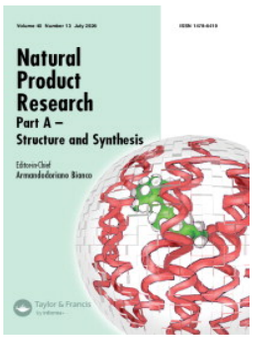

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Phytochemical investigation, antimicrobial activities, and molecular docking studies on endemic *Gelasia sericea* (Aucher ex DC.) Zaika, Sukhor. & N.Kilian grown in Türkiye

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Phytochemical investigation, antimicrobial activities, and molecular docking studies on endemic *Gelasia sericea* (Aucher ex DC.) Zaika, Sukhor. & N.Kilian grown in Türkiye

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ABSTRACT

In this study, activity-guided isolation of the endemic *Gelasia sericea* (Aucher ex DC.) Zaika, Sukhor. & N.Kilian yielded five new compounds (8-*O*-*β*-*D*-glucopyranosyl-6-hydroxy-3-(4-hydroxyphenyl)-1*H*-isochromen-1-one (**1**), *rel.* (3*R*,3′*S*)-8,8′-oxy*bis*[6-hydroxy-3-(4-hydroxyphenyl)-3,4-dihydro-1*H*-isochromen-1-one] (**2**), 3-*O*-(4-*O*-glyceryl)-*α*-*D*-xylopyranosyl-5-methyl-4*H*-pyran-4-one (**3**), 2-carboxyl-3-hydroxy-4′-methoxy-5-*O*-(3-*O*-glyceryl)-*β*-*D*-xylopyranosylbibenzyl (**4**), and 2-carboxyl-3,4′-dihydroxy-5-*O*-(*β*-*D*-apiofuranosyl)-(1→6)-*β*-D-glucopyranosylbibenzyl (**5**). Five known compounds as *p*-coumaric acid (**6**), scorzopigmecosite (**7**), scorzocreticin (**8**), quercetin (**9**), and kelampayoside A (**10**). Spectroscopic methods were used to characterise the structures of compounds **1–10**. All the isolated compounds, except compound **10**, exhibited an inhibition zone diameter of 10–12 mm against at least one of the nine different microorganisms tested. Compound **8** was found to be the most effective with an MIC value of 12.5 µg/mL against *Pseudomonas aeruginosa*. Additionally, molecular docking analysis of compounds **1–10** was performed, targeting *P. aeruginosa* RhlR and DNA gyrase B enzymes. Among the identified compounds, compound 2 exhibited the most promising inhibitory activity against both targets, with binding energies of −12.0 and −11.3 kcal/mol, respectively.

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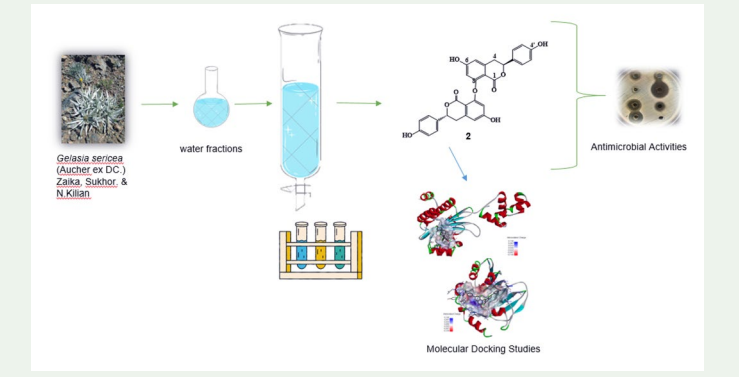

1. Introduction

The genus *Scorzonera* L. belongs to the Asteraceae family, comprising approximately 180 species worldwide, and is widely distributed in the barren lands of Eurasia and Africa (Senol Sezer et al. 2014; Chamberlain 1975). Although there are only 28 species in the European flora, more than 50 species of the genus *Scorzonera* grow in Türkiye, 31 of which are endemic (Chamberlain 1975; Acikara et al. 2010; Makbul et al. 2010; Altinordu et al. 2015; Coşkunçelebi et al. 2015). This means that Türkiye is an essential centre of diversity for this genus. Most *Scorzonera* species are consumed as vegetables in Türkiye, particularly in the Eastern Anatolia region. *Scorzonera* species are traditionally known for their use as fodder, and the roots and green buds of the plants are consumed fresh or after cooking. The *Scorzonera sericea* species has now been transferred to *Gelasia sericea* (Aucher ex DC.) Zaika, Sukhor. & N.Kilian. *G. sericea* is characterised by short, linear leaves with blunt tips. It also has a solitary, obconical flower head and a dark-pubescent involucre. It typically reaches a height of only 5–10 cm and thrives in rocky, alpine environments at elevations ranging from 1,800 to 3,200 m (Zaika et al. 2020).

Some edible *Scorzonera* species include *Scorzonera mollis* Bieb., *Scorzonera suberosa* C. Koch, *Scorzonera cana* (C. A. Meyer) Hoffm., and *Scorzonera latifolia* (Fisch. et Mey.) DC. (Edrada et al. 2006; Tsevegsuren et al. 2007; Senol Sezer et al. 2014). In addition to their edible uses, several Scorzonera species are also utilised in traditional medicine. For instance, *Scorzonera radiata* Fisch., *Scorzonera divaricata* Turcz., *Scorzonera pseudodivaricata* Lipsch., *Scorzonera cretica* Willd., *Scorzonera mongolica* Maxim., *Scorzonera austriaca* Willd., *Scorzonera hispanica* L., and *Scorzonera humilis* L. are used in Türkiye (Baytop 1999; Acikara et al. 2010, 2015; Citoglu et al. 2010; Akkol et al. 2011, 2019), China (Zhu et al. 2009), Mongolia (Wang Y et al. 2009a), and various European countries (Zidorn et al. 2000a, 2000b; Paraschos et al. 2001; Tsevegsuren et al. 2007; Acikara 2010).

Secondary metabolites are complex natural compounds with a remarkable diversity of chemical structures. Phenolic, terpenic, and alkaloid class compounds are essential secondary compounds and show biological activity in a broad spectrum, either as a total extract or as a pure compound. Numerous studies on the development of new

drugs have been conducted using natural compounds (Newman and Cragg 2007). Efforts to develop new drugs from natural compounds are increasing interest in isolating and characterising secondary metabolites. Flavonoids are a significant class of naturally occurring compounds with a polyphenolic structure. Flavonoid molecules are known to possess antioxidant activity and are associated with conditions such as atherosclerosis, cancer, and Alzheimer's disease. Because they can alter the activity of cellular enzymes, phenolic compounds have anti-inflammatory, anticarcinogenic, antimutagenic, and antioxidative properties. In alternative medicine, polyphenolic substances are frequently utilised in nutraceutical, pharmacological, medicinal, and cosmetic applications (Panche et al. 2016).

Many different natural compounds like guaianolide class sesquiterpene lactones, lignans, stilbenoids, triterpenoids, flavonoids (such as apigenin, kaempferol, luteolin, and quercetin), caffeoylquinic acids, and coumarins have been isolated from *Scorzonera* species (Lendzion et al. 2021). Literature review has shown that terpenic and phenolic compounds are quite rich in *Scorzonera* species (Ertürk and Demirdağ 2003; Tsevegsuren et al. 2007; Zidorn 2008; Sari et al. 2009; Sareedenchai and Zidorn 2010; Ugur et al. 2010; Bader et al. 2011; Wu QX et al. 2018; Sweidan et al. 2020; Erik, Yaylı, et al. 2021; Erik, Coşkunçelebi, et al. 2021; Korkmaz et al. 2023a, 2023b). Antimicrobial and antifungal activity on the various solvent extracts and fractions of the genus *Scorzonera* were also reported (Ertürk and Demirdağ 2003; Sari et al. 2009; Ugur et al. 2010; Wu QX et al. 2018; Ayromlou et al. 2020; Mohammed et al. 2020; Sweidan et al. 2020; Erik, Yaylı, et al. 2021; Erik, Coşkunçelebi, et al. 2021; Korkmaz et al. 2023a, 2023b).

A literature search revealed antioxidant and enzyme inhibition properties for the aqueous methanol extract of *G. sericea* (*S. sericea*) (Senol Sezer et al. 2014). Still, no studies on the isolation of secondary metabolites or antimicrobial activity were found. In our ongoing activity-guided work, clarifying the new bioactive compounds of the *G. sericea* species is essential. Therefore, phytochemical studies led to the characterisation of five new compounds (**1–5**) and five known compounds (**6–10**). Furthermore, we evaluated the antimicrobial activity of all isolated compounds (**1–10**) against nine different microorganisms—the first such report for compounds derived from *G. sericea*.

2. Results and discussion

Fractionation of the methanol extract of *G. sericea* was carried out using solvents of increasing polarity, yielding *n*-hexane, chloroform, ethyl acetate, and water fractions. As this study was conducted in a bio-guided manner, the isolation of the compounds was guided by the antimicrobial activity results of the extracts. The most bioactive ethyl acetate fraction of *G. sericea*, a new 8-*O*-*β*-*D*-glucopyranosyl-6-hydroxy-3-(4-hydroxyphenyl)-1*H*-isochromen-1-one (**1**), and four known compounds *p*-coumaric acid (**6**) (Karthikeyan et al. 2014; Deveci 2021; Abbey et al. 2023; Anwar et al. 2023; Rios and Gómez-Calvario 2023), scorzopigmecosite (**7**) (Şahin et al. 2020; Erik, Yaylı, et al. 2021), scorzocreticin (**8**) (Paraschos et al. 2001; Zidorn et al. 2008; Srinivas et al. 2014), and quercetin (**9**) (Ghosh et al. 2015; Mostafa 2020; Wang R et al. 2023) were isolated. The water fraction of *G. sericea* was also subjected to reversed-phase silica gel column chromatography, then ordinary-phase CC, and finally, normal phase preparative TLC (PTLC) to afford four new compounds as *rel*. (3 *R*,3′*S*)-8,8′-oxy*bis*[6-hydroxy-3-(4-hydroxyphenyl)-3,4-

dihydro-1*H*-isochromen-1-one] (**2**), 3-*O*-(4-*O*-glyceryl)-*α*-*D*-xylopyranosyl-5-methyl-4*H*-pyran-4-one (**3**), 2-carboxyl-3-hydroxy-4′-methoxy-5-*O*-(3-*O*-glyceryl)-*β*-*D*-xylopyranosyl-bibenzyl (**4**), and 2-carboxyl-3,4′-dihydroxy-5-*O*-(*β*-*D*-apiofuranosyl)-(1→6)-*β*-*D*-glucopyranosylbibenzyl (**5**), together with a known kelampayoside A (**10**) (Sunghwa and Koketsu 2009; He et al. 2017). In addition to the new compounds (**1**–**5**), five previously known natural products (**6**–**10**) were also identified in this study. Among the known compounds, *p*-coumaric acid (6) and quercetin (9) are widely distributed phenolic compounds previously reported in several members of the Asteraceae family, including *Scorzonera* species such as *S. suberosa* and *S. latifolia* (Senol Sezer et al. 2014; Zidorn et al. 2000a). Scorzopigmecosite (7) and scorzocreticin (8) have also been reported in *S. cretica* and *Scorzonera papposa* DC., respectively (Zidorn et al. 2005). Kelampayoside A (10), although more commonly reported in other plant families such as Lamiaceae and Rutaceae (Sunghwa and Koketsu 2009; He et al. 2017), has not previously been isolated from the Scorzonera genus or Asteraceae family to the best of our knowledge. Therefore, this is the first report of compounds 6–10 from *G. sericea*, expanding the known phytochemical diversity of the species. As this represents the first phytochemical and antimicrobial investigation on *G. sericea*, all these compounds were reported from this species for the first time.

The LC-QTOF-MS of **1** gave an ion peak at *m/z* $[M\text{-}H_2O]^+$ 413.2647 (100) (calc. 413.2644); $[M\text{-}CH_2OH+Na+H]^+$ 425.2134 (28) (calc. 425.2133) and the molecular formula was determined as $C_{21}H_{20}O_{10}$. FT-IR spectrum of **1** showed absorption bands at 3286 cm^{-1} (-OH), 3054 cm^{-1} (sp^2-CH), 2954 cm^{-1} (sp^3-CH), 1643 cm^{-1} (C=O), 1450 cm^{-1} (C=C), 1286 cm^{-1}, and 1111 cm^{-1} (C–O), suggestive of a 4-hydroxyphenyl-1*H*-isochromen-1-one glycoside structure. UV spectra showed absorption maxima (log Ɛ) at 300 (5.43) nm. The optical activity of **1** was observed as $[\alpha]_d^{24}$ +4.28 (c: 0.021 CH_3OH). ^{1}H NMR spectrum of **1** revealed peak at δ_H 6.83 ppm (d, J = 2.3 Hz), δ_H 6.82 ppm (d, J = 2.3, 2.0 Hz), and δ_H 6.40 ppm (d, J = 2.0 Hz) that were assigned to H-4, H-5, and H-7, respectively. In addition, peaks at δ_H 7.38 ppm (d, J = 8.8 Hz, H-2′,6′) and δ_H 6.74 ppm (d, J = 8.8 Hz, H-3′,5′) were assigned for the B ring of **1** and prove that ring B is para-substituted. These NMR data are compatible with the scorzonerol (Sahin et al. 2020), thunberginol B (Yoshikawa et al. 1992), polyisocoumarin (Jiang et al. 2020), and 6,8-dimethoxy-3-(4-methoxyphenyl) isocoumarin (Saeed 2006). When the FT-IR, UV,^{1}H NMR, and ^{13}C NMR spectra of **1** are examined, the aglycone part of the compound coincides with the peaks of the scorzonerol compound isolated from *Scorzonera pygmaea* Sibth. & Sm. (Sahin et al. 2020). In the ^{1}H NMR spectrum, the peak observed at δ_H 4.96 ppm, besides the water peak (solvent), was attributed to the anomeric proton of glucose. The ^{13}C-NMR spectrum of the glycone part of **1** yielded six carbon signals. The anomeric C-1′ carbon peak was observed at δ_C 106.61 ppm. When the HMBC spectrum was examined, a correlation was observed from the anomeric proton of glucose (δ_H 4.96 ppm) to the C-8 (δ_C 161.08 ppm) position, indicating that glucose was linked to the C-8 position of the aglycone. As a result of all these findings, the structure of compound **1** was 8-(*O*-*β*-*D*-glucopyranosyl)-6-hydroxy-3-(4-hydroxyphenyl)-1*H*-isochromen-1-one (scorzonerol 8-*O*-*β*-*D*-glucopyranoside (Sahin et al. 2020) and given the trivial name scorzosericoside I that was introduced to the literature as a new compound. NMR, FT-IR, UV-VIS, and LC-QTOF-MS data of **1** are shown in the supplementary data Figures S1–S7.

Compound **2** was isolated as a white powder (mp. 53–55 °C), and its molecular formula was determined as $C_{30}H_{22}O_9$ by HR LC-QTOF-MS (*m/z* $[M+H]^+$: 525.28672 (89), calc.: 525.28670); $[M+2Na\text{-}H]^+$ 569.31290 (100) (calc. 569.3173). The UV spectra showed absorption maxima (log Ɛ) at 285 nm (5.89) and 305 nm (5.91). The FT-IR spectrum of 2 showed absorption bands at 3285 cm-1 (–OH), 2954 cm-1 (sp3 C-H), 1651 cm-1 (C=O), and 1560, 1450 cm^{-1} (C=C). Comparison of the ^1H and ^{13}C NMR data of **2** with the literature (Paraschos et al. 2001; Saeed 2006; Sari et al. 2007; Harkati et al. 2010; Li and Wang 2010; Donia 2016; Çiçek et al. 2018; Sahin et al. 2020; Erik, Yaylı, et al. 2021), the structure of **2** is in the dihydroisocoumarin form. The ^1H NMR spectrum of **2** showed a proton peak at δ_H 5.43 ppm (d, J = 12 Hz, H-3) coupled with two methylene proton peaks at δ_H 3.18 ppm (dd, J = 17, 12 Hz, H-4a) and δ_H 2.92 ppm (d, J = 17, 3 Hz, H-4b), and two meta-coupled aromatic protons on a disubstituted A-ring at δ_H 6.40 ppm (bs, 1H, H-5) and δ_H 6.90 ppm (bs, 1H, H-7). Additionally, the presence of ortho-coupled aromatic protons (δ_H δ 6.80 ppm, d, J = 8.0 Hz, H-3′,5′ and δ_H 7.31 ppm, d, J = 8.0 Hz, H-2′,6′) suggested a *p*-substituted B-ring. The ^{13}C NMR spectrum showed the presence of one carbonyl group (δ_C 175.89 ppm, C-1) characteristic of dihydroisocoumarins (Paraschos et al. 2001; Sahin et al. 2020; Erik, Yaylı, et al. 2021). Moreover, the ^{13}C/APT NMR spectrum for compound **2** revealed 13 carbons (three oxygenated quaternary, three quaternary, and four protonated), one methylene, one oxygenated methine, and one carbonyl. In literature, H-5 and H-7 peaks of thunberginol C have been located at δ_H 6.24 ppm (s, H-5) and δ_H 6.21 ppm (s, H-7) (Yoshikawa et al. 1992, 1996; Rasool et al. 2016; Park et al. 2018; Sahin et al. 2020; Erik, Yaylı, et al. 2021). The ^1H NMR data of 2 for the H-5 and H-7 proton peaks were observed at δH 6.90 ppm and δH 6.40 ppm, respectively, which are shifted downfield, indicating the dimeric form of the dihydroisocoumarin. In addition, the expected C_8-OH peak could not be observed in the ^1H NMR spectrum of **2** due to the chelation of the C_8-OH peak with the C_1 carbonyl group. This clearly showed the bis-linkage at C_8-*O*-$C_{8'}$ position of **2** and named as 8,8′-oxy*bis*[3,4-dihydro-3-(4-hydroxyphenyl)-1*H*-2-benzopyran-1-one. The proton and carbon peaks for the *bis*-aglycone part of compound **2** were found to overlap (Table S1). The bis structure of **2** is also demonstrated by the mass spectrum LC-QTOF-MS ($C_{30}H_{22}O_9$, (*m/z* $[M+H]^+$: 525.28672 (89), calc.: 525.28670)). Compound 2 exhibited no optical activity, indicating that the relative configuration at the C-3 and C-3′ positions of the *bis*-aglycone is R and S, respectively. Consequently, compound **2** was assigned as *rel.* (3*R*,3′*S*)-8,8′-oxy*bis*[3,4-dihydro-3-(4-hydroxyphenyl)-1*H*-2-benzopyran-1-one and given the trivial name as scorzosericol. The literature reports a cyclic form of dimeric phenyl dihydroisocoumarin, previously identified under various names including tragoponol, nitidissimol A/B, trichonoides A, and scorzoaucherioside III (Rasool et al. 2016; Çiçek et al. 2018; Erik, Yaylı, et al. 2021; Wang R et al. 2023). Compound 2 was determined to be a dimeric dihydroisocoumarin, representing a novel class of dimers-phenol ethers-distinct from the previously known macrocyclic dilactone, tragoponol. (Zidorn et al. 2010; Çiçek et al. 2018). NMR, FT-IR, UV-VIS, and LC-QTOF-MS data of **2** are shown in the supplementary data Figures S8-S13.

Compound **3** has five unsaturations with the formula $C_{14}H_{20}O_9$, which was determined from the LC-QTOF-MS (*m/z*) as $[M\text{-}CH_2OH+Na+H]^+$ 325.22673 (100%) (calc. 325.22673). FT-IR spectrum of **3** showed absorption bands at 3280 cm^{-1} (-OH), 1643 cm^{-1} (C=O), and 1450 cm^{-1} (C=C). UV spectra of **3** showed absorption maxima (log Ɛ) at

275 nm (5.0) and 285 nm (5.02). All these data are suggestive of a 4*H*-pyran-4-one glycoside structure (Yaylı et al. 2001; D'Abrosca et al. 2013; Adams et al. 2015; Woo et al. 2017; Tu et al. 2020). The optical activity of **3** was observed as $[\alpha]_d^{24}$ −2.67 (c:0.03 CH_3OH). ^1H NMR spectrum of **3** resulted in singlet peaks at δ_H 8.31 ppm and δ_H 8.18 ppm, which indicated the *O*-olefinic H-2 and H-6 protons of the 3,5-disubstituted-4*H*-pyran-4-one. In addition, a methyl peak was observed at δ_H 1.81 ppm. ^1H NMR data indicated that the aglycone part of **3** was the isomeric form of maltol (Tu et al. 2020; Yaylı et al. 2001) (Table S2). The peak at δ_H 5.96 ppm (d, 1H) was assigned to the anomeric proton of the sugar H-1′ with a coupling constant (*J*) value of 6.36 Hz, indicating that the sugar has an α-glycosidic linkage. All proton and carbon correlations of the glycone moiety of **3** were determined using 2D NMR data (COSY, TOCSY, and HSQC), confirming that it is a five-carbon aldopentose unit. ^{13}C/APT NMR spectrum of the **3** revealed 13 carbon peaks, which were assigned to pyrone ring (5 carbons), one methyl, 5 glycone, 1 CH, and 1 CH_2 peaks. The anomeric carbon signal was observed at δ_C 91.40 ppm (HSQC NMR), and the anomeric proton coupling (6.36 Hz) indicates that the sugar has an *α*-configuration. APT NMR data for the glycone part of **3** showed the *α-D*-xylopyranoside. Two extra -OCH (δ_C 74.01 ppm) and 2x-OCH_2 (δ_C 64.56 ppm) peaks were observed in the ^{13}C/APT NMR spectra of compound 3, which was assigned as glycerol. The Xylose C-4′ carbon peak was observed at δ_C 88.34 ppm, indicating glycerol linked from this position. As a result of 2D COSY, TOCY, HSQC, HMQC data, ACD NMR analysis, and literature comparisons, it was shown that xylose bonded from the C_3 position of 4*H*-pyran-4-one. The NMR data of 3 were highly similar to those of maltol-*β-D*-glucopyranoside (dianthoside), which has been reported in various literature sources (Yaylı et al. 2001; D'Abrosca et al. 2013; Woo et al. 2017; Tu et al. 2020). As a result of all these findings and comparison of literature data, compound **3** was assigned as 3-*O*-(4-*O*-glyceryl)-*α-D*-xylopyranosyl-5-methyl-4*H*-pyran-4-one (*iso*-maltol-4-*O*-(glyceryl)-*α-D*-xylopyranoside) and given the trivial name scorzosericoside II, which was introduced to the literature as a new compound. NMR, FT-IR, UV-VIS, and LC-QTOF-MS data of **3** are shown in supplementary data Figures S14–S23.

Compound **4** was isolated as a white, amorphous solid. The molecular formula, $C_{24}H_{30}O_{11}$, was determined by HR LC-QTOF-MS at *m/z* $[M\text{-}CH_3OH+K]^+$ 501.15678 (100) (calc. 501.15676), which showed ten unsaturations. The FT-IR spectrum of 4 exhibited absorption bands at 3309 cm-1 (–OH), 1643 cm-1 (C=O), 1565 cm^{-1} (C=C), and 1458 cm^{-1}, suggestive of a bibenzyl glycoside structure. UV spectra of **4** showed absorption maxima (logε) at 285 nm (5.95) and 290 nm (5.96). The optical activity of **4** was observed as $[\alpha]_d^{24}$ +3.3 (c: 0.0006 CH_3OH). The ^1H NMR spectrum of **4** showed signals of one *p*-substituted phenyl ring at δ_H 7.05 ppm (2H, d, $J = 8.6$ Hz, H-2′, H-6′) and δ_H 6.65 ppm (2H, d, $J = 8.6$ Hz, H-3′, H-4′), one 1,2,3,5-tetrasubstituted aromatic ring at δ_H 6.33 ppm (1H, bs, H-4) and δ_H 6.22 ppm (1H, bs, H-6), two methylene groups at δ_H 3.16 ppm (1H, m, Hα), δ_H 3.10 ppm (1H, m, Hα′), and δ_H 2.76 (2H, dd, $J = 8.2$, 8.1 Hz, Hβ), one methoxy peak at δ_H 3.82 ppm (3H, s), one -OCH at δ_H 3.70 ppm (1H, m), two -OCH_2 at δ_H 3.52 ppm (4H, m), and one anomeric proton at δ_H 4.76 ppm (1H, d, $J = 7.6$ Hz) (Hashimoto et al. 1988; Fang et al. 2012). Analysis of the ^{13}C NMR and HSQC spectra of compound **4** indicated a total of 21 carbon signals, including seven quaternary carbons, nine methines, four methylenes, and one

methoxy group. Analysis of the NMR data suggested that structure **4** was 2-carboxyl-3,4′-dihydroxy-5-*O*-*β*-*D*-xylopyranosylbibenzyl isolated from *Tragopogon porrifolius* subs. *porrifolius* L. (Zidorn et al. 2005). The ^{13}C-NMR chemical shifts for the sugar unit for **4** are δ_C 102.79, 74.84, 77.82, 71.21, and 67.01, and the multiplicity of the anomeric proton at δ_H 4.76 (d, $J = 7.6$ Hz) is assignable for *β*-*D*-xylopyranosyl (Zidorn et al. 2005) (Table S3). The position of the sugar was assigned at C-5 of **4** by HMBC correlations between xylose H-1′′ (δ_H 4.76) and C-5 (δ_C 160.59) (Figure S30). The location of the methoxy group at C-4′ was proven by HMBC correlations between the methoxy (δ_H 3.82) and C-4′ peak (δ_C 156.74). Two extra -OCH (δ_C 74.01 ppm) and 2x-OCH_2 (δ_C 64.57 ppm) peaks were observed in the 60–80 ppm region of the ^{13}C/APT NMR spectra of **4,** and this group was determined to be glycerol. As a result of the 2D NMR spectra (COSY, TOCSY, HSQC, and HMBC) and literature comparisons, xylose was linked from the C_5 position of the bibenzyl structure, and the glycerol unit was substituted from the C_3 (δ_C 77.82) of xylose. Compound **4** is like cudrabibenzyl A (Zidorn et al. 2005; Sahakitpichan et al. 2017; Shin et al. 2019) and vittarin C (Wu PL et al. 2005). However, it is noted that the glycone unit of cudrabibenzyl A and vittarin C was reported to be glucose. Consequently, the structure of **4** was confirmed by spectroscopic methods and identified as 2-carboxyl-3-hydroxy-4′-methoxy-5-*O*-(3-glyceryl)-*β*-*D*-xylopyranosylbibenzyl, which was given the trivial name scorzosericoside III and introduced to the literature as a new compound. NMR, FT-IR, UV-VIS, and LC-QTOF-MS data of **4** are shown in supplementary data Figures S24–S33.

Compound **5** was obtained as a white amorphous powder, possessing the molecular formula $C_{26}H_{32}O_{14}$ as deduced from the HR-LC-QTOF-MS at *m/z* [M-CH_2OH+Na + H]$^+$ 561.15644(100) (calc. 561.15740). UV absorption (log Ɛ) of **5** was observed at 285(9.52) and 295(10.54) nm. FT-IR spectrum of **5** showed hydroxyl (3309 cm^{-1}), carbonyl (1643 cm^{-1}), and aromatic ring (1549 cm^{-1}). The ^{1}H NMR spectrum of **5** showed signals of one *p*-substituted phenyl ring at δ_H 7.05 ppm (2H, d, $J = 8.6$ Hz, H-2′, H-6′) and δ_H 6.65 ppm (2H, d, $J = 8.6$ Hz, H-3′, H-4′), one 1,2,3,5-tetrasubstituted aromatic ring at δ_H 6.36 ppm (1H, bs, H-4) and δ_H 6.22 ppm (1H, bs, H-6), two methylene groups at δ_H 3.16 ppm (1H, m, Hα), δ_H 3.10 ppm (1H, m, Hα′) and δ_H 2.78 ppm (2H, dd, $J = 8.2$, 8.01 Hz, Hβ), and two anomeric protons at δ_H 4.76 ppm (1H, d, $J = 7.6$ Hz, glucose H-1) and δ_H 5.06 ppm (1H, bs, apiose H-1), assigned to a disaccharide. The ^{13}C/APT NMR and HSQC spectra of **5** gave 24 carbon signals, of which 12 carbons were assigned to a dihydrostilbene moiety; one carbon -COOH; six carbons to a *β*-*D*-glucopyranosyl unit at δ_C 102.24 (C-1), 76.12 (C-2), 78.11 (C-3), 74.10 (C-4), 77.26 (C-5), 65.27 (C-6); and five carbons for a *β*-*D*-apiofuranosyl unit at δ_C 109.48 (C-1), 75.29 (C-2), 80.59 (C-3), 74.69 (C-4), and 64.54 (C-5) (Table S3). Comparison of these NMR data with those of 3,4′-dihydroxydihydrostilbene-5-*O*-*β*-*D*-glucopyranoside (Wu PL et al. 2005; Sahakitpichan et al. 2017; Sahin et al. 2020) indicated the addition of an apiofuranosyl group linked to a glucose at C-6′′. The HMBC correlations between H-2′/H-6′ (δ_H 7.05 ppm) and C-4′ (δ_C 156.71 ppm), H-3′/5′ (δ_H 6.65 ppm) and C-1′ (δ_C 135.37 ppm), between H-4 (δ_H 6.36 ppm) and C-6 (δ_C 109.49 ppm) confirmed positions of the hydroxy groups at C-3 and C-4′. The position of the *β*-*D*-glucopyranosyl moiety at C-5 was confirmed by the HMBC correlation from glucose H-1′′ (δ_H 4.76 ppm) to C-5 (δ_C 160.53 ppm). The position of the apiofuranosyl group at glucose C-6′′ was confirmed

by HMBC correlation from glucose H-6′′ (δH 3.64 and 3.48) to apiose C-1′′′ (δ_C 109.48 ppm). NMR data for the glycone part of **5** revealed an additional terminal sugar as apiose, which was linked to the C-6 position of glucose, a standard disaccharide chain known in natural compounds as apiofuranosyl-(1→6)-glucoside (Sahakitpichan et al. 2017; Korkmaz et al. 2023a, 2023b). The ^{1}H and ^{13}C NMR data for the aglycone part of **5** were found to be superimposable on those of cudrabibenzyl A (Zidorn et al. 2005; Sahakitpichan et al. 2017; Shin et al. 2019) and vittarin C (Wu PL et al. 2005). Based on the above evidence, the structure of **5** was elucidated as 2-carboxyl-3,4′-dihydroxy-5-*O*-[(*β*-D-apiofuranosyl)-(1→6)-*β*-*D*-glucopyranosyl]bibenzyl and given the trivial name scorzosericoside IV, which was introduced to the literature as a new compound. NMR, FT-IR, UV-VIS, and LC-QTOF-MS data of **5** are shown in supplementary data Figures S34–S43. The chemical structures of compounds **1–10** are illustrated in Figures S44.

Several phytochemical investigations on different *Scorzonera* species have led to the isolation of various compounds. For instance: *Scorzonera tomentosa* L.: hydrrangenol-8-*O*-β-D-glucopyranoside, (±)-hydrangenol, (-)-hydrangenol-4′-*O*-β-glucoside, (±)-scorzotomenthosine, and (-)-scorzotomentosin-4′-*O*-β-glucoside (Sari et al. 2007; Acıkara et al. 2015); *Scorzonera divaricata* Turcz.: 7-hydroxycoumarin, scopoletin, and skopolin (Wu QX et al. 2018; Meng et al. 2020); *Scorzonera undulata* ssp. *delicosa* (Guss.) Maire: coumarin-*O*-β-glucoside (Harkati et al. 2010); *Scorzonera latifolia*: (-)-scorzotomentosin-4′-*O*-β-glucoside, (±)-hydrangenol, and hydrrangenol-8-*O*-β-D-glucopyranoside (Çitoğlu et al. 2010; Özbek et al. 2017); *Scorzonera alexandriana*: xanthotoxin and scopoletin (Donia 2016); *S. pseudodivaricata*: scopoletin (Edrada et al. 2006); *Scorzonera judaica* Eig: (±)-scorzotomenthosine, (±)-hydrangenol, (-)-hydrangenol-4′-*O*-β-glucoside, 3S-hydrangenol derivatives (Bader et al. 2011); *S. pygmaea*: scorzopigmecoside, scorzonerol, thunberginol C, scorzocreticoside I–II (Sahin et al. 2020); *S. papposa*: thunberginol G (Milella et al. 2014); *S. cretica*: scorzocretin and scorzocreticosides I–II (Paraschos et al. 2001). These findings demonstrate the rich diversity of secondary metabolites in *Scorzonera* species.

Phenolic acid and glycoside derivatives have been isolated and reported from *S. divaricata* (Edrada et al. 2006; Yang et al. 2013; Meng et al. 2020), *S. radiata* (Wang Y et al. 2012), *Scorzonera aristata* Ramond ex DC. (Jehle et al. 2010), *S. pseudodivaricata* (Tsevegsuren et al. 2007), *Scorzonera tomentosa* L. (Acıkara et al. 2015), *Scorzonera veratrifolia* Fenzl (Sari 2010; Beceren et al. 2016), *Scorzonera baetica*, *Scorzonera austriaca* Willd., *Scorzonera crispatula* (DC.) Boiss., *S. hispanica*, *Scorzonera trachysperma* Guss., *Scorzonera villosa* Scop. (Granica et al. 2015), and *S. latifolia* (Sari 2012). Quercetin was detected by HPLC analysis in *S. latifolia*, *S. suberosa*, and *Scorzonera laciniata* L. species (Erden et al. 2013) and isolated from *Scorzonera columnae* Guss. (Menichini et al. 1994). The presence of quercetin-3-*O*-rhamnohexoside, quercetin-3-*O*-malonylhexoside, quercetin-3-*O*-glucuronide in *S. hispanica* (Granica and Zidorn 2015); quercetin-3-*O*-galactoside from *Scorzonera cinerea* Boiss., *Scorzonera cana* var. *jacquiniana* (W.D.J.Koch) D.F.Chamb., *Scorzonera eriophora* DC., *S. tomentosa*, *Scorzonera parviflora* Jacq., *Scorzonera mollis* ssp. *Szowitsii* (DC.) D.F.Chamb., *S. latifolia* and *S. hispanica* were determined by HPLC (Wang et al. 2009a; Wang et al. 2010; Akkol et al. 2011; Acikara et al. 2013, 2015; Granica et al. 2015; Granica and Zidorn 2015). Bibenzyl derivatives isolated and reported from *S. radiata* (Wang Y et al.

2009a), *S. tomentosa* (Sari et al. 2007), *S. humilis* (Zidorn et al. 2000b; 2002; 2003) and *S. pygmaea* (Sahin et al. 2020). Significant differences were observed in the antioxidant activity and total phenolic content of *S. latifolia* samples collected from Kars, Kayseri, and Bayburt regions. Notably, the samples from the Kars region exhibited lower antioxidant activity and phenolic compound content compared to those from the other regions (Acikara et al. 2017). Natural products belonging to various chemical classes, including sesquiterpene lactones, stilbenoids, lignans, triterpenoids, flavonoids (e.g. apigenin, kaempferol, luteolin, and quercetin), caffeoylquinic acids, and coumarins, have been identified in species of *Scorzonera* (Lendzion et al. 2021). Literature has shown that terpenic and phenolic compounds are abundant in Scorzonera species (Tsevegsuren et al. 2007; Zidorn 2008; Sareedenchai and Zidorn 2010; Erik, Coşkunçelebi, et al. 2021; Korkmaz et al. 2023a, 2023b).

The resistance of microorganisms to antimicrobial agents is recognised as a significant health issue. The use of new antibiotic agents, especially in infectious diseases, can be considered an innovation (Gajdács and Albericio 2019); thus, the use of new antimicrobials is increasing. *Scorzonera* species have been reported to be used in traditional medicine for the treatment of diabetes, hypertension, rheumatism, and wound healing.

In this work, isolated compounds **1–10** were tested against nine microorganisms (Table S4) (Barry 1999; Woods et al. 2011). The antimicrobial activities of isolated compounds **6** (Cho et al. 1998), 9 (Zhang et al. 2023), and 10 (Sinan et al. 2021) against specific microorganisms have been reported in the literature. However, antimicrobial analyses of the other isolated compounds **1–5** and **7–8** were performed for the first time in this study. Some of the isolated compounds showed inhibition in the range of 10–12 mm, depending on the specific microorganisms tested. Inhibition zone of **1** is 10 mm against the *Mycobacterium smegmatis* (ATCC607) and *Candida albicans* (ATCC 60193)*;* **2** is 10 mm against only *Pseudomonas aeruginosa* (ATCC 43288); **3** is 10 mm against the *Escherichia coli* (ATCC 25922), *P. aeruginosa*, and *C. albicans;* **4** is 10 mm against only *P. aeruginosa*; **5** is 10 mm against *E. coli*, *Yersinia pseudotuberculosis* (ATCC 911), and *Staphylococcus aureus* (ATCC 25923); **6** is 10 mm against the *P. aeruginosa*, *S. aureus*; *M. smegmatis* and *C. albicans;* **7** is 10 mm against the *P. aeruginosa* and *C. albicans;* **8** is 10 mm against the *P. aeruginosa* and *Enterococcus faecalis*; **9** is 12 mm against *Bacillus cereus* and *M. smegmatis*; **10** is 8 mm against the *P. aeruginosa* and *S.aureus* (Table S4). It was observed that the isolated compounds were more active against Gram-negative bacteria. The most effective inhibition was observed against *P. aeruginosa* among the tested compounds. The inhibition zones of isolated compounds **1–10** were found to be the most effective antimicrobials against *P. aeruginosa*. When the MIC values of **1–10** were calculated against the *P. aeruginosa*, they were found to be 25 µg/mL, 55 µg/mL, 20 µg/mL, 40 µg/mL, 110 µg/mL, 70 µg/mL, 32.5 µg/mL, 12.5 µg/mL, 20 µg/mL, and 220 µg/mL, respectively. Compound **8** was found to be the most effective with an MIC value of 12.5 µg/mL. Results indicated that the antimicrobial activity of dihydroisocoumarins and bibenzyl derivatives is associated with the presence of free hydroxyl groups or their substitution *via* glycosidic bonds.

Antimicrobial and antifungal activity on the genus *Scorzonera*; using microdilution technique for the ethanol extract and petroleum ether, ethyl acetate, and *n*-butanol

fractions from *S. latifolia,* and *S. veratrifolia* against *S. aureus, S. epidermidis* against *E. coli, K. pneumoniae, P. aeruginosa, Proteus mirabilis, Shigella flexneri, Salmonella typhi,* and *C. albicans* was reported. The ethyl acetate fractions of both *S. latifolia* and *S. veratrifolia* demonstrated the most potent antimicrobial activity against *S. aureus*, exhibiting minimum inhibitory concentration (MIC) values of 19.52 µg/mL and 39.06 µg/mL, respectively. (Sari et al. 2009). The essential oil of *S. undulata* subsp. *deliciosa* demonstrated notable antibacterial activity against both Gram-positive and Gram-negative bacterial strains, except for *Pseudomonas aeruginosa*. However, no antifungal activity was observed (Boussaada et al. 2008). The ethyl acetate and petroleum ether extracts obtained from the roots of *Scorzonera undulata* exhibited antibacterial activity against *S. aureus*, *E. faecalis*, and *Citrobacter freundii*. Notably, the petroleum ether extract demonstrated superior efficacy, with a minimum inhibitory concentration (MIC) of 500 µg/mL against *S. aureus*. Overall, both extracts showed stronger antibacterial activity against Gram-positive bacteria compared to Gram-negative strains (Abdelkader et al. 2010). The methanol extract of *Scorzonera semicana* exhibited the highest phytochemical richness and demonstrated superior antimicrobial activity against *Listeria monocytogenes* and *Klebsiella pneumoniae* compared to the standard antibiotic. Additionally, it demonstrated significant anticancer activity against the LNCaP and HCT-116 cell lines (Keser and Kak 2021). Antimicrobial activity of *n*-hexane, chloroform, ethyl acetate, and ethanol extracts of aerial parts of *Scorzonera sandrasica* Hartvig Et Strid. against *Enterobacter aerogenes, E. coli, P. aeruginosa, Micrococcus luteus, S. aureus, Bacillus subtilis, Streptococcus mutans, C. albicans, C. tropicalis,* and *Stenotrophomonas maltophilia* were reported. Although ethanol and chloroform extracts showed significant antibacterial activity against *S. maltophilia*, no antifungal activity was detected against two fungi (Ugur et al. 2010). Antimicrobial activities of chloroform, ethyl acetate, acetone, ethanol, methanol, and water extracts (containing dimethyl sulfoxide (DMSO) and 5% tween 20) obtained from the roots and leaves of *S. mollis* against *E. coli, S. aureus, B. subtilis, P. aeruginosa, E. cloacae, Proteus vulgaris,* and *C. albicans* were mentioned. While significant antibacterial activity was observed against some gram-positive and gram-negative bacteria in some of the leaf and root extracts, antifungal activity was detected only in ethyl-acetate, ethanol, and acetone extracts obtained from the leaf against *C. albicans* (Ertürk and Demirdağ 2003). Sulfocorzonine D and sulfocorzonine E, glucosaluzanin C, oleanolic acid isolated from *S. divaricata*, loop-20(29)-en-3β,28-diol, (22*E*)-5α,8α-epidioxyergosta-6,22-diene-3β-ol, ergosta-3β,5α,6β-trialcol, sacrolite A, vomifoliol, trans-caffeic acid, *trans-p*-hydroxycoumaric acid, 4-hydroxy-3-methoxyphenyl ferulate, tricine, luteolin, diosmetin, 5,7-dihydroxy-8-methoxyflavone, 5,7-dihydroxy-6-methoxyflavone, methyl-3,4-dihydroxy benzoate, *m*-hydroxy benzoic acid, 7-hydroxycoumarin and scopoletin compounds gram-positive (*Bacillus megaterium, B. subtilis, Clostridium perfringens Micrococcus tetragenus*, MRSA (methicillin-resistant *S. aureus*), RN4220, Mu50, and Newman WT)) and gram-negative (*E. coli*) bacteria were tested for their antimicrobial activity. Sulfocorzonine D exhibited the same antibacterial activity against *C. perfringens* as erythromycin and streptomycin but stronger than ampicillin, with an MIC of 50 µg/mL. Sacrolite A showed more significant activity against Newman WT than streptomycin and ampicillin (Wu QX et al. 2018). Antimicrobial activities of *Scorzonera mackmeliana* Boiss. Antimicrobial activity against *Staphylococcus*, *Enterococcus*, *Escherichia*, and *Pseudomonas* species was

investigated using water and ethanol extracts of whole plants, flowers, stems, leaves, and roots. The stem water extract was found to have the most active activity, with a MIC value of 48.98 mg/mL (Sweidan et al. 2020). The antibacterial activity of ethanol extracts from *S. papposa*, collected in Iraq and Turkey, was tested against *E. faecalis, E. coli, P. aeruginosa*, and *Acinetobacter baumannii* using the agar dilution method. The results showed that the above-ground parts of plant samples collected from Türkiye exhibited high antifungal activity, and the samples collected from Iraq demonstrated high activity against *A. baumannii* (Mohammed et al. 2020). MIC and MBC concentrations of the methanol extract obtained from the aerial parts of *Scorzonera calyculata* were determined, and their antimicrobial activities against *S. aureus, B. subtilis, S. pyogenes, K. pneumoniae, P. aeruginosa,* and *Listeria monocytogenes* were evaluated. The best efficacy was demonstrated against *S. aureus*, with the lowest MIC value reported (Ayromlou et al. 2020). Scorzoaucherioside II and iso-scorzopygmaecoside, isolated from *S. aucheriana*, exhibited anti-tuberculosis activity (MIC, 21.2 µg/mL and 25.6 µg/mL, respectively) (Erik, Yaylı, et al. 2021). In this study, differences were observed in the antimicrobial activities of extracts and pure isolated compounds, as in the literature.

Among the isolated compounds, compound 8 exhibited the most potent antimicrobial activity, with a minimum inhibitory concentration (MIC) value of 12.5 µg/mL against *P. aeruginosa*.

Molecular docking analyses revealed that some of the isolated *G. sericea* compounds exhibit a high binding affinity to the RhlR transcriptional regulatory protein, an activator of numerous genes responsible for the establishment of virulence and biofilm formation in *P. aeruginosa*. The same compounds were also found to have high binding affinity to the catalytic core of *P. aeruginosa* DNA gyrase B, which plays a vital role in DNA replication processes. In this context, especially the compound **2** was found to exhibit the highest binding affinity to *P. aeruginosa* protein RhlR in the presence of low binding free energy (−12.0 kcal/mol) (Table S5). Structural analyses further revealed that compound **2** exhibits a typical key-lock arrangement at the active site of RhlR (Figure S45A,B). Upon examining the binding modes, it was found that compound **2** exhibited a remarkably strong inhibitory potential, characterised by three strong hydrogen bonds to RhlR active site residues, as well as numerous hydrophobic interactions (Figure S45C). Furthermore, the *G. sericea* metabolite of **5** was also identified as having potent inhibitory activity against *P. aeruginosa* RhlR, with a binding free energy of −9.5 kcal/mol and 6 hydrogen bonding potential (Figure S46).

When the isolated *G. sericea* compounds were analysed for their affinity for DNA gyrase B, **2** was again found to be the most promising inhibitory compound for GyrB with a binding free energy of −11.3 kcal/mol (Figure S47). Cartoon and surface visualisations of the targeted protein provided robust data to demonstrate the strong binding potential and consistent localisation of compound **2** in the active site (Figure S47A,B). In-depth binding mode analyses revealed that **2** could potentially form **4** strong hydrogen bonds with the catalytic core residues of GyrB (Figure S47C). Furthermore, among all *G. sericea compounds*, compound **1** was identified as the second highest inhibitory compound for *Pa* GyrB in the presence of a binding free energy of −9.6 kcal/mol (Figure S48). The binding mode analysis revealed that both **2** and **1** resulted in **4** strong hydrogen bonds with the catalytic residues of the *Pa* GyrB protein. Taken together, molecular docking studies provided strong evidence of

the high inhibitory potential of *G. sericea* compounds on both RhlR, the transcription activator of genes responsible for biofilm formation, and the DNA gyrase enzyme, which is involved in DNA replication, transcription, and recombination.

The identified natural compounds (**1–10**) of *G. sericea* were utilised to target two *P. aeruginosa* targets: the transcription factor receptor RhlR, which plays a key role in biofilm formation, and the DNA gyrase subunit B (GyrB) protein, a type II topoisomerase enzyme that catalyses the introduction of negative supercoiling into DNA molecules. *P. aeruginosa* utilises a sophisticated quorum-sensing (QS) network to control virulence, with the RhlR protein playing a central role in this regulatory framework. RhlR, a LuxR-type transcription factor, is activated by its cognate autoinducer, *N*-butanoyl-*L*-homoserine lactone (C4-HSL), produced by the RhlI synthase. Upon binding C4-HSL, RhlR undergoes multimerization, a crucial step for its transcriptional activity, allowing it to regulate a broad array of virulence genes. The RhlI/R system is particularly pivotal in late-stage and chronic infections, where RhlR governs both RhlI-dependent and RhlI-independent gene networks. In the absence of RhlI, RhlR can still function by collaborating with alternative ligands to control target gene expression (Borgert et al. 2022). A key modulator of RhlR activity is PqsE, a thioesterase encoded within the *Pseudomonas* Quinolone Signal (PQS) biosynthesis pathway. Although PqsE is dispensable for PQS production, it is essential for RhlR-mediated virulence. PqsE interacts directly with RhlR, forming a 2:2 protein complex that solubilises and stabilises RhlR, rendering the otherwise insoluble transcription factor active. Structural studies have elucidated the PqsE-RhlR interaction, identifying specific residues crucial for this binding. These findings underscore the unique regulatory role of PqsE in modulating RhlR, highlighting its potential as a target for novel anti-virulence therapies against *P. aeruginosa* (Letizia et al. 2022). Considering the tight interaction between both RhlR and PqsE proteins described here and their importance for *P. aeruginosa* infection, we targeted both proteins for molecular docking studies.

DNA gyrase B (GyrB), another essential enzyme of *P. aeruginosa*, pivotal to DNA replication, transcription, and recombination, has garnered significant attention as a viable target for antibacterial therapeutics. DNA gyrase, a type II topoisomerase, catalyses the introduction of negative supercoils into DNA while alleviating the accumulation of positive supercoils that occur during replication and transcription, rendering it a critical antibacterial target (Cotman et al. 2023). This enzyme is indispensable for multiple stages of DNA replication, including initiation, chain elongation, and termination. Inhibition of gyrase activity, whether through pharmacological inhibitors or temperature-sensitive mutations, results in the arrest of DNA replication; however, the specific step primarily affected by such inhibition often remains unclear. Structurally, DNA gyrase is a heterotetrameric complex composed of two GyrA and two GyrB subunits (A2B2). The identification of natural compounds that inhibit GyrB has the potential to disrupt bacterial DNA replication, ultimately leading to cell death. This mechanism highlights the therapeutic potential of targeting GyrB in the development of novel antibacterial agents (Alotaibi et al. 2024). Although compound 8 showed the highest antimicrobial activity *in vitro*, compound 2 showed the strongest binding affinities in silico against both RhlR (−12.0 kcal/mol) and DNA gyrase B (−11.3 kcal/mol), suggesting potential inhibitory effects through different mechanisms.

3. Experimental

See Supplementary Material.

4. Conclusions

In this study, phytochemical investigations of the ethyl acetate and water fractions of the methanol extract of *G. sericea* led to the isolation of ten compounds, including five previously undescribed natural products. Antimicrobial screening revealed that compounds **2–4** and **6–9** exhibited noteworthy antibacterial activity against *P. aeruginosa* with a 10 mm inhibition zone. Among them, compound **9** showed the most potent inhibition zones (12 mm) against *B. cereus* and *M. Smegmatis*. The inhibition zones of isolated compounds **1–10** were found to be the most effective antimicrobial agents against *P. aeruginosa,* and compound **8** was the most effective, having an MIC value of 12.5 µg/mL. Compound 8 was the most effective antimicrobial agent, demonstrating an MIC value of 12.5 µg/mL against *P. aeruginosa*, while compound 5 showed only moderate activity with a 10 mm inhibition zone and no measurable MIC. The *in vitro* results were further supported by molecular docking analyses, in which compound **2** showed strong binding affinity to both RhlR and DNA gyrase B, key proteins associated with *P. aeruginosa* pathogenicity. These findings suggest that *G. sericea* is a promising source of antimicrobial agents, with compound **2** serving as a valuable scaffold for the development of future antibacterial or anti-virulence therapeutics. Overall, this study provides the first comprehensive insight into the secondary metabolites of *G. sericea* and their potential biological activities. Further studies, including cytotoxicity assays, structure–activity relationship analysis, and *in vivo* evaluations, are warranted better to understand the pharmacological potential of the active compounds. In conclusion, compound 8 demonstrated the most promising antimicrobial activity with a MIC of 12.5 µg/mL, whereas compound 2 showed superior binding affinity in molecular docking simulations, making both compounds potential candidates for further pharmacological evaluation.

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Authors contributions

CRediT: **Gözde Bozdal**: Conceptualization, Project administration, Resources, Validation, Visualization, Writing – original draft, Writing – review & editing; **Büşra Korkmaz**: Methodology, Writing – review & editing; **Murat Emre Abanoz**: Formal analysis, Visualization, Writing – original draft; **Büşra Şahin**: Resources, Writing – review & editing; **Ugur Uzuner**: Methodology, Validation, Writing – original draft; **Arif Bozdeveci**: Methodology; **Serdar Makbul**: Conceptualization, Methodology; **Nurettin Yaylı**: Validation, Writing – original draft, Writing – review & editing.

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