

Insights Into Blood-Brain Barrier Permeability

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The Blood-Brain Barrier (BBB) is a very important barrier between systemic circulation and central nervous system (CNS). Drugs targeting CNS-related disorders need to overcome this barrier to show pharmacological activity. The most common parameter to quantify BBB permeability is the logBB.

$$\log BB = \log \left(\frac{C_{Brain}}{C_{Blood}} \right) \quad (1)$$

Unfortunately it is time-consuming and expensive to measure experimentally and therefore highly interesting for structure property relationships (SPR) [1].

We established high-throughput cell culture models for two closely related problems to BBB: Drug-induced phospholipidosis (PLD) and functional inhibition of acid sphingomyelinase (ASM) [2]. We measured a large set of over 200 FDA approved drugs from a broad range of clinical application and indications.

When focusing on BBB permeable compounds, it is important to highlight that a large part of these compounds are also ASM inhibitors and PLD inducing drugs. These results were in agreement with our expectations, as all three topics require compounds to overcome two membranes.

Combining all experimental data we were able to establish predictive relationships for BBB permeability, ASM inhibition and PLD induction solely. In addition to that it also allowed us to create a biological profile with respect to membrane permeability.

[1] A.R. Mehdipour, *Drug Discovery Today*, 14(21-22), (2009), p. 1030-1036.

[2] J. Kornhuber, *Cellular Physiology and Biochemistry*, 26(1), (2010), p. 9-20.