

Oily Solutions and Suspensions

Partition coefficient of the drug in solution or suspension is the most important factor affecting release of the drug from the oil into the tissue. For solutions, the drug is soluble in oil, so it will have a relatively slow release due to its naturally high partition coefficient. For suspensions, the drug is not soluble in oil, but has to dissolve in the oil phase, then partition from the oil phase to the aqueous tissue. Oily injectable suspensions are formulated as sustained release dosage forms, e.g., amoxicillin, penicillin procaine G, haloperidol decanoate, fluphenazine decanoate, testosterone enanthate, others (Chapter 6). Oily injection vehicles tend to remain in tissue as oily cysts for a long time. Olive oil is thought to reside the least amount of time in tissue while castor oil resides the longest.

Oil-in-Water and Water-in-Oil Emulsions

The first word of these two emulsions is the internal phase where the drug is dissolved. For oil-in-water emulsions the drug is dissolved in the oil either for solubilization purposes or for sustained release purposes. The drug must partition from the oil phase to the aqueous phase, then diffuse into the surrounding tissue, then diffuse and partition into the bloodstream. For water-in-oil emulsions, the drug is dissolved in water with these dosage forms formulated for sustained release purposes. It takes a longer period of time for drug to partition from the aqueous phase to the external oil phase and then to the surrounding tissue fluid.

Sustained or Controlled Release Dosage Forms

Included in this category of dosage form are complexes, polymeric systems, liposomes, and other microparticulate delivery systems. Many biopharmaceuticals have very short biological half-lives that are especially applicable to being formulated in sustained release dosage forms that will reduce the requirement for daily injections. Controlled release formulations are important for injectable drugs whose therapeutic doses are very small yet have a relatively high therapeutic index such that inadvertent dose dumping would not cause life-threatening reactions. Leuprolide acetate perhaps is the best example of an injectable drug that meets these requirements. The rate and extent of absorption of sustained and controlled released drugs from injection sites and from depot locations are heavily dependent upon formulation factors such as the type of polymer, drug solubility in the polymer matrix, partition coefficient, particle size, and other properties of the formulation (3).

PHYSIOLOGICAL FACTORS AFFECTING DRUGS ADMINISTERED BY INJECTION

Blood and Lymphatic Circulation

Table 33-3 gives a comparison of volume, rate, and pressure for various parts of the circulatory or arteriovenous system (4). What is especially interesting and relevant to injections is the fact that the capillary system is only 250 mL or 7% of the body's blood volume and has a flow rate much slower than other blood vessels, especially the arteries and vena cava vein. Injections other than intravascular depend on the capillary vessel system to transport drugs to the major blood vessels, so this further explains why IM/SC injections take time for the drug to reach the site of action.

Table 33-3 Comparison of Volume, Rate, and Pressure for Various Parts of the Circulatory or Arteriovenous System (4)

System	Volume (cm ³)	Rate (cm/sec)	Pressure (mm Hg)
Aorta	100	40	100
Arteries	325	40–10	100–40
Arterioles	50	10–0.1	40–25
Capillaries	250	0.1	25–12
Venules	300	0.3	12–8
Veins	2200	0.3–5	10–5
Vena Cava	300	30–5	2