



Original article

Mosquito and tick repellency of two *Anthemis* essential oils from Saudi Arabia[☆]

Hasan Soliman Yusufoglu^{a,*}, Nurhayat Tabanca^b, Ulrich R. Bernier^c, Andrew Y. Li^d, Mohammed Ayman Salkini^a, Saleh Ibrahim Alqasoumi^e, Betül Demirci^f

^a Department of Pharmacognosy, College of Pharmacy, Prince Sattam Bin Abdulaziz University, Saudi Arabia

^b USDA-ARS, Subtropical Horticulture Research Station, Miami, FL 33158, USA

^c USDA-ARS, Center for Medical, Agricultural, and Veterinary Entomology, Gainesville, FL 32608, USA

^d USDA-ARS, Invasive Insect Biocontrol and Behavior Laboratory, Beltsville, MD 20705, USA

^e Pharmacognosy Department, College of Pharmacy, King Saud University, Riyadh, Saudi Arabia

^f Department of Pharmacognosy, Faculty of Pharmacy, Anadolu University, Eskisehir 26470, Turkey

ARTICLE INFO

Article history:

Received 19 January 2018

Accepted 25 March 2018

Available online xxxxx

Keywords:

Anthemis melampodina

Anthemis scrobicularis

Natural repellents

Aedes aegypti

Amblyomma americanum

ABSTRACT

The essential oils (EOs) of *Anthemis melampodina* (Am) and *Anthemis scrobicularis* (As) (Asteraceae) were extracted from the aerial parts of the plants by hydrodistillation, and their chemical compositions were analyzed using GC-FID and GC-MS. Fifty-six components representing 85.5% of the oil composition of *Anthemis melampodina* were identified, and the major components were α -pinene (17.1%) and β -eudesmol (13.8%). Forty-one components representing 86% of the oil composition of *Anthemis scrobicularis* were identified, and the major component was β -eudesmol (12.8%). Laboratory bioassays were conducted to determine repellency of Am and As EOs against the yellow fever mosquito *Aedes aegypti* L. and the lone star tick *Amblyomma americanum* L. The minimum effective doses (MEDs) of the Am and As EOs against mosquitoes were 0.187 ± 0.000 and 0.312 ± 0.063 mg/cm² respectively, which were significantly higher than that of DEET (0.023 ± 0.000 mg/cm²) in human-based repellent bioassays. The As EO was more repellent than Am EO against nymphal ticks but was less effective than DEET in vertical paper bioassays.

© 2018 Production and hosting by Elsevier B.V. on behalf of King Saud University. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Mosquitoes are a major vector for the transmission of several life-threatening diseases (Rajkumar and Jebanesan, 2010). The Kingdom of Saudi Arabia (KSA) is one of the Eastern Mediterranean countries that is part of the World Health Organization. KSA bears 11% of the world burden of vector-borne diseases, such as malaria and several arboviral diseases (WHO, 2004). Malaria has been

endemic in KSA since 1900 (Mattingly and Knight, 1956). Since 1995, the most reported arboviral diseases in KSA have been dengue fever (DF) and Rift Valley fever (RVF); however, other arboviral diseases have also been reported (Khater et al., 2013). There are 46 mosquito species recorded in the Arabian Peninsula, including 15 in the Riyadh Region (Alahmed et al., 2007). Species from the major three genera *Anopheles*, *Culex*, and *Aedes* are present in KSA (Mattingly and Knight, 1956). Ticks are vectors of bacteria, viruses, and protozoa that cause diseases affecting human and animal health (Meng et al., 2016). Given its vast geographical area and being a center of the Islamic world, with millions of pilgrimages visiting the holy sites during the annual sessions of pilgrimage and Umrah, the kingdom of Saudi Arabia faces a high risk of vector-borne disease epidemics (Ahmed, 2015). After the appearance of Rift Valley Fever (RVF) in Saudi Arabia for the first time in September 2000, the Ministry of Health in Saudi Arabia developed and implemented plans to prevent this disease in the Hajj period (Madani, 2005).

Effective vector control and management are vital in the prevention of disease transmission. *Anthemis* L. (Asteraceae) is one

* Corresponding author.

E-mail address: h.yusufoglu@psau.edu.sa (H.S. Yusufoglu).

[☆] This article reports the results of research only. Mention of a proprietary product does not constitute an endorsement or a recommendation by the USDA for its use. USDA is an equal opportunity provider and employer.

Peer review under responsibility of King Saud University.



Production and hosting by Elsevier

<https://doi.org/10.1016/j.jsps.2018.03.012>

1319-0164/© 2018 Production and hosting by Elsevier B.V. on behalf of King Saud University.

This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Please cite this article in press as: Yusufoglu, H.S., et al. Mosquito and tick repellency of two *Anthemis* essential oils from Saudi Arabia[☆]. Saudi Pharmaceutical Journal (2018), <https://doi.org/10.1016/j.jsps.2018.03.012>

of the largest genera of Anthemideae tribe (Mohammed et al., 2017). It is represented by 19 species in Saudi Arabia (Konstantinopoulou et al., 2003) and nearly 210 species distributed in different areas around the world (Mohammed et al., 2017). *Anthemis scrobicularis* Yavin and *A. melampodina* Dei are annual herbs growing in sandy areas of the Arabian Peninsula, Jordan, Palestine and Egyptian desert (Mohammed et al., 2017; Ghafoor, 2010; Chaudhary 2000; Takholm, 1974). Studies of the *Anthemis* species have led to the reports on the chemical composition and diverse biological activities, such as their antioxidant, antifungal (Papaioannou et al., 2007), antiplasmodial, antitumor, schistosomicidal, cytotoxic, anthelmintic, phytotoxic, analgesic (Amjad et al., 2012) effects and for the treatment of afflictions and cystitis (Burim et al., 1999). Tinctures, extracts, tisanes, salves, decoction, infusion and other traditional formulations of *Anthemis* species are widely used for the treatment of dysmenorrhea, inflammation, hemorrhoid, hepatotoxicity, abdominal pain and different types of skin inflammation in the European folk medicine (Mann and Staba, 1986; Ugurlu and Secmen, 2008; ManganenelliUncini and Tomei, 1999; Baltaci et al., 2011; Petkeviciute et al., 2010). Several types of active compounds like flavonoids, sesquiterpene lactones, fatty acids, sterols, essential oils and polyacetylenes have been reported in previous reports on *Anthemis* species (Mohammed et al., 2017; Hajdu et al., 2010; Masterova et al., 2005; Pavlovic et al., 2007; Vuckovic et al., 2005). Anti-inflammatory and hepatoprotective activities have been reported previously for *A. scrobicularis* methanolic extract (Yusufoglu et al., 2014), and there are four new sesquiterpene lactones isolated from the same species (Zaghloul et al., 2014). In this present study, *A. melampodina* (Am) and *A. scrobicularis* (As) essential oils (EOs) were tested, for the first time, for repellency against the mosquito *Aedes aegypti* L. (*Ae. aegypti*) and lone star tick *Amblyomma americanum* L. (*Am. americanum*).

2. Materials and methods

2.1. Plant material

The aerial parts of Am and As were collected during the flowering period from the Al-shadida, Province of Alkharj, Saudi Arabia, in February 2014, and March 2015, respectively. The plant species were authenticated by Dr. Osman Almekki using morphological features of the plant samples. The voucher specimen was deposited in the Herbarium, College of Pharmacy (PSAU-CPH-11-2014, PSAU-CPH-5-2015), Prince Sattam bin Abdulaziz University, Al-Kharj, KSA.

2.2. Preparation and analysis of the oil

Air-dried aerial parts of Am (250 g) and As (500 g) were ground and subjected, separately, to hydrodistillation for 4 h using a Clevenger-type apparatus with 5 L rounded-bottomed flask. After decanting and drying over anhydrous sodium sulfate, the corresponding oils were purified, resulting in a yield of 0.095% and 0.25% w/w, respectively.

2.3. GC-MS analysis

The GC-MS analysis was carried out with an Agilent 5975 GC-MSD system. An Innowax fused silica capillary column (60 m × 0.25 mm, 0.25 μm film thickness) was used with helium as the carrier gas (0.8 ml/min). The GC oven temperature was held at 60 °C for 10 min after injection and then ramped to 220 °C at a rate of 4 °C/min, and held at 220 °C for 10 min, followed by a second ramp to 240 °C at a rate of 1 °C/min. The split ratio was

set at 40:1. The injector temperature was set at 250 °C. Mass spectra were recorded using 70 eV electrons in Election Ionization (EI) mode. The mass analyzer was scanned from m/z 35–450 at a scan rate of (3.46) s⁻¹.

2.4. GC analysis

The GC analysis was carried out on an Agilent 6890N GC system. The FID detector temperature was set to 300 °C. To obtain the same elution order with GC-MS, simultaneous auto-injection was performed on the GC-MS system using a similar column operated with identical GC parameters. Relative percentages of the separated compounds were calculated from peaks in the GC-FID chromatograms. Identification of the essential oil components was carried out by comparison of their relative retention times with those of authentic samples or by comparison of their relative retention index (RRI) to a series of *n*-alkanes. Computer matching against commercial (Wiley GC/MS Library, MassFinder 3 Library) (Zaghloul et al., 1989; McLafferty and Stauffer, 1989) and in-house “Başer Library of Essential Oil Constituents” built up by genuine compounds and components of known oils, as well as MS literature data (Koenig et al., 2004; Joulain and Koenig, 1998), were also used for the identification.

2.5. Bioassays

2.5.1. Insects

Mosquitoes used in all bioassays were female *Ae. aegypti* (Orlando strain, 1952) from the colony maintained at the Center for Medical, Agricultural, and Veterinary Entomology (CMAVE-USDA-ARS) in Gainesville, FL. Pupae were obtained from the onsite colony and maintained in laboratory cages until ready for use in experiments (ESO, 2000). Laboratory-reared nymphs of the lone star tick, *Am. americanum*, maintained at the USDA-ARS, Invasive Insect Biocontrol and Behavior Laboratory in Beltsville, MD, USA. Nymphs were 1–3 months old at the time of the experiments. Technical DEET (97% active ingredient; Sigma-Aldrich, USA) was used as positive control for mosquito and tick bioassays (Tabanca et al., 2016a).

2.5.2. Mosquito repellent bioassays (Cloth patch assay)

Repellency was determined as the minimum effective dosage (MED) of Am and As EOs against *Ae. aegypti* mosquitoes. The methods are as described in the literatures (Posey and Schreck, 1981; Schreck et al., 1977; Katritzky et al., 2010). Tests were conducted on each control or treated patch for 1 min. A control patch (acetone solvent only) was tested before the start of experiments and after every 10 tests. If fewer than five landings occurred on the control patch in 30 s, then tests were discontinued for 60 min. At the conclusion of testing, the control patch was tested again. If five landings were not received within 30 s, the data for the replicate was discarded. When testing a patch treated with a candidate repellent, if ≈1% or five mosquito bites were received during this one min test, this compound was considered to have failed, that is, was not repellent at that concentration. Observed Minimum Effective Dosage (MED) values for each candidate compound were averaged across participants and reported as a mean MED ± SE. Additional explanation of this type of bioassay can be found in (Tabanca et al., 2016b). Written informed consent was obtained for all human subjects used in this study in accordance with protocol #636-2005, as approved by the University of Florida Institutional Review Board (IRB-01).

2.5.3. Tick repellency bioassay

Tick repellency against *Am. americanum* was determined by using a bioassay technique (vertical paper assay) described by

Carroll et al. (Carroll et al., 2011). Briefly, a 4 × 7 cm rectangle of Whatman No. 4 filter paper was prepared by treating the central 4 × 5 cm zone with a volume of 165 µl of test solution. After drying, the paper strip was suspended from a bulldog clip hung from a holder. Ten *Am. americanum* nymphs were released from a glass vial on the lower untreated end of the paper strip. Locations of the nymphs were recorded at 1, 3, 5, 10 and 15 min. Ticks were considered repelled if they stayed on the lower untreated zone or fell off the filter paper without having crossed into the upper untreated zone (Meng et al., 2016). Each treatment/concentration included three replicates. The mean percent repellency was generated for DEET and each essential oil concentrations for comparison.

3. Results and discussion

The hydrodistillation of the herbal parts of As and Am yielded 0.095% w/w (calculated to dry weight) and 0.25% w/w (calculated to fresh weight) with dark brownish colored oils, respectively. In the As EO, the GC-MS revealed at least 56 components representing 85.5% of the As EO (Table 1). The major component was oxygenated sesquiterpene β -eudesmol (12.8%). The oil was characterized by a high percentage of oxygenated sesquiterpenes (55.4%), followed by oxygenated monoterpenes (20.1%). Monoterpene hydrocarbons and sesquiterpene hydrocarbons represented only 1.7% and 4.0% of the oil, respectively (Table 1).

The chemical composition of Am EO from Saudi Arabia and Egypt has been previously investigated (Al-Humaidi, 2015; Grace, 2002), however, we found significant quantitative and qualitative differences in Am EO from region to regions even in the same country of origin. The GC-MS analyses of Am EO revealed at least 41 components representing 86% of the volatile Am EO (Table 1). The oil was characterized by a high percentage of monoterpene hydrocarbons (31.6%), with α -pinene (17.1%) as the main component, followed by oxygenated monoterpenes (23.7%) and oxygenated sesquiterpenes (22.2%). The same plant which collected from Tabuk (Saudi Arabia), the northwest part of the kingdom and has been reported by Al-Humaidi (2015) has shown 42 components with the highest percentage of α -pinene (15.33%) and followed by other components belonged to oxygenated sesquiterpenes (31.22%). Another sample collected from the east part of Cairo (Egypt) (Grace, 2002) had santolinatriene (27.33%), monoterpene hydrocarbons (49.94%) and oxygenated sesquiterpene (11.43%).

The preliminary evaluation of feeding deterrent effects using this oil was done with three human volunteers using the “cloth patch assay”. The Am EO showed better repellency with minimum effective dose (MED) of 0.187 ± 0.000 mg/cm² than As EO (MED = 0.312 ± 0.063 mg/cm²), which had significantly lower potency compared to reference standard *N,N*-diethyl-3-methylbenzamide, DEET (0.023 ± 0.000 mg/cm²) (Table 2). However, based on our laboratory repellent bioassays on essential oils, plant extracts or essential oils with a MED value of ≤ 0.375 mg/cm² are promising to the investigation of active components (Tabanca et al., 2016b). The Am EO is rich in monoterpene hydrocarbons (31.6%) of which the major constituent is α -pinene (17.1%), but it is hard to attribute the repellent activity to monoterpene hydrocarbons. An earlier study showed that pinenes did not seem to contribute to the biting-deterrent activity in the *in vitro* assays against *Ae. aegypti* (Tabanca et al., 2015). Sesquiterpene compounds in essential oils isolated from *Amyris balsamifera* and *Fokienia hodginsii* were assayed for spatial and contact repellency against *Ae. aegypti* to determine the quantitative structure-activity relationship. Two sesquiterpenes, 10-epi- γ -eudesmol, and β -eudesmol, showed the highest levels of repellent activity (Paluch et al., 2009). According

Table 1

Composition of the Essential Oils of *Anthemis melampodina* (Am) and *A. scrobicularis* (As).

RRI	Compound	Am (%)	As (%)	IM
1032	α -Pinene	17.1	1.0	RRI, MS
1076	Camphene	2.5	0.2	RRI, MS
1118	β -Pinene	0.6	0.2	RRI, MS
1132	Sabinene	0.1	–	RRI, MS
1174	Myrcene	5.6	–	RRI, MS
1203	Limonene	4.5	0.3	RRI, MS
1213	1,8-Cineole	4.7	1.5	RRI, MS
1244	2-Pentyl furan	–	0.1	MS
1280	<i>p</i> -Cymene	2.4	1.0	RRI, MS
1285	Isoamyl isovalerate	tr	tr	MS
1299	2-Methylbutyl isovalerate	0.3	–	MS
1482	(<i>Z</i>)-3-Hexenyl-2-methyl butyrate	2.9	0.3	MS
1494	(<i>Z</i>)-3-Hexenyl 3-methylbutyrate	0.5	–	MS
1499	α -Campholene aldehyde	–	0.5	MS
1532	Camphor	–	1.4	RRI, MS
1541	Benzaldehyde	1.8	2.7	RRI, MS
1562	Isopinocampone	0.3	0.5	MS
1586	Pinocarvone	–	0.4	RRI, MS
1591	Bornyl acetate	0.1	–	RRI, MS
1611	Terpinen-4-ol	0.5	–	RRI, MS
1612	β -Caryophyllene	0.2	–	RRI, MS
1648	Myrtenal	0.1	0.5	MS
1668	(<i>Z</i>)- β -Farnesene	1.2	–	MS
1670	<i>trans</i> -Pinocarveol	0.3	1.2	RRI, MS
1683	<i>trans</i> -Verbenol	0.8	1.2	RRI, MS
1704	γ -Muuroleone	–	0.2	MS
1719	Borneol	4.8	4.0	RRI, MS
1725	Verbenone	0.7	0.7	MS
1740	α -Muuroleone	–	1.0	MS
1742	β -Selinene	2.1	–	MS
1773	δ -Cadinene	–	1.8	MS
1776	γ -Cadinene	tr	0.8	MS
1786	Kessane	–	0.3	MS
1797	<i>p</i> -Methyl acetophenone	–	0.3	MS
1804	Myrtenol	0.4	0.7	MS
1838	(<i>E</i>)- β -Damascenone	–	0.3	MS
1845	<i>trans</i> -Carveol	0.3	0.8	RRI, MS
1849	Calamenene	–	0.2	MS
1864	<i>p</i> -Cymen-8-ol	–	1.1	RRI, MS
1871	Neryl isovalerate	–	0.3	MS
1958	(<i>E</i>)- β -Ionone	–	0.2	MS
1969	<i>cis</i> -Jasmone	1.1	0.4	MS
2008	Caryophyllene oxide	1.7	3.1	RRI, MS
2050	(<i>E</i>)-Nerolidol	–	0.4	MS
2080	Cubenol	–	0.5	MS
2144	Spathulenol	0.6	2.9	MS
2148	(<i>Z</i>)-3-Hexen-1-yl benzoate	1.6	0.7	MS
2187	T-Cadinol	3.2	6.7	MS
2200	α -Guaialol	–	0.3	MS
2204	Eremoligenol	0.6	1.9	MS
2209	T-Muurolol	–	2.3	MS
2214	<i>ar</i> -Turmerol	–	0.7	MS
2219	δ -Cadinol	–	0.4	MS
2250	α -Eudesmol	0.9	3.2	MS
2255	α -Cadinol	–	7.2	MS
2257	β -Eudesmol	13.8	12.8	MS
2264	Intermedeol	–	8.7	MS
2278	α -Kessy alcohol	1.4	–	MS
2298	Decanoic acid	–	1.3	RRI, MS
2312	9-Geranyl- <i>p</i> -cymene	1.1	0.4	MS
2365	(<i>Z</i>)-Methyl jasmonate	1.7	0.8	MS
2388	(<i>E</i>)-Nuciferol	0.5	1.9	MS
2503	Dodecanoic acid	–	0.5	RRI, MS
2586	(<i>E</i>)-Nuciferol	–	0.5	MS
2604	α -Costol	0.9	0.8	MS
2931	Hexadecanoic acid	2.1	1.4	RRI, MS
	Total	86.0	85.5	

RRI: Relative retention indices calculated against *n*-alkanes; % calculated from FID data; tr Trace (<0.1%); IM: Identification method based on the relative retention indices (RRI) of authentic compounds on the HP Innowax column; MS, identified on the basis of computer matching of the mass spectra with those of the Wiley and MassFinder libraries and comparison with literature data.

Table 2

Minimum effective doses (MED) for repellency values for *Anthemis melampodina* (Am) and *A. scrobicularis* (As) EOs against *Ae. aegypti* mosquitoes.

Samples	MED ± SE (mg/cm ²)
Am EO	0.187 ± 0.000
As EO	0.312 ± 0.063
DEET*	0.023 ± 0.000

* DEET, *N,N*-diethyl-3-methylbenzamide, commercial standard repellent.

Table 3

Comparison of lone start tick (*Am. americanum*) repellency between *Anthemis melampodina* (Am) and *A. scrobicularis* (As) EOs and DEET.

		Mean repellency		
		%	Stdev	Sterr
Am EO	2.50%	80.00	10.00	5.77
Am EO	1.25%	66.67	20.82	12.02
Am EO	0.625%	26.67	15.28	8.82
As EO	2.50%	96.67	5.77	3.33
As EO	1.25%	90.00	17.32	10.00
As EO	0.625%	80.00	10.00	5.77
As EO	0.3125%	83.33	11.55	6.67
As EO	0.1562%	20.00	10.00	5.77
DEET*	0.625%	95.00	7.07	5.00

* DEET, *N,N*-diethyl-3-methylbenzamide, commercial standard repellent.

to our study, β -eudesmol was the second major constituent (13.8%) in Am EO and the most abundant compound (12.8%) of As EO. It is difficult to attribute the repellency of Am EO to β -eudesmol because As EO has that component at a similar percentage and the EO exhibited weak repellency.

In tick bioassays, *A. melampodina* and *A. scrobicularis* EOs showed 80.0% and 96.7% repellency against *Am. americanum* at a concentration of 2.50% As EO (80.0%) showed higher repellency than Am EO (26.7%) and the two plants showed significantly lower repellency when compared with the positive control DEET, which was 95% repellent at a concentration of 0.625% (Table 3). The moderate repellency of As EO is likely due to its high sesquiterpene content (59.4%)

According to previous studies on essential oils derived from plants, the repellency was attributed to the high percentage of sesquiterpenes, especially oxygenated sesquiterpenes, like farnesol. Farnesol is the major component of oxygenated sesquiterpenes of the essential oil isolated from *Pluchea dioscoridis*. This compound showed marked mosquito larvicidal activity against *Culex pipiens* (Grace, 2002). Germacrene D, pregeijerene and geijerene namely norsequiterpenes, the major constituents isolated from the oil of *Chloroxylon swietenia* leaves, were repellent against *Ae. aegypti* and *Anopheles gambiae* (Ravi Kiran and Pushpalatha). The sesquiterpene alcohol, (–)-10-epi- γ -eudesmol, components of essential oils isolated from some plant species were found to be repellent against *Am. americanum* (Tabanca et al., 2013). Previous studies indicated that terpenoids (sesquiterpenes) that contain two functional groups are biologically active against mosquitoes. One of these functional groups on the negatively charged end contains either ester/ether bonds or an ethanol hydroxyl group and the other group on the positively charged end contains an alkyl group (Kalita et al., 2013).

In conclusion, this is the first report of a comprehensive study where GC–FID and GC–MS were employed to characterize the volatile constituents of *A. melampodina* and *A. scrobicularis* essential oils. Differences in the chemical compositions of these two species play an important role in the repellent activities. The essential

oil of *A. melampodina* as a mosquito repellent was more effective than that of *A. scrobicularis*, but both were less efficacious than DEET. On the contrary, the essential oil of *A. scrobicularis* performed moderately as a repellent against ticks, while the essential oil of *A. melampodina* was less repellent. In tests with mosquitoes, both EOs were less repellent than DEET. As we mentioned above the mosquito repellency cannot be attributed to the high percentage of α -pinene (17.1%) in the Am EO, but the high amount of monoterpane hydrocarbons (31.6%), oxygenated monoterpenes (23.7%) and oxygenated sesquiterpenes (22.2%) may be acting synergistically to produce the repellency. The tick repellency of As EO is likely due to the high relative amount of β -eudesmol or possibly to the effect additional compounds in the mixture acting together. This EO contains a high amount of oxygenated sesquiterpenes (55.4%) and oxygenated monoterpenes (20.1%). These Am and As EOs will be further evaluated in bioassay-guided studies to determine the active compound(s) that are responsible for their repellency against mosquitoes and ticks.

Declaration

No financial/commercial conflicts of interest are reported by the authors.

Acknowledgments

This study was in part funded by a Deployed War-Fighter Protection Research Program Grant by the U.S. Department of Defense – United States through the Armed Forces Pest Management Board. We thank Natasha M. Agramonte, Greg Allen, Ingeborg Cuba and Erin O'Reilly (USDA, ARS, CMAVE, Gainesville, FL) for mosquito and James McCrary (USDA, ARS, IIBBL, Beltsville, MD) for tick bioassays.

References

- Ahmed, A.E., 2015. Tropical diseases in Saudi Arabia. *SOJ Immunol.* 3 (2), 1–4.
- Alahmed, A.M., Al Kuriji, M.A., Kheir, S.M., 2007. Distribution and habitat of mosquito larvae (Diptera: Culicidae) in Riyadh Region, Saudi Arabia. *J. King Saud Univ. (Agric. Sci.)* 9 (2), 39–55.
- Al-Humaidi, J., 2015. Chemical composition of the essential oils for *Anthemis melampodina* from North Saudi Arabia. *Oriental J. Chem.* 31 (4), 2265–2270.
- Amjad, L., Madani, M., Rezvani, Z., 2012. Potential activity of the *Anthemis gayana* leaves on fungi. *World Acad. Sci. Eng. Technol.* 61, 901–902.
- Baltaci, S., Kolatan, H.E., Yilmaz, O., Kivcak, B., 2011. Anti-inflammatory activity of *Anthemis aciphylla* var. *aciphylla* Boiss. *Turk. J. Biol.* 35, 757–762.
- Burim, R.V., Canalle, R., Lopes, J.L.C., Takahashi, C.S., 1999. Genotoxic action of the sesquiterpene lactone glaucolide B on mammalian cells in vitro and in vivo. *Genet. Mol. Biol.* 22, 401–406.
- Carroll, J.F., Tabanca, N., Kramer, M., Elejalde, N.M., Wedge, D.E., Bernier, U.R., Coy, M., Becnel, J.J., Demirci, B., Baser, K.H.C., Zhang, J., Zhang, S., 2011. Activity of *Cupressus funebris*, *Juniperus communis*, and *J. chinensis* (Cupressaceae) essential oils as repellents against ticks (Acari: Ixodidae) and as repellents and toxicants against mosquitoes (Diptera: Culicidae). *J. Vector Ecol.* 36, 258–268.
- Chaudhary, S., 2000. Flora of the Kingdom of Saudi Arabia, vol. 2 (Part 3), Ministry of Agri. & Water, Riyadh.
- ESO 2000. The Complete Database of Essential Oils, Boelens Aroma Chemical Information Service, the Netherlands, 1999.
- Ghafoor, A., 2010. The genus *Anthemis* L. (Compositae-anthemideae) in Arabia peninsula: a taxonomic study. *Pak. J. Bot.* 42, 79–98.
- Grace, M.H., 2002. Chemical composition and biological activity of the volatiles of *Anthemis melampodina* and *Pluchea dioscoridis*. *Phytother. Res.* 16, 183–185.
- Hajdu, Z., Zupko, I., Rethy, B., Forgo, P., Hohmann, J., 2010. Bioactivity-guided isolation of cytotoxic sesquiterpenes and flavonoids from *Anthemis ruthenica*. *Planta Med.* 76, 94–96.
- Joulain, D., Koenig, W.A., 1998. The Atlas of Spectra Data of Sesquiterpene Hydrocarbons. EB-Verlag, Hamburg.
- Kalita, B., Bora, S., Sharma, A.K., 2013. Plant essential oils as mosquito repellent—a review. *Int. J. Res. Dev. Pharm. Life Sci.* 3 (1), 741–747.
- Katritzky, A.R., Wang, Z., Slavov, S., Dobchev, D., Hall, C.D., Tskolika, M., Bernier, U.R., Elejalde, N.M., Clark, G.G., Linthicum, K.J., 2010. Novel carboxamides as potential mosquito repellents. *J. Med. Entomol.* 47, 924–938.
- Khater, E.I., Sowilem, M.M., Sallam, M.F., Alahmed, A.M., 2013. Ecology and habitat characterization of mosquitoes in Saudi Arabia. *Trop. Biomed.* 30 (3), 409–427.

- Koenig, W.A., Joulain, D., Hochmuth, D.H., 2004. Terpenoids and related constituents of essential oils. MassFinder 3, Hamburg, Germany.
- Konstantinopoulou, M., Karioti, A., Skaltsas, S., Skaltsa, H., 2003. Sesquiterpene lactones from *Anthemis altissima* and their anti-helicobacter pylori activity. *J. Nat. Prod.* 66, 699–702.
- Madani, T.A., 2005. Alkhurma virus infection, a new viral hemorrhagic fever in Saudi Arabia. *J. Infect.* 51 (2), 91–97.
- ManganelliUncini, R.E., Tomei, P.E., 1999. Ethnopharmacobotanical studies of the Tuscan Archipelago. *J. Ethnopharmacol.* 65, 181–202.
- Mann, C., Staba, E.J., 1986. The chemistry, pharmacology, and commercial formulations of chamomile. In: Craker, L.E., Simon, J.E. (Eds.), *Herbs, Spices, and Medicinal Plants: Recent Advances in Botany, Horticulture and Pharmacology*, vol. 1. Oryx Press Phoenix, AZ, pp. 235–280.
- Masterova, I., Grancai, D., Grancaiova, Z., Pour, M., Ubik, K., 2005. A new flavonoid: tinctosid from *Anthemis tinctoria* L. *Pharmazie*. 60, 956–967.
- Mattingly, P.F., Knight, K.L., 1956. The mosquito of Arabia. I. *Bull. Brit. Mus. (Nat. Hist.) Entomol* 4 (3), 89–141.
- McLafferty, F.W., Stauffer, D.B., 1989. *The Wiley/NBS Registry of Mass Spectral Data*. J Wiley and Sons, New York.
- Meng, H., Li, A.Y., Costa Junior, L.M., Castro-Arellano, I., Liu, J., 2016. Evaluation of DEET and eight essential oils for repellency against nymphs of the lone star tick, *Amblyomma americanum* (Acari: Ixodidae). *Exp. Appl. Acarol.* 68 (2), 241–249.
- Mohammed, A.A., Sharma, A., Saied, M.A.M., Osman, O.H., Al-Balawi, M.H., Salih, D. A., Singla, L.D., 2017. Lack of Evidence for Infection of Camels with tick-borne Diseases in Riyadh Region. Saudi Arabia. *Sudan J. Vet. Res.* 32, 39–40.
- Paluch, G., Grodnitzky, J., Bartholomay, L., Coats, J., 2009. Quantitative structure-activity relationship of botanical sesquiterpenes: spatial and contact repellency to the yellow fever mosquito *Aedes aegypti*. *J. Agric. Food Chem.* 57, 7618–7625.
- Papaioannou, P., Lalaria, D., Karioti, A., Souleles, C., Heilmann, J., Hadjipavlou-Litina, D., Skaltsas, H., 2007. Phenolic compounds with antioxidant activity from *Anthemis tinctoria* L. (Asteraceae). *Z. Naturforsch.* 62, 326–330.
- Pavlovic, M., Kovacevic, N., Tzakou, O., Couladis, M., 2007. Components of cyclohexane extract of *Anthemis triumfetti*. *Chem. Nat. Compd.* 43, 512–514.
- Petkeviciute, Z., Savickiene, N., Savickas, A., Bernatoniene, J., Simaitiene, Z., Kalveniene, Z., Pranskunas, A., Lazauskas, R., Mekas, T.A., 2010. Urban ethnobotany study in Samogitia region, Lithuania. *J. Med. Plants Res.* 4, 64–71.
- Posey, K.H., Schreck, C.E., 1981. An airflow apparatus for selecting female mosquitoes for use in repellent and attraction studies. *Mosquito News* 41, 566–568.
- Rajkumar, S., Jebanesan, A., 2010. Chemical composition and larvicidal activity of leaf essential oil from *Clausena dentata* (Willd) M. Roam. (Rutaceae) against the chikungunya vector, *Aedes aegypti* Linn. (Diptera: Culicidae). *J. Asia Pac. Entomol.* 13, 107–109.
- Ravi Kiran, S., Pushpalatha, K.C., 2013. Repellency of essential oil and sesquiterpenes from leaves of *Chloroxylon swietenia* DC against mosquito bites. *VRI Phytomedicine* 1 (3), 103–108.
- Schreck, C.E., Posey, K., Smith, D., 1977. Repellent activity of compounds submitted by Walter Reed Army Institute of Research. Part I. Protection time and minimum effective dosage against *Aedes aegypti* mosquitoes. *Tech. Bull.*, 1549.
- Takholm, V., 1974. *Student Flora of Egypt*. Cairo University, Cairo.
- Tabanca, N., Wang, M., Avonto, C., Chittiboyina, A.G., Parcher, J.F., Carroll, J.F., Kramer, M., Khan, I.A., 2013. Bioactivity-guided investigation of *Geranium* essential oils as natural tick repellents. *J. Agric. Food Chem.* 61, 4101–4107.
- Tabanca, N., Demirci, B., Ali, A., Khan, S.I., Jacob, M.R., Aytac, Z., Khan, I.A., 2015. Chemical composition, biting deterrent, antimalarial and antimicrobial activity of essential oil from *Hypericum scabrum* L. *Curr. Bioact. Compd.* 11, 62–72.
- Tabanca, N., Nalbantsoy, A., Bernier, U.R., Agramonte, N.M., Ali, A., Li, A.Y., Yalcin, T., Guzel, S., Demirci, B., 2016a. Essential oil composition of *Pimpinella cypria* and its insecticidal, cytotoxic, and antimicrobial activity. *Nat. Prod. Commun.* 11, 1531–11354.
- Tabanca, N., Bernier, U.R., Agramonte, N.M., Tsikolia, M., Bloomquist, J.R., 2016b. Discovery of repellents from natural products. *Curr. Org. Chem.* 20, 2690–2702.
- Vuckovic, I., Vujusic, L., Milosavljevic, S., 2005. Phytochemical investigation of *Anthemis cotula* L. *Serb. Chem. Soc.* 71, 127–133.
- Ugurlu, E., Secmen, O., 2008. Medicinal plants popularly used in the villages of Yunt Mountain (Manisa-Turkey). *Fitoterapia* 79, 126–131.
- WHO (World Health Organization), 2004. *Integrated vector management strategic framework for the Eastern. The Mediterranean Region 2004–2010*. The WHO Regional Office for the Eastern Mediterranean, Cairo.
- Yusufoglu, H.S., Alam, A., Salkini, M.A., Zaghoul, A.M., 2014. Anti-inflammatory and hepatoprotective activities of methanolic extract of *Anthemis scrobicularis* herbs. *Pharmacognosy* 6 (3), 55–61.
- Zaghoul, A.M., Abo El-fattah, H., Hali, A.F., 1989. Chemical investigation of the aerial parts of *Anthemis helahpdina* Del. Mans. *J. Pharm. Sci.* 5 (1), 23–33.
- Zaghoul, A.M., Yusufoglu, H.A., Salkini, M.A., Alam, A., 2014. New cytotoxic sesquiterpene lactones from *Anthemis scrobicularis*. *J. Asian Nat. Prod. Res.* 16 (9), 922–929.