Research Article

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Antifeedant effect of polygodial and drimenol derivatives against *Spodoptera frugiperda* and *Epilachna paenulata* and quantitative structure-activity analysis

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Abstract

BACKGROUND: The antifeedant activity of 18 sesquiterpenoids of the drimane family (polygodial, drimenol and derivatives) was investigated.

RESULTS: Polygodial, drimanic and nordrimanic derivatives were found to exert antifeedant effects against two insect species, *Spodoptera frugiperda* and *Epilachna paenulata*, which are pests of agronomic interest, indicating that they have potential as biopesticide agents. Among the 18 compounds tested, the epoxynordrimane compound (11) and isonordrimenone (4) showed the highest activity [50% effective concentration (EC_{50}) = 23.28 and 25.63 nmol cm^{-2}, respectively, against *S. frugiperda*, and 50.50 and 59.00 nmol/cm^2, respectively, against *E. paenulata*].

CONCLUSION: The results suggest that drimanic compounds have potential as new agents against *S. frugiperda* and *E. paenulata*. A quantitative structure–activity relationship (QSAR) analysis of the whole series, supported by electronic studies, suggested that drimanic compounds have structural features necessary for increasing antifeedant activity, namely a C-9 carbonyl group and an epoxide at C-8 and C-9.

Supporting information may be found in the online version of this article.

Keywords: polygodial; nordrimane; *Spodoptera frugiperda*; *Epilachana paenulata*

1 INTRODUCTION

The use of synthetic insecticides for pest control continues to be the most common method for keeping pest populations below the economic threshold. The continuous use of conventional insecticides, however, has caused the emergence of resistant individuals,[1] and numerous environmental problems are associated with their use.[2] Many researchers have become involved in the search for new chemical structures that affect the development and survival of insect pests in order to identify new candidates for natural insecticides that may replace synthetic insecticides.[3] Natural insecticides derived from plants, either crude extracts or naturally occurring chemicals, constitute an environmentally acceptable option for pest control in view of their quick degradation and reduced impact on the environment, human health, and non-target organisms.[4–6]

Drimys winteri J.R. Forster et G. Forster (Winteraceae) is a tree native to southern Chile and Argentina, commonly found in humid and even marshy areas.[7,8] This tree produces drimane sesquiterpenes with bicyclic farnesane-type skeletons. Several important bioactivities, such as antimicrobial,[9] cytotoxic,[9,10] insect

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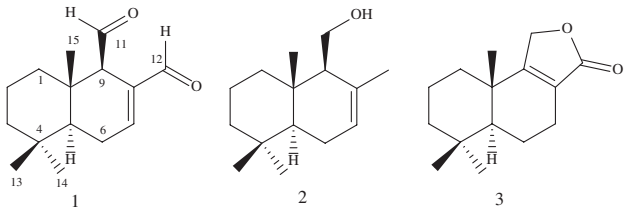

Figure 1. Natural compounds evaluated for activity against *S. frugiperda* and *E. paenulata*.

antifeedant.[11] and larvicidal.[12] activities, have been reported for these sesquiterpenes. Antifeedant activity against the insect *Spodoptera litoralis* (Boisduval) (Lepidoptera: Noctuidae) has been studied at the larval level.[13] It has been reported that the variation in antifeedant activity of polygodial (**1**; see Fig. 1) and other drimanic compounds is consistent with a mode of action proposed for antifeedant compounds; that is, the formation of an adduct between the drimane aldehyde and amino groups on molecular targets in the insect [8,12–15]. Furthermore, Prota *et al.* reported an antifeedant effect of **1** against *Myzus persicae*,[16] and also against lepidopteran larvae belonging to the genera *Heliothis*,[17] *Pieris* and *Plutella*,[17–21] as well as the coleopteran *Leptinotarsa decemlineata* Say.[22] Polygodial (**1**) also interrupts feeding and prevents colony formation in aphids.[23–25] In addition, drimenol (**2**), a homoallylic alcohol drimane also occurring in *D. winteri*, showed various biological activities, including (but not limited to) antifungal, antibacterial, cytotoxic and antifeedant effects.[26] In view of the importance of the biological activities associated with this type of compound, several synthetic derivatives of drimanes have been prepared.[26] The aim of this study was to assess the potential of 18 polygodial and drimenol hemisynthetic derivatives as antifeedants against two insect pests, the generalist *Spodoptera frugiperda* (Smith J.E.) (Lepidoptera: Noctuidae) and the specialist *Epilachna paenulata* ((Germar 1824) (Coleoptera: Coccinelidae), by determination of the 50% effective concentration (EC_{50}). Furthermore, the EC_{50} values of these compounds were used to develop quantitative structure–activity relationships (QSARs) that may facilitate the design of more effective dimanic antifeedants and provide insight into the structural properties responsible for the activity, as well as providing information about receptor–ligand interactions.

The polyphagous fall armyworm *S. frugiperda* is an economically important pest in the production of grain and many other crops in North, Central and South America.[27] and its control has become a serious problem because it has become resistant to many synthetic insecticides.[28] and has adapted to transgenic Bacillus thuringiensis-maize.[29] In contrast, *E. paenulata* is a specialist insect, a native of South America, that affects cucurbits by feeding on their leaves.

2 MATERIALS AND METHODS

2.1 Chemicals

Azadirachtin (**19**) was purchased from Sigma Chemical Co. Inc. (St. Louis, MO, USA). All solvents were high-performance liquid chromatography (HPLC) grade and were purchased from Merck (Darmstadt, Germany) and Fisher Scientific (New Jersey, NJ, USA).

2.2 Plant material

Stem bark of *D. winteri* adult trees was collected from the Malleco Province (Región de La Araucanía, Chile; 38°15′ S, 72°15′ W), in March 2012. A voucher specimen (N° Dw-10114) was deposited at the Herbarium of the Natural Products Laboratory, "Dr. Herbert Appel A.", Department of Chemistry, Universidad Técnica Federico Santa María, Valparaíso, Chile. The plant material was botanically identified by Forest Engineer Patricio Novoa, Botanical Expert, Horticulture Department Chief, "Jardín Botánico Nacional", Viña del Mar, Chile. Fresh bark was carefully washed with abundant distilled water to remove any residue. Afterwards, the bark was dried in an oven at 35 °C to a constant weight. Once dried, it was stored in hermetically sealed plastic containers at 4 °C.

2.3 Isolation of natural compounds 1–3

Polygodial (**1**), drimenol (**2**) and confertifolin (**3**) were isolated from a dichloromethane extract of *D. winteri* bark. The extraction methodology and isolation of pure compounds were performed according to reported procedures.[12] Compounds **1**–**3** were identified by melting point, optical rotation, and spectroscopic data (see Supporting Information Methods S1), including ^{1}H- and ^{13}C-nuclear magnetic resonance (NMR), and comparisons with data reported in the literature.[12]

2.4 Preparation of polygodial derivatives and drimenol derivatives

Compounds **6**–**8** and **13**–**18** were synthesized by treating **1** using different protocols reported in the literature.[12,30] Then, compounds **4**, **5** and **9**–**12** were synthesized by treating **2** using different synthetic procedures reported previously.[12,30] All compounds were identified by melting point, optical rotation, and spectroscopic data (see Methods S1).

2.5 Insects

Spodoptera frugiperda larvae were obtained from a laboratory colony, reared on an artificial diet of distilled water, agar, bean meal, yeast extract, wheat germ, sorbic acid, ascorbic acid, and formaldehyde, prepared as previously described,[31] and *E. paenulata* larvae were obtained from a laboratory colony, reared on a natural diet of *Cucurbita maxima* leaves. Both insects were maintained in a growth chamber at 26 ± 1 °C and 70-75% relative humidity, with a photoperiod of 16:8 light:dark, and periodically renewed with field specimens.[32]

2.6 Feeding choice assay

The feeding choice assays for compounds **1**–**19** were carried out as previously described in the literature.[32,33] Two circular sections of *Lactuca sativa* leaves (1 cm^2) or two sections of *Curcubita maxima* seedling (1 cm^2) were placed in a Petri dish. A starved, third-instar *S. frugiperda* larva or third-instar *E. paenulata* larva was placed equidistant from a treated (10 µL of test solution) and untreated (10 µL of acetone; solvent control) leaf disk. Test solutions were prepared by dissolving the necessary amount of **1**–**19** in 10 mL of HPLC-grade acetone. The dosages for each compound, applied with a Hamilton syringe, were 0.015, 0.15, 1.5, 15.0, 150.0 and 300.0 nmol/cm^2. Ten replicates were run for each treatment at 50 µg/cm^2. Larvae were allowed to feed until 50% of the available food had been eaten. The relative amounts (recorded in percentages from 0 to 100%) of the treated and untreated substrate area eaten in each test were estimated visually by dividing the food area into imaginary quarters or by determining the area of the leaf disks consumed by the larvae using the ImageJ screener software program (Fiji project; available online: http://imagej.net/Downloads).

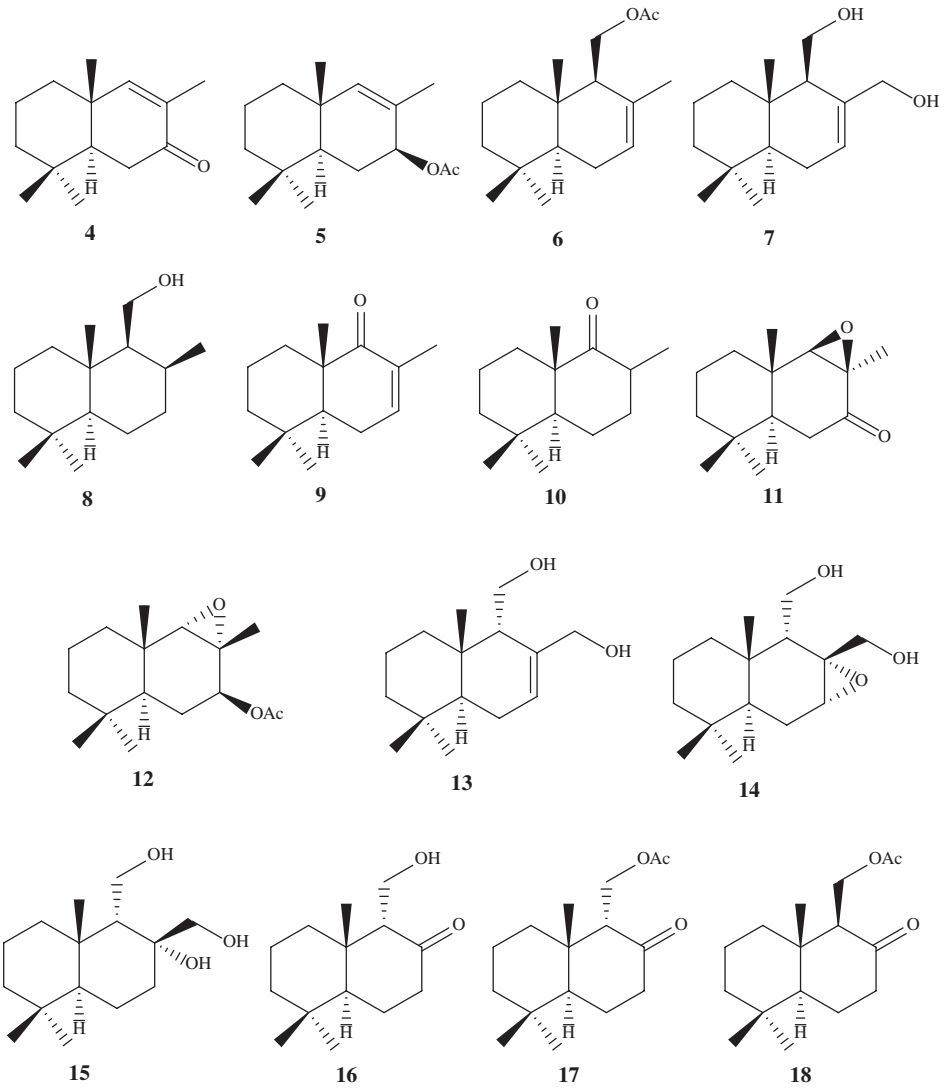

Figure 2. Synthetic compounds evaluated for activity against *S. frugiperda* and *E. paenulata*.

An antifeedant index (AI%)[32,34] was calculated as:

$$(\mathrm{AI}\%) = \left[1 - (T/C)\right] 100 \quad (1)$$

where T and C represent consumption of treated and untreated foods, respectively.

2.7 2D-QSAR modeling

Full unconstrained geometry optimizations of the studied compounds (Fig. 1) were carried out using the Gaussian 09 program, the most widely used exchange-correlation function, with the suggested exchange potential from Becke; the gradient-corrected correlation provided by Lee, Yang and Parr (B3LYP); a Gaussian Double-Z 6-31G basis set (Gaussian Inc., Wallingford, CT, USA); and double polarized and d orbital expansions. Optimized geometries were verified by means of frequency calculations and characterized as minima (no imaginary frequency) in their potential energy surface. The reactivity descriptors were dipolar moment (DM), Mülliken's charge of the drimanic skeleton, highest occupied molecular orbital (HOMO), lowest unoccupied molecular orbital (LUMO), chemical potential (μ), hardness (η), softness (S), and electrophilicity global index (ω), which were calculated with the following equations[35]:

$$\mu = \frac{\left(E_{LUMO} + E_{HOMO}\right)}{2};\quad \eta = \frac{\left(E_{LUMO} - E_{HOMO}\right)}{2};\quad S = \frac{1}{2\eta};\omega = \frac{\mu^2}{2\eta} \quad (2)$$

In addition, the molecular weight (MW), molecular surface (MS), molecular volume (MV), H-bond acceptor (HBA), H-bond donor (HBD), molar refractivity (MR), lipophilicity index (Clog*P*), Balaban's index (BI), molecular topological index (MTI), rotatable bond number (RBN), polar surface (PS), shape attempt (SA), topological diameter (TD) and Wiener's index (WI) were calculated with ChemDraw software (CambridgeSoft, Cambridge, UK) after geometry optimization using molecular mechanics second parameterization (MM2). 2D-QSAR analyses were performed using the above-mentioned descriptors, and cross-validation of QSAR models was carried out with the Golbraikh methodology.[36] and using the following equation:

$$q^2 = 1 - \frac{\sum \left(y_{obs} - \hat{y}\right)^2}{\sum \left(y_{obs} - \bar{y}\right)^2} \quad (3)$$

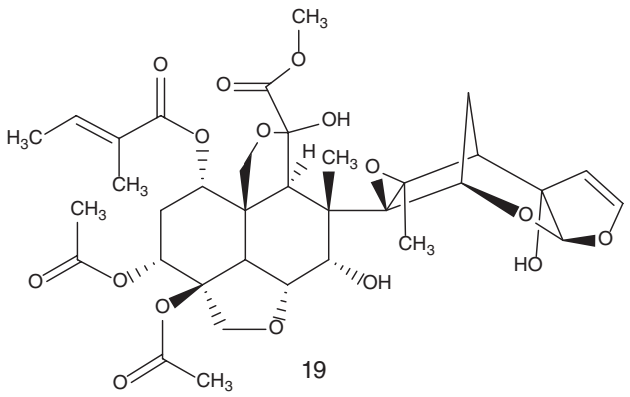

Figure 3. Positive control evaluated for activity against *S. frugiperda* and *E. paenulata*.

where y_{obs} is pEC_{50} is defined as the negative logarithm of EC_{50}. we can show some examples associated, similar to Ka and pKa If EC_{50} is The molar concentration of an agonist that produces 50% of the maximal possible effect of that agonist, pEC_{50} is the negative logarithm to base 10 of the EC_{50}.

2.8 Statistical analysis

Results from feeding choice assays were analyzed using the Wilcoxon signed-rank test. Differences were considered significant at $P \leq 0.05$. The AI% values obtained for different doses were used to calculate the EC_{50}. Probit analysis (Harvard Programming; Hg1, 2) was used to analyze the dose–antifeedant response.

Table 1. Effect of drimane and nordrimane compounds on the inhibition of feeding of *Spodoptera frugiperda* and *Epilachna paenulata* by leaf-disk choice assay

	AI%	
Compound	*Spodoptera frugiperda*	*Epilachna paenulata*
1	99*	93*
2	88*	33
3	69	82*
4	89*	100*
5	82*	64
6	48	67
7	79*	74*
8	26	-145
9	44	80*
10	86*	100*
11	94*	100*
12	94*	100*
13	74*	76*
14	69	-36
15	0	27
16	26	61
17	0	-4
18	0	0
19	100	100

The antifeedant index was calculated as AI% = [1(*T*/*C*)]100; values are means of 10 replicates at 50 μg/cm^2.
*Significant difference between consumption on treated and control leaves (Wilcoxon signed-rank test) at $P < 0.05$.

3 RESULTS AND DISCUSSION

Sesquiterpenes **1**–**3** (Fig. 1) obtained from *D. winteri*,[12] and the synthetic compounds **4-18** prepared from polygodial and drimenol[10,28] (Fig. 2) were assayed by choice test for activity against two phylogenetically separated insect species, the generalist *S. frugiperda* and the specialist *E. paenulata*. The obtained antifeedant index (AI%) of **1**–**18** and the positive control azadirachtin (**19**) (Fig. 3) are listed in Table 1.

Considering that significant feeding inhibition occurs when the AI% is >70 ($P < 0.05$),[37] the results obtained at 50 μg/cm^2 for each compound (Table 1) indicated that nine drimanes exhibit moderate to excellent activities against the fall armyworm *S. frugiperda*. Among the 18 tested compounds, **1**, the epoxy derivatives **11** and **12**, and the α,β-unsaturated ketone derivatives **4** and **2** were the most active, displaying similar activities.

In other lepidopteran larvae, polygodial (**1**) can block stimulant effects of glucose, sucrose, and inositol on cellular chemoreceptors in insect mouth parts.[8,38] The significant antifeedant activity found for the drimane derivatives tested in this work suggested that they could act on the same chemoreceptor of *S. frugiperda*.

Nine compounds also had antifeedant effects against *E. paenulata* at 50 μg/cm^2. The larvae totally rejected, for feeding, leaves treated with **4**, **10**, **11** and **12** (AI% = 100) ($P < 0.05$) while **1**, **3**, **9**, and **13** possessed significant, although slightly lower, activity against *E. paenulata* (AI% = 93, 82, 80, and 76, respectively) ($P < 0.05$).

The determination of EC_{50} for **1**–**18** against *S. frugiperda* demonstrated that **11** and **1** were the most active compounds, with EC_{50} = 23.28 and 23.84 nmol/cm^2, respectively. Nevertheless, an EC_{50} of 3002 nmol/cm^2 has previously been reported for the dialdehyde **1** against *Spodoptera littoralis* larvae.[8] The third most active compound was the α,β-unsaturated ketone **4**, known as isonordrimanone, with an EC_{50} of 25.63 nmol/cm^2 for *S. frugiperda* (Table 2). These values indicate that **11**, **1** and **4** are potent antifeedant compounds, although less active than azadirachtin (EC_{50} = 0.1 nmol/cm^2; Table 2). In addition, it was observed that 80% of larvae exposed to **4** (25.63 nmol/cm^2) died during the choice assay, indicating that this compound has a strong antifeedant activity against *S. frugiperda* larvae. This mortality rate was observed for treatments at 51.26 and 25.63 nmol/cm^2, but not for the other evaluated doses of this compound.

Comparing the activities of **1**–**18** against *E. paenulata*, food rejection effects for these compounds appeared at dosages higher than those observed for *S. frugiperda*. Compound **11** was the most active against *E. paenulata*, with feeding inhibition at EC_{50} = 50.5 nmol/cm^2, while compound **19** showed an EC_{50} of 0.59 nmol/cm^2. Compound **4** was the second most active compound against *E. paenulata* (EC_{50} = 59.0 nmol/cm^2), while **10**, **7**, **9**, **5**, **13**, **6, 1** and **3** had lower activity against this insect, showing EC_{50} values of 64.57, 83.99, 83.99, 104.1, 104.1, 133.1, and 142.0 nmol/cm^2, respectively (Table 2).

Comparing the EC_{50} values for the two insects, **11** and **4** were among the most active compounds against *S. frugiperda* and *E. paenulata*, both being more effective against *S. frugiperda* than against *E. paenulata*. In the latter species, the compound probably acted as a secondary anti-nutrient, where the reduction of food intake was caused by the initial consumption of the treated leaf, which resulted in a rejection or deterrent effect on subsequent consumption.[38] Compounds **11** and **12**, derived from enone **4**, showed good to high activity against both species. The presence of

Table 2. Effective concentrations (EC_{50}) of compounds **1**–**19** for the inhibition of feeding of *Epilachna paenulata* and *Spodoptera frugiperda* determined by leaf-disk choice assay

Compound	EC_{50} (nmol/cm^2)	
	Spodoptera frugiperda	*Epilachna paenulata*
1	23.84 (17.70-32.10)	133.1 (85.73-207.0)
2	124 (94.8-164.0)	>300
3	175 (109.0-294.0)	142 (64.8-205.0)
4	25.63 (19.0-35.0)	59.0 (48.0-74.3)
5	104.1 (56.3-184.0)	104.1 (93.0-260.0)
6	>300	105.7 (76.0-148.0)
7	182.7 (102.0-280.0)	83.99 (56.0-126.0)
8	>300	>300
9	>300	83.99 (75.0-129.0)
10	ND	64.57 (45.0-75.6)
11	23.28 (16.6-30.6)	50.5 (39.8-64.0)
12	54.24 (14.9-197.0)	ND
13	142.6 (78.3-259.0)	104.1 (73.0-148.0)
14	160.1 (83.2-276.0)	>300
15	>300	>300
16	>300	>300
17	>300	>300
18	>300	>300
19	0.1 (0.01-0.2)	0.59 (0.07-0.49)

Values are mean (95% confidence interval).
ND, not determined.

an epoxide group and a double bond between C-8 and C-9 in the B-ring of decalin increased the activity of nordrimanic compounds against *S. frugiperda* and *E. paenulata*.

Compounds **3**, **5**, **7** and **13** were also active against both insects but they were more effective against *E. paenulata*. Comparison of the EC_{50} values of diol **7** (182.7 nmol/cm^2 for *S. frugiperda* and 83.99 nmol/cm^2 for *E. paenulata*) indicates that *E. paenulata* was more sensitive to this compound than *S. frugiperda*. The same was found for diol **13** (drimendiol), which presented EC_{50} values of 104.1 nmol/cm^2 for *E. paenulata* and 142.6 nmol/cm^2 for *S. frugiperda*. Antifeedant activity found for **13** in this work was different from that reported in previous studies. Kubo and Ganjian reported that none of the sesquiterpene compounds isolated from different plants of the family Canellaceae had activity against *S. littoralis*.[39] Subsequently, the same authors reported that **13** (drimendiol) significantly reduced the relative consumption of leaf disks at all tested concentrations, showing EC_{50} values of ≥1260 nmol/cm^2.

In general, insects are able to metabolize a large variety of exogenous compounds, including secondary metabolites present in seedlings, through the activity of their detoxification enzymes.[41,42] Approximately 20 enzyme systems are involved in the detoxification of allelochemicals in insects.[43] Among the most important of these enzymes are monooxygenases, glutathione-S-transferases and esterases.[44–46] The induction of metabolic detoxification systems plays an important role in the adaptation of insects to their host plants. It is known that specialized insects (e.g. *E. paenulata*) are less susceptible to plant allelochemicals produced by their host plants, while generalists (e.g. *S. frugiperda*) are able to adapt to a great number of compounds from different plants.[46] Both situations are reflected in our findings; *E. paenulata* was more tolerant than *S. frugiperda* of the drimane compounds. Recent studies have shown that insects that eat plants containing furanocoumarins, monoterpenes present in essential oils, produce monooxygenases responsible for metabolizing these phytotoxins, which do not contain these compounds do not induce detoxifying enzymes.[46,47]

Table 3. Quantum descriptors with antifeedant activity correlation in 2D-QSAR analysis for *Spodoptera frugiperda*

Compound	μ	μ^2	pEC_{50} obs	pEC_{50} calc	Residual
2	−0.127	0.016	6.907	6.83	0.076
4	−0.156	0.024	7.591	7.675	−0.084
5	−0.13	0.017	6.983	6.89	0.092
7	−0.124	0.015	6.738	6.792	−0.054
11	−0.152	0.023	7.633	7.489	0.144
12	−0.146	0.021	7.266	7.29	−0.025
13	−0.127	0.016	6.846	6.835	0.011
14	−0.34	0.018	6.796	6.957	−0.162

obs, observed; calc, calculated.

The identification of drimanic compounds with activity against *S. frugiperda* and *E. paenulata* opens up a new field of research, especially for *S. frugiperda*, which causes serious damage in corn fields and can affect up to 80–90% of the total area of cultivation. The coleopteran pest *E. paenulata* causes substantial yield losses in pumpkin and melon crops, with serious economic consequences for producers. Thus, the development of new compounds using logical syntheses can generate new lines of research with applications in the productive sector, and specifically agrofood production.

3.1 Structure–activity relationship

QSAR analyses using multiple linear regressions have been attempted in order to identify structural features of the drimanic derivatives that may have an influence on observed antifeedant activity against *S. fugiperda* and *E. paenulata*. Because of mathematical fit, the compounds with EC50 indeterminate can not be used in the equation.

3.1.1 Spodoptera frugiperda QSAR

Initially, each descriptor was correlated with pEC_{50} and it was found that HDB, HDB^2, LUMO, LUMO^2, μ, μ^2, *S* and *S*^{2} were significant in the QSAR model ($P < 0.05$). Furthermore, the antifeedant activities of synthetic and hemisynthetic drimanic compounds against *S. fugiperda* were related to the chemical potential (μ) in its linear and quadratic forms with 99.99% certainty:

$$pEC_{50} = 13.22\ (\pm 9.72) + 114.5\ (\pm 14.0)\,\mu + 506.2\ (\pm 50.1)\,\mu^2 \quad (4)$$

$$n = 8, r = 0.959, r^2 = 0.919, \mathrm{SD} = 0.120, F = 28.50, q^2 = 0.919 \quad (5)$$

This descriptor, from the physical point of view, corresponds to the ability of a molecule to donate or retain its electrons, depending on its positive or negative nature, respectively. In the case of the evaluated compounds, all have negative values (Table 3), so they have a tendency to retain their electrons, consistent with the presence of carbonyl groups within the drimanic skeleton of **4**, **11** and **12**. Additionally, the result obtained for the QSAR model is in agreement with reports[12,30] of the mechanism of action for larvicidal activity of organic compounds with a skeletal structure, which

Table 4. Topological and quantum descriptors with antifeedant activity correlation in 2D-QSAR analysis for *Epilachnna paenulata*

Compound	TD	C9	pEC_{50} obs	pEC_{50} calc	Residual
1	7	−0.403	6.876	6.869	0.007
3	7	−0.357	6.848	6.891	−0.043
5	8	−0.05	6.983	6.969	0.014
6	8	0.032	6.976	7.007	−0.032
7	7	−0.118	7.076	7.004	0.072
9	6	−0.097	7.076	7.08	−0.005
10	6	0.258	7.19	7.248	−0.058
11	6	0.268	7.297	7.252	0.044

TD, topological diameter; C9, Mülliken charge on carbon skeleton C9.

have indicated that nucleophiles can react by nucleophilic additions to carbonyl and α,β-unsaturated carbonyl groups.

3.1.2 *Epilachna paenulata* QSAR

Initially, each descriptor was correlated with pEC_{50} and it was found that TD, TD^2, C1, C3 $C3^2$, C9, C10 and $C10^2$ were significant in the QSAR model ($p < 0.05$). Furthermore, the antifeedant activity of the compounds evaluated against *E. paenulata* was related to TD and the Mülliken charge of C9 of the drimanic skeleton with 99.99% certainty, as shown in Eqn 5. The parameters used for this correlation are listed in Table 4.

$$pEC_{50} = 7.53\ (\pm 0.17) - 0.07\ (\pm 0.02)\,TD + 0.47\ (\pm 0.08)\,C9 \quad (6)$$

$$n = 8, r = 0.957, r^2 = 0.916, SD = 0.05, F = 27.29, q^2 = 0.916 \quad (7)$$

In addition, the last descriptor is the most important feature of the set of compounds examined, because it has a slope 6.7 times greater than TD. The Mülliken charge is a descriptor indicating the electronegativity of the atoms.[48] in this case, compounds **9** and **10** have a C-9 carbonyl group, while **11** has an epoxide at C-8 and C-9 epoxy groups. In addition, TD is a descriptor related to the size and shape of the molecules.[49] from this perspective, compounds with compressed structures, such as **9**–**11**, show better activity than do bulky compounds **5** and **6**. The findings of the QSAR analysis of the antifeedant activity of drimanic compounds against *E. paenulata* are concordant with those of similar studies reported with drimanic skeletons compound. There must be deficient areas of electrons for this compound to be able to react with nucleophiles, as is the case for compounds **9**–**11**.[26]

4 CONCLUSION

The data obtained in this study indicate that nine drimanes exhibit good activities against the species *S. frugiperda* and *E. paenulata*. Comparing the EC_{50} values for these insects, **11** and **4** were among the most active compounds against *S. frugiperda* and *E. paenulata*, both compounds being more effective against *S. frugiperda* than against *E. paenulata*. Antifeedant index values obtained indicate that compounds **1**, **4** and **11** are potent antifeedant compounds, although less active than azadirachtin. The QSAR analysis of antifeedant activity against *S. frugiperda* and *E. paenulata* showed that the presence of carbonyl groups within the drimanic skeleton provides selectivity for the bioactivity against each of the tested species. The identification of drimanic compounds with activity against *S. frugiperda* and *E. paenulata* opens up new possibilities for the control of these species, which affect large areas of cultivation at enormous cost to farmers. Thus, research on new compounds using logical syntheses can generate new molecules with important applications in the productive sector, and specifically the agrofood industry.

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SUPPORTING INFORMATION

Supporting information may be found in the online version of this article.

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