

Measuring accurate doses of semi-solids with an applicator tends to be relatively difficult, while tablets, capsules, and films offer the advantage of unit-dose delivery.

### Ideal vaginal dosage form

Some of the important characteristics of an ideal vaginal dosage form are:

- should be long acting, reducing the frequency of administration
- should be stable in a range of climatic conditions
- should not lead to any irritation, burning or itching
- should not cause any leakage
- should not cause staining or discolouring of under garments
- the formulation should be colourless and odourless
- the formulation should not adversely affect sexual activity
- women should be able to use it without the knowledge of a male partner
- should be easy to insert and/or apply, without the need for an applicator.

### Drug characteristics

The physicochemical properties of active ingredient(s) influence the formulation design and performance. The following is a brief outline of the most important properties. Many of these factors are similar to those for rectal administration discussed above.

**Particle size.** Insoluble particles larger than 50  $\mu\text{m}$  are likely to cause mechanical irritation after administration. At the same time, particles greater than 150  $\mu\text{m}$  have the potential for rapid sedimentation during manufacturing, i.e. during molten mixture stage, before setting.

**Solubility.** The aqueous solubility of the drug is a critical preformulation parameter that dictates formulation options, for example, a lipophilic drug will solubilize in fatty bases, while a hydrophilic drug will be suspended.

**Dose or drug loading.** It can be difficult to incorporate high unit doses in formulations, e.g. fatty pessaries are difficult to optimize when they contain greater than 10% of oily drugs, while maintaining the required mechanical strength and the melting point.

**Bulk density.** Drugs insoluble in the vehicle with low bulk density, especially those with high doses, can be difficult to incorporate into the formulation.

**Surface characteristics.** Addition of surfactant may be required to help with some drugs to permit rapid wetting after administration.

### Pessaries

Pessaries are solid, single-dose preparations for vaginal insertion. Pessaries can be prepared in various shapes, usually ovoid, with a volume and consistency suitable for insertion into the vagina. Typically, they weigh around one gram. Pessaries contain one or more active substances dissolved or dispersed in a suitable base that may be soluble or dispersible in water, or may melt at body temperature. Additionally, they may contain diluents, adsorbents, surface-active agents, lubricants, antimicrobial preservatives, colouring matter and other stabilizers if necessary. The particle size of the active and excipients, if suspended in the vehicle, is controlled to avoid any irritation.

### Selection of a pessary base

A number of factors influence the selection of a base for pessaries. Many of these considerations are similar to those for rectal suppositories discussed above.

Vaginal suppositories (pessaries) are most often prepared with glycerol-gelatin bases, since this mixture is well tolerated. Polyethylene glycols are less common, since they are said to promote irritation. Fatty excipients are little used. Most drug delivery forms for vaginal application demand an auxiliary device, in order to obtain deep insertion of the dosage form.

The following are some of the important factors that should be critically evaluated during the development phase for large-scale manufacture of pessaries.

**Drug solubility and release.** The solubility of a drug in the vehicle and body fluids affects the release profile from the formulation. Because of partitioning, the drug tends to prefer the phase where it is more soluble. Additionally, the miscibility of a base with body fluids affects the drug release profile. If the drug is highly lipophilic and poorly hydrophilic, a water-soluble base is preferred. Similarly, if the drug is more hydrophilic, a lipid base will be