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Detoxifying Enzymes in Insecticide Resistance in *Nilaparvata Lugens* (Stål) (Delphacidae: Hemiptera)

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Introduction:

- Brown plant hopper (BPH), *Nilaparvata lugens* (Stål.), is the primary insect pest that attacks rice and is responsible for a significant decline in yield in the rice ecosystem (Jena *et al*., 2018).
- Chemical insecticides have been the mainstay of the fight against *N. lugens*; however, repeated and widespread use of these pesticides has resulted in resistance to most of the insecticides currently in use, including carbamates, pyrethroids, pyridines, neonicotinoids, and organophosphates (Liao *et al*., 2021). However, BPH can quickly become resistant to pesticides due to abuse and misuse (Zhang *et al*., 2016).
- Understanding the molecular mechanisms behind BPH's pesticide resistance is crucial for creating strategies to counteract the significant danger posed to crop productivity by the rapid evolution of insecticide resistance, for effective management strategies implementation.

Detoxifying enzymes involved in IR in BPH:

It is known that pesticide resistance is either caused by altered target sites, such as amino acid changes in voltage-gated sodium channels in some insects (Soderland & Knipple, 2003) or by increased amounts of detoxifying enzymes. The most prevalent resistance mechanism is the upregulation of these detoxification enzymes. *Nilaparvata lugens*, is one of the four principal (major) detoxifying enzymes included in the IR in BPH (Lu *et al*., 2021a), which are:

- Cytochrome P450 monooxygenase (P450s),
- Glutathione-S-Transferase (GSTs)
- Carboxylesterases (CarEs), and
- UDP-glycosyltransferases (UGTs)

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Like other insect species, insecticide resistance of BPH is most often acquired through the enhancement of metabolic detoxification (metabolic resistance) and alterations in the target sites causing reduced binding affinity of insecticides (target-site resistance) (Tang *et al*., 2022). The roles of various detoxifying enzymes involved in insecticide resistance of BPH are;

1. **Mixed Function Oxidase (MFO):** The enhanced resistance in BPH is mostly caused by cytochrome P450s, as demonstrated by metabolic enzyme activity primarily related to detoxification, synergism test, and RNA interference (RNA interference) (Abbas *et al*., 2016). Neonicotinoid resistance in BPH is primarily caused by enhanced detoxification by cytochrome P450s, which results in cross-resistance because of broad-spectrum detoxification by cytochrome P450s (Wen *et al*., 2009). Buprofezin resistance is also conferred by BPH cytochrome P450 CYP6AY1, which has been shown to metabolize imidacloprid well (Ding *et al*., 2013).
2. **Glutathione-S-Transferase (GSTs):** Previous research in *Nilaparvata lugens* suggested that it has been noted that, perhaps through metabolic and antioxidant defense, GSTs gave BPH resistance to pyrethroids (Vontas e*t al.*, 2000). It has been observed that overexpression of GST genes in BPH results in resistance to insecticides, including fipronil and pyrethroids (permethrin and λ-cyhalothrin) (Zhang et al., 2016). Neonicotinoid pesticide resistance is influenced by glutathione-S-transferase and these GST genes' functions in imidacloprid resistance were validated by their constitutive overexpression and expression induction (Garrood *et al*., 2016).

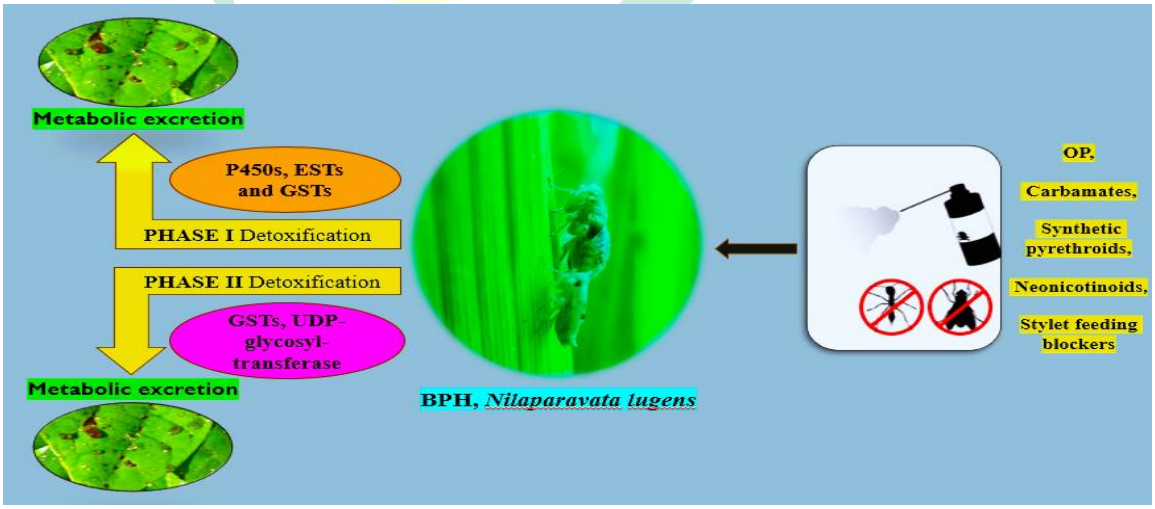

Fig. Xenobiotic detoxification of insecticides inside rice brown planthopper, *Nilaparvata lugens* (Stål)

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3. Carboxylesterases (ESTs): In insects, *CarE* acts as a Phase I detoxification enzyme to directly metabolize xenobiotic compounds, such as insecticides and phytochemicals (Li *et al*., 2007). Esterases that function by sequestration are known to be elevated through gene amplification and have been reported in OP-resistant strains of *Nilaparvata lugens* (Small and Hennigway, 2000) to insecticides like malathion, methamidophos, acephate, carbosulfan, etc. In BPH, several studies have shown that increased *CarE* activity is involved in the development of resistance to nitenpyram, sulfoxaflor, ethiprole, and acephate (Liao *et al.*, 2019).

4. UDP Glycosyl-transferases (UGTs): According to Bajda *et al*. (2015), Phase II UDP glycosyltransferases (UGTs) catalyze the conjugation of Phase I detoxification intermediates for solubilization and transport. As a key enzyme in Phase II detoxification, UGTs catalyze the conjugation of various small lipophilic compounds with sugar donors that create UDPs to produce water-soluble molecules that aid in the removal of hazardous substrates and help with detoxification (Dimunova *et al*., 2022). There are 21 known UGTs, and recent case studies have revealed that the HNF4 factor may also function in UGTs to control BPH's resistance to imidacloprid (Rowland *et al*., 2013). A recent study (Zhang *et al*., 2021b) functionally clarified their involvement in nitenpyram resistance. In BPH extensive work is still going on regarding organophosphorus and other insecticide resistance related to UGTs.

Examples of some recent research conducted on detoxification enzymes in IR in BPH:

Sl. No.	Test insect	Insecticide resistant to BPH	Detoxifying enzymes	References
1	The brown planthopper, *Nilaparvata lugens*, (Stål) (Delphacidae: Hemiptera), and White-backed plant hopper, *Sogatella furcifera*	Triflumezopyrim	Cytochrome P450s	Gong *et al*., 2022
2		Chlorpyrifos	Carboxyl-esterase (CarE)	Lu *et al*., 2022
3		Acephate, Thiamethoxam, and Buprofezin	Esterases [ESTs], Glutathione *S*-transferases [GSTs], and mixed-function oxidases [MFOs]	Malathi *et al*., 2017
4		Imidacloprid	Cytochrome P450 monooxygenase	Elzaki *et al*., 2016
5		Triflumezopyrim	Glutathione *S*-transferases [GSTs]	Zhang *et al*. (2020)

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6	(Delphacidae: Hemiptera),	Nitenpyram	Cytochrome P450 monooxygenase, and Esterases [ESTs],	Zhang *et al.*, 2017
7		Nitenpyram, Dinotefuran, and Chlorpyrifos	Cytochrome P450 monooxygenase	Jin *et al.* (2019)

***IR – Insecticide Resistance, BPH – Brown planthopper**

Conclusion:

The detoxification enzymes have inhibitory effects on xenobiotic compounds utilizing detoxification through various pathways. This makes an insect pest resistant to synthetic chemicals by causing huge crop loss. Various molecular mechanisms should be adopted to alter the genetic configuration of the amino acids that constitute the enzymes and proteins so that the overexpression of that particular gene will be stopped and the functioning of the detoxification process (xenobiotic degradation) can be erased, which will not favor the pest against the insecticides and ultimately the crop yield will be enhanced.

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