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RESEARCH ARTICLE

Biological Activities of the Endemic Plant *Colchicum figlalii*: Cytotoxic, Antioxidant, and Antimicrobial Properties

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Biological Activities of the Endemic Plant Colchicum figlalii: Cytotoxic, Antioxidant, and Antimicrobial Properties

SUMMARY

Throughout history, plants have been used in the treatment of various diseases, forming the foundation of traditional medicine and inspiring modern pharmaceutical research. In particular, Colchicum species, known for their therapeutic potential, represent an important group of plants considered in both traditional use and modern pharmacology. In this study, the in vitro cytotoxic, antioxidant, and antimicrobial activities of the methanol extract of Colchicum figlalii, an endemic species found in Muğla, Türkiye, were investigated. Cytotoxic effects were evaluated using the MTT assay in prostate (PC-3), liver (Huh-7), colon (HT-29, SW-48, Caco-2), and malignant mesothelioma (CARM-L12 TG3) cancer cell lines. The extract exhibited the lowest IC_{50} values in HT-29 and Caco-2 cells at both treatment times, with IC_{50} values of 4.8 and 4.3 µg/mL, respectively, at 48 h. Antioxidant activity was evaluated using the DPPH radical scavenging assay. Extract solutions prepared at concentrations of 0.4, 0.8, and 1.0 mg/mL showed radical scavenging activities of 82.6 ± 12.3%, 80.9 ± 15.2%, and 80.3 ± 13.5%, respectively, while the corresponding BHA solutions showed activities of 85.7 ± 8.9%, 86.0 ± 9.1%, and 88.8 ± 9.4%, respectively. In antimicrobial assays, the extract produced inhibition zones against several of the tested microorganisms, including 17 mm against Staphylococcus aureus and 14 mm against Candida albicans at 10 mg/mL, whereas no inhibition was observed against Enterococcus faecalis. These findings demonstrate that C. figlalii exhibited cytotoxic, antioxidant, and antimicrobial activities under the experimental conditions used. Overall, these findings provide important evidence regarding the biological activities of C. figlalii under the experimental conditions examined.

Keywords: *Colchicum figlalii, endemic, cytotoxic, antioxidant, antimicrobial.*

Endemik Bitki Colchicum figlalii'nin Biyolojik Aktiviteleri: Sitotoksik, Antioksidan ve Antimikrobiyal Özellikler

ÖZ

Tarih boyunca bitkiler, çeşitli hastalıkların tedavisinde kullanılmış, geleneksel tıbbın temelini oluşturmuş ve modern farmasötik araştırmalara ilham kaynağı olmuştur. Özellikle terapötik potansiyeli ile bilinen Colchicum türleri, hem geleneksel kullanım hem de modern farmakoloji açısından değerlendirilen önemli bir bitki grubunu temsil etmektedir. Bu çalışmada, Muğla, Türkiye'de bulunan endemik bir tür olan Colchicum figlalii'nin metanol ekstraktının in vitro sitotoksik, antioksidan ve antimikrobiyal aktiviteleri araştırılmıştır. Sitotoksik etkiler, prostat (PC-3), karaciğer (Huh-7), kolon (HT-29, SW-48, Caco-2) ve malign mezotelyoma (CARM-L12 TG3) kanser hücre hatlarında MTT testi kullanılarak değerlendirilmiştir. Ekstrakt, her iki uygulama süresinde de HT-29 ve Caco-2 hücrelerinde en düşük IC_{50} değerlerini göstermiş; 48 saatte IC_{50} değerleri sırasıyla 4,8 ve 4,3 µg/mL olarak belirlenmiştir. Antioksidan aktivite, DPPH radikal süpürme testi kullanılarak değerlendirilmiştir. 0,4; 0,8 ve 1,0 mg/mL konsantrasyonlarında hazırlanan ekstrakt çözeltileri sırasıyla %82,6 ± 12,3, %80,9 ± 15,2 ve %80,3 ± 13,5 radikal süpürme aktivitesi gösterirken, karşılık gelen BHA çözeltilerinde bu değerler sırasıyla %85,7 ± 8,9, %86,0 ± 9,1 ve %88,8 ± 9,4 olarak bulunmuştur. Antimikrobiyal testlerde ekstrakt, 10 mg/mL konsantrasyonda Staphylococcus aureus üzerinde 17 mm ve Candida albicans üzerinde 14 mm dahil olmak üzere test edilen çeşitli mikroorganizmalar üzerinde inhibisyon zonları oluşturmuş, buna karşılık Enterococcus faecalis üzerinde herhangi bir inhibisyon gözlenmemiştir. Bu bulgular, C. figlalii'nin kullanılan deneysel koşullar altında sitotoksik, antioksidan ve antimikrobiyal aktiviteler gösterdiğini ortaya koymaktadır. Genel olarak, bu bulgular C. figlalii'nin incelenen deneysel koşullar altında biyolojik aktivitelerine ilişkin önemli kanıtlar sunmaktadır.

Anahtar Kelimeler: *Colchicum figlalii, endemik, sitotoksik, antioksidan, antimikrobiyal.*

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INTRODUCTION

Throughout history, people have relied on natural plants for the management of various diseases and infections. Such practices formed the basis of traditional medicine and later contributed to the emergence of modern pharmacology through natural product–derived therapeutics. In this regard, medicinal plants represent a key link between traditional knowledge and contemporary medicine, as they constitute rich sources of bioactive molecules. These plants contain a wide range of phytochemicals, including alkaloids, flavonoids, phenolic compounds, and tannins (Toplan, Gürer, & Mat, 2016). Among them, *Colchicum* species—well known for their therapeutic properties—occupy an important position in both ethnopharmacological use and modern scientific research (Toplan et al., 2016).

Colchicum is a significant genus within the family Colchicaceae, currently comprising 162 accepted species distributed across Europe, North Africa, and western to central Asia (Keskin, Sonay, & Balos, 2025). The genus is distinguished by specialized morphological characteristics, notably subterranean, bulb-like corms and ovaries that remain below ground during fertilization. Flowers possess six tepals arranged in two distinct whorls (Figure 1.) (Düşen & Sümbül, 2007). In Türkiye, Brickell (1984) documented 26 well-defined and 5 incompletely known species of *Colchicum*, while Düşen (2012) later reported a total of 47 species, 35 of which are endemic to the region (Brickell, 1984; Düşen, 2012; Keskin et al., 2025).

The name *Colchicum* is derived from the ancient region of Colchis on the Black Sea coast, indicating the plant's historical geographical origin. Known as "*kolkikon*" in Anatolia, *Colchicum* species are also referred to as autumn crocus and meadow saffron (Toplan et al., 2016).

The *Colchicum* genus is known to contain tropolone alkaloids, including bioactive compounds such as colchicine, demecolcine, and colchicoside, which have been associated with various pharmacological activities (Al-Fayyad, Alali, Alkofahi, & Tell, 2002). Colchicine, which is photosensitive, loses its tropolone structure upon exposure to light and is converted into its derivative compounds. Colchicine has been detected in different parts of *Colchicum* species; however, higher concentrations have generally been reported in the seeds and bulbs compared with other plant parts (Nasreen, Gundlach, & Zenk, 1997; Ondra, Válka, Vičar, Sütlüpinar, & Šimánek, 1995; Rosso & Zuccaro, 1998).

In one study, Alali et al. (2010) isolated five different colchicinoids from *C. crocifolium*. Among these compounds, a novel colchicinoid analogue, N, N-dimethyl-N-deacetyl-(–)-cornigerin, was identified, and the cytotoxic effects of all five compounds were evaluated against human cancer cell lines. All five isolated compounds showed cytotoxic activity against the tested cancer cell lines (Alali et al., 2010). In a separate study, researchers reported that loss of the tropolone structure of colchicine was associated with a loss of its antitumor activity (Toplan et al., 2016). In addition to its well-established antitumor activity, colchicine has also been reported to exhibit anti-inflammatory properties and has been used in the treatment of various inflammatory disorders, including gout, Familial Mediterranean Fever (FMF), Behçet's disease, and liver cirrhosis (Slămnoiu-Teodorescu et al., 2017; Zemer, Livneh, Danon, Pras, & Sohar, 1991).

The pharmacological properties of *Colchicum* species are not solely associated with tropolone alkaloids; phenolic constituents have also been reported to contribute to their antioxidant capacity and other biological activities. Commonly reported phenolic compounds in this genus include phenolic acids such as vanillin, vanillic acid, p-coumaric acid, and caffeic acid. In addition, flavonoids, particularly luteolin (3′,4′,5,7-tetrahydroxyflavone), have been reported as important components of the bioactive phytochemical profile of *Colchicum* species (Sevim et al., 2010).

Research on *Colchicum figlalii*, an endemic spe-

cies unique to Türkiye, is quite limited. The existing literature contains only a few studies on this plant, such as those investigating its cholinesterase inhibitory activity and DPPH antioxidant capacity (Sevim et al., 2010). In contrast to other *Colchicum* species, the cytotoxic and antimicrobial activities of *C. figlalii* remain insufficiently investigated. Therefore, this study aimed to provide additional data on the biological activities of *C. figlalii* by investigating its cytotoxic, antioxidant, and antimicrobial activities.

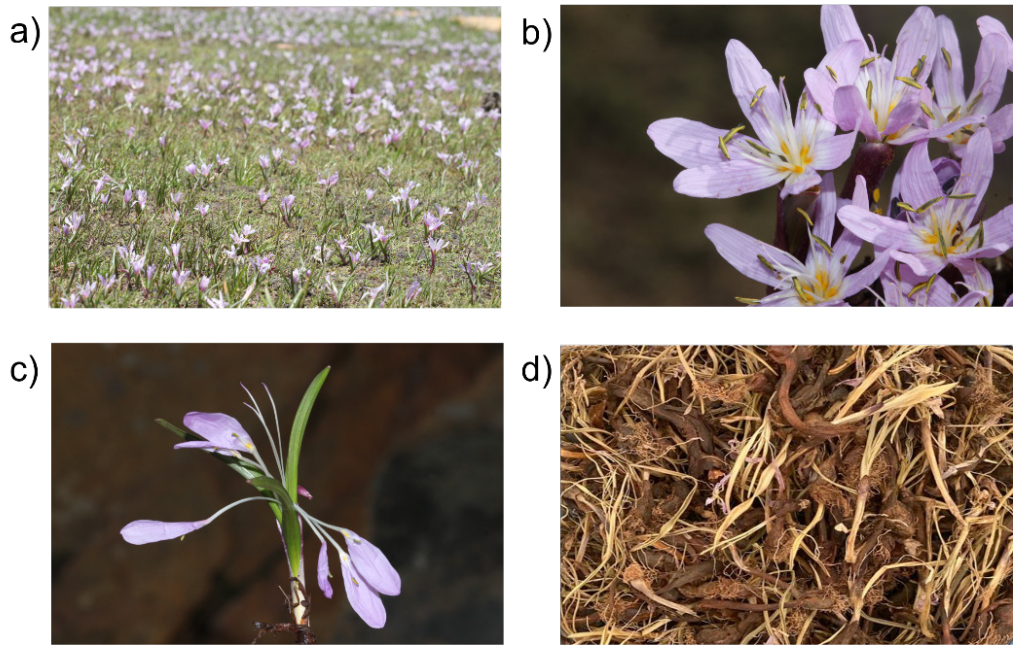

Figure 1. General view and parts of the *C. figlalii* plant. a) A field view of a natural population and habitat of *C. figlalii*, b) A close-up view of the plant's flowers, c) The general morphology of a single *C. figlalii* plant, including its leaves and flower, d) Dried aerial parts and corms of the *C. figlalii* plant

MATERIALS AND METHODS

Plant material

The plant material used in the experimental studies was photographed, collected, and identified by Kenan Akbaş on June 14, 2019, from wet meadows around the Gökçeova Pond on Sandras Mountain (Köyceğiz, Muğla) at an elevation of 1758 m. The corresponding specimen is deposited in the herbarium of Muğla Sıtkı Koçman University under herbarium number K.A.911-6.

Extraction procedure

The extraction procedure was developed by adapting methods from previous studies and optimizing them for *C. figlalii* (Babayeva, Mammadov, Atay, & Çöl, 2025). Briefly, the leaves, stems, and flowers of the plant were dried and then homogenized into a fine powder using a laboratory blender. A 6 g portion of this plant material was mixed with methanol at a 1:15 (w/v) ratio (6 g plant in 90 mL methanol) in Erlenmeyer flasks. Each flask was sealed with Parafilm and aluminum foil, then incubated in a shaker at 150 rpm, 25 °C overnight. To increase extraction efficiency, the residual plant material (marc) was collected after the first extraction, an additional 100 mL of methanol was added, and the extraction process was repeated under the same conditions. The filtrates from the two extraction steps were combined.

The combined filtrate was concentrated by removing methanol under reduced pressure using a rotary

evaporator. The resulting crude extract was re-dissolved in a minimal volume (8.5 mL) of methanol solely to facilitate the complete (quantitative) transfer of the extract from the rotary evaporation flask to a Falcon tube. The extract was briefly sonicated to ensure complete dissolution and quantitative transfer. Subsequently, the Falcon tube was left uncapped in a fume hood at room temperature to allow complete evaporation of the residual methanol. After complete solvent removal, the tube was sealed with Parafilm, frozen at −80 °C, and subsequently lyophilized (freeze-dried). The dried extract was then carefully scraped from the tube, transferred to Eppendorf tubes, and stored at −20 °C until further analysis (Turan & Mammadov, 2018). All procedures were carried out under light-protected conditions to prevent the degradation of light-sensitive compounds.

Cytotoxicity assays

Cell lines and reagents

The experimental protocol utilized a panel of six distinct human cancer cell lines, specifically targeting colorectal (Caco-2, SW-48, and HT-29), liver (Huh-7), prostate (PC-3), and malignant mesothelioma (CARM-L12 TG3) cancers. Every cell line involved in the assays was sourced from the American Type Culture Collection (ATCC, USA). Standard cultivation media, including RPMI-1640 and DMEM, along with fetal bovine serum (FBS), were acquired from Gibco. Additional essential supplements, such as L-glutamine and penicillin-streptomycin, were provided by Capricorn, while Trypsin-EDTA was obtained from Pan-Biotech. Finally, key analytical reagents, comprising MTT, DMSO, trypan blue, and DPBS, were purchased from Sigma-Aldrich.

Cell culture

Cells were cultured in DMEM and RPMI media supplemented with 1% L-glutamine, 10% fetal bovine serum (FBS), and 1% penicillin–streptomycin. DMEM was used for Caco-2, HT-29, Huh-7, and CARM-L12 TG3 cells, whereas RPMI was used for SW-48 and PC-3 cells. Cell cultures were maintained at 37 °C in a humidified incubator with 5% CO_2. When the cells reached 80–90% confluence, they were detached by trypsinization, and cell viability was determined using the trypan blue exclusion method with a Thoma hemocytometer. For the experimental assays, cells were seeded into 96-well plates at a density of 4 x 10^3 cells per well and allowed to attach for 24 h. The culture medium was then replaced with fresh medium containing different concentrations of *C. figlalii* methanol extract (0, 6.25, 12.5, 25, 50, 100, and 200 µg/mL). Doxorubicin (0.625, 1.25, 2.5, 5, 10, and 20 µg/mL) was included as the positive control and applied under the same experimental conditions. The cells were subsequently incubated under identical culture conditions for an additional 48 or 72 h (Öztürkel Kabakaş, Sezer Kürkçü, Onat Taşdelen, & Çöl, 2024).

MTT assay

Cytotoxicity was assessed using the MTT assay (Boyraz, Shekhany, & Süzergöz, 2021). This colorimetric assay measures mitochondrial reductase activity as an indicator of cell viability. At the end of each treatment period, the medium in each well was aspirated, and 200 µL of MTT solution (5 mg/mL in DPBS) was added to each well. Plates were incubated at 37 °C for 4 hours in the dark to allow viable cells to convert MTT into insoluble formazan crystals. Then, 100 µL of DMSO was added to each well and gently mixed to dissolve the formazan. After 15 minutes, the absorbance of each well was measured at 570 nm using a microplate reader. The percentage of viable cells at each extract concentration was calculated relative to untreated controls, and the concentration of extract that inhibited cell growth by 50% (IC_{50}) was determined for each cell line (Çöl, Sezer Kürkçü, & Sorucu, 2021; Öztürkel Kabakaş et al., 2024). Data are presented as mean ± SEM from three independent experiments, each performed in triplicate (Babayeva, Dibek, Kıvrak, & Çöl, 2024).

Statistical analysis

IC_{50} values were calculated from dose–response curves (log concentration versus cell viability) using GraphPad Prism v8.0.1 (GraphPad Software, San Diego, CA, USA) (Babayeva et al., 2024).

Antioxidant activity

DPPH radical scavenging assay

The antioxidant capacity of the extracts was evaluated using the DPPH free radical scavenging assay, and spectrophotometric measurements were performed at a wavelength of 517 nm. A 0.004% (w/v) DPPH solution was prepared by dissolving 0.0011 g of DPPH in 25 mL of methanol. Pure methanol was used as the negative control, while butylated hydroxyanisole (BHA) was used as the positive control. A 1 mg/mL BHA stock solution was prepared by dissolving 0.001 g of BHA in 1 mL (1000 µL) of methanol.

The plant extract and BHA solutions were prepared at three different concentrations (1.0, 0.8, and 0.4 mg/mL). The assay was performed in microplate wells. A volume of 200 µL of DPPH solution was added to each well. Subsequently, 50 µL of methanol was added to the negative control wells, while 50 µL of each prepared extract or BHA solution was added to the respective wells. The reported extract concentrations (1.0, 0.8, and 0.4 mg/mL) refer to the concentrations of the extract solutions before their addition to the assay wells. Since 50 µL of each extract solution was combined with 200 µL of DPPH solution, the final extract concentrations in the wells differed from the initial concentrations. The wells were mixed using a microplate vortex mixer, and the microplate was covered with aluminum foil to protect it from light and incubated in the dark at room temperature for 30 min. Following incubation, absorbance values were measured at 517 nm using a microplate reader.

The DPPH radical scavenging activity (%) of the extracts was calculated using Equation (1) (Ayaz Seyhan, 2019).

$$\%DPPH\ activity = \frac{Absorbance\ Control - Absorbance\ Sample}{Absorbance\ Control} X\ 100 \quad \text{(Eq 1.)}$$

The experiments were conducted as two independent biological experiments, each consisting of three technical replicates. The results are presented as mean ± standard deviation (SD) (n = 6), calculated by combining the data obtained from both independent biological experiments.

Antimicrobial activity

Agar well diffusion method

To evaluate the antimicrobial efficacy of the *Colchicum figlalii* extract, an agar well diffusion technique was employed against a panel of six microorganisms, including *Candida albicans* yeast and five bacterial strains (*Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Enterococcus faecalis*, and *Bacillus subtilis*). Initially, the test strains were revived from cryopreserved stocks (-80 °C) and cultivated overnight at 37 °C to isolate individual colonies. These colonies were then inoculated into 5 mL of LB-Miller broth and kept in a shaking incubator at 37 °C. The resulting cultures were standardized to a 0.5 McFarland turbidity and adjusted to a final concentration of $1x10^8$ CFU/mL using PBS. After spreading these suspensions onto Mueller-Hinton agar, 6 mm diameter wells were created using a sterile punch. Various extract concentrations, ranging from 10 mg/mL down to 0.312 mg/mL, were prepared, and 20 µl of each dilution was carefully introduced into the designated wells. Methanol, the solvent used to dissolve the extracts, was included as the negative control. Kanamycin (Kan) was used as the positive control for *E. coli*, *B. subtilis*, and *S. aureus*, ampicillin (Amp) for *E. faecalis*, and erythromycin (Erm) for *P. aeruginosa*. After a brief period to allow for extract diffusion, the plates were incubated at 37 °C. Following 24 hours of incubation, the diameters of the inhibition zones were measured in millimeters and recorded (Babayeva et al., 2025; Perez, Pauli M., & Bazerque P., 1990).

RESULTS

Cytotoxic activity of *C. figlalii* methanol extract

The cytotoxic effects of the *C. figlalii* methanol extract were evaluated in six different cancer cell lines (HT-29, SW-48, Caco-2, Huh-7, CARM-L12 TG3, and PC-3). Doxorubicin was included as the positive control and evaluated under the same experimental conditions. Cell viability was determined using the MTT assay following treatment with different concentrations of *C. figlalii* methanol extract (0, 6.25, 12.5, 25, 50, 100, and 200 µg/mL) and doxorubicin (0.625, 1.25, 2.5, 5, 10, and 20 µg/mL) for 48 and 72 h. The results were analyzed and plotted using GraphPad Prism 8.0.1 software.

The *C. figlalii* methanol extract reduced cell viability in all tested cancer cell lines, with responses varying according to cell line and treatment duration (Figure 2.).

In the 48 h (panel a) and 72 h (panel b) treatment graphs (Figure 2.), the left panels show the percentage of cell viability, the middle panels present the $\log_{10}$-transformed dose–response curves, and the right panels display the calculated IC_{50} values for each cell line. Cell line abbreviations are indicated within the figure. Data are presented as mean ± SEM from three independent experiments, each performed in triplicate.

Based on the calculated IC_{50} values, different responses were observed among the tested cell lines at 48 and 72 h. HT-29 and Caco-2 cells exhibited the lowest IC_{50} values at both time points. At 48 h, Huh-7 cells showed the highest IC_{50} value, whereas at 72 h, the highest IC_{50} value was observed in CARM-L12 TG3 cells. The IC_{50} values of SW-48 and PC-3 remained within an intermediate range at both treatment times.

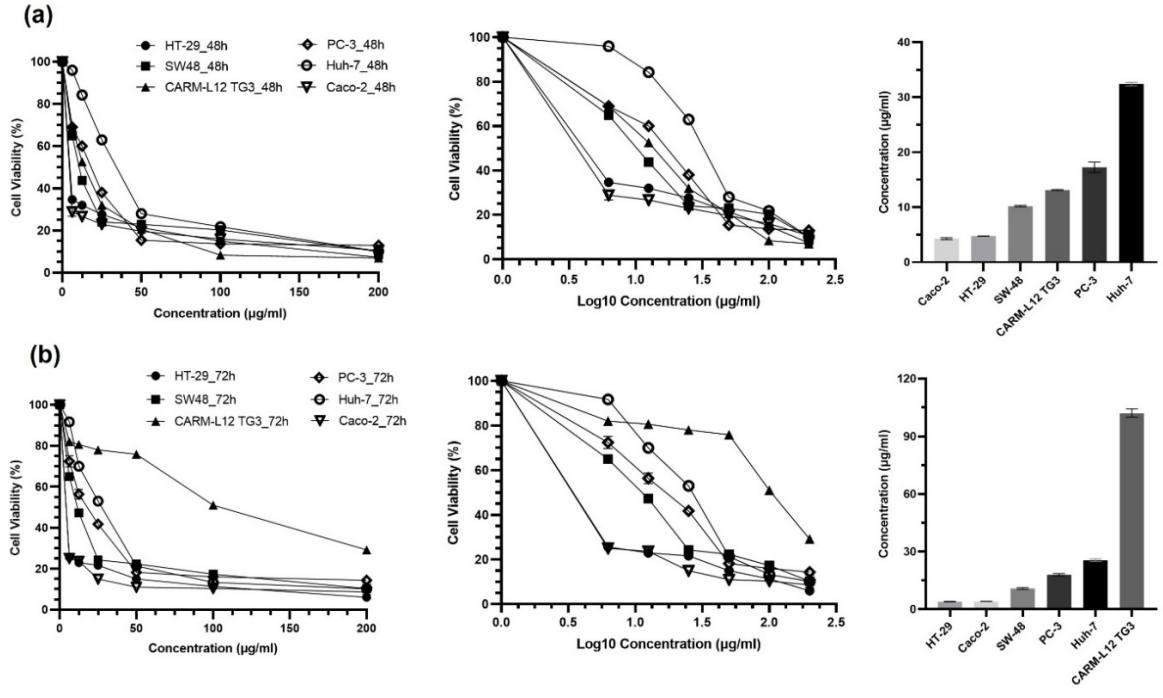

Figure 2. Graphical representation of the cytotoxic effect of *C. figlalii* methanol extract on various cancer cell lines after 48 hours (a) and 72 hours (b) of exposure

The cytotoxic effects of doxorubicin, used as the positive control, are presented in Figure 3. In the 48 h (panel a) and 72 h (panel b) treatment graphs, the left panels show the percentage of cell viability, the middle panels present the log_{10}-transformed dose–response curves, and the right panels display the calculated IC_{50} values for each cell line. For improved visualization of the log_{10}-transformed dose–response curves, doxorubicin concentrations are expressed in ng/mL. Cell line abbreviations are indicated within the figure. Data are presented as mean ± SEM from three independent experiments, each performed in triplicate.

According to the calculated IC_{50} values, doxorubicin showed different cytotoxic responses among the tested cell lines at 48 and 72 h. At 48 h, PC-3 cells exhibited the highest IC_{50} value, followed by Huh-7 cells, whereas CARM-L12 TG3 cells showed the lowest IC_{50} value. At 72 h, CARM-L12 TG3 cells exhibited the highest IC_{50} value, followed by Huh-7 cells, while SW-48 and Caco-2 cells showed the lowest IC_{50} values.

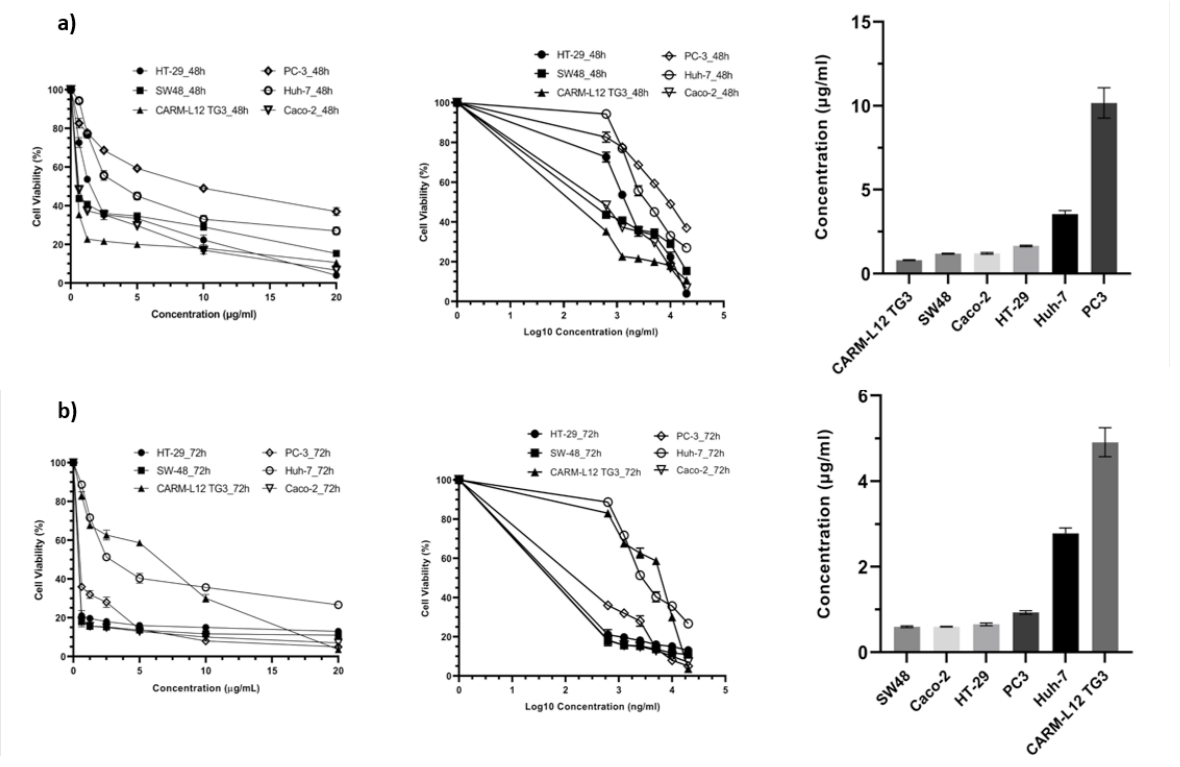

Figure 3. Graphical representation of the cytotoxic effect of doxorubicin on various cancer cell lines after 48 h (a) and 72 h (b) of exposure. Dose–response curves (left), log-transformed dose–response curves (middle), and corresponding IC_{50} values (right) are shown for each cell line.

Doxorubicin concentrations are expressed in ng/mL in the log_{10}-transformed curves

The *C. figlalii* methanol extract exhibited cytotoxic activity against all tested cancer cell lines. In the HT-29 cell line, the IC_{50} values were 4.8 ± 0.02 µg/mL at 48 h and 4.0 ± 0.1 µg/mL at 72 h. Similarly, the Caco-2 cell line exhibited IC_{50} values of 4.3 ± 0.2 µg/mL and 4.1 ± 0.1 µg/mL at 48 and 72 h, respectively. The SW-48 cell line showed IC_{50} values of 10.2 ± 0.1 µg/mL at 48 h and 10.8 ± 0.5 µg/mL at 72 h. In the prostate cancer cell line PC-3, the IC_{50} values were 17.3 ± 0.9 µg/mL at 48 h and 18.0 ± 0.6 µg/mL at 72 h. The liver cancer cell line Huh-7 exhibited IC_{50} values of 32.4 ± 0.3 µg/mL at 48 h and 25.5 ± 0.7 µg/mL at 72 h. In the CARM-L12 TG3 cell line, the IC_{50} value was 13.1 ± 0.1 µg/mL at 48 h and 102.0 ± 2.1 µg/mL at 72 h. The IC_{50} values of the *C. figlalii* methanol extract and doxorubicin are summarized in Table 1.

Table 1. Comparison of IC_{50} values of *C. figlalii* methanol extract and doxorubicin in various cancer cell lines after 48 and 72 h of treatment

Cell Line	*C. figlalii* IC_{50} (µg/mL) at 48 h [a]	Doxorubicin IC_{50} (µg/mL) at 48 h [a]	*C. figlalii* IC_{50} (µg/mL) at 72 h [a]	Doxorubicin IC_{50} (µg/mL) at 72 h [a]
HT-29	4.8 ± 0.02	1.6 ± 0.04	4.0 ± 0.1	0.6 ± 0.03
Huh-7	32.4 ± 0.3	3.5 ± 0.2	25.5 ± 0.7	2.7 ± 0.12
SW-48	10.2 ± 0.1	1.1 ± 0.02	10.8 ± 0.5	0.5 ± 0.02
CARM-L12 TG3	13.1 ± 0.1	0.8 ± 0.02	102.0 ± 2.1	4.9 ± 0.3
Caco-2	4.3 ± 0.2	1.2 ± 0.04	4.1 ± 0.1	0.5 ± 0.008
PC-3	17.3 ± 0.9	10.1 ± 0.9	18.0 ± 0.6	0.9 ± 0.04

[a] IC_{50} (half-maximal inhibitory concentration) values represent the concentrations of *C. figlalii* methanol extract and doxorubicin required to reduce cell viability by 50%. Values are presented as mean ± SEM from three independent experiments, each performed in triplicate. All assays were performed using the MTT cell viability assay. Doxorubicin was used as the positive control.

Antioxidant effect of *C. figlalii* methanol extract

The antioxidant capacity of the *C. figlalii* methanol extract was evaluated using the DPPH free radical scavenging assay. The DPPH radical scavenging activities of the extract solutions prepared at concentrations of 0.4, 0.8, and 1 mg/mL were compared with those of butylated hydroxyanisole (BHA), which was used as the positive control. The results are presented as the mean ± standard deviation (SD) (n = 6), calculated by combining data obtained from two independent biological experiments, each performed in triplicate.

According to the results, the DPPH radical scavenging activities of BHA solutions prepared at concentrations of 1.0, 0.8, and 0.4 mg/mL were 88.8 ± 9.4%, 86.0 ± 9.1%, and 85.7 ± 8.9%, respectively. Under the same experimental conditions, the DPPH radical scavenging activities of the *C. figlalii* methanol extract solutions prepared at the corresponding concentrations were 80.3 ± 13.5%, 80.9 ± 15.2%, and 82.6 ± 12.3%, respectively (Table 2.).

The *C. figlalii* methanol extract exhibited substantial DPPH radical scavenging activity across all tested extract solution concentrations. At the lowest tested concentration (0.4 mg/mL), the extract showed a radical scavenging activity of 82.6 ± 12.3%, compared with 85.7 ± 8.9% for the corresponding BHA solution (Table 2.). Overall, these findings indicate that the *C. figlalii* methanol extract exhibited considerable DPPH radical scavenging activity under the experimental conditions used.

Table 2. DPPH free radical scavenging activity (%) of *C. figlalii* methanol extract versus BHA (positive control) [a]

DPPH free radical scavenging capacity (%)		
Prepared solution Concentration (mg/mL)	BHA (PC) (Mean ± SD)	*C. figlalii* methanol extract (Mean ± SD)
1 mg/mL	88.8% ± 9.4	80.3% ± 13.5
0.8 mg/mL	86.0% ± 9.1	80.9% ± 15.2
0.4 mg/mL	85.7% ± 8.9	82.6% ± 12.3

[a] Values are presented as mean ± SD (n = 6) from two independent biological experiments, each performed in triplicate. BHA (butylated hydroxyanisole) was used as the positive control. The concentrations refer to the prepared BHA and extract solutions prior to addition to the assay wells.

Antimicrobial activity of *C. figlalii* methanol extract

This study also evaluated the inhibitory effect of the *C. figlalii* methanol extract against selected microorganisms, including five bacteria (*B. subtilis*, *E. faecalis*, *E. coli*, *P. aeruginosa*, *S. aureus*) and the yeast *C. albicans*. The extract, tested across concentrations from 0.312 mg/mL up to 10 mg/mL, produced inhibition zones of various diameters on agar plates (Table 3.).

Upon examining the antimicrobial activity results, the *C. figlalii* extract showed microorganism-specific effects. Notably, a distinct inhibition zone of 17 mm in diameter was observed against *S. aureus* at the highest extract concentration (10 mg/mL). Even at a relatively low concentration of 0.625 mg/mL, the extract produced a 10 mm zone of inhibition against *S. aureus*, indicating inhibitory activity against this Gram-positive bacterium (Table 3.). In contrast, the extract showed no detectable inhibition zone against *E. faecalis* at any concentration, suggesting that the extract showed no detectable inhibitory activity against *E. faecalis* under the tested conditions. For *E. coli* (Gram-negative), inhibition zones ranged from 12 mm at 10 mg/mL to 10 mm at 2.5 mg/mL, with no zone at the lower concentrations (≤1.25 mg/mL).

B. subtilis (Gram-positive) also showed inhibition, with a zone of 13 mm at 10 mg/mL, decreasing to 10 mm at 1.25 mg/mL. At the two lowest concentrations, only a negligible inhibition zone of 0.8 mm was recorded, which may fall within the measurement error and was therefore not considered evidence of meaningful inhibitory activity. The yeast *C. albicans* exhibited inhibition zones of 14 mm at 10 mg/mL and 10 mm at the lowest tested concentration (0.312 mg/mL), indicating antifungal inhibitory activity under the tested conditions.

The extract's effect on *P. aeruginosa* (Gram-negative) was limited, with a maximum zone of 11 mm at 10 mg/mL and much smaller zones (≤ 0.8 mm) at lower concentrations, indicating limited activity against this organism (Table 3.). The positive control antibiotics produced inhibition zones of 25 mm for kanamycin against *E. coli*, 21 mm for kanamycin against *B. subtilis*, 20 mm for kanamycin against *S. aureus*, 12 mm for ampicillin against *E. faecalis*, and 11 mm for erythromycin against *P. aeruginosa* (Table 3.). These results served as reference controls for the antimicrobial assay.

Table 3. Inhibition zone diameters (mm) indicating antimicrobial activity of *C. figlalii* methanol extract against various microorganisms [a]

Inhibition zone diameter (mm)							
Microorganism	Concentration (mg/mL)						Positive Control
	0.312	0.625	1.25	2.5	5	10	
E. coli	-	-	-	10 mm	11 mm	12 mm	Kan (25 mm)
B. subtilis	0.8 mm	0.8 mm	10 mm	11 mm	12 mm	13 mm	Kan (21 mm)
E. faecalis	-	-	-	-	-	-	Amp (12 mm)
S. aureus	0.8 mm	10 mm	11 mm	15 mm	15 mm	17 mm	Kan (20 mm)
C. albicans	10 mm	11 mm	12 mm	12 mm	13 mm	14 mm	NC
P. aeruginosa	-	-	0.8 mm	0.8 mm	10 mm	11 mm	Erm (11 mm)

[a] "–" indicates no inhibition zone observed. Values are the diameters of clear zones (in mm) around wells containing the extract at the given concentration. These results represent mean measurements from duplicate plates. NC (Not Included) indicates that no positive control was included for *C. albicans*. Positive controls: Kan, kanamycin; Amp, ampicillin; Erm, erythromycin.

DISCUSSION

Although cytotoxic activity assays for various *Colchicum* species exist in the literature, no prior studies have specifically examined the cytotoxic effects of *C. figlalii*. In our study, we investigated the cytotoxicity of a prepared *C. figlalii* methanol extract on a panel of human cancer cell lines (HT-29, SW-48, Caco-2, Huh-7, CARM-L12 TG3, and PC-3).

The *C. figlalii* methanol extract reduced cell viability in a concentration-dependent manner in all tested cell lines at both 48 and 72 h (Figure 2.). However, the IC_{50} values varied among cell lines and between the two treatment durations. HT-29 and Caco-2 cells exhibited the lowest IC_{50} values at both 48 and 72 h, indicating greater sensitivity to the extract under the experimental conditions used in this study (Table 1.). In contrast, the IC_{50} values of SW-48 and PC-3 were slightly higher at 72 h than at 48 h, while a marked increase was observed in CARM-L12 TG3 cells, from 13.1 ± 0.1 µg/mL at 48 h to 102.0 ± 2.1 µg/mL at 72 h. Therefore, the cytotoxic response did not consistently increase with prolonged exposure across all cell lines.

Considering the relatively lower IC_{50} values observed in the colon cancer cell lines, it is possible that certain bioactive compounds present in *C. figlalii* contribute to the observed cytotoxic activity. To contextualize our findings, we reviewed related studies. Huang et al. (2015) investigated the effect of colchicine-the primary active alkaloid the *Colchicum* genus-on HT-29 human colon cancer cells. They observed a dose-dependent decrease in HT-29 viability and the induction of early apoptosis at a colchicine concentration of 1 µg/mL. Additionally, it has been reported that colchicine treatment in HT-29 cells results in the loss of mitochondrial membrane potential, an increase in intracellular reactive oxygen species (ROS) levels, activation of caspase-3, upregulation of the pro-apoptotic protein BAX, and downregulation of the anti-apoptotic protein Bcl-2. The study indicated that this sequence of events is associated with the activation of the p38 MAPK signaling pathway, and concluded that colchicine induces apoptosis via the mitochondrial (intrinsic) pathway and the p38 signaling cascade (Huang, Xu, & Peng, 2015). Based on these findings, it may be hypothesized that the *C. figlalii* extract could potentially induce apoptosis in colon cancer cells through related mechanisms. However, since the specific compounds responsible for the observed cytotoxic activity were not identified in the present study, this possibility remains speculative and requires further investigation. The lower IC_{50} values observed in the colon cancer cell lines compared with the other tested cell lines indicate that these cells were more responsive to the extract under the experimental conditions used in this study. However, the molecular mechanisms responsible for this differential response remain to be elucidated.

Another relevant study examined the impact of colchicine on the MCF-7 breast cancer cell line. Bakar-Ateş et al. (2018) treated MCF-7 cells with colchicine at concentrations of 0.1, 10, and 100 µg/mL and evaluated cell viability using the MTT assay. They found that colchicine at 10 and 100 µg/mL significantly inhibited MCF-7 cell proliferation and suggested that colchicine may be considered a potential anticancer compound for further investigation (Bakar Ateş, Özmen, Kaya Sezginer, & Kurt, 2018). Collectively, these studies demonstrate that colchicine exhibits cytotoxic activity against different cancer cell types, although the effective concentrations and underlying mechanisms may vary depending on the cell line. Consistent with these findings, the *C. figlalii* methanol extract evaluated in the present study exhibited cytotoxic activity, while the degree of sensitivity differed among the tested cell lines (Alali et al., 2010; Bakar Ateş et al., 2018; Toplan et al., 2016).

Among the cell lines we tested, Huh-7 (liver cancer) was the least sensitive to the *C. figlalii* extract at 48 hours, having a much higher IC_{50} than the other cell lines at that time point (Table 1.). These findings indicate variability in the cytotoxic response among the tested cancer cell lines. Meanwhile, PC-3 (pros-

tate) and SW-48 (colon) showed intermediate IC_{50} values that remained relatively similar between 48 and 72 hours. Thus, the *C. figlalii* extract exhibited cytotoxic activity across different cancer cell types, with sensitivity varying among the tested cell lines (Table 1.). Our results are supported by the literature on the cytotoxic potential of other *Colchicum* species. For instance, Pirildar et al. (2010) reported that methanol extracts of *C. baytopiorum* were cytotoxic to human leukemia cell lines (K562 and HL-60). They found that all methanolic extracts (except seed extract) were more cytotoxic to HL-60 cells (IC_{50} ranging from 6.5 to <0.1 µg/mL) than to K562 cells (IC_{50} ranging from >500 to 44 µg/mL). This indicates some selectivity of *Colchicum* extracts even among cancer cell types (Pirildar et al., 2010).

Similarly, Falahianshafiei et al. (2023) compared the cytotoxic effects of *C. autumnale* extract on MCF-7 breast cancer cells vs. normal human fibroblast (HFF2) cells. After 48 and 72 hours, *C. autumnale* extract had a stronger cytotoxic effect on MCF-7 cancer cells than on normal fibroblasts. Moreover, *C. autumnale* extract's potency was comparable to that of the chemotherapy drug doxorubicin in the same study. These reports suggest that certain *Colchicum* species extracts may exhibit cytotoxic activity and, in studies where both cancer and normal cell lines were evaluated, a degree of selectivity toward cancer cells has also been reported (Falahianshafiei, Akhtari, Davoodi, & Pasha, 2023).

An interesting observation in the present study was the marked increase in the IC_{50} value of the CARM-L12 TG3 cell line after 72 h of treatment compared with 48 h. This finding suggests that prolonged exposure to the extract may be associated with changes in the cellular response. Similar observations have been linked to several adaptive mechanisms reported in cancer cells, including enhanced drug metabolism, increased drug efflux, and alterations in cell-cycle regulation (Dewanjee et al., 2017; Liu, Wang, Xia, & Li, 2024; Pandey et al., 2024; Shah & Schwartz, 2001). However, the molecular mechanisms underlying this observation were not investigated in the present study and therefore require further experimental validation.

Overall, the IC_{50} data indicate that HT-29 and Caco-2 cells were the most responsive to the *C. figlalii* extract at both treatment times, whereas Huh-7 cells showed the highest IC_{50} value at 48 h. At 72 h, CARM-L12 TG3 cells exhibited the highest IC_{50} value, with a marked increase compared with 48 h. SW-48 and PC-3 showed relatively similar IC_{50} values between the two treatment durations. These findings indicate that the cytotoxic response to the *C. figlalii* methanol extract varied among the tested cell lines and treatment durations (Table 1.). Further studies are needed to identify the bioactive compounds responsible for the observed effects and to elucidate their underlying molecular mechanisms.

Oxidative stress arises when the physiological equilibrium between oxidants and antioxidants is disrupted, acting as a critical factor in oncogenesis and tumor progression (Birben, Sahiner, Sackesen, Erzurum, & Kalayci, 2012). In this study, in addition to cytotoxicity, the antioxidant potential of the *C. figlalii* methanol extract was assessed using the DPPH free radical scavenging assay. Our results (Table 2.) show that the *C. figlalii* methanol extract possesses considerable free radical scavenging activity in the DPPH assay. The extract solutions prepared at concentrations of 0.4, 0.8, and 1.0 mg/mL showed DPPH radical scavenging activities of 82.6 ± 12.3%, 80.9 ± 15.2%, and 80.3 ± 13.5%, respectively, while the corresponding BHA solutions showed activities of 85.7 ± 8.9%, 86.0 ± 9.1%, and 88.8 ± 9.4%, respectively. These findings indicate that the *C. figlalii* methanol extract exhibited DPPH radical scavenging activity within a range comparable to that observed for BHA under the experimental conditions used. The observed antioxidant activity may be associated with the presence of bioactive compounds capable of scavenging free radicals; however, the specific compounds responsible for this activity were not identified in the present study.

Further phytochemical characterization is therefore required to determine the compounds contributing to the observed antioxidant activity.

When the antioxidant results are considered together with the cytotoxic findings, *C. figlalii* appears to exhibit multiple biological activities. The cytotoxic activity observed in the present study indicates that the methanol extract can reduce the viability of the tested cancer cell lines, while the DPPH assay demonstrated its free radical scavenging activity. Although the simultaneous observation of cytotoxic and antioxidant activities may appear contradictory, plant extracts contain complex mixtures of bioactive compounds that may exert different biological effects. Oxidative and redox-related processes may also influence cellular responses to bioactive compounds (Gould & Templin, 2023). However, the specific mechanisms underlying the observed cytotoxic and antioxidant activities could not be determined in the present study.

Previous studies have shown that *Colchicum* species generally exhibit antioxidant activity; however, the level of activity may vary considerably depending on the species, plant organ used, and extraction method. Researchers investigated the DPPH radical scavenging activities of methanol extracts prepared from the bulbs and seeds of 49 *Colchicum* taxa, including *C. figlalii*, collected from different regions of Türkiye, and reported a DPPH radical scavenging activity of 29.00 ± 2.45% for *C. figlalii* (Sevim et al., 2010). In contrast, the methanol extract prepared from the aerial parts (leaves, stems, and flowers) of *C. figlalii* in the present study exhibited DPPH radical scavenging activities exceeding 80% at all tested extract solution concentrations, and these values were substantially higher than those previously reported by Sevim et al. (2010). This difference may be attributed to variations in the plant organs used, extraction procedures, and environmental conditions (such as season, soil characteristics, and habitat); all of these factors may influence the phytochemical composition of plant extracts.

In a different study, researchers reported that the antioxidant activity of ethanol extracts of *C. autumnale* varied depending on the plant organ used. The extract prepared from the corms exhibited approximately 34% DPPH radical scavenging activity, whereas the flower extract showed approximately 52% scavenging activity (Slămnoiu-Teodorescu et al., 2017). These findings indicate that different organs of the same plant may possess different antioxidant capacities.

Similarly, Mammadov et al. (2009) prepared extracts from the leaves and corms of *C. balansae* using different solvents and reported that the ethanol extract prepared from the leaves exhibited higher antioxidant activity (64% DPPH radical scavenging activity) than the extracts obtained from the underground organs. In addition, Özcan et al. (2020) reported that the aerial parts of *C. turcicum* and *C. bornmuelleri* exhibited higher antioxidant activity than their corms. These findings are consistent with the antioxidant activity observed in the present study and highlight the potential contribution of plant material and extraction conditions to the antioxidant properties of *Colchicum* extracts.

Indeed, Karakaya et al. (2022) demonstrated that the leaf extract of *C. speciosum* possessed the highest total phenolic content and the strongest antioxidant activity among the different plant parts examined. These findings further support the potential contribution of aerial plant parts to the antioxidant activity observed in some *Colchicum* species.

In summary, the methanol extract of *C. figlalii* exhibited cytotoxic activity against the tested cancer cell lines and demonstrated considerable antioxidant activity in the DPPH assay. These findings suggest that bioactive constituents may contribute to the observed biological activities of *C. figlalii*. However, further studies involving phytochemical characterization, mechanism-of-action analyses, and evaluation in normal cell lines and in vivo models are required to better understand the biological properties and potential applications of *C. figlalii*.

In this study, the antimicrobial activity of *C. figlalii* extract was also investigated, and this activity is reported for the first time for this species. The extract showed inhibitory activity against several of the tested microorganisms. Against *S. aureus*, the *C. figlalii* extract produced a 17 mm inhibition zone at 10 mg/mL, while the kanamycin positive control produced a 20 mm inhibition zone. Similarly, against *B. subtilis*, the extract produced a 13 mm inhibition zone at 10 mg/mL, whereas kanamycin produced a 21 mm inhibition zone. For *E. coli*, the extract produced a 12 mm inhibition zone at 10 mg/mL compared with 25 mm for the kanamycin positive control. Against *P. aeruginosa*, the extract produced an 11 mm inhibition zone at 10 mg/mL, which was the same diameter as the inhibition zone observed for the erythromycin positive control. No inhibition was observed against *E. faecalis*, whereas the ampicillin positive control produced a 12 mm inhibition zone (Table 3.). These findings demonstrate that the *C. figlalii* extract exhibited inhibitory activity against several of the tested microorganisms under the experimental conditions used.

When considering studies conducted on *Colchicum* species, Mammadov et al. (2009) reported that the ethanol extract of *C. balansae* (a related species) produced a 10 mm inhibition zone against *S. aureus* (ATCC 25923). In this study, the extract was applied at a volume of 20 µL to 6 mm-diameter discs using the disc diffusion method. In another study, the methanol extract of *C. luteum* was reported to exhibit approximately 58% inhibition against *B. subtilis* in a turbidity-based assay (Ahmad, Khan, Bashir, & Ali, 2006). When the findings of the present study were evaluated, the methanol extract of *C. figlalii* produced inhibition zones of 17 mm against *S. aureus* and 13 mm against *B. subtilis* at a concentration of 10 mg/mL (Table 3.). Although the methodologies and measurement parameters used in these studies differed, these reports provide additional evidence of antimicrobial activity among the investigated *Colchicum* species.

Against Gram-negative bacteria, the *C. figlalii* extract showed inhibitory activity under the tested conditions, producing inhibition zones of 12 mm against *E. coli* and 11 mm against *P. aeruginosa* at a concentration of 10 mg/mL. Özcan et al. (2020) reported a 7 mm inhibition zone against *E. coli* for *C. turcicum* extract using the disc diffusion method. However, differences in the diffusion methods and experimental conditions limit the direct equivalence of the results between the two studies. Nevertheless, these findings indicate that the *C. figlalii* extract exhibited inhibitory activity against the tested Gram-negative bacteria under the experimental conditions used.

When evaluating the antifungal activity of *Colchicum* species, previous researchers reported that the flower extract of *C. coum* produced an 11 mm inhibition zone against *C. albicans* using the disc diffusion method (Özcan, Semerci, & Tunç, 2020). In the present study, the *C. figlalii* extract produced a 14 mm inhibition zone against *C. albicans* at a concentration of 10 mg/mL and a 10 mm inhibition zone even at the lowest tested concentration of 0.312 mg/mL (Table 3.). In another study, researchers reported that ethanol and aqueous extracts of *C. luteum* corms exhibited antifungal activity against *Colletotrichum* and *Fusarium* species, producing inhibition zones of approximately 17–19 mm at high concentrations (Rather et al., 2022). However, these studies were conducted using different fungal species and different experimental methodologies. Therefore, the results of these studies should be considered as findings reported in the literature regarding the antifungal activity of *Colchicum* species rather than being directly compared. A limitation of the present study is that a reference antifungal agent was not included as a positive control for *C. albicans*. Therefore, the observed inhibition should not be interpreted as a comparative measure of antifungal efficacy. Rather, these findings should be considered as preliminary evidence of the potential antifungal activity of the *C. figlalii* extract under the tested experimental conditions.

On the other hand, the *C. figlalii* extract did not show inhibition against *E. faecalis* at any concentration tested in our experiments. The specific reason for the lack of inhibition against *E. faecalis* could not be determined within the scope of the present study. This finding indicates that the antimicrobial activity of the extract varied among the tested microorganisms under the experimental conditions used.

In conclusion, the methanol extract of *C. figlalii* exhibited antimicrobial activity against several tested microorganisms, including Gram-positive bacteria, a Gram-negative bacterium, and a yeast, while no activity was observed against *E. faecalis*. These findings indicate that the antimicrobial activity of the extract varied among the tested microorganisms under the experimental conditions used. Identifying the specific compounds responsible for these effects and elucidating their mechanisms of action will be important areas for future research. Further phytochemical and biological studies may help to clarify the compounds and mechanisms underlying the observed antimicrobial activity of *C. figlalii*.

CONCLUSION

This study indicates that *C. figlalii* exhibits cytotoxic, antioxidant, and antimicrobial activities under the experimental conditions used. The lower IC_{50} values observed in the colon cancer cell lines and the DPPH radical scavenging and antimicrobial activities observed in this study highlight the biological potential of the species. However, the specific bioactive compounds responsible for these activities were not identified in the present study. Further investigations involving phytochemical characterization, structural identification of the compounds present in the extract, and elucidation of their mechanisms of action are therefore warranted. Such studies may provide a better understanding of the biological properties and potential applications of *C. figlalii*.

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AUTHOR CONTRIBUTION STATEMENT

TK, ÇY, and AB carried out the experimental studies. The endemic plant used in the study was collected from the field, photographed, and provided by KA. The manuscript was written by TK. ED and BÇ supervised the study and contributed to data analysis and interpretation, providing important scientific revisions. All authors reviewed and approved the final version of the manuscript.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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