

From Screening to Mechanism: Curcumin Emerges as a Key Natural Compound Against Israeli Acute Paralysis Virus in *Apis mellifera*

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The honeybee (*Apis mellifera*), a cornerstone species in global ecosystems, sustains biodiversity and agricultural productivity through pollination and bee products generation. However, recent years have witnessed significant threats to honeybee health from diverse factors, including parasites and pathogens. Israeli acute paralysis virus (IAPV) is widely prevalent in honeybee colonies, inducing paralysis and tremors in honeybees that lead to mortality, severely compromising colony health, and is recognized as a critical factor to colony collapse disorder (CCD). Despite its devastating impact, no targeted antiviral therapies are currently available for IAPV management. Natural products, with their structural diversity, multi-target potential, and low environmental toxicity, offer a promising yet underexplored avenue for combating viral infections in honeybee.

In this study, we screened eight natural products (myrcene, citral, menthol, chlorogenic acid, resveratrol, curcumin, quercetin, and tea polyphenol) for their efficacy in reducing IAPV loads in honeybee. By administering these compounds to artificially or naturally IAPV-infected honeybees and quantifying viral titers via qRT-PCR, we identified curcumin as the most effective candidate for significantly suppressing IAPV replication. After 7 days of feeding with a 50% sucrose solution containing 10 μ M curcumin, artificially and naturally IAPV-infected honeybees exhibited significant reductions in viral titers by 46.2% and 84.0%, respectively. Transcriptomic analysis revealed that curcumin upregulated genes associated with nutrient metabolism (Vg, Hex110, Hex70a, Vhdl), suggesting improved physiological resilience, alongside antiviral genes such as Dicer and Argonaute-2 (core RNA interference pathway components) and Tep7 (a gene implicated in pathogen defense). Concurrently, curcumin downregulated antimicrobial peptide genes (Hymenoptaecin, Abaecin, Defensin), indicating a strategic shift in immune resource allocation. These findings indicate that curcumin combats IAPV by enhancing honeybee health and reallocating physiological resources to prioritize the RNAi pathway and other antiviral mechanisms, thereby amplifying targeted viral suppression.

This study identifies curcumin as a novel, eco-friendly candidate for IAPV mitigation. By suppressing viral replication without compromising the safety of bee products, it resolves existing deficiencies in apicultural viral management and provides a sustainable solution to enhance healthy beekeeping practices and ensure the production of safe bee products.

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Background



**Experimental
Design**

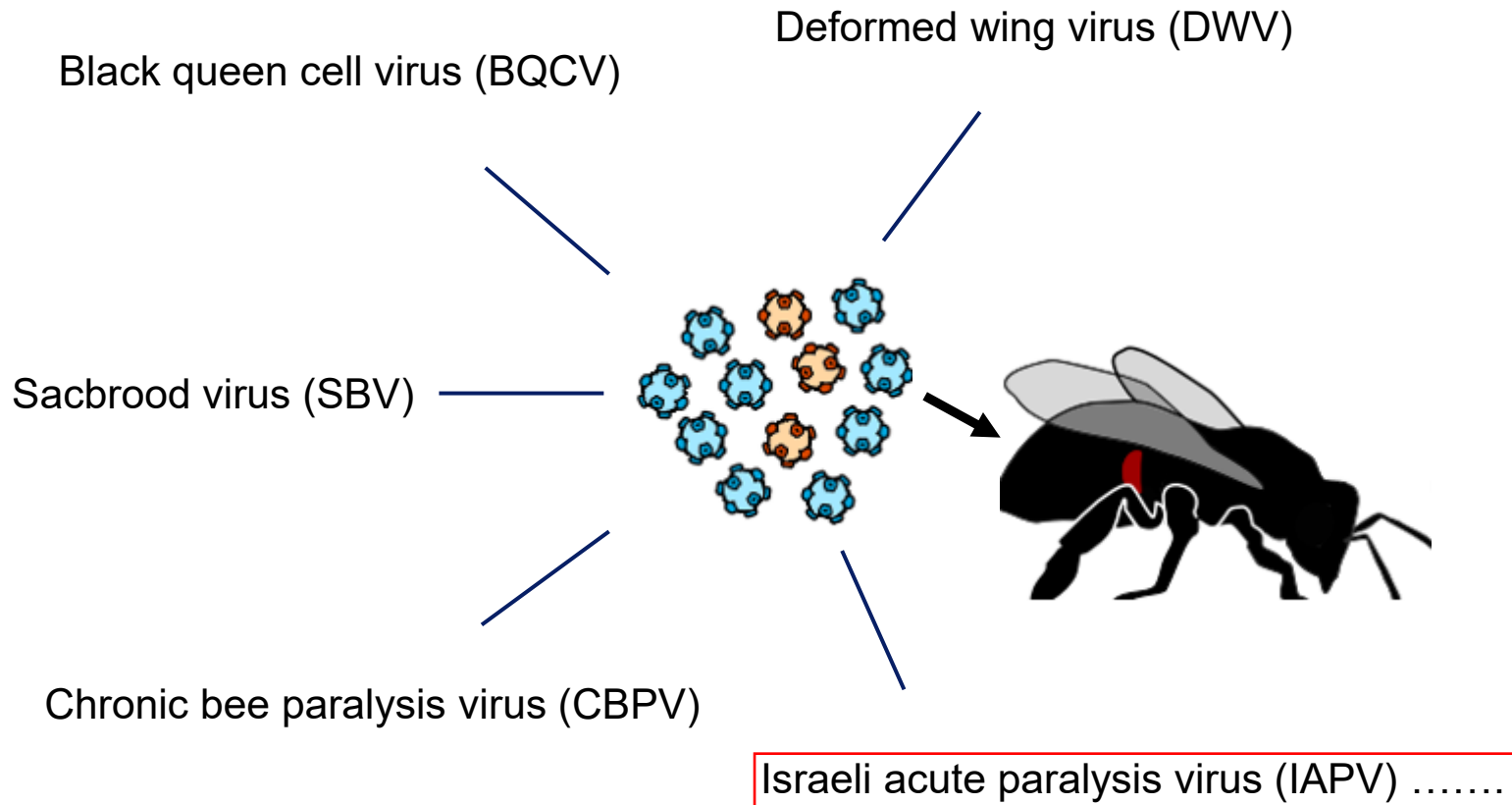


Result



**Conclusion and
Future Work**

Background | Bee Viruses

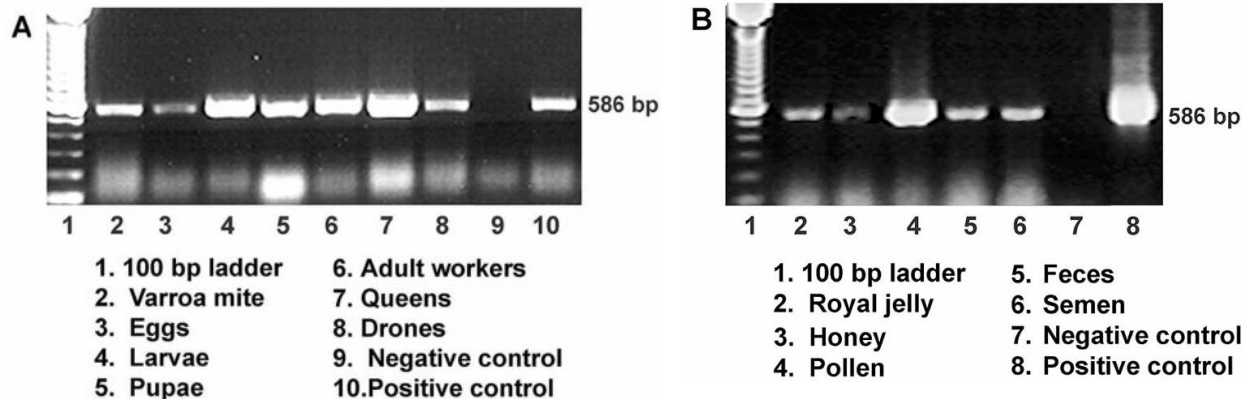


(Traynor *et al.*, 2020, Trends Parasitol)

Background | Israeli acute paralysis virus

Agent	CCD (n = 30)	Non-CCD (n = 21)	Total (n = 51)	Positive predictive value (%)	Sensitivity (%)	Specificity (%)
IAPV	25 (83.3%)	1 (4.8%)	26 (51.0%)	96.1	83.3	95.2
KBV	30 (100%)	16 (76.2%)	46 (90.2%)	65.2	100	23.8
<i>N. apis</i>	27 (90%)	10 (47.6%)	37 (72.5%)	73.0	90.0	52.4
<i>N. ceranae</i>	30 (100%)	17 (80.9%)	47 (92.1%)	63.8	100	19.0
All four agents	23 (76.7%)	0 (0%)	23 (45.0%)	100	76.7	100

(Cox-Foster *et al.*, 2007, Science)



(Chen *et al.*, 2014, PLOS Pathogens)

Background | Natural Compounds Exhibit Diverse Biological Activities



Curcumin



Tea
Polyphenols

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Resveratrol

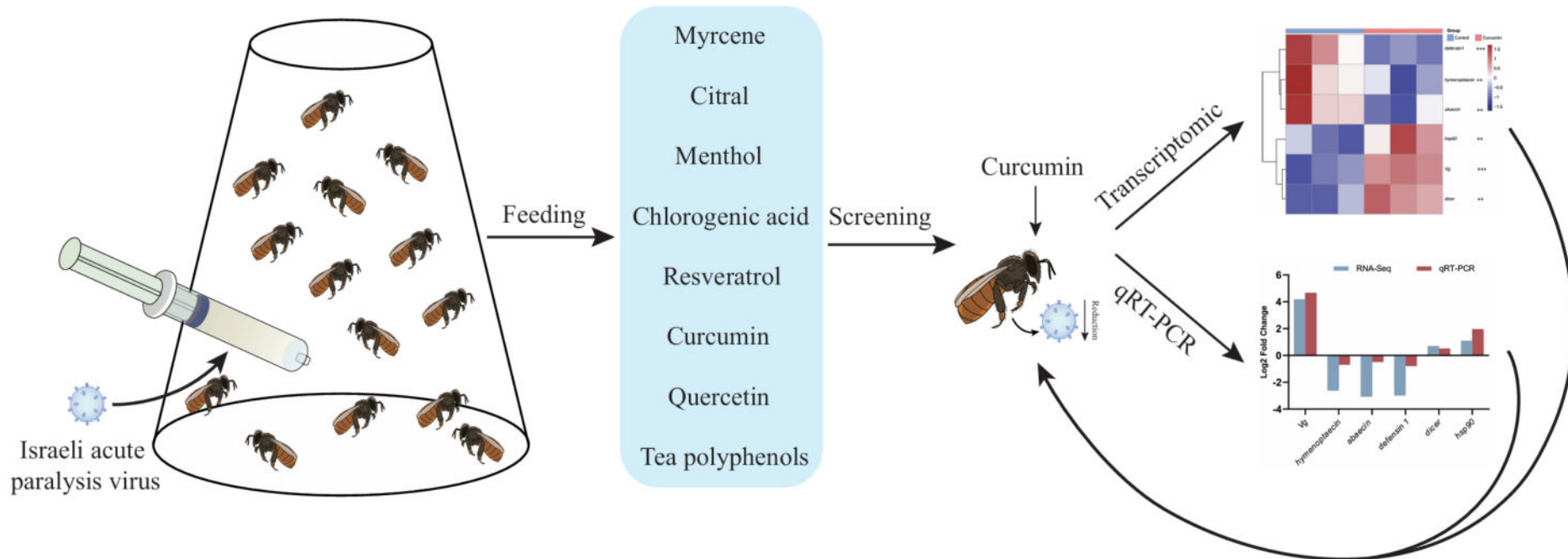
Antioxidant

Anti-
inflammatory

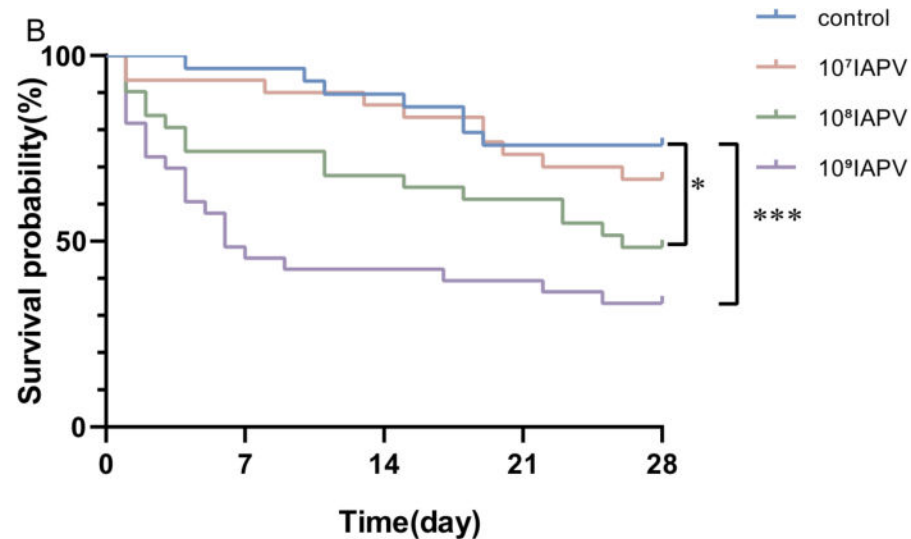
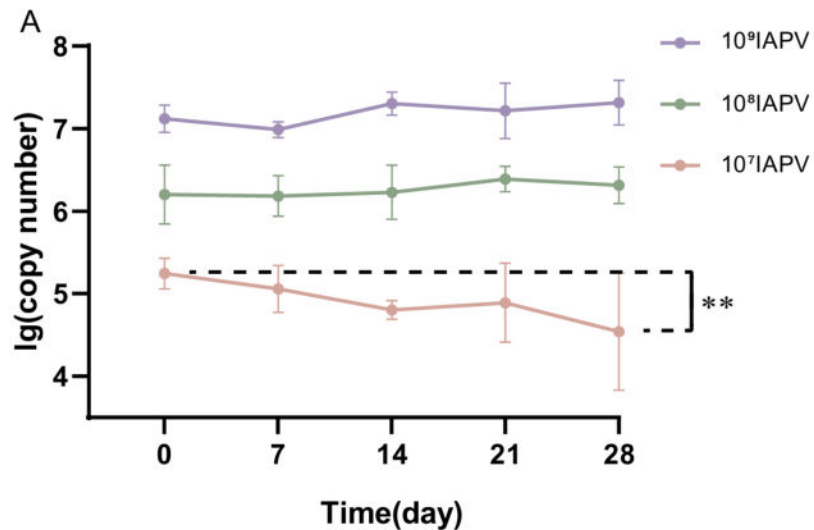
Antiviral

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Experimental Design



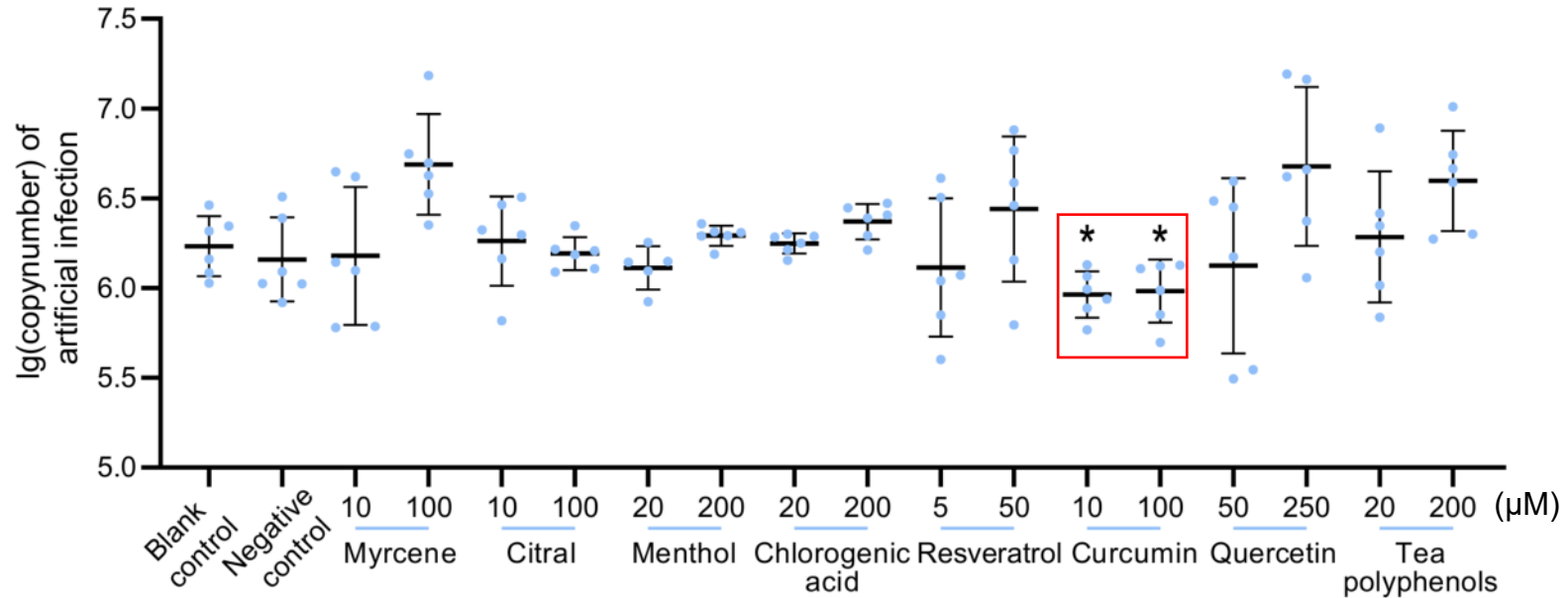
Result | Screening of Experimental Concentrations for IAPV



IAPV inoculum at 1×10^8 copies/ μ L maintains stable titers over time with no severe bee mortality.

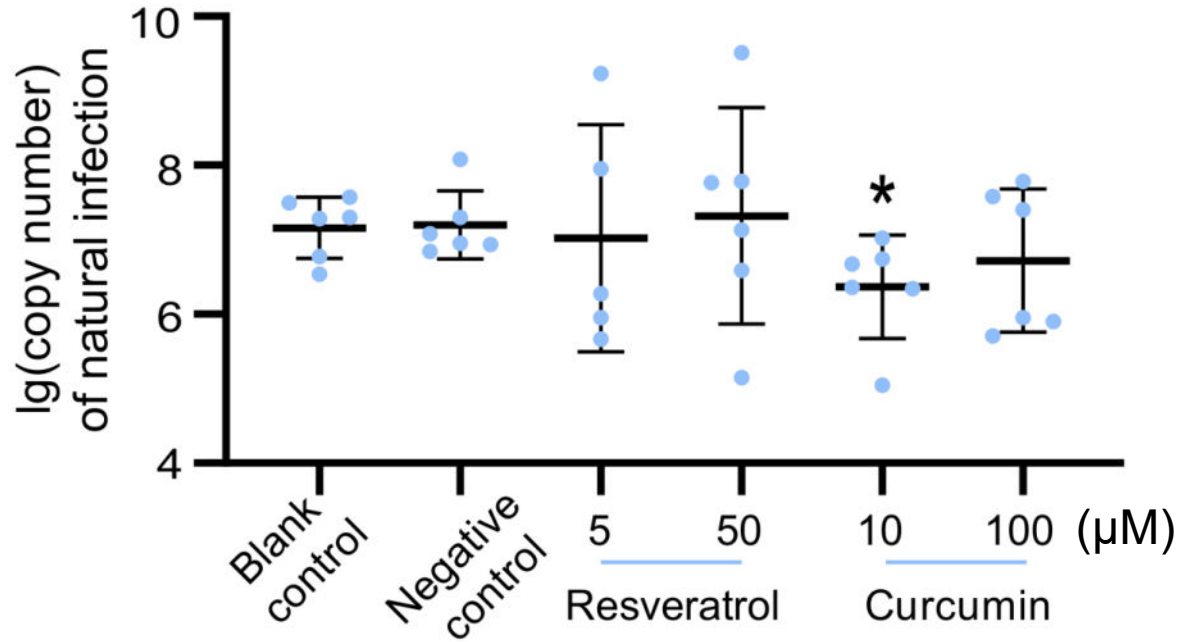
Result

Screening Natural Products for Efficacy Against Artificial IAPV Inoculation



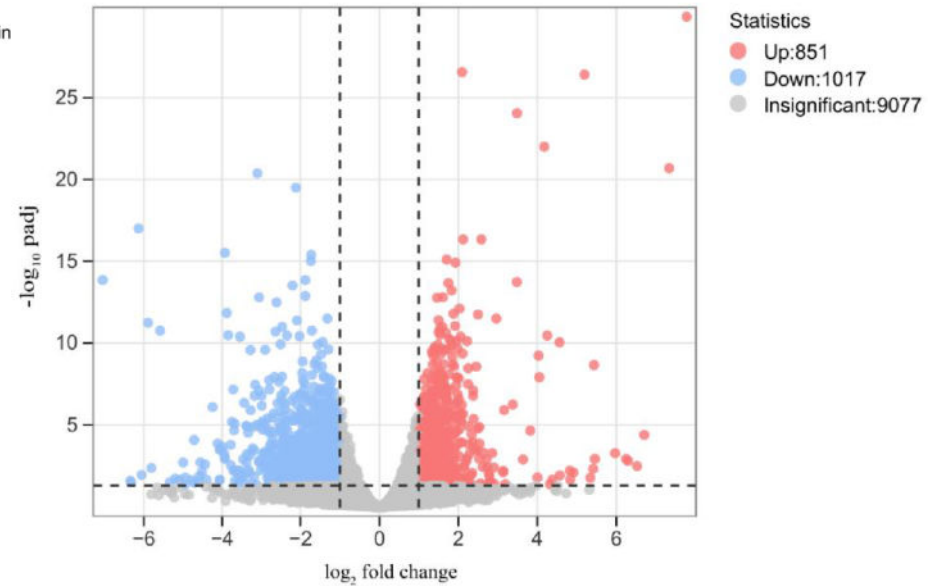
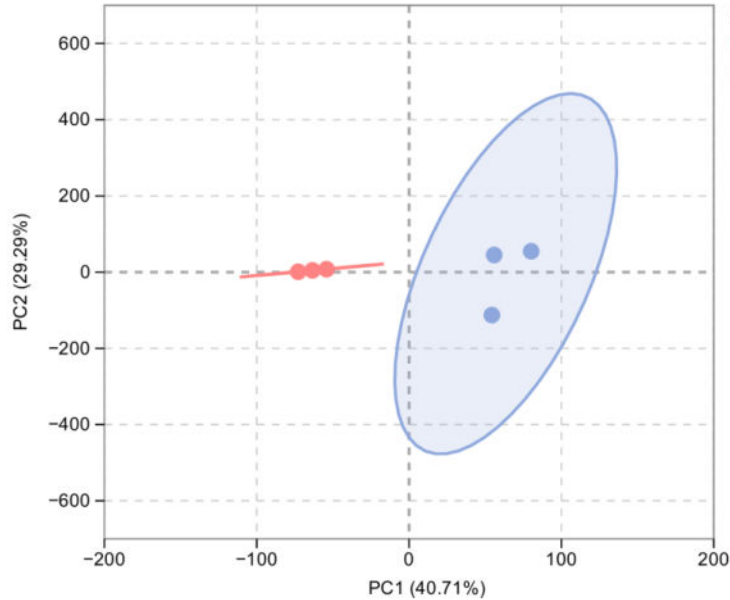
Both concentrations of curcumin significantly reduced IAPV viral load in **laboratory-infected** honey bees.

Result | Screening Natural Products for Efficacy Against Natural IAPV Infection



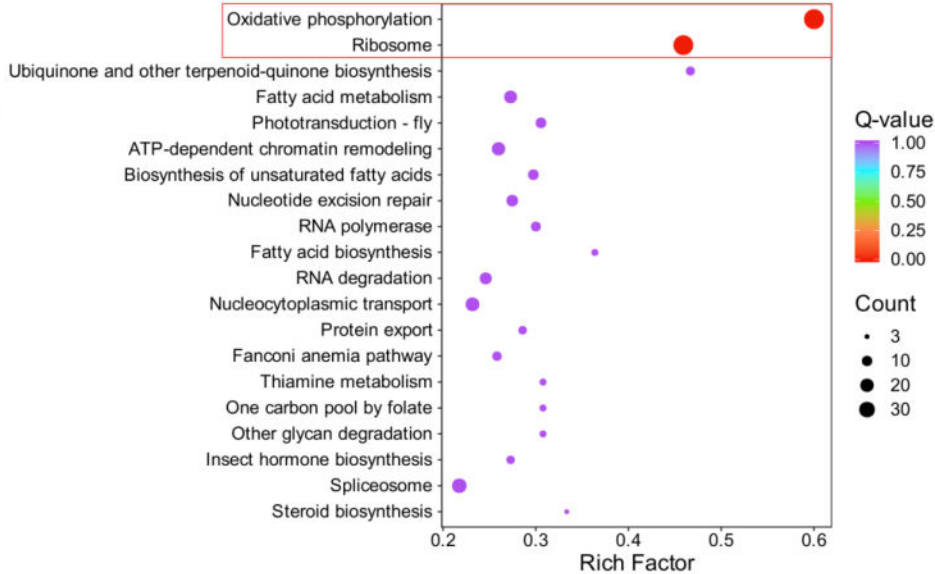
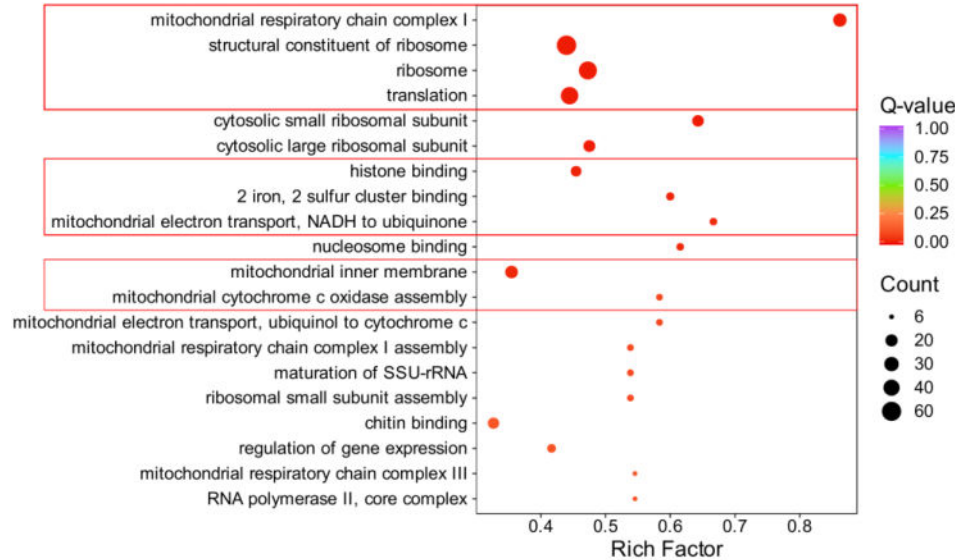
Curcumin feeding at 10 μ M significantly reduced IAPV viral load in **naturally infected** honey bees.

Result | Identification of Differentially Expressed Genes



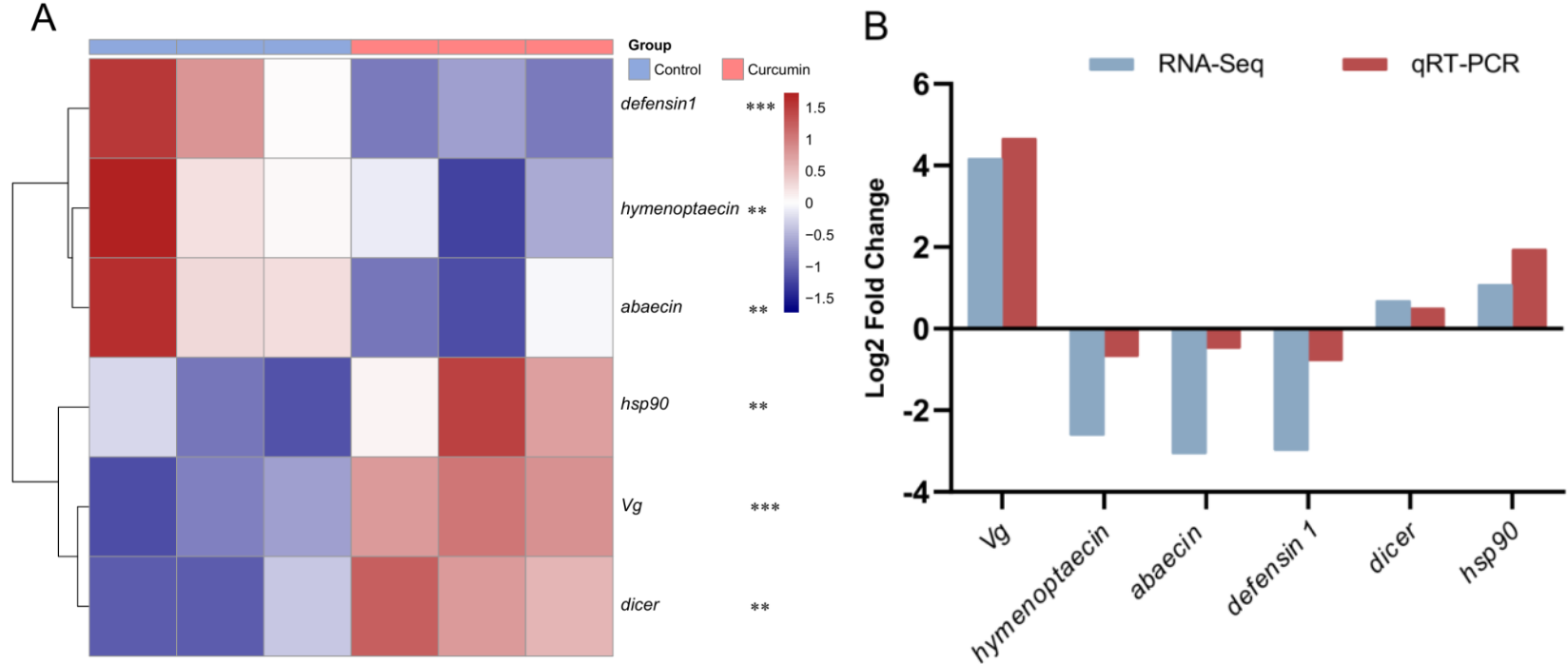
A total of 1,868 differentially expressed genes (DEGs) were identified between curcumin-treated and control groups, with **851 upregulated** and **1,017 downregulated** genes.

Result | Functional Enrichment Analysis of DEGs



Differentially expressed genes were primarily enriched in pathways and biological functions related to **energy metabolism** and **protein synthesis**.

Result | Elucidating the Antiviral Mechanism of Curcumin against IAPV



Upregulation of **Vg** and **RNAi** pathway genes, with downregulation of **antimicrobial peptide** genes.

Conclusion and Future Work

- Curcumin significantly reduces IAPV load in both laboratory-infected and naturally infected honey bees.
 - Curcumin-mediated IAPV suppression through enhanced honey bee fitness parameters and activated RNAi pathway factors.
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- Unraveling the molecular basis of curcumin's action on honey bee viral pathogens.
 - Exploring delivery methods and dosage optimization of curcumin in honey bee colonies.

Acknowledgement



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Thank You

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