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Insecticidal Efficacy of Piper Nigrum–DerivedPhytochemicals for Sustainable Pest Management

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ABSTRACT
The widespread use of synthetic insecticides has raised concerns regarding environmental persistence, resistance development, and non-target toxicity, necessitating the exploration of sustainable alternatives. Piper nigrum derived phytochemicals have attracted considerable attention due to their broad spectrum bioactivity and ecological compatibility. The present study investigates the phytochemical composition of P. nigrum and their molecular interactions with key insect targets. Major constituents, including Piperin and related alkaloids, were identified and evaluated for their binding affinity and interaction stability with proteins involved in insect metabolic pathways. Molecular interaction analysis revealed strong and specific ligand–target associations, suggesting potential mechanisms underlying insecticidal activity. These findings provide significant insights into the insecticidal potential of P. nigrum phytochemicals and support their development as eco-friendly alternatives to synthetic insecticides.
Keywords: *bioinformatics, black pepper, pest, phytochemical, sustainability.*

1. INTRODUCTION

The management of insect pests in agriculture and public health has long relied on the extensive use of chemical pesticides, which are widely regarded as quick, convenient, and cost-effective control measures (Aktar et al., 2009). As a result, chemical pesticides remain the primary choice for many farmers, despite limited awareness regarding their potential health risks and appropriate handling practices (Rijal et 2 al, 2018). The selection of these pesticides is largely influenced by economic considerations and ease of accessibility rather than safety or environmental sustainability (Sharifzadeh et al., 2018). However, growing evidence indicates that chemical pesticides contribute to a range of human health disorders and exert detrimental effects on the environment (Nicolopoulou-Stamati et al., 2016).

In response to these concerns, biopesticides have emerged as viable alternatives to conventional pest management strategies, offering several advantages such as reduced toxicity and improved environmental compatibility (Mishra et al., 2018). Among these, plant-derived essential oils have gained particular attention due to their repellent, insecticidal, and growth-inhibitory effects against a wide variety of insect species (Regnault et al., 2012).

Piper nigrum L., belonging to the family Piperaceae, is recognized for its diverse biological properties. Previous studies have reported its antioxidant and antimicrobial potential (Singh et al., 2013; Bagheri et al., 2014), as well as its insecticidal activity against insect pests (Wagan et al., 2017). In Thailand, Piper nigrum is a well-known medicinal plant and has demonstrated broad biological activity against insect pests, including Sitophilus oryzae (Vanichpakorn et al. 2017). The insecticidal and repellent properties of Piper nigrum extracts have also been previously documented (Khani et al. 2012).

Recent advances in computer-based technologies have enabled the design of studies that begin with in silico models, thereby reducing experimental time, cost, and the use of trial organisms. In silico approaches in drug discovery have significantly improved the prediction of pharmacokinetic, metabolic, and toxicity parameters, thus accelerating the overall discovery process (Waterbeemd & Gifford, 2003). These computational techniques have been successfully applied in the evaluation of potential anticancer compounds (San Lucas et al., 2014) and in studies aimed at the control of disease vectors such as mosquitoes (Elamathi et al., 2014).

In the present study, computer-based drug design approaches are employed to investigate the insecticidal efficacy of phytochemicals derived from Piper nigrum. Glutathione S-transferase (GST) is selected as the target receptor for molecular docking analysis. GST is a key detoxification enzyme that catalyzes the conjugation of exogenous xenobiotic compounds with glutathione, thereby facilitating their elimination from the insect system (Enayati et al., 2005). Inhibition of this enzyme may compromise the insect's natural detoxification mechanism, increasing susceptibility to toxic compounds.

By integrating phytochemical characterization with molecular interaction analysis, this study aims to elucidate the potential of P. nigrum bioactive compounds as sustainable and eco-friendly alternatives for insect pest management.s

2. METHODOLOGY

2.1. Extract Preparation:

The extraction was carried out following established methodologies (Abubakar and Haque, 2020; Sasidharan et al., 2011). Seeds of P. nigrum were shade-dried and mechanically ground into a fine powder. The powdered material was subjected to Soxhlet extraction using methanol as the solvent for the preparation of the test extract. The resulting extract was concentrated and dried in a hot air oven (Hot Air Oven–NSW 143) maintained at 40 °C and subsequently stored in clean glass bottles for further analysis.

2.2. Phytochemical Analysis

Phytochemical Analysis was performed in accordance with previously described procedures (Mohammed et al., 2016). The prepared crude extracts were screened for phytochemical constituents using gas chromatography–mass spectrometry (GC–MS) analysis (ISQ-7000).

2.3. In silico Analysis

2.3.1. Preparation of receptor and ligand structures

The molecular structure of the receptor Glutathione S- Transferase (1GNW) was downloaded from RCBS PDB (Research Collaborators for structural Bioinformatics Protein Data Bank) database (https://www.rcsb.org/) (Berman et al., 2000). The ligand, selected active components of black pepper was downloaded from Zinc database (https://zinc.docking.org/) which is a free database of commercially available compounds especially prepared for virtual screening (Irwin and Shoichet, 2005). For the present study we download Piperin (ZINC000169711394)

2.3.2. Molecular docking

Molecular docking was performed to predict the possible molecular interactions between the receptors and the ligand molecules using docking software, Molegro Virtual Docker (MVD 2010.4.0 for Windows). MVD identifies ligand binding modes by iteratively evaluating a number of candidate solutions (ligand conformations) and estimating the energy of their interactions with the macromolecule (Bitencourt-Ferreira and de Azevedo, 2019).

2.3.3. Visualization

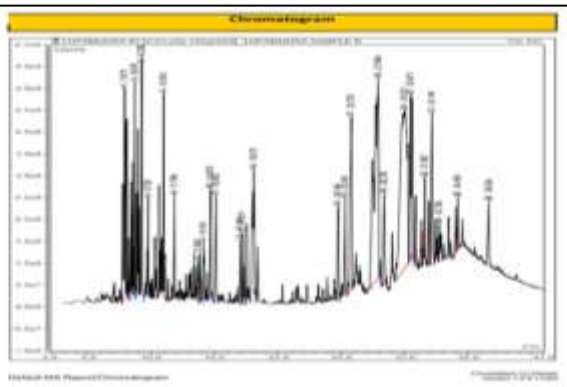
The data acquired from the docking simulation was further analyzed using visualization software Biovia Discovery Studio. The receptor ligand interactions are visualized using both 3 dimensional and 2 Dimensional images (BIOVIA, 2021).

3. RESULTS AND DISCUSSION

To evaluate the insecticidal efficacy of Piper nigrum, a methanolic extract was prepared using Soxhlet extraction, which facilitates efficient and exhaustive extraction of bioactive constituents. Methanol was selected as the solvent due to its effectiveness in extracting a wide range of phytochemicals with known biological activity. The chemical composition of the obtained extract was subsequently characterized using GC–MS analysis. The GC–MS profiling revealed the presence of several bioactive compounds (Fig. 1).

Table: List of compounds

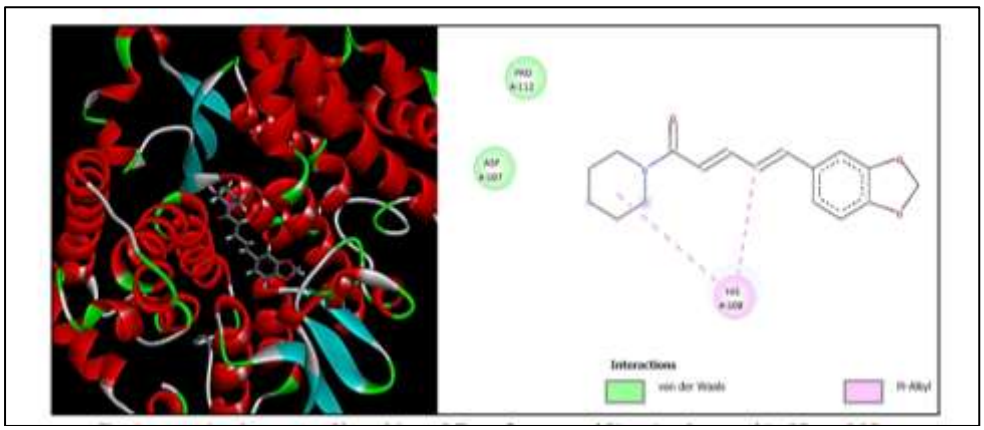
Sl No.	Compound Name	Retention Factor (min)
1	Piperin	29.971
2	Caryophyllene	7.871
3	ß-Bisabolene	8.670
4	Humulenol-II	9.728
5	11-Elemadiol	11.796
6	Limonen-6-ol	13.881
7	Arctiol	14.105
8	n-Hexadecanoic acid	15.092
9	9,12-Octadecadienoic acid	17.211
10	Oleic acid	18.071
11	cis-11-Eicosenoic acid	24.744



a. b.

Fig 1: Results of GC-MS Analysis Piper nigrum, a. List of compounds present in the sample with their Retention factors, b. Chromatogram obtained after analysis of the sample.
A comprehensive list of the phytochemicals present in Piper nigrum is prepared. From available literature it was noted that Piperin is a major component of Piper nigrum.

Investigations on Piperin bioactivities have reported the very high spectrum of physiological effects, including antihypertensive, antiaggregant, antioxidant, antitumor, antispasmodic, antiasthmatic, antidepressant, anxiolytic, and many others (Damanhouri, 2014). Along with an array of biological activities, Piperinis known for its ability to increase the bioavailability of drugs, and thus enhance their therapeutic potential (Salehi et al., 2019, Mhaske et al., 2018). The potential of Piperin as an insecticide is further analysed using in silico methods.
Molecular docking was performed to study the interaction between Piperin and the target receptors Glutathione S-Transferase (1GNW). Docking scores, -89.9858 obtained from Molegro Virtual Docker indicate the binding affinity of piperin with the receptor. Lower docking scores suggest stronger and more stable receptor–ligand interactions.
Piperin showed stable binding within the active site of Glutathione S-Transferase. The ligand formed hydrogen bonds and hydrophobic interactions with key amino acid residues. These interactions may interfere with the detoxification function of the enzyme.



a. b.

Fig. 2: Interaction between Glutathione S Transferase and Piperin observed in a. 3D and b. 2D

The receptor–ligand complexes obtained from docking simulations were further visualized using BIOVIA Discovery Studio to better understand the spatial orientation and interaction patterns of Piperin within the binding pockets. Both two-dimensional and three-dimensional interaction maps revealed the involvement of key functional groups of Piperinin forming stable interactions with the receptors (Fig. 2). The visualization analysis corroborates the docking scores and interaction data, providing structural evidence for the potential inhibitory action of Piperin against GST.
The strong binding affinity and stable interactions of Piperin with both Glutathione S-Transferase support its potential role as an effective insecticidal compound. Together, these molecular interactions provide a mechanistic explanation for the insecticidal activity observed for Piper nigrum, reinforcing its suitability as a natural and eco-friendly pest control agent.

4. CONCLUSION

The present study demonstrates the insecticidal potential of Piper nigrum, supported by both phytochemical and molecular docking analyses. Soxhlet extraction using methanol yielded a bioactive extract containing compounds with potential insecticidal properties, as confirmed by GC–MS analysis. Molecular docking results showed strong binding affinity of Piperin with Glutathione S-Transferase and Alpha-amylase, indicating possible inhibition of detoxification and digestive enzymes in insects. These interactions provide a molecular basis for the observed insecticidal activity. Overall, the findings suggest that Piper nigrum and its bioactive constituent Piperin may serve as effective, natural alternatives to synthetic insecticides. Further in vivo and field-based studies are recommended to validate their practical application.

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