Saudi Journal of Biological Sciences 28 (2021) 157–162

Contents lists available at ScienceDirect

Saudi Journal of Biological Sciences

journal homepage: www.sciencedirect.com

Original article

Larvicidal activity of novel anthraquinone analogues and their molecular docking studies

Keerthana Selvaraj [a], Daoud Ali [b], Saud Alarifi [b], Sathish Kumar Chidambaram [a], Surendrakumar Radhakrishnan [a], Idhayadhulla Akbar [a,*]

[a] Research Department of Chemistry, Nehru Memorial College (Affiliated to Bharathidasan University), Puthanampatti-621007, Tiruchirappalli District, Tamil Nadu, India
[b] Department of Zoology, College of Sciences, King Saud University (KSU), P.O. Box 2455, Riyadh 11451, Saudi Arabia

ARTICLE INFO

Article history:
Received 18 July 2020
Revised 9 September 2020
Accepted 14 September 2020
Available online 21 September 2020

Keywords:
Anthraquinone
Culex quinquefasciatus
Larvicidal activity
Molecular docking
Odorant-binding protein (OBP)

ABSTRACT

To investigate the larvicidal activities of novel anthraquinones (**1a-1k**) against *Culex quinquefasciatus* mosquito larvae. Novel anthraquinones (**1a-1k**) derivatives were synthesis via condensation method. The compounds were confirmed through FT-IR spectroscopy, ^{1}H & ^{13}C NMR spectrum, and mass spectral studies. The larvicidal activity of compound **1c** was highly active LD_{50} 20.92 μg/mL against *Culex quinquefasciatus* compared standard **permethrin** with LD_{50} 25.49 μg/mL. Molecular docking studies were carried out for compound **1c** against Odorant-binding protein of *Culex quinquefasciatus*. The compound **1c** (−9.8 Kcal/mol) was a potent larvicide with more binding energy than control **permethrin** (−9.7 Kcal/mol). Therefore, compound (**1c**) may be more significant inhibitors of mosquito larvicidal.

1. Introduction

Mosquitoes are disreputable as the main vectors for the spread a number of diseases, such as malaria, dengue fever, schistosomiasis Japanese encephalitis, filariasis, and yellow fever (Georges et al., 2008; Govindarajan, 2010). These types of disease reason an affect the economic and social impact in all over the word, especially *Culex quinquefasciatus* is vectors which are obtained frequently from urban and rural human habitat. Control of mosquito has been used big challenge and currently using most effective mosquito inhibitors such as organophosphates, fenthion, chlorpyrifos, menthoprene, and temephos, then usage of this big challenge in various environmental condition. In this reason, we selected anthraquinones, which is most suitable environmental safe secondary metabolites. Anthraquinones analogues are a large group of pigmented polyketides extensively formed by fungi. Basically, different substituted anthraquinone derivatives are most active in biological systems, such as the addition of methyl (—CH_3), carboxyl (—COOH), hydroxyl (—OH), and methoxyl (—OCH_3) groups of 9,10-anthracenedione outcomes in a broad-spectrum of medicinal properties (Tutin et al., 1911). Fig. 1 shows important larvicidal active compounds that based on structure, relation of target compounds. Larvicidal activities of benzoquinone (LC_{50}: 90 μg/mL) were evaluated on third-instar larvae *of A. aegypti* (De Sousa et al., 2010). 2-methoxy-1,4-naphthoquinone (LC_{50}: 0.085 μg/mL) against *Estagio larval* and isolated from Balsaminaceae (*Impatiens glandulifera*), (Kim and Ahn, 2017). Naphthalene-1,4-dione (LC_{50}: 1.64 μg/mL) against *Culex pipiens pallens*, (Jeon et al., 2015), anthracence-9,10-dione (LC_{50}: >25.0 μg/mL) (A. aegypti), tectoquinone LC_{50}: 3.3 μg/mL (*A. aegypti*), and emodin LC_{50}: 5.3 μg/mL (A. aegypti) (Cheng et al., 2008). However, the above chemicals are problems for usage of environmental factor, such as widespread development of resistance, leading to occurrences of mosquito species, disrupted natural biological control systems, and effects of infection from soil, water, air (Park et al., 2005). Therefore, the above drawback requires the new selective control of mosquito larvae (Yang et al., 2013). Odorant-binding proteins were transporting the odorants to olfactory receptors, which plays in major activities of host-seeking (Bazaes et al., 2013; De March and Golebiowski, 2014; Pechlaner and Oostenbrink, 2015). The above scientific information, we have chosen a hydroxyanthraquinone target against *Culex quinquefasciatus* and using odorant-binding protein (PDB ID: 3OGN) for molecular docking studies. In the present study, synthe-

* Corresponding author.
E-mail addresses: idhayadhulla@nmc.ac.in, a.idhayadhulla@gmail.com (I. Akbar).
Peer review under responsibility of King Saud University.

Production and hosting by Elsevier

https://doi.org/10.1016/j.sjbs.2020.09.028
1319-562X/

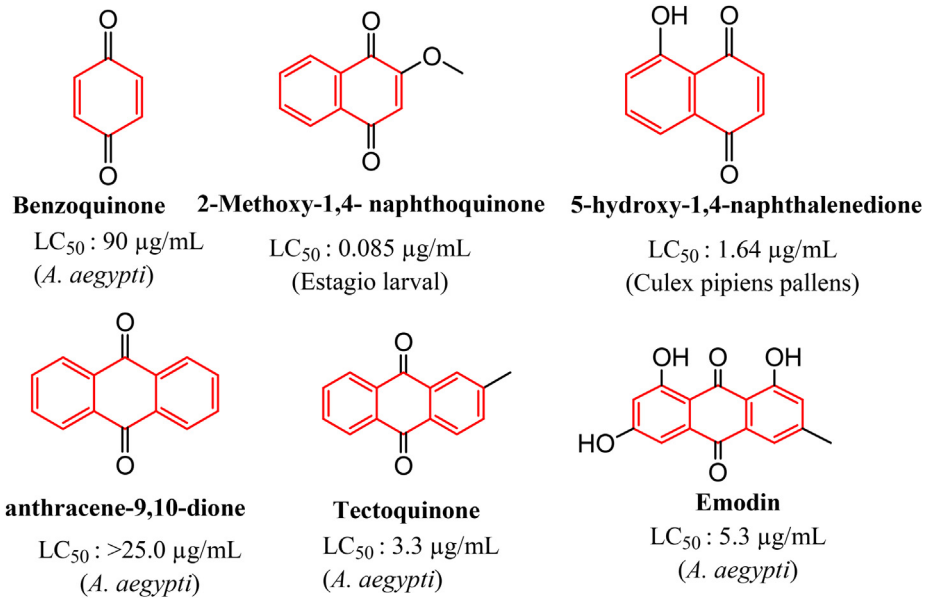


Fig. 1. Some important Larvicidal active compounds.

sis of new hydroxyanthraquinone Mannich base derivatives for evaluation of larvicidal activity.

2. Materials and methods

2.1. Chemistry

The chemicals were obtained from commercially and fully purified all chemicals before using the reactions. The FT-IR Shimadzu 8201PC (4000–400 cm^{-1}), and ^{1}H & ^{13}C NMR spectra of Bruker DRX-300 MHz were used by analysis all newly synthesized compounds. Thin layer chromatography (TLC) technique was used by check purity of the compounds with using silica gel plates.

*2.1.1. General method for preparation of 4,11-dihydroxy-2-phenyl-2,3-dihydro-1H-naphtho[2,3-f]isoin dole-5,10-dione (**1a**).*

A mixture of 1,4-dihydroxy anthraquinone (0.0005 mol, 0.1 mg), benzaldehyde (0.002 mol, 0.5 ml) and aniline (0.001 mol, 0.5 ml) are dissolved in ethanol. The mixture was reflexes by 24 h at 60 °C. The final target compound was monitored by TLC. The product was recrystallized in suitable alcohol. The same experimental method was used for preparation of other compounds **1b-k.**

*2.1.2. 4,11-dihydroxy-2-phenyl-2,3-dihydro-1H-naphtho[2,3-f] isoindole-5,10-dione (**1a**)*

IR (kBr, cm^{-1}): 1714, 1691, 1462, 822, 752; ^{1}H NMR (300 MHz): δ ppm 8.37–8.33 (d, *J* = 13.74 Hz, 2H), 7.82–7.80 (d, *J* = 13.74 Hz, 2H), 7.21–7.18 (dd, *J* = 7.72 Hz, *J* = 7.75 Hz, 2H), 6.95–6.93 (d, *J* = 7.75 Hz, 2H), 6.79–6.77 (d, *J* = 7.75 Hz, 1H), 5.30(s, 2H), 4.61 (s, 4H); ^{13}C NMR (75 MHz): δ 187.9, 152.5, 149.1, 133.0, 132.9, 129.0, 128.2, 126.1, 114.6, 114.1, 121.4, 54.9; EI-MS *m*/*z*(rel.int): 358.4 (M^{+}, 26%); Anal $C_{22}H_{15}NO_4$: C,73.94; H,4.23; N,3.92; Found: C, 73.92; H, 4.26; N, 3.91;

*2.1.3. 4,11-dihydroxy-2-phenyl-1,3-di((E)-prop-1-en-1-yl)-2,3-dihydro-1H-naphtho[2,3-f]isoin dole-5,10-dione (**1b**)*

IR (kBr, cm^{-1}): 1762, 1689, 1452, 812, 741; ^{1}H NMR (300 MHz): δ 8.38–8.36 (d, *J* = 13.74 Hz, 2H), 7.82–7.80 (d, *J* = 13.74 Hz, 2H), 7.21–7.18 (dd, *J* = 7.72 Hz, *J* = 7.75 Hz, 2H), 6.95–6.93 (d, *J* = 7.75 Hz, 2H), 6.77–6.75 (d, *J* = 7.75 Hz, 1H), 6.10(s, 2H), 5.48–5.46 (q, 2H), 5.36 (s, 2H), 4.49 (s, 2H), 2.12(d, 6H); ^{13}C NMR (75 MHz, δ (ppm)): 187.8, 152.4, 148.9, 133.9, 132.7, 129.1, 128.8, 125.6, 125.0, 124.3, 122.1, 115.8, 115.1, 72.6, 17.5; EI-MS *m*/*z*(rel.int): 438.0 [M^{+}, 26%); Anal $C_{28}H_{23}NO_4$: C,76.87; H,5.30; N,3.20; Found: C, 76.88; H, 5.32; N, 3.21;

*2.1.4. 4,11-dihydroxy-1-((E)-4-methylpenta-1,3-dien-1-yl)-3-((Z)-4-methylpenta-1,3-dien-1-yl)-2-phenyl-2,3-dihydro-1H-naphtho[2,3-f] isoindole-5,10-dione (**1c**)*

IR (kBr, cm^{-1}): 1744, 1678, 1451, 816, 738; ^{1}H NMR (300 MHz): δ 8.31–8.28 (d, *J* = 13.04 Hz, 2H), 7.80–7.78 (d, *J* = 13.04 Hz, 2H), 7.26–7.22 (dd, *J* = 7.70 Hz, 2H), 6.95–6.93 (d, *J* = 7.70 Hz, 2H), 6.76–6.75(d, *J* = 7.71 Hz, 1H), 6.20(s, 2H), 6.10(d, 2H), 5.90(d, 2H), 5.34(s, 2H), 4.69 (s, 2H), 2.14(s, 6H), 1.98(s, 6H); ^{13}C NMR (75 MHz, DMSO d_6, δ (ppm)): 187.5, 151.6, 148.5, 135.9, 133.2, 132.5, 129.5, 128.9, 128.2, 128.0, 126.3, 126.1, 122.3, 113.9, 114.1, 70.6, 27.6, 20.5 ; EI-MS *m*/*z*(rel.int): 518.25 (M^{+}, 35%); Anal $C_{34}H_{31}NO_4$: C,78.88; H,6.04; N, 2.71; Found: C, 78.86; H, 6.08; N, 2.70;

*2.1.5. 4,11-dihydroxy-2-phenyl-1,3-di((E)-styryl)-2,3-dihydro-1H-naphtho[2,3-f]isoindole-5,10 –dione (**1d**)*

IR (kBr, cm^{-1}): 1769, 1674, 1462, 812, 738; ^{1}H NMR(300 MHz): δ 8.32–8.30 (d, *J* = 13.70 Hz, 2H), 7.86–7.84 (d, *J* = 13.72 Hz, 2H), 7.42–7.44(m, Ph), 7.26–7.24 (dd, *J* = 7.70 Hz, 2H), 6.92–6.87 (d, *J* = 7.70 Hz, 2H), 6.69–6.67 (d, *J* = 7.70 Hz, 1H), 5.32 (s, 2H), 4.59 (s, 2H), 6.69(s, 2H),6.21(s, 2H); ^{13}C NMR (75 MHz, δ (ppm)): 187.9, 152.5, 149.1, 138.5, 132.9, 132.7, 129.0, 128.5, 128.2, 126.1, 121.4, 114.6, 114.1, 125.9, 71.2, 124.2, 128.9, 54.9; EI-MS *m*/*z*(rel.int): 562.21(M^{+}, 45%); 44(18); Anal $C_{38}H_{27}NO_4$: C,81.27; H,4.85; N,2.49; Found: C, 81.25; H, 4.81; N, 2.48;

*2.1.6. 1,3-di(furan-2-yl)-4,11-dihydroxy-2-phenyl-2,3-dihydro-1H-naphtho[2,3-f]isoindole-5,10 –dione (**1e**)*

IR (kBr, cm^{-1}): 1725, 1681, 1461, 823, 712; ^{1}H NMR (300 MHz): δ 8.39–8.36 (d, *J* = 13.74 Hz, 2H), 7.86–7.82 (d, *J* = 13.74 Hz, 2H), 7.62(d, *J* = 7.62 Hz, 2H), 7.22–7.20 (dd, *J* = 7.72 Hz, 2H), 6.94–6.91 (d, *J* = 7.75 Hz, 2H), 6.71–6.68 (d, *J* = 7.75 Hz, 1H), 6.25–6.21 (d, *J* = 7.62 Hz, 2H), 6.45–6.42(d, *J* = 7.62 Hz, 2H), 5.38(s, 2H), 5.36 (s, 2H); ^{13}C NMR(75 MHz, δ (ppm)): 187.4, 151.9, 150.6,

147.9, 141.0, 135.6, 131.9, 128.2, 127.9, 127.8, 122.6, 115.7, 115.2, 109.1, 67.1, 53.7; EI-MS *m/z*(rel.int): 490(M^+, 78%); Anal $C_{30}H_{19}NO_6$: C,73.61; H, 3.91; N, 2.86; Found: C, 73.60; H, 3.90; N, 2.84;

*2.1.7. 4,11-dihydroxy-1,2,3-triphenyl-2,3-dihydro-1H-naphtho[2,3-f] isoindole-5,10-dione (**1f**)*

IR (kBr, cm^{-1}): 1747, 1697, 1455, 809, 744; ^{1}H NMR(300 MHz): δ 8.40–8.36(d, *J* = 13.72 Hz, 2H), 7.85–7.83 (d, *J* = 13.72 Hz, 2H), 7.36–7.28(m 10*H*, Ph), 7.26–7.23 (dd, *J* = 7.72 Hz, 2H), 6.99–6.97 (d, *J* = 7.71 Hz, 2H), 6.78–6.75 (d, *J* = 7.71 Hz, 1H), 5.36 (s, 2H), 5.22 (s, 2H); ^{13}C NMR (75 MHz, δ (ppm)): 187.2, 153.6, 149.8, 146.2, 133.6, 132.2, 132.9, 130.0, 128.9, 125.6, 128.9, 126.2, 122.6, 114.5, 113.8, 71.6; EIMS *m/z*(rel.int): 510.23(M^+, 56%); Anal $C_{34}H_{23}NO_4$: C, 80.14; H,4.55; N,2.75; Found: C, 80.15; H, 4.56; N, 2.76;

*2.1.8. 1,3-bis(4-chlorophenyl)-4,11-dihydroxy-2-phenyl-2,3-dihydro-1H-naphtho[2,3-f]isoin do le-5,10-dione (**1g**)*

IR (kBr, cm^{-1}): 1741, 1641, 1462, 821, 765, 659; ^{1}H NMR (300 MHz): δ 8.34–8.30 (d, *J* = 13.69 Hz, 2H), 7.86–7.81 (d, *J* = 13.69 Hz, 2H), 7.33–7.30(d, *J* = 7.69 Hz, 4H), 7.24–7.21(dd, *J* = 7.72 Hz, 2H), 7.20–7.18(d, *J* = 7.69 Hz, 4H), 6.97–6.91(d, *J* = 7.72 Hz, 2H), 6.71–6.69(d, *J* = 7.72 Hz, 1H), 5.39(s, 2H), 5.12(s, 2H); ^{13}C NMR (75 MHz, δ (ppm)): 187.0, 153.6, 147.8, 140.4, 133.5, 132.9, 132.2, 128.6, 128.0, 127.9, 127.3, 125.2, 121.2, 115.8, 113.7, 71.0; EI-MS *m/z*(rel.int): 578.23 (M^+, 47%); Anal $C_{34}H_{21}Cl_2NO_4$: C, 70.60; H, 3.66; N,2.42; Found: C, 71.25; H, 3.67; N, 3.68;

*2.1.9. 4,11-dihydroxy-1,3-bis(4-hydroxyphenyl)-2-phenyl-2,3-dihydro-1H-naphtho[2,3-f]isoind ole-5,10-dione (**1h**)*

IR (kBr, cm^{-1}): 3232, 1749, 1680, 1461, 810, 741; ^{1}H NMR (300 MHz): δ 8.43–8.40 (d, *J* = 13.63 Hz, 2H), 7.81–7.78 (d, *J* = 13.63 Hz, 2H), 7.24–7.22 (dd, *J* = 7.74 Hz, *J* = 7.72 Hz, 2H), 7.10–7.08(d, *J* = 7.70 Hz, 4H), 6.96–6.94 (d, *J* = 7.74 Hz, 2H), 6.73–6.70 (d, *J* = 7.72 Hz, 1H), 6.68–6.63(d, *J* = 7.70 Hz, 4H), 5.42 (s, 2H), 5.25 (s, 2H); ^{13}C NMR (75 MHz, δ (ppm)): 187.9, 157.2, 152.5, 149.1, 135.9, 132.9, 132.2, 128.9, 128.6, 128.2, 126.0, 122.9, 118.6, 113.9, 114.1, 71.2; EIMS *m/z*(rel.int): 542.12 (M^+, 22%); Anal $C_{34}H_{23}NO_6$: C, 75.41; H,4.28; N,2.59; Found: C, 75.40; H, 4.21; N, 2.55;

*2.1.10. 4,11-dihydroxy-1,3-bis(3-nitrophenyl)-2-phenyl-2,3-dihydro-1H-naphtho[2,3-f]isoindole-5,10-dione (**1i**)*

IR (kBr, cm^{-1}): 1752, 1684, 1545, 1465, 804, 745; ^{1}H NMR (300 MHz): δ 8.40–8.38 (d, *J* = 13.78 Hz, 2H), 8.12(d, *J* = 7.70 Hz, 4H), 7.90–7.87 (d, *J* = 13.78 Hz, 2H), 7.58–7.56(d, *J* = 7.70 Hz, 4H), 7.26–7.24 (dd, *J* = 7.72 Hz, *J* = 7.75 Hz, 2H), 6.95–6.93 (d, *J* = 7.75 Hz, 2H), 6.83–6.80 (d, *J* = 7.75 Hz, 1H), 5.38 (s, 2H), 5.26 (s, 2H); ^{13}C NMR (75 MHz, δ (ppm)): 187.1, 152.5, 149.1, 146.8, 142.9, 135.8, 133.3, 133.0, 131.1, 129.0, 127.9, 126.5, 126.1, 122.9, 121.4, 114.1, 113.9, 68.5; EIMS *m/z*(rel.int): 600.21 (M^+, 36%); Anal $C_{34}H_{21}N_3O_8$: C, 68.11; H,3.53; N,7.01; Found: C, 68.17; H, 3.57; N, 7.18;

*2.1.11. 1,3-bis(4-(dimethylamino)phenyl)-4,11-dihydroxy-2-phenyl-2,3-dihydro-1H-naphth o [2, 3-f]isoindole-5,10-dione (**1j**)*

IR (kBr, cm^{-1}): 1753, 1681, 1469, 795, 745; ^{1}H NMR(300 MHz): δ 8.37–8.34 (d, *J* = 13.74 Hz, 2H), 7.82–7.80 (d, *J* = 13.74 Hz, 2H), 7.23–7.19 (dd, *J* = 7.72 Hz, 2H), 7.08–7.05(d, *J* = 7.75 Hz, 4H), 6.95–6.93 (d, *J* = 7.75 Hz, 2H), 6.79–6.76 (d, *J* = 7.75 Hz, 1H), 6.68–6.62(d, *J* = 7.75 Hz, 4H), 5.29(s, 2H), 5.22 (s, 2H), 3.04(s, 12H); ^{13}C NMR (75 MHz, δ (ppm)): 187.9, 152.5, 149.1, 148.9, 133.2, 133.1, 132.9, 128.0, 128.6, 128.2, 125.9, 121.4, 113.8, 114.1, 114.1, 70.2, 42.3; EIMS *m/z*(rel.int): 596.32 (M^+, 20%); Anal $C_{38}H_{33}N_3O_4$: C, 76.62; H,5.58; N,7.05; Found: C,76.63; H, 5.59; N, 7.09;

*2.1.12. 4,11-dihydroxy-1,3-bis(4-methoxyphenyl)-2-phenyl-2,3-dihydro-1H-naphtho[2,3-f]iso in dole-5,10-dione (**1k**)*

IR (kBr, cm^{-1}): 2821, 1742, 1682, 1469, 812, 740; ^{1}H NMR (300 MHz): δ 8.56–8.41 (d, *J* = 13.70 Hz, 2H), 7.89–7.86 (d, *J* = 13.65 Hz, 2H), 7.22–7.19(dd, *J* = 6.65 Hz, *J* = 7.71 Hz, 2H), 7.16 (4H, CH), 6.90–6.88 (d, *J* = 7.71 Hz, 2H), 6.75–6.73 (d, *J* = 7.71 Hz, 1H), 6.69(4H, CH), 5.27(s, 2H), 5.15 (s, 2H), 3.85(s, 6H); ^{13}C NMR (75 MHz, δ (ppm)): 187.1, 159.8, 153.0, 148.9, 136.8, 133.2, 132.8, 129.3, 129.1, 128.1, 127.3, 122.2, 116.1, 114.2, 115.6, 70.5, 55.9; EIMS *m/z*(rel.int): 570.10 (M^+, 30%); Anal $C_{36}H_{27}NO_6$: C, 75.91; H, 4.78; N, 2.46; Found: C, 75.05; H, 4.77; N, 2.45;

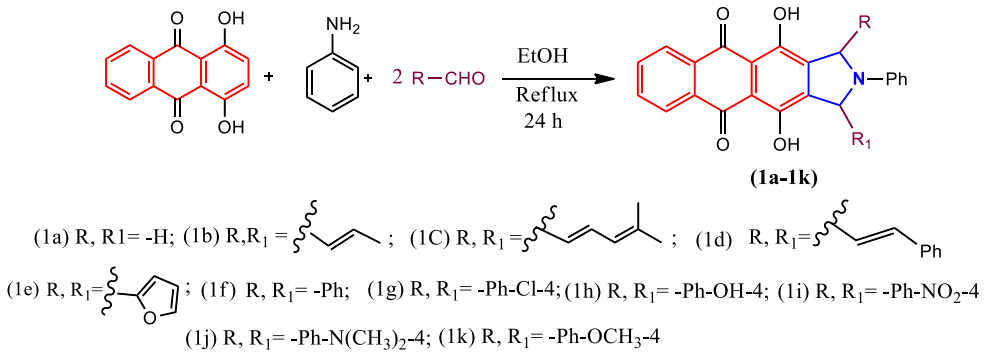
2.2. Biological activity

2.2.1. Larvicidal activity

Larvicidal activities of 10, 25, 50 and 100 μg/mL of compounds (**1a-1k**) were screened as we previously described in publication Idhayadhulla et al., (SathishKumar et al., 2020). Mortality caused by the compounds was evaluated as ratios (%) of the numbers of dead vs. live larvae. The 50% lethal doses (LD_{50}) values of the compounds were calculated using probit analysis and statistically analyzed using SPSS version 16.0 software.

2.2.2. Statistical analysis

Larvicidal activities results were calculated through 3 independent evaluations and Microsoft Excel was used to analysis the standard deviations (SD) of each compound.



Scheme 1. Route of synthesis larvicidal active target molecules.

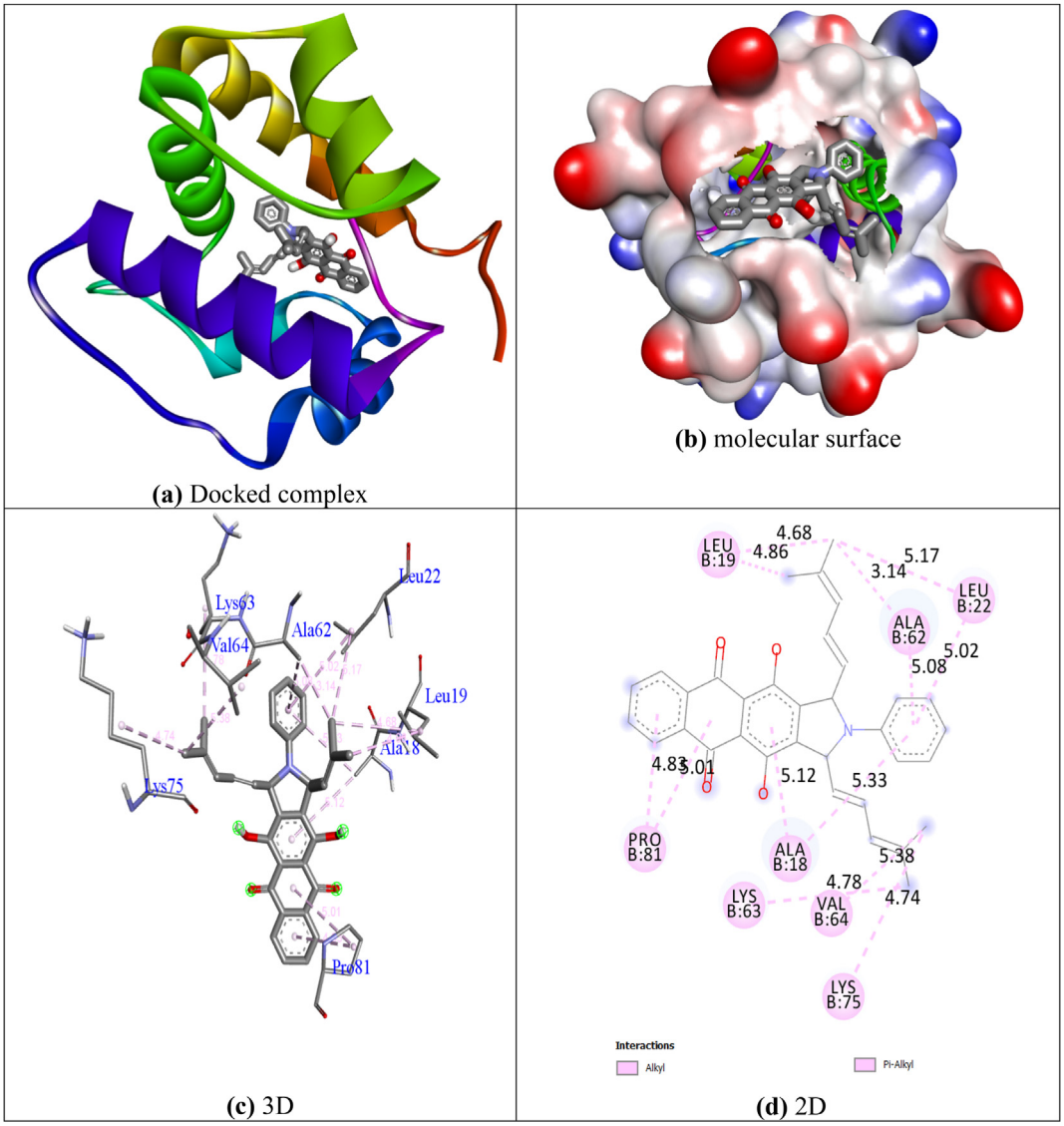


Fig. 2. Molecular docked modes of **1c** with binding site of 3OGN.

2.2.3. Molecular docking

This study was carried out via Autodock vina 1.1.2. (Trott and Olson, 2010), which using to interpret the binding mode of compounds (**1c**) and permethrin with mosquito odorant protein. Crystal structure of mosquito odorant binding protein (PDB ID: 3OGN) was collected from protein data bank web link. The 3D association of the compound (**1c**) and permethrin was accomplished through Chem Draw Ultra 12.0 software. The 3OGN protein was fixed at

Table 1
Larvicidal activity of anthraquinone analogues (**1a-1k**) and **permethrin.**

Compounds	Concentration (μg/mL)/Mortality (%)				LD_{50} (μg/mL)
	10	25	50	100	
1a	–	0 ± 0.00	16 ± 0.27	36 ± 0.97	>100
1b	7 ± 0.89	23 ± 1.25	36 ± 0.96	55 ± 0.00	85.42
1c	41 ± 0.00	65 ± 1.31	100 ± 1.34	–	20.92
1d	5 ± 1.76	22 ± 1.12	43 ± 1.87	60 ± 1.61	74.17
1e	4 ± 1.14	15 ± 1.48	38 ± 1.46	54 ± 0.88	86.27
1f	–	–	0 ± 0.00	20 ± 0.47	>100
1g	22 ± 1.87	46 ± 1.21	62 ± 0.56	88 ± 0.30	37.95
1h	0 ± 0.00	10 ± 1.87	20 ± 0.67	40 ± 1.89	>100
1i	–	–	21 ± 0.00	38 ± 0.09	>100
1j	22 ± 0.95	36 ± 1.65	57 ± 1.41	100 ± 1.14	37.59
1k	–	–	0 ± 0.00	40 ± 1.23	>100
Permethrin	23 ± 1.76	55 ± 1.23	82 ± 1.94	100 ± 0.00	25.49

[a]Values are the means of three replicates ± SD.

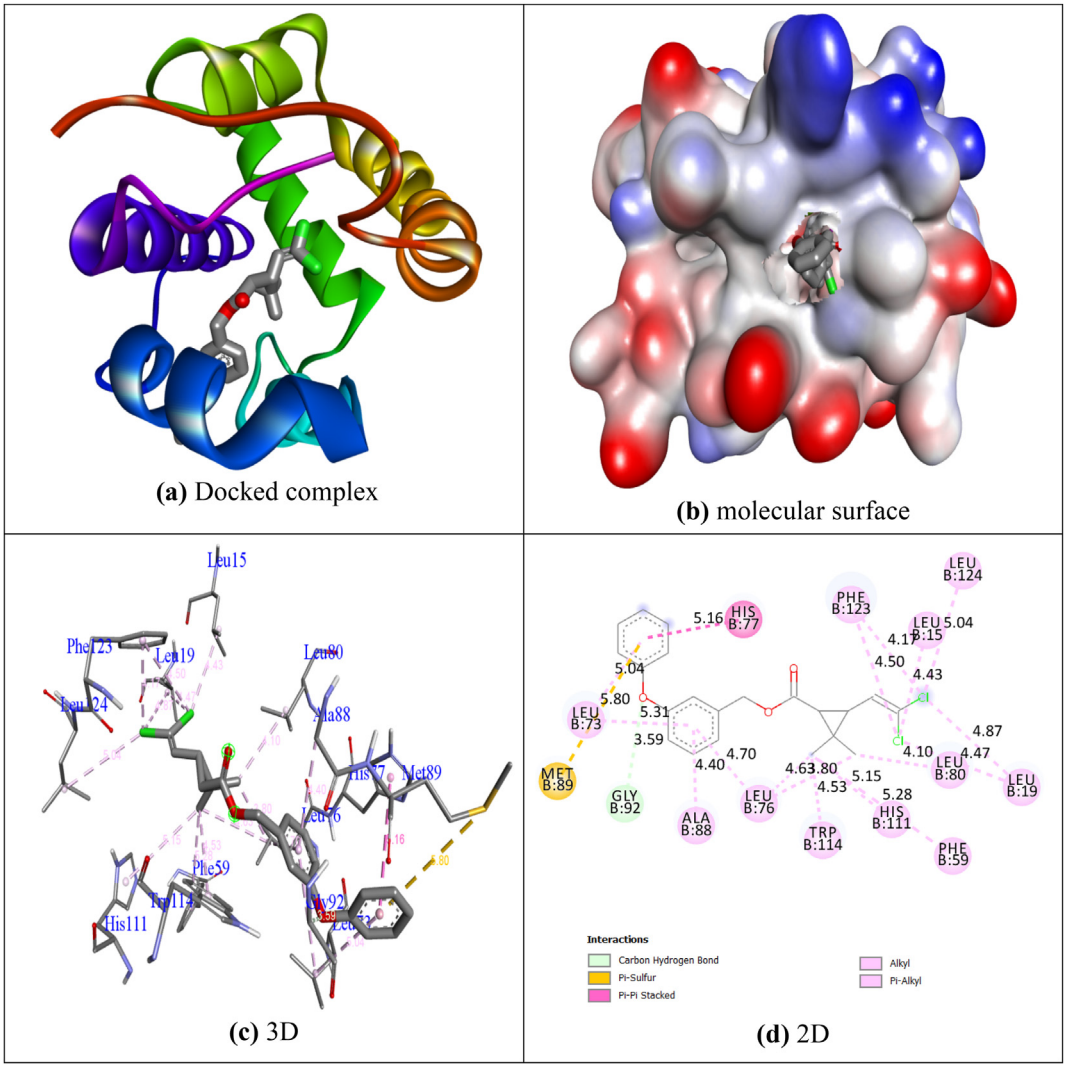


Fig. 3. Molecular docked modes of **permethrin** with binding site of 3OGN protein.

Table 2
Molecular docking interaction of compound **1c** and control **permethrin.**

Comp. No.	Mosquito odorant-binding protein 3OGN		
	Binding affinity (kcal/mol)	No. of H-bonds	H-bonding residues
1c	−9.8	0	–
Permethrin	−9.7	0	–

center_x: 18.681, center_y: 49.66, and center_z: 11.409 with size_x: 22, size_y: 20, and size_z: 22 with spacing of 1.0 Å. Discovery studio 2019 program was used for analysis visually of results compared with the least binding affinity value of docking compounds.

3. Result and discussion

3.1. Chemistry

The compound **1a-1k** was synthesized from anthraquinone reached with aldehyde and primary amine in the ethanol medium by condensation method. The mixture was reflexed by 24 hr at 60 °C. The final products were obtained yield between 80 and 89 %. The method of preparation was outlined in scheme 1. Structures **1a-1k** were definite via FT-IR, ^{1}H and ^{13}C NMR, mass spectral studies, the importance of the IR spectral peak at C—N—C, C═O, OH corresponding to the average peak at 1641–1697, 174–1769, and 1451–1469 cm^{-1} respectively. ^{1}H NMR spectral obtained important proton peaks range between δ 4.49–5.26, and 5.32–5.42 ppm conforming to the protons HC-N, and OH respectively. The ^{13}C NMR carbon peaks were obtained the range of value between at δ 54.9–72.6, 187.0–187.9, and 151.6–153.6 conforming to the C—N—C, C═O, and C—OH carbons respectively. All compounds were conformed the mass values according to the molecular ion peak obtain in mass spectral values.

3.2. Larvicidal activity

Larvicidal activity was screened for all synthesized anthraquinones (**1a-1k**) derivatives against second instar *C. quinquefasciatus* larvae. Compound **1c** exerted more larvicidal activity (LD_{50} 20.92 μg/mL) than other compounds and standard permethrin LD_{50} 25.49 μg/mL. Compounds **1a, 1f, 1h, 1i,** and **1k** were less active against *C. quinquefasciatus* with LD_{50} values of above >100 μg/mL LD_{50} value. All values are represented in Table 1.

3.3. Docked results with AutoDock Vina

The Autodock Vina program was used to study for compound (**1c**) and **permethrin** docking with 3OGN protein. The compound **1c** shows significant binding affinity (−9.8 kcal/mol) than **permethrin** (−9.7 kcal/mol). Stability of protein and ligand was confirmed through the bond distance calculation, which is less than 3.5 Å form H-donor and the H-acceptor of bond distance (Taha et al., 2015). The compound **1c** was not conceded for any hydrogen bond in 3OGN. The residues Ala18, Leu19, Leu22, Ala62, Lys63, Val64, Lys75 and Pro81 were complex with hydrophobic connections. The molecular interaction of compound **1c** and 3OGN were shown in Fig. 2. The control **permethrin** was also not conceded any hydrogen bond in 3OGN. The hydrophobic interactions were involved due to the formation of Leu15, Leu19, Phe59, Leu73, Leu76, His77, Leu80, Ala88, Met89, Gly92, His111, Trp114, Phe123, and Leu124. Fig. 3 shows that the molecular interaction of **permethrin** with 3OGN. Therefore, the compound **1c** having remarkable inhibition capability than **permethrin** in mosquito odorant-binding protein. The results are presented in Table 2.

4. Conclusion

Novel anthraquiones (**1a-1k**) moiety were synthesized and screened for larvicidal activity. The Compound **1c** was highly active (LD_{50} 20.92 μg/mL) against second instar *C. quinquefasciatus* mosquito larvae than **permethrin** with LD_{50}: 25.49 μg/mL. Molecular docking findings supported the potent larvicidal activity of compound **1c** (-9.8 Kcal/mol) compared with Permethrin with binding energy values of (-9.7 Kcal/mol). Therefore, these compounds might serve as a new class of products with larvicidal activity and prospective foundation for emerging ecologically important bioactive compound.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

This work was funded by Researchers Supporting Project number (RSP-2020/27), King Saud University, Riyadh, Saudi Arabia.

References

Bazaes, A., Olivares, J., Schmachtenberg, O., 2013. Properties, projections and tuning of teleost olfactory receptor neurons. J. Chem. Ecol. 39, 451–464.
De March, C.A., Golebiowski, J., 2014. A computational microscope focused on the sense of smell. Biochimie. 107, 3–10.
De Sousa, D.P., Vieira, Y.W., Uliana, M.P., Melo, M.A., Brocksom, T.J., Sócrates, C.H., Cavalcanti, S.C.H., 2010. Larvicidal activity of para-Benzoquinones. Parasitol. Res. 107, 741–745.
Georges, K., Jayaprakasam, B., Dalavoy, S.S., Nair, M.G., 2008. Pestmanaging activities of plant extracts and anthraquinones from Cassia nigricans from Burkina Faso. Bioresour. Technol. 99, 2037–2045.
Govindarajan, M., 2010. Chemical composition and larvicidal activity of leaf essential oil from Clausena anisata (Willd.) Hook. f. ex Benth (Rutaceae) against three mosquito species. Asian Pac. J. Trop. Med., 874–877
Jeon, J.-H., Kim, M.-G., Lee, H.-S., 2015. Larvicidal activity of naturally occurring naphthalenedione and its structurally related analogs against three mosquito species. J. Am. Mosq. Control. Assoc. 31 (1), 71–76.
Kim, S.I., Ahn, Y.J., 2017. Larvicidal activity of lignans and alkaloid identified in *Zanthoxylum piperitum* bark toward insecticide-susceptible and wild *Culex pipiens pallens* and *Aedes aegypti*. Parasit Vectors 10 (1), 221–230.
Park, I.K., Shin, S.C., Kim, C.S., Lee, H.J., Choi, W.S., Ahn, Y.J., 2005. Larvicidal activity of lignans identified in Phryma leptostachya Var. asiatica roots against tree mosquito species. J. Agric. Food Chem. 53, 969–972.
Pechlaner, M., Oostenbrink, C., 2015. Multiple binding poses in the hydrophobic cavity of bee odorant binding protein AmelOBP14. J. Chem. Inform. Model. 55, 2633–2643.
SathishKumar, C., Selvaraj Keerthana, S., Anis, A., Ibrahim, A.A., SurendraKumar, R., Idhayadhulla, A., 2020. Cu^{II}-tyrosinase enzyme catalyst-mediated synthesis of 2- thioxopyrimidine derivatives with potential mosquito larvicidal activity: spectroscopic and computational investigation as well as molecular docking interaction with OBPs of *Culex quinquefasciatus*. Chem. Sel., 4567–4574
Cheng, S.-S., Huang, C.-G., Chen, W.-J., Kuo, Y.-H., Chang, S.-T., 2008. Larvicidal activity of tectoquinone isolated from red heartwood-type Cryptomeria japonica against two mosquito species. Bioresource Technol. 99, 3617–3622.
Taha, M., Ismail, N.H., Khan, A., Shah, S.A.A., Anwar, A., Halim, S.A., QFatmi, M., Imran, S., Rahim, F., Kha, K.M. 2015. Synthesis of novel derivatives of oxindole, their urease inhibition and molecular docking studies. Bioorg. Med. Chem. Lett. 25, 3285–3289.
Trott, O., Olson, A.J., 2010. AutoDock Vina: improving the speed and accuracy of docking with a new scoring function, efficient optimization and multithreading. J. Comput. Chem. 31, 455–461.
Tutin, F., Clewer, H.W.B. XCIX. 1911. The constituents of rhubarb. J. Chem. Soc. Trans. 36, 946–967.
Yang, J.Y., Cho, K.S., Chung, N.H., Kim, C.H., Suh, J.W., Lee, H.S., 2013. Constituents of volatile compounds derived from Melaleuca alternifolia leaf oil and acaricidal toxicities against house dust mites. J. Korean Soc. Appl. Biol. Chem. 56, 91–94.