

## **IQB-9302, A NEW POTENT LOCAL ANESTHETIC**

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A series of novel amide local anesthetics bearing a cyclopropyl group linked to the side chain have been synthesized. From this series, IQB-9302 [dl(1-methylcyclopropyl)-2-(2,6-xylyl carbamoyl) piperidine] was the most active derivative in some standard pharmacological tests in comparison with mepivacaine: a) **Palpebral reflex in the rabbit**: IQB-9302 (1%) induced 100% anesthesia lasting 30 min; 45 min after dosing, anesthesia was still 83%. Mepivacaine (1%) only induced 80% anesthesia lasting 15 min. b) **Intradermal anesthesia in guinea-pig**: IQB-9302 (0.1%) induced 100% anesthesia for more than 50 min and effect was still evident (80%) after 60 min; conversely, duration of Mepivacaine (1%) induced anesthesia was only 10-15 minutes. c) **In rat sciatic nerve** electrically stimulated, conduction was totally blocked by IQB-9302 (0.1%) and Mepivacaine (0.5%) for 2 hours. Anesthesia was maintained after washing with saline in both cases. Onset of anesthesia was lower for IQB-9302. Acute subcutaneous toxicity in conscious mice of IQB-9302 was compared with those of bupivacaine and mepivacaine. DL 50 were 89, 74 and 280 mg/kg, respectively. Therapeutic indexes **[TI]** (calculated from the mean of anesthetic activity in the above pharmacological tests, the DL50 values and data from literature <sup>1</sup>) were: IQB-9302  $\geq$  8.93 ; mepivacaine = 4.16 ; bupivacaine = 4; lidocaine = 3.1.

From these preliminary experiments, it can be concluded that IQB-9302 exhibits the best therapeutic index of all up to date described local anesthetics. In particular, the TI of IQB-9302 is approximately twice of those of Lidocaine, mepivacaine and bupivacaine that are today the most prescribed drugs.

1)Covino, B: Pharmacology of local anesthetic agents. *Br.J.Anaesth.*, (1986) **58**: 701-716