The solvent system

Aqueous solvents

The majority of pharmaceutical solutions are water-based. Water is the most commonly used solvent due to its many advantages, such as its lack of toxicity and low cost. Different types of 'water' have been defined in the pharmacopoeias, related to its purity. Those defined in the *British Pharmacopoeia* are given as representative examples in Table 24.1. Other pharmacopoeias, such as the *United States Pharmacopoeia*, have additional types, such as 'Bacteriostactic Water for Injection'.

Tap (drinking) water is not normally used for the manufacture of pharmaceutical solutions or for extemporaneous compounding, as it contains dissolved substances which could interfere with the formulation, for example, reduce drug solubility and stability. Tap water is therefore purified, for example, by distillation, ion exchange or reverse osmosis to produce Purified Water. The latter is used for the preparation of non-parenteral solutions. For parenteral solutions, tap water is further purified in order to remove pyrogens (water-soluble, fever-producing compounds) thereby producing *Water for Injections*. In certain instances, for example, in extemporaneous dispensing, drinking tap (potable) water, freshly drawn from a mains supply, boiled and cooled, can be used to prepare oral or external solutions that are not intended to be sterile.

Table 24.1 Different types of water, as defined by the British Pharmacopoeia

Type of water	Use
Purified Water	Used for the preparation of medicines that do not have to be sterile and apyrogenic.
Highly Purified Water	Used for the preparation of medicines where water of high biological quality is needed, except where Water for Injections is required.
Water for Injections	Used for medicines for parenteral administration. Must be pyrogen-free.
Sterilized Water for Injections	Used for medicines for parenteral administration. Water has been sterilized by heat and is suitably packaged.

On its own, water does not dissolve many drug compounds to a sufficient degree to enable the preparation of a pharmaceutical solution. Other water-miscible liquids with greater drug solubility may therefore be added to water to enhance drug solubility. These liquids are called co-solvents. Commonly used examples include glycerol, propylene glycol, ethanol and poly(ethylene glycol). Co-solvents are generally less innocuous than water and the concentration used in an aqueous solution is limited primarily by their toxicity, by drug solubility in the formulation and finally cost. The mechanism of action of co-solvents is discussed in greater detail below.

Non-aqueous solvents

Non-aqueous solvent systems are used when the drug is insufficiently soluble or stable in aqueous systems, or when a solution is intended for specific properties, such as sustained drug absorption. Non-aqueous solutions are however limited to certain delivery routes, such as intramuscular and topical, due to their unpalatibility, toxicity, irritancy or immiscibility with physiological fluids. Although there is a huge number of organic liquids in which drugs can dissolve, the majority are toxic, and only a few are used in pharmaceutical solutions. Examples of commonly used organic liquids are shown in Table 24.2. These liquids are used as co-solvents with water, as co-solvents with other organic liquids, or on their own.

The drug

The drug could be a small molecule like aspirin, or a large biotherapeutic molecule, such as insulin or an antibody. As defined in Chapter 2, the drug is present as molecules or ions throughout the solvent. It is usual to ensure that the drug concentration in a pharmaceutical solution is well below its saturation solubility in order to avoid the possibility of drug precipitating out of the solvent as a result of subsequent temperature changes during storage and use.

The excipients

Excipients – substances other than the drug or prodrug which are included in pharmaceutical