Laboratory 4 – Paracetamol Suspension

Background

In this laboratory class, and the associated pharmacy practice role-playing session, you will be testing and supplying a suspension formulation of the active pharmaceutical ingredient (API) paracetamol.

A suspension formulation is where the API is provided in the form of solid particles dispersed within a liquid medium. The important thing to note is that the API is not dissolved, or only minimally dissolved, in the medium. This is in contrast to a solution or an elixir, where the API is fully dissolved.

A suspension formulation can be preferred over other oral dosage forms, such as tablets and capsules, when the intended patient is not able to swallow or having them swallow a solid formulation may be dangerous (e.g. babies and children). An extra advantage is that a suspension dosage form also allows for different doses to be drawn from the bottle. This is especially useful for children as children of different ages and weights require different quantities of API. As such, it is common for many children's oral formulations to be supplied as suspensions.

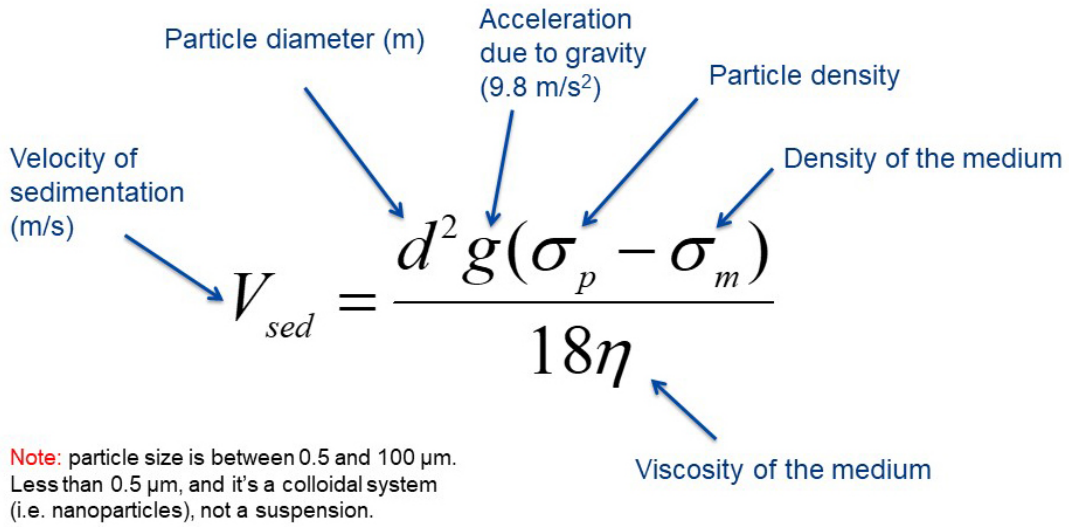
Two examples of children's suspension formulations

Stability of suspensions

While there are a number of stability issues that have the potential to impact suspension formulations, like chemical degradation of the API or changes in the solid state of the API from amorphous to crystalline or one form of crystalline to another crystalline form, the major stability issue is physical stability of the dispersion of the particles.

Because the API particles in a suspension have mass, they are acted upon by gravity, which means over time, the particles will be less dispersed as they sink and settle to the bottom of the bottle. For this reason it is always important to counsel patients as to the need to Shake Before Use of any suspension formulation (to redisperse the API particles).

When the bottle is not shaken before use, or if the suspension is poorly designed and the particles settle quickly, then this will result in an inaccurate amount of API particles being draw up. The result would then be underdosing of the child when liquid is drawn from a newly opened bottle to the more serious overdosing of the child when the last remnants of the bottle are being drawn out. It is therefore very important to design a suitably stable formulation and to remind patients to shake before use.



The Stokes equation

The Stokes equation provides a mathematical explanation for how fast the particles in a suspension will settle in the bottle. What it shows is that the sedimentation rate (rate of settling of the API particles) can be slowed in two easy ways: (1) by increasing the viscosity of the medium or (2) by increasing the density of the medium. The viscosity and density of the medium can be changed through the addition of selected excipients into the formulation.

Ingredients in a suspension formulation

In any general suspension formulation there are a range of excipient ingredients that are used for varying purposes. These can include, as examples:

Role	Examples
Medium	Water, ethanol
Preservative	Hydroxybenzoate, methyl/propyl paraben, phenoxyethanol
Sweetener	Sugar (syrup), artificial sweeteners (e.g. saccharin sodium)
Density modifier	Glycerol, sugar (syrup)
Viscosity modifier	Xanthum gum, dispersible cellulose, carboxymethylcellulose, sugar (syrup)
Colour	Artificial (e.g. amaranth) and natural (e.g. purple colour extract) dyes
Flavour	Cherry, vanilla, tutti frutti
pH modifier	Citric acid

Experimental

This laboratory class is to be completed in two parts.

Part 1 Preparation and testing of a paracetamol suspension formulation

Part 2 Counselling and supply of paracetamol suspension to a parent of a baby, followed by a product recall

Part 1 – Preparation and testing of a paracetamol suspension formulation

1. Using a sharpie marker, label 3 dispensing flat bottles (shown below) with the labels: A, B, and C.

Dispensing flat bottle

2. Using a measuring cylinder, add 100 mL of water to each bottle and then use a sharpie marker to indicate the water level. When done, tip out the water (there is no need to dry the inside of the bottle).

3. Into each bottle, add the ingredients listed below, in the order shown.

Bottle A	Bottle B	Bottle C
25 mL water	25 mL water	25 mL water
25 mL CMC solution	25 mL CMC solution	
25 ml syrup solution		25 mL syrup solution
1 mL hydroxy benzoate	1 mL hydroxy benzoate	1 mL hydroxy benzoate
5 grams paracetamol	5 grams paracetamol	5 grams paracetamol
Make up to 100 mL with water	Make up to 100 mL with water	Make up to 100 mL with water

4. Note that Bottle A contains all the ingredients, while bottle B is missing the syrup ingredient, and bottle C is missing the CMC ingredient.

5. Screw the caps on each bottle and invert (do not shake) them until lumps are no longer observed; this may take up to 10 minutes.

Inversion of a dispensing flat bottle to disperse the particles video

6. Place the bottles to the side and prepare your volumetric flasks and beakers.

7. Label 12 of the 100 mL volumetric flasks as A0, A1, A5, A10, B0, B1, B5, B10, C0, C1, C5, C10. These are for different time samples (0 min, 1 min, 5 min, and 10 min) for each of bottles A, B, and C.

8. Label 12 of the 100 mL beakers with the same labels as in step 7.

9. And label 12 of the 50 mL volumetric flasks with the same labels as in step 7.

10. Read steps 11 to 16 before you continue. It's important that you know what you are doing before you start because timing is important.

11. Have a micropipette ready and set to 1.000 mL. Put one tip on the micropipette and have another two tips ready.

12. Invert each bottle for exactly 60 seconds. It is important that all three bottles are inverted at the same time for the same amount of time.

13. As soon as the 60 seconds is up, and as quickly as you can, with the pipette withdraw 1 mL from each bottle (aim for the pipette tip to be about 1 cm below the top of the liquid). It is important that you try not to move the bottle when drawing up samples, otherwise you may redisperse the particles.

14. inject it into its appropriately labelled 100 mL volumetric flask (these will be A0, B0, and C0). These are your time zero samples.

15. Using a fresh micropipette tip for each sample, wait 1 another minute (2 minutes since you first started the timer), and withdrawn another 1 mL from each bottle and inject the samples into the volumetric flasks labelled A1, B1, and C1. These are your 1 minute samples.

16. Wait 4 more minutes (6 minutes since you first started the timer), and withdraw another 1 mL from each bottle and inject the samples into the volumetric flasks labelled A5, B5, and C5. These are your 5 minute samples.

17. Wait 5 more minutes (11 minutes since you first started the timer), and withdrawn another 1 mL from each bottle and inject the samples into the volumetric flasks labelled A10, B10, and C10. These are your 10 minute samples.

18. Make each of the 100 volumetric flasks up to the mark with water.

19. Pour approximately 10 mL of each volumetric flask into its respective beaker.

20. Using a micropipette, transfer 1.000 mL of solution from each beaker into its respective 50 mL volumetric flask and make up to the mark with water.

21. Using the sipper functions on the UV machines (see video below), measure the UV absorbance (wavelength 243 nm) for each sample and record the values in the table in your report form.

How to use the sipper function on the UV machines

22. Use the UV absorbance values to calculate the percentage drop in paracetamol concentration at each time point when compared with the absorbance at time zero.

23. Using the percentage drop data, answer the questions on the report form.

Part 2 – Counselling and supply of paracetamol suspension to a parent of a baby

Counselling and supply. In the second half of this laboratory class you will be required to undertake a related pharmacy practice role play.

Your lab demonstrator will play the role of the patient/customer and you will play the role of the pharmacist in a shopping centre pharmacy.

The scenario is that the customer's baby, which is 11 months of age, was knocked over while they were playing in the shopping centre and has a large scrap on their leg. The baby's leg been hurting since it happened 10 minutes ago.

The baby has no medical conditions and isn't on any other medications.

The parent has come to your pharmacy in the shopping centre to buy a bottle of children's paracetamol suspension to help with the kid's pain.

When you supply the medication to the parent it will be important for you counsel them on the need to shake the bottle before use.

Product recall. In the second half of the role playing, your demonstrator will provide you with a recall notice issued by the TGA for the paracetamol suspension you just supplied.

You will need to explain to the patient why the product was recalled and what effect it can have on product, and then provide a different product.

End of lab 4