AI-Guided Discovery of Anti-Inflammatory Peptides from Edible Rhizomes and Root Vegetables

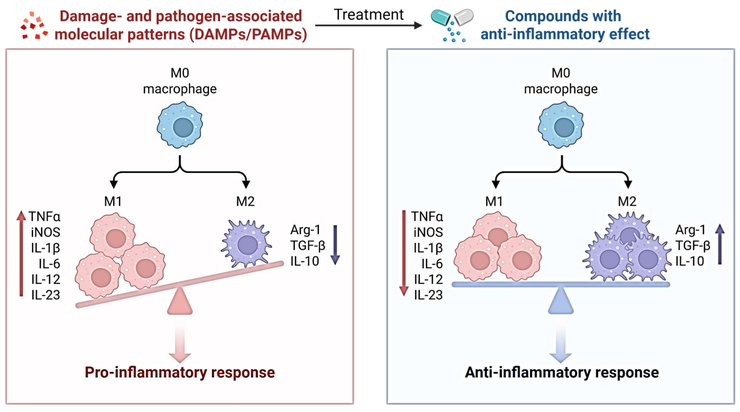
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CONNECT WITH ME

Chronic Inflammation a central driver of metabolic dysregulation & lifestyle-associated disorders [1]



Why Edible Rhizomes & Root Vegetables ?

- Underexplored as sources of bioactive peptides [2,3]
- Recognised in Traditional Medicinal Systems [2,3]

Objectives

- Mine hydrolysates by AI-guided QSAR/QSPR triage (sequence + structure based predictors).
- Validate predicted lead candidate at the bench.
- Resolve bioactivity mechanism across metabolic & proteomic endpoints.

Discovery pipeline — AI as the triage step prioritizes candidates & shrinks the search space

EXTRACT
4 root-vegetable protein matrices
Ginger . Sweet Potato. Red Radish . Purple Carrot

→

HYDROLYSE
15 food-grade protease Configurations
Individual/ Sequential/ Concurrent

→

SEQUENCE
10,049
unique peptides identified by LC-MS/MS

→

AI TRIAGE
36
5 Sequence-based bioactivity predictors + Molecular Docking + Toxicity Predictor

→

VALIDATE
7
Biochemical and cell-based In vitro assays

Nitric oxide Inhibition

Griess assay · LPS-stimulated RAW 264.7 (murine) macrophages

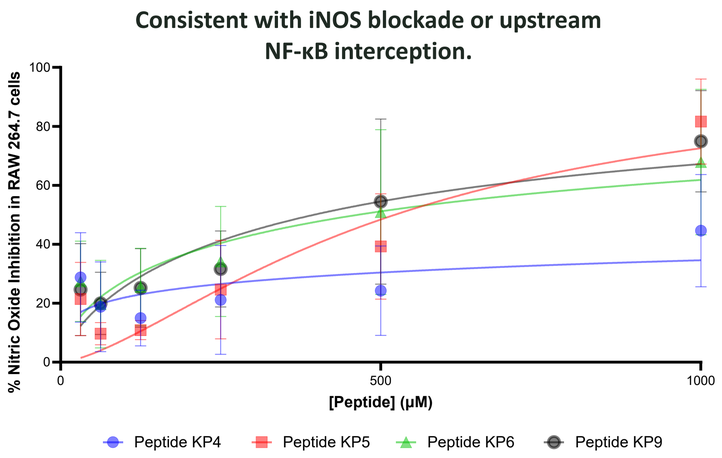


Figure 1. NO inhibition (%) relative to LPS-positive control. Mean ± SEM, n = 9.

Cyclooxygenase-2 Inhibition

Cell-free COX-2 enzyme inhibition quantified via PGE_2 product formation (LC-MS/MS)

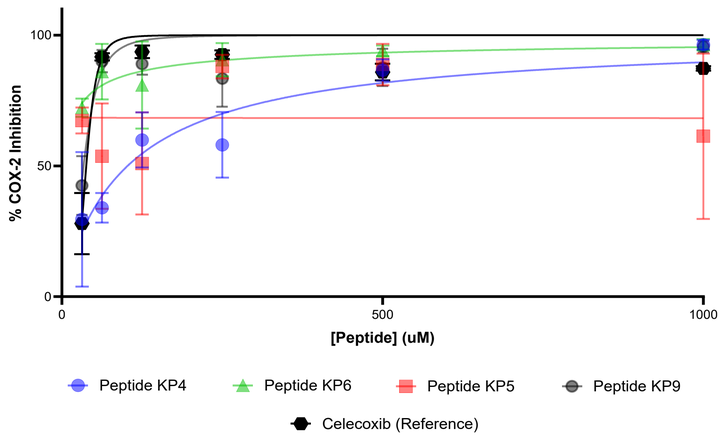


Figure 2. COX-2 inhibition (%) relative to Celecoxib reference. Mean ± SEM, n = 3.

Pro-Inflammatory Cytokine Release

IL-6 and TNF-α ELISA · RAW 264.7 (murine) macrophages

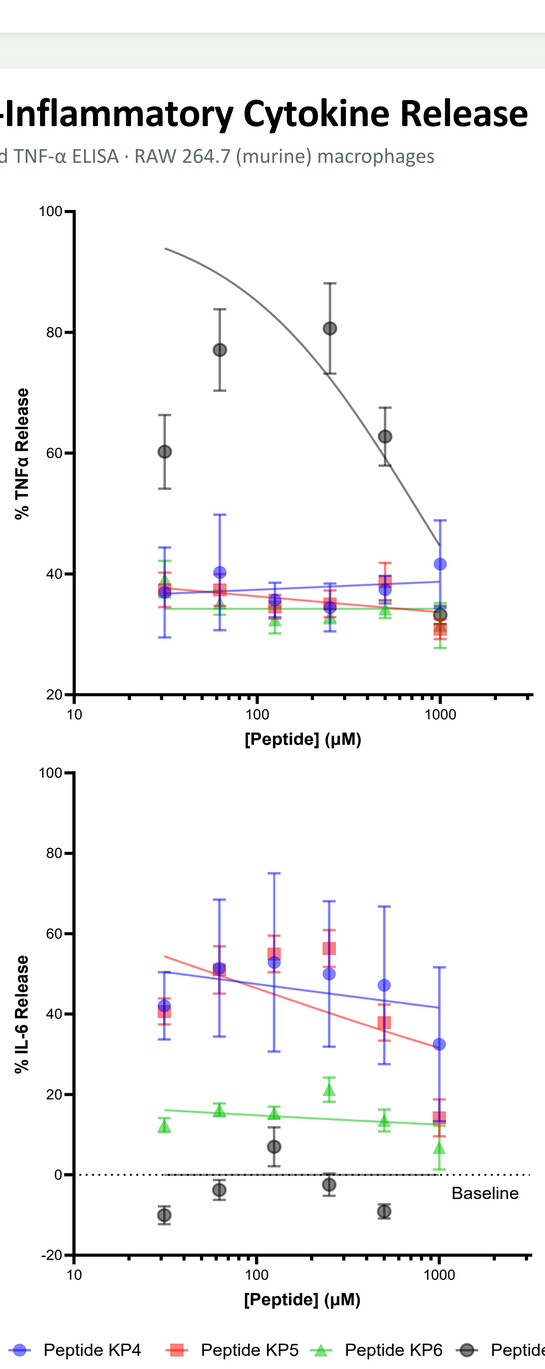


Figure 3. Pro-inflammatory cytokine release in LPS-stimulated macrophages. Mean ± SEM, n = 9.

Dual suppressors: Peptides **KP4**, **KP5** & **KP6** lowered both IL-6 and TNF-α pro-inflammatory cytokines.

Divergent responder: Peptide **KP9** suppressed IL-6 below baseline, while inducing TNF-α

Metabolic reprogramming of inflamed macrophage

LPS-stimulated RAW 264.7 (murine) macrophages

Figure 4. Untargeted metabolomics of peptide-treated versus LPS-stimulated macrophages. (A) PCA scores. (B) Profiling for NO-pathway metabolite changes (top 25 abundant metabolites).

Peptide KP4 Anti-inflammatory pathway enrichment

Peptide KP9 Pro-inflammatory pathway blockade

Peptide KP6 Distinct reprogramming, unrelated to LPS reversal

Mechanistic Evaluation

Tail MM/GBSA binding free energies across inflammatory targets· Orthosteric vs interfacial binding sites

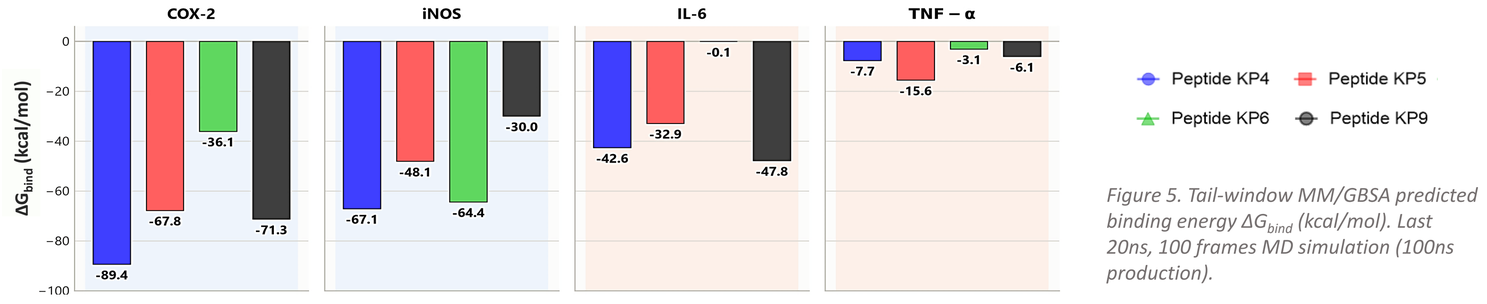


Figure 5. Tail-window MM/GBSA predicted binding energy ΔG_{bind} (kcal/mol). Last 20ns, 100 frames MD simulation (100ns production).

Peptide KP4 is the strongest overall anti-inflammatory lead — dual IL-6/TNF-α suppression, NO inhibition, and dose-dependent COX inhibition — consistent with its most favourable predicted binding across targets.

Peptide KP6 binds the studied targets weakly yet is potently active, suggesting its anti-inflammatory effect is driven through an off-target/alternative mechanism.

Conclusions

- AI triage compressed 10,049 sequences to 36 candidates, 7 of which entered lab validation.
- **4 of 7 leads were active in LPS-stimulated macrophages across Nitric Oxide Pathway, Pro-inflammatory cytokines and Cyclooxygenase endpoints.**
- Root vegetables are a credible, sustainable source of anti-inflammatory bioactive peptide with further implications for metabolic syndrome management.

Next Steps

- Proteomic profiling of peptide-treated inflamed murine RAW 264.7 macrophages (ongoing).
- Replicate metabolic and proteomic analysis in differentiated human THP-1 monocytes (ongoing).
- Antidiabetic and antihypertensive bioactivity profiling – metabolic syndrome.
- Deep mutational scanning to optimise affinity, potency and stability.

SUSTAINABLE DEVELOPMENT GOALS

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References [1] Furman D et al. *Nat Med* 2019; 25:1822–1832. [2] Purohit K et al. *Food Chem* 2025; 484:144432. [3] Purohit K et al. *IJMS* 2024; 25(3):1391.