Novel Local Anesthetics Demonstrate Isomer-dependent Analgesia in Mice

Clinically there is a need for local anesthetics with a greater specificity of action and longer duration. We have synthesized a series of local anesthetic derivatives called boronicaines in which the aromatic, phenyl ring of lidocaine was replaced with an isomeric, polyhedral carborane cluster. A carborane cluster is an icosahedral cage comprised of ten boron and two carbon atoms (C2B10H12), and is more hydrophobic than a benzene ring. The boronicaine derivatives were tested for their analgesic activity and compared to lidocaine using a standard hot plate tests in mice following plantar injections. The use of mice in these studies was approved by the University of Missouri Animal Care and Use Committee. Results showed that the compounds differed in their analgesic activity in the following order: ortho-carborane = C, C′-dimethyl meta-carborane > para-carborane > lidocaine > meta-carborane derivative. Both ortho-boronicaine and C, C′-dimethyl meta-boronicaine had longer durations of analgesia than lidocaine. No analgesia was seen when the phenyl ring of lidocaine was replaced by either an adamantane or cyclohexane group. Differences in analgesic activity are rationalized by variations in chemical structure and protein binding characteristics.