Biodistribution, Pharmacokinetics and Acute Toxicity of Disulfide Crosslinked P(AAm-co-MAA) Nanogels

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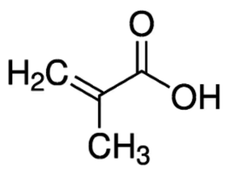
NEURO IMMUNO ENGINEERING COLLECTIVE

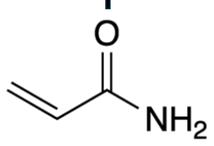
INTRODUCTION

Our Goal is to evaluate pharmacokinetics (PK), biodistribution (BD), and acute toxicity study of Poly (acrylamide-co-methacrylic acid) Nanogels as a potential platform delivery system

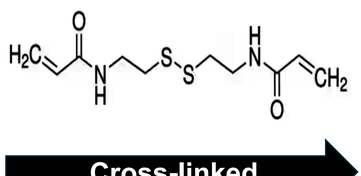


Methacrylic Acid (MAA)

+

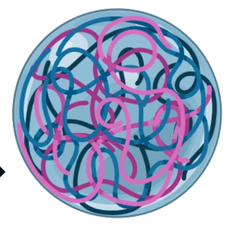


Acrylamide (AAm)



Cross-linked

N,N′-bis(acryloyl) cystamine



Poly(acrylamide-co-methacrylic acid) Nanogels

Clinical Translation

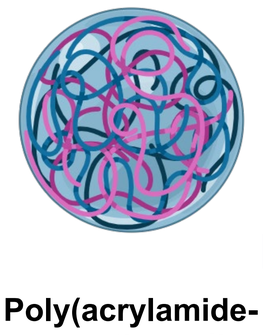
- **Pharmaco-kinetics (PK)**
- **Bio-distribution (BD)**
- **Toxicity**

Key Features

- **Highly tunable**
- **Stimuli responsive (pH)**
- **High Drug loading for hydrophilic molecules**
- **Robust synthesis**
- **Biocompatible**

METHODOLOGY

Nanogels were synthesized by inverse emulsion polymerization. Alexa647 was conjugated via EDC/NHS reaction

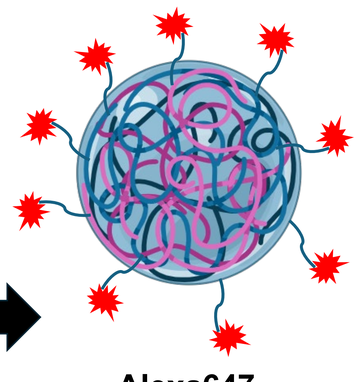


Poly(acrylamide-co-methacrylic acid) Nanogels

Alexa 647

Cross-linked

EDC/NHS reaction



Alexa647 conjugated Nanogels

Mice: C57BL/6
Routes: I.V. and IP
Dose: 10mg/kg of body weight
Control: Saline

Blood and tissues collection: 1h, 6h, 24h and 48h

- **Pharmaco-kinetics (PK)**
- **Bio-distribution (BD)**

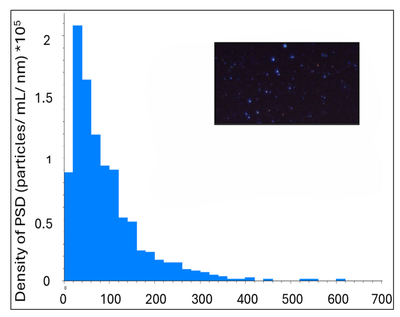
Blood and tissues collection: Day 1 & 7

- **Systemic immunogenicity**
- **Histology**
- **Blood Chemistry**

RESULTS

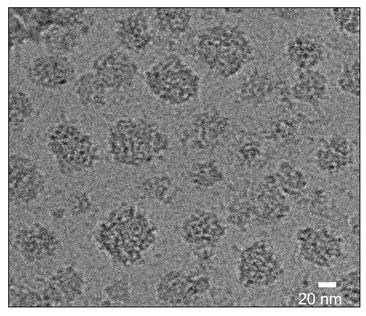
Characterization of Nanogel

NTA



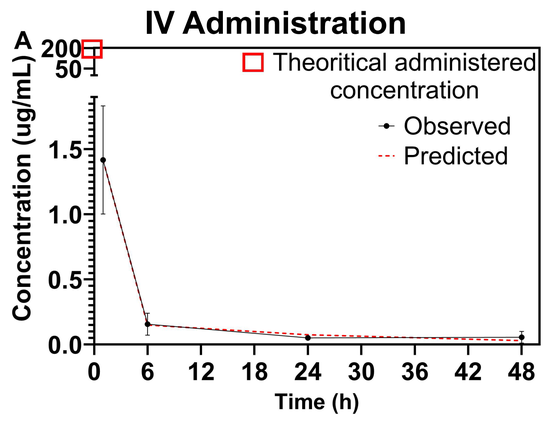
Mode Size: 75 nm

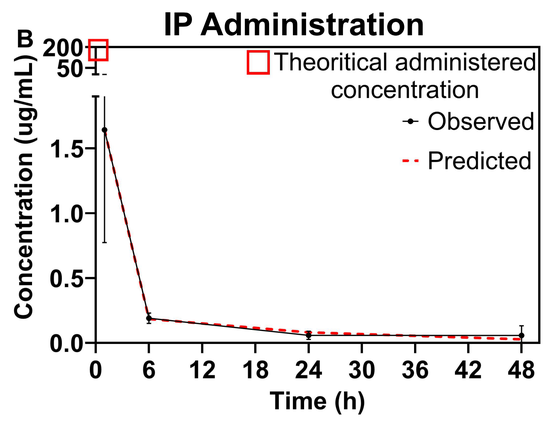
Cryo-EM



Rough, spherical particles

Pharmacokinetics Study

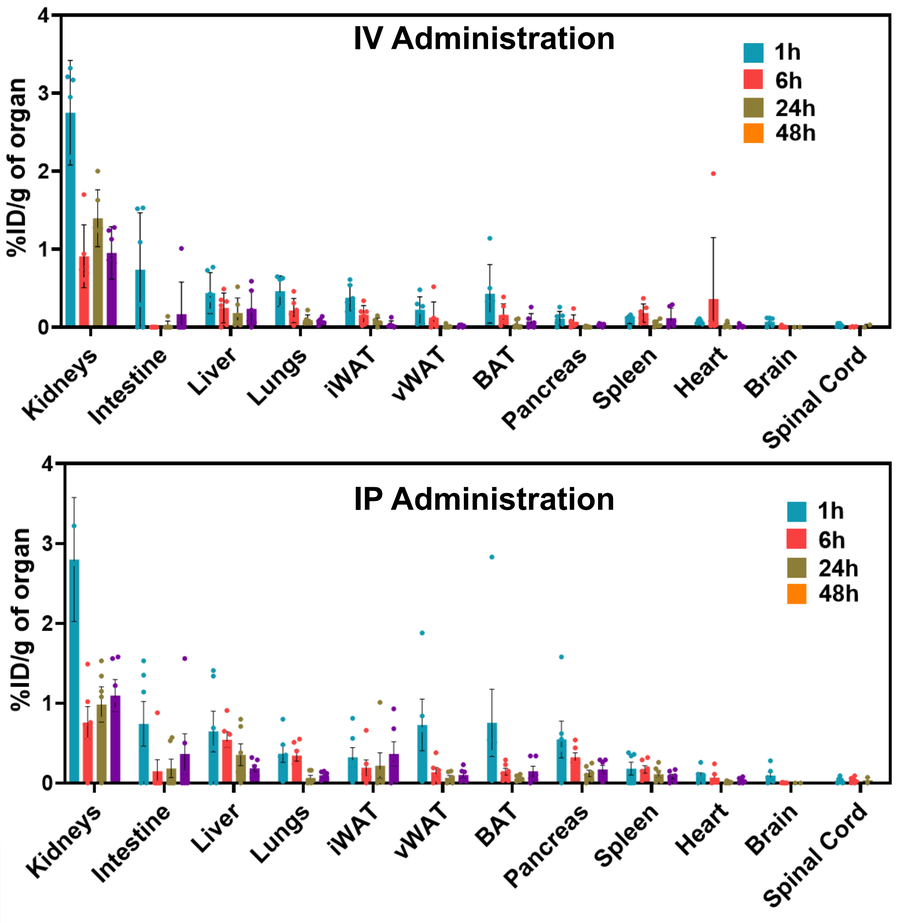




Parameters	IV	IP
T1/2 α (h)	0.14	0.14
T1/2 β (h)	18.23	15.24
CL ((µg)/(µg/ml)/h)	4.52	4.38
CL2 (µg)/(µg/ml)/h)	0.56	0.57
AUMC (µg/ml*h^2)	137.63	125.04
MRT (h)	3.11	2.74

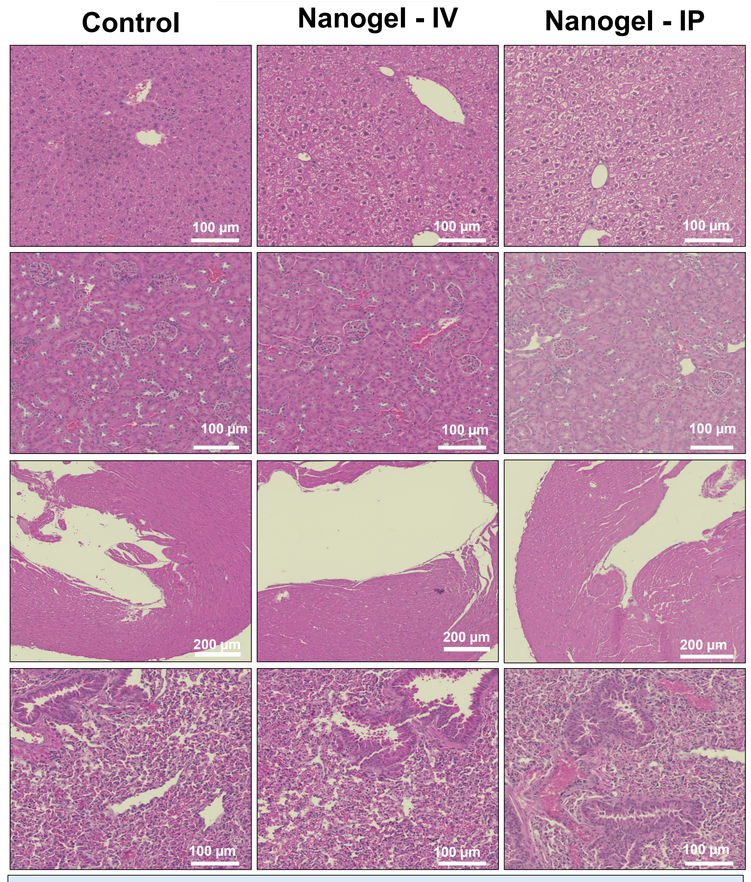
P(AAm-co-MAA) Nanogel is efficient in both distribution and elimination via both routes

Biodistribution Study



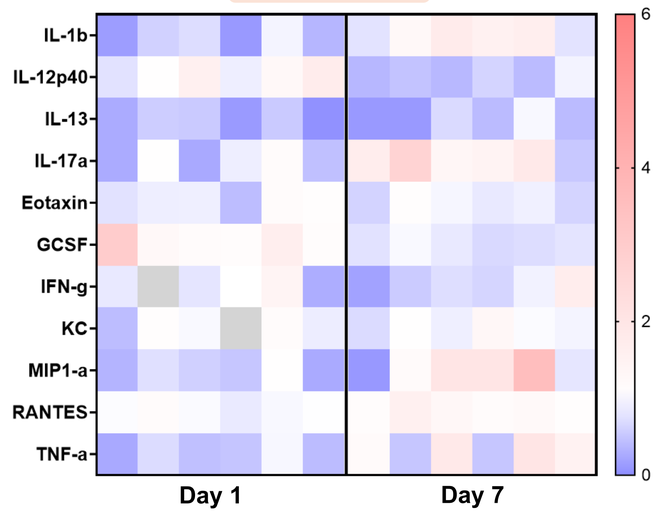
P(AAm-co-MAA) Nanogel accumulation via IV and IP: Kidneys > Intestine > Liver > Lung

Acute Toxicity

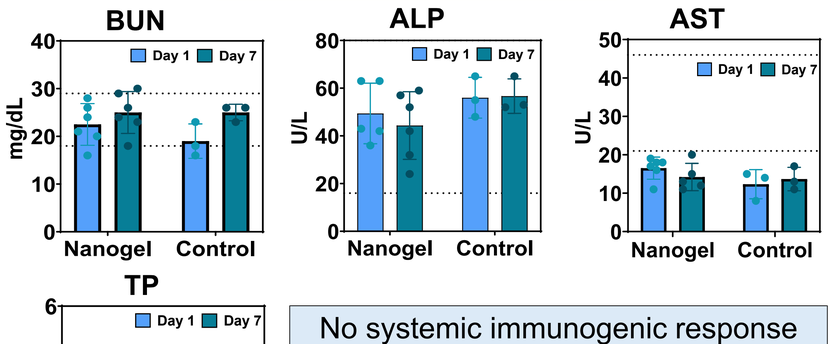


Normal tissue morphology. No histopathological changes observed.

Bio-Plex



Biochemical Markers



No systemic immunogenic response after Day 1 and 7.

Kidney, liver and metabolic function markers showed no significant changes compared to control.

CONCLUSION

- Rapid tissue distribution (Vss ~14mL, t1/2α: 0.14h) and efficient renal clearance (CL: ~4 mL/h) suggests **potential for target distribution and safe repeat dosage regime**.
- **Targeted biodistribution:** Primary accumulation in kidney, followed by intestine, liver, suggest efficient clearance pathways.
- **Favorable safety profile:** No remarkable immunogenic response observed in Bio-plex analysis. Liver, Kidney, and total protein markers similar to control. Histology showed no sign of tissue damage in major organs
- **These findings highlight the nanogel's promising therapeutic potential with a strong safety margin.**

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