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Efficiency of Certain Neonicotinoid Mixtures Against the Cowpea Aphid, *Aphis craccivora* (Koch)

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ABSTRACT

Insecticide combinations are a strategy for increasing toxicity, combating resistance, and overcoming resistance. Neonicotinoid mixtures have been recommended to control a variety of sucking insects. In this study, the combination index (CI) was used to examine the synergistic interactions of certain neonicotinoids (acetamiprid, thiamethoxam, and dinotefuran) with various insecticides. The interactions of neonicotinoid mixtures were assessed by using the experimental combinations (1:1) and the commercial formulation mixtures ratio. The results clarified that the combination between neonicotinoids and acetylcholinesterase inhibitors insecticides had a strong synergistic effect, with (CI) values ranging between 0.05 -0.56. On the other hand, the lowest combination index (CI) value was 0.05 in thiamethoxam/profenofos mixtures, indicating the strongest synergism. Likewise, similar results were obtained with the antifeedant pymetrozine, with CI values ranging between 0.34- 0.68. Neonicotinoids had an additive effect when mixed with the tested pyrethroids and abamectin. Synergized mixtures can help to establish a resistance management strategy, reduce costs, and provide broad spectrum activity to cover multiple target pests at the same time.

INTRODUCTION

The cowpea aphid *Aphis craccivora* (Koch, 1854) (Homoptera: Aphididae) is a serious pest in Egypt that attacks legumes(El-Ghareeb *et al.* 2002). Direct feeding, virus transmission, and honeydew excretion all reduce their yield (Schepers, 1988). The use of various insecticide classes such as organophosphates, carbamates, and synthetic pyrethroids is essential for aphid control (Ahmad *et al.* 2009; Herron *et al.* 2001; Mokbel 2013). However, the widespread use of these conventional insecticides had resulted in an increase in insecticide resistance (Devonshire, 1989). Then, neonicotinoids insecticides were introduced in the 1990s and widely used in agricultural systems to combat resistant populations (Wang *et al.*, 2020). Unfortunately, The first report of neonicotinoid resistance in the whitefly, *Bemisia tabaci*, was reported with imidacloprid (Cahill *et al.*, 1996). Since then, several neonicotinoid

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resistance issues in different pest insects were documented. The Arthropod Pesticide Resistance Database (APRD) lists more than 330 cases of imidacloprid resistance, followed by 130 and 50 cases of thiamethoxam and acetamiprid resistance, respectively (Bass *et al*. 2015). A prior study suggested that *A. craccivora* could develop insecticide resistance to different neonicotinoids (Mokbel *et al.,* 2017).

Developing new insecticides is costly and time-consuming. So optimizing the use of current insecticides is critical for effective resistance management (Yang & Lai 2019). Therefore, there was an urgent need to combine newer and more traditional insecticides to combat insecticide resistance (Saddiq *et al.,* 2017). As a result, new formulations of neonicotinoid combinations were introduced to improve pesticide efficiency and restore sensitivity in resistant populations (Khan et al., 2013b; Taillebois and Thany, 2016). In addition, The investigation of synergistic interactions between mixtures is very critical for employing highly effective combinations in the control strategy (World Health Organization 2010).

Mixtures can broaden the spectrum of activity, postpone resistance, reduce the number of applications, and lower costs (Ahmad *et al.,* 2009; Brattsten *et al.,* 1986; Cloyd, 2009; Roush, 1989). The synergistic interactions with different insecticides are extremely powerful for insect control (Attique *et al.,* 2006; Basit *et al.,* 2013; Corbel *et al.,* 2004, 2006; Gunning *et al.,* 1999; Ullah *et al.,* 2017; Taillebois and Thany, 2022)**.** Insecticide mixtures have been proposed depending on the absence of cross-resistance to any of the mixture components.

In Egypt, several neonicotinoids mixtures were introduced and recommended to control sucking piercing insects, (*Egyptian Agricultural Pesticides Committee*, 2021) The aim of the current study is to evaluate the joint action and synergistic interactions of neonicotinoids mixtures with various insecticide classes such as organophosphates, pyrethroids, abamectin, and pymetrozine by using combination index (CI) values. The findings can be valuable for reducing current insecticides rates, saving time and money, and preserving or restoring neonicotinoid efficacy.

MATERIALS AND METHODS

Insecticides:

Commercial formulations of the following insecticides were used: acetamiprid (Acetamiprid 20 % SP, Barighat, India), dinotefuran (Oshin 20% SG, Mitsui Chemicals, Inc., Japan), thiamethoxam (Actara 25% WP, Syngenta Agro., Switzerland), malathion (Nasr lathion 57% Ec, Coromandel Fertilizers Co., Ltd., India), profenofos (Teliton 72% EC, The National Company for Agrochemicals &Investment, Egypt), pirimicarb (Aphox 50% DG, Syngenta Agro., Switzerland), lambdacyhalothrin (Lambdacyhalothrin 5% EC, Barighat, India), cypermethrin (Cyperco 20% EC, United Phosphorus Ltd., India), abamectin (Vapcomic 1.8% EC, VAPCO, Jordan), pymetrozine (Chess 25% WP, Syngenta Agro., Switzerland,

Insect:

The study used a cowpea aphid, *A. craccivora* (Koch) colony originated from a field collection from Sharkia Governorate, Egypt. Insects were reared in laboratory setting (22 degrees Celsius, 75% relative humidity, and a 12:12 light-dark photoperiod). Aphids were raised on seedlings of faba bean (Vicia fabae) cultivated in plastic pots (15 cm diameter). Pots carrying faba bean seedlings were kept in another chamber until needed.

Bioassays:

Leaf-dip Bioassay:

The leaf-dip bioassay technique was adopted from (Moores et al., 1996) with minor modifications. Faba bean leaves were immersed in the pesticides' aqueous solutions for about 10 seconds before drying on a paper towel. In Petri plates (60mm diameter), leaves were placed upside down on an agar bed. On the treated leaf, ten apterous adults of *A. craccivora* were inserted, whereas leaves dipped in water served as control. Each pesticide had five to seven concentrations and each concentration had five replicates. After 48 hours, the mortality rate was calculated. Adults were regarded as dead if they showed no coordinated forward movement when they were prodded with a fine paintbrush.

Mixture Leaf-Dip Bioassay:

The LC_{50} values for each binary pesticide mixture were determined using leaf-dip bioassays. Binary mixtures were made with active ingredients in a 1:1 ratio. The registered formulations in Egypt, on the other hand, were. (2 acetamiprid:1 cypermethrin), (5 thiamethoxam:1 abamectin), (3 thiamethoxam:4 pymetrozine), and (2 acetamiprid:1 cypermethrin) (1 acetamiprid:1.75 lambda-cyhalothrin). The Combination Index (CI) equation was used to examine the results.

Data Analysis:

Abbott's formula was used to correct mortality (Abbott, 1925). The data were then subjected to probit analysis (Finney, 1971) included in the Probit-MSChart computer program (Chi, 2020). The combination index (CI) technique, suggested by (Chou and Talalay, 1984), was used in this investigation. The following formula was used to compute the CI at the LC_{50} level:

$$\mathrm{CI} = \frac{\mathrm{LC_{50}}^{1m}}{\mathrm{LC_{50}}^{1}} + \frac{\mathrm{LC_{50}}^{2m}}{\mathrm{LC_{50}}^{2}} + \left(\frac{\mathrm{LC_{50}}^{1m}}{\mathrm{LC_{50}}^{1}} \times \frac{\mathrm{LC_{50}}^{2m}}{\mathrm{LC_{50}}^{2}}\right)$$

LC_{50} 1: LC_{50} value of the first pesticide in the mixture alone.
LC_{50}2: LC_{50} of the second pesticide in the mixture used alone.
LC_{50}1M: the proportionality of the dose of the first pesticide in the LC_{50} of the mixture
LC_{50}2M: the proportionality of the dose of the second pesticide in the LC_{50} of the mixture
Based on CI values, the interaction categories were classified according to (Gisi, 1996; Kosman and Cohen, 1996):
CI < 0.5, the mixture components were strongly synergistic.
CI 0.5 to 0.77, the mixture components were less synergistic.
CI > 0.77 to 1.43, the mixture components were additive.
CI > 1.43, the mixture components were antagonistic.

RESULTS

Table 1 shows the LC_{50} values of the investigated insecticides in the current investigation. Lambda-cyhalothrin, with an LC_{50} of 0.021 g/mL, was the most effective insecticide against cowpea aphids, followed by cypermethrin, with an LC_{50} of 0.056 g/mL. Furthermore, different neonicotinoid pesticides had different LC_{50} values against the cowpea aphid. Dinotefuran showed the greatest efficiency (0.89g/mL), followed by acetamiprid (0.95g/mL), and thiamethoxam showed the least harmful effect (3.82g/mL). Pirimicarb, a carbamate insecticide, with an LC_{50} of 0.68g/mL. The organophosphorus insecticide profenofos had an LC_{50} of 1.96 g/mL, while malathion had an LC_{50} of 88.74 g/mL. Pymetrozine had an LC_{50} of 9.87 g/mL and abamectin had an LC_{50} of (418.5 g/mL), respectively.

Table1. Response of cowpea aphid, *Aphis craccivora* (Koch) to the individual tested insecticides.

Pesticide (Common name)	LC_{50} µg/mL (95% CI)	Fit of probit line			
		Slope± SE	χ2	df	*P*
Thiamethoxam	3.825 (2.758 - 5.612)	1.36± 0.18	4.15	5	0.528
Acetamiprid	0.95 (0.69 - 1.27)	1.05±0.19	0.98	4	0.912
Dinotefuran	0.89 (0.58- 1.26)	1.32± 0.21	3.17	4	0.529
Pymetrozine	9.87 (6.97-14.89)	1.82± 0.37	0.262	3	0.967
Cypermethrin	0.056 (0.006-0.145)	0.65± 0.22	0.442	3	0.931
Lambda-cyhalothrin	0.021 (0.012- 0.030)	2.13±0.47	1.143	2	0.564
Malathion	88.74 (75.03-109.66)	2.81±0.61	3.573	2	0.167
Profenofos	1.96 (1.37 - 2.67)	2.53 ±0.40	3.254	3	0.354
Pirimicarb	0.68 (0.25-1.47)	0.79± 0.18	4.771	3	0.189
Abamectin	418.53 (99.16- 151571.4)	0.57±0.19	4.004	2	0.135

The binary combination of neonicotinoids with other pesticides revealed that (acetamiprid + lambda cyhalothrin) with mixture ratio of (1 : 1.75) had the lowest LC_{50} values (0.04 µg/mL) followed by thiamethoxam + profenofos with mixture ratio of (1: 1) (0.12 µg/mL), acetamiprid + cypermethrin with mixture ratio of (2: 1) (0.18 µg/mL), acetamiprid + malathion (0.43 µg/mL), thiamethoxam + malathion with mixture ratio of (1: 1) (0.45 µg/mL), acetamiprid + pirimicarb with mixture ratio of (1: 1) (0.50 µg/mL), dinotefuran + malathion with mixture ratio of (1: 1) (1.01 µg/mL), thiamethoxam + pymetrozine with mixture ratio of (3: 4) (1.91 µg/mL) and thiamethoxam + abamectin with mixture ratio of (5: 1) (6.21 µg/mL) as shown in Table 2 .

Table2. Response of cowpea aphid, Aphis craccivora (Koch) to the tested binary pesticide mixtures.

Mixture (common names)	Mixture ratio	LC50 µg/mL (95% CI)	Fit of probit line			
Commercial formulation mixtures			**Slope ± SE**	**χ2**	**df**	***P***
Thiamethoxam + abamectin	5:1	6.21 (4.71- 8.16)	1.36 ±0.30	0.544	3	0.909
Thiamethoxam+ pymetrozine	3:4	1.91 (1.53 - 2.38)	1.05 ±0.25	0.260	3	0.967
Acetamiprid + cypermethrin	2:1	0.18(0.11 - 0.28)	1.27± 0.21	3.665	5	0.598
Acetamiprid+ λ-cyhalothrin	1 : 1.75	0.04(0.02 - 0.08)	1.02± 0.16	4.203	6	0.649
Experimental mixtures						
Thiamethoxam + abamectin	1:1	1.43(0.75 - 2.31)	1.37±0.41	0.437	2	0.803
Thiamethoxam+ pymetrozine	1:1	3.34(2.08- 4.98)	1.51± 0.34	0.579	2	0.748
Thiamethoxam + malathion	1:1	0.45 (0.39 - 0.50)	1.18 ±0.22	0.124	4	0.998
Thiamethoxam + profenofos	1: 1	0.12(0.07 - 0.15)	0.94 ±0.26	0.271	3	0.965
Acetamiprid + malathion	1:1	0.44 (0.06 - 0.95)	0.98± 0.24	4.74	3	0.191
Dinotefuran + malathion	1:1	1.01(0.82 - 1.28)	1.46 ±0.32	0.487	4	0.974
Acetamiprid + pirimicarb	1:1	0.50(0.28 - 0.81)	1.89± 0.38	2.179	3	0.536
Acetamiprid + cypermethrin	1:1	0.22 (0.12 - 0.37)	1.27 ± 0.24	2.48	3	0.478
Acetamiprid+ λ-cyhalothrin	1:1	0.07(0.05 - 0.09)	1.26± 0.18	1.850	6	0.932

The combination index (CI) was calculated for each mixture in Table 3 to assess the interaction effect of insecticide mixtures. Except for thiamethoxam + pymetrozine with a mixture ratio (3:4), which showed Strong synergism with a CI value of (0.34), commercial formulation mixture ratios exhibited an additive effect. Regarding experimental mixtures, the greatest synergistic effect was obtained with thiamethoxam - profenofos mixture (CI = 0.05), followed by thiamethoxam -malathion mixture (0.06), acetamiprid - malathion mixture (0.23), and thiamethoxam - pymetrozine mixture (0.23). (0.68). Dinotefuran-malathion and acetamiprid-pirimicarb mixtures showed less synergism, with CI values of 0.56 and 0.73, respectively. Acetamiprid-cypermethrin and lambda-cyhalothrin mixtures, on the other hand, showed antagonism with CI values of 2.0 and 1.85, respectively.

Table 3. Combination index of the tested mixtures on the cowpea aphid, *Aphis craccivora* (Koch).

Mixture (Common names) Commercial formulation mixtures	$LC_{50}1$	$LC_{50}2$	Mixture ratio	$LC_{50}M$	LC_{50} 1M	LC_{50} 2M	CI	Classification
Acetamiprid + λ-cyhalothrin	0.95	0.02	1: 1.75	0.04	0.014	0.02	1.02	Additive
Thiamethoxam + abamectin	3.82	418.5	5:1	6.21	5.09	1.16	1.33	additive
Thiamethoxam+ pymetrozine	3.82	9.87	3:4	1.91	0.82	1.09	0.34	Strong synergism
Acetamiprid + cypermethrin	0.95	0.065	2:1	0.17	0.11	0.056	1.07	Additive
Experimental mixtures								
Acetamiprid + malathion	0.95	88.74	1:1	0.43	0.215	0.215	0.23	Strong synergism
Acetamiprid + pirimicarb	0.95	0.68	1:1	0.5	0.25	0.25	0.73	Less synergism
Acetamiprid + cypermethrin	0.95	0.065	1:1	0.22	0.11	0.11	2.00	Antagonism
Acetamiprid + λ-cyhalothrin	0.95	0.02	1:1	0.07	0.035	0.035	1.85	Antagonism
Dinotefuran + malathion	0.84	88.74	1:1	1.01	0.5	0.5	0.56	Less synergism
Thiamethoxam + abamectin	3.82	418.5	1:1	1.43	0.72	0.72	0.19	Strong synergism
Thiamethoxam + pymetrozine	3.82	9.87	1:1	3.34	1.67	1.67	0.68	Less synergistic
Thiamethoxam + malathion	3.82	88.74	1:1	0.45	0.22	0.22	0.06	Strong synergism
Thiamethoxam + profenofos	3.82	1.96	1: 1	0.13	0.065	0.065	0.05	Strong synergism

DISCUSSION

As a result of widespread use, insecticide resistance had emerged by the time. As a result, various strategies, such as the use of pesticide mixtures, are required to prevent or delay the appearance of resistance (Chou, 2006). Insecticide mixtures with different modes of action have been shown to increase efficacy, combat, and/or delay resistance in pest species (Curtis, 1985). The current study was carried out to assess the toxicity of neonicotinoids and their combinations with other insecticides with different modes of action against the cowpea aphid.

The data obtained revealed that the mode of action of the mixture component had a significant impact on the combined toxicity of mixtures. Our findings demonstrated that the combination of neonicotinoids and organophosphates had strong synergistic effects That consistent with the findings of (Taillebois and Thany, 2016), who found that an acetamiprid-chlorpyrifos mixture had a synergistic effect against the pea aphid, *Acyrthosiphon pisumi* (Harris) (Hemiptera: Aphididae). Similarly, after topical treatment with 1:0.5 chlorpyrifos-imidacloprid mixture on *Nilaparvata lugens* (Stål) (Hemiptera: Delphacidae) with a combination index value of 0.18. (Xu *et al.*, 2020). The interaction of neonicotinoids and acetylcholinesterase inhibitors can be interpreted as enhancing the nerve impulse in the postsynaptic membrane due to acetylcholine accumulation at the neuromuscular junction. As a result, both cholinesterase inhibitors and neonicotinoids have a similar net effect on nerve impulse transmission. Furthermore, acetylcholinesterase inhibitors can inhibit esterases and/or monooxygenase, which are involved in neonicotinoid detoxification in *A. craccivora*. As a result, metabolic enzyme inhibition can be used to interpret neonicotinoids' synergism when combined with Ops compounds (Khan *et al.,* 2013a).

Mixtures of neonicotinoids and pyrethroids had an additive effect. Our findings are consistent with those of (Reddy *et al.*, 2018), who discovered that thiamethoxam mixtures with lambda-cyhalothrin significantly reduced *A. craccivora* numbers in cowpea. The additive effect may be due to the fact that neonicotinoids and pyrethroids are complementary in an ideal way: Pyrethroids have a quick knockdown effect and work through contact; neonicotinoids are systemic, meaning they are distributed throughout the plant and can reach hidden pests. As a result, IRAC recommends these mixtures for agricultural use, provided that the pest populations are not resistant to one of the components (Housset *et al.*, 2009).

There have been few studies on neonicotinoids-abamectin or neonicotinoids-pymetrozine mixtures. The interaction patterns of thiamethoxam-abamectin mixtures were studied in this study. Mixtures with a 5:1 ratio (thiamethoxam: abamectin) showed an additive effect, whereas mixtures with a 1:1 ratio showed strong synergism. Similarly, (Levchenko and Silivanova, 2019) found that a 1:2.5 ivermectin/acetamiprid mixture had strong synergistic effects. Furthermore, the combination of abamectin and thiamethoxam had the highest residual toxicity against the *Asian citrus psyllid* (ACP), *Diaphorina citri* Kuwayama (Hemiptera: Liviidae) (Vanaclocha *et al.*, 2019). Concerning neonicotinoids–pymetrozine mixtures, thiamethoxam-pymetrozine mixture with a ratio of 3:4 demonstrated strong synergism, whereas the mixture with a ratio of 1:1 demonstrated low synergism. On the melon aphid, *Aphis gossypii* Glover (Hemiptera: Aphididae), similar results were obtained with imidacloprid:pymetrozine mixtures. The ratio of 1:1 produced the greatest synergistic effect (Olfati Somar *et al.*, 2019).

The current study found that neonicotinoid mixtures, particularly those with cholinesterase inhibitors, abamectin, and pyrethroids, had either additive or synergistic effects. The current finding suggests that synergistic neonicotinoid mixtures can extend the use of neonicotinoids against the cowpea aphid. Furthermore, it can overcome aphid resistance to certain conventional insecticides. The obtained results allow us to provide useful indications about combinations that may be interesting in pest management applications.

Conclusions

Several strategies had been used to avoid pesticide resistance and environmental hazards as a result of these drawbacks, Insecticide mixtures are an effective way to achieve these goals. Our findings show that neonicotinoid mixtures can have additive, synergistic, or antagonistic effects. The interaction effect is determined by the pesticide category and the mixing ratio. Our findings provide some hints as to which combinations may be useful in future *Aphis craccivora* management applications.

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