Bulleyaconitine A Preferably Blocks Voltage-gated Sodium Channels of Dorsal Root Ganglion Neurons in Neuropathic Conditions

Man-Xiu Xie, Jie-Yang, Kai-Feng Shen, Jin Xu, Xiong-Xiong Zhong, Shao-Kun Wang, Xiao-Long Zhang, Rui-Ping Pang and Xian-Guo Liu*

Pain Research Center and Department of Physiology, Zhongshan School of Medicine of Sun Yat-sen University, 74 Zhongshan Rd. 2, Guangzhou 510080, China, liuxg@mail.sysu.edu.cn, Tel: 0086-20-87331956

Background: Oral Bulleyaconitine A (BLA) is effective for treating chronic pain in human patients but the underlying mechanisms is poorly understood. **Methods:** The effects of BLA on Na^+ channels were evaluated with the whole cell patch clamp technique in intact dorsal root ganglion (DRG) neurons of sham-operated rats, in injured and uninjured neurons in L4-6 DRGs of spared nerve injury (SNI) rats and in the uninjured neurons in L4 and L6 DRGs of L5 spinal nerve ligation (L5-SNL) rats. Mechanical allodynia and thermal hyperalgesia were accessed with von Frey hairs and the plantar tester. **Results:** Compared to sham rats, IC_{50} values for resting and inactivated Na^+ channels were 93 and 81 times lower in DRG neurons of SNI rats (5.3±0.3 nM and 0.72±0.04 nM), and 624 and 586 times lower in the neurons of L5-SNL rats. The use-dependent blockage of BLA on Na^+ channels was more potent in SNI and L5-SNL rats than that in sham rats at corresponding IC_{50} concentrations. BLA facilitated the inactivation of VGSCs in each group. In cell lines, IC_{50} values for resting and inactivated Nav1.3, Nav1.7 were at least 140 times lower than those for Nav1.8. The use-dependent blockage was most profound in Nav1.7, less in Nav1.3 and least in Nav1.8 at IC_{50} concentrations. Local application of BLA onto L4-6 DRGs at 0.1-10 nM dose-dependently reversed the mechanical allodynia and thermal hyperalgesia in L5-SNL model. **Conclusions:** Preferable blockage of Na^+ channels including Nav1.7 and Nav1.3 in neuropathic conditions may contribute to BLA's anti-neuropathic pain effect.

- 适用于离子通道作为疼痛治疗靶点