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Resumo	BACKGROUND: Our research group has recently developed liposomes with ionic gradient and in a combined manner as donor and acceptor vesicles containing ropivacaine (RVC; at 2% or 0.75%). Looking for applications of such novel formulations for postoperative pain control, we evaluated the duration of anesthesia, pharmacokinetics, and tissue reaction evoked by these new RVC formulations. METHODS: The formulations used in this study were large multivesicular vesicle (LMVV) containing sodium acetate buffer at pH 5.5 or in a combined manner with LMVV as donor and large unilamellar vesicles (LUVs) as acceptor vesicles with an external pH of 7.4. Wistar rats were divided into 6 groups (n = 6) and received sciatic nerve block (0.4 mL) with 6 formulations of RVC (LMVVRVC0.75%, LMVV/LUVRVC0.75%, LMVVRVC2%, LMVV/LUVRVC2%, RVC 0.75%, and RVC 2%). To verify the anesthetic effect, the animals were submitted to the pain pressure test and the motor block was also monitored. Histopathology of the tissues surrounding the sciatic nerve region was also assessed 2 and 7 days after treatment. Rats (n = 6) were submitted to a hind paw incision, and mechanical hypersensitivity was measured via the withdrawal response using von Frey filaments after injection of the 6 formulations. Finally, New Zealand white rabbits (n = 6) received sciatic nerve block (3 mL) with 1 of the 6 formulations of RVC. Blood samples were collected predose (0 minutes) and at 15, 30, 45, 60, 90, 120, 180, 240, 300, 360, 420, 480, and 540 minutes after injection. RVC plasma levels were determined using a triple-stage quadrupole mass spectrometer. RESULTS: Duration and intensity of the sensory block were longer with all liposomal formulations, when compared to the plain RVC solution (P < .05). Histopathological

	evaluation showed greater toxicity for the positive control (lidocaine 10%), when compared to all formulations (P < .05). After the hind paw incision, all animals presented postincisional hypersensitivity and liposomal formulations showed longer analgesia (P < .05). LMVVRVC0.75% presented higher time to reach maximum concentration and mean residence time than the remaining formulations with RVC 0.75% (P < .05), so LMVV was able to reduce systemic exposure of RVC due to slow release from this liposomal system. CONCLUSIONS: All new liposomal formulations containing 0.75% RVC were able to change the pharmacokinetics and enhance anesthesia duration due to slow release of RVC from liposomes without inducing significant toxic effects to local tissues.
Fomento	