

Capsaicin enhances hypothermia tolerance and accelerates recovery from hypothermic shock

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INTRODUCTION & AIM

Sub-zero temperatures threaten organismal survival through synergistic cellular damage and ice crystal effects, causing irreversible tissue injury. This phenomenon influences evolution, species distribution, and biomedical fields like cryopreservation. With rising extreme cold events, elucidating cold tolerance mechanisms becomes imperative for understanding adaptation and identifying targets for biodiversity conservation and cryo-pharmaceutical development.

This study examines the cryoprotective role of capsaicin (CS), a natural TRPV channel agonist from Capsicum plants, in *C. elegans*. Capsaicin activates TRPV channels, triggering conserved calcium signaling through the OSM-9/OCR-2 complex, and subsequently engaging downstream DAF-2/DAF-16 insulin and PMK-1 p38 MAPK pathways.

While previous research demonstrated capsaicin's protective effects under mild cold conditions, its efficacy against extreme cold shock remains unexplored. Our investigation reveals that capsaicin significantly enhances post-thaw recovery following both single and repeated cold shocks. These findings not only advance the mechanistic understanding of capsaicin's cryoprotective actions but also provide an experimental foundation for developing capsaicin-based protective strategies.

METHOD

Synchronization of *C. elegans*

Synchronized L1 larvae were obtained through hypochlorite-alkaline lysis of gravid adults, followed by washing, centrifugation, and overnight incubation at 15°C. The larvae were then cultured on NGM plates containing specified capsaicin concentrations and seeded with *E. coli* OP50 at 20°C.

Cold Adaptation Assay

Both capsaicin-treated and control worms were exposed to 4°C for 30 min. Locomotor activity was assessed post-exposure to evaluate the potential protective effect of capsaicin on neuromuscular function and metabolic activity under low-temperature stress.

Recovery Assay After Cold Shock

Capsaicin-treated and control worms were exposed to −20°C for 5 min before returning to room temperature. Recovery capacity was assessed by recording the minimum and maximum time to movement resumption.

Measurement of Locomotor Behavior

Locomotor parameters were quantified under a stereomicroscope: pharyngeal pumping rate was scored as swallows per 20-second interval; body bends were counted when posterior curvature reached maximal alternation; and head thrash frequency was measured in M9 buffer by counting lateral movements over 20 seconds.

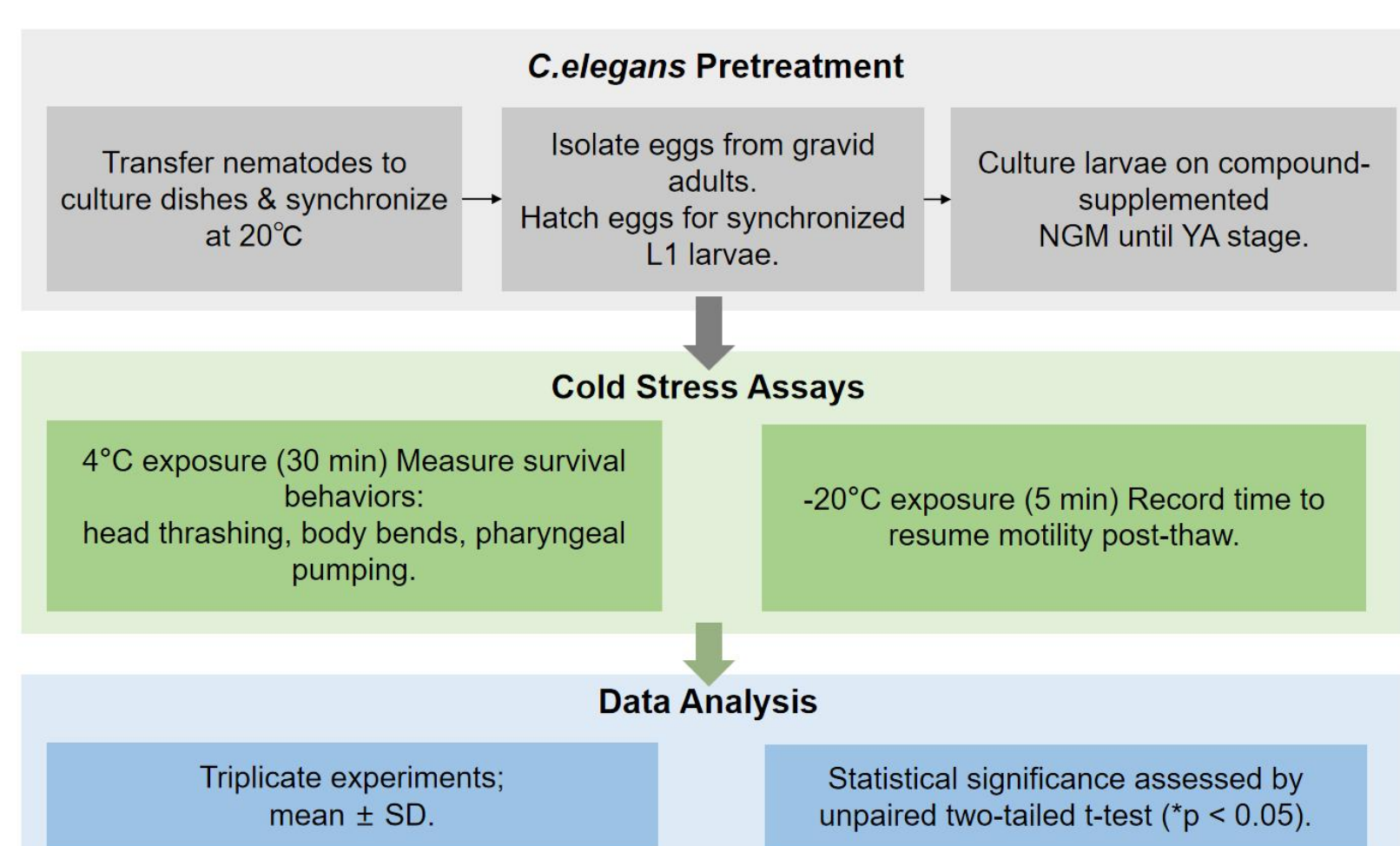


Fig 1. Experimental Design for Capsaicin Investigation

CONCLUSION

Based on our findings, the cold adaptation assay demonstrates that capsaicin significantly enhances pharyngeal pumping, head thrashing, and body bending rates in *C. elegans* following cold exposure, thereby improving locomotor capacity under low-temperature conditions. Furthermore, results from the cryoshock recovery assay indicate that capsaicin not only accelerates recovery from cold shock but also acts synergistically with the organism's inherent adaptive memory mechanism, collectively enhancing self-protection and cold adaptation in *C. elegans*.

RESULTS & DISCUSSION

Capsaicin Enhances *C. elegans* Locomotion under Cold Stress

To investigate the role of capsaicin in protecting *C. elegans* against cold stress, we conducted a cold adaptation assay and measured multiple locomotor parameters following a 30-minute exposure to 4°C. The results are summarized in Figure 2.

Post-chill locomotor analysis revealed that worms reared in capsaicin-supplemented medium from the L1 stage exhibited significantly greater motor activity after cold treatment compared to untreated controls.

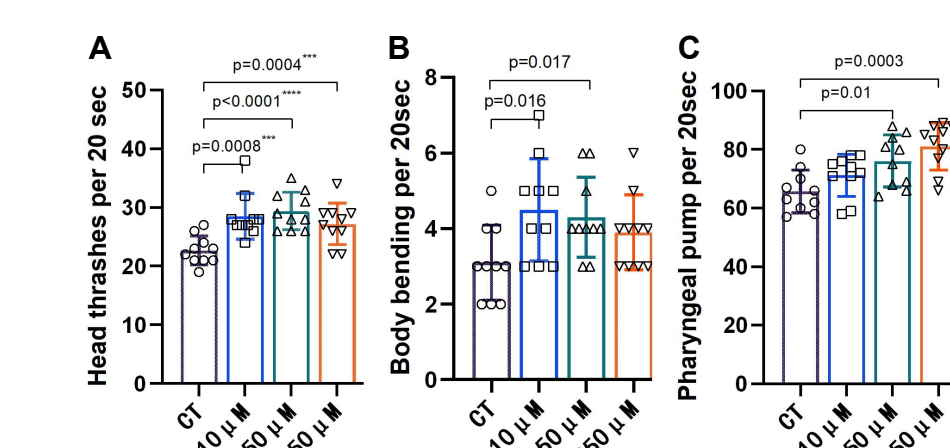


Fig 2. Effect of Capsaicin on Cold Adaptation in *C. elegans*

Capsaicin Enhances *C. elegans* Locomotion under Cold Stress

Exposure of *C. elegans* to −20°C for several minutes induces a cold shock state. Based on evidence that capsaicin enhances low-temperature locomotor activity, we hypothesized that it protects muscular cells and preserves motor function. To evaluate capsaicin's effect on cold shock recovery and adaptation, we performed recovery assays with worms cultured at different capsaicin concentrations (Figure 3).

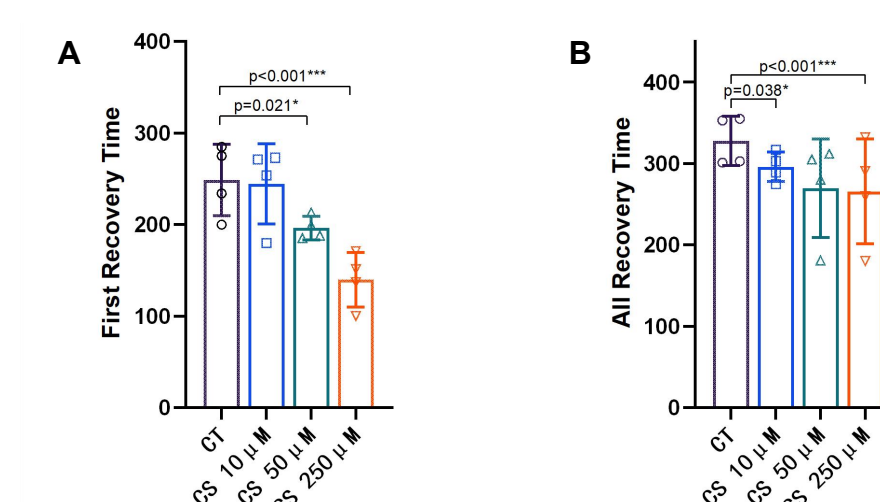


Fig 3. Effect of Capsaicin on Post-Cryoshock Recovery in *C. elegans*

Capsaicin at 250 µM significantly accelerated the time to first recovery by 31.5% compared to controls, indicating rapid neuromuscular activation. While the 50 µM group showed a moderate yet distinct improvement, the 10 µM group remained ineffective. Both 50 µM and 250 µM capsaicin consistently shortened the time to full population recovery by 40.6%, suggesting a coordinated mechanism involving metabolic and neuromuscular pathways.

Capsaicin Enhances *C. elegans* Locomotion under Cold Stress

Repeated cold shocks induced accelerated recovery in *C. elegans*, demonstrating physiological memory for cold adaptation. To test capsaicin's effect on this response, we conducted consecutive cold shock trials with worms pre-treated at varying capsaicin concentrations (Figure 4).

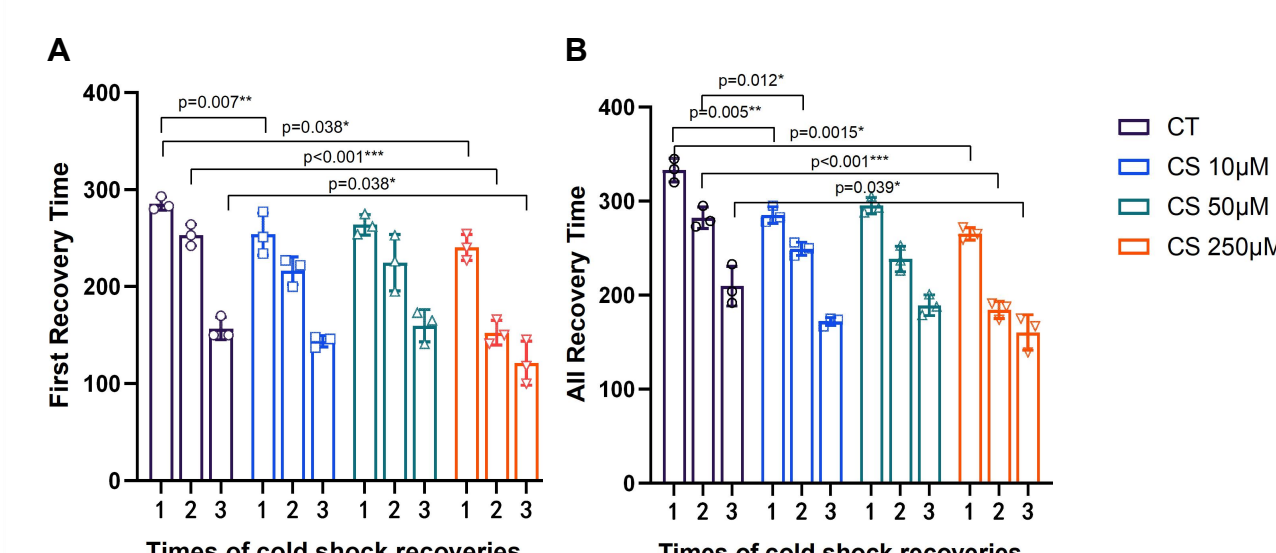


Fig 4. Effect of capsaicin on cryoshock recovery in *C. elegans*

Control worms demonstrated inherent cold adaptation through progressively shorter recovery times, whereas the 250 µM capsaicin group exhibited significantly enhanced recovery, suggesting a synergistic effect with physiological memory.

FUTURE WORK

In subsequent investigations, we will further elucidate the mechanistic basis of capsaicin's effects by integrating genomic sequencing and RNAi-based functional validation to delineate its complete signaling pathway. These findings will be substantiated through complementary bioinformatic analyses to provide a comprehensive interpretation of capsaicin's mode of action.