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# JOINT TOXICITY OF INSECTICIDES

Tulasi B[1] and Godavari[2]

[1,2] Division of Entomology, ICAR- Indian Agricultural Research Institute, New Delhi

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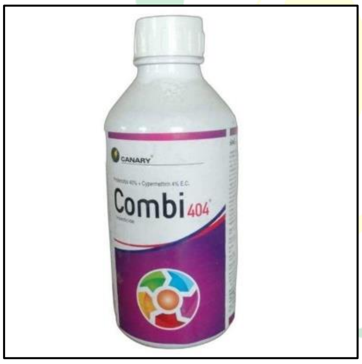
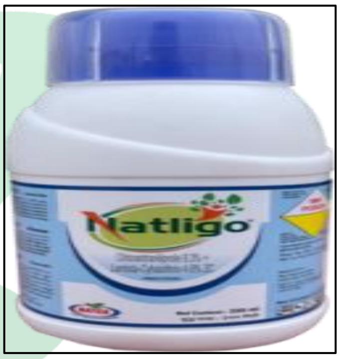
## Introduction

- Joint toxicity of insecticides refers to the combined toxic effects observed when two or more insecticides are used together or sequentially. **Ex: NATVOL:** Chlorantraniliprole 8.8% + Thiamethoxam 17.5% SC; and **NATLIGO:** Chlorantraniliprole 9.3% + Lambda-cyhalothrin 4.6% ZC.




- This phenomenon occurs when the toxic effects of individual insecticides are enhanced or potentiated by their interaction, resulting in a greater overall toxicity than would be expected from the sum of the toxicities of the individual insecticides alone. Understanding joint toxicity is crucial for pesticide risk assessment and management to ensure the safety of agricultural practices and environmental protection

## I. Compatability and Incompatability

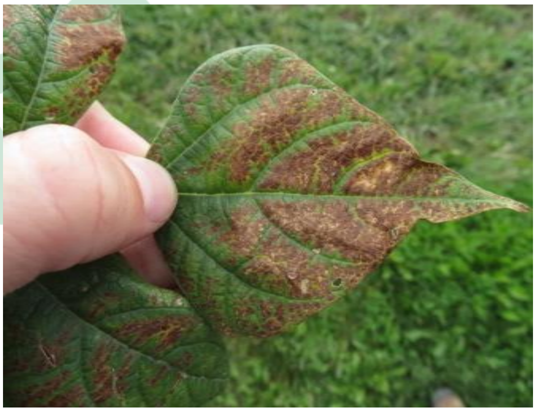
- **Compatability**: Pesticides are compatible when they can be mixed and applied without reducing the effectiveness or changing the physical and chemical properties of the mixture
- **Incompatability**: Two chemicals were mixed together such reactions from the either of one chemical may results in undesirable effect

a. Chemical - Some insecticides can react chemically with each other when mixed, leading to the formation of compounds that are less effective or more toxic than the individual insecticides. For instance, mixing certain insecticides with strong acids or bases can lead to chemical reactions that degrade the active ingredients or produce harmful byproducts.

b. Physical - Insecticides may have different formulations or adjuvants that are not compatible with each other. For example, mixing an emulsifiable concentrate insecticide with a wettable powder insecticide may result in precipitation or phase separation, reducing the efficacy of the mixture.

c. Phytotoxic - Incompatible mixtures can also pose risks of phytotoxicity when applied to crops. Some combinations of insecticides may cause leaf burn, discoloration, or other damage to plants due to their chemical properties or interactions with plant tissues.

**Interveinal chlorosis**



**Pesticide toxicity**

II. **Types of joint action of two poisons in a mixture:**

a. **Independent joint action:** The poisons or drugs act independently and have different modes of action. The susceptibility to one compound may or may not be co-related with the susceptibility with other. The toxicity of mixture can he predicted from the dose-mortality curve for each constituent applied alone and the correlation in susceptibility to the two poisons: the observed toxicity can be computed on this basis whatever relative proportions of components.

b. **Similar joint action:** The poisons or drugs produce similar but independent effects so that one component can be substituted at a constant proportion for the other. Variation in individual susceptibility to the two components is completely co-related or parallel. The toxicity of a mixture is predictable directly from that of the constituents, if their relative proportions are known.

**Calculations or mixed formulation of two toxicants:**

- Sun and Johnson have suggested a method of calculating the joint action of insecticides which is not only simple but also gives an approximation of the gain or loss of toxicity as well as the type of joint action for a mixture.
- There method involves determination of

  i) Actual toxicity indices of the components and their mixture from dosage -mortality curves.

  ii) Theoretical toxicity index of the same mixture which is equal to the sum of toxicity indices of two components

  iii) Joint toxicity or co-toxicity coefficient of the mixture which is equal to
- $\textbf{Joint toxicity or co} - \textbf{toxicity coefficient} = \frac{\text{Actual toxicity index of a mixture}}{\text{Theoretical toxicity index of a mixture}} * 100$

- Coefficient of a mixture near 100 indicates possibility of Similar action, coefficient less than 100 indicate independent action, while a coefficient significantly above 100 indicates synergism and the same significantly less than that shows antagonism.

- **Actual toxicity index (ATI)** $= \frac{\text{LD50 of A}}{\text{LD50 of mixture}} * 100$

- **Theoretical toxicity index = (Toxicity index of A*% of A in mixture) + (Toxicity index of** B*% of B in mixture

- **Toxicity index of A and B**= Relative toxicity of each *100

- **Relative toxicity** $= \frac{\text{LC50 of more toxic indecticide}}{\text{LC50 of less toxic insecticide}}$

**Types of Interactions**

a. **Synergism** – Increase in the bioactivity of two compounds to produce an effect greater than the one expected from a single algebraic summation of the effects of two compounds individually administered. One compound is non-toxic and other compound is toxic

b. **Potentiation** – Two toxic compounds applied together elicit a response greater than that expected from the sum of the individual toxicants

c. **Antagonism** – Decrease in lower activity of two compounds than the summation of activity when they are administered individually

**SYNERGISTS**

- **Synergists:** Often one component is not toxic or far less active than the counterpoint component at the dosage employed, but when combined with the later markedly increases the activity is called a 'Synergist'.

- Synergists are grouped into two types:

- **Analog synergists** – Structural resemblance to the insecticide and compete with it for detoxifying enzyme site

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- **MDP type synergists** – Inhibit or reduce the activity of microsomal enzymes as a result rate of detoxification of insecticides is reduced

**Non-toxic compounds which act as synergist**

**1. Compounds containing Methylene-dioxyphenyl (MDP) function**

**2. Compounds containing methylene-dioxyphenyl function along with other synergophores:**

a. MDP function and ether: ex: sesamin, sesamolin, piperonyl butoxide (PBO), safroxane, sesamex, etc. Best synergists have 3-4 ether linkages. PBO has three and sesamex contains four ether linkages.

b. MDP function and ether acetal: Tropital and dibenzylidene.

c. MDP function and amide: fagaramide.

d. MDP function and sulfoxide: sulfoxide

e. MDP function and carboxylic group : n-propyl isomer and buoarpolate.

f. MDP and α, β unsaturated carbonyl: piperonyl cylonene

**3. Compounds containing ether function:** ex: S-421, EUGENOL, methyl eugenol, tetramethoxy benzene

**4. N-Substituted amides:** ex: IN-930, MGK-264

**5. Pine oil and terpene derivatives:** ex: Isobornyl thiocyano acetate (Thanite)

**6. Miscellaneous compounds:**

a. α, β unsaturated carbonyl function: ex: Lipid associated of *Pongamia glabra* Vent.

b. Acylated 1, 3-Indandiones: ex: Valone

c. Established Insecticides ex: Nicotine

d. Other compounds: Imidazole, Phthalates

**7. Structural analogue:** WARF anti resistant, DMC, FDMC etc.

**Mechanism of synergistic action**

a. **Direct Enzyme Inhibition**: Some synergists directly bind to detoxification enzymes, inhibiting their activity. This binding may occur at the active site of the enzyme, blocking substrate binding or catalytic activity. Alternatively, the synergist may bind to allosteric sites, inducing conformational changes that inhibit enzyme function. For example, certain compounds may bind to cytochrome P-450 enzymes, preventing them from metabolizing insecticides effectively.

b. **Competitive Inhibition**: Synergists can compete with substrates (e.g., insecticides) for binding to detoxification enzymes. By occupying the active site or binding site of the enzyme, the synergist prevents the insecticide from being metabolized, thereby increasing its concentration and toxicity. This competitive inhibition reduces the rate of insecticide detoxification, leading to enhanced insecticidal activity.

c. **Non-competitive Inhibition**: In some cases, synergists may inhibit detoxification enzymes through non-competitive mechanisms. Instead of directly competing with substrates for binding sites, these synergists bind to other regions of the enzyme, causing structural changes that impair enzyme function. This type of inhibition may be more difficult to overcome than competitive inhibition because it does not rely on substrate concentration.

d. **Indirect Enzyme Modulation**: Synergists may also modulate the activity of detoxification enzymes indirectly by affecting enzyme expression, stability, or post-translational modifications. For example, certain synergists may upregulate the expression of enzymes involved in insecticide detoxification, counteracting the inhibitory effects of the synergist. Alternatively, synergists may promote the degradation of detoxification enzymes or interfere with their activation processes.

**Synergistic ratios:**

- Brondbent and Grubber (1971) worked out the synergistic ratios for the evaluation of synergistic effect of various non-toxic chemicals in mixtures with different insecticides.

A synergistic ratio is defined as the increase in toxicity caused by the non-toxic compound. Synergistic ratios are given for arbitrary combinations (commonly 10 parts of synergist to 1 part of insecticide) and is calculated as

- **Synergistic ratio** $= \frac{\text{LC50 of toxicant alone}}{\text{LC50 of mixture}}$
- If R> 1- Synergism
- If R <1 – Antagonism

- Synergistic ratio does not involve the multiplication factor of 100 used in the case of co-toxicity coefficient. Otherwise, the conclusion drew on the basis of co-toxicity coefficient is valid for the synergistic ratio as well.

- The terminology used in denoting such actions by co-toxicity coefficient or synergistic ratio also appears to have inherent drawbacks because the former is suitable only for the evaluation of the co-toxicity coefficient of two toxicants in the mixture and not of one toxicant and another non-toxic chemical in the mixture, and the latter may not only Indicate synergistic action but also antagonistic action.

**Advantages of using mixed formulations**

In the search for new and effective methods for controlling insect pests and in solving some of the problems created by the use of insecticides, mixed formulations of insecticides offer many possibilities. The mixed formulations of insecticides may be advantageously used for a number of different purposes.

- ✓ Although many of the modern insecticides control a wide spectrum of insect pests, yet the same insecticide is not the most suitable for controlling different species of insects attacking the same crop. To provide better **control of the different pests infesting the same crop**, the insecticides are mixed. Also, this avoids repeated application of individual insecticides on the same crop.
- ✓ Insecticides are often characterized with group specificity. Some of the new synthetic pyrethroids and insecticides of other groups are not effective against mite and increase

their population. To **overcome this problem of resurgence of secondary pests**, good formulated mixture of two insecticides can check the Increase of other pests.

- ✓ Pyrethrins are mixed with other Insecticides like DDT or lindane to exploit the knockdown effect along with quick action to control pests.
- ✓ Sometimes insecticides are mixed to **avoid hazardous effect of the individual insecticides**. For example, In EDCT mixture, the component carbon tetrachloride is added to reduce the fire and explosion hazards.
- ✓ There is a possibility of prevention **of development of resistance** by the use of mixtures of toxicants because the individuals resistant to one insecticide are the ones which become susceptible to the other insecticides.
- ✓ Combinations of some of the insecticides greatly increase the combined potency against insect pests i.e., their mixture shows synergism, The word 'Synergism' owe, its origin to the greek word (Syn: with, ergon: to work), meaning to work with or to co-operate.
- ✓ Lower rates may be used compared to using products containing single active substances (additive or synergistic action)
- ✓ The mixture may provide higher and/or more consistent levels of control against the same species

### Disadvantages of using mixed-formulations

- ❖ Added cost to already expensive insecticides
- ❖ Most insecticide treatments are related to economic thresholds. The presence of two pests at threshold levels controlled by different active substances of a mixture may coincide. However in many cases it is possible that one active will be applied when its target pest either does not reach the treatment threshold, or indeed may not be present in the crop. Either situation would constitute an overuse or unnecessary use of insecticide and not be considered good agricultural practice;
- ❖ Complexity of insecticide formulation and application
- ❖ In many cases insecticide solo product labels have different individual doses recommended for different targets, even for individual species within a particular group. In this situation, when the mixture is targeting a wide range of pests, there will be less flexibility in being able to differentiate doses for individual species.

- For many insect pests the application timing is critical in achieving an effective treatment, and additionally there may be a relatively short window within which treatments should be applied. Adults, but particularly juvenile stages, often quickly migrate or burrow into relatively inaccessible, sheltered parts of the crop. If the mixture is targeting different pests, the timing may not be optimal for all, resulting in reduced effectiveness
- Detrimental effects on non-target organisms, and may do more overall harm than using single active products in sequence
- Regulatory challenges in registration of these products and it takes more time