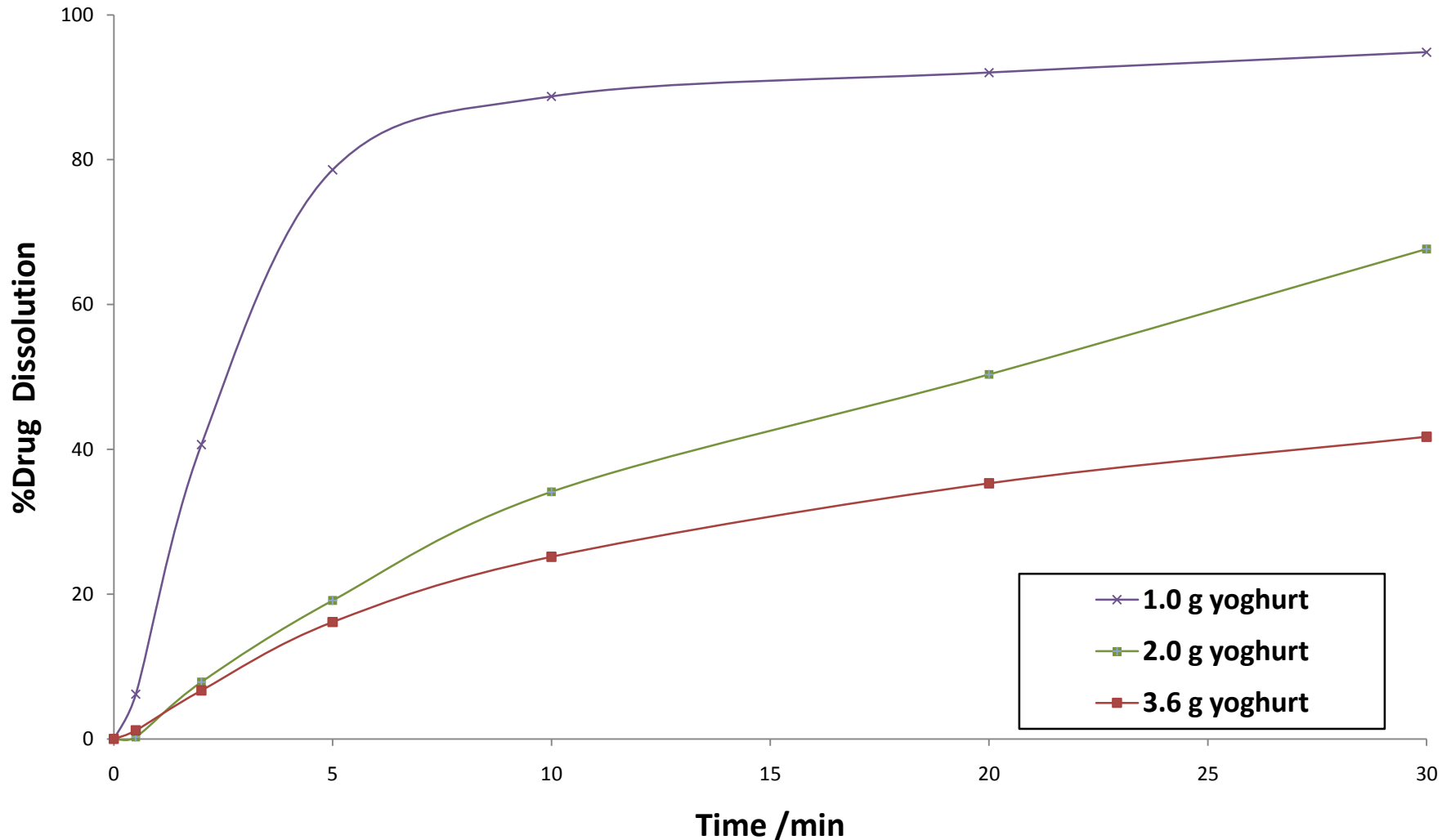


Figure 3. Dissolution profiles of crushed tablet mixed with various amounts of yogurt

Results- Dissolution



Figure 4. Crushed Panamax tablet + 1.0 g of yogurt

Summary

- Is it acceptable to crush paracetamol and administer it in yoghurt ?
 - **Yes** as stability is not adversely affected
- Is there an effect on the dissolution profile of paracetamol once it is crushed and mixed with yoghurt?
 - **Yes**
- Does the amount of yoghurt used affect dissolution?
 - **Yes**

Is the dilemma solved?

- NO!

Amount of vehicle (yoghurt)used in the practice =
3.6g or more.

- The amount of vehicle (yoghurt) necessary to
 - Comply with the USP Standard for dissolution is 1.0 g
- 1.0 g yoghurt + 1 tablet is a thick paste
 - Not palatable
 - Not easy to swallow

Solving the dilemma

- The process of testing the extracted drug validated.
- Scope to test other vehicles / amounts
 - Custard
 - Jam
 - Chocolate syrup
 - Designer formulation
- Scope to test other medications
 - Thyroxine
 - Warfarin
 - Frusemide



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Thank you

