

A Tunable Nanoparticle-based Botulinum Toxin Formulation for Extended Duration of Therapeutic Effect



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Introduction

- Botulinum toxins (BoNT) are increasingly popular neuromodulators with an array of aesthetic and neurological indications.
- BoNT has limited duration of effect (8-12 wks.), requiring frequent redosing causing inconvenience, increased cost, and heightened risk of complications for patients.
- Aim: Nanoparticle-based delivery system to extend BoNT release, characterize its release profile, assess the kinetics of neuromodulation *in vivo*, and understand its effects at the neuromuscular junction.

Methods

- Botulinum toxin A (BoNTa) neuromodulators were encapsulated within polymeric nanoparticles (NPs) using a kinetically controlled microfluidic assembly method
- Neuromodulator formulations were injected into a rat forelimb model and grip strength was assessed weekly for 20 weeks
- Histological quantification of neuromuscular junctions was performed at 1 hour, 2 days, 2 weeks, and 6 weeks after administration of neuromodulators.

Figure 1: Sustained Release of NPs

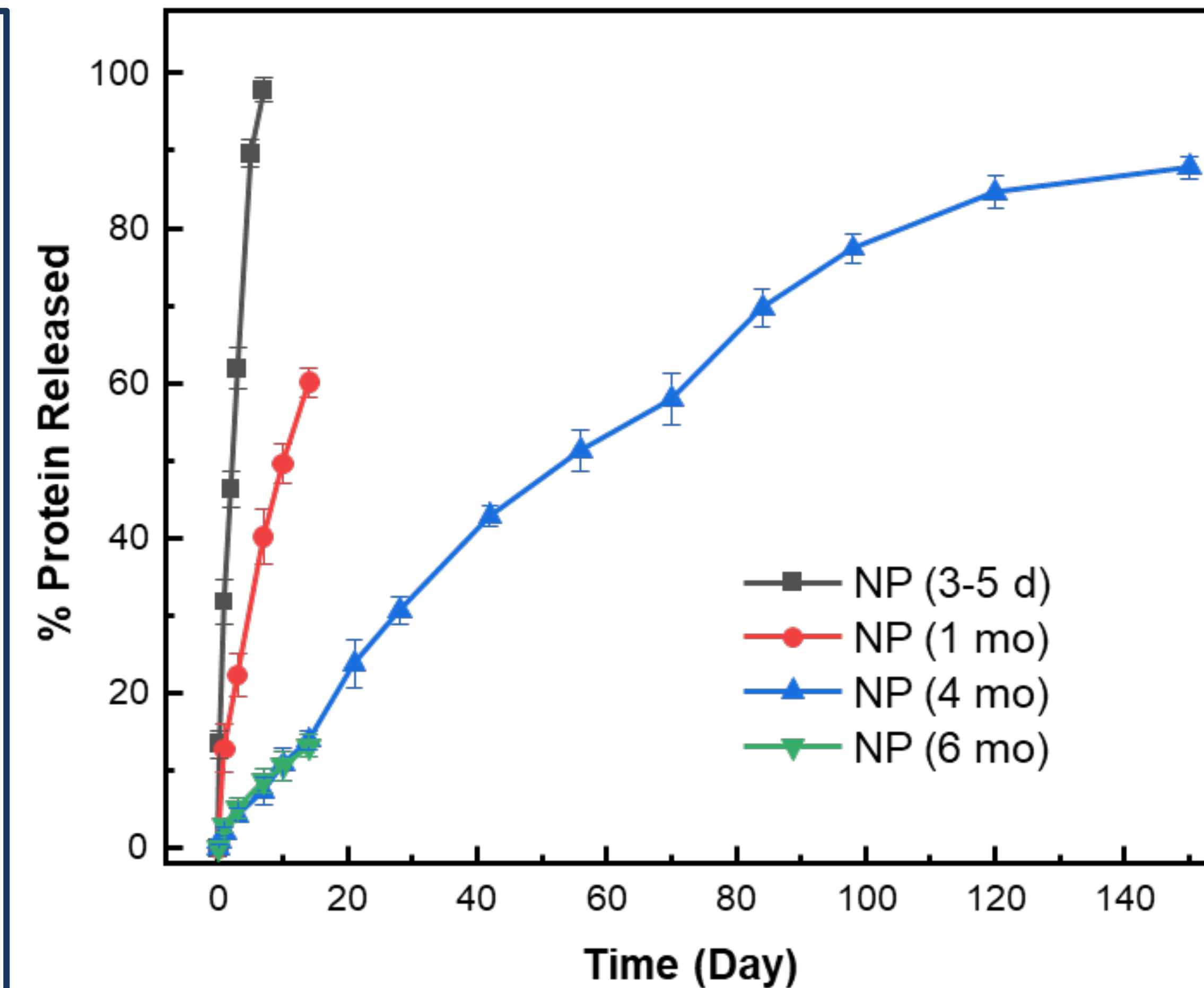
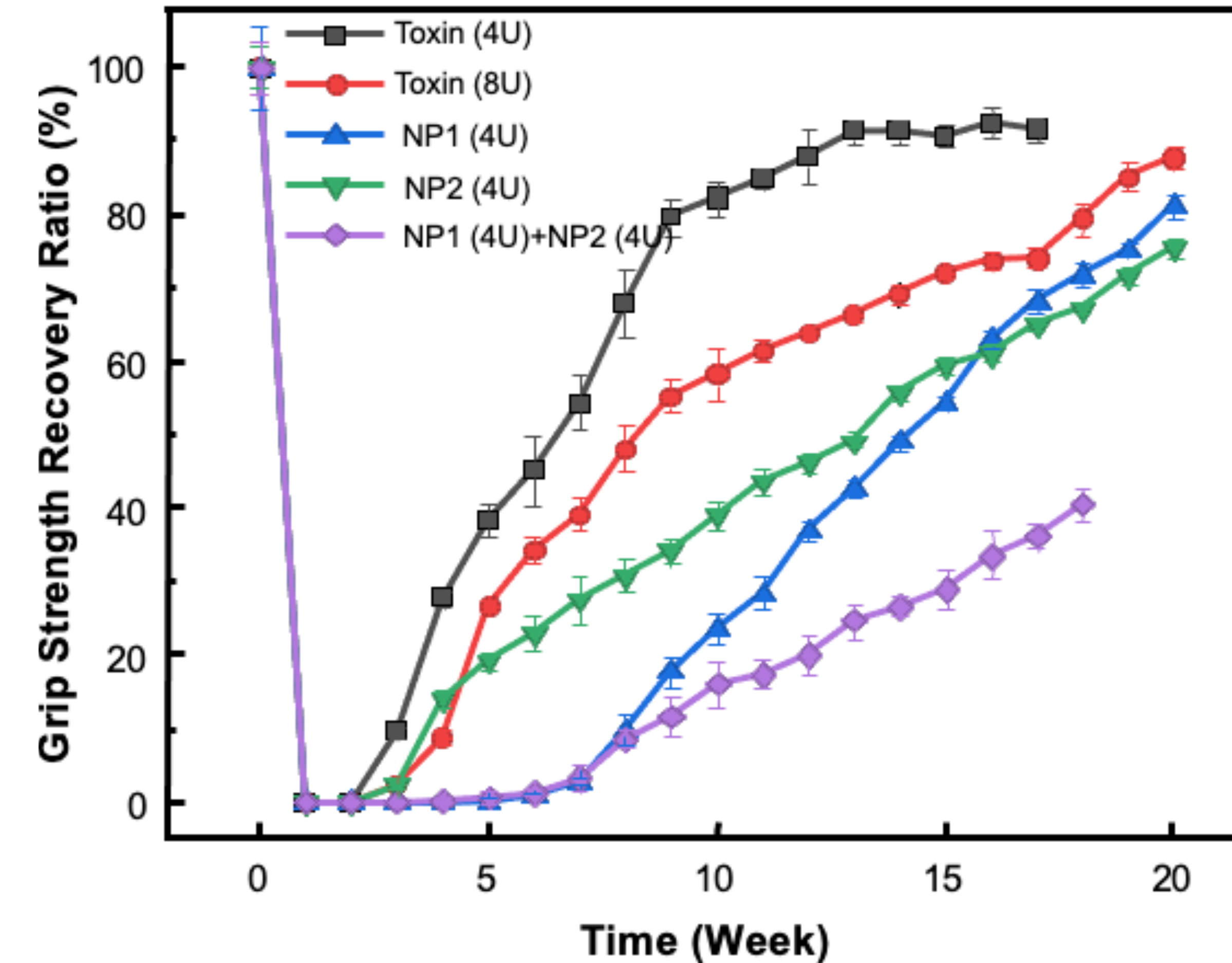


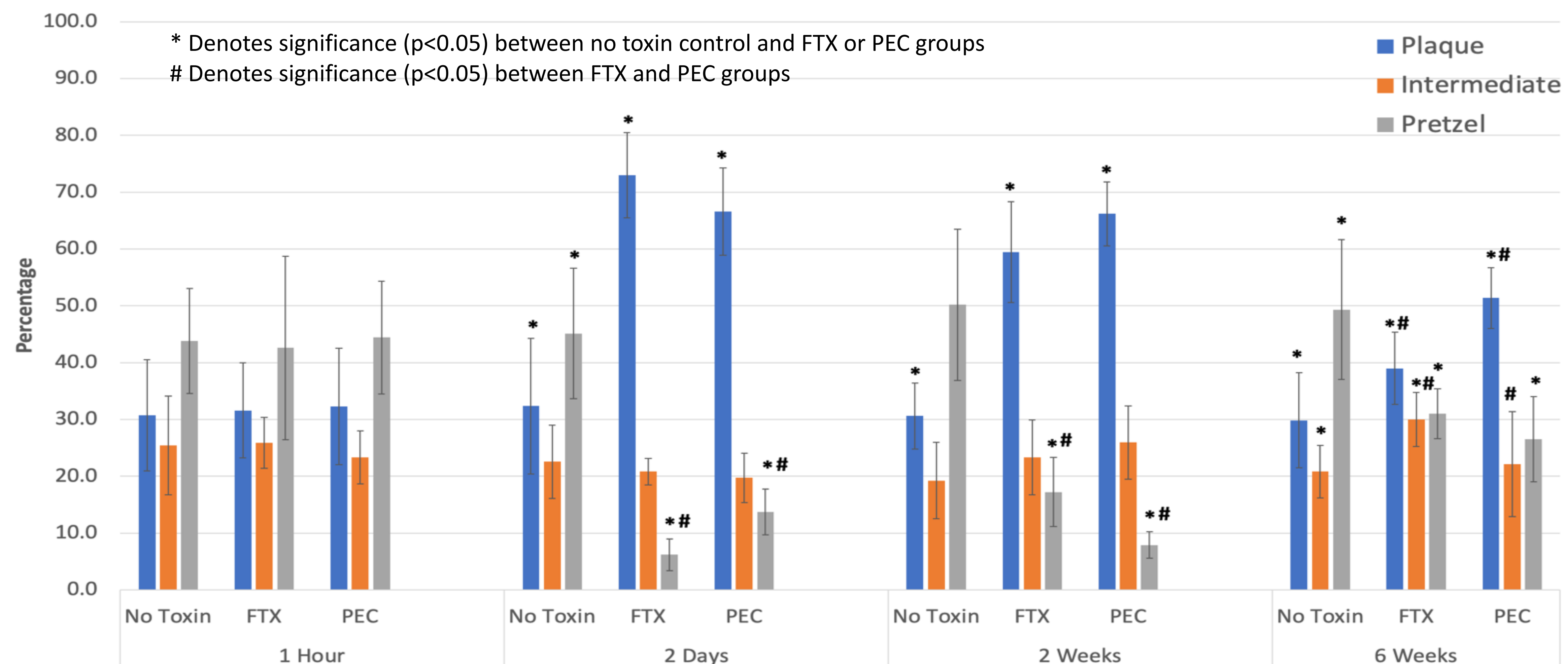
Figure 2: Functional Recovery



Results

- A tunable release profile was achieved, in which BoNTa could be released linearly or with an initial bolus followed by sustained release at the desired rate (Figure 1)
- In vivo* studies demonstrated extended duration of therapeutic effect in a rat model (Figure 2)
- BoNTa and NP1 had a significantly greater proportion of immature neuromuscular junctions (“plaques”) and a smaller proportion of mature neuromuscular junctions (“pretzels”) than the no toxin control starting at 2 days and continuing at 2 weeks and 6 weeks after administration (Figure 3)
- These data align with our functional grip testing results and support that the botulinum toxin formulations are likely to cause paralysis by decreasing the proportion of mature (i.e., fully functional) neuromuscular junctions.

Figure 3: Neuromuscular Junction Morphological Analysis



Conclusion

- We developed a novel nanoparticle-based botulinum toxin formulation capable of providing long-acting release of neuromodulator with tunable kinetics at designated dosage
- This sustained release delivery modality enables superior therapeutic outcomes with less frequent re-dosing.

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