

years, data from thermal analysis techniques, particularly microcalorimetry and differential scanning calorimetry (DSC), when critically examined, have been found useful in rapid screening for possible drug-additive and drug-drug interactions. For example, DSC has revealed that the widely used tableting lubricant magnesium stearate interacts with aspirin and should be avoided in formulations containing this drug.

## Organoleptic properties

Modern medicines require that pharmaceutical dosage forms are acceptable to the patient. Unfortunately, many drug substances in use today are unpalatable and unattractive in their natural state and dosage forms containing such drugs, particularly oral preparations, may require the addition of approved flavours and/or colours.

The use of flavours applies primarily to liquid dosage forms intended for oral administration. Available as concentrated extracts, solutions, adsorbed onto powders or microencapsulated, flavours are usually composed of mixtures of natural and synthetic materials. The taste buds of the tongue respond quickly to bitter, sweet, salt or acid elements of a flavour. Unpleasant taste can be overcome by using water-insoluble derivatives of drugs which have little or no taste. An example is the use of amitriptyline pamoate, although other factors, such as bioavailability, must remain unchanged. If an insoluble derivative is unavailable or cannot be used, a flavour or perfume can be used. However, unpleasant drugs in capsules or prepared as coated particles or tablets may be easily swallowed, avoiding the taste buds.

Selection of flavour depends upon several factors but particularly on the taste of the drug substance. Certain flavours are more effective at masking various taste elements; for example, citrus flavours are frequently used to combat sour or acid-tasting drugs. Solubility and stability of the flavour in the vehicle are also important. In addition, the age of the intended patient should also be considered, since children for example prefer sweet tastes, as well as the psychological links between colours and flavours (e.g. yellow colour is associated with lemon flavour). Sweetening agents may also be required to mask bitter tastes. Sucrose continues to be used but alternatives, such as sodium saccharin which is 200–700 times sweeter depending on concentration, are

available. Sorbitol is recommended for diabetic preparations.

Colours are employed to standardize or improve an existing drug colour, to mask a colour change or complement a flavour. Whilst colours are obtained both from natural sources (e.g. carotenoids) or synthesized (e.g. amaranth), the majority used are synthetically produced. Dyes may be aqueous (e.g. amaranth) or oil soluble (e.g. Sudan IV) or insoluble in both (e.g. aluminium lakes). Lakes, which are generally calcium or aluminium complexes of water-soluble dyes, are particularly useful in tablets and tablet coatings because of greater stability to light than corresponding dyes, which also vary in their stability to pH and reducing agents. However, in recent years, the inclusion of colours in formulations has become extremely complex because of the banning of many traditionally used colours in many countries.

## Other drug properties

At the same time as ensuring that dosage forms are chemically and physically stable and are therapeutically efficacious, it is also relevant to establish that the selected formulation is capable of efficient and, in most cases, large-scale manufacture. In addition to those properties previously discussed such as particle size and crystal form, other characteristics such as hygroscopicity, flowability and compactability are particularly valuable when preparing solid dosage forms where the drugs constitute a large percentage of the formulation. Hygroscopic drugs can require low moisture manufacturing environments and need to avoid water during preparation. Poorly flowing formulations may require the addition of flow agents (e.g. fumed silica). Studies of the compactability of drug substances are frequently undertaken using instrumented tablet machines in formulation laboratories to examine the tableting potential of the material in order to foresee any potential problems during compaction, such as lamination or sticking, which may require modification of the formulation or processing conditions.

## Therapeutic considerations in dosage form design

The nature of the clinical indication, disease or illness for which the drug is intended is an important