Target-Based Design and Hit to Lead Optimization of Pyrimidinylpyrazole Insecticides

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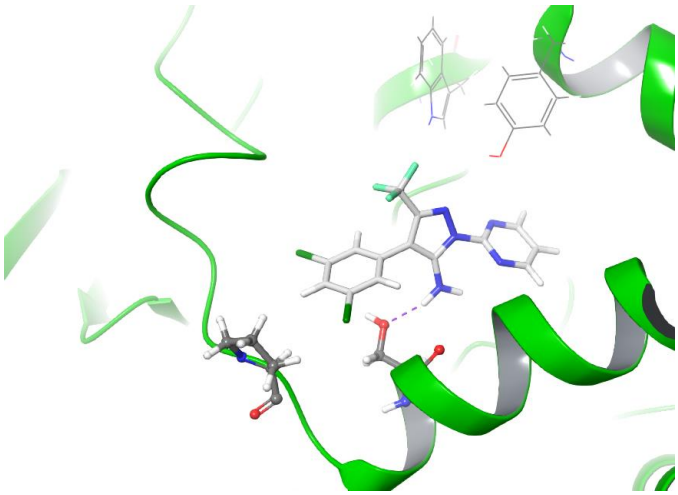
The urgent need for selective, effective, and environmentally sustainable crop protection solutions remains paramount in addressing global pest control challenges. Arthropod pests, particularly insects, cause significant damage to global agriculture, with current worldwide yield losses ranging from 17-30% on major food crops[1]- a figure projected to increase under warming climate conditions[2]. These substantial yield reductions threaten food security, farmer livelihoods, and agricultural sustainability across the globe.

This presentation outlines our exploration of novel insecticides, beginning with pyrimidinylpyrazoles identified in patent literature[3] as promising chemical scaffolds. We will systematically outline our research journey from initial hit discovery through lead optimization, encompassing mode of action elucidation, development of specialized tools and capabilities for target-based design, structure-activity relationship studies informing our working hypothesis of ligand-target binding interactions, and strategic alignment of compound optimization with commercial target product profiles - the essential features a product must possess for market viability.

This case study illustrates how modern insecticide discovery integrates multiple scientific disciplines to address the complex challenges of sustainable crop protection.



[1] Savary, S., Willocquet, L., Pethybridge, S. J., Esker, P., McRoberts, N., & Nelson, A. (2019). The global burden of pathogens and pests on major food crops. Nature Ecology & Evolution, 3(3), 430-439.

[2] Deutsch, C. A., Tewksbury, J. J., Tigchelaar, M., Battisti, D. S., Merrill, S. C., Huey, R. B., & Naylor, R. L. (2018). Increase in crop losses to insect pests in a warming climate. Science, 361(6405), 916-919.

[3] WO08077483