glucuronides, can be deconjugated by intestinal enzymes and bacteria that reside in the gut, providing additional opportunity for the compounds to be reabsorbed into the body.[68]

IN VITRO ADME SCREENING METHODS

Ideally, it would be possible to examine the *in vivo* ADME characteristics of large numbers of compounds in a given program in order to select the compounds with best overall ADME properties. In practice, however, this is simply not possible as *in vivo* experiments are both expensive and time-consuming. Fortunately, a number of *in vitro* assays that are useful predictors of *in vivo* ADME properties have been developed. Insight into compound absorption, for example, can be obtained by determining a compound's solubility in aqueous media. High-throughput solubility assays can be performed using commercially available 96-well plate platforms. Measuring the solubility of a compound in a range of biologically relevant buffer system will provide insight into how soluble a compound will be in the various section of the gastrointestinal tract.

Absorption is also driven by compound permeability, and *in vitro* assays have been developed to model this as well. Permeability across a biological barrier can be assessed in an *in vitro* setting in a parallel artificial membrane permeability assay, also known as PAMPA (Figure 6.45).[69] In

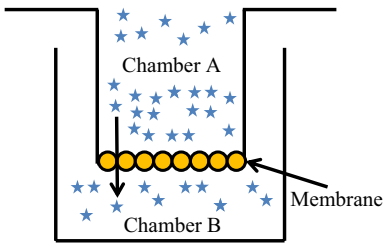

FIGURE 6.45 In parallel artificial membrane permeability assay, an artificial membrane (orange) separates two compartments. The test compound is placed in one compartment and after an incubation period, the concentration in each compartment is measured to assess membrane permeability.

this experiment, two compartments are separated by an artificial membrane and the test compound is placed in one side of the two compartments. After an incubation period, the amount of compound in each of the two compartments is measured. The change in compound concentration in each chamber provides direct insight into its ability to passively diffuse across a biological barrier.

Transporter activity, which as discussed earlier can impact absorption, distribution, and excretion, can be assessed in a similar manner