PLGA nanoparticles to deliver GnRH analogues as fertility control agents to the brushtail possum

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In New Zealand, the Australian brushtail possum is a significant pest animal and administering control agents to this wild population is challenging. The current control strategy is poisoning, however disrupting fertility is a more humane and effective method to reduce the population of this pest.[1, 2] Gonadotropin releasing hormone (GnRH) is a neurohormone that controls the reproductive function in the possums. D-Lys^6-GnRH is an analogue of GnRH and chronic exposure downregulates GnRH receptors and causes infertility in brushtail possums.[3] Nanoparticles are used successfully for drug and gene delivery and humans, however their application in a wildlife setting is untested. Formulation of peptides into nanoparticles can enhance gut absorption after oral administration and improve stability of the drug by protecting the therapeutic agent from enzymatic degradation, thus improving bioavailability. Oral delivery is the most effective strategy to administer control agents to brushtail possums in the wild. A crucial aspect to consider for application of nanoparticles in wildlife control that is yet to be addressed is the stability of the nanoparticles under field conditions.

Utilizing the technique of microfluidics with a staggered herringbone configuration, we have synthesized poly-lactic-*co*-glycolic acid (PLGA) nanoparticles with an average size of 242 nm and zeta potential of -15 mV. The encapsulation of D-Lys^6-GnRH in PLGA nanoparticles was performed using an *in situ* microfluidics approach and quantified using RP-HPLC. Encapsulation efficiency of D-Lys^6-GnRH in PLGA nanoparticles was 92.20 ± 1.07%. The size, PDI and zeta potential of D-Lys^6-GnRH-loaded nanoparticles was approximately 220 nm, 0.14, and -9 mV, respectively.

To assess the stability of the drug-loaded nanoparticles, two different stability tests will be performed: one in controlled conditions and one in field conditions. The drug-loaded nanoparticles will be incubated under different temperatures and humidity, where the controlled conditions will follow the ICH guidelines for accelerated stability studies. To evaluate the stability in field and controlled conditions, RP-HPLC will be used to measure the degradation D-Lys^6-GnRH.

We have demonstrated that D-Lys^6-GnRH can be entrapped efficiently in PLGA nanoparticles using microfluidics. This information along with field stability are important for the development of nanomedicines for use in wildlife control.

[1] McDowell, A.; et al. *Advanced Drug Delivery Reviews* **2007**, 59, 1121-32.
[2] McDowell, A.; et al. *New Zealand Veterinary Journal* **2009**, 57, 370-7.
[3] Eymann, J.; et al. *Reproduction, Fertility and Development* **2007**, 19, 899-909.