amorphous crystals of no uniform shape but not exceeding 2 μm in size, and 70% crystalline insulin consisting of rhombohedral crystals between 10 to 40 μm in size. Insulin Zinc Suspension is obtained by adding a suitable zinc salt such as zinc chloride to soluble insulin.

Oily intramuscular injections are solutions or suspensions of drug substances, often steroids, hormones or fat soluble vitamins in a suitable metabolizable oil, such as arachis or sesame oils, as the vehicle. This approach can be used to administer drugs that are insoluble in water, or water soluble drug substances can be chemically modified to produce an oil soluble compound specifically for administration in an oily injection. The use of undecanoate, enanthate or propionate esters to obtain the oil soluble form of a drug is commonplace. As oily injections are much more viscous than aqueous injections, the injected solution does not spread along the muscle fascias when injected intramuscularly. This means a depot is formed in the muscle tissue. The drug must partition from the oil into the aqueous tissue fluid before it can be absorbed, therefore release from oily intramuscular injections is very slow. Many antipsychotic medicines are given as oily intramuscular injections as they require dosing only every 2 to 4 weeks rather than daily oral dosing, thus compliance with treatment can be better managed.

Excipients

It is very unusual for an injectable medicine to be composed entirely of the drug substance and no other ingredient. The drug, unless presented as a dried powder for reconstitution before use, will be dissolved or suspended in a vehicle such as water or a saline solution, or a non-aqueous liquid. Other ingredients (excipients) may be present in the formulation to aid the dissolution or suspension of the drug in the vehicle. Other excipients may be incorporated to comply with pharmacopoeial requirements such as the incorporation of a preservative if the preparation is for multiple use rather than a single dose product. Excipients are often included in parenteral products to prevent, reduce or delay the degradation of the drug product over time and thus improve the product's shelf-life. Finally, excipients are frequently added to adjust the pH and tonicity of the product to make it comparable to the physiological pH and tonicity of the tissue into which it is being injected (usually comparable to human plasma values). This is done to reduce pain and irritation that may otherwise be caused to blood vessels or tissues by the administration process.

Vehicles for injections

'Water for injections' is the most common vehicle used for parenteral products. Water for injections is a highly purified grade of water which is subject to pharmacopoeial standards with respect to production methods and purity. Water is of course well tolerated by the body and it is a solvent for a wide range of drug substances. For those drugs which are poorly soluble in water, water-miscible non-aqueous solvents such as ethanol, glycerol or propylene glycol may be added as co-solvents to improve the solubility of a drug substance.

Solubilizing agents may be added to an injection formulation to aid the dissolution of drugs with poor aqueous solubility. Polyoxyethylene castor oil derivatives will solubilize hydrophobic drugs into aqueous solutions for injections and are used, for instance, for formulations of paclitaxel, diazepam and cisplatin. Cyclodextrins are cyclic oligosaccharide molecules (see Fig. 24.1) with a bucket-like structure containing a hydrophobic central cavity, while the outer surface is hydrophilic. Cyclodextrins can form inclusion complexes with a variety of poorly soluble drug molecules. The 'hydrophobic' drugs are held within the cyclodextrin 'bucket' with the outer surface of the complex remaining hydrophilic. Both alpha and gamma-cyclodextrin can be used in parenteral products, but beta-cyclodextrin should not be used as it causes severe kidney damage.

Water-insoluble drugs may be administered parenterally by dissolving the drug in a suitable oil and forming an oil-in-water emulsion using a suitable emulsifying agent to stabilize the emulsion (see Chapter 27 for further details on emulsions). Droplet size must be controlled and is usually less than 3 μm in diameter to prevent oil embolisms forming in the blood-stream. Lecithin and various sorbitan fatty acid esters have been used as emulsifying agents in parenteral products. Finally, oils such as arachis oil or sesame oil may be chosen as a vehicle for intramuscular injections, for drug release over a prolonged period of time (depot injections).