1,3-Propanedisulfonic acid is a sulfonic acid containing two sulfonate units. Its salts are called eprodisates and have been evaluated as a protector of renal function in AA amyloidosis

CCL2 (MCP-1) and CCL5 (RANTES) are pro-inflammatory chemokines that mediate neuroimmune responses to acute insults, and aspects of brain injury and neurodegenerative diseases; however, a blood-to-brain transport system has not been evaluated for either chemokine in vivo. Therefore, Quaranta et al. determined whether CCL2 and CCL5 in blood can cross the intact BBB and enter the brain. Using CD-1 mice, they found that 125I-labeled CCL2 and CCL5 crossed the BBB, and entered the brain parenchyma. They next aimed to identify the mechanisms of 125I-CCL2 and 125I-CCL5 transport in an in-situ brain perfusion model. They found that both heparin and eprodisate inhibited brain uptake of 125I-CCL2 and 125I-CCL5 in situ, whereas antagonists of their receptors, CCR2 or CCR5 respectively, did not, suggesting that heparan sulfates at the endothelial surface mediate BBB transport. Finally, they showed that CCL2 and CCL5 transport across the BBB increased following a single injection of 0.3mg/kg lipopolysaccharide. These data demonstrate that CCL2 and CCL5 in the brain can derive, in part, from the circulation, especially during systemic inflammation. Further, binding to the BBB-associated heparan sulfate is a mechanism by which both chemokines can cross the intact BBB, highlighting a novel therapeutic target for treating neuroinflammation. The work demonstrates that CCL2 and CCL5 can cross the intact BBB, and that transport is robustly increased during inflammation. These data suggest that circulating CCL2 and CCL5 can contribute to brain levels of each chemokine. They further showed that the transport of both chemokines is inhibited by heparin and eprodisate, suggesting that CCL2/CCL5-heparan sulfate interactions could be therapeutically targeted to limit accumulation of these chemokines in the brain ¹⁾.

1)

Quaranta DV, Weaver RR, Baumann KK, Fujimoto T, Williams LM, Kim HC, Logsdon AF, Omer M, Reed MJ, Banks WA, Erickson MA. Transport of the pro-inflammatory chemokines CCL2 (MCP-1) and CCL5 (RANTES) across the intact mouse blood-brain barrier is inhibited by heparin and eprodisate and increased with systemic inflammation. J Pharmacol Exp Ther. 2022 Oct 30:JPET-AR-2022-001380. doi: 10.1124/jpet.122.001380. Epub ahead of print. PMID: 36310035.

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