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Acaricidal activities of new potential oxadiazole derivatives on *Tetranychus urticae* Koch (Prostigmata: Tetranychidae)

Yeni potansiyel oksadiazol türevlerinin *Tetranychus urticae* Koch (Prostigmata: Tetranychidae)'de akarisidal aktiveleri

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ABSTRACT

Tetranychus urticae Koch, 1836 (Prostigmata: Tetranychidae) is a cosmopolitan species known for developing resistance to many pesticides. One strategy to address this challenge is to discover of new groups of active substances. However, the high cost and time required for discovering new molecules have prompted researchers to focus on modifying existing active substances. Etoxazole is an active ingredient reported to be effective against several economically important mite species. Therefore, derivatization studies have been carried out using this compound as a lead structure. In the present study, target molecules containing modifiable oxadiazole groups were designed through a bioisosterism approach, in which the oxazoline ring was replaced with an oxadiazole ring, and substituted phenyl groups were introduced at the C-2 and C-4 positions. When the toxic effects of seven synthesized active substances (3a, 3b, 3c, 3d, 3e, 3f, and 3g) were tested against the nymphal stages of *T. urticae*, the highest mortality rates were observed for compounds 3b, 3a, and 3g (66%, 64%, and 58%, respectively), following the etoxazole-treated control group. At the egg stage, compound 3a exhibited toxic effects comparable to that of etoxazole, whereas the remaining derivatives displayed relatively lower levels of activity. In conclusion, the findings indicate that derivatives of the oxadiazole group, showing stage-specific activity against *T. urticae*, represent a promising approach for the development of new control strategies against this pest.

INTRODUCTION

Tetranychus urticae Koch (Acari: Tetranychidae) is one of the most important pest species worldwide. It is a phytophagous mite with a broad host range, short life cycle, high reproductive capacity, and remarkable ability to develop resistance to pesticides, making it a serious threat to agriculture (Agrawal 2000, Assouguem et al. 2022, Rincón et al. 2019, Van Leeuwen et al. 2015). To date, over 1.100 plant species from more than 140 families have been recorded worldwide, including economically important crops such as fruit trees, vegetables, and ornamental plants (Attia et al. 2013, Grbić et al. 2011, Rioja et al. 2017). A range of cultural, chemical, and biological methods have been employed for its control, but synthetic acaricides and insecticides remain the most commonly used approach (Ay et al. 2005, Opit et al. 2004, Sato et al. 2011, Van Leeuwen et al. 2006). Despite their effectiveness, reliance on chemical pesticides has resulted in resistance development and residue problems in *T. urticae* populations (Khanahmadi et al. 2017, Kim et al. 2004). According to recent data, *T. urticae* has been reported to develop resistance to at least 96 active substances, including organophosphates, pyrethroids, and several newly developed pesticides (Wu et al. 2023). Moreover, the continual withdrawal of active substances due to resistance further complicates chemical control and increases economic losses (Denholm and Rowland 1992). To address this challenge, the discovery of new active substances is considered a promising solution (Jutsum et al. 1998, Sparks et al. 2021). However, the high costs and long timelines associated with developing novel compounds have directed research efforts toward structural modification of existing active ingredients as a more feasible strategy (Das 2016).

Molecules containing N-heterocyclic structures are considered promising candidates for the development of new pesticides. Incorporation of a nitrogen atom into a molecule can enhance cell permeability, water solubility, and interaction with biological targets (Romanov-Michailidis and Rovis 2015). An analysis of the U.S. Food and Drug Administration (FDA) database indicates that more than 59% of approved drug molecules contain an N-heterocyclic structure, and such scaffolds are also widely represented among potent pesticide molecules (Jiang et al. 2020, Liu et al. 2017, Vitaku et al. 2014, Zhang 2017, Zu et al. 2020). A well-known example is etoxazole, a 2,4-diphenyl-1,3-oxazoline derivative that acts as a chitin biosynthesis inhibitor. Etoxazole is a novel acaricide with high specificity and strong activity against several phytophagous mite species, including *Brevipalpus* spp., *Tetranychus cinnabarinus*, *Panonychus ulmi*, and *Tetranychus urticae* (Suzuki et al. 2001). Importantly, it exhibits low toxicity to non-target organisms such as aquatic species, birds, and mammals (Nauen and Smagghe 2006). In addition, etoxazole demonstrates broad-spectrum efficacy against multiple developmental stages of mites, particularly eggs, larvae, and nymphs (Li et al. 2014).

Recently, the development of new acaricides based on the chemical scaffold of etoxazole has attracted considerable attention. Several studies have reported structural modifications to etoxazole, integrating different functional groups such as ether (Zhang et al. 2022), oxime ether (Li et al. 2014), and sulfide (Chen et al. 2019, Chen et al. 2024) (Figure 1). In another approach, oxazoline derivatives containing disulfide (S–S) bonds were synthesized, and their acaricidal potential against *Tetranychus cinnabarinus* eggs and larvae was evaluated (Tian et al. 2024).Oxadiazoles are five-membered aromatic heterocycles composed of two carbon atoms, two nitrogen atoms, and one oxygen atom. They have recently drawn significant interest as bioisosteric replacements for carbonyl-containing functional groups. Compounds incorporating oxadiazole rings display diverse pharmacological activities, including antituberculosis, antifungal, analgesic, anti-inflammatory, antiviral, anticancer, antihypertensive, anticonvulsant, and antibacterial properties (Ziyaev and Ismailova 2017). Bioisosterism is a well-established strategy in medicinal chemistry that involves modifying the structure of precursor compounds to achieve improved stability, optimized pharmacokinetic properties, or enhanced biological activity, while retaining the essential features responsible for efficacy (Lima and Barreiro 2005, Patani and LaVoie 1996, Wagener and Lommerse 2006). This approach has also been widely adopted in agrochemical discovery, where pharmaceutical R&D methodologies have contributed to the development of new insecticides and acaricides. Given the proven acaricidal potential of etoxazole and the promising outcomes of derivatization studies, we designed a new series of target molecules using a bioisosterism approach. In these compounds, the oxazoline ring of etoxazole was replaced with an oxadiazole ring, and substituted phenyl groups were introduced at the C-2 and C-4 positions. The structural modifications were intended to evaluate the influence of: the number and position of fluorine atoms on the C-4 phenyl ring, the incorporation of a second nitrogen atom within the oxadiazole ring, and the presence of a substituted phenyl group at the C-2 position.

In this study, the acaricidal effects of seven newly synthesized oxadiazole derivatives were assessed against the nymphal and egg stages of *T. urticae*. The results were used to evaluate their potential as candidate acaricides for future pest management strategies.

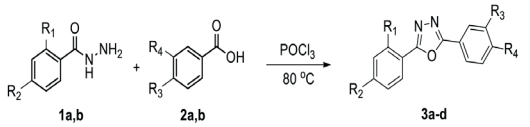
MATERIALS AND METHODS

Tetranychus urticae population and mass production

In this study, the German Susceptible Strain (GSS) population of *Tetranychus urticae*, which has been maintained without exposure to pesticides since 2001 in the insect rearing rooms of the Plant Protection Department, Faculty of Agriculture, Isparta University of Applied Sciences, was used. The GSS colony was continuously reared on bean plants (*Phaseolus vulgaris*) without pesticide application, under controlled conditions of 26 ± 1 °C, 50–60% relative humidity, and a photoperiod of 16:8 h (light:dark) provided by fluorescent lamps.

Synthesis and characterization of compounds

In this study, commercially available hydrazide compounds (1a,b) were subjected to intramolecular cyclization reactions with two different aryl carboxylic acids (2a,b) in the presence of phosphoryl chloride to obtain oxadiazole derivatives (3a–d). Hydrazide (1a,b) (10 mmol) and the corresponding carboxylic acid (2a,b) were mixed, followed by the addition of $POCl_3$ (4 ml). The mixture was stirred under reflux at 80 °C until the reaction was completed, as monitored by Thin Layer Chromatography (TLC). After completion, the reaction mixture was slowly poured into ice water with stirring, and the resulting precipitate was collected by filtration, dried, and purified by recrystallization from a suitable solvent.



Compounds	R_1	R_2	R_3	R_4
3a	-F	-H	$-OCH_3$	$-OCH_3$
3b	-F	-H	$-OCH_2CH_3$	$-OCH_2CH_3$
3c	-F	-F	$-OCH_3$	$-OCH_3$
3d	-H	-F	$-OCH_2CH_3$	$-OCH_2CH_3$

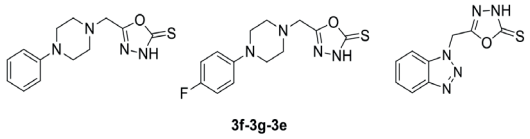


Figure 1. The chemical structures of the novel oxadiazole derivatives

The molecular structures of the synthesized compounds were characterized using FTIR and NMR spectroscopic techniques. Examination of the FTIR spectra revealed the disappearance of the amino group bands present in the hydrazide precursors, while the C=N stretching bands indicative of oxadiazole ring formation were observed in the range of 1519–1572 cm^{-1}. Additionally, the absence of C=O stretching bands corresponding to the hydrazide and carboxylic acid groups in the FTIR spectra of the synthesized oxadiazole derivatives further supported the successful formation of the target structures.

Analysis of the ^1H NMR spectra of compounds 3a–d showed resonances of aromatic protons (arH) in the range of 7.11–8.15 ppm, along with the disappearance of -NH and $-NH_2$ protons from the hydrazide precursors, and the absence of the carboxylic acid (-COOH) proton, confirming the molecular structures. Another important evidence was provided by the ^{13}C NMR spectra, in which the C-2 and C-5 carbons of the oxadiazole ring were observed at 151.79–152.36 ppm and 164.48–164.55 ppm, respectively. Compounds 3e–g were synthesized and characterized according to previously reported methods (Figure 1) (Mermer et al. 2019, Ozdemir et al. 2017, Zhang et al. 2013).

Acaricidal activity assays

The acaricidal activities of the synthesized compounds against *Tetranychus urticae* were evaluated using the dry residue method. To determine the effects of the oxadiazole derivatives, applications were carried out on two developmental stages of the two-spotted spider mite: eggs and nymphs. These stages were selected because etoxazole, a commercially registered acaricide containing an oxazoline moiety, is typically applied during the pre-adult stages of this pest. To ensure uniformity in the test material, a preliminary preparation was performed to obtain eggs and nymphs of the same age. For this purpose, 10 adult female mites were transferred onto bean leaves placed in petri dishes (9 cm diameter). After a few days, eggs of the same age laid by the females were used for the egg assays, while the nymphs that hatched from these eggs were used for the nymph assays. The experiments were designed with one control group and three treatment concentrations, each with three replicates. Each synthesized compound was first dissolved in N,N-dimethylformamide and subsequently diluted in distilled water to final concentrations of 125 mg L^{-1}, 250 mg L^{-1}, and 375 mg L^{-1} (0.1 mg L^{-1} in solvent), which were then used in the biological activity assays. These doses were determined based on preliminary trials. Twenty-five mite eggs or nymphs were transferred onto clean bean leaves under a binocular microscope. The leaves were treated with 2 ml of the prepared solutions using a spray tower, ensuring coverage of the leaf surface. The control group was treated with distilled water only. Additionally, a commercially registered preparation containing etoxazole, an oxazoline-based compound, was used as a reference treatment. Mortality assessments for nymphs were conducted on the fourth day after application, while egg hatchability was recorded once all eggs in the

control group had hatched. The acaricidal activities of the synthesized compounds at different concentrations were calculated based on the observed mortality and analyzed using probit analysis.

RESULTS

Reaction times were determined to be 11 h for compounds 3a and 3b, and 10 h for compounds 3c and 3d. The reactions were monitored by Thin Layer Chromatography ($CHCl_3$:EtOH (9:1)). The obtained crude compounds were purified by recrystallization using ethanol (for 3a and 3d) or ethyl acetate (3b and 3c). The yields of compounds 3a-d after purification were found to be 82%, 79%, 86%, and 89%, respectively.

The effects of the active compounds on *T. urticae* nymphs varied depending on the applied concentration. At a concentration of 125 mg L^{-1}, treatments with 3a (29%) and 3b (36%) exhibited moderate activity, whereas 3c, 3d, and 3e showed no mortality (0%), and 3f induced only 2% mortality. Compound 3g caused 14% mortality, indicating limited efficacy at this concentration. In contrast, etoxazole achieved complete mortality (100%), demonstrating complete activity. At 250 mg L^{-1}, mortality rates increased noticeably for 3a and 3b, reaching 45% and 48%, respectively, compared to the previous concentration. Other treatments, including 3c (5%), 3d (2%), 3e (0%), and 3f (8%), remained at low activity levels, while 3g exhibited moderate activity with 38% mortality. At the highest tested concentration of 375 mg L^{-1}, the highest efficacies were observed for compounds 3a (64%), 3b (66%), and 3g (58%). Limited activity was observed for 3c (11%), 3d (2%), 3e (0%), and 3f (17%). Etoxazole consistently showed 100% mortality across all three concentration levels, confirming its superior biological activity (Table 1). Overall, compounds 3a, 3b, and 3g demonstrated a marked increase in efficacy with increasing concentration, whereas the effects of the other compounds on *T. urticae* nymphs remained limited.

At 125 mg L^{-1}, the active compounds caused low mortality in *T. urticae* eggs, ranging from 0% to 21% across the tested groups, whereas etoxazole achieved 100% mortality. At 250 mg L^{-1}, mortality slightly increased (e.g., 38% in 3a, 25% in 3g), but remained low in most groups. At the highest concentration (375 mg L^{-1}), mortality reached 60% in 3a and 34% in 3b, while remaining between 2–8% in other groups. In contrast, etoxazole consistently resulted in 100% mortality at all concentrations (Table 2). These results demonstrate that although mortality generally increased with concentration, the overall efficacy of the compounds remained limited compared to etoxazole.

DISCUSSION

Studies in the literature indicate that oxadiazole, oxazoline, and their derivatives provide promising results in terms of acaricidal and insecticidal potential. Dai et al. (2017) reported that pyrazoloxime derivatives containing oxadiazole exhibited significant acaricidal and insecticidal activity against *Tetranychus cinnabarinus*, *Aphis medicaginis*, *Mythimna separata*, and *Nilaparvata lugens*. The authors

Table 1. The acaricidal effect of the active compounds on *Tetranychus urticae* nymphs

Observation Time (days)	Active Substances	Mortality Rate (%)		
		Concentrations (mg L^{-1})		
		125	250	375
4	3a	%29±0.59 bC*	%45±0.55 bB	%64±0.25 bA
	3b	%36±0.35 bB	%48±1.59 bB	%66±0.80 bA
	3c	%0±0.25 cB	%5±0.65 cB	%11±0.48 cA
	3d	%0±0.15 cA	%2±1.05 cA	%2±0.75 dA
	3e	%0±0.88 cA	%0±0.35 cA	%0±0.25 dA
	3f	%2±0.45 cB	%8±0.15 cA	%17±1.05 cA
	3g	%14±0.48 bB	%38±0.75 bA	%58±0.25 bA
	Etoxazole	%100±0.15 aA	%100±0.25 aA	%100±0.25 aA

*Different lowercase letters in the same column and different uppercase letters in the same row indicate that the means are significantly different according to the active ingredient and the applied concentrations, respectively ($p < 0.05$)

Table 2. Toxicity of active compounds on *Tetranychus urticae* eggs

Observation Time (days)	Active Substances	Mortality Rate (%)		
		Concentrations (mg L^{-1})		
		125	250	375
4-5	3a	%21±0.25 bC*	%38±0.38 bB	%60±0.65 bA
	3b	%9±0.55 cC	%22±0.74 Bb	%34±0.15 Ac
	3c	%0±0.35 cA	%2±0.85 cA	%2±0.15 dA
	3d	%4±0.25 cA	%5±0.13 cA	%8±0.50 dA
	3e	%1±1.50 cA	%2±0.50 cA	%6±0.25 dA
	3f	%2±0.65 cA	%5±0.36 cA	%6±0.78 dA
	3g	%10±0.80 cB	%25±0.42 bB	%31±0.28 cA
	Etoxazole	%100±0.20 aA	%100±0.15 aA	%100±0.15 aA

*Different lowercase letters in the same column and different uppercase letters in the same row indicate that the means are significantly different according to the active ingredient and the applied concentrations, respectively ($p < 0.05$)

established their experimental protocols based on methodologies adapted from various previous studies. Specifically, bioassays conducted on *T. cinnabarinus* targeted both egg and larval stages, employing the leaf-dipping method with an immersion duration of 3 seconds for each stage. Each replicate comprised 60–100 individuals, and mortality evaluations were performed on the fourth day post-treatment (Yu et al. 2015). For *A. medicaginis*, apterous adult individuals were used, with treatments applied using the dipping method for 5 seconds, followed by mortality assessments after 24 hours (Shao et al. 2010). In the case of *M. separata*, ten fourth-instar larvae were treated with the test compounds via foliar application, and observations were recorded on the fourth day (Yu et al. 2015). Finally, for *N. lugens*, macropterous females (30 individuals per replicate) were subjected to microtopical application of the tested compounds, and mortality assessments were conducted 48 hours after treatment (Shao et al. 2010). In particular, some compounds demonstrated good to excellent acaricidal activity on *T. cinnabarinus* at 500 μg/ml, with compounds 7a, 7h, 7p, and 7q achieving mortality rates of 100%, 100%, 90%, and 90%, respectively, comparable to the commercial acaricide fenpyroximate. Similarly, Suzuki et al. (2002) investigated the acaricidal and insecticidal activities of several 2,4-biphenyl-1,3-oxazoline derivatives using the leaf-dipping method to determine their effects on the egg and larval stages of *Tetranychus urticae*. Concentrations ranging from 0.001 to 1000 ppm were applied to the eggs, while a concentration of 1000 ppm was used to evaluate larvicidal activity. Mortality assessments for both developmental stages were conducted one week after treatment. The study revealed that halogen substitutions at the ortho positions of the 2-phenyl ring resulted in marked ovicidal activity against *Tetranychus* spp. eggs. Moreover, in 2-(2,6-difluorophenyl)-4-phenyl-1,3-oxazoline, hydrophobic substitutions on the 4-phenyl group enhanced acaricidal activity, and the compound exhibited significant insecticidal effects against *Nephotettix cincticeps*, *Plutella xylostella*, and *Myzus persicae*. For *N. cincticeps*, four rice seedlings were dipped into a 500 ppm solution, and after drying, 10–15 nymphs were transferred onto them. In the case of *P. xylostella*, leaves exposed to a 500 ppm concentration using the same method were allowed to dry before transferring 10–15 larvae. Similarly, for *M. persicae*, 10–15 nymphs of the same age were transferred onto leaves previously dipped in a 500 ppm solution. For all three insect species, mortality observations were made three days after treatment. Furthermore, replacement of the 1,3-oxazoline ring with 1,3-oxazole or 4-methyl-1,3-oxazoline resulted in a substantial reduction in biological activity. Chen et al. (2021) evaluated novel 2,4-diphenyl-1,3-oxazoline derivatives synthesized from a 4-(4-(chloromethyl)phenyl)-2-(2,6-difluorophenyl)-4,5-dihydrooxazole intermediate via a modified Ritter reaction. Most of these compounds, which included one phthalimidyl-substituted and four indolyl-substituted derivatives, exhibited good to excellent larvicidal and ovicidal activity against *T. cinnabarinus* in leaf-dip bioassays. Notably, some compounds demonstrated

lower LC_{50} values than those of etoxazole (0.088 mg/l for larvae and 0.128 mg/l for eggs). More recently, Chen et al. (2024) reported that 2,5-diphenyl-1,3-oxazoline derivatives with substitutions at the 5-phenyl position exhibited lower biological activity against mite eggs and larvae compared to their 2,4-diphenyl analogues. Overall, these studies demonstrate that oxadiazole, oxazoline, and their various derivatives can exert strong acaricidal and insecticidal activities against both mites and insect pests. In particular, structurally modified compounds with specific substitutions have shown high biological activity, in some cases comparable to or exceeding that of commercial acaricides. These findings highlight the importance of carefully considering structure–activity relationships in the development of new-generation pesticides and indicate the need for more comprehensive molecular design strategies in future research.

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ÖZET

Tetranychus urticae Koch, 1836 (Prostigmata: Tetranychidae) birçok pestisite direnç geliştirdiği rapor edilen kozmopolit bir türdür. Bu sorunu önleme yöntemlerinden biri yeni etken madde gruplarının keşfidir. Yeni etken madde keşfinin maliyet ve zaman açısından önemli dezavantajları olması araştırmacıları mevcut etken maddelerde değişiklik yapmaya yöneltmiştir. Etoxazole, bazı önemli zararlı akar türlerine karşı etkili olduğu bildirilen bir etken maddedir. Bu nedenle çeşitli maddelerle türevlendirme çalışmaları yapılmaktadır. Bu çalışmada, kimyasal yapıları değiştirilebilen oxidazole grubuna bağlı hedef moleküller, biyoizosterizm yaklaşımı kullanılarak oxazoline halkasının oksadiazole ile değiştirilmesi ve halkanın C-2 ve C-4 pozisyonlarına ikame edilmiş fenil halkaları eklenmesiyle tasarlanmıştır. Yedi etken maddenin (3a, 3b, 3c, 3d, 3e, 3f, 3g) *T. urticae*'nin nimf dönemleri üzerindeki toksik etkileri incelendiğinde, etoxazole uygulanan kontrol grubundan sonra sırasıyla en yüksek toksik etkiler %66, %64 ve %58 oranlarında 3b, 3a ve 3g etken maddelerinde tespit edilmiştir. Yumurta dönemindeki toksik etkiler incelendiğinde ise 3a grubunun benzer toksik etki gösterdiği, diğer etkin maddelerin ise nispeten daha düşük toksik etki gösterdiği belirlenmiştir. Sonuç olarak *T. urticae*'nin farklı dönemlerinde etkili olan oxidazole grubu bileşiklerin türevlerinin varlığı bu zararlının kontrolünde umut verici bir yaklaşım olarak görünmektedir.

Anahtar kelimeler: *Tetranychus urticae*, etoxazole, oxadiazole, akarisit

REFERENCES

Agrawal A.A., 2000. Host-range evolution: adaptation and trade-offs in fitness of mites on alternative hosts. Ecology, 81 (2), 500-508.

Assouguem A., Kara M., Mechchate H., Korkmaz Y.B., Benmessaoud S., Ramzi A., Abdullah K.R., Noman O.M., Farah A., Lazraq A., 2022. Current situation of *Tetranychus urticae* (Acari: Tetranychidae) in Northern Africa: The sustainable control methods and priorities for future research. Sustainability, 14 (4), 2395.

Attia S., Grissa K.L., Lognay G., Bitume E., Hance T., Mailleux A.C., 2013. A review of the major biological approaches to control the worldwide pest *Tetranychus urticae* (Acari: Tetranychidae) with special reference to natural pesticides: Biological approaches to control *Tetranychus urticae*. Journal of Pest Science, 86 (3), 361-386.

Ay R., Sökeli E., Karaca I., Gürkan M.O., 2005. Response to some acaricides of the two-spotted spider mite (*Tetranychus urticae* Koch) from protected vegetables in Isparta. Turkish Journal of Agriculture and Forestry, 29 (3), 165-171.

Chen Y., Tian J., Tan Y., Liu Y., Wang Q., 2024. Design, synthesis, and acaricidal activity of 2, 5-Diphenyl-1, 3-oxazoline compounds. Molecules, 29 (17), 4149.

Chen S., Zhang Y., Liu Y., Wang Q., 2021. Highly efficient synthesis and acaricidal and insecticidal activities of novel oxazolines with N-heterocyclic substituents. Journal of Agricultural and Food Chemistry, 69 (12), 3601-3606.

Chen S., Zhang Y., Liu Y., Wang Q., 2019. Design, synthesis, acaricidal activities, and structure–activity relationship studies of novel oxazolines containing sulfonate moieties. Journal of Agricultural and Food Chemistry, 67 (49), 13544-13549.

Dai H., Chen J., Li G., Ge S., Shi Y., Fang Y., Ling Y., 2017. Design, synthesis, and bioactivities of novel oxadiazole-substituted pyrazole oximes. Bioorganic & Medicinal Chemistry Letters, 27 (4), 950-953.

Das S.K. 2016. Screening of bioactive compounds for development of new pesticides: a mini review. Universal Journal of Agricultural Research 4 (1), 15-20.

Denholm I., Rowland M.W., 1992. Tactics for managing pesticide resistance in arthropods: theory and practice. Annual Review of Entomology, 37, 91-112.

Grbić, M., Van Leeuwen T., Clark R.M., Rombauts S., Rouzé P., Grbić V., Osborne E.J., Dermauw W., Ngoc P.C.T., Ortego F., Hernández-Crespo P., Diaz I., Martinez M., Navajas M., Sucena E., Magalhães S., Nagy L., Pace R.M., Djuranović S., Smagghe G., Iga M., Christiaens O., Veenstra J.A., Ewer J., Mancilla Villalobos R., Hutter J.L., HudsonS.D., Velez M., Yi S.V., Zeng J., Pires-daSilva A., Roch F., Cazaux M., Navarro M., Zhurov V., Acevedo G., Bjelica A., Fawcett J.A., Bonnet E., Martens C., Baele G., Lothar Wissler L., Sanchez-Rodriguez A., Tirry L., Blais C., Demeestere K., Henz S.R., Gregory T.R., Mathieu J., Verdon L., Farinelli L., Schmutz J., Lindquist E., Feyereisen R., Van de Peer Y., 2011. The genome of *Tetranychus urticae* reveals herbivorous pest adaptations. Nature, 479 (7374), 487-492.

Jiang B., Jin X., Dong Y., Guo B., Cui L., Deng X., Zhang L., Yang Q., Li Y., Yang X., Smagghe G., 2020. Design, synthesis, and biological activity of novel heptacyclic pyrazolamide derivatives: a new candidate of dual-target insect growth regulators. Journal of Agricultural and Food Chemistry, 68 (23), 6347-6354.

Jutsum A.R., Heaney S.P., Perrin B.M., Wege P.J., 1998. Pesticide resistance: assessment of risk and the development and implementation of effective management strategies. Pesticide Science, 54 (4), 435-446.

Khanahmadi M., Pakravan P., Hemati A., Azandaryani M.N., Ghamari E., 2017. Fumigant toxicity of *Artemisia haussknechtii* essential oil and its nano-encapsulated form. Pharma, 2, 1776-1783.

Kim Y.J., Lee S.H., Lee S.W., Ahn Y.J., 2004. Fenpyroximate resistance in *Tetranychus urticae* (Acari: Tetranychidae): cross-resistance and biochemical resistance mechanisms. Pest Management Science: formerly Pesticide Science, 60 (10), 1001-1006.

Li Y., Li C., Zheng Y., Wei X., Ma Q., Wei P., Ma Q., Wei P., Liu Y., Qin Y., Yang N., Sun Y., Ling Y., Yang X., Wang Q., 2014. Design, synthesis, acaricidal activity, and mechanism of oxazoline derivatives containing an oxime ether moiety. Journal of Agricultural and Food Chemistry, 62 (14), 3064-3072.

Li Y., Yang N., Wei X., Ling Y., Yang X., Wang Q., 2014. Evaluation of etoxazole against insects and acari in vegetables in China. Journal of Insect Science, 14 (1), 104.

Lima L.M., Barreiro E.J., 2005. Bioisosterism: a useful strategy for molecular modification and drug design. Current Medicinal Chemistry, 12 (1), 23-49.

Liu Q., Zhu R., Gao S., Ma S.H., Tang H.J., Yang J.J., Diao Y., Wang H., Zhu H.J., 2017. Structure-based bioisosterism design, synthesis, insecticidal activity and structure–activity relationship (SAR) of anthranilic diamide analogues containing 1, 2, 4-oxadiazole rings. Pest Management Science, 73 (5), 917-924.

Mermer A., Faiz O., Demirbas A., Demirbas N., Alagumuthu M., Arumugam S., 2019. Piperazine-azole-fluoroquinolone hybrids: Conventional and microwave irradiated synthesis, biological activity screening and molecular docking studies. Bioorganic Chemistry, 85, 308-318.

Nauen R., Smagghe G., 2006. Mode of action of etoxazole. Pest Management Science: formerly Pesticide Science, 62 (5), 379-382.

Opit, G.P., Nechols J.R., Margolies D.C., 2004. Biological control of twospotted spider mites, *Tetranychus urticae* Koch (Acari: Tetranychidae), using *Phytoseiulus persimilis* Athias-Henriot (Acari: Phytoseidae) on ivy geranium: assessment of predator release ratios. Biological Control, 29 (3), 445-452.

Ozdemir S.B., Demirbas N., Cebeci Y.U., Bayrak H., Mermer A., Ceylan S., DemirbasA., 2017. Synthesis and antimicrobial activities of hybrid heterocyclic molecules based on 1-(4-fluorophenyl) piperazine skeleton. Letters in Drug Design & Discovery, 14 (9), 1014-1034.

Patani G.A., LaVoie E.J., 1996. Bioisosterism: a rational approach in drug design. Chemical Reviews, 96 (8), 3147-3176.

Rincón R.A., Rodríguez D., Coy-Barrera E., 2019. Botanicals against *Tetranychus urticae* Koch under laboratory conditions: A survey of alternatives for controlling pest mites. Plants, 8 (8), 272.

Rioja C., Zhurov V., Bruinsma K., Grbic M., Grbic V., 2017. Plant-herbivore interactions: a case of an extreme generalist, the two-spotted spider mite *Tetranychus urticae*. Molecular Plant-Microbe Interactions, 30 (12), 935-945.

Romanov-Michailidis F., Rovis T., 2015. Natural polarity inverted. Nature, 523 (7561), 417-418.

Sato M.E., Da Silva M.Z., Raga A., Cangani K. G., Veronez B., Nicastro R.L., 2011. Spiromesifen toxicity to the spider mite *Tetranychus urticae* and selectivity to the predator *Neoseiulus californicus*. Phytoparasitica, 39 (5), 437-445.

Shao X., Fu H., Xu X., Xu X., Liu Z., Li Z., Qian X., 2010. Divalent and oxabridged neonicotinoids constructed by dialdehydes and nitromethylene analogues of imidacloprid: design, synthesis, crystal structure, and insecticidal activities. Journal of Agricultural and Food Chemistry, 58 (5), 2696-2702.

Sparks T.C., Storer N., Porter A., Slater R., Nauen R., 2021. Insecticide resistance management and industry: the origins and evolution of the I nsecticide R esistance A ction C ommittee (IRAC) and the mode of action classification scheme. Pest Management Science, 77 (6), 2609-2619.

Suzuki J., Ishida T., Kikuchi Y., Ito Y., Morikawa C., Tsukidate Y., Tanji I., Ota Y., TodaK., 2002. Synthesis and activity of novel acaricidal/ınsecticidal 2, 4-Diphenyl-1, 3-oxazolines. Journal of Pesticide Science, 27 (1), 1-8.

Suzuki J., Ishida T., Shibuya, I., Toda K., 2001. Development of a new acaricide, etoxazole. Journal of Pesticide Science, 26 (2), 215-223.

Tian Q., Du T., Xu A., Li Y., 2024. Design, synthesis, and 3D-QASR of oxazoline derivatives containing an S–S moiety as potential acaricide. Journal of Agricultural and Food Chemistry, 72 (43), 23727-23735.

Van Leeuwen T., Tirry L., Yamamoto A., Nauen R., Dermauw W., 2015. The economic importance of acaricides in the control of phytophagous mites and an update on recent acaricide mode of action research. Pesticide Biochemistry and Physiology, 121, 12-21.

Van Leeuwen T., Van Pottelberge S., Tirry,L., 2006. Biochemical analysis of a chlorfenapyr-selected resistant strain of *Tetranychus urticae* Koch. Pest Management Science: Formerly Pesticide Science, 62 (5), 425-433.

Vitaku E., Smith D.T., Njardarson J.T., 2014. Analysis of the structural diversity, substitution patterns, and frequency of nitrogen heterocycles among US FDA approved pharmaceuticals: miniperspective. Journal of Medicinal Chemistry, 57 (24), 10257-10274.

Wagener M., Lommerse J.P., 2006. The quest for bioisosteric replacements. Journal of Chemical Information and Modeling, 46 (2), 677-685.

Wu M., Zhang Y., Tian T., Xu D., Wu Q., Xie W., ZhangY., Crickmore N., Guo Z., Wang S. 2023. Assessment of the role of an ABCC transporter TuMRP1 in the toxicity of abamectin to *Tetranychus urticae*. Pesticide Biochemistry and Physiology, 195 105543.

Yu X., Liu Y., Li Y., Wang Q., 2015. Design, synthesis, and acaricidal/insecticidal activities of oxazoline derivatives containing a sulfur ether moiety. Journal of Agricultural and Food Chemistry, 63 (44), 9690-9695.

Zhang W., 2017. Mesoionic pyrido [1, 2-a] pyrimidinone insecticides: from discovery to triflumezopyrim and dicloromezotiaz. Accounts of Chemical Research, 50 (9), 2381-2388.

Zhang Y., Chen Y., Xun X., Chen S., Liu Y., Wang Q., 2022. Design, synthesis, acaricidal activities, and structure–activity relationship studies of oxazolines containing ether moieties. Journal of Agricultural and Food Chemistry, 70 (42), 13538-13544.

Zhang S., Luo Y., He L.Q., Liu Z.J., Jiang A.Q., Yang Y.H., Zhu H.L., 2013. Synthesis, biological evaluation, and molecular docking studies of novel 1, 3, 4-oxadiazole derivatives possessing benzotriazole moiety as FAK inhibitors with anticancer activity. Bioorganic & Medicinal Chemistry, 21 (13), 3723-3729.

Ziyaev A.A., Ismailova D.S., 2017. Biological activity of 5-(2, 3, 4-Pyridyl)-1, 3, 4-oxadiazol-2-thiones and their derivatives. World Journal of Pharmaceutical Research, 6 (4), 52-77.

Zu G., Gan X., Xie D., Yang H., Zhang A., Li S., Hu D., Song B., 2020. Design, synthesis, and anti-ToCV activity of novel 4 (3 H)-quinazolinone derivatives bearing dithioacetal moiety. Journal of Agricultural and Food Chemistry, 68 (20), 5539-5544.

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