The Efficacy of a Dual-Acting, Peripherally-Restricted kappa/delta Opioid Agonist (CAV1001) in Neuropathic Pain in the Rat

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Background

Nerve injury can precipitate a neuroimmune inflammatory response.1 This response might lead to the activation of peripheral delta opioid receptors, allowing delta opioid agonists in the periphery to become analgesic directly and through allosteric modulation of peripheral kappa opioid receptors.2

This study evaluated the efficacy of a single intraperitoneal injection of CA1001 (a novel peripherally-restricted dual-acting kappa/delta opioid agonist) and the comparator, gabapentin, in the spinal nerve ligation (SNL) model for neuropathic pain in the rat.

Methods

• Following IACUC approval, neuropathy was induced by surgically ligating the 5th and 6th lumbar spinal nerves (L5 and L6);
• Mechanical sensitivity was assessed via paw compression thresholds (PCTs) using a digital Randall-Selitto device;
• 50 animals that met the inclusion criteria were randomly assigned to 5 groups with 10 animals per group (Power: 80%);
• Animals were administered a single dose of vehicle, CAV1001 (1 mg/kg, 5 mg/kg, or 10 mg/kg IP), or control compound (gabapentin 100 mg/kg PO; active control: internal validity) on day 0 (15 days after SNL) and PCTs were determined 1, 2, and 4 hours after compound administration;
• All behavioral evaluations were performed by a blinded observer.

Results

Gabapentin significantly reversed SNL-induced mechanical hyperalgesia at 1, 2, and 4-hours (p<0.01 versus vehicle, t test).

Conclusion

The reversal of mechanical hyperalgesia by CAV1001 at 5 mg/kg and 10 mg/kg did not differ significantly from the active control, gabapentin.

References


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