Senthil-Nathan, 2020). Essential oils from various plants have been shown to cause neuroexcitation or inhibition by modulating acetylcholine receptors and other neural targets, which impairs mosquito motor functions and feeding behavior (Duque et al., 2023).

In addition to direct neurotoxicity, some plant compounds disrupt mitochondrial function within nerve cells by inhibiting electron transport chain enzymes, thereby reducing ATP production essential for nerve signal propagation (Duque et al., 2023). This dual action on both synaptic transmission and cellular energy metabolism enhances the overall insecticidal efficacy of botanical extracts. Such neurotoxic mechanisms are crucial for developing plant-based insecticides that can overcome resistance issues associated with synthetic chemicals.

6.2 Inhibition of key enzyme activities

A major mode of action for many plant-derived insecticides involves the inhibition of acetylcholinesterase (AChE), an enzyme critical for terminating nerve impulses by hydrolyzing the neurotransmitter acetylcholine. Several studies have demonstrated that essential oils and phytochemicals bind to AChE active sites, preventing its function and causing accumulation of acetylcholine at synapses, which results in continuous nerve stimulation and eventual paralysis of mosquitoes (Duque et al., 2023; Montaño-Campaz et al., 2025). Molecular docking analyses support these findings by showing stable interactions between plant compounds such as γ-elemene and germacrene D with mosquito AChE enzymes (Montaño-Campaz et al., 2025).

Beyond AChE inhibition, other enzymes involved in detoxification processes like glutathione S-transferase and cytochrome P450 monooxygenases are also targeted by certain plant extracts, impairing the mosquito's ability to metabolize toxic substances (Pavela et al., 2019; Senthil-Nathan, 2020). This multi-enzyme inhibition not only increases toxicity but may also reduce the development of resistance by attacking several biochemical pathways simultaneously.

6.3 Toxicological effects at cellular and tissue levels

At the cellular level, plant extracts induce a range of toxic effects including disruption of cell membranes, oxidative stress, and damage to vital organelles such as mitochondria. These effects compromise cell integrity and function in mosquito larvae and adults (Pavela et al., 2019; Baz et al., 2024). Histopathological examinations reveal degeneration in tissues critical for survival such as midgut epithelium, *Malpighian tubules*, muscles, and reproductive organs following exposure to botanical insecticides (Baz et al., 2024).

Such tissue-level damage impairs digestion, excretion, locomotion, and reproduction in mosquitoes, contributing to reduced population growth beyond immediate mortality effects. For example, essential oils from *Ageratum conyzoides* caused ovarian cell degeneration in adult mosquitoes alongside gut epithelial damage (Baz et al., 2024), indicating that botanical extracts can exert prolonged sublethal impacts that affect vector capacity. These multifaceted toxicological actions highlight the potential of plant-based products as effective tools for integrated mosquito management.

7 Safety and Environmental Impact Assessment

7.1 Toxicity evaluation on non-target organisms

Plant-based extracts used for mosquito control generally exhibit lower toxicity to non-target organisms compared to synthetic insecticides, making them safer alternatives in integrated vector management. Studies have shown that many botanical insecticides, including neem oil and various essential oils, are target-specific and biodegradable, causing minimal harm to beneficial insects, aquatic organisms, and mammals (Demirak and Canpolat, 2022; Chatterjee et al., 2023). For example, methanolic extracts from certain plants demonstrated larvicidal activity against mosquitoes while showing weak or no toxicity in zebrafish embryos, a common model for assessing environmental safety (Figure 4) (Alqurashi et al., 2025). This selective toxicity is attributed to the complex mixtures of bioactive compounds in plant extracts that often act on specific mosquito physiological pathways without broadly affecting other species.