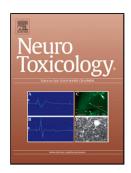
### Accepted Manuscript

Title: Brain Uptake of Deltamethrin in Rats as a Function of Plasma Protein Binding and Blood-Brain Barrier Maturation

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## ACCEPTED MANUSCRIPT

#### Brain Uptake of Deltamethrin in Rats as a Function of Plasma Protein Binding and Blood-Brain Barrier Maturation

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#### ABSTRACT

Pyrethroids, including permethrin and deltamethrin (DLM), are very widely used of insecticides. It was hypothesized that lower plasma binding and increased blood-brain barrier (BBB) penetration of DLM in immature rats contribute to the higher brain concentrations of DLM and more pronounced neurotoxicity reported in this age-group. The left brain of anesthetized adult rats was perfused for 2 min via a carotid artery with 1  $\mu$ M <sup>14</sup>C-DLM in: 2 – 5% human serum albumin (HSA); plasma from adults and 15- and 21-day-old rats; and plasma from human donors of: birth – 1 week, 1 – 4 weeks, 4 weeks – 1 year, 1 – 3 years and adults. The fraction of DLM bound and brain uptake of DLM did not vary significantly with the HSA concentration nor with the age of rat or human plasma donors. One, 10 and 50  $\mu$ M <sup>14</sup>C-DLM were perfused into the left brain of anesthetized adult, 15-day and 21-day-old rats. DLM deposition in the brain was linear over this range of concentrations and inversely related to age. The results of this investigation indicate that increased BBB permeability in the youngest rats enhances brain deposition of the insecticide. Plasma protein binding of DLM in immature rats and humans is not sufficiently diminished to impact its brain uptake.

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