Oral Powders

Oral powders may be formulated as divided powders, with each dose packaged individually or undivided, as a bulk powder. Undivided oral powders are usually non-potent medicaments, such as antacids, where the accuracy by which the patient measures the dose is not critical. When dosage accuracy and repeatability is of greater importance, as is the case for potent medicaments, individually packaged powders for each separate dose are used. The latter are known as divided powders, and are presented as powders wrapped in sachets or packaged in capsules.

Oral undivided powders are usually formulated by a simple mixture of the prescribed medicaments without the addition of other ingredients. Examples of powders prepared in bulk include light magnesium carbonate, heavy magnesium carbonate and magnesium trisilicate.

Oral divided powders may contain one or more active ingredients together mixed with inert diluents. A pharmaceutical balance is used to measure a minimum quantity, which is usually taken to be 200 mg. Oral powders can be either prepared from the active pharmaceutical ingredient or from a solid dosage form of the respective medicinal.

200mg of powder is usually chosen since:

- It can be safely and reproducibly weighed on a Class II balance or electronic equivalent since it exceeds the minimum weighable amount of the balance
- It is easy to calculate multiples and divisions of 200 during pharmaceutical calculations
- It normally fits into a size 3 capsule and it enables the compounder to use the same calculations for both powders in sachets and capsules

The usual diluent used to provide ‘bulk’ is pharmacopoeial grade lactose monohydrate because it is water-soluble, colourless, odourless and generally harmless. Lactose is generally considered to be inert with most active ingredients.
Remember:
When weighing any pharmaceutical ingredient, it is imperative to give due consideration to the accuracy of the instrument being used. The three main types of balance used in pharmacy are given below. However, every balance has its own range and tolerance so it is important to check the accuracy, tolerance and range of each balance being used. It is imperative to use the correct balance depending on the procedure that is being carried out.

<table>
<thead>
<tr>
<th>Type of balance</th>
<th>Typical Minimum weight</th>
<th>Typical Maximum weight</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Large balance</td>
<td>50 g and upwards</td>
<td>VARIABLE</td>
<td>VARIABLE</td>
</tr>
<tr>
<td>Class II dispensing balance* or electronic equivalent</td>
<td>100mg (non-potent) 150mg (potent)</td>
<td>25g</td>
<td>± 10 mg</td>
</tr>
<tr>
<td>Sensitive analytical balance</td>
<td>50 mg (non-potent) 100 mg (potent)</td>
<td>100 – 500 g</td>
<td>± 1 mg</td>
</tr>
</tbody>
</table>

Table 1. Types of balances and recommended minimum and maximum weights (Adopted from Mariott JF, Wilson KA, Langley CA, Belcher D. Pharmaceutical compounding and dispensing. London: Pharmaceutical Press; 2010: 55)

*Class B beam balances were traditionally used before Class II balances and for the purpose of this practical, they can be considered to be functionally similar

**MIXING OF SOLIDS**

Since powders do not mix spontaneously, it may be very difficult to ensure a final homogenous mixture of powders and energy must be introduced for the successful mixing of powders. This problem is increased when the proportion of one ingredient is very small. Localised shear forces move the particles relative to one another and a general circular motion brings the bulk of the powder in the region of shear. A porcelain mortar is generally used as the mixing vessel except for compounds that stain (in which case a glass mortar is used). A sufficiently large mortar should be used to ensure enough space for adequate mixing. Mortars should be perfectly dry before mixing dry powders. The doubling-up technique is used to ensure a final homogenous mixture:

1. Add the ingredient present in the lowest bulk to the mortar
2. Add the second ingredient in approximately the same amount that is present in the mortar, therefore doubling-up the bulk already in the mortar
3. Mix lightly since undue pressure may cause caking
4. The bottom of the mortar can be loosened by scraping the sides of the powder using a large flexible spatula
5. At each addition, add a quantity that approximately doubles the bulk in the mortar.
PREPARATION OF UNDIVIDED POWDERS

Add all ingredients to a mortar using the doubling-up technique and mix well. Pass the mixed powder through a 250µm sieve and lightly re-mixed using a spatula, since sieving may cause partial separation of the gradients. The powder may then be packed.

PREPARATION OF DIVIDED ORAL POWDERS

Manipulative losses are inevitable when small quantities are weighed from bulk, therefore it is necessary to prepare for at least one powder extra to requirement. If the amount of active ingredient is less than 200mg, a diluents (lactose or any other compatible inert diluent) must be incorporated in proportional quantities to a minimum of 200 mg of active ingredient so as to enable the formulation of a homogeneous bulk mix containing the required dose per each aliquot of 200 mg mix.

Example

1. Prepare 4 sachets each containing 8 mg of propranolol
2. Prepare mix for 5 sachets to account for manipulative losses. Therefore 5 x 8 = 40 mg of active ingredient are required
3. The minimum weighable amount of active ingredient on the balance is of 200 mg (assuming a class B balance) therefore a minimum of 200 mg propranolol can be weighed
4. By simple proportion, if each sachet of 8mg active ingredient requires the addition of 192 mg lactose (200mg minus 8mg), how much lactose must be added to 200 mg active ingredient?
5. 192 mg x 200 mg/8 mg = 4800 mg of lactose have to be added to 200 mg of the active ingredient
6. These are mixed and individual aliquots of 200 mg are then taken, each containing 8mg of propranolol

The above described technique is what we commonly refer to as a ‘single dilution’. Potent substances in small amounts require a ‘double dilution’ (also known as ‘serial dilution’). The latter technique, as its name implies involves more than one dilution step and is mainly aimed at lessening the technical possibility of ‘clumping of active ingredients’ which phenomenon could potentially pose fatal consequences.
METHOD FOR WRAPPING DIVIDED POWDERS

1. Refer to Figure 1 below.
2. White glazed paper (known as demy paper) is used. Carry out the wrapping on a clean tile or a large sheet of demy to protect the product.
3. Arrange the papers with their long edge parallel to the front of the bench and turn up the long edge of each paper to about one-seventh of its width.
4. Weigh out the powder and place towards the front of the paper.
5. Carry the front of the paper over to the turned up edge, bring the turn up down and then fold this edge forward until it covers about two thirds of the distance to the near edge of the packet. Turn the edges of the packet so that the overlap is equal at both ends.
6. Firm the creases using a clean flexible spatula but avoid excessive pressure which would cause caking of the enclosed powder.
7. The packets are best packed in pairs, flap to flap and restrained with an elastic band.
8. In a well wrapped product there should not be powder within the flaps or folds. When opened by the user, the powder should appear in the centre of the paper, easily available for administration.

Figure 1: Wrapping of divided powders
ASPIRIN SACHETS

Consider the following prescription:

Aldo Scerri  
22, Newstreet  
B/Kara  
Age: 45

Rx

Aspirin 75 mg Pulv.

M. 5 sachets

Once daily

Dr. Abraham Fillet MD Reg: 111  
The Clinic, 128, High Street  
High Town  
Tel: 79000000

Calculations:

What is the minimum mass each sachet must be at?

______________________________
What is the minimum mass of active ingredient that can be weighed using a class B balance?

______________________________

Total amount of aspirin added: ________________________________
Total amount of lactose added: ________________________________

Briefly describe the method of preparation used:

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________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________

Can such a preparation be prepared from Aspirin E.C. tablets? Substantiate your answer with a justification.

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________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
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Write down the master label to be used for each sachet:
What are two possible problems with the use of lactose as diluent?

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________________________________________________________________________

In the eventuality of such problems, what can be used instead?

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If you had to use Aspirin 75mg tablets as the starting material, how would you proceed?
(Describe in a stepwise manner)

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________________________________________________________________________
Consider the following prescription:

Aldo Scerri
22, Newstreet
B/Kara
Age: 45

Rx

Compound magnesium carbonate powder  B.P.C. Pulv.
S. to be mixed with little water after meals
M. 5g

Dr. Abraham Fillet MD Reg: 111
The Clinic, 128, High Street
High Town
Tel: 79000000

Calculations:
Formula:

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Amounts added</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heavy Magnesium carbonate 940 mg</td>
<td></td>
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<tr>
<td>Sodium bicarbonate 310 mg</td>
<td></td>
</tr>
<tr>
<td>Magnesium trisilicate 230 mg</td>
<td></td>
</tr>
<tr>
<td>Light Kaolin 75 mg</td>
<td></td>
</tr>
<tr>
<td>Prepared Chalk 945 mg</td>
<td></td>
</tr>
<tr>
<td>Peppermint oil 0.5 mls</td>
<td></td>
</tr>
</tbody>
</table>

Briefly describe the method of preparation used:

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________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________

What is the indication for this preparation?

________________________________________________________________________
________________________________________________________________________

Write down the master label to be used for each sachet:
Why were other diluents given preference over lactose here?
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________

What advice would you give to the patient when dispensing the prescription?
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________

What are the appropriate storage conditions and shelf-life?
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________________________________________________________________________
________________________________________________________________________
**Powders: General Questions**

1. Explain when the use of a double (serial) dilution is preferred over a single dilution when preparing a bulk mix for the preparation of sachets.

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2. What is the process by which one can ensure that a given mixing process for a particular sachet type is yielding a homogeneous mix?

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   ________________________________________________________________________

3. List two advantages and disadvantages of extemporaneously prepared powders over extemporaneously prepared oral liquids?

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4. What is the main difference between bulk powders and divided powders?

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<table>
<thead>
<tr>
<th>Demonstrator Name</th>
<th>Signature</th>
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