

ORAL LIQUID PREPARATIONS

The British Pharmacopoeia (B.P.) 1998 and the European Pharmacopoeia (Ph. Eur.) 1997 define Oral Liquids:

“Liquids for oral use are usually solutions, emulsions or suspensions containing one or more active ingredients in a suitable vehicle; some liquids for oral administration may consist of liquid active ingredients as such they are intended to be swallowed either undiluted or after dilution. These preparations may also be prepared before use from concentrated liquid preparations, or from powders, granules or tablets for the preparation of oral solutions or suspensions using a suitable vehicle. Liquids for oral use may contain suitable antimicrobial preservatives, antioxidants and other excipients such as dispersing, suspending, thickening, emulsifying, buffering, wetting, solubilising, stabilising, flavouring and sweetening agents and colouring matter authorised by the competent authority

Additional subclasses of Oral Liquid are also defined in the B.P.:

Oral Solutions are Oral Liquids containing one or more active ingredients dissolved in a suitable vehicle.

Oral Suspensions are Oral Liquids containing one or more active ingredients suspended in a suitable vehicle. Suspended solids may slowly separate on standing but are easily redispersed.

Oral Emulsions are Oral Liquids containing one or more active ingredients. They are stabilised oil-in-water dispersions, either or both phases of which may contain dissolved solids. Solids may also be suspended in Oral Emulsions.

Mixtures are Oral Liquids containing one or more active ingredients dissolved, suspended or dispersed in a suitable vehicle. Suspended solids may separate slowly on standing but are easily redispersed on shaking.

Oral Drops are Oral Liquids that are intended to be administered in small volumes with the aid of a suitable measuring device.

Elixirs are clear, flavoured Oral Liquids containing one or more active ingredients dissolved in a vehicle that usually contains a high proportion of sucrose or a suitable polyhydric alcohol or alcohols and may contain Ethanol (96%) or a Dilute Ethanol.

Elixirs tend to be used for potent or nauseous drugs. Although ethanol is a widely used solvent in elixirs, high concentrations may produce a pharmacological effect, hence the inclusion of polyhydric alcohols such as glycerol, propylene or sorbitol as co-solvents.

Linctuses are viscous Oral Liquids that may contain one or more active ingredients in solution. The vehicle usually contains a high proportion of sucrose, other sugars or a suitable polyhydric alcohol. Linctuses are intended for use in the treatment or relief of cough, and are sipped and swallowed slowly without the addition of water. Linctuses may possess demulcent, antitussive or expectorant properties. Sorbitol is a useful substitute for sucrose in linctuses for diabetics, but it does cause diarrhoea in large quantities.

DOSE VOLUMES OF ORAL LIQUIDS

A 5mL spoon is used as a standard measure for liquid oral medicines and doses are generally administered in multiples of 5mL. Thus 5mL and 10mL are common dosage volumes. The label should bear the phrase, “One 5mL spoonful to be taken ...” or “Two 5mL spoonfuls to be taken...”. When a 20mL dosage is to be administered, patients are often provided with a measuring cup which allows for more accurate dosage.

Phrases such as “teaspoonful”, “tablespoonful”, etc. are not to be used.

Traditionally if a dose was prescribed which was less than 5mL or not a multiple of 5mL, the liquid was suitable diluted to achieve a dose volume which was a multiple of 5mL. For “ official preparations”, i.e. those described in the pharmacopoeia, appropriate diluents may be specified in the monograph. Suitable diluents for a proprietary preparation are generally listed by the manufacturer in the product’s data sheet. Dilution may affect the stability of a preparation. Nowadays if a dose, which is less than 5mL, is prescribed (e.g. 2 mL), this will be measured using an oral syringe, which is calibrated from 1mL to 5mL divisions. The oral syringe is used in preference to dilution of oral liquids.

PRESCRIBING OF ORAL LIQUIDS

Oral Liquids may be prescribed in either of two ways:

1. As an official preparation. Reference to the British Pharmaceutical Codex 1973 will reveal the complete formula. Nothing extra should be added; it is completely wrong to add anything, which is not in the formula, unless so directed by the prescriber.
2. As an extemporaneous preparation, in which the prescriber names the drugs required, their dose and the type of dosage forms, but does not specify any formula or excipients. In such cases, the pharmacist must decide what wetting agent, suspending agent, etc., are required, and how much. There is no need to refer back to the prescriber regarding the types and concentrations of the excipients. The pharmacist may also be called upon to prepare a suspension of a drug that is only commercially available in tablet form. The required number of tablets are crushed to a fine powder (or the contents of capsules used) and formulated into a stable

suspension for oral administration. These are intended primarily for paediatric patients where fractions of the unit dose have been prescribed. Information relating to the most suitable diluents and shelf-life of the product is frequently available from the relevant pharmaceutical company or from hospital drug information centres.

Oral Solutions:

The main factor to be considered in the preparation of solutions is the solubility of the solute(s) in the required vehicle. The vehicle is usually aqueous but may be oily or alcoholic. Information on solubility will be found in monographs and reference books, and consideration of this information will usually indicate the most appropriate method of preparation.

Solutes exhibiting adequate solubility usually present few problems. Insoluble or sparingly soluble materials may be brought into solution by a number of formulation techniques. These are:

- (a) Adjustment of pH
- (b) Use of cosolvents such as alcohol or glycerol
- (c) Solubilisation
- (d) Formulation of soluble complexes

In general, the easiest way to prepare a solution is to add the solute to some of the vehicle in a beaker or a measure and then stir. A given weight of small particles will usually dissolve more quickly than the same weight of larger particles. Substances such as potassium permanganate are slow to dissolve and they yield an optically dense solution which makes it difficult to determine when solution is complete. The easiest method in this case is to triturate the crystals in a glass mortar with a small amount of the vehicle. After allowing a few moments for undissolved solid to settle, the supernatant solution is carefully decanted from the solid. A further portion of the vehicle is added and the process is repeated until no undissolved solid remains after decantation.

The resulting solution must then be examined for the presence of extraneous material such as fibres, in order to assess if it requires clarification before it can be used. The standard of clarity applied depends on the mode of use of the product, freedom from particles being more important in the case of injections and eye-drops than with gargles. Clarification is usually achieved by filtration.

The solution is finally adjusted to volume or occasionally to weight, packed and labelled.

Mixtures

Mixtures are defined in the B.P. as oral liquids containing one or more active ingredients dissolved, suspended or dispersed in a suitable vehicle. Suspended solids may separate slowly on standing but are easily redispersed on shaking.

Mixtures may contain soluble substances only (i.e. solutions). In mixtures containing diffusible solids the solids are insoluble but on shaking the powder is evenly dispersed for sufficient time for the patient to obtain a uniform dose. A "Shake the bottle" label is essential for these types of mixtures. Examples of some diffusible solids not requiring suspending agents for aqueous vehicles are bismuth carbonate, compound kaolin powder, magnesium trisilicate, magnesium oxide and light kaolin.

Oral Suspensions

A suspension consists of a finely divided powder (the disperse phase) distributed in a liquid vehicle (the continuous phase). It is important that the suspended material is efficiently dispersed, and remains so dispersed throughout the period of time the dose is being measured by the patient. This is achieved by:

1. Suspending the powder in a finely divided state. Finely divided solids have a large surface area, and therefore a large surface energy. For this reason they often resist being wetted by the liquid phase, and float on the surface. In this situation, a wetting agent is required.
2. Increasing the viscosity of the continuous phase. This is done by adding a suspending agent. Most suspending agents can also function as wetting agents.

Some solids form acceptable suspensions on addition to the vehicle, followed by vigorous stirring. Another simple method sometimes useful with these substances is to add the solid to some of the vehicle in a calibrated bottle, seal and then shake vigorously. Other ingredients may then be added before adjusting the volume with more vehicle up to the calibration mark.

Other solids require the application of shear forces to effect adequate dispersion. On a small scale, this is usually attained by use of a mortar and pestle (trituration). The solids are finely powdered and mixed in the mortar and then a small amount of liquid is added. The resulting mixture is triturated to form a smooth paste, to which more liquid is added, accompanied by further trituration. When the suspension becomes pourable, it may be transferred to a calibrated container using further quantities of vehicle for rinsing. Any liquid ingredients may then be added and the volume adjusted as before. This is the most appropriate method for extemporaneous preparations. On a large scale, blending of ingredients is carried out using mechanical mixers, blenders, colloid mills, etc.

ESSENTIAL READING

B.P. 1998; pp. 1440-1442