Permeability Measurements under Hydrodynamic Control

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The PAMPA assay has been used as in vitro assay in drug discovery for over a decade. It has been shown that the measured permeability is a combination of two separate factors: the membrane permeability and the permeability of the unstirred water layer (UWL). Separation of the membrane permeation from UWL contribution leads to a better correlation with in vivo absorption and eliminates low permeability response of highly lipophilic drugs (false negative). Here, we present a single-channel variation of this assay with in situ drug analysis in the acceptor compartment and controlled hydrodynamic conditions in both donor and acceptor compartment. These conditions allow both permeability-time profiles and the membrane permeability to be assessed. The membrane permeability can be approached both from the dependence of the measured (effective) permeability on the stirring rate and permeability-pH profiles. Comparison of the two approaches is presented for a weak acid (warfarin) and a weak base (verapamil).