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The effectiveness of PLGA nanoparticles encapsulating two NSAIDs simultaneously using a double emulsification method in producing potent analgesic effects in chronic inflammation

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Abstract Background: Pain is regarded as a disease and needs to be treated in a timely manner, avoiding the consequences that affect not only affect one individual but also affect the family and society, not only in terms of emotional but also economic and social influences in general. It is a fact that there is still a lack of hydrophilic drug Ketorolac Tromethamine (KT) and hydrophobic drug Prednisolone (PRED) were concurrently entrapped in poly (lactic-co-glycolic acid) (PLGA) nanoparticles (NPs), achieving dual encapsulation to ensure high compatibility, benefit in the long-term efficacy of pain relief and reduce side effects. Method: Dual drug nanocarriers (KT-PRED-PLGA NPs) were characterized for particle size, encapsulation efficiency, drug loading efficiency, drug release, and biocompatibility. Vero cell viability and cytotoxicity were measured and demonstrated under different drug concentrations. The ICR mice were used to induce pain model by Complete Freund's adjuvant (CFA) injection in the hind paw. The measuring pain-induced model changes in thresholds mechanical pressure via Dixon's up-down method. Tissue samples of the liver, stomach, and kidney were harvested and tested for toxicology in animal models up to 14 days after drug application. The presence of the two cyclooxygenases (COX) and prostaglandin E2 (PGE2) in the hind paw was examined via immunohistochemistry to quantify the pain relief pathway after intravenous dual nanocarrier administration. Results: The dual-emulsion drug encapsulation in PLGA NPs demonstrated that a nanomedicine with KT and PRED can reduce chronic pain, clearly proven to be non-toxicity, and have no side effects in both in vitro and in vivo studies. Conclusion: Our study explored and developed the potential of a highly effective dose of pain relief and the safety factors, reduced side effects, and unnecessary elimination to avoid wasting medicine.

Importance of Research: The most commonly used clinical analgesics can be broadly classified into strong opioids and nonsteroidal anti-inflammatory drugs (NSAIDs). We developed a new pharmacological treatment with long-term efficacy and few side effects in the study of chronic inflammatory pain based on the development of a single-step method of water-in-oilin-water (W/O/W) synthesis poly (lactic-co-glycolic acid) (PLGA) nanoparticles. These PLGA nanoparticles achieve dual encapsulation of the hydrophilic NSAID Ketorolac Tromethamine (KT) and a widely used corticosteroid hydrophobic drug Prednisolone (Pred). The nanocarriers ensure compatibility, benefit in long-term efficacy treatment, and reduce side effects such as some severe complications of therapy with KT, such as GI ulceration, bleeding and perforation, postoperative bleeding, acute renal failure, anaphylactic and anaphylactoid reactions, and liver failure. Besides that, implementation of single-step synthesis of PLGA with a steroid (proposed as hydrophobic Pred) to prolong the absorption time for chronic inflammatory pain. The double emulsification nanocarriers are not only an effective treatment combination but also a reduction in dosage as well as a reduction in side effects and treatment costs.

Keywords: PLGA Nanoparticles; Ketorolac Tromethamine; Prednisolone; Nanomedicine; Inflammatory Chronic pain; NSAIDs.

Biography

The creative researcher is a Ph.D. candidate at National Cheng Kung University. In addition, I am an enthusiastic research assistant currently engaged in the R&D program in university-industry cooperation.

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