Abstract:

The blood-brain barrier (BBB) is a dynamic interface between the cerebral circulation and the brain tissue, and it is essential for maintaining the micro-environment within brain. Although it has its advantages for protecting brain from blood-born neurotoxins, however, the BBB extremely limits the therapeutic efficacy of drugs into the CNS. Thus, determination of the permeability of cerebral microvessels to various drugs across the BBB is important for the drug development for CNS disorders such as multiple sclerosis, Alzheimer's disease, HIV infection and brain tumors. One of objectives of the current study is to develop non-invasive quantitative fluorescence method to measure BBB permeability to hydrophilic solutes. Employing this method, we examined the charge effects of the BBB on various-charged solute transport as well as the modulation of the BBB permeability by plasma polyanionic glycoprotein orosomucoid. Furthermore, combining the in vivo measured permeability data and a theoretical model, we could predict the charge densities of the endothelial glycocalyx layer and the basement membrane in the BBB under normal conditions and under orosomucoid treatment.