

Quercetin Mitigates ALNP-Induced Cognitive and Hippocampal Damage via Akt/GSK3 β Pathway Modulation

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BACKGROUND

- Human exposure to **aluminum nanoparticles (ALNPs)** is increasing via consumer, cosmetic, and industrial products.
- **ALNPs cross the blood–brain barrier** and accumulate in hippocampal circuits.
- Hippocampal ALNP accumulation triggers **oxidative stress, neuroinflammation, and tau/A β abnormalities**.
- The **Akt/GSK3 β signaling pathway** is a key regulator of **synaptic plasticity** and is disrupted in **Alzheimer's disease**.
- **Quercetin**, a dietary flavonoid, has **antioxidant, anti-inflammatory, and anti-amyloid** properties.
- Its protective effect against **acute ALNP-induced hippocampal damage** is not fully characterized.

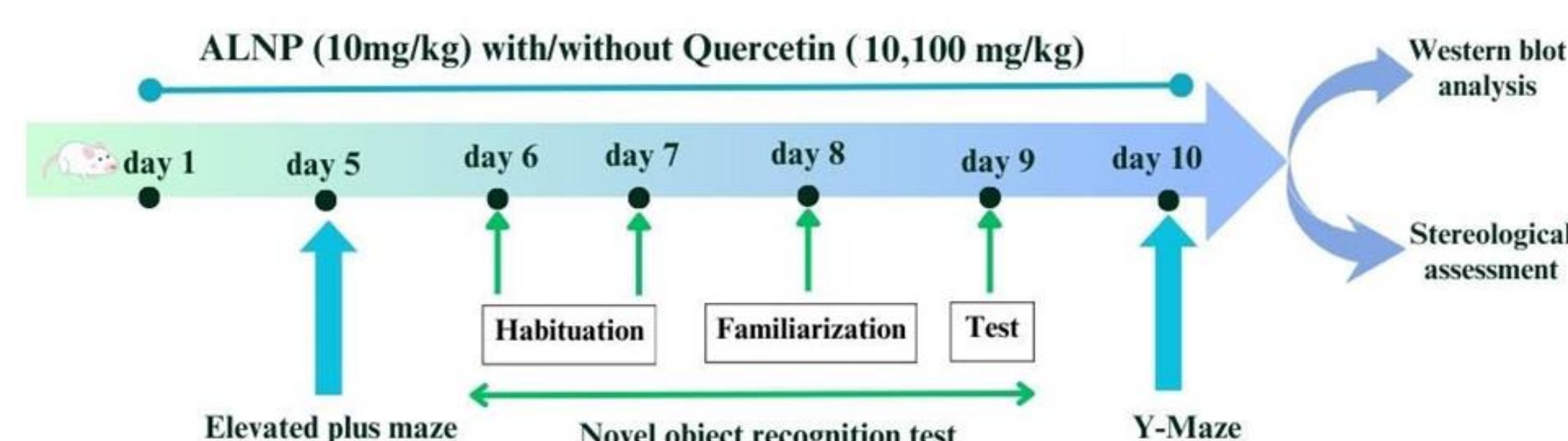
OBJECTIVE

- To evaluate whether **quercetin prevents ALNP-induced hippocampal-dependent memory deficits**.
- To determine the effect of quercetin on **Akt/GSK3 β signaling** and **hippocampal neuronal integrity**.

METHODS

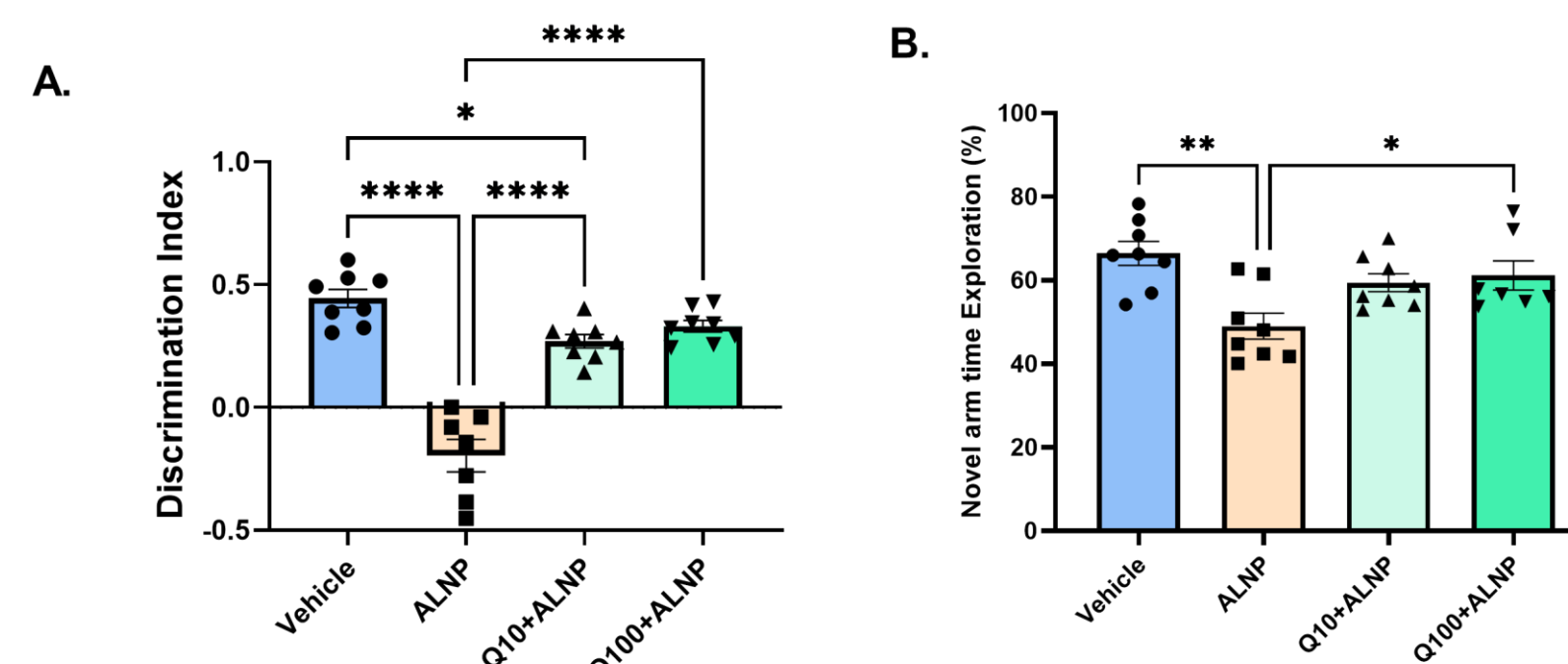
- **Animals:** Adult male Swiss mice, 4 groups
- **Groups:** Control | ALNP (10 mg/kg, i.p.) | ALNP + Quercetin 10 mg/kg | ALNP + Quercetin 100 mg/kg
- **Duration:** 10 days, daily oral quercetin
- **Behavioral Tests:**
 - Day 5: **Elevated Plus Maze** (anxiety)
 - Days 6–9: **Novel Object Recognition (NOR)** (recognition memory)
 - Day 10: **Y-Maze** (spatial memory)
- **Post-Mortem Analyses:**
 - **Unbiased stereology:** CA1 & dentate gyrus, neuronal counts
 - **Western blot:** p-Akt, GSK3 β

FIGURE 1 – Experimental Design Flowchart



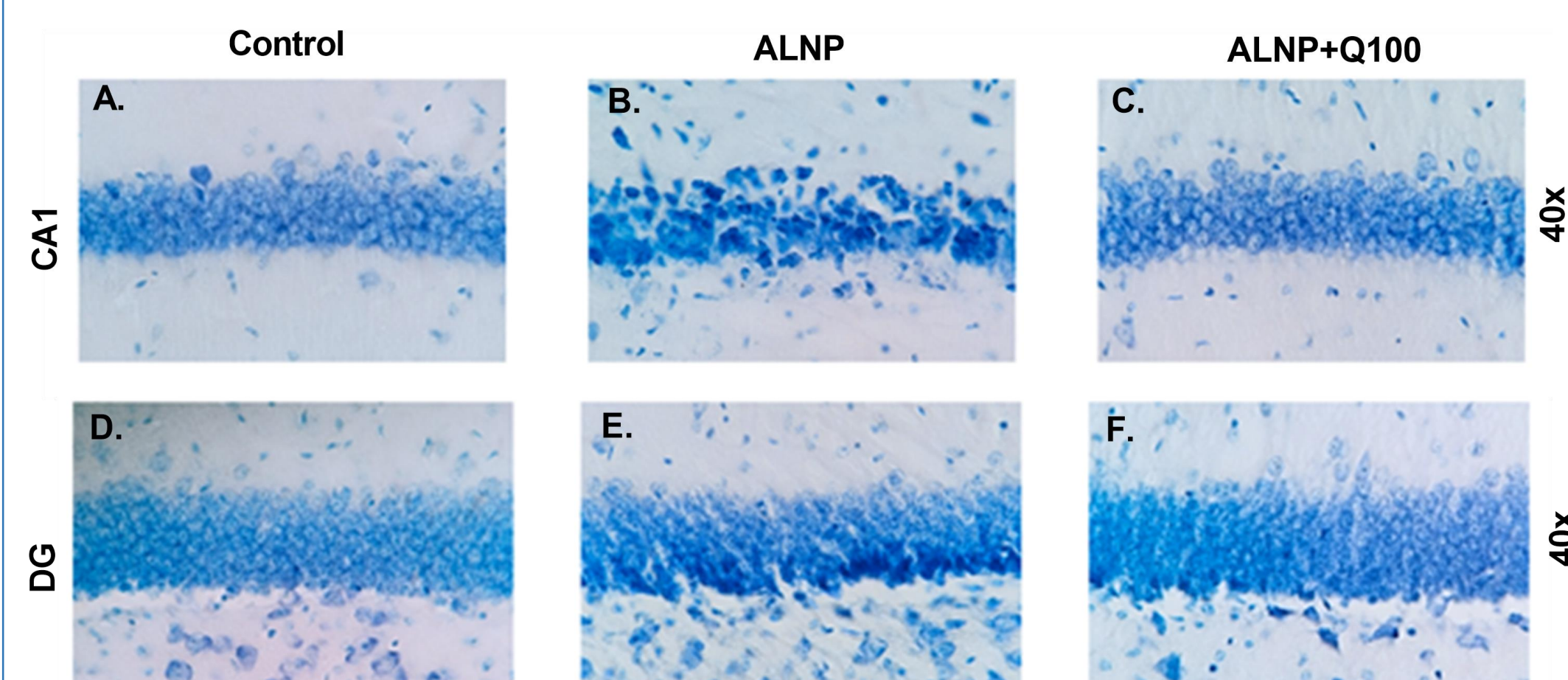
RESULTS

FIGURE 2 – Behavioral Graphs



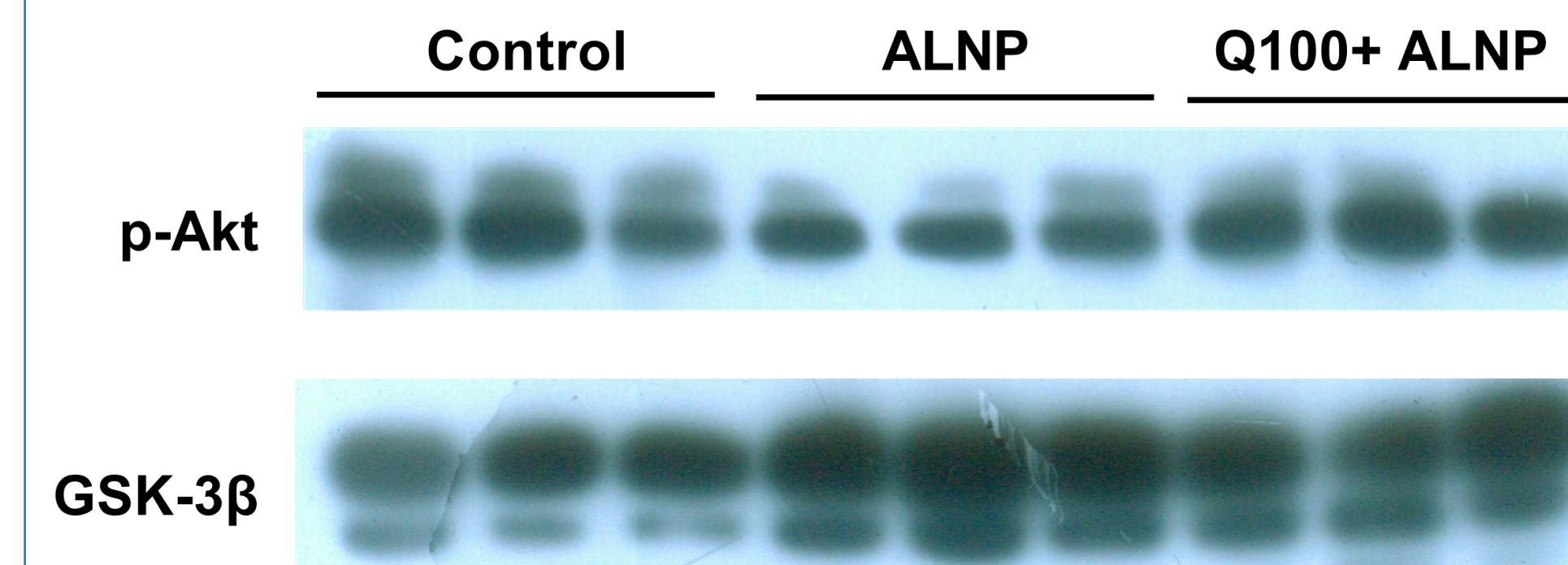
- **ALNP significantly impaired** recognition memory and spatial memory ($p < 0.01$ vs. Control).
- **Quercetin 100 mg/kg fully prevented** both memory deficits.
- Quercetin 10 mg/kg showed partial, non-significant protection.
- No effect on **anxiety-like behavior** in any group.

FIGURE 3 – Stereology: CA1 & DG Neuronal Count



- **ALNP significantly reduced** CA1 and dentate gyrus neuronal density.
- **Quercetin 100 mg/kg fully restored** hippocampal neuronal counts.

FIGURE 4 – Western Blot Images



- **ALNP markedly suppressed p-Akt and enhanced GSK3 β** .
- **Quercetin 100 mg/kg normalized Akt/GSK3 β signaling**.

CONCLUSION

- **Acute ALNP exposure** induces hippocampal structural and functional impairments via **Akt/GSK3 β downregulation**.
- **Quercetin at 100 mg/kg** confers strong **neuroprotection** across behavioral, structural, and molecular domains.
- **ALNP exposure** represents a relevant environmental risk factor for **Alzheimer's-related pathology**.
- **Quercetin** is a promising modulator of **Akt/GSK3 β -dependent neurotoxicity**.

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