Enhancing Soybean Drought Resilience with Natural Compounds: How Curcumin and Lupenone Influence Heme Oxygenase-1

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INTRODUCTION

- Climate change has intensified challenges for crops, leading to increased abiotic stresses, such as drought, that impact yield and economic viability.
- Modulating phytohormone signaling pathways offers a promising strategy to enhance crop resistance to environmental stressors.
- This study investigates the role of heme oxygenase 1 (HO-1), a vital enzyme in plant stress response pathways, including phytohormonal interactions.
- The focus is on improving soybean's drought resilience through the synergistic action of the naturally derived bioactive compounds Curcumin and Lupenone.

OBJECTIVE

This research aims to investigate the **potential of Curcumin and Lupenone to enhance drought resistance in soybeans by modulating HO-1 activity** through molecular docking and dynamics simulations, elucidating their role in reinforcing adaptive responses via phytohormone signaling pathways.

MATERIALS AND METHODS

Potential Target preparation

3D structure of HO-1 (PDB ID: 7CKA) was downloaded from the RCSB Protein Data Bank

Structure imported using Discovery Studio Visualizer 4.0

Core protein structure isolated by removal of co-crystal ligands and heteroatoms

Optimization of the protein structure for energy minimization

Curcumin and Lupenone downloaded as .sdf files from PubChem.

.sdf files were converted into .pdb format using Discovery Studio Visualizer 4.0

Molecular docking

Docking Software: Docking simulations were performed on the HO-1 structure with Curcumin and Lupenone using AutoDock Vina.

Receptor Grid Definition: A grid was defined around the co-crystal ligand binding site (4.57 Å radius) using AutoDock MGL tools 1.5.6.

File Preparation: The protein and ligand structures were converted to PDBQT format (including merging nonpolar hydrogens) using MGL tools.

Docking Parameters: An equilateral grid box (X=25 Å, Y=35 Å, Z=45 Å, spacing=5.64 Å) and Lamarckian Genetic Algorithm (LGA) were used for docking.

Molecular dynamic simulations

Simulation Software: A 100 ns MD simulation was performed using Desmond software (Schrödinger LLC).

System Setup: Orthorhombic fluid box models with OPLS 2005 force fields were utilized. The NaCl concentration was set to 0.15 M, and counterions were added for system stability.

Data Collection: RMSD of the protein and ligand, as well as MD trajectories, were recorded every 100 ps. RMSF was utilized to analyze protein backbone flexibility during the simulation.

Simulation Conditions: The temperature was maintained at 300 K, and the pressure was maintained at 1 atmosphere throughout the simulation.

RESULTS

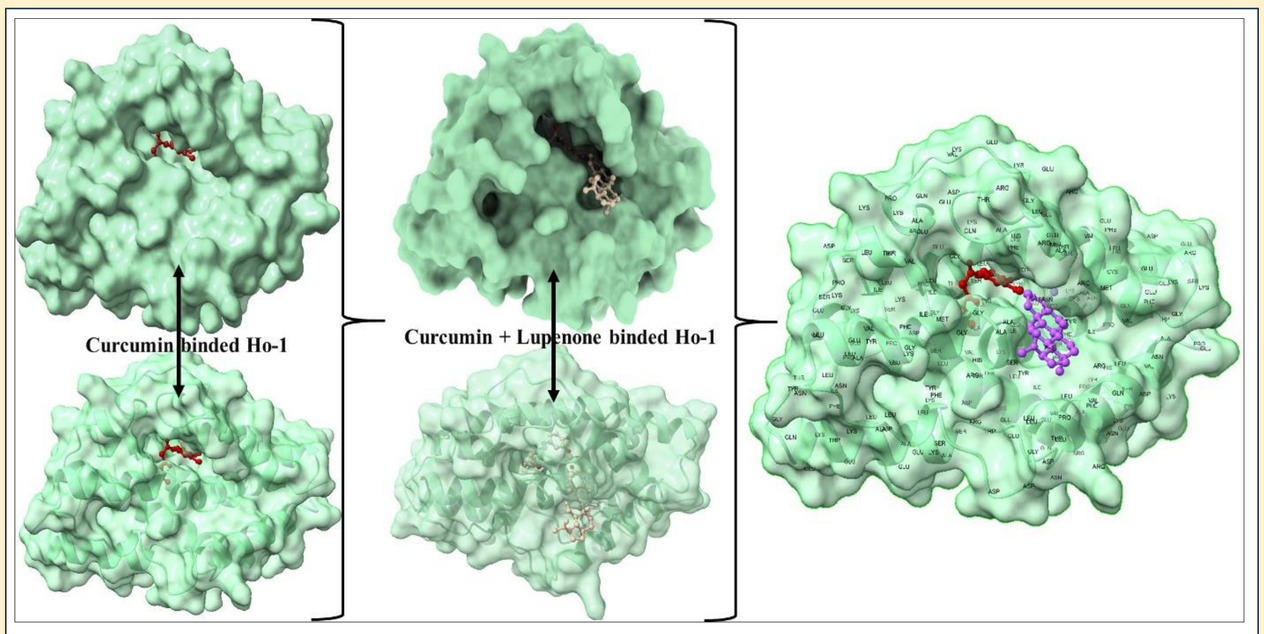

Figure 1 - Analysis of the docked posture of 7CKA-Curcumin+Lupenone; were displayed the ligand bound at the pocket of the receptor 7CKA and the binding pocket residues interacted with the ligand displayed.

Table 1. Molecular Docking of 10 selected Phyto-chemicals upon prior binding with Curcumin.

Sl. No.	Primary ligand selected	Second phytochemical compound names	Binding energy (Kcal/mol)
1.	**Curcumin (-7.81 kcal/ mol)**	Mangiferin	-5.60
2.		Barbalonin	-4.56
3.		Jasmonic acid	-4.87
4.		Brassino steroid	-7.33
5.		Capilobenzofuranol	-5.22
6.		**Lupenone**	**-12.57**
7.		Salicylic acid	-8.41
8.		Strigolactones	-7.12
9.		Ethylene	-6.37
10.		Wedelosin	-5.67

- **Re-docking indicated deep binding in the protein pocket** with a binding energy of -10.97 kcal/mol and Ki of 0.12 mM, underscoring their synergistic effect.
- The **C-α backbone RMSD** of the 7CKA protein showed high stability, fluctuating only by 1.1 Å, while the Curcumin-Lupenone complex remained consistent over 100 ns.
- The **RMSF analysis** confirmed stability, but after 100 ns, the Curcumin-Lupenone-bound protein showed a 2 Å deviation at residues 37, 50-52, 150, 67, and 200 from the reference structure.
- The **Rg plot of the C-α backbone** revealed that the 7CKA protein exhibited Rg values between 14.7 to 15.0 Å, reflecting significant compactness with an average change of only 0.4 Å over the 100 ns simulation.
- The simulation formed **three hydrogen bonds**, enhancing binding and drought resistance, indicating a stable interaction of the complex.
- **MM-GBSA analysis** revealed ΔGbindCoulomb, ΔGbindvdW, and ΔGbindLipo significantly contributed to complex stability, while ΔGbindCovalent and ΔGbindSolvGB indicated instability.

CONCLUSION

This study paves the way for experimental validation of the Curcumin + Lupenone complex's effects on HO-1 activity and its role in phytohormone signaling, enhancing our understanding of drought resistance mechanisms in soybean and informing strategies to improve crop drought tolerance.

REFERENCES

Competing interests: All authors announce that no conflict of interest exists.