ACS OMEGA

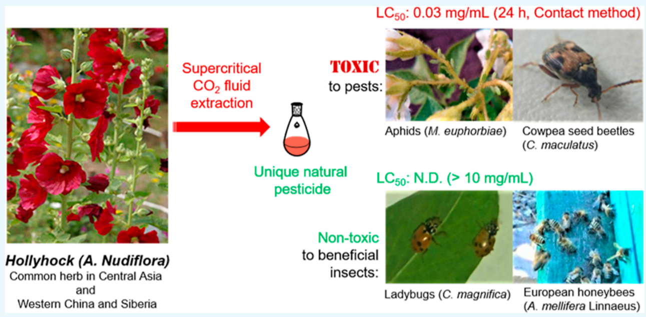
http://pubs.acs.org/journal/acsodf Article

Compositional Analysis and Potent Insecticidal Activity of Supercritical CO_2 Fluid Extracts of *Alcea nudiflora* L. Leaves

Nazira K. Khidyrova, Saida M. Turaeva, Malohat J. Rakhmatova, Khayrulla M. Bobakulov, Shamansur S. Sagdullaev, Rano P. Zakirova, Khamid U. Khodjaniyazov,* and Kohei Torikai*

Cite This: *ACS Omega* 2022, 7, 19892–19897 Read Online

ACCESS | Metrics & More | Article Recommendations



ABSTRACT: To mitigate potentially severe food shortages due to the exponential growth of the global population, it is of paramount importance to improve the yield and quality of globally harvested food crops. As pest control contributes to both these aspects, the development of safe and effective pesticides is one of the main strategies pursued in this direction in the context of agricultural chemistry. During our investigation of natural pesticides, a supercritical CO_2 fluid extract of *Alcea nudiflora* L. was found to exert extremely potent insecticidal activity against aphids (*Macrosiphum euphorbiae*) and cowpea seed beetles (*Callosobruchus maculatus*) with LC_{50} values of 0.03 mg/mL (24 h exposure, contact method). The facts that their insecticidal activity is in the most potent class among the essential oils known to date, and that the extract did not show any toxicity toward beneficial insects such as ladybugs (*Coccinella magnifica*) and European honeybees (*Apis mellifera* Linnaeus), indicate that this extract could be a good, natural, and safe new pesticide candidate. A compositional analysis of this extract was carried out using GC/MS.

■ INTRODUCTION

Due to the improved quality of life, and especially medical care, the global population has reached 7.8 billion and continues to grow.[1] One study estimates that it will grow to 10 and 11 billion in 2050 and 2100, respectively.[2] To manage the associated potentially severe shortages of food, improving crop yield and quality are of paramount global importance. There are many strategies to increase the yield and quality of crops, among which pest control to decrease crop loss is one of the most essential. Thus, to date, hundreds of artificial pesticides have been developed and made commercially available.[3] Chemical pesticides are powerful, scalable, and inexpensive, but they have historically caused health problems in humans, although recently developed ones are often much less harmful.[4]

On the other hand, various plant-derived materials, such as essential oils, plant extracts, and fermentation products (e.g., vinegars) have also been used as natural pesticides[5] and medicines;[6] these are believed to be superior to their chemical counterparts on account of their greater safety for both humans and the environment. Among these, supercritical CO_2 extracts (SCE) of plants have attracted great attention, as CO_2 can achieve the extraction of unique substances that conventional solvents (e.g., organic solvents and water) cannot afford.[7] Furthermore, unlike organic solvents, CO_2 is easily removed by evaporation, and even if it remains in the products until their distribution, it is completely harmless.

During our investigations to identify useful plant extracts, we found that a frequently observed hollyhock, *Alcea nudiflora*, contains a variety of natural substances such as astragalin and polyprenols, which can be extracted using organic solvents.[8] Although there is no evidence that plants belonging to the *Alcea* genus have historically been used to control pests, we have previously detected some insecticidal compounds such as β-amyrin, β-sitosterol, phytol, and lupeol[9] in the EtOH infusion extract (EIE) and EtOH sonication extract (ESE) of *A. nudiflora* leaves, which prompted us to further investigate the extracts of this plant. In particular, the SCE, if sufficiently insecticidal, might represent a good candidate for new, safe, and inexpensive natural pesticides, since *A. nudiflora* is commonly encountered in Central Asia, Western China, and Western Siberia. Herein, we report the insecticidal activity of SCE of *A. nudiflora* L. against pests such as aphids (*Macrosiphum euphorbiae*) and cowpea weevils (*Callosobruchus*

Received: March 20, 2022
Accepted: May 20, 2022
Published: June 2, 2022

maculatus). Furthermore, we examined its insecticidal activity against beneficial insects such as ladybugs (*Coccinella magnifica*) and European honeybees (*Apis mellifera* Linnaeus). Identification of molecular components in the SCE was accomplished using gas chromatography/mass spectrometry (GC/MS) and comparison of the MS characteristics and retention indices (RIs) with data in databases.[10] As far as we know, this work is the first to demonstrate the insecticidal activity of extracts of *A. nudiflora*.

■ MATERIALS AND METHODS

Plant Materials. Leaves of *A. nudiflora* L. {identified by an experienced botanist, Dr. Alimjan M. Nigmatullaev, and kept at the herbarium of the S. Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan (administrative number: 1338)} were collected in the vicinity of Chortak village, Namangan region, Uzbekistan (August 2015), dried in the shade, and crushed (4−6 mm) before the extraction.

Extraction. The crushed dry leaves of *A. nudiflora* L. (1 kg) were extracted with fluidic supercritical CO_2 at 40−50 °C under 28−30 MPa for 100 min to give 3.00 g of SCE. Additional samples of dry leaves (10.0 g each) were extracted three times with EtOH (96%, 80 mL, 60 mL, and 60 mL, respectively) under sonication (90 min) or by infusion (24 h) at room temperature. Evaporation at 40 °C afforded an ESE (1.73 g, dark green oily mass) and an EIE (1.44 g, dark green oily mass), respectively.

Further Separation of the CO_2 Extract. The SCE (2.00 g) was further separated into three fractions using column chromatography on silica gel. Fraction (Fr) 1 (450 mg, yellow oil after the removal of solvents), Fr 2 (275 mg, colorless amorphous mass), and Fr 3 (720 mg, colorless oil) were eluted using hexane−$CHCl_3$ = 1:1, 1:5, and 1:10, respectively.

Insects. Dozens of *C. maculatus* were collected from the institutional storage house and kept separately in a cage with tap-water-washed and dried mung beans (*Vigna radiata*) to prevent infestation. Adult *C. maculatus* were reared at 25 ± 1 °C and 55 ± 5% relative humidity with a photoperiod of 12 h. Three-day-old *C. maculatus* adults were selected and used in assays. The laboratory population of *M. euphorbiae* was kept on seedlings of the potato variety Sante at 22 ± 2 °C with a photoperiod of 16 h. Adult *C. magnifica* and *A. mellifera* Linnaeus were collected at a farm in Tashkent, Uzbekistan and kept in separate cylindrical glass bottles closed with a mosquito net.

Insecticidal Assays. Each extract (1.00 g) and a drop of Tween 80 or OP-10 were diluted with distilled H_2O to give 100 mL of stock solution (10 mg/mL). These stock solutions were further diluted with H_2O to prepare samples with lower concentrations. The various sample solutions (1.00 mL) were added to Petri dishes (diameter: 9 cm) in which a filter paper had been placed. After 10 min, insects (*M. euphorbiae* and *C. maculatus*, 10 adults each), together with their feed plants [potatoes (*Solanum tuberosum* L.) and mung beans (*Vigna radiate*), respectively] were placed on each dish, and the insect mortality was determined 5, 10, 30, and 60 min and 24 h after exposure. After obtaining three independent replicates at each concentration, the insecticidal activity of each extract was determined as percentage mortality of the insects.

Identification of the Components in the CO_2 Extract. A solution of the SCE (1.0 mg) in hexane (1 mL) was injected (1.0 μL) into a GC/MS (5975C inert MSD/7890A GC system, Agilent Technologies, USA, 2009), equipped with a quartz capillary column: HP-INNOWax, 30 m (length) × 0.25 mm (diameter) × 0.25 μm (thickness), Agilent Technologies. The separation and analysis were carried out under the following conditions: injector temperature: 220 °C; temperature mode: 50 °C (1 min) → 200 °C (heating rate: 4 °C/min followed by a constant temperature of 200 °C for 6 min) → 250 °C (heating rate: 15 °C/min followed a constant temperature of 250 °C for 25 min); recorded EI-MS *m/z* range: 10−550; carrier gas: helium; flow rate: 1.1 mL/min. The components were identified by comparison of the observed MS characteristics with MS libraries, that is, the Wiley Registry of Mass Spectral Data, 9th Ed., and the National Institute of Standards and Technology (USA) Mass Spectral Library (2011). The Kratz RIs of compounds, which were determined relative to a mixture of *n*-alkanes (C_9−C_{20}), were also compared with a previous literature report.[10]

■ RESULTS AND DISCUSSION

Insecticidal Activity of the EtOH and CO_2 Extracts. We first examined the insecticidal activity of the EtOH and CO_2 extracts (10 mg/mL each) against aphids, *M. euphorbiae* (Figure 1), with negative and positive control experiments using H_2O and the known synthetic pyrethroid cypermethrin (0.10 mg/mL).

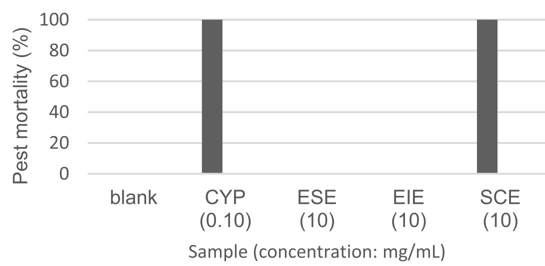


Figure 1. Insecticidal activity of the ESE, EIE, and SCE of *A. nudiflora* against *M. euphorbiae* (5 min exposure).

After 5 min of exposure, only SCE exhibited potent insecticidal activity, whereas both EtOH extracts, that is, ESE and EIE, were inactive. These results were surprising given that we have detected some insecticidal compounds (e.g., β-amyrin, β-sitosterol, phytol, and lupeol) in our preliminary study of ESE and EIE. We concluded that neither ESE nor EIE were active due to the (very) low concentration of insecticidal compounds. On the other hand, these results were also very interesting as they indicate that supercritical CO_2 is able to extract more/other insecticidal compounds than those mentioned above and/or different unique insecticidal plant substances that EtOH cannot.

Insecticidal Activity of the CO_2 Extract against *M. euphorbiae* and *C. maculatus*. As preliminary insecticidal activity was only detected for SCE, we further investigated the dose responses of *M. euphorbiae* and *C. maculatus* to SCE. Treatment of *M. euphorbiae* with systematically diluted SCE solutions (0.050−5 mg/mL) revealed that the SCE of *A. nudiflora* L. exhibits potent pesticidal activity (Figure 2). At the highest concentration of 5.0 mg/mL, 87% of the aphids were dead within 10 min (blue bar), with the death rate reaching 100% after 30 min of exposure (red bar). Even at concentrations of 0.10−1.0 mg/mL, the potent insecticidal activity was maintained especially after 60 min (green bar) and

https://doi.org/10.1021/acsomega.2c01688
ACS Omega 2022, 7, 19892−19897

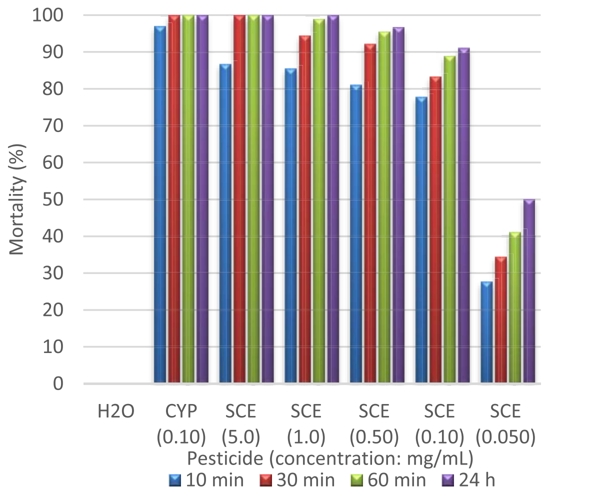


Figure 2. Insecticidal activity of SCE of *A. nudiflora* against *M. euphorbiae*.

24 h (purple bar) of exposure, with mortality rates of >80%. At 0.050 mg/mL, the activity dropped to <50%. The lethal concentration (LC_{50}) value after 24 h was calculated to be 0.03 mg/mL.

The SCE of *A. nudiflora* also exhibited potent insecticidal activity against the larger pest *C. maculatus* (Figure 3). The activity was almost identical to that against *M. euphorbiae*, with its LC_{50} value for *C. maculatus* after 24 h also being found to be 0.03 mg/mL. Ikbal and Pavela have reported in their excellent review article that potent insecticidal essential oils show LC_{50} values on the order of 10^1 to 10^2 μL/mL (≈mg/mL for solids) against aphids in contact applications.[11] Only 9% (7 examples) of the 77 examples in the literature showed an LC_{50} of <0.1 μL/mL, and only 4% (3 examples) were more potent than the SCE of *A. nudiflora*. This comparison clearly shows that among materials of plant origin, the SCE of *A. nudiflora* exhibits excellent potency against aphids. Moreover, it is noteworthy that the SCE of *A. nudiflora* is completely harmless to the beneficial insects *C. magnifica* and *A. mellifera* L. as well as to human skin, even at a concentration of 10 mg/mL (data not shown). These results indicate that the SCE of *A. nudiflora* is a good candidate as a novel natural insecticide, although the scalability of the extraction should further be addressed.

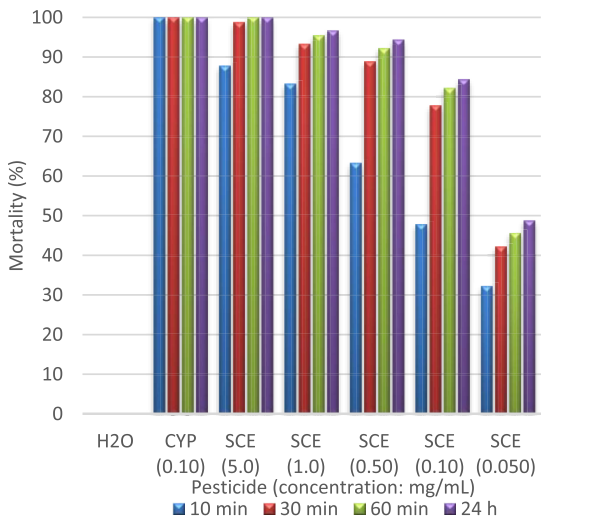


Figure 3. Insecticidal activity of SCE of *A. nudiflora* against *C. maculatus*.

Insecticidal Activity of Further-Fractionated SCE. To investigate the active species, we further separated the SCE using column chromatography on silica gel to give three fractions. The obtained Frs. 1 (eluted with hexane/$CHCl_3$ = 1/1), 2 (hexane/$CHCl_3$ = 1/5), and 3 (hexane/$CHCl_3$ = 1/10) were subsequently subjected to insecticidal assays and the mortality (%) was calculated for insects exposed to the fractions for 24 h. Frs. 1 and 2 exhibited potent insecticidal activity against both *M. euphorbiae* (Figure 4) and *C. maculatus* (Figure 5), while Fr. 3 did not. The LC_{50} values of Fr. 1 against *M. euphorbiae* and *C. maculatus* were 0.09 and 0.08 mg/mL, while those of Fr. 2 were 0.1 and 0.08 mg/mL, respectively. Since these LC_{50} values are almost identical to those of the parent SCE mixture, these results indicate that less-polar organic compounds extracted by supercritical CO_2 fluid are responsible for the insecticidal activity.

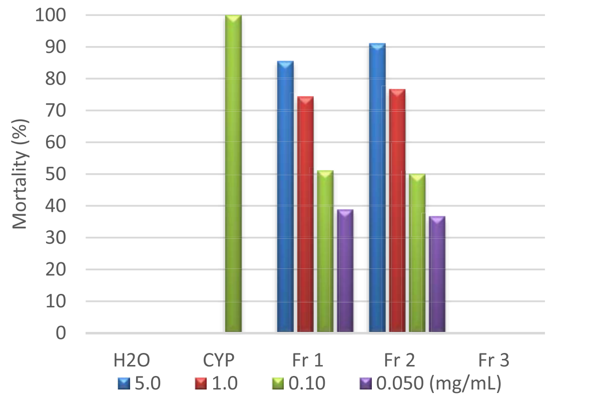


Figure 4. Insecticidal activity of fractionated SCE against *M. euphorbiae*.

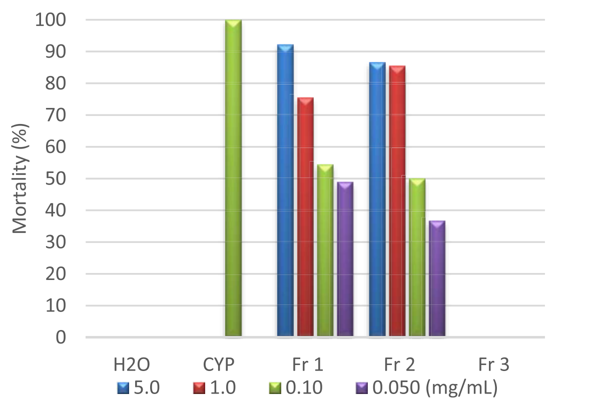
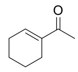
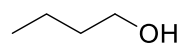
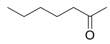
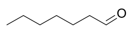
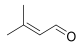
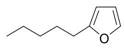
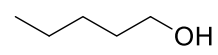
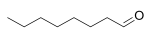
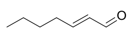
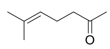
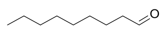
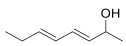
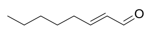
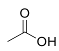
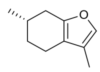
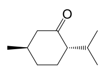
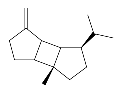
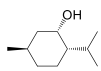
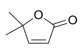
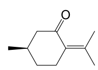
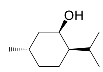
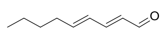
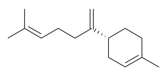
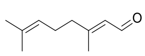
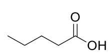
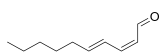
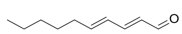
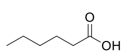
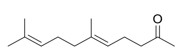
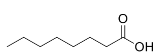
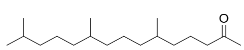
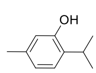


Figure 5. Insecticidal activity of fractionated SCE against *C. maculatus*.

Components in the SCE Detected by GC/MS and a Comparison of Their Insecticidal Activity with Literature Precedents. Finally, we analyzed the chemical components of the SCE of *A. nudiflora* using GC/MS. Each component was identified via comparison of its Kratz RI with literature values, as well as its EI-MS fragmentation pattern. As a result, 32 compounds were identified (Table 1). Among these, thymol is known to be pesticidal against many pests,

https://doi.org/10.1021/acsomega.2c01688
ACS Omega 2022, 7, 19892−19897

Table 1. Composition of SCE of *A. nudiflora* Analyzed by GC/MS

No	Compound name	Structure	Retention time (min)	Kratz retention index (experimental)	Kratz retention index (reported)[10a]
1	1-acetylcyclohexene		5.40	1126	
2	*n*-butanol		5.89	1136	1139
3	heptan-2-one		6.57	1177	1182
4	*n*-heptanal		6.68	1181	1185
5	3-methyl-but-2-enal		6.99	1195	1202[10b]
6	2-*n*-pentylfuran		7.84	1226	1232
7	pentan-1-ol		8.05	1240	1247
8	octanal		9.39	1280	1287
9	2-heptenal		10.35	1313	1321
10	6-methyl-5-hepten-2-one		10.78	1328	1336
11	nonanal		12.44	1386	1391
12	3,5-octadien-2-ol		12.79	1398	
13	(*E*)-2-octenal		13.45	1420	1429
14	acetic acid		14.37	1450	1446
15	menthofuran[17]		15.00	1471	1482
16	L-menthone (*trans*-menthone)[13,14,16]		15.17	1477	1465
17	β-bourbonene		16.03	1505	1523
18	(+)-neomenthol		16.56	1585	1578
19	5,5-dimethyl-2(5H)-furanone		17.38	1593	1590[10c]
20	pulegone		19.69	1627	1654
21	D-neoisomenthol		20.50	1654	1646[10d]
22	(2*E*,4*E*)-2,4-nonadienal		21.12	1685	1696
23	β-bisabolene		22.22	1712	1727
24	citral[14]		22.33	1716	1733[10e]
25	*n*-pentanoic acid		22.74	1730	1734[10f]
26	*cis,trans*-deca-2,4-dienal		23.29	1749	1756
27	*trans,trans*-deca-2,4-dienal		24.51	1790	1808
28	*n*-hexanoic acid		25.79	1834	1843
29	geranyl acetone		25.88	1850	1854
30	*n*-octanoic acid		32.09	2045	2057
31	hexahydrofarnesyl acetone		34.49	2124	2124
32	thymol[12-17]		35.81	2180	2164

such as tobacco cutworms (*Spodoptera litura* Fab),[12] bed bugs (*Cimex lectularius* L),[13] houseflies (*Musca domestica*),[14] red spider mites (*Tetranychus urticae*),[14] Western corn rootworms (*Diabrotica virgifera*), and click beetles (*Agriotes obscurus* L).[15] Pulegone is known to be toxic against *S. litura* Fab.,[12] maize weevils (*Sitophilus zeamais*),[16] *M. domestica*,[14] *D. virgifera*[14] and vine mealybugs (*Planococcus ficus*).[17] Menthone acts pesticidally against *C. lectularius* L.,[13] *C. lectularius* L.,[13] *S. zeamais*,[16] *M. domestica*,[14] and *D. virgifera*,[14] while citral is pesticidal against *M. domestica*,[14] and *D. virgifera*.[14] Therefore, the main active insecticidal compounds in the SCE of *A. nudiflora* are most likely menthone, thymol, pulegone, and citral which differ from those in the EIE and ESE (β-amyrin, β-sitosterol, phytol, and lupeol), albeit that the presence of novel, structurally unknown natural products and/or synergistic effects with some minor components cannot be ruled out at this point. The good insecticidal selectivity of the SCE of *A. nudiflora* against beneficial/pest insects might be derived from the presence of thymol and pulegone, given that they are safe for European honeybees, which has recently been reported.[18]

CONCLUSIONS

In summary, *A. nudiflora* L. leaves have been extracted with supercritical CO_2 under fluidic conditions and been subjected to insecticidal assays for the first time. The supercritical CO_2 extract (SCE) of *A. nudiflora* exhibited potent insecticidal activity against aphids (*M. euphorbiae*) and cowpea seed beetles (*C. maculatus*) with LC_{50} values of 0.03 mg/mL (24 h exposure, contact method). It is worth noting that the EtOH extract of *A. nudiflora* is not pesticidal and that the SCE is harmless to beneficial insects such as ladybugs (*C. magnifica*) and European honeybees (*A. mellifera* Linnaeus) at the tested concentrations (<10 mg/mL). These findings indicate that the SCE of *A. nudiflora* exhibits promising potential as an excellent lead for a safe pesticide of natural origin. Further investigations into the development of practical methods to enable the large-scale production of *A. nudiflora* SCE and the application of supercritical CO_2 extraction to various other plants native to Uzbekistan are currently in progress in our laboratory.

AUTHOR INFORMATION

Corresponding Authors

Khamid U. Khodjaniyazov − *A. S. Sadikov Institute of the Bioorganic Chemistry, Academy of Sciences of the Republic of Uzbekistan, Tashkent 100125, Uzbekistan; Faculty of Chemistry, National University of Uzbekistan named after Mirzo Ulugbek, Tashkent 100174, Uzbekistan*; Email: hamidkhodjaniyazov@yandex.ru

Kohei Torikai − *Faculty of Chemistry, National University of Uzbekistan named after Mirzo Ulugbek, Tashkent 100174, Uzbekistan; Department of Chemistry, Faculty of Science, Kyushu University, Fukuoka 819-0395, Japan*; orcid.org/0000-0002-9928-4300; Email: torikai@chem.kyushu-univ.jp

Authors

Nazira K. Khidyrova − *S. Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, Tashkent 100170, Uzbekistan*

Saida M. Turaeva − *S. Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, Tashkent 100170, Uzbekistan*

Malohat J. Rakhmatova − *S. Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, Tashkent 100170, Uzbekistan*

Khayrulla M. Bobakulov − *S. Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, Tashkent 100170, Uzbekistan; "Tashkent Institute of Irrigation and Agricultural Mechanization Engineers", National Research University, Tashkent 100000, Uzbekistan*

Shamansur S. Sagdullaev − *S. Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, Tashkent 100170, Uzbekistan*

Rano P. Zakirova − *S. Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, Tashkent 100170, Uzbekistan*

Complete contact information is available at: https://pubs.acs.org/10.1021/acsomega.2c01688

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

We thank Dr. Alimjan M. Nigmatullaev {S. Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan (ICPS), Uzbekistan} for his identification of *A. nudiflora*. This work was supported by a Basic Grant from the Innovation Ministry of the Republic of Uzbekistan (VA-ACS-5-008 to N.K.K.). K.U.K. and K.T. are grateful to ICPS for financial support to send K.U.K. to K.T.'s laboratory (Kyushu University, Japan) and to invite K.T. to ICPS, which enabled their smooth collaboration.

REFERENCES

(1) Clark, M.; Tilman, D. Comparative analysis of environmental impacts of agricultural production systems, agricultural input efficiency, and food choice. *Environ. Res. Lett.* **2017**, *12*, 064016.

(2) WIKIPEDIA. Projections of population growth. https://en.wikipedia.org/wiki/Projections_of_population_growth (accessed Mar 17, 2022).

(3) Zikankuba, V. L.; Mwanyika, G.; Ntwenya, J. E.; James, A. Pesticide regulations and their malpractice implications on food and environment safety. *Cogent Food Agric.* **2019**, *5*, 1601544.

(4) (a) Lamberth, C.; Jeanmart, S.; Luksch, T.; Plant, A. Current challenges and trends in the discovery of agrochemicals. *Science* **2013**, *341*, 742−746. (b) Zhao, X.; Cui, H.; Wang, Y.; Sun, C.; Cui, B.; Zeng, Z. Development strategies and prospects of nano-based smart pesticide formulation. *J. Agric. Food Chem.* **2018**, *66*, 6504−6512.

(5) (a) Sparks, T. C.; Wessels, F. J.; Lorsbach, B. A.; Nugent, B. M.; Watson, G. B. The new age of insecticide discovery-the crop protection industry and the impact of natural products. *Pestic. Biochem. Physiol.* **2019**, *161*, 12−22. (b) Beck, J. J.; Alborn, H. T.; Block, A. K.; Christensen, S. A.; Hunter, C. T.; Rering, C. C.; Seidl-Adams, I.; Stuhl, C. J.; Torto, B.; Tumlinson, J. H. Interactions among plants, insects, and microbes: Elucidation of inter-organismal chemical communications in agricultural ecology. *J. Agric. Food Chem.* **2018**, *66*, 6663−6674.

(6) Plant extracts are not necessarily safe. For a recent example, see: Phupong, C.; Suenaga, M.; Bhoopong, P.; Chunglok, W.; Jaritngam, G.; Karak, M.; Yoshida, K.; Phupong, W.; Torikai, K. Precise ^{1}H- and ^{13}C-NMR reassignment of dehydrocrebanine by 10-mg INADEQUATE and in silico analysis: With an alert for its toxicity. *Tetrahedron* **2020**, *76*, 131310.

(7) (a) Palavra, A. M. F.; Coelho, J. P.; Barroso, J. G.; Rauter, A. P.; Fareleira, J. M. N. A.; Mainar, A.; Urieta, J. S.; Nobre, B. P.; Gouveia, L.; Mendes, R. L.; Cabral, J. M. S.; Novais, J. M. Supercritical carbon

dioxide extraction of bioactive compounds from microalgae and volatile oils from aromatic plants. *J. Supercrit. Fluids* **2011**, *60*, 21−27. (b) Jozwiak, A.; Brzozowski, R.; Bujnowski, Z.; Chojnacki, T.; Swiezewska, E. Application of supercritical CO_2 for extraction of polyisoprenoid alcohols and their esters from plant tissues. *J. Lipid Res.* **2013**, *54*, 2023−2028. (c) Abd Hamid, I. A.; Ismail, N.; Abd Rahman, N. Supercritical carbon dioxide extraction of selected herbal leaves: An overview. *IOP Conf. Ser.: Mater. Sci. Eng.* **2018**, *358*, 012037.

(8) (a) Rahmatova, M. J.; Mamatkulova, N. M.; Khodjaniyazov, K. U.; Mukarramov, N. I.; Khidyrova, N. K. Accumulation dynamics of polyprenols in Alcea nudiflora: Identification and comparative HPTLC analysis. *Int. J. Sci. Res. Methodol.* **2016**, *4*, 82−91. (b) Syrov, V. N.; Vais, E. V.; Khidyrova, N. K.; Rakhmatova, M. D.; Shakhidoyatov, R. K.; Khushbaktova, Z. A. Results of experimental studies of the immunotropic action of polyprenols extracted from Alcea nudiflora. *Pharm. Chem. J.* **2016**, *50*, 29−32. (c) Kukina, T. P.; Sal'nikova, O. I.; Khidyrova, N. K.; Rakhmatova, M. D.; Pankrushina, N. A.; Grazhdannikov, A. E. Aliphatic and terpene constituents of Alcea nudiflora extracts. *Chem. Nat. Compd.* **2016**, *52*, 285−287. (d) Khidyrova, N. K.; Rakhmatova, M. Z.; Kukina, T. P.; Shakhidoyatov, R. K.; Shakhidoyatov, K. M. Polyprenols and triterpenoids from leaves of Alcea nudiflora. *Chem. Nat. Compd.* **2012**, *48*, 180−184.

(9) Opiyo, S. A. Insecticidal Activity of Ocimum Suave Willd Extracts and Compounds against Sitophilus Zeamais Motschulsky. *Basic Sci. Med.* **2020**, *9*, 32−37.

(10) (a) Babushok, V. I.; Linstrom, P. J.; Zenkevich, I. G. Retention indices for frequently reported compounds of plant essential oils. *J. Phys. Chem. Ref. Data* **2011**, *40*, 043101. (b) Chung, H. Y.; Yung, I. K. S.; Ma, W. C. J.; Kim, J.-S. Analysis of volatile components in frozen and dried scallops (Patinopecten yessoensis) by gas chromatography/mass spectrometry. *Food Res. Int.* **2002**, *35*, 43−53. (c) Wei, A.; Mura, K.; Shibamoto, T. Antioxidative activity of volatile chemicals extracted from beer. *J. Agric. Food Chem.* **2001**, *49*, 4097−4101. (d) Chung, T. Y.; Eiserich, J. P.; Shibamoto, T. Volatile compounds isolated from edible Korean chamchwi (Aster scaber Thunb). *J. Agric. Food Chem.* **1993**, *41*, 1693−1697. (e) Choi, H.-S. Lipolytic effects of citrus peel oils and their components. *J. Agric. Food Chem.* **2006**, *54*, 3254−3258. (f) Quijano, C. E.; Linares, D.; Pino, J. A. Changes in Volatile compounds of fermented Cereza Agria [Phyllanthus acidus (L.) Skeels] fruit. *Flavour Fragr. J.* **2007**, *22*, 392−394.

(11) Ikbal, C.; Pavela, R. Essential oils as active ingredients of botanical insecticides against aphids. *J. Pestic. Sci.* **2019**, *92*, 971−986.

(12) Hummelbrunner, L. A.; Isman, M. B. Acute, sublethal, antifeedant, and synergistic effects of monoterpenoid essential oil compounds on the tobacco cutworm, Spodoptera litura (Lep., Noctuidae). *J. Agric. Food Chem.* **2001**, *49*, 715−720.

(13) Gaire, S.; Scharf, M. E.; Gondhalekar, A. D. Toxicity and neurophysiological impacts of plant essential oil components on bed bugs (Cimicidae: Hemiptera). *Sci. Rep.* **2019**, *9*, 3961.

(14) Lee, S.; Tsao, R.; Peterson, C.; Coats, J. R. Insecticidal activity of monoterpenoids to Western corn rootworm (Coleoptera: Chrysomelidae), twospotted spider mite (Acari: Tetranychidae), and house fly (Diptera: Muscidae). *J. Econ. Entomol.* **1997**, *90*, 883−892.

(15) Waliwitiya, R.; Isman, M. B.; Vernon, R. S.; Riseman, A. Insecticidal activity of selected monoterpenoids and rosemary oil to Agriotes obscurus (Coleoptera: Elateridae). *J. Econ. Etnomol.* **2005**, *98*, 1560−1565.

(16) Herrera, J. M.; Zunino, M. P.; Massuh, Y.; Pizzollito, R. P.; Dambolena, J. S.; Gañan, N. A.; Zygadlo, J. A. Fumigant toxicity of five essential oils rich in ketones against Sitophilus zeamais (Motschulsky). *Agriscientia* **2014**, *31*, 35−41.

(17) Peschiutta, M. L.; Pizzolitto, R. P.; Ordano, M. A.; Zaio, Y. P.; Zygadlo, J. A. Laboratory evaluation of insecticidal activity of plant essential oils against the vine mealybug. *Planococcus ficus. Vitis* **2017**, *56*, 79−83.

(18) (a) Charpentier, G.; Vidau, C.; Ferdy, J.-B.; Tabart, J.; Vetillard, A. Lethal and sub-lethal effects of thymol on honeybee (Apis mellifera) larvae reared in vitro. *Pest Manag. Sci.* **2014**, *70*, 140−147. (b) Papadimitriou, D. M.; Petrakis, E. A.; Arvaniti, K. A.; Kimbaris, A. C.; Polissiou, M. G.; Perdikis, D. C. Comparative bioactivity of essential oils from two Mentha pulegium (Lamiaceae) chemotypes against Aphis gossypii, Aphis spiraecola, Tetranychus urticae and the generalist predator Nesidiocoris tenuis. *Phytoparasitica* **2019**, *47*, 683−692.

https://doi.org/10.1021/acsomega.2c01688
ACS Omega 2022, 7, 19892−19897