Tween 80. It is interesting to note that when Taxol is administered with Cremophor EL, the pharmacokinetics of the drug turns out to be nonlinear. For intravenous administration, a small particle size of less than 150 nm is desirable only in cases where one wants to pass fenestrated endothelia (e.g., treatment of tumors); however, this is a very limited case. More realistic and short-term achievable goal is passive targeting of drugs to treat mononuclear phagocytic system (MPS) infections (i.e., targeting the macrophages, e.g., treatment of *Mycobacterium tuberculosis* and *Mycobacterium avium* infections, especially in human immunodeficiency virus [HIV]-infected patients). Here, it is more desirable to have larger particles to ensure fast and efficient removal from the bloodstreams by the macrophages. Another therapeutic goal is the creation of stealth drug nanoparticles circulating in the blood, minimizing free-drug concentration, and simultaneously prolonging the drug release by slow dissolution. For this purpose, very small particles are not suitable, because they will dissolve too fast. Another therapeutic goal is targeting the non-MPS targets, for example, the brain and the bone marrow.

The particle size should be customized depending on the therapeutic requirements and purpose. The nanoparticle suspensions are physically stable for a long period of time if they are stabilized by emulsifiers or polymers in optimized composition. However, aqueous suspensions might not be the most convenient dosage form for the patient. The nanoparticle suspension can be used as granulation fluid for tablet production or as wetting liquid for pellet production. The dispersions can also be spray-dried to be filled into hard gelatin capsules or sachets. Drug nanoparticles produced in PEG 600 or Miglyol can directly be filled into soft gelatin capsules. Lyophilization of drug nanoparticles produced in a water-reduced media can be used to produce fast-dissolving delivery systems. For parenteral application, nanoparticles can be lyophilized and reconstituted with isotonic media prior to injection (e.g., water with glycerol). There are also other areas of application, for example, ocular delivery (prolonged retention time) and topical application (increased saturation solubility, leading to increased diffusion pressure into the skin).

5.3 Assay Systems

As the U.S. FDA has begun accepting recommendations for waiver of bioequivalence requirement, protocols proving extremely expensive in the drug development cycle, there is a greater need to develop surrogate models that might prove useful sometime in securing waivers for all classes of drugs. Generally, the methods available currently show that the complexity of assay is directly proportional to its correlation with the absorption of drugs in humans (Figure 5.3). Studies that correlated log *P* with human absorption profile and the suitability or lead candidates are elaborated in Chapter 4. In this chapter, we will examine more complex assay systems.

Drug transport across epithelial cell barriers, especially the human small intestine, is difficult to predict. The intestinal epithelial cell barrier is a sophisticated organ that has evolved over hundreds of millions of years to become a “smart,” effective, and selective xenobiotic screen. Nevertheless, there is large interindividual variability in the intestinal transport of drugs. Genetic variability in key proteins is believed to be causal. There is a pressing need to better understand the key processes and how the system components interact at the molecular, cellular, and tissue levels to control drug transport and determine drug absorption in small intestines.