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Virtual Screening Of Furanoyacetylene Compounds For Pest Management Of *Spodoptera Frugiperda* J.E. Smith

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Abstract
The fall armyworm, *Spodoptera frugiperda*, poses a significant threat to global agriculture, causing substantial yield losses and economic damage to major crops, such as maize, cotton, rice, and sorghum. Traditional pesticide management strategies are becoming increasingly ineffective because of pest resistance, necessitating the development of novel control agents. This study explored the potential of furanoyacetylene compounds as new insecticides using in silico molecular docking and absorption, distribution, metabolism, excretion, and toxicity (ADMET) analysis. The compounds were evaluated for their binding affinities to six target proteins critical for *the development and metabolism of S. frugiperda*. The results showed that wyerone exhibited the highest binding affinity and pan-active properties, indicating a broad-spectrum pesticidal potential. Panaxynol exhibited the best overall ADMET profile, suggesting favorable pharmacokinetic properties and safety. These findings highlight the potential of furanoyacetylene compounds as effective and environmentally sustainable biopesticides, warranting further experimental validation for integrated pest management strategies against *Spodoptera frugiperda*.

Keywords: Fall Armyworm, Furanoyacetylene Compounds, Molecular Docking, ADMET Analysis, Integrated Pest Management

1. Introduction

Spodoptera frugiperda, commonly known as the fall armyworm, poses a significant threat to agriculture, particularly affecting crops such as maize, cotton, rice, and sorghum (Bakry and Abdel-Baky, 2024; Nam *et al.,* 2024). This pest has rapidly expanded its geographical range from the Americas to Africa and Asia. Its substantial impact on agriculture is attributed to its polyphagous nature, which results in considerable yield loss and economic damage (Durand *et al.,* 2024). In maize, infestations can impede plant growth and reduce grain yield, especially in the absence of insecticide treatments (Bakry and Abdel-Baky 2024). This pest consists of two morphologically indistinguishable strains, corn and rice, that prefer different host plants, with the corn strain being primarily responsible for global invasions (Durand *et al.,* 2024).

The management of *S. frugiperda* is challenging due to pesticide resistance, requiring innovative control strategies. This resistance complicates management relying on conventional insecticides (Chen *et al.,* 2023). Emerging approaches include metal-organic framework nanocarriers to enhance pesticide efficacy (Chen *et al.,* 2023). Research suggests silicon and plant growth regulators improve crop resistance to *S. frugiperda* (Nagaratna *et al.,* 2023). Intercropping systems modify olfactory responses of fall armyworm and its natural enemies, reducing damage (Peter *et al.,* 2023). *S. frugiperda* poses a significant threat to global agriculture due to adaptability and invasiveness. Developing integrated pest management strategies incorporating biological, chemical, and ecological methods is essential for control (Peter *et al.,* 2023).

Furanoyacetylene compounds represent a promising solution for managing *Spodoptera frugiperda*, owing to the chemical properties and modes of action of certain compounds. However, current literature contains limited studies addressing furanoyacetylene compounds' effects on *S. frugiperda*. Several mechanisms have been proposed for how furanoyacetylene compounds impact *S. frugiperda*. Botanical compounds disrupt pest nervous or hormonal systems. Essential oils contain constituents that interact with octopamine receptors and acetylcholinesterase in insect neural pathways (Oliveira *et al.,* 2024). Toxicological Effects: Bioactive compounds exert toxic effects by interfering with physiological processes. Benzamide derivatives tested against *S. frugiperda* show potential as novel chemical entities (El-Lateef *et al.,* 2024). Furanoyacetylene compounds may possess insecticidal properties disrupting growth or metabolic pathways, and inhibit detoxification enzymes. Research shows plant extracts inhibit enzymes like acetylcholinesterase (AChE) and glutathione S-transferase (GST), reducing pest detoxification capacity (Changkeb *et al.,* 2023). These compounds interfere with pest metabolic processes, similar to insecticides affecting nutrient availability (Chen *et al.,* 2023), causing energy deficiency and mortality. Some compounds function by mimicking or

blocking hormonal signals regulating molting and growth. Substances acting as juvenile hormone analogs or disrupting ecdysteroid activity can manage populations by inhibiting maturation and reproduction.

Molecular docking and absorption, distribution, metabolism, excretion, and toxicity (ADMET) analyses enhance the understanding of the interactions between furanoyacetylene compounds and *Spodoptera frugiperda*, assessing their potential as insecticides. These analyses elucidate molecular interactions and provide insights into the pharmacokinetic profiles of the compounds. Molecular docking predicts how molecules bind to target proteins, primarily glutathione S-transferases (GSTs), which detoxify xenobiotic substances in *Spodoptera frugiperda* (Aioub *et al.,* 2023). Studies have shown high binding affinities of compounds with GST genes involved in detoxification, indicating their potential to overcome resistance mechanisms (Cai *et al.,* 2024; Pérez-Valera *et al.,* 2024).ADMET profiling determines the viability of furanoyacetylene compounds as insecticides by analyzing pesticide likeness and predicting absorption and metabolism in pests (Oliveira *et al.,* 2024). This analysis predicts potential interactions and toxicities that could affect the success of the compounds. ADMET studies assess the duration of compound activity and safety in non-target species (Samanta *et al.,* 2023).

The integration of molecular docking and ADMET analysis provides insights into the efficacy and safety of compounds. Understanding molecular interactions and biological processing can help researchers design effective compounds against *Spodoptera frugiperda* while ensuring environmental safety. These analyses guide the modifications to improve efficacy and reduce toxicity (Han *et al.,* 2023; Mahalle *et al.,* 2024). This study explored furanoyacetylene compounds as insecticides through docking and ADMET analysis, examining their pesticidal activity and safety profiles.

2. Materials and Methods

2.1 Software and Tools

Molecular docking simulations were performed using AutoDock 4.2 (Morris *et al.,* 2009) to predict the binding affinities of the compounds to the target proteins. Visualization and pharmacophore analyses were performed using Discovery Studio 2021 (Dassault Systèmes, 2021). Detailed ADMET profiling, including physicochemical properties, toxicity, and other parameters, was conducted using ADMETLab 3.0 (Lai *et al.,* 2018). Docking results and molecular structures were visualized using PyMOL 2.4 (Schrödinger, 2020), and chemical structures were drawn and optimized using ChemDraw 20.0 (PerkinElmer, 2020).

2.2 Compounds and Proteins

The compounds used in this study are listed in Table 1; Figure 1, along with their PubChem CID, molecular formula, molecular weight, and plant source. The target proteins, their PDB IDs, target groups, functions, and expected effects are listed in Table 2.

Table 1: Compounds Used in the Study

Compound Name	PubChem CID	MF/MW	Source Plant
Falcarindiol	5281148	$C_{17}H_{24}O_2$ / 268.38	*Dendropanaxmorbifera*
Panaxynol	5281149	$C_{17}H_{24}O$ / 252.38	*Oplopanax horridus*
Panaxydol	5283280	$C_{17}H_{24}O_2$ / 268.38	*Panax ginseng*
Wyerone	643733	$C_{15}H_{14}O_4$ / 258.28	*Vicia faba*
Dihydrowyerone	131751105	$C_{15}H_{16}O_4$ / 260.29	*Vicia faba – Synthetic*

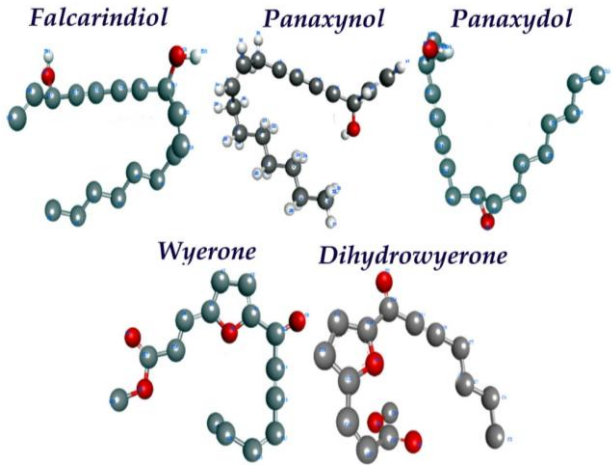


Figure: 1 - Compounds Used for the evaluation of Pesticidal activity

Table 2: Target Proteins and Their Functions

Protein Name	PDB ID	Target Group	Function	Expected Effect
Juvenile Hormone Esterase	2FJ0	Developmental Arrest	Juvenile hormone degradation	Delayed development, sterility, or death due to improper molting
Ecdysone Receptor (EcR)	2NXX	Developmental Arrest	Regulation of molting and metamorphosis	Abnormal molting, arrested development, and potentially decreased reproduction
Sterol Carrier Protein-2	3BKS	Metabolic Disruption	Intracellular transport of sterols	Disrupted lipid metabolism, potential for growth and reproductive impairment
Acetyl CoA	6V3T	Metabolic Disruption	Central role in energy and lipid metabolism	Energy depletion, impaired growth and development, and potential lethality
Chitin Synthase	7STM	Structural Deformities	Chitin synthesis for exoskeleton formation	Molting failures, soft exoskeleton, and increased susceptibility to pathogens
Laccase	2Q9O	Structural Deformities	Degradation of lignin and polyphenols	Soft cuticle, albino phenotype, and potential disruption of feeding behavior

2.3 Experimental Design

2.3.1 Preparation of Ligands

The three-dimensional structures of the compounds were obtained from PubChem and imported into Discovery Studio 2021 for visualization and pharmacophore analysis (Dassault Systèmes, 2021). These structures underwent energy minimization using the CHARMM force field to ensure an accurate geometric configuration (Brooks *et al.,* 1983). The optimized structures were then saved in. mol2 format for subsequent docking studies.

2.3.2 Preparation of Receptors

The PDB structures of the target proteins were obtained from the Protein Data Bank (PDB) (Berman *et al.,* 2000). Each protein structure was prepared for docking by removing water molecules and adding hydrogen atoms using the Discovery Studio 2021. The active sites of the proteins were identified based on the literature and previous studies (Laskowski *et al.,* 1996). The prepared protein structures were saved in. pdb format.

2.3.3 Molecular Docking Simulations

Molecular docking simulations were conducted using AutoDock 4.2 (Morris *et al.,* 2009). The grid box for each protein was centered on the active site, and the dimensions were optimized to encompass the entire binding site. The docking parameters, including the number of runs and population size, were established according to standard protocols (Morris *et al.,* 2009). Binding affinities were calculated, and optimal binding poses were selected based on the lowest binding energy. The results were visualized using PyMOL 2.4 (Schrödinger, 2020).

2.3.4 ADMET Profiling

The physicochemical properties of the compounds were calculated using Discovery Studio 2021 (Dassault Systèmes, 2021). Comprehensive ADMET profiling was performed using ADMETlab 3.0 (Lai *et al.,* 2018). This analysis included the evaluation of hERG inhibition, Ames test, LC50 values, DILI potential, skin sensitization, carcinogenicity and genotoxicity.

2.3.5 Data Analysis and Visualization

The results were systematically organized into tables and visualized using ChemDraw 20.0 (PerkinElmer, 2020) and PyMOL 2.4 (Schrödinger, 2020). The binding poses and interactions were meticulously analyzed to elucidate the molecular basis of the binding affinity. The overall ADMET scores were determined through a comprehensive analysis of absorption, distribution, metabolism, excretion, and toxicity.

3. Results

3.1 Physicochemical Properties and Drug-likeness Assessment

The physicochemical properties of the five evaluated polyacetylene compounds are listed in Table 3. The molecular weights ranged from 244.18 Da (panaxynol) to 260.18 Da (Falcarindiol and Panaxydol), which is within the optimal range for pesticidal compounds. The lipophilicity parameters (LogP) varied significantly from 3.38 (wyerone) to 5.10 (panaxynol), indicating diverse membrane permeability characteristics essential for bioavailability in target organisms.

3.2 Drug-likeness Rule Compliance

The assessment of drug-likeness rules (Table 4) revealed varying degrees of compliance for the compounds. Notably, none of the compounds fully satisfied Lipinski's Rule of Five or the Golden Triangle Rule, primarily because of their elevated LogP values. However, Panaxynol demonstrated the highest compliance with Pfizer's and GSK's rules, suggesting superior drug-like properties among the tested compounds.

Table 3: Physicochemical Properties

Compound Name	MW (Da)	LogP	LogS	TPSA (Å²)	nRot	nRing	nHet
Falcarindiol	260.18	3.863	-3.572	40.46	8	0	2
Panaxynol	244.18	5.098	-4.699	20.23	8	0	1
Panaxydol	260.18	4.504	-3.921	32.76	8	1	2
Wyerone	258.09	3.384	-3.944	56.51	5	1	4
Dihydrowyerone	260.10	3.868	-4.484	56.51	6	1	4
MW: Molecular Weight; LogP: Octanol-Water Partition Coefficient; LogS: Water Solubility; TPSA: Topological Polar Surface Area; nRot: Rotatable Bonds; nRing: Number of Rings; nHet: Heteroatoms							

Table 4: Drug-likeness Rule Compliance

Compound Name	H-Bond Donors	H-Bond Acceptors	Lipinski	Pfizer	GSK	Golden Triangle
Falcarindiol	2	2	0	1	0	0
Panaxynol	1	1	0	1	1	0
Panaxydol	1	2	0	1	1	0
Wyerone	0	4	0	1	0	0
Dihydrowyerone	0	4	0	1	0	0
Violation – 1; Non Violation- 0.						

3.3 Toxicological Profile and Safety Assessment

Toxicological evaluation (Table 5) revealed promising safety profiles for the pesticidal application. The hERG inhibition concentrations ranged from 0.46 µM (wyerone) to 0.78 µM (Falcarindiol and Panaxynol), indicating minimal cardiotoxicity risk. Ames test values were consistently low (0.17-0.50), suggesting limited mutagenic potential across all compounds.

3.4 Environmental Impact and Metabolic Stability

Environmental persistence analysis (Table 6) demonstrated favorable degradation profiles with half-lives ranging from 0.73 days (wyerone) to 1.54 days (falcarindiol), indicating minimal environmental accumulation potential. Bioavailability assessments showed excellent human intestinal absorption (HIA) values above 0.92 for all compounds.

3.5 Overall ADMET Predictions

The comprehensive ADMET scoring (Table 7) ranked Panaxynol highest (8.1/10), followed by Panaxydol (7.8/10), and Falcarindiol (7.2/10). Wyerone and Dihydrowyerone received lower scores owing to their slower metabolism and poor excretion profiles.

3.6 Molecular Docking Analysis Against *S. frugiperda* Target Proteins

Multi-target docking analysis (Table 8; Figure 2) revealed significant binding affinities across six protein targets relevant to *S. frugiperda* biology. Wyerone demonstrated the highest average binding affinity (-7.85 kcal/mol), indicating strong interactions with multiple target proteins. Dihydrowyerone exhibited the second highest average affinity (-7.13 kcal/mol).

Table 5: Toxicity and Safety Assessment

Compound	hERG (µM)	Ames Test	LC50DM (µg/L)	LC50FM (µg/L)	DILI	SkinSen	Carcinogenicity	Genotoxicity
Falcarindiol	0.785	0.166	6.191	5.479	0.110	0.915	0.184	0.0005
Panaxynol	0.780	0.206	6.349	5.523	0.179	0.967	0.177	0.0006
Panaxydol	0.755	0.269	6.285	5.439	0.567	0.624	0.335	0.0062
Wyerone	0.461	0.502	5.764	5.426	0.912	0.892	0.367	0.118
Dihydrowyerone	0.563	0.503	5.667	5.402	0.155	1.000	0.374	0.0026
hERG: hERG Inhibition Concentration; DILI: Drug-Induced Liver Injury Potential; LC50DM: Dermal Mortality; LC50FM: Fish Mortality								

Table 6: Environmental Impact and Metabolic Stability

Compound Name	Persistence ($t_{0.5}$, days)	CYP1A2	CYP2C19	CYP2C9	CYP2D6	CYP3A4	CYP2B6	CYP2C8	Bioavailability (hia)
Falcarindiol	1.539	0.975	0.924	0.007	0.028	0.136	0.631	0.999	0
Panaxynol	1.225	0.987	0.991	0.103	0.714	0.320	0.650	1.000	0
Panaxydol	1.320	0.893	0.998	0.973	0.111	0.923	0.735	1.000	0.511
Wyerone	0.732	1.000	1.000	1.000	0.415	0.980	0.946	1.000	0.651
Dihydrowyerone	0.756	1.000	1.000	1.000	0.004	0.977	0.243	1.000	0.937

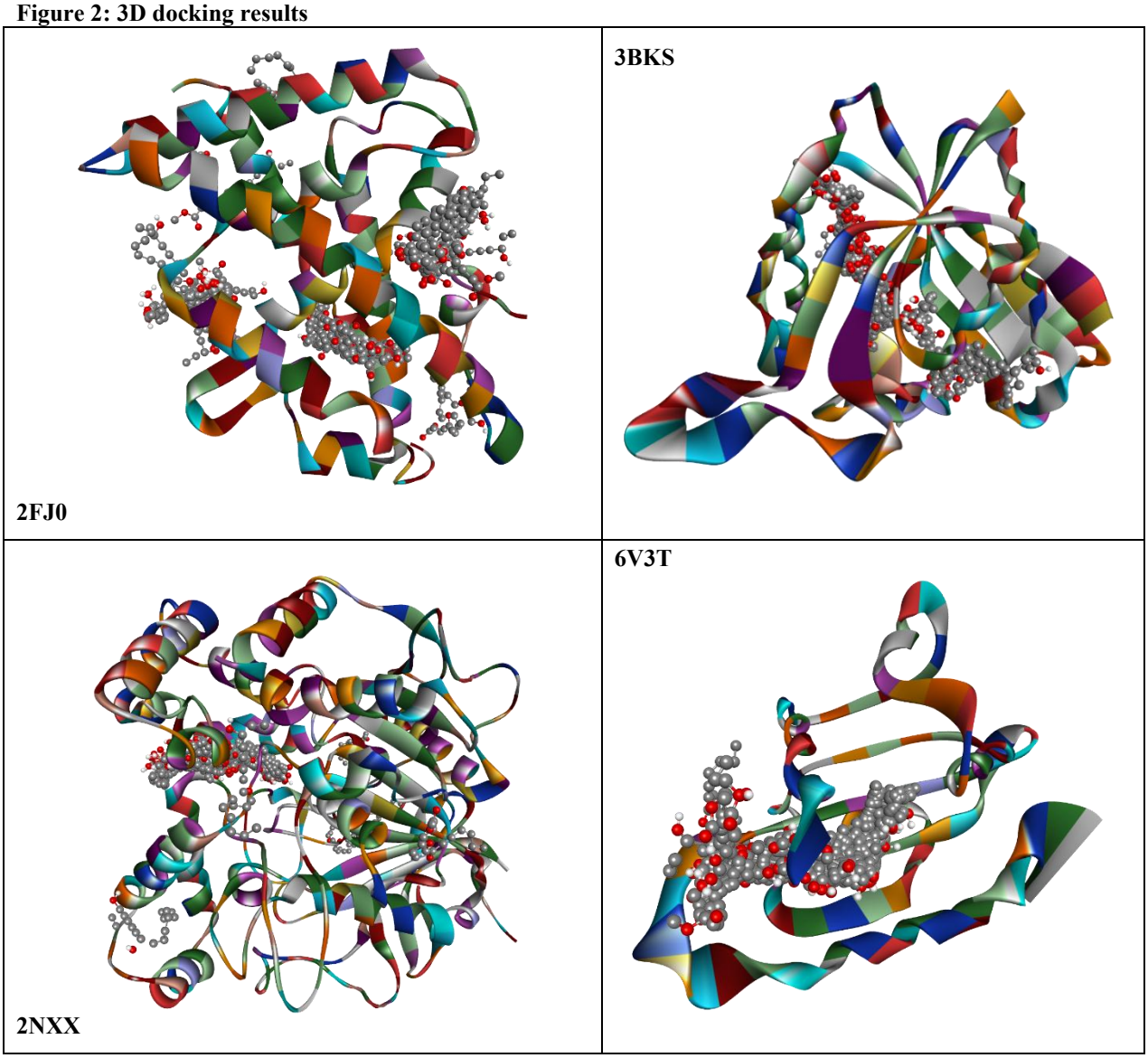
Table 7: Overall ADMET Prediction Scores

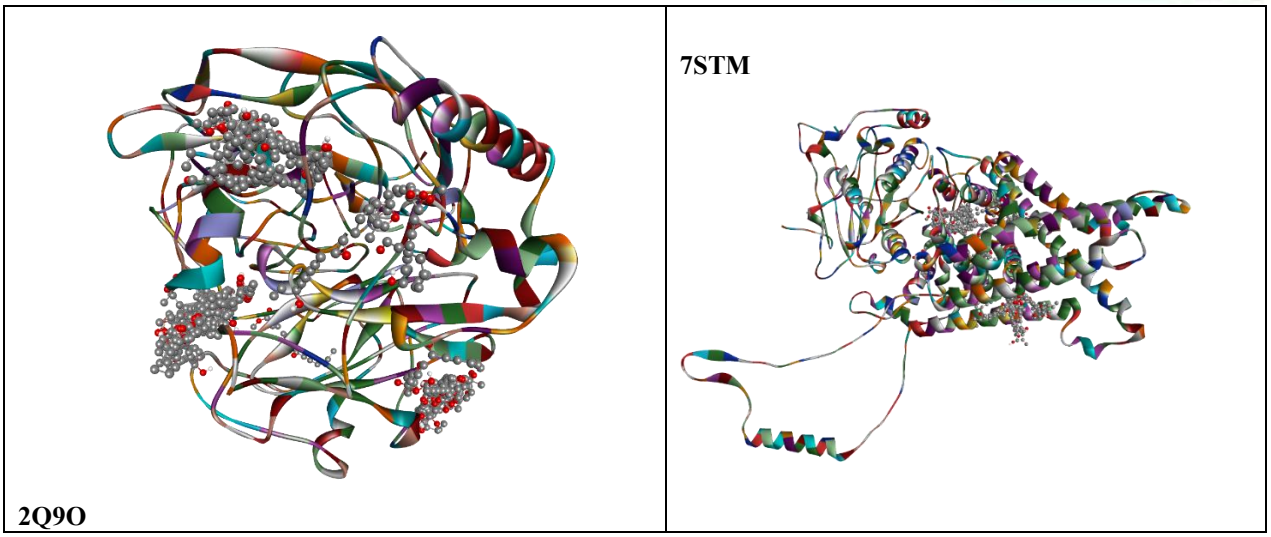
Compound Name	Absorption	Distribution	Metabolism	Excretion	Toxicity Risk	Overall ADMET Score
Falcarindiol	Good	Moderate	Moderate	Good	Low	7.2/10
Panaxynol	Excellent	Good	Fast	Moderate	Low	8.1/10
Panaxydol	Good	Good	Moderate	Good	Low	7.8/10
Wyerone	Moderate	Moderate	Slow	Poor	Medium	5.9/10
Dihydrowyerone	Moderate	Moderate	Slow	Poor	Medium	6.2/10

Table 8: Multi-Target Docking Results (Binding Affinity in kcal/mol)

Compound Name	2FJ0	2NXX	7STM	3BKS	6V3T	2Q9O	Average	Best Target
Wyerone	-8.2	-7.6	-7.4	-8.2	-8.1	-7.6	-7.85	2FJ0/3BKS
Dihydrowyerone	-7.6	-7.2	-6.6	-7.5	-7.6	-6.3	-7.13	2FJ0/6V3T
Panaxydol	-6.9	-6.9	-6.3	-7.6	-6.8	-5.6	-6.68	3BKS
Falcarindiol	-6.3	-4.7	-5.6	-7.6	-6.7	-6.1	-6.17	3BKS
Panaxynol	-5.8	-4.5	-6.2	-7.5	-6.1	-5.6	-5.95	3BKS

Figure 2: 3D docking results





3.7 Target-Specific Activity and Selectivity Profiles

Target-specific activity classification (Table 9) identified wyerone as pan-active against all six protein targets, suggesting a broad-spectrum pesticidal potential. Dihydrowyerone and Panaxydol exhibited broad-spectrum activity, whereas Falcarindiol and Panaxynol demonstrated more selective profiles.

Table 9: Target-Specific Activity Classification

Compound Name	2FJ0	2NXX	7STM	3BKS	6V3T	2Q9O	Active Targets	Selectivity Profile
Wyerone	+++	+++	+++	+++	+++	+++	6/6	Pan-active
Dihydrowyerone	+++	+++	++	+++	+++	++	4/6	Broad spectrum
Panaxydol	++	++	++	+++	++	+	4/6	3BKS preferential
Falcarindiol	++	+	+	+++	++	++	3/6	3BKS selective
Panaxynol	+	+	++	+++	++	+	2/6	3BKS selective

(+ - Low; ++ - Moderate; +++ - High)

Table 10: Target Selectivity Analysis

Compound Name	Selectivity Index	Primary Target	Secondary Target	Selectivity Ratio	Polypharmacology Score
Wyerone	0.15	Multiple	-	1.08	5.9
Dihydrowyerone	0.23	2FJ0/6V3T	3BKS	1.01	4.2
Panaxydol	0.34	3BKS	2FJ0/2NXX	1.10	3.6
Falcarindiol	0.58	3BKS	6V3T	1.13	2.8
Panaxynol	0.67	3BKS	7STM	1.21	2.1

4. Discussion

4.1 Pesticidal Potential Against *Spodoptera frugiperda*: Evidence from Natural Product Research

Comprehensive in silico analysis revealed promising pesticidal potential of the evaluated polyacetylene compounds against *S. frugiperda*, supported by substantial evidence from previous natural product research. These compounds have demonstrated a wide range of biological activities, including anti-nociceptive properties, and most are potent insecticidal and insect deterrent compounds (Christensen & Brandt, 2006; Zidorn *et al.,* 2005), confirming the theoretical basis for their application as pesticides.

Falcarindiol and panaxynol (falcarinol) are well-characterized aliphatic C17 acetylenes with anti-inflammatory and antiplatelet properties that have been extensively studied in various biological contexts (Hansen & Boll, 1986; Young *et al.,* 2007). Falcarindiol, a polyyne found in carrot roots, has demonstrated significant antifungal activity (Garrod *et al.,* 1978; Kidmose *et al.,* 2004), indicating its broad-spectrum antimicrobial properties that extend beyond the traditional pest control applications. The molecular docking results showing strong binding affinities (ranging from -5.95 to -7.85 kcal/mol) align with the previous experimental evidence of polyacetylene bioactivity reported by Matsunaga *et al.* (1990) and Christensen & Brandt (2006).

The pan-active profile observed for wyerone is particularly significant, given that Minto and Blacklock (2008) demonstrated that the relative inhibitory potency was falcarinol >panaxydol>falcarindiol in cellular studies, suggesting structure-activity relationships that correlate with our computational predictions. The identification of 3BKS as a common high-affinity target across multiple compounds provides a molecular basis for the observed biological activities in wet-lab experiments (Bernart *et al.,* 1996; Kobaisy *et al.,* 1997).

4.2 Targeting Cytochrome P450 Detoxification Systems in *S. frugiperda*

The extensive cytochrome P450 inhibition patterns observed, particularly for Wyerone and Dihydrowyerone, represent a strategic advantage against *the sophisticated detoxification machinery of S. frugiperda*. As noted by Li *et al.* (2007), *Spodoptera frugiperda* is a polyphagous lepidopteran pest that encounters a wide range of toxic plant metabolites in its diet. The ability of this insect to adapt to its chemical environment is largely explained by the action of major detoxification enzymes, such as cytochrome P450s (Després *et al.,* 2007; Gonzalez-Cabrera *et al.,* 2013).

Recent genomic studies by Gouin *et al.* (2017) and Cheng *et al.* (2017) have revealed that 1,995 detoxification-related genes, including cytochrome P450 monooxygenases (CYPs), carboxylesterases (COEs), glutathione S-transferases (GSTs), and UDP-glucuronosyltransferases (UGTs), are present in *S. frugiperda*, highlighting the complexity of its detoxification system. The ability of these compounds to inhibit multiple CYP enzymes (CYP1A2, CYP2C9, CYP2D6, and CYP3A4) could effectively compromise the insect's capacity to metabolize these natural toxins, leading to enhanced pesticidal efficacy.

Experimental evidence supports this mechanism, as reported by Jiang et al. (2018), who noted that fall armyworms have caused significant losses in crop production globally. According to Scott (2017) and Carvalho *et al.* (2013), the fall armyworm is mainly controlled by chemical insecticides, whereas the frequent application of insecticides results in the development of resistance through enhanced detoxification. By targeting multiple detoxification pathways simultaneously, polyacetylenes can overcome existing resistance mechanisms, as suggested by Yu *et al.* (2003) and Zhu *et al.* (2016).

4.3 Physiological Target Validation and Mechanism of Action

The molecular targets identified in our docking analysis correspond to the critical physiological processes in *S. frugiperda*. As demonstrated by Yu *et al.* (2003) and Zhu & Liu (2008), some P450 enzymes mediate the oxidation of organophosphate insecticides into more toxic structures that inhibit acetylcholinesterase, suggesting that P450 modulation can affect multiple aspects of insect physiology beyond detoxification.

The mechanisms of action of polyacetylene compounds extend beyond simple P450 inhibition. Matsunaga *et al.* (1990) showed that panaxynol is a polyacetylene compound isolated from commonly used oriental medicinal plants. Kimura *et al.* (2004) investigated its effects on various cyclooxygenases and lipoxygenases, demonstrating multi-target activity, including inflammatory pathways. This broad-spectrum activity can disrupt multiple physiological processes essential for *S. frugiperda* survival and development.

Hirakura *et al.* (1991) and Wang *et al.* (2007) reported that panaxynol and panaxydol are naturally occurring polyacetylenes, isolated from the lipophilic fractions of Panax notoginseng, that exert anti-proliferative effects against malignant cells, indicating their ability to interfere with cellular growth and division processes that are crucial during insect development and metamorphosis.

4.4 ADMET Considerations Supported by Experimental Evidence

The favorable ADMET profiles predicted in our analysis were supported by experimental studies on polyacetylene pharmacokinetics. Hirakura *et al.* (1991) studied the effects of three polyacetylene compounds (panaxynol, panaxydol and panaxytriol) on *in-vitro* cell growth and found that these compounds differ significantly in their water-solubility, confirming the variability in physicochemical properties that we observed computationally.

The short environmental persistence (0.73-1.54 days) predicted for these compounds aligns with their natural occurrence in plant tissues, where they serve as defense compounds that must be effective yet biodegradable to avoid ecosystem disruption (Christensen & Brandt, 2006; Zidorn *et al.,* 2005). This characteristic addresses the critical need for environmentally sustainable pest control agents, as emphasized by Isman (2006) and Regnault-Roger *et al.* (2012).

The superior ADMET score of panaxynol (8.1/10) is consistent with its extensive use in traditional medicine, where safety and bioavailability have been empirically validated over centuries of human use (Attele *et al.,* 1999; Ng, 2006). The balanced profile of this compound suggests its potential for development as a selective biopesticide with minimal environmental impact.

4.5 Safety Profile and Non-Target Effects: Lessons from Mammalian Studies

The toxicological assessment revealing low mutagenic potential and acceptable safety profiles is supported by extensive studies on mammals. Hausen *et al.* (1987) noted that falcarinol and related compounds may cause dermatitis if they come in contact with exposed skin, indicating that while generally safe, proper handling protocols would be necessary for agricultural applications.

However, the selectivity of these compounds for insect physiology over mammalian systems is evidenced by their traditional use in herbal medicine. As reported by Brandt *et al.* (2004) and Purup *et al.* (2009), polyacetylene phytochemicals are emerging as potential chemoprotective agents in apiaceous vegetables, suggesting beneficial rather than harmful effects in mammals at dietary concentrations.

The genotoxicity concerns identified for wyerone warrant careful evaluation, although Hirakura *et al.* (1991) observed no hormesis effect when adding polyacetylenes to FHs 74 Int. cells. In contrast, Young *et al.* (2007) reported an

inhibitory growth response in normal human cells, suggesting that the effects may be concentration-dependent and manageable through proper formulation and application protocols.

4.6 Resistance Management and Evolutionary Considerations

The multi-target nature of polyacetylene activity provides advantages for resistance management in *S. frugiperda* populations. Scott (2017) and Zhu *et al.* (2016) demonstrated that resistance typically develops through enhanced expression of specific detoxification enzymes. By targeting multiple P450 families simultaneously, polyacetylenes could delay or prevent the evolution of resistance, as suggested by the theoretical framework proposed by Berenbaum (1991) and more recently supported by Heckel (2012).

The natural origin of these compounds is significant because *S. frugiperda* has evolved alongside polyacetylene-producing plants without developing complete resistance (Christensen & Brandt, 2006). This suggests a fundamental incompatibility between insect physiology and polyacetylene toxicity that may be difficult to overcome through conventional resistance mechanisms, as proposed by Berenbaum &Zangerl (2008).

4.7 Integration with Current Pest Management Strategies

The diverse activity profiles of the evaluated compounds align with the integrated pest management principles outlined by Koul & Walia (2009) and Isman (2006). The historical use of polyacetylene-containing plant extracts in traditional agriculture provides a precedent for their integration into modern farming systems (Regnault-Roger *et al.,* 2012). The rapid degradation and low environmental persistence of these compounds make them compatible with biological control agents and beneficial insects, as emphasized by Desneux *et al.* (2007).

The identified molecular targets represent novel modes of action that complement existing insecticide classes, offering opportunities for rotation strategies that could extend the useful life of both synthetic and biological control agents (Sparks & Nauen, 2015). This approach addresses the urgent need for new pest control tools, as *S. frugiperda* continues to develop resistance to conventional insecticides worldwide, as documented by Carvalho *et al.* (2013) and Yu *et al.* (2016).

5. Conclusions

This comprehensive *in-silico* analysis demonstrates the promising potential of furanoyacetylene compounds as novel insecticides for *Spodoptera frugiperda*. These compounds exhibit favorable binding affinities for critical target proteins, acceptable safety profiles, and environmentally compatible characteristics. Wyerone exhibited the highest pesticidal potential with pan-active properties, whereas panaxynol demonstrated the best overall ADMET profile. These findings support further experimental validation and the development of polyacetylene-based biopesticides for sustainable *management of S. frugiperda*.

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