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The Na⁺-dependent L-ascorbic acid transporter SVCT2 expressed in brainstem cells, neurons, and neuroblastoma cells is inhibited by flavonoids.

[Caprile T](#), [Salazar K](#), [Astuya A](#), [Cisternas P](#), [Silva-Alvarez C](#), [Montecinos H](#), [Millán C](#), [de Los Angeles García M](#), [Nualart F](#).

Department of Cellular Biology, Faculty of Biological Sciences, University of Concepcion, Concepcion, Chile.

Ascorbic acid (AA) is best known for its role as an essential nutrient in humans and other species. As the brain does not synthesize AA, high levels are achieved in this organ by specific uptake mechanisms, which concentrate AA from the bloodstream to the CSF and from the CSF to the intracellular compartment. Two different isoforms of sodium-vitamin C co-transporters (SVCT1 and SVCT2) have been cloned. Both SVCT proteins mediate high affinity Na⁽⁺⁾-dependent L-AA transport and are necessary for the uptake of vitamin C in many tissues. In the adult brain the expression of SVCT2 was observed in the hippocampus and cortical neurons by in situ hybridization; however, there is no data regarding the expression and distribution of this transporter in the fetal brain. The expression of SVCT2 in embryonal mesencephalic neurons has been shown by RT-PCR suggesting an important role for vitamin C in dopaminergic neuronal differentiation. We analyze SVCT2 expression in human and rat developing brain by RT-PCR. Additionally, we study the normal localization of SVCT2 in rat fetal brain by immunohistochemistry and in situ hybridization demonstrating that SVCT2 is highly expressed in the ventricular and subventricular area of the rat brain. SVCT2 expression and function was also confirmed in neurons isolated from brain cortex and cerebellum. The kinetic parameters associated with the transport of AA in cultured neurons and neuroblastoma cell lines were also studied. We demonstrate two different affinity transport components for AA in these cells. Finally, we show the ability of different flavonoids to inhibit AA uptake in normal or immortalized neurons. Our data demonstrates that brain cortex and cerebellar stem cells, neurons and neuroblastoma cells express SVCT2. Dose-dependent inhibition analysis showed that quercetin inhibited AA transport in cortical neurons and Neuro2a cells.

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