DOI 10.1007/s10600-021-03572-y
Chemistry of Natural Compounds, Vol. 57, No. 6, November, 2021

ANTIBIOFILM, ANTI-QUORUM SENSING ACTIVITIES, AND MOLECULAR DOCKING STUDIES OF *Seriphidium quettense* ESSENTIAL OIL

Rubina Naz Qaisrani,[1] Shah Iram Niaz,[1*] Muhammad Akram,[2] Abdul Rafey,[3] Amanullah,[3] Fakhar Ul Mahmood,[3] Luc Pieters,[4] and Adnan Amin[3*]

Bacterial quorum sensing (QS) is generally referred to as cell-to-cell communication where specific signals (auto-inducing peptide, acyl-homoserine lactone, etc.) are activated to synchronize pathogenicity and facilitate bacteria to make biofilms [1]. Biofilm formation also produces basic changes in gene expression and thus contributes towards antibiotic resistance [2]. The genus *Seriphidium* consists of 125 species reported from various parts of the world, including Asia, Europe, and North America [3], and mainly includes medicinal plants [4] that are traditionally used for treating G.I.T disorders [5] and scabies and that have antimicrobial, antidiabetic, and antihypertensive properties [6]. The plant *Seriphidium quettense* (Podlech) Y. R. Ling is endemic to Balochistan Province of Pakistan and traditionally employed for the treatment of various G. I. T problems [7]. Various compounds have previously been isolated, including ilicic acid [2] and 6α-hydroxy-8(10)-oplopen-14-one, from leaves that showed excellent anti urease activity [8]. This is the first report that describes anti-quorum sensing and anti-biofilm properties of *S. quettense* essential oil (EO).

The fresh leaves of *S. quettense* were collected from Hazar Ganji Baochistan (Pakistan) and authenticated by Islamabad Herbarium (Quaid I Azam University Islamabad Pakistan). Hydrodistillation of *S. quettense* yielded 2 mL ± 0.10 mL/100 g of an aromatic pale yellow EO. The essential oil analysis was performed using GC-MS (Shimadzu GC 2010, Japan) equipped with a flame ionization detector (FID) and AOC-20i autosampler using a DB-5 MS (30 m × 0.25 mm id, 0.25 μm film thickness) capillary column. The component identification was carried out on a GCMS-QP 2010 Plus (Shimadzu, Japan) system operating in electron ionization mode at 70 eV. Mass units were monitored from 35 to 500 AMU. A DB-5 MS (30 m × 0.25 mm i.d., 0.25 μm film thickness) capillary column was used. The linear retention indices were calculated using a homologous series of *n*-alkanes (C8–C25) under the same temperature-programmed conditions. The components were identified by comparison with linear retention indices (RI), mass spectra with those of NIST mass spectral library, or co-injection with standards. The GC-MS spectra were quite complex, and a total of 20 compounds was identified (Table 1). Camphor was present in highest amount (28.8%), followed by β-thujone (24.9%) and 3-thujanone (24.3%). Other major components included eucalyptol (3.8%), methylbenzene (3.3%), davanone (2.8%), δ-elemene (2.8%), *trans*-farnesol (2.6%), and α-terpinyl acetate (2.4%). The components were identified by comparison with linear retention indices (RI) with *n*-alkanes (C8–C25), and mass spectra with those of NIST mass spectral library. Molecular docking studies of the test compounds were performed in the active pocket of transcriptional regulators PqsE (2Q0J) and LasR (2UV0) and quorum sensing regulators CviR (3QP5). The essential oil was analyzed for antibiofilm and antiquorum sensing activities, and violacine production was quantified.

During analysis for the Lipinski rule of five, *trans*-farnesol and δ-elemene violated rule 1; however, they still displayed druglike properties in the experimental studies *in vitro.* In the ADMET analysis, the TPSA of all compounds was less than 100, suggesting good oral absorption or membrane permeability [9]. Similarly, all compounds showed ideal lipophilicity (AlogP98 ≤ 5) [10], high Caco-2 permeability, excellent absorption, and low distribution volume.

1) Institute of Chemical Sciences, Gomal University, D. I. Khan, Pakistan; 2) Pakistan Council for Scientific and Industrial Research (PCSIR), Peshawar, Pakistan; 3) NPRL, Department of Pharmacognosy, Faculty of Pharmacy, Gomal University, D. I. Khan, Pakistan, e-mail: adnan.amin@gu.edu.pk; 4) Natural Products & Food Research and Analysis, Department of Pharmaceutical Sciences, University of Antwerpen, Belgium. Published in *Khimiya Prirodnykh Soedinenii*, No. 6, November–December, 2021, pp. 979–980. Original article submitted August 21, 2020.

TABLE 1. GC-MS Profile of *S. quettense*

Compound	RI	%	Compound	RI	%
Methylbenzene	884.0	3.3	Borneol	1292.5	0.2
β-Myrcene	1125.2	0.7	4-Terpineol	1299.3	0.4
4-Carene	1151.9	0.5	*p*-Cymen-8-ol	1304.3	0.3
Cymene	1159.8	1.6	α-Terpeniol	1308.5	0.3
Eucalyptol	1166.8	3.8	δ-Elemene	1338.0	2.8
Maylene	1194.9	0.1	Thymol	1363.0	0.3
β-Linalool	1242.5	0.3	Carvacol	1365.6	0.1
3-Thujanone	1246.4	24.3	α-Terpineol acetate	1385.6	2.4
β-Thujone	1256.8	24.9	Davanone	1467.6	2.8
Camphor	1277.7	28.8	*trans*-Farnesol	1479.0	2.6

TABLE 2. Antibiofilm and Anti-quorum Sensing Inhibition by *S. quettense* EO

Concentration, %	Antibiofilm, % inhibition	Anti-quorum sensing, mm
5	5	0
10	19	3
20	30	5
30	38	9
40	51	13

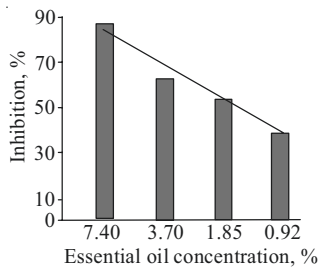

Fig. 1. Violacine inhibition assay of *S. quettense* essential oil.

Likewise, all tested compounds showed significant BBB absorption and high renal clearance. Among them, davanone showed the highest number of H-bonding interaction (His 71; His 159; Arg 288) with other notable interactions included in the Leu 277, Phe 195, Leu 193, His 221, Leu 112, and Tyr 72 and 2D representation. For transcriptional regulator LasR (2UV0), camphor, 3-thujanone, and davanone showed the highest number of H-bonding interaction and 2D representation. Finally, during docking inside the active pocket of quorum sensing regulator CviR (3QP5), it was observed that Asn 77 was the active site residue taking part in the formation of H-bonding interactions with the test compounds camphor and β-thujone. Other interactions included pi-sigma (Tyr 80 and Tyr 88) and 2D representation. Finally, in order to validate the docking results, antibiofilm and anti-quorum sensing activities of the EO was performed. The EO presented excellent inhibition (51%) against *Pseudomonas aeruginosa* in a concentration-dependent manner using the maximum tested dose (40%) (Table 2). Further, during the anti-quorum sensing assay, the EO (using *C. violaceum* as biomarker strain for quorum sensing) showed the highest inhibition (13 mm at 40% concentration) (Table 2), whereas significant inhibition (88% at 7.4% concentration) of violacine production was noticed (Fig. 1). Based on earlier reports [10–13] and docking results, it was concluded that antibiofilm and quorum sensing activities of the EO are possibly due to camphor, β-thujone, and 3-thujanone, which may act both individually and through synergistic effects.

ACKNOWLEDGMENT

The Foundation "Plants for Health" is kindly acknowledged for financial support to Dr. Adnan Amin.

REFERENCES

1. Q. Jiang, J. Chen, C. Yang, Y. Yin, and K. Yao, *Biomed. Res. Int*., doi: 10.1155/2019/2015978 (2019).
2. S. Keerlara, S. Thakur, and J. P. Patel, *Foodborne Pathol. Dis*., **13** (9), 509 (2016).
3. A. Ghafoor, S. I. Ali, and M. Qaiser (Eds.), *Flora of Pakistan, (Asteraceae) Anthemideae*, No. 207, University of Karachi, 2002, 117 pp.
4. N. C. Shah, *The Scitech J*., **1** (1), 29 (2014).
5. M. Hayat, Q. Ashraf, M. Khan, M. A. Yasmin, G. Yasmin, N. Shaheen, and M. Jabeen, *Int. J. Agric. Biol.,* **11**, 4 (2009).
6. M. J. Durrani, A. M. Taj, and F. J. Hussain, *Sci. Technol*., **27**, 4 (2003).
7. Q. N. Muhamad, T. Zohra, T. A. Khalil, S. Saqib, S. M. Ayaz, A. Ahmad, and Z. K. Shinwari, *Green. Chem. Lett. Rev*., **12**, 3 (2019).
8. M. I. Tousif, N. Riaz, M. Nazir, S. Ahmad, M. Saleem, A. Jabbar, M. Ashraf, and R. B. Tareen, *Rec. Nat. Prod*., **11**, 223 (2017).
9. T. Qidwai, in: *Silico. Pharmacol*., **5**, 6 (2017).
10. P. Fonteh, A. Elkhadir, B. Omondi, I. Guzei, J. Darkwa, and D. Meyer, *Biometals*., **28**, 6 (2015).
11. R. K. Manoharan, J. H. Lee, and J. Leem, *Front. Microbiol*., **8**, 1476 (2017).
12. X. Zhao, F. Zhao, J. Wang, and N. Zhong, *R.S.C. Adv.,* **7**, 6 (2017).
13. S. Alves, A. Duarte, S. Sousa, and F. C. Domingues, *J. Bioadhesion. Biofilm. Res*., **32**, 2 (2016).