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ORIGINAL PAPER

Laboratory evaluation of five novel pyrrole derivatives as grain protectants against *Tribolium confusum* and *Ephestia kuehniella* larvae

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Abstract Several naturally discovered or laboratory-synthesized pyrrole compounds have insecticidal, acaricidal and microbial properties. The novel sulfanyl 5*H*-dihydro-pyrrole derivatives exhibit certain antioxidant activities. However, there is a knowledge gap whether these substances are potent grain protectants against stored-product insect pest species. In this context, we evaluated the insecticidal activity of five novel pyrrole derivatives (under the trivial names 3a, 3g, 3l, 3m, 3h), against larvae of *Tribolium confusum* Jaquelin du Val and *Ephestia kuehniella* Zeller at different doses (0.1, 1 and 10 ppm), exposure intervals (7, 14 and 21 days or 1, 2, 7, 14, 21 days), temperatures (20, 25 and 30 °C), relative humidity (RH) (55 and 75 %) levels and commodities (wheat, maize, barley). The pyrrole derivative 3a exhibited the highest insecticidal activity, while 3g, 3l, 3m and 3h caused similar mortality against larvae of *T. confusum*. Apart of the level of efficacy, all tested pyrrole derivatives performed similarly according temperature. We found that increase in temperature increased mortality in the majority of the tested combinations. Generally, the pyrrole derivatives caused the highest mortality levels at 30 °C. The pyrrole derivatives 3a, 3g, 3l and 3m were affected by relative humidity at almost all combinations tested. The 75 % level of RH moderated the efficacy of the pyrrole derivatives, while the 55 % enhanced it. Mortality of *T. confusum* and *E. kuehniella* on maize was much lower on treated maize than barley or wheat. However, 100 % control of both species was recorded only on treated barley. The results of the present study indicate that the pyrrole derivatives tested could serve as grain protectants against noxious stored-product insects under certain biotic and abiotic conditions.

Keywords Pyrrole derivatives · Stored-product insects · Dose · Exposure · RH · Temperature · Commodity

Key message

- There is a gap of knowledge whether novel sulfanyl 5*H*-dihydro-pyrrole derivatives are potent grain protectants.
- We evaluated five pyrrole derivatives against *T. confusum* and *E. kuehniella* larvae at different doses, exposure intervals, temperatures, RH levels and commodities.

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- Insect mortality was favored at 30 °C and 55 % RH.
- Insects were harder to be controlled on maize than on barley or wheat.
- Insecticidal performance of the pyrrole derivatives is elevated under certain biotic and abiotic conditions.

Introduction

One of the most critical issues on the management of stored-product pests is the development of resistance to synthetic pesticides (Pimentel et al. 2007, 2009; Kumar et al. 2010). Thus, there is an ongoing interest on finding novel insecticidal or repellent active ingredients that will enhance stored-product protection (Bedini et al. 2015; Germinara et al. 2015; Abdelgaleil et al. 2016; Boukouvala et al. 2016a, b). Pyrrole is a five-member heterocyclic aromatic organic substance that corresponds to the chemical formula C_4H_5N. In the last two decades, research has documented different types of biological activities that numerous pyrrole derivatives exhibit, either synthesized in the laboratory or discovered from natural resources. Thus, pyrrole derivatives can serve as enzyme inhibitors or anticancer, antimicrobial, antitubercular, anti-inflammatory, antioxidant, cytotoxic, insecticidal and acaricidal agents (Gholap 2016) or mimicking natural products (Zaidi et al. 2006; Lucas et al. 2013).

A critical examination of the international bibliography reveals several studies showing that certain pyrrole derivatives are capable to kill a wide spectrum of insect and mite species of both agricultural and public health importance. For example, Ito et al. (2003) reported high toxicity of a series synthesized of *N*-sulfanyl-, *N*-sulfinyl- and *N*-sulfonyldihydropyrrole derivatives against *Nilaparvata lugens* (Stål) (Hemiptera: Delphacidae) and *Nephotettix cincticeps* (Uhler) (Hemiptera: Cicadellidae) at 1 ppm after 5 days of exposure to the material. Similarly, Zhao et al. (2008a, b) found that several 2-aryl-pyrrole derivatives caused 100 % mortality of larvae of *Mythimna separata* Walker (Lepidoptera: Noctuidae), larvae of *Culex pipiens* L. ssp. *pallens* Coquillett (Diptera: Culicidae) and adults of *Tetranychus cinnabarinus* (Boisduval) (Acari: Tetranychidae) after 2 days of exposure at 10–20, 0.1–0.5 and 50–200 ppm, respectively. The pure compound, 5-(2, 4-dimethylbenzyl)pyrrolidin-2-one, that was extracted by the marine actinobacteria *Streptomyces* VITSVK5 sp., caused 100 % mortality to larvae of *Rhipicephalus microplus* (Canestrini) (Ixodida: Ixodidae), *Anopheles stephensi* Liston (Diptera: Culicidae) and *Culex tritaeniorhynchus* Giles (Diptera: Culicidae) at 500 ppm after 1 day of exposure (Saurav et al. 2013).

Also, pyrrole derivatives from natural resources such as the compound 5-azidomethyl-3-(2-ethoxy carbonyl-ethyl)-4-ethoxycarbonylmethyl-1H-pyrrole-2-carboxylic acid, ethyl ester, extracted from the marine *Streptomyces* VITSVK7 sp. exhibited 61, 69, 57 and 52 % mortality to *Haemaphysalis bispinosa* Neumann (Ixodida: Ixodidae), *R. microplus*, *Anopheles subpictus* Meigen (Diptera: Culicidae) and *Culex quinquefasciatus* Say (Diptera: Culicidae), respectively, after 1 day of exposure (Thenmozhi et al. 2013).

All above pyrrole derivatives can be potential insecticides that merit commercialization as in the case of chlorfenapyr, i.e., 4-bromo-2-(4-chlorophenyl)-1-ethoxymethyl-5-(trifluoromethyl)pyrrole-3-carbonitrile (Zhao et al. 2008a, b). Chlorfenapyr causes oxidative phosphorylation in the mitochondria, which disrupts the synthesis of ATP and has low mammalian toxicity (Hunt 1996; Tomlin 2000; McLeod et al. 2002). Chlorfenapyr exhibits elevated toxicity against several stored-product insects either as surface treatment, i.e., *Liposcelis bostrychophila* Badonnel (Psocoptera: Liposcelididae), *Liposcelis entomophila* (Enderlein) (Psocoptera: Liposcelididae), *Liposcelis paeta* Pearman (Psocoptera: Liposcelididae), *Tribolium castaneum* (Hertz) and *T. confusum* (Guedes et al. 2008; Arthur 2013, 2015; Athanassiou et al. 2014a) or as grain protectant, i.e., *Prostephanus truncatus* (Horn) (Coleoptera: Bostrychidae), *Rhyzopertha dominica* (F.) (Coleoptera: Bostrychidae), *Sitophilus oryzae* (L.) (Coleoptera: Curculionidae) and *Tribolium confusum* Jaquelin du Val (Coleoptera: Tenebrionidae) (Kavallieratos et al. 2011). However, so far it has been registered in the USA for application in cracks and crevices against urban pest species including stored-product insects associated with food processing or storage (Arthur 2013; Athanassiou et al. 2014a).

It has been previously documented that novel sulfanyl 5*H*-dihydro-pyrrole derivatives exhibit strong antioxidant activity (Georgiou et al. 2012; Oikonomou et al. 2015). Furthermore, Boukouvala et al. (2016a, b) examined two of these compounds, the ethyl 3-(benzylthio)-4,6-dioxo-5-phenyl-2,4,5,6-tetrahydropyrrolo[3,4-*c*]pyrrole-carboxylate (under the trivial name 3i) and the isopropyl 3-(benzylthio)-4,6-dioxo-5-phenyl-2,4,5,6-tetrahydropyrrolo[3,4-*c*]pyrrole-carboxylate (under the trivial name 3k) against adults of *T. confusum* and larvae of *Ephestia kuehniella* Zeller (Lepidoptera: Pyralidae) and found that under certain combinations of biotic and abiotic factors mortality of the exposed individuals can be complete. It is well known that food sources favor larval development (Loschiavo and Okumura 1979; Cuperus et al. 1990; Platt et al. 1998; Arthur and Phillips 2003; Arthur and Campbell 2008) and that immature instars predominate in insect resident infestations in storage facilities (Campbell et al. 2010a, b). Thus, Wolly Wijayaratne et al. (2012) suggested the enhancement of insecticidal treatments against immature individuals to be considered in insect management programs. Considering also the fact that the activity of several other pyrrole derivatives is not known against any insect species and based on the need of development of new insecticides, the objective of the current study was to examine the insecticidal effect of five novel pyrrole derivatives against larvae of the highly destructive stored-product insects *T. confusum* and *E. kuehniella* (Aitken 1975; Hill 2003; Mahroof and Hagstrum 2012) under different combinations of temperature, relative humidity, commodity, dose and exposure interval.

Materials and methods

Insects

The insects used in tests were reared at the Laboratory of Agricultural Zoology and Entomology, Agricultural University of Athens, at continuous darkness. The cultures, initially collected from Greek storage facilities, have been kept at Agricultural University of Athens since 2014. *T. confusum* was reared in wheat flour including 5 % brewer's yeast (w/w) at 30 °C and 60 % RH. *E. kuehniella* was reared in wheat flour at 25 °C and 60 % RH. First instar larvae of *T. confusum* or *E. kuehniella* were used in the tests. For that purpose, *T. confusum* or *E. kuehniella* eggs were collected from flour by using a sieve of 60 mesh (250 micron, WS Tyler, Mentor, OH, USA), then placed in incubators at 25 °C and 60 % RH, or 30 °C and 60 % RH, respectively, and first instar larvae were collected after hatching.

Commodities

Untreated, clean and free of infestation and pesticides, hard wheat, *Triticum durum* Desf. (var. Mexa), barley *Hordeum vulgare* L. (var. Persephone) and maize, *Zea mays* L. (var. Dias) were used for the experimentation. The moisture content of the tested grain commodities was 11, 11.3 and 10.9 % for wheat, barley and maize, respectively, as determined by a Dickey-John moisture meter (mini GAC plus, Dickey-John Europe SAS., Colombes, France) at the beginning of the tests.

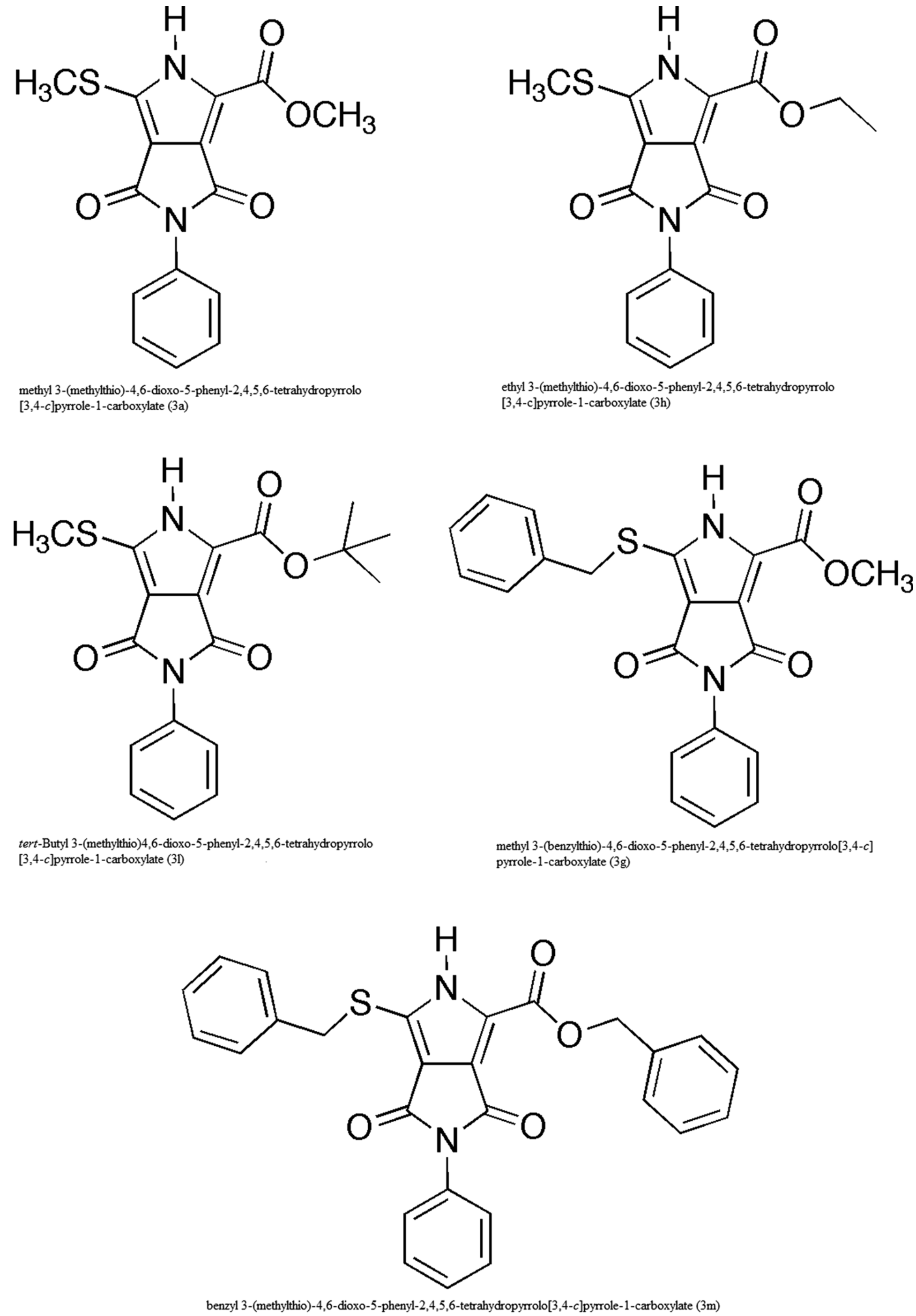
Pyrrole derivatives

Five pyrrole derivatives, i.e., methyl 3-(methylthio)-4,6-dioxo-5-phenyl-2,4,5,6-tetrahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate [molecular weight (mw) = 316.33 g/mol, melting point (mp) = 171–172 °C], methyl 3-(benzylthio)-4,6-dioxo-5-phenyl-2,4,5,6-tetrahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (mw = 392.43, mp = 185–186 °C), *tert*-Butyl 3-(methylthio) 4,6-dioxo-5-phenyl-2,4,5,6-tetrahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (mw = 358.41, mp = 173–174 °C), benzyl 3-(methylthio)-4,6-dioxo-5-phenyl-2,4,5,6-tetrahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (mw = 392.43, mp = 186–187 °C) and ethyl 3-(methylthio)-4,6-dioxo-5-phenyl-2,4,5,6-tetrahydropyrrolo[3,4-c]pyrrole-1-carboxylate (mw = 330.36, mp = 161–162 °C), given the trivial names 3a, 3g, 3l, 3m and 3h, respectively (Fig. 1), were used for experimentation. These substances were synthesized by Oikonomou et al. (2015) at the Laboratory of Organic Chemistry, Department of Chemistry, University of Ioannina and used as powders in the tests. Details on their synthesis can be found in Oikonomou et al. (2015).

Bioassays series 1

One-kg lots of wheat were placed in cylindrical glass jars and treated with the pyrrole derivatives separately at three doses: 0.1, 1 and 10 ppm. The jars were shaken manually for 5 min to achieve the equal distribution of the particles of the pyrrole derivatives in the entire wheat mass. An additional 1 kg of untreated wheat was served as control. From each lot, three samples, of 10 g each, were taken and placed in small cylindrical glass vials (7 cm in diameter, 12 cm in height) with a different scoop that was inside each jar. The quantity of 10 g was weighed with a Precisa XB3200D compact balance (Alpha Analytical Instruments, Gerakas, Greece). The closure of the vials had a 1.5-cm-diameter hole in the middle, which was covered by gauze, to allow sufficient aeration inside the vial. The *T. confusum* larvae were tested on wheat treated with all pyrrole derivatives, while *E. kuehniella* larvae were tested on wheat treated with 3h. Ten larvae of *T. confusum* or *E. kuehniella* were separately placed inside each vial. The internal "necks" of the vials were covered by Fluon (Northern Products Inc., Woonsocket, USA), to prevent insects from escaping. Subsequently, six series of bioassays of each compound were placed in controlled chambers under the following conditions: 20 °C and 55 % RH, 25 °C and 55 % RH, 30 °C and 55 % RH, 20 °C and 75 % RH, 25 °C and 75 % RH and 30 °C and 75 % RH for the duration of the experimental period. Mortality of the treated individuals was assessed after 7, 14 and 21 days of exposure. Dead larvae were determined by prodding with a brush to detect movement under an Olympus stereomicroscope (Olympus SZX9, Bacacos SA, Athens, Greece). The brush was carefully washed after the examination of each vial. All tests were repeated three times for each species, by preparing new lots each time. Control mortality was very low (<5 %), and thus, no correction was necessary for the mortality data. Data were analyzed separately for each of the tested species according to the repeated-measures model (Sall et al. 2001). The repeated factor was

Fig. 1 Chemical structures of the pyrrole derivatives examined



exposure interval, while mortality was the response variable. Temperature, RH, pyrrole derivative and dose were the main effects in the case of *T. confusum* larvae, whereas temperature, RH and dose were the main effects in the case of *E. kuehniella* larvae. The associated interactions of the main effects were incorporated in the analysis. All analyses were conducted using the JMP 11 software (SAS Institute 2013). Means were separated by the Tukey–Kramer (HSD) test at 0.05 probability (Sokal and Rohlf 1995).

Bioassays series 2

One-kg lots of barley or maize were treated and proceeded with the same pyrrole derivatives as in Bioassays series 1. The *T. confusum* larvae were tested on maize or barley treated with all pyrrole derivatives, while *E. kuehniella* larvae were tested on maize or barley treated with 3h. The tests were conducted in incubators set at 25 °C and 60 % RH during the entire experimental period. Mortality of the treated individuals was assessed after 1, 2, 7, 14 and 21 days of exposure. Dead larvae were determined as above. Control mortality was very low (<5 %), and thus, no correction was necessary for the mortality data. Data were analyzed separately for each of the tested species according to the repeated-measures model as in Bioassays series 1. Pyrrole derivative, commodity and dose were the main effects in the case of *T. confusum* larvae, whereas commodity and dose were the main effects in the case of *E. kuehniella* larvae.

Results

Bioassays series 1

Mortality of T. confusum larvae

Between exposure intervals, all main effects and the associated interactions temperature × RH, pyrrole derivative × dose, temperature × pyrrole derivative, RH × pyrrole derivative, RH × dose and temperature × RH × pyrrole derivative were significant (Table 1). Within exposure intervals, all main effects and associated interactions were significant except exposure × temperature × dose, exposure × temperature × RH × dose and exposure × temperature × RH × ryrrole derivative × dose.

After 7 days of exposure, mortality on wheat treated with 3a remained low at 0.1 and 1 ppm in all tested combinations (Table 2). However, mortality reached almost 79 % on wheat treated with 10 ppm 3a at 30 °C and 55 % RH while it did not exceed 55.6 % at 30 °C and 75 % RH. After 14 days post-exposure, on wheat treated with 1 ppm at 30 °C, mortality was 70 and 64.4 % at 55 and 75 % RH, respectively. In 10 ppm mortality was >94 % at 30 °C and 55 % RH, whereas it ranged from 57.8 to 72.2 % at the same temperature and 75 % RH. Seven days later mortality notably increased at all tested combinations. Thus, even in 0.1 ppm, mortality was 80 % but it reached 98.9 % in 10 ppm at 30 °C and 55 % RH. The increase in temperature from 20 or 25 °C to 30 °C significantly increased mortality at all tested combinations at 55 % RH.

Regarding pyrrole derivative 3g, after 7 or 14 days of exposure the overall mortality was negligible to average (Table 3). However, after 21 days of exposure, at 25 and 30 °C mortality was 90 and 97.8 % at 55 % RH. In contrast, mortality was average at 75 % RH and did not exceed 56.7 % at 30 °C.

Mortality of *T. confusum* larvae was low or average on wheat treated with the pyrrole derivative 3l after 7 and 14 days of exposure and did not exceed 56.7 % in 10 ppm at 30 °C and 75 % RH (Table 4). However, after 21 days of exposure, mortality was 84.4 and 95.6 % in 10 ppm of 3l at 25 and 30 °C and 55 % RH. In contrast, at 75 %, mortality was average and did not exceed 67.8 % at 30 °C. Generally, the mortality values at 55 % RH were higher that at 75 % RH.

For both tested RH levels, after 7 days of exposure, mortality of *T. confusum* larvae was little to average in the case of the pyrrole derivative 3m (Table 5). Seven days later, mortality further increased and reached 76.7 % in 10 ppm at 30 °C and 55 % RH. At 21 days post-exposure, mortality was >84 and >95 % in 10 ppm at 25 °C and 30 °C and 55 % RH.

Mortality of *T. confusum* larvae was similarly ranged from 12.2 to 46.7 % and from 10 to 42.2 % at 55 and 75 % RH, respectively, on wheat treated with the pyrrole derivative 3h after 7 days of exposure (Table 6). Seven days later, mortality was still average for both RH levels tested. After 21 days of exposure, in 1 ppm mortality was >80 % at 30 °C and 55 % RH. However, at temperatures ≥25 °C, mortality was >88 %. At 75 % RH, mortality was generally similar to 55 % RH.

Mortality of E. kuehniella larvae

Between exposure intervals, all main effects and the associated interactions temperature × RH and temperature × RH × dose were significant (Table 1). Within exposure intervals, the main effects exposure × temperature and exposure × dose were significant. All associated interactions were significant except exposure × RH × dose.

After 7 days of exposure, mortality of *E. kuehniella* on wheat treated with 3h exhibited great range for both RH levels among temperatures (Table 7). Similar trend was recorded at 14 and 21 days of exposure. The highest mortality values were noted in 10 ppm at 30 °C, i.e., 87.9 % (at 55 % RH) and 90 % (at 75 % RH). Similarly, after 14 days of exposure, mortality still greatly ranged as previously described. At this exposure, mortality was almost complete (98.9 %) at 30 °C and 55 % RH while it reached 95.6 % at 30 °C and 75 % RH.

Bioassays series 2

Mortality of T. confusum larvae

Between exposure intervals, all main effects and the associated interaction pyrrole derivative × commodity were significant (Table 8). Within exposure intervals, all main effects and associated interactions were significant.

No mortality was noted on maize treated with 0.1 ppm of any the tested pyrrole derivatives after 1 and 2 days of exposure. Yet, mortality was low in 1 or 10 ppm of all pyrrole derivatives (Table 9). After 7 days of exposure, no

Table 1 MANOVA parameters for main effects and associated interactions for mortality levels of *T. confusum* larvae and *E. kuehniella* larvae between and within exposure intervals (error *df* = 720 for *T. confusum* larvae and error *df* = 76 for *E. kuehniella* larvae)

Source	*df*	*T. confusum* (larvae)		*E. kuehniella* (larvae)	
		F	*P*	*F*	*P*
Between exposure intervals					
Temperature	2	110.4	<0.01	29.5	<0.01
RH	1	240.3	<0.01	13.9	0.01
Pyrrole derivative	4	88.6	<0.01	–	–
Dose	2	210.8	<0.01	268.7	<0.01
Temperature × RH	2	11.6	<0.01	3.7	0.03
Pyrrole derivative × dose	8	3.7	0.01	–	–
Temperature × pyrrole derivative	8	22.8	<0.01	–	–
RH × pyrrole derivative	4	34.0	<0.01	–	–
Temperature × dose	4	0.5	0.76	0.9	0.48
RH × dose	2	7.8	0.01	2.2	0.11
Temperature × RH × pyrrole derivative	8	19.3	<0.01	–	–
Temperature × RH × dose	4	0.9	0.45	2.5	0.05
Temperature × pyrrole derivative × dose	16	1.1	0.31	–	–
RH × pyrrole derivative × dose	8	1.1	0.35	–	–
Temperature × RH × pyrrole derivative × dose	16	0.7	0.75	–	–
Within exposure intervals					
Exposure × temperature	4	4.2	0.01	10.3	<0.01
Exposure × RH	2	87.7	<0.01	0.9	0.40
Exposure × dose	4	20.4	<0.01	15.5	<0.01
Exposure × pyrrole derivative	8	19.6	<0.01	–	–
Exposure × RH × dose	4	9.1	<0.01	2.1	0.09
Exposure × temperature × RH	4	7.1	<0.01	4.3	0.01
Exposure × pyrrole derivative × dose	16	6.2	<0.01	–	–
Exposure × temperature × dose	8	1.8	0.08	7.2	<0.01
Exposure × temperature × pyrrole derivative	16	8.0	<0.01	–	–
Exposure × RH × pyrrole derivative	8	4.0	0.01	–	–
Exposure × temperature × pyrrole derivative × dose	32	1.9	0.01	–	–
Exposure × RH × pyrrole derivative × dose	16	3.2	<0.01	–	–
Exposure × temperature × RH × dose	8	0.8	0.62	2.3	0.02
Exposure × temperature × RH × pyrrole derivative	32	1.9	0.01	–	–
Exposure × temperature × RH × pyrrole derivative × dose	32	1.1	0.37	–	–

mortality was recorded in 0.1 ppm of 3h, while it was still low for all other pyrrole derivatives. In 1 and 10 ppm, mortality was average. After 14 days of exposure, mortality further increased but it did not exceed 74.4 % (3a at 10 ppm). Interestingly, mortality reached 91.1 % on maize treated with 10 ppm 3a, followed by pyrrole derivative 3h which provided mortality almost 80 % at 10 ppm. Regarding barley, after 1 day of exposure, low or no mortality was recorded for any of the tested substances. Yet, after 2 days of exposure, despite mortality increased in all combinations it was low or average. At 7 days post-exposure, the pyrrole derivative 3a caused 82.2 % mortality to *T. confusum* larvae. Seven days later, complete mortality was recorded in 10 ppm of 3a and 3m followed by 3g at 10 ppm that provided 97.8 % mortality. After 21 days of exposure, complete mortality was also recorded in 1 ppm of 3a and 10 ppm of 3g, 3l and 3h.

Mortality of E. kuehniella larvae

Between and within exposure intervals, all main effects were significant while the associated interactions were not (Table 8). After 1, 2 and 7 days of exposure on maize, the 3h pyrrole derivative caused average or no mortality to *E.*

Table 2 Mean mortality (% ±SE) of *T. confusum* larvae after 7, 14 and 21 days on wheat treated with 3a at three doses under three temperatures and two RH levels

RH	55 %			F	P	75 %			F	P
Temperature Dose	20 °C	25 °C	30 °C			20 °C	25 °C	30 °C		
7 days										
0.1 ppm	15.6 ± 4.4b	17.8 ± 6.2b	18.9 ± 3.5b	0.1	0.89	12.2 ± 4.0Bb	11.0 ± 3.1Bb	32.2 ± 7.2A	5.4	0.01
1 ppm	28.9 ± 5.1b	25.6 ± 7.7b	32.2 ± 3.2b	0.3	0.71	16.6 ± 5.5Bb	26.6 ± 5.0Bb	43.3 ± 4.1A	7.6	0.01
10 ppm	50.0 ± 4.4Ba	64.4 ± 8.4ABa	78.9 ± 4.8Aa	5.6	0.01	43.3 ± 6.2a	46.7 ± 5.0a	55.6 ± 7.8	1.0	0.39
F	13.8	11.3	64.3			9.9	16.0	3.2		
P	0.01	0.01	<0.01			0.01	<0.01	0.06		
14 days										
0.1 ppm	33.3 ± 6.0Bb	30.0 ± 7.3Bb	62.2 ± 4.3Ab	8.7	0.01	16.6 ± 5.0Bb	26.7 ± 4.1Bb	58.9 ± 7.0A	16.2	<0.01
1 ppm	48.9 ± 4.2ABb	45.6 ± 10.2Bb	70.0 ± 4.7Ab	3.7	0.04	31.1 ± 7.0Bb	43.3 ± 5.7Bab	64.4 ± 4.1A	8.6	0.01
10 ppm	68.9 ± 5.9Ba	76.7 ± 6.9ABa	94.4 ± 2.9Aa	5.7	0.01	57.8 ± 6.6a	58.9 ± 5.1a	72.2 ± 6.0	1.8	0.18
F	10.8	8.3	17.1			11.1	10.2	1.3		
P	0.01	0.01	<0.01			0.01	0.01	0.28		
21 days										
0.1 ppm	47.8 ± 4.6Bc	50.0 ± 10.4Bb	80.0 ± 3.3Ab	6.8	0.01	31.1 ± 7.3Bb	33.3 ± 4.1Bb	67.8 ± 5.5A	12.6	0.01
1 ppm	63.3 ± 4.4Bb	64.4 ± 7.5Bab	86.7 ± 2.9Ab	6.2	0.01	46.7 ± 7.6Bab	54.4 ± 4.4ABa	73.3 ± 4.4A	5.8	0.01
10 ppm	81.1 ± 3.5Ba	86.7 ± 4.4Ba	98.9 ± 1.1Aa	7.5	0.01	66.7 ± 6.2a	66.7 ± 6.2a	78.9 ± 6.5	1.2	0.31
F	15.6	5.6	13.3			6.3	11.3	1.0		
P	<0.01	0.01	0.01			0.01	0.01	0.38		

Within each column, exposure and RH, means followed by the same lowercase letter are not significantly different; $df = 2, 26$. Within each row, exposure and RH, means followed by the same uppercase letter are not significantly different; $df = 2, 26$, Tukey–Kramer (HSD) test at $P = 0.05$. Where no letters exist, no significant differences were recorded

kuehniella. Mortality arose to 71.1 % after 14 days of exposure in 10 ppm and finally to 82.2 % seven days later (Table 10). On barley, after 1, 2 and 7 days, mortality was low or average. However, 7 days later it arose to 91.1 % and became 100 % after 21 days of exposure at the same dose.

Discussion

The findings of the present study indicate that the efficacy of the tested pyrrole derivatives varied according the pyrrole derivative, dose, exposure interval, temperature, RH and commodity. Considering the overall data, the pyrrole derivative 3a exhibited the highest insecticidal activity, while 3g, 3l, 3m and 3h caused similar mortality against larvae of *T. confusum*. Apart of the level of efficacy, all tested pyrrole derivatives performed similarly according temperature. Actually, temperature seemed to be a key factor that significantly regulated mortality. Thus, increase in temperature increased mortality in the majority of combinations tested. Generally, the pyrrole derivatives caused the highest mortality levels at 30 °C and 55 % RH. It has been previously documented that increase in temperature increases the loss of water, through increased insect respiration, as well as the mobility of insects and therefore their ability to have elevated contact with substrates that have been treated with insecticides, i.e., diatomaceous earths, organophosphates, abamectin (Turnbull and Harris 1986; Arthur 2000; Kavallieratos et al. 2009; Athanassiou et al. 2014b). In a recent study, however, Boukouvala et al. (2016a) reported that the pyrrole derivatives 3i and 3k were more efficacious at 25 than at 20 or 30 °C against the same target species. This interesting finding shows that compounds with close chemical structure can perform differently under the change of temperature. For two insecticides both of which are based on metabolites (spinosyns) of the actinomycete *Saccharopolyspora spinosa* Mertz and Yao (Actinomycetales: Pseudonocardiaceae), i.e., spinosad that contains the spinosyn A and spinosyn D and spinetoram that contains spinosyn L and spinosyn J (Dripps et al. 2011), it is evident that temperature may or may not play a role in their efficacy against stored-product insects. For example, Athanassiou et al. (2008) reported that *S. oryzae* mortality on wheat treated with a liquid formulation of spinosad was positively affected at temperatures ranging from 20 to 30 °C. In contrast, mortality of the same species was not much affected

Table 3 Mean mortality (% ±SE) of *T. confusum* larvae after 7, 14 and 21 days on wheat treated with 3g at three doses under three temperatures and two RH levels

RH	55 %			*F*	*P*	75 %			*F*	*P*
Temperature Dose	20 °C	25 °C	30 °C			20 °C	25 °C	30 °C		
7 days										
0.1 ppm	5.6 ± 1.8Bc	25.6 ± 2.9Ab	26.7 ± 4.7Ab	12.2	0.01	0.0 ± 0.0B	0.0 ± 0.0B	3.3 ± 1.7Ab	4.0	0.03
1 ppm	15.6 ± 1.8Bb	30.0 ± 4.4Ab	40.0 ± 2.4Aa	16.1	<0.01	0.0 ± 0.0B	0.0 ± 0.0B	11.1 ± 2.6Aab	18.2	<0.01
10 ppm	25.6 ± 2.9Ba	52.2 ± 3.6Aa	45.6 ± 1.8Aa	23.1	<0.01	0.0 ± 0.0B	0.0 ± 0.0B	17.8 ± 2.8Aa	41.0	<0.01
F	20.3	14.8	9.2			–	–	9.1		
P	<0.01	<0.01	0.01			–	–	0.01		
14 days										
0.1 ppm	7.8 ± 1.5Bc	44.4 ± 4.4Ab	46.7 ± 3.7Ab	40.0	<0.01	0.0 ± 0.0B	10.0 ± 2.9A	10.0 ± 2.4Ab	7.2	0.01
1 ppm	20.0 ± 1.7Bb	52.2 ± 4.7Aab	57.8 ± 2.8Aab	38.9	<0.01	1.1 ± 1.1B	15.6 ± 3.4A	15.6 ± 3.4Aab	8.7	0.01
10 ppm	34.4 ± 2.4Ba	64.4 ± 3.8Aa	66.7 ± 2.9Aa	34.2	<0.01	4.4 ± 2.4B	20.0 ± 4.4A	23.3 ± 3.3Aa	8.4	0.01
F	49.5	5.5	10.1			2.3	1.9	4.8		
P	<0.01	0.01	0.01			0.13	0.17	0.02		
21 days										
0.1 ppm	8.9 ± 2.0Bc	57.8 ± 6.8Ab	64.4 ± 5.0Ac	36.4	<0.01	8.9 ± 2.0	10.0 ± 2.9b	17.8 ± 4.7c	2.1	0.15
1 ppm	28.9 ± 3.5Bb	73.3 ± 4.1Aab	77.8 ± 2.8Ab	59.7	<0.01	11.1 ± 3.1B	20.0 ± 4.1ABab	35.6 ± 6.3Ab	7.0	0.01
10 ppm	55.6 ± 3.8Ba	90.0 ± 2.4Aa	97.8 ± 1.5Aa	69.1	<0.01	12.2 ± 3.2C	24.4 ± 4.1Ba	56.7 ± 2.4Aa	47.9	<0.01
F	53.8	11.3	24.0			0.4	3.9	17.1		
P	<0.01	0.01	<0.01			0.70	0.03	<0.01		

Within each column, exposure and RH, means followed by the same lowercase letter are not significantly different; $df = 2, 26$. Within each row, exposure and RH, means followed by the same uppercase letter are not significantly different; $df = 2, 26$, Tukey–Kramer (HSD) test at $P = 0.05$. Where no letters exist, no significant differences were recorded

Table 4 Mean mortality (% ±SE) of *T. confusum* larvae after 7, 14 and 21 days on wheat treated with 3l at three doses under three temperatures and two RH levels

RH	55 %			*F*	*P*	75 %			*F*	*P*
Temperature Dose	20 °C	25 °C	30 °C			20 °C	25 °C	30 °C		
7 days										
0.1 ppm	1.1 ± 4.2	12.2 ± 2.2b	20.0 ± 5.5b	1.3	0.29	0.0 ± 0.0Bb	2.2 ± 1.5B	20.0 ± 4.4A	16.7	<0.01
1 ppm	4.4 ± 2.4B	16.7 ± 3.7Bb	32.2 ± 5.7Aab	11.1	0.01	3.3 ± 1.7Bab	12.2 ± 4.3B	26.7 ± 4.7A	9.5	0.01
10 ppm	7.7 ± 2.8B	32.2 ± 5.2Aa	37.8 ± 3.2Aa	16.8	<0.01	6.7 ± 1.7Ba	13.3 ± 5.8B	28.9 ± 4.5A	6.9	0.01
F	1.1	7.1	3.4			6.0	2.2	1.0		
P	0.36	0.01	0.05			0.01	0.15	0.37		
14 days										
0.1 ppm	24.4 ± 6.3	26.7 ± 3.3Bb	45.6 ± 5.6A	5.0	0.02	13.3 ± 4.4B	14.4 ± 4.1B	35.6 ± 7.7A	4.9	0.02
1 ppm	31.1 ± 2.6B	38.9 ± 5.4ABab	54.4 ± 6.5A	5.4	0.01	15.6 ± 2.4B	24.4 ± 7.8B	47.8 ± 7.8A	6.5	0.01
10 ppm	33.3 ± 6.2B	50.0 ± 6.0ABa	55.6 ± 4.1A	4.4	0.02	25.6 ± 3.8B	34.4 ± 4.4B	56.7 ± 3.7A	16.1	<0.01
F	0.8	5.4	1.0			3.2	3.1	2.5		
P	0.48	0.01	0.38			0.06	0.07	0.10		
21 days										
0.1 ppm	30.0 ± 5.8Ba	40.0 ± 5.3ABb	54.4 ± 4.1Ab	5.8	0.01	17.7 ± 4.6B	21.1 ± 4.5Bb	44.4 ± 6.5Ab	7.5	0.01
1 ppm	46.7 ± 6.5ab	53.3 ± 5.5b	62.2 ± 5.5b	1.8	0.19	27.8 ± 4.0B	35.6 ± 7.3Bab	58.9 ± 6.0Aab	6.9	0.01
10 ppm	60.0 ± 6.5Ba	84.4 ± 1.8Aa	95.6 ± 1.8Aa	20.8	<0.01	30.0 ± 3.3B	40.0 ± 3.3Ba	67.8 ± 5.7Aa	20.9	<0.01
F	5.8	25.4	28.6			2.6	3.4	3.5		
P	0.01	<0.01	<0.01			0.10	0.05	0.05		

Within each column, exposure and RH, means followed by the same lowercase letter are not significantly different; $df = 2, 26$. Within each row, exposure and RH, means followed by the same uppercase letter are not significantly different; $df = 2, 26$, Tukey–Kramer (HSD) test at $P = 0.05$. Where no letters exist, no significant differences were recorded

Table 5 Mean mortality (% ±SE) of *T. confusum* larvae after 7, 14 and 21 days on wheat treated with 3m at three doses under three temperatures and two RH levels

RH	55 %			*F*	*P*	75 %			*F*	*P*
Temperature Dose	20 °C	25 °C	30 °C			20 °C	25 °C	30 °C		
7 days										
0.1 ppm	4.4 ± 1.8B	22.2 ± 8.6AB	31.1 ± 5.4Ab	5.2	0.01	8.8 ± 4.6B	3.3 ± 1.7Bb	30.0 ± 4.7Ab	13.0	0.01
1 ppm	8.9 ± 2.6B	28.9 ± 8.7AB	46.7 ± 6.0Aab	8.9	0.01	12.2 ± 2.2B	4.4 ± 1.8Bab	44.4 ± 6.0A	30.4	<0.01
10 ppm	13.3 ± 4.1B	40.0 ± 7.8A	50.0 ± 4.1Aa	11.4	0.01	15.6 ± 4.1B	11.1 ± 2.6Ba	48.9 ± 2.6Aa	48.9	<0.01
F	2.2	1.1	3.7			0.8	4.2	4.5		
P	0.13	0.34	0.01			0.47	0.03	0.02		
14 days										
0.1 ppm	15.6 ± 3.4B	30.0 ± 9.1AB	40.0 ± 5.8Aa	3.5	0.05	20.0 ± 6.5B	17.8 ± 2.8B	40.0 ± 8.5A	3.4	0.05
1 ppm	26.7 ± 2.4Bab	45.6 ± 8.7AB	67.8 ± 7.8Aa	9.0	0.01	28.9 ± 5.9B	21.1 ± 3.1B	50.0 ± 6.2A	8.1	0.01
10 ppm	31.1 ± 5.1Ba	56.7 ± 9.1A	76.7 ± 2.9Aa	13.3	0.01	32.2 ± 4.0B	24.4 ± 1.8B	63.3 ± 5.8A	24.2	<0.01
F	4.5	2.2	10.7			1.3	1.6	2.9		
P	0.02	0.13	0.01			0.29	0.22	0.08		
21 days										
0.1 ppm	32.2 ± 2.2Bc	51.1 ± 7.7Ab	54.4 ± 3.4Ac	5.7	0.01	26.7 ± 6.7	24.4 ± 2.4	43.3 ± 8.0	2.8	0.08
1 ppm	50.0 ± 3.3Bb	66.7 ± 5.8ABb	78.9 ± 6.1Ab	7.7	0.01	36.7 ± 7.1	27.8 ± 2.8B	53.3 ± 6.5A	5.1	0.01
10 ppm	65.6 ± 1.8Ca	84.4 ± 4.1Ba	95.6 ± 1.8Aa	29.8	<0.01	46.7 ± 6.7AB	33.3 ± 2.9B	65.6 ± 5.0A	10.1	0.01
F	43.6	7.6	24.7			2.2	2.8	2.8		
P	<0.01	0.01	<0.01			0.14	0.08	0.08		

Within each column, exposure and RH, means followed by the same lowercase letter are not significantly different; $df = 2, 26$. Within each row, exposure and RH, means followed by the same uppercase letter are not significantly different; $df = 2, 26$, Tukey–Kramer (HSD) test at $P = 0.05$. Where no letters exist, no significant differences were recorded

Table 6 Mean mortality (% ±SE) of *T. confusum* larvae after 7, 14 and 21 days on wheat treated with 3h at three doses under three temperatures and two RH levels

RH	55 %			*F*	*P*	75 %			*F*	*P*
Temperature Dose	20 °C	25 °C	30 °C			20 °C	25 °C	30 °C		
7 days										
0.1 ppm	14.4 ± 4.4B	12.2 ± 3.6B	30.0 ± 4.4Ab	5.4	0.01	10.0 ± 2.9Bb	17.8 ± 3.2ABb	24.4 ± 5.0Ab	3.6	0.04
1 ppm	16.7 ± 3.7B	18.9 ± 4.2B	35.6 ± 3.8Aab	7.0	0.01	17.8 ± 3.6ab	34.4 ± 7.1ab	31.1 ± 3.5ab	3.1	0.07
10 ppm	26.7 ± 8.0AB	20.0 ± 6.7B	46.7 ± 5.3Aa	4.2	0.03	26.7 ± 5.5a	36.7 ± 3.7a	42.2 ± 5.2a	2.6	0.10
F	1.3	0.7	3.5			4.0	4.3	3.7		
P	0.29	0.51	0.05			0.03	0.03	0.04		
14 days										
0.1 ppm	27.8 ± 4.0Bb	30.0 ± 4.1Bb	62.2 ± 4.6A	20.5	<0.01	37.8 ± 4.0b	35.6 ± 2.4b	43.3 ± 3.3b	1.5	0.25
1 ppm	35.6 ± 4.1Bab	55.6 ± 4.7Aa	68.9 ± 4.8A	13.4	0.01	45.6 ± 7.8ab	56.7 ± 6.7a	52.2 ± 3.6b	0.8	0.47
10 ppm	50.0 ± 6.5Ba	58.9 ± 5.9ABa	74.4 ± 3.8A	5.1	0.01	65.6 ± 6.7a	63.3 ± 4.1a	70.0 ± 3.7a	0.5	0.64
F	5.1	10.2	1.9			5.0	9.4	14.5		
P	0.01	0.01	0.17			0.01	0.01	<0.01		
21 days										
0.1 ppm	41.1 ± 3.5Bb	42.2 ± 4.9Bb	66.7 ± 6.0Ab	8.6	0.01	51.1 ± 6.5b	44.4 ± 3.8b	54.4 ± 4.4b	1.0	0.38
1 ppm	47.8 ± 5.2Bb	75.6 ± 4.4Aa	81.1 ± 4.8Aab	13.6	0.01	64.4 ± 5.3ab	68.9 ± 6.8a	61.1 ± 4.5ab	0.5	0.62
10 ppm	73.3 ± 7.3Ba	88.9 ± 2.6ABa	91.1 ± 2.0Aa	4.4	0.02	81.1 ± 5.9a	76.7 ± 5.0a	72.2 ± 3.2a	0.9	0.44
F	9.4	34.0	7.1			6.4	10.0	4.6		
P	0.01	<0.01	0.01			0.01	0.01	0.02		

Within each column, exposure and RH, means followed by the same lowercase letter are not significantly different; $df = 2, 26$. Within each row, exposure and RH, means followed by the same uppercase letter are not significantly different; $df = 2, 26$, Tukey–Kramer (HSD) test at $P = 0.05$. Where no letters exist, no significant differences were recorded

by temperature on wheat treated with spinetoram at certain combinations (Vassilakos and Athanassiou 2013). From practical point of view, a potential application of the tested pyrrole derivatives, especially 3a, on wheat could optimize the control measures at elevated temperatures (30 °C) against *T. confusum* given that the developmental period from egg to adult and the fecundity of females are favored at temperatures ranging between 29 and 34 °C (Park and Burton Frank 1948; Aitken 1975). In contrast, temperatures ≥31 °C inhibit the development of *E. kuehniella* from egg to adult but 25 °C fastens it (Jacob and Cox 1977). Thus, a combined treatment of the pyrrole derivatives 3i or 3k with the pyrrole derivatives tested here, as grain protectants, could offer substantial control of both species by limiting the influence of variation of temperature at least between 25 and 30 °C. The concept of the combined treatments could be extended with other insecticides that already used as grain protectants (e.g., spinosad, pyrethroids, diatomaceous earths). These assumptions, however, merit further experimental work on the same or other stored-product insects on different commodities given that previous studies have shown that combinations of insecticides could be or could not be more effective than the applications of the same insecticides alone. For example, Nayak and Daglish (2007) found that the combination of 1 ppm spinosad with 10 ppm chlorpyrifos-methyl was able to provide complete control of *L. bostrychophila*, *Liposcelis decolor* (Pearman) (Psocoptera: Liposcelididae), *L. entomophila* and *L. paeta* for 3 months on wheat contrary to spinosad or chlorpyrifos-methyl alone. However, Daglish (2008) did not find significant differences in the mortality of *S. oryzae* on wheat treated with chlorpyrifos-methyl or combinations of chlorpyrifos-methyl with spinosad or *s*-methoprene. Similar results were reported by Athanassiou and Kavallieratos (2014) for the combination of spinosad and spinetoram on wheat against *P. truncatus*, *R. dominica*, *S. oryzae* and *T. confusum*.

The pyrrole derivatives 3a, 3g, 3l and 3m were affected by RH at almost all combinations tested. The 75 % level of RH moderated the efficacy of the pyrrole derivatives, while the 55 % enhanced it. This observation was also evident for the pyrrole derivatives 3i and 3k (Boukouvala et al. 2016a). Despite the fact that the mode of actions of these novel substances are not known, based on the fact that we applied the pyrrole derivatives as dusts and having the humidity and temperature dependence of their efficacy

Table 7 Mean mortality (% ±SE) of *E. kuehniella* larvae after 7, 14 and 21 days on wheat treated with 3h at three doses under three temperatures and two RH levels

RH	55 %			F	P	75 %			F	P
Temperature Dose	20 °C	25 °C	30 °C			20 °C	25 °C	30 °C		
7 days										
0.1 ppm	8.8 ± 2.9b	14.4 ± 4.4b	18.9 ± 4.5b	1.5	0.22	5.6 ± 2.4b	7.8 ± 2.2b	7.8 ± 3.2b	0.2	0.79
1 ppm	11.1 ± 3.5Bb	20.0 ± 3.3ABb	26.7 ± 5.5Ab	3.4	0.05	14.4 ± 1.8b	14.4 ± 2.9b	15.6 ± 4.1b	0.1	0.96
10 ppm	42.2 ± 4.3Ba	54.4 ± 9.1ABa	72.2 ± 8.3Aa	4.0	0.03	27.8 ± 4.3Ba	38.9 ± 4.2Ba	80.0 ± 5.8Aa	32.4	<0.01
F	27.4	12.3	20.7			13.5	25.6	77.5		
P	<0.01	0.01	<0.01			0.01	<0.01	<0.01		
14 days										
0.1 ppm	20.0 ± 5.0Bb	21.1 ± 5.4Bb	41.1 ± 7.3Ab	3.9	0.03	15.6 ± 5.3b	12.2 ± 3.6b	8.9 ± 3.1c	0.7	0.53
1 ppm	24.4 ± 4.4Bb	33.3 ± 4.4ABb	44.4 ± 5.3Ab	4.5	0.02	25.6 ± 5.0Bb	20.0 ± 3.7Bb	43.3 ± 3.7Ab	8.4	0.01
10 ppm	73.3 ± 5.3a	84.4 ± 5.6a	87.9 ± 5.7a	1.9	0.17	81.1 ± 2.6ABa	67.8 ± 6.2Ba	90.0 ± 3.3Aa	6.7	0.01
F	36.2	42.7	17.7			62.2	41.5	143.8		
P	<0.01	<0.01	<0.01			<0.01	<0.01	<0.01		
21 days										
0.1 ppm	22.2 ± 6.0Bb	25.6 ± 5.9Bb	62.2 ± 7.6Ab	11.6	0.01	17.8 ± 4.6c	15.6 ± 5.3b	21.1 ± 3.5c	0.4	0.69
1 ppm	26.7 ± 5.0Bb	42.2 ± 6.4Bb	66.7 ± 7.1Ab	10.5	0.01	33.3 ± 5.0Bb	27.8 ± 5.2Bb	54.4 ± 6.0Ab	6.7	0.01
10 ppm	78.9 ± 6.8Ba	88.9 ± 4.8ABa	98.9 ± 1.1Aa	4.3	0.03	88.9 ± 2.6ABa	75.6 ± 6.0Ba	95.6 ± 1.8Aa	6.7	0.01
F	28.1	32.9	11.0			78.5	32.9	80.5		
P	<0.01	<0.01	0.01			<0.01	<0.01	<0.01		

Within each column, exposure and RH, means followed by the same lowercase letter are not significantly different; $df = 2, 26$. Within each row, exposure and RH, means followed by the same uppercase letter are not significantly different; $df = 2, 26$, Tukey–Kramer (HSD) test at $P = 0.05$. Where no letters exist, no significant differences were recorded

Table 8 Repeated measures MANOVA parameters for main effects and associated interactions for mortality levels of *T. confusum* larvae and *E. kuehniella* larvae between and within exposure intervals (error $df = 240$ for *T. confusum* larvae and error $df = 76$ for *E. kuehniella* larvae)

Source	*df*	*T. confusum* (larvae)		*E. kuehniella* (larvae)	
		F	*P*	*F*	*P*
Between exposure intervals					
Pyrrole derivative	4	20.9	<0.01	–	–
Commodity	1	235.1	<0.01	20.4	<0.01
Dose	2	449.7	<0.01	54.3	<0.01
Commodity × dose	2	2.2	0.12	0.7	0.49
Pyrrole derivative × dose	8	1.9	0.06	–	–
Pyrrole derivative × commodity	4	2.7	0.03	–	–
Pyrrole derivative × commodity × dose	8	0.9	0.56	–	–
Within exposure intervals					
Exposure × dose	8	60.7	<0.01	6.7	<0.01
Exposure × commodity	4	45.9	<0.01	4.2	0.01
Exposure × pyrrole derivative	16	5.7	<0.01	–	–
Exposure × commodity × dose	8	4.8	<0.01	1.3	0.24
Exposure × pyrrole derivative × dose	32	3.5	<0.01	–	–
Exposure × pyrrole derivative × commodity	16	2.1	0.01	–	–
Exposure × pyrrole derivative × commodity × dose	32	2.2	0.01	–	–

Table 9 Mean mortality (% ±SE) of *T. confusum* larvae after 1, 2, 7, 14 and 21 days on maize or barley treated with the pyrrole derivatives 3a, 3g, 3l, 3m, 3h

Exposure Pyrrole derivative	Dose	1 day	2 days	7 days	14 days	21 days	*F*	*P*
Commodity: Maize								
3a	0.1 ppm	0.0 ± 0.0Cc	0.0 ± 0.0Cc	11.1 ± 2.0Befg	15.6 ± 2.4Bef	25.6 ± 2.4Aef	37.6	<0.01
	1 ppm	10.0 ± 4.1Cab	25.6 ± 5.3Bab	45.6 ± 7.8ABabcd	55.6 ± 7.5Aabcd	61.1 ± 6.6Abc	11.1	<0.01
	10 ppm	14.4 ± 2.4Ca	32.2 ± 6.2Ca	64.4 ± 6.0Ba	74.4 ± 5.0ABa	91.1 ± 2.6Aa	43.7	<0.01
3g	0.1 ppm	0.0 ± 0.0Bc	0.0 ± 0.0Bc	5.6 ± 2.4Bfg	10.0 ± 2.4ABf	18.9 ± 4.8Ade	9.0	<0.01
	1 ppm	3.3 ± 1.7Cbc	11.1 ± 3.5Cbc	27.8 ± 2.8Bde	38.9 ± 5.4ABcde	51.1 ± 4.8Ac	25.5	<0.01
	10 ppm	7.8 ± 2.8Cabc	21.1 ± 4.2BCab	40.0 ± 5.3Bbcd	62.2 ± 5.2Aabc	75.6 ± 5.6Aab	35.3	<0.01
3l	0.1 ppm	0.0 ± 0.0Bc	0.0 ± 0.0Bc	2.2 ± 1.5Bg	5.6 ± 2.4Bf	14.4 ± 2.9Ae	10.9	<0.01
	1 ppm	4.4 ± 2.4Cbc	18.9 ± 5.1BCab	31.1 ± 7.0ABcde	46.7 ± 6.0Abcd	50.0 ± 7.5Ac	10.6	<0.01
	10 ppm	8.9 ± 2.6Dabc	32.2 ± 4.9Ca	55.6 ± 5.0Bab	68.9 ± 5.1ABab	75.6 ± 4.8Aab	36.0	<0.01
3m	0.1 ppm	0.0 ± 0.0Cc	0.0 ± 0.0Cc	4.4 ± 1.8BCfg	8.9 ± 2.0Bf	16.7 ± 2.4Ae	19.4	<0.01
	1 ppm	3.3 ± 1.7Cbc	10.0 ± 2.9CbcB	28.9 ± 4.5Bde	52.2 ± 6.8Aabcd	58.9 ± 6.8Abc	24.6	<0.01
	10 ppm	6.7 ± 2.4Dabc	24.4 ± 2.4Cab	51.1 ± 2.6Babc	70.0 ± 3.3Aab	75.6 ± 3.8Aab	100.1	<0.01
3h	0.1 ppm	0.0 ± 0.0Bc	0.0 ± 0.0Bc	0.0 ± 0.0Bg	4.4 ± 1.8ABf	7.8 ± 2.8Ae	5.8	0.01
	1 ppm	6.7 ± 2.4Babc	10.0 ± 3.3Bbc	25.6 ± 6.9ABdef	34.4 ± 7.3Ade	41.1 ± 7.9Acd	6.3	0.01
	10 ppm	12.2 ± 1.5Eab	28.9 ± 2.0Da	45.6 ± 2.4Cabcd	60.0 ± 2.4Babc	78.9 ± 2.0Aab	156.7	<0.01
F		5.6	13.5	21.8	28.9	31.3		
P		<0.01	<0.01	<0.01	<0.01	<0.01		
Commodity: Barley								
3a	0.1 ppm	6.6 ± 2.4Dbcde	13.3 ± 2.9Defg	32.2 ± 3.2Cefgh	50.0 ± 2.4Bcdef	67.8 ± 3.2Abc	79.6	<0.01
	1 ppm	12.2 ± 1.5Ebcd	31.1 ± 2.0Dbcd	56.7 ± 3.7Cbcd	86.7 ± 3.3Bab	100.0 ± 0.0Aa	216.7	<0.01
	10 ppm	23.3 ± 1.7Da	51.1 ± 2.6Ca	82.2 ± 1.5Ba	100.0 ± 0.0Aa	100.0 ± 0.0Aa	477.0	<0.01
3g	0.1 ppm	5.6 ± 2.4Ccde	13.3 ± 3.7Cefg	32.2 ± 6.0Befgh	41.1 ± 4.6ABefg	56.7 ± 3.7Acd	23.9	<0.01
	1 ppm	11.1 ± 1.1Cbcd	21.1 ± 2.0Ccdef	51.1 ± 4.8Bbcde	68.9 ± 4.8Abc	80.0 ± 3.7Ab	67.0	<0.01
	10 ppm	16.7 ± 1.7Dab	34.4 ± 4.1Cbc	66.7 ± 4.7Babc	97.8 ± 1.5Aa	100.0 ± 0.0Aa	157.3	<0.01
3l	0.1 ppm	4.4 ± 1.8Bde	12.2 ± 1.5Bfg	31.1 ± 6.3Aefgh	38.9 ± 5.6Afg	44.4 ± 5.0Ade	14.5	<0.01
	1 ppm	10.0 ± 1.7Dbcde	17.8 ± 1.5Ddefg	40.0 ± 1.7Cdefg	58.9 ± 2.6Bcde	74.4 ± 2.4Ab	180.2	<0.01
	10 ppm	12.2 ± 3.2Dbcd	31.1 ± 5.1Cbcd	67.8 ± 5.7Babc	87.8 ± 4.0Aab	100.0 ± 0.0Aa	81.1	<0.01
3m	0.1 ppm	0.0 ± 0.0Ce	3.3 ± 5.0BCg	21.1 ± 5.4ABgh	33.3 ± 6.0Afg	35.6 ± 7.3Ae	11.3	<0.01
	1 ppm	15.0 ± 2.7Eabc	28.0 ± 3.3Dbcde	46.7 ± 2.9Ccdef	63.3 ± 2.4ABcd	77.8 ± 2.2Ab	83.7	<0.01
	10 ppm	15.6 ± 2.4Dabc	42.2 ± 3.2Cab	68.9 ± 3.9Bab	100.0 ± 0.0Aa	100.0 ± 0.0Aa	204.9	<0.01
3h	0.1 ppm	4.4 ± 2.4Bde	8.9 ± 3.1Bfg	17.8 ± 4.3ABh	28.9 ± 5.9Ag	32.2 ± 4.7Ae	8.1	<0.01
	1 ppm	7.8 ± 2.2Cbcde	13.3 ± 3.3BCefg	28.9 ± 3.9Bfgh	45.6 ± 5.0Adefg	52.2 ± 4.9Acd	23.0	<0.01
	10 ppm	15.6 ± 2.4Eabc	30.0 ± 3.3Dbcd	56.7 ± 4.1Cbcd	83.3 ± 3.3Bab	100.0 ± 0.0Aa	139.4	<0.01
F		8.3	19.0	19.9	42.2	55.7		
P		<0.01	<0.01	<0.01	<0.01	<0.01		

Within each column, means followed by the same lowercase letter are not significantly different; $df = 14, 134$. Within each row, means followed by the same uppercase letter are not significantly different; $df = 4, 44$, Tukey–Kramer (HSD) test at $P = 0.05$. Where no letters exist, no significant differences were recorded

could suggest these compounds have both physical and biochemical mode of action. The inactivation of their particles through absorption of water from the highly humid environment as in the case of diatomaceous earths could significantly reduce their water adsorption capacity and directly impact their efficacy (Subramanyam and Roesli 2000; Korunic 1998; Fields and Korunic 2000). Improved efficacy at higher temperature is well known in case of dust and desiccant-based insecticides and can be explained by higher evaporation rate of water from insects' body and improved adsorption performance (Arthur 2000; Fields and Korunic 2000). The fact that the

Table 10 Mean mortality (% ±SE) of *E. kuehniella* larvae after 1, 2, 7, 14 and 21 days on maize or barley treated with the pyrrole derivative 3h

Exposure	Dose	1 day	2 days	7 days	14 days	21 days	*F*	*P*
Commodity: Maize								
	0.1 ppm	0.0 ± 0.0Bb	3.3 ± 1.7Bb	7.8 ± 2.8Bb	14.4 ± 4.1ABc	27.8 ± 7.2Ac	7.6	0.01
	1 ppm	5.6 ± 1.8Bab	16.7 ± 3.3Ba	38.9 ± 4.6Aa	51.1 ± 6.3Ab	54.4 ± 7.1Ab	18.4	<0.01
	10 ppm	11.1 ± 3.1Ca	24.4 ± 3.8Ca	47.8 ± 5.5Ba	71.1 ± 5.6Aa	82.2 ± 4.0Aa	50.0	<0.01
F		7.3	12.2	22.7	31.9	18.8		
P		0.01	0.01	<0.01	<0.01	<0.01		
Commodity: Barley								
	0.1 ppm	2.2 ± 1.5Cc	8.9 ± 2.6BCc	33.3 ± 7.5ABb	38.9 ± 7.9Ab	42.2 ± 8.5Ac	8.4	<0.01
	1 ppm	12.2 ± 1.5Bb	24.4 ± 3.8Bb	50.0 ± 4.7Ab	58.9 ± 5.6Ab	64.4 ± 6.5Ab	22.8	<0.01
	10 ppm	20.0 ± 2.4Da	40.0 ± 3.7Ca	72.2 ± 4.0Ba	91.1 ± 2.6Aa	100.0 ± 0.0Aa	136.2	<0.01
F		24.1	20.8	12.2	20.6	22.4		
P		<0.01	<0.01	0.01	<0.01	<0.01		

Within each column, means followed by the same lowercase letter are not significantly different; $df = 2, 26$. Within each row, means followed by the same uppercase letter are not significantly different; $df = 4, 44$, Tukey–Kramer (HSD) test at $P = 0.05$. Where no letters exist, no significant differences were recorded

tested pyrrole derivatives exhibit elevated insecticidal efficacy under low RH is important since *T. confusum* is tolerant at dry conditions (Aitken 1975). The efficacy of 3h was affected by RH as above under certain combinations according to species, i.e., at 30 °C, for exposures >7 days in the case of *T. confusum*, or at 25 °C for any exposure in the case of *E. kuehniella*. These findings stand in accordance with the influence of RH on the insecticidal efficacy of chlorfenapyr as wheat protectant that it varies among different species, doses, temperatures and exposure intervals (Kavallieratos et al. 2011). Furthermore, the majority of the tested pyrrole derivatives caused the maximum mortality levels against both insect species at 10 ppm. Similar dose performance has been observed for chlorfenapyr as grain protectant against *L. bostrychophila*, *R. dominica*, *S. oryzae* and *T. confusum* (Kavallieratos et al. 2011). These results strongly indicated that biochemical mode of action could additionally explain observed insecticidal performance of sulfanyl 5H-dihydropyrrole pyrrole-based compound studied in this work. The mode of action of commercially available pyrrole-based pesticide (chlorfenapyr) is based on the disruption of production of adenosine triphosphate (ATP) and cellular death, through an oxidative removal of the N-ethoxymethyl group of molecule which is not present in these compounds. All sulfanyl 5H-dihydropyrrole pyrrole compounds explored in this work are the NH derivatives with active groups that could act as binding sites to receptors related to the voltage-gated sodium channels (vgSCh) and blocking their activities. Their different insecticidal activities can be explained by influence of linked groups to the surrounding O and S atoms (methyl, ethyl, terc-butyl, phenyl) on N–H affinity to these receptors. However, more studies compared with control compounds and different ligands are required to elucidate the proposed biochemical mode of actions.

Taking into account the results of both bioassay series, commodity was an important factor that influences the performance of the pyrrole derivatives as grain protectants. Mortality of *T. confusum* and *E. kuehniella* on maize was much lower on treated maize than barley or wheat. However, 100 % control of both species was recorded only on treated barley. Similar results have also been reported for the pyrrole derivatives 3i and 3k against adults or larvae of *T. confusum* and larvae of *E. kuehniella* (Boukouvala et al. 2016a, b). Thus, it can be concluded that all so-far-tested pyrrole derivatives exhibit unified insecticidal activity on certain commodities, at least for the grain varieties and insect species tested.

However, insecticides perform differently against the same stored-product insects, such as *R. dominica* and *S. oryzae*, among varieties of the same grain (Kavallieratos et al. 2010); further experimental work would reveal potential differentiation of the efficacy of the pyrrole derivatives examined here within grain species. Kavallieratos et al. (2005) related the high efficacy of DEs against *R. dominica* adults with the high (>82 %) retention of DEs on the surface of whole (rough) barley kernels vs. lower DE efficacy corresponding to lower DE adherence (<52 %) on the surface of peeled (smooth) barley kernels. Given that maize kernels are much smoother than barley or wheat kernels, we assume that the lower efficacy of the pyrrole derivatives could also be related to the reduced adherence of their particles on maize. The use of high-performance liquid chromatography/mass spectrometry method (LC/MS) showed that a dust formulation of spinosad was degraded >80 % on maize kernels contrary to its limited degradation on barley and wheat. Consequently, the low and high efficacy of spinosad on maize and barley or wheat, respectively, against *R. dominica* and *S. oryzae* could be attributed on this phenomenon (Chintzoglou et al. 2008). Further experimentation in this direction could confirm or not a similar assumption for the pyrrole derivatives. It is well known that *T. confusum* and *E. kuehniella* are resistant to various insecticides (Attia et al. 1979; Zettler 1991; Arthur and Zettler 1992; Zettler and Arthur 1997; Rossi et al. 2010). Furthermore, *T. confusum* is tolerant against several insecticides (Athanassiou et al. 2008; Athanassiou and Kavallieratos 2014; Rumbos et al. 2013; Kavallieratos et al. 2015).

In conclusion five novel sulfanyl 5H-dihydropyrrole pyrrole-based compounds were synthesized and their insecticidal performance against *T. confusum* and *E. kuehniella* were evaluated for the first time. Their activities were found to be influenced by temperature, humidity, commodity and dosage and indicate their combined physical and biochemical mode of the action. More studies are required to further evaluate the performance of these novel active ingredients for the protection of grains against other noxious insects at the post-harvest stage given that different species exhibit variant susceptibility to insecticides (Kavallieratos et al. 2011). The present study documented that sulfanyl 5H-dihydropyrrole pyrrole compounds can work as promising grain protectants under certain biotic and abiotic factors, a fact that may help in promoting them toward the formation of new class of insecticides. The involvement of quantitative structure–activity relationship (QSAR) modeling experts in future work to assist the synthesis of pyrrole compound with optimized performance should be considered.

Author contribution statement

MCB, NGK, CGA, LPH and YE conceived and designed research. MCB conducted experiments. MCB, NGK and CGA analyzed data. MCB, NGK, CGA and DL wrote the manuscript.

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Compliance with ethical standards

Conflict of interest The authors declare no competing interests.

Ethical approval This article does not contain any studies with human participants performed by any of the authors.

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