**2-LBS-22** Late-Breaking Session

# The relationships of pharmacological effects and radical scavenging abilities on BBB permeable $Ca^{2+}$/Calmodulin antagonist CV-159.

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Redox imbalances by overproduction of reactive oxygen species (ROS) are known to play an essential role in the pathological events of cerebral and cardiac ischemic injury, hypertension, inflammation and cancer. Widely used calcium channel antagonists such as nifedipine, nicardipine, amlodipine are not effective for ischemia-reperfusion (I/R) injuries at clinical used low dose on animal models.

BBB permeable $Ca^{2+}$ /calmodulin antagonist CV-159, 1,4- Dihydro -2,6-dimethyl- 4-(3-nitrophenyl) -3,5-pyridinedicarboxylic acid methyl 6-(5-phenyl-3-pyrazolyloxy)hexyl ester characterized by markedly inhibitory effects for infarct size and edema on cerebral I/R injury. In cyclic voltammetry and ESR studies, hydroxyl radical scavenging ability of CV-159 was detected 100 times stronger than that of nicardipine, and it also suppressed mitochondrial superoxide and iNOS generation. Radical spin trapper G-CYPMPO (CAS No.1350616-52-2) and CV-159 markedly relaxed the high concentration of $K^+$-induced contractions in isolated endothelium-denuded rat aortic strips, suggesting the existence of a novel role of oxygen radical in smooth muscle signal transduction.