Table 21.1 Some of the models available for predicting or measuring drug absorption

Model type	Model	Description
Computational/ In silico	clog P	Commercial software that calculates n-octanol/ water partition coefficient based on fragment analysis, known as the Leo-Hansch method
	mlog P	Method of calculating log P, known as the Moriguchi method (see text)
Physicochemical	Partition coefficient	Measure of lipophilicity of drug, usually measured between n-octanol and aqueous buffer via a shake-flask method
	Immobilized artificial membrane	Measures partition into more sophisticated lipidic phase on an HPLC column
Cell culture	Caco-2 monolayer	Measures transport across monolayers of differentiated human colon adenocarcinoma cells
	HT-29	Measures transport across polarized cell monolayer with mucin-producing cells
Excised tissues	Cells	Measures uptake into cell suspensions, e.g. erythrocytes
	Freshly isolated cells	Measures uptake into enterocytes; however; the cells are difficult to prepare and are short-lived
	Membrane vesicles	Measures uptake into brush border membrane vesicles prepared from intestinal scrapings or isolated enterocytes
	Everted sacs	Measures uptake into intestinal segments/sacs
	Everted intestinal rings	Studies the kinetics of uptake into the intestinal mucosa
	Isolated sheets	Measures the transport across sheets of intestine
In situ studies	In situ perfusion	Measures drug disappearance from either closed or open loop perfusate of segments of intestine of anaesthetized animals
	Vascularly perfused intestine	Measures drug disappearance from perfusate and its appearance in blood
In vivo studies	Intestinal loop	Measures drug disappearance from perfusate of loop of intestine in awake animal
Human data	Loc-I-Gut	Measures drug disappearance from perfusate of human intestine
	High-frequency capsule	Non-invasive method; measures drug in systemic circulation
	InteliSite capsule	Non-invasive method; measures drug in systemic circulation
	Bioavailability	Deconvolution of pharmacokinetic data

length of the gastrointestinal tract, the potential of degradation or metabolism by bacterial enzymes should be assessed. If a drug is metabolized to a metabolite which can be absorbed, the potential toxicity of this metabolite should be considered.

Permeability

There is a wealth of techniques available for either estimating or measuring the rate of permeation across membranes that are used to gain an assessment of oral absorption in humans. These range from computational (in silico) predictions to both physicochemical and biological methods. The biological methods can be further subdivided into in vitro, in situ and in vivo methods. In general, the more complex the technique, the more information that can be gained and the more accurate is the assessment of oral absorption in humans. The range of techniques is summarized in Table 21.1. Some of the more widely used ones are discussed below.

Partition coefficients

One of the first properties of a molecule that should be predicted or measured is its *partition coefficient* between oil and a water phase (log*P*). This gives a measure of the lipophilicity of a molecule, which can be used to predict how well it will be able to cross a biological membrane. It is a very useful parameter for many reasons relating to formulation design and drug absorption and is discussed