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Research Article

Cyperus fuscus: A natural source for anti-aging via elastase and collagenase inhibition

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Abstract: The skin is the largest organ and protects against extrinsic factors while maintaining essential functions. Skin aging, influenced by pollution, ultraviolet radiation, stress, and unhealthy habits, involves intrinsic and extrinsic processes that degrade collagen and elastin fibers. This study examined *Cyperus fuscus*—a medicinal plant from the Cyperaceae family—for its potential to slow skin aging by inhibiting elastase and collagenase activity. Biological assays assessed the plant's enzyme inhibition, while GC-MS profiling identified active compounds. *C. fuscus* extracts significantly inhibited elastase and collagenase activity. Methanol extracts had the strongest elastase inhibition, with underground-derived methanol extracts showing 35.39% inhibition at 2 µg/mL. For collagenase, underground methanol extracts had the greatest inhibitory effect (62.46% at 2 µg/mL), while the aerial water extract showed the lowest effect (22.21% at 2 µg/mL). Antioxidant assays confirmed high phenolic content, particularly in methanol extracts from aerial parts of the plant. The DPPH assay revealed antioxidative potential, with water extracts performing similarly to synthetic antioxidants. GC-MS analysis identified bioactive compounds, including benzoic acid, ginsenol, and hexadecanoic acid, suggestive of the plant's therapeutic properties. These findings suggest *C. fuscus* as a promising natural anti-aging agent; however, further research is required to confirm its clinical potential.

INTRODUCTION

The skin is the body's largest organ and its primary function is to act as a barrier between the body's intrinsic and extrinsic environments (Kendall & Nicolaou, 2013). Human skin supports all physicochemical phenomena required for life internally and acts as a protective shield against external mechanical forces. Furthermore, the skin is a sensitive organ that is susceptible to infections and diseases. Skin aging has become an important issue in recent years; accordingly, the number of studies on this subject is increasing and gaining importance.

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Environmental pollution, excessive ultraviolet (UV) radiation exposure, harmful microorganisms, age, dietary habits, stress, and chemicals can all cause skin problems. Premature skin aging is a leading cause of serious skin problems worldwide. Skin aging falls within two categories: intrinsic or extrinsic aging. Intrinsic aging, also known as natural aging, is caused by changes in skin elasticity in time. Extrinsic skin aging is caused primarily by exposure to solar radiation. Free radicals produced by oxidative stress are important for both intrinsic and extrinsic aging (Lavker, 1995). The epidermis, dermis, and subcutis are the three main layers of human skin. Collagen and elastin fibers are the primary components of the dermis and wrinkles form due to a decrease in these fibers (Xu *et al*., 2008). The breakdown of elastin and collagen is the primary cause of sagging skin and wrinkle formation. Collagenase and elastase enzymes are responsible for the breakdown of collagen and elastin respectively, both of which are extracellular matrix (ECM) components. Elastin is a protein that keeps the skin supple and taut and helps the skin return to its original position after being stretched. Collagen is a unique fibrous protein with high tensile strength, which gives skin its firmness. Wrinkles are caused by a combination of intrinsic and extrinsic aging, and increased levels of collagenase and elastase (Fisher *et al*., 1997). The effect of UV irradiation on extrinsic damage is well established and is commonly referred to as photoaging (Sveikata *et al*., 2011). UV irradiation damages DNA and causes oxidative stress by producing reactive oxygen species (ROS) (Brem *et al*., 2010; Rinnerthaler *et al*., 2015). These damages increase the synthesis and activity of proteases, which degrade the ECM that contains collagen and elastin fibers (Cavinato *et al*., 2017; Fisher *et al*., 1997; Takeuchi *et al*., 2010). Recent studies have shown that long-term skin aging causes spots and wrinkles, even when exposed to normal amounts of light UV as opposed to excessive sunburn (Miyamoto *et al*., 2017). As a result, in addition to traditional sunscreens that protect the skin from UV light, supplements that suppress ROS formation by absorbing or reflecting UV light along with activating ECM-degrading proteases have received a lot of attention. Skincare cosmetics treat the epidermal surface layer, providing better environmental protection than untreated skin (Antczak *et al*., 2001). In particular, there is a growing demand for facial skincare cosmetics. According to Gasco-Buisson (2015), the global skincare market was projected to reach $82 billion by 2012, driven by rising consumer demand and anti-aging trends. Two-thirds of these consumption expenditures were for facial skincare, and the segment is expected to continue to dominate the market. The increasing demand for anti-aging products, and the growing concern about the use of natural and organic skincare products, are the main factors driving the skincare industry in this context (Raghavan, 2013). Cosmetics alone are insufficient for skin and body-part care; active ingredients should be combined to control skin damage and aging. As a result, herbal actives containing active ingredients are crucial for maintaining skin health. Cosmetics containing herbal actives are emerging as a viable solution to the current issue (Datta & Paramesh, 2010). Plants contain various compounds, including polyphenols, such as flavonoids, tocopherols, phenolic acids, and tannins, which provide collagenase inhibiting compounds or a platform on which active molecules can be synthesized. Numerous studies have analyzed plant secondary metabolites and entire extracts and have shown that they contain anti-collagenase and anti-elastase properties (Pientaweeratch *et al*., 2016; Thring *et al*., 2009; Younis *et al*., 2022). Anti-elastase activity in plants refers to the ability of plant-derived compounds to inhibit the activity of elastase enzymes. Elastase is a protease enzyme that breaks down elastin, a protein found in elastic tissues, such as the lungs and skin. Overactive elastase activity can lead to tissue damage and is implicated in various diseases, such as emphysema and dermatitis. Therefore, plant-derived compounds that exhibit anti-elastase activity might have potential therapeutic applications (Liu *et al*., 2021). Collagenase is an enzyme that breaks down collagen, and excessive collagenase activity can lead to tissue damage and aging. Many plants produce compounds that have been shown to inhibit collagenase activity and therefore, could have anti-aging and wound healing properties (Thring *et al*., 2009).

Cyperus, a genus of the Cyperaceae family, is a well-known medicinal plant that has been used in traditional medicine for various ailments. Particularly, *Cyperus rotundus* (commonly known as nagarmotha or nut grass) is recognized for its anti-inflammatory, analgesic, and antipyretic properties. Singh *et al*. (2020) investigated the pharmacological effects of *C. rotundus* and reported its anti-inflammatory, antipyretic, and analgesic activities (Singh *et al*., 2020). Seo *et al*. (2019) reported that methanol extracts of *C. rotundus* rhizomes inhibited nitric oxide and superoxide production in RAW 264.7 cell lines, demonstrating their potential as an anti-inflammatory agent (Seo *et al*., 2019). Gupta *et al*. (2018) explored the anti-inflammatory, antipyretic, and analgesic activities of bioactive compounds isolated from *C. rotundus* and found significant and positive effects (Gupta *et al*., 2018). Kilani *et al*. (2017) evaluated the antibacterial, antioxidative, cytotoxic, and apoptotic activities of *C. rotundus* infusions and extracts *in vitro*, confirming its therapeutic potential (Kilani *et al*., 2017). Thebtaranonth *et al*. (2016) isolated antimalarial sesquiterpenes from *C. rotundus* rhizomes, highlighting its potential for treating malaria (Thebtaranonth *et al*., 2016). In recent years, *Cyperus* species have gained increasing attention as a promising source of natural compounds with anti-aging, anti-inflammatory, and antioxidative properties. Specifically, some *Cyperus* species contain compounds exhibiting potent antioxidative activity. Moreover, members of the *Cyperus* genus have been used to alleviate pain, fever, diarrhea, dysentery, and other digestive issues (Umerie & Ezeuzo, 2000). The presence of quinones (Nassar *et al*., 2007; Abdel-Razik *et al*., 2005), flavonoids (Chau *et al*., 2013), and sesquiterpenes (Xu *et al*., 2008) distinguishes *Cyperus* species from other plant genera, highlighting their unique biochemical profile. The chemical makeup of essential oils from several *Cyperus* species has been described, with monoterpenes and sesquiterpenes being the most common molecules found in oil samples (Feizbakhsh *et al*., 2012; Aghassi *et al*., 2013; Nassar *et al*., 2015).

The purpose of this study was to investigate the inhibitory effects of the methanol extract of *C. fuscus* on elastase and collagenase activity, and the biological activities of this extract, which could be developed into anti-aging treatments for human skin.

METHOD

Plant Material and Preparation of Extracts

C. fuscus samples were collected from Adana, Türkiye, during the autumn season when the plant's vegetation period was under stress. The plant parts were air-dried and cut into small pieces. 10 g of dried plant material was extracted with 200 mL of methanol and distilled water. A rotavapor (Heidolph, Laborota 4000) was used to concentrate the extract at a temperature less than 50°C under reduced pressure.

Enzyme Assays

Anti-elastase assay

Anti-elastase activity was established using a modified version of the method described by Kraunsoe (1996). In the first step, 25 µL of 0.1 M HEPES buffer (pH 7.5) was added to each well of a 96-well plate, followed by 25 µL of plant extracts (ie, 1 µg/mL, 1.5 µg/mL, and 2 µg/mL), and lastly, 25 µL of elastase enzyme (1 µg/mL). For the negative control, 75 µL of HEPES buffer was loaded and for the negative control, 25 µL of elastase enzyme and 50 µL of HEPES buffer were loaded. For the experimental groups, the solvent control used the same dilution of plant extract, after which the plate was incubated at room temperature for 20 minutes. Then, 100 µL of substrate (N-methoxysuccinyl-Ala-Ala-Pro-Val-pnitroanilid) at a concentration of 1 mM was added, and the plate was incubated for an additional 40 minutes at 25°C. The absorbance was measured at 405 nm using an ELISA plate reader.

$$\% \text{ of inhibition} = [(A \text{ control} - A \text{ sample}) / A \text{ control}] \times 100$$

Anti-collagenase assay

The anti-collagenase activity was determined using a modified protocol according to Barrantes and Guinea (2003). First, 25 µL of elastase enzyme (0.8 units/mL) and 50 mM Tris buffer (pH 7.5) were added to each well of a 96-well plate, followed by 25 µL of plant extract (ie, 1 µg/mL, 1.5 µg/mL, and 2 µg/mL). DMSO was used as a negative control. For the positive control, 25 µL of elastase enzyme, 25 µL of Tris buffer, and 25 µL of N-methoxysuccinyl-Ala-Ala-ProCholoro (10 µg/mL) were used. After 15 minutes of incubation, 50 µL of substrate (N-(3-[2-furyl]acryloyl)-Leu-Gly-Pro-Ala) was added. The absorbance was measured at 340 nm using an ELISA plate reader. The percentage inhibition was calculated using the formula:

$$\% \text{ of inhibition} = 100 - [(A \text{ sample} / A \text{ control}) \times 100]$$

Antioxidant Assays

The DPPH (2,2-diphenyl-1-picrylhydrazyl) radical scavenging activity was applied by modifying the DPPH method (Sharma & Bhat, 2009). The DPPH solution was prepared fresh in methanol at 250 µM and protected from light. Extract stock solutions were diluted to 5 mg/mL. Ascorbic acid (used as a positive control) was prepared in methanol at of 100 µg/mL. Each sample was analyzed with its own blank sample, and experimental samples and positive controls were tested in duplicate. The plate was then incubated in the dark at room temperature for 30 minutes prior to absorbance measurement. The absorbance was then measured at 520 nm. The DPPH radical scavenging activity was calculated in terms of DPPH inhibition using the following formula:

$$\% \text{ of DPPH inhibition} = [As (As - Ab] / Ac \times 100$$

Ac=control absorbance, As=sample absorbance, Ab=blank

The total phenolic content was established using the Folin–Ciocalteu method (Marinova, 2005) adapted for a 96-well plate. Plant extracts were diluted with DMSO at different concentrations ranging 0.1–5 mg/mL. For each well, 10 µL of sample, standard, or blank was mixed with 90 µL of distilled water, followed by the addition of 10 µL of the Folin–Ciocalteu reagent (FCR). The mixture was shaken for 5 minutes at room temperature. Subsequently, 100 µL of 7% sodium carbonate (Na_2CO_3) and 40 µL of distilled water were added to each well, and the plate was incubated at room temperature for 90 minutes. Then, the absorbance of the mixture was measured at 760 nm. Gallic acid was used as the calibration standard, and the total phenolic content of the extracts was expressed as mg of gallic acid equivalents (GAE) per gram of extract.

Gas Chromatography-Mass Spectroscopy (GC-MS) Analysis

The chemical composition of *C. fuscus* extracts in methanol, and distilled water was determined using gas chromatography-mass spectrometry (GC-MS; Shmadzu, QP2010 Ultra). The GC-MS analysis was performed using a capillary column (30 m × 0.25 mm i.d., 0.25 µm film thickness). Helium was used as the carrier gas at a constant flow rate of 0.90 mL/minute. The oven temperature program was set as an initial hold at 60°C for 2 minutes, followed by a linear increase at a rate of 1°C per minute to a final temperature of 280°C.

RESULTS

In this study, we used methanol and water extracts of *C. fuscus* to investigate its potential anti-aging effect using elastase and collagenase inhibition assays. Additionally, we conducted an antioxidant activity assay and performed GC-MS analysis to identify potential anti-aging compounds present in the extracts. We found that the methanol extract yields of the underground and aerial parts of *C. fuscus* species were higher compared with the water extract yields.

We assessed the extracts' anti-aging capabilities by evaluating their ability to inhibit elastase and collagenase activities (Tables 1 and 2). The extracts obtained from both the underground

and aerial parts of *C. fuscus* inhibited both collagenase and elastase in a dose-dependent and solvent-dependent manner. These findings align with previous studies highlighting the role of natural plant extracts in protecting skin integrity and delaying aging-related structural degradation (Smith *et al*., 2020; Lee & Kim, 2019). The significant enzyme inhibition observed in this study suggests that *C. fuscus* could contribute to skin elasticity and firmness by reducing enzymatic degradation of the ECM, a key factor in maintaining youthful skin (Jones *et al*., 2021). Further mechanistic studies are required to elucidate the bioactive compounds responsible for these effects and their potential applications in dermatological formulations.

Anti-Elastase Assay

The inhibition activity of the elastase enzyme was examined for *C. fuscus* revealed that the extracts obtained with methanol showed higher activity compared with the extracts obtained using water. Analyzing the results of water extracts, the extracts from the aerial parts of *C. fuscus* showed higher activity than those obtained from the underground parts. When the methanol extracts were compared with each other, the underground parts showed significantly higher activity on the elastase enzyme. Overall, based on the results, it can be concluded that the methanol extracts of *C. fuscus* plant had a significant elastase inhibitory activity (Table 1).

Table 1. Elastase inhibitory activity of *Cyperus fuscus* extracts (%).

Cyperus fuscus	*Elastase inhibition (%)*		
Concentration	1 µg/mL	1.5 µg/mL	2 µg/mL
Aerial: methanol	8.33±0.72	26.32±0.81	32.80±0.72
Aerial: water	3.45±0.64	8.70±0.72	11.58±0.63
Underground: water	0.00±0.0	1.18±0.08	2.33±0.55
Underground: *methanol*	24.33±0.62	31.15±0.81	35.39±0.64
N-methoxysuccinyl-Ala-Ala-ProCholoro (10 µg/mL)	42.49±1.68		

Anti-Collagenase Assay

For the analysis of the anti-collagenase effect of *C. fuscus* species, plant extracts were tested at three different concentrations: 1 µg/mL, 1.5 µg/mL, and 2 µg/mL. Each analysis was performed in triplicate. The results of the observation indicated that the extracts obtained using methanol had higher activity compared with the extracts obtained using water (Table 2 and Figure 1). The extracts obtained with methanol from the aerial parts of the plant showed significantly higher activity compared with the extracts obtained from the underground parts. Among all the obtained extracts, the highest activity percentage was 62.46%, which was obtained from the underground parts of *C. fuscus* using methanol. The lowest observed inhibition percentage was 16.66%, which was obtained from the aerial parts of the plant using water as the extracting solvent.

Table 2. Collagenase inhibitory activity (%) of Cyperus fuscus extracts.

Cyperus fuscus	*Collagenase inhibition (%)*		
Concentration	1 µg/mL	1.5 µg/mL	2 µg/mL
Aerial: methanol	26.50±0.12	27.40±0.38	31.48±0.13
Aerial: water	16.66±0.17	17.62±0.76	22.21±0.76
Underground: water	24.85±0.33	28.36±0.24	28.53±0.24
Underground: *methanol*	30.74±0.69	32.59±0.69	62.46±0.94
EGCG (250 µM)	74.44±0.00		

EGCG=epigallocatechin gallate.

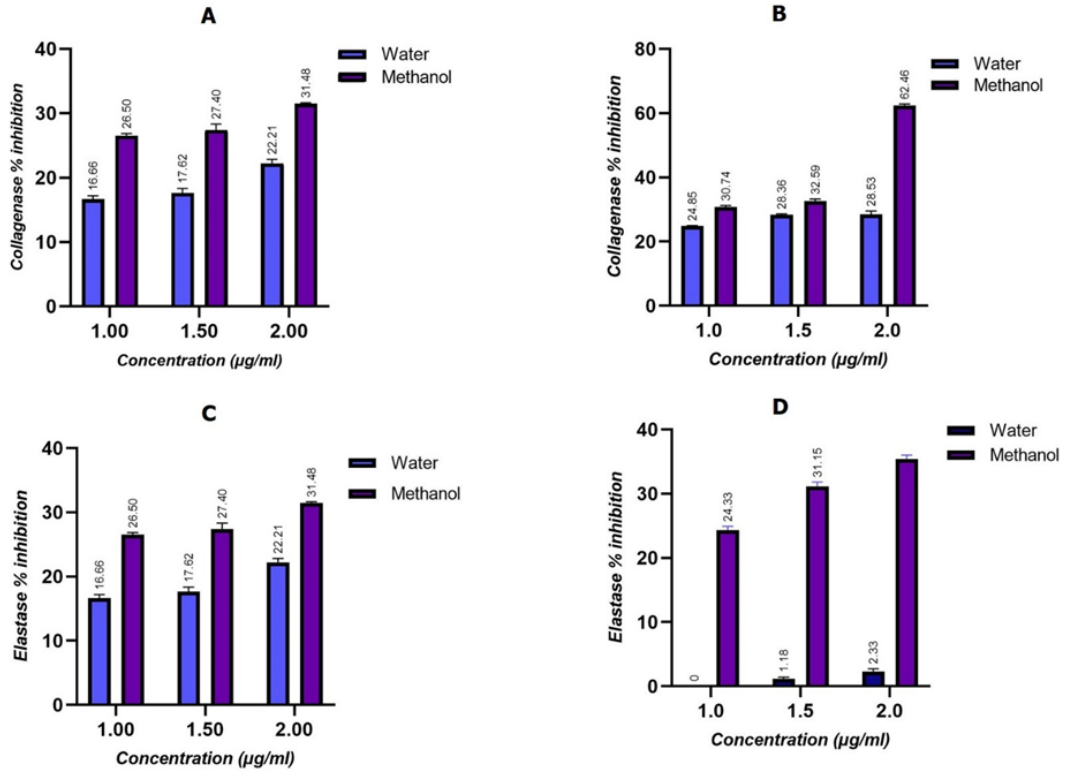


Figure 1. (A) Collagenase: *aerial*, (B) collagenase: *underground*, (C) elastase: *aerial*, and (D) elastase: *underground*.

Antioxidant Assays

To establish the total phenolic compound content, FCR was used. In the presence of phenolic substances, the addition of FCR resulted in the formation of products that exhibited maximum absorbance at 760 nm. Six different concentrations of plant samples were analyzed, namely 0.1 mg/mL, 0.5 mg/mL, 1.0 mg/mL, 2.0 mg/mL, 4.0 mg/mL, and 5.0 mg/mL. The amounts of phenolic compounds contained in each concentration were determined as GAE using the standard Gallic acid curve (Table 3 and Figure 2). When examining the results of the total phenolic content of *C. fuscus* species, the highest total phenolic content was observed in the methanol extract obtained from the aerial parts of the plant. However, in this study, trials were conducted at six different concentrations and no phenolic content was observed at the lowest concentration of 0.1 mg/mL. At the second lowest concentration of 0.5 mg/mL, a small amount of phenolic content was only detected in the extracts obtained from the aerial parts of the plant. However, as the concentration increased, a significant increase in the phenolic content of the plant was observed. We found the highest total phenolic content in the methanol extracts of *C. fuscus*. In conclusion, *C. fuscus* species had a significant amount of total phenolic content and has the potential to be used as an antioxidant. The DPPH assay was used to evaluate the free radical scavenging activity of natural antioxidants. In this study, the free radical scavenging effects of the extracts obtained from the plant were established using the DPPH radical. As a standard substance, a solution of synthetic antioxidant, ascorbic acid, was used. The effective antioxidant concentration required to neutralize 50% of the DPPH radicals in the reaction medium is defined as the IC50 value, and a low IC50 value indicates high radical scavenging activity. IC50 values for each *C. fuscus* extract were determined as a concentration of percentage inhibition (Figure 2). When examining the results of the DPPH radical scavenging activity of *C. fuscus* species, the highest total phenolic content was observed in the methanol extract obtained from the aerial parts of the plant. As the concentration increased, a significant increase in the phenolic content of the plant was also observed. According to the study findings, the highest activity was observed in the water extracts of *C. fuscus* species. Ascorbic acid was used as the positive control, which is a well-known potent antioxidant. Ascorbic acid was tested

simultaneously with our samples, and the activity level of our samples was compared. As a result, it was concluded that *C. fuscus* has DPPH radical scavenging activity similar to natural antioxidants and has the potential to be used as an antioxidant.

Table 3. Total phenolic content amount of *Cyperus fuscus*.

Cyperus fuscus	Total phenolic content amount (GAE/g)				
Concentration	0.1 mg/mL	0.5 mg/mL	1 mg/mL	2 mg/mL	4 mg/mL
Aerial: methanol	-	3.8±0.1	8.64±0.26	18.01±0.21	34.39±0.57
Aerial: water	-	0.26±0.01	2.55±0.31	8.05±0.54	16.55±0.35
Underground: water	-	-	-	1.05±0.04	5.1±0.05
Underground: methanol	-	-	0.26±0.03	2.72±0.63	4.21±0.19

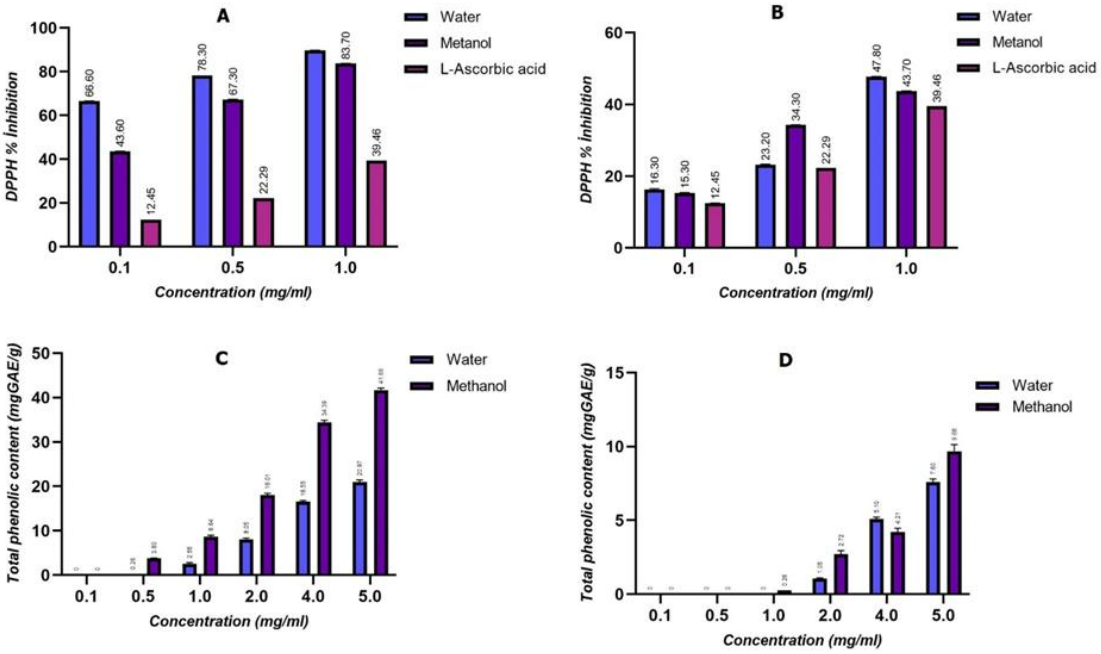


Figure 2. (A) DPPH: above ground, (B) DPPH: subsoil, (C) total phenolic content above ground, and (D) total phenolic content subsoil.

Gas Chromatography-Mass Spectroscopy (GC-MS) Analysis

The GC-MS results of plant extracts obtained from the underground parts of *C. fuscus* identified 20 components for water extracts and 21 components for methanol extracts (Tables 4 and 5). The top three components in water extracts were benzoic acid, 3-methyl-2-trimethylsilyloxy-trimethylsilyl ester (9.27%), ginsenol (7.93%), and 12-hydroxy-3-keto-bisnor-4-cholenic acid (6.74%). For the methanol-soluble extracts, the top three components were 2,6-lutidine, 3,5-dicholoro-4-dodecylthiol (25.95%), ginsenol (16.55%), and 1,3-benzenedicarboxylic acid, bis (2-ethylhexyl) ester (13.14%; Table 4 and Figure 3).

In comparison, when the GC-MS results of plant extracts obtained from the aerial parts of *C. fuscus* were examined, 22 components were identified for water extracts and 18 components for methanol extracts. The top three components in water extracts were hexadecanoic acid, methylester (CAS; 45.27%), 14α-Cheilanth-13(14)-enic methyl ester (6.55%), and ethyl 2-butyramido-3,3,3-trifluoro-2-(3-fluoroanilino)propionate (5.88%). For the methanol-soluble extracts, the top three components were podocarpan-14α-ol (14.86%), ginsenol (11.72%), and 14α-Cheilanth-13(14)-enic methyl ester (6.90%; Table 5 and Figure 3). The known activities of the compounds identified from GC-MS analyses are provided in Table 6.

Table 4. GC-MS analysis results of water and methanol extracts of the underground part of *Cyperus fuscus*.

Components	Water (area %)	Methanol (area %)
1. Mibemycin b, 13-chloro-5-demethoxy-28-deoxy-6,28-epoxy-5-(hydroxyimino)-25-(1-methylethyl)-(6R,13R,25R)-	3.68	-
2. Barbituric acid, 5-allyl-5-(cyclohex-2-en-1-yl)-	3.12	-
3. Lanosta-7,9(11)-dien-18-oic acid, 22,25-epoxy-3,17,20-trihydroxy-γ-lactone, (3β)-	4.31	-
4. İsolongifolan-8-ol	3.81	-
5. 6-Hydroxyimino-9-decanolide	4.21	-
6. 6-Hexadecenoic acid, 7-methyl, methyl ester (E)	6.53	-
7. N-(2-furylmethyl)-1-piperidinecarboxamide	5.11	-
8. Quercetin 7,3',4'-trimethoxy	3.63	1.97
9. Pinane-2,3-diol, 2,3-O-ethaneboronate-	4.00	-
10. 12-hydroxy-3-keto-bisnor-4-cholenic acid	6.74	-
11. Imidazole, 2-bromo-4-methyl-5-nitro-	5.61	-
12. 3α,4α,9β,11-diepoxymuurolan-10-ol	4.03	-
13. Strychane,1-acetyl-20α-hydroxy-16-methylene-	4.41	-
14. 14α-Cheilanth-12-enic methyl ester	4.11	2.47
15. 2-(N-methylpyrrolyl) thienoate	3.48	-
16. Naphtho[2,1-d][1,3]dioxepin, dodecahydro-5a,8,811a-tetramethyl-,[5Ar-(5aα,7aβ,11aα,11bβ)]-	6.62	-
17. Benzoic acid, 3-methyl-2-trimethylsilyloxy-, trimethylsilyl ester	9.27	-
18. Cheilanth-13(14)-enic methyl ester	3.11	1.92
19. 2,6-Lutidine 3,5-dicholoro-4-dodecylthio-	6.29	25.95
20. Ginsenol	7.93	16.55
21. Acetic acid, choloro-(CAS)	-	1.42
22. 1,3,4-Trimethoxy-butan-2-ol	-	0.92
23. 2-Bromopropionic acid, 6-ethyl-3-octyl ester	-	1.14
24. Geranyl isovalerate	-	5.68
25. 15,16-dinorlab-12-ene,8,13-epoxy-	-	2.08
26. Isochiapin b	-	2.71
27. Quassin	-	1.25
28. Dasycarpidan-1-methanol, acetate (ester)	-	1.26
29. Prost-13-en-1-oic acid,9,11,15-trihydroxy-6-oxo-, methyl ester, (9α,11α, 13E, 15S)-	-	1.06
30. 2,4-di-tert-butylthiophenol	-	1.06
31. Desacyl-kondurangogenins a	-	6.07
32. 1,3-Benzenedicarboxylic acid,bis(2-ethylhexyl) ester	-	13.14
33. Glutaric acid, di(2-isopropoxyphenyl) ester	-	1.88
34. Benzo[f]chromene, perhydro-7,7,10a-trimethyl	-	1.83
35. 14α-Cheilanth-13(14)-enic methyl ester	-	5.58
36. (+)-18-norisoambrox	-	4.06

However, when the GC-MS results of plant extracts obtained from the Aerial parts of *C. fuscus* using water and methanol were examined, 22 components were identified for water extracts, while 18 components were determined for methanol extracts. The top three components in water extracts were found to be Hexadecanoic acid, methyl ester (CAS) (45.27%), 14.alpha.-Cheilanth-13(14)-enic methyl ester (6.55%), and Ethyl 2-butyramido-3,3,3-trifluoro-2-(3-fluoroanilino)propionate (5.88%). For the methanol-soluble extracts, the top three components were identified as Podocarpan-14.alpha. -ol (14.86%), Ginsenol (11.72%), and 14.alpha. Cheilanth-13(14)-enic methyl ester (6.90%) (Table 5, Figure 3). Based on the GC-MS results of the extracts of *C. fuscus*, the known activities of the compounds are provided in Table 6.

Table 5. GC-MS analysis results of water and methanol extracts of the above ground part of *Cyperus fuscus.*

Components	Water (area %)	Methanol (area %)
1. Hexadecanoic acid, methyl ester(CAS)	45.27	-
2. 1-Oxaspirol[2.5]octan-4-one,2,26-trimethyl-, cis-(CAS)	3.03	-
3. d,l-Xylitol, 1-O-under-10-enoyl-	1.43	-
4. 1-(β-d-ribo furanosyl)-4-difluormethoxy-uracil	1.85	-
5. Myrtanol, 2-mercapto-	1.20	-
6. α-D-glucopyranoside, methyl 4,6-O-nonylidene-	2.61	-
7. (5-isopropyl-2-methylphenoxy)trimethylsilane	1.22	-
8. Cytidine, 2'-deoxy-(CAS)	1.64	-
9. Cholesta-5, 17(20)-dien-3-ol, acetate, (3β,17E)-	1.56	-
10. N-Methyl-1-adamantaneacetamide	3.27	-
11. Benzoic acid, 5-methyl-2-trimethylsilyloxy-, trimethylsilyl ester	1.31	-
12. Milbemycin b, 13-chloro-5-demethoxy-28-deoxy-6,28-epoxy-5-(hydroxyimino)-25-(1-methylethyl)-,(6R,13R,25R)-	4.28	-
13. Abeo-humulinone	1.44	-
14. Taraxasterol	1.64	-
15. 2,6-lutidine 3,5-dichloro-4-dodecylthio-	1.44	-
16. Megastrol acetate	3.20	-
17. Dihydroartemisinin, 10-O-(t-butyloxy)-	2.42	-
18. Methanone, (4-bromophenyl)(5-cyclohexyl-5-hydroxy-3-methyl-2-imidazolin-1-yl)-	5.47	-
19. 14α-Cheilanth-13(14)-enic methyl ester	6.55	6.90
20. Ethyl 2-butyramido-3,3,3-trifluoro-2-(3-fluoroanilino)propionate	5.88	-
21. (-)-18-noramborx	1.27	-
22. 1-iso-propyl-3,6-diazahomoadamantan-9-one	2.02	-
23. Diethylmalonic acid, monochloride, undercyl ester	-	3.34
24. Sclaral (sclareolide lactol)	-	4.21
25. Picrotoxinin	-	4.54
26. n-Octyl guanidine	-	3.66
27. (2,14-Dioxocyclotetradecyl)acetic acid methyl ester	-	5.74
28. Pyranol [4,3-b]benzopyran-1,9-dione,5a-methoxy-9a-methyl-3-(1-propenyl) perhydro-	-	3.08
29. Phenanthrol[1,2-b]oxirene-4-carboxylic acid, tetradecahydro-1b,9-dihydroxy-4,7a-dimethyl-9a- (1-methylethyl)-, methyl ester, [1ar	-	3.83
30. 1,1,3,3-D4-dihydro-2-ketomanoyl oxide	-	3.20
31. 1-monolinoleoylglycerol trimethylsilyl ether	-	4.72
32. 18,19-secolupan-3-ol, (3β,17ξ)-	-	3.23
33. 14α-Chelianth-12-enic methyl ester	-	4.19
34. Podocarpan-14α-ol	-	14.86
35. Benzothiophene-3-carboxylic acid,4,5,6,7-tetrahydro-2-amino-6-ethyl-, ethyl ester	-	7.22
36. Ginsenol	-	11.72
37. Haloxazolam	-	3.24
38. Cholestane, 3-ethoxy-, (3β,5α)-	-	4.56
39. (-)-isolongifolol, trimethylsilyl ether	-	3.47

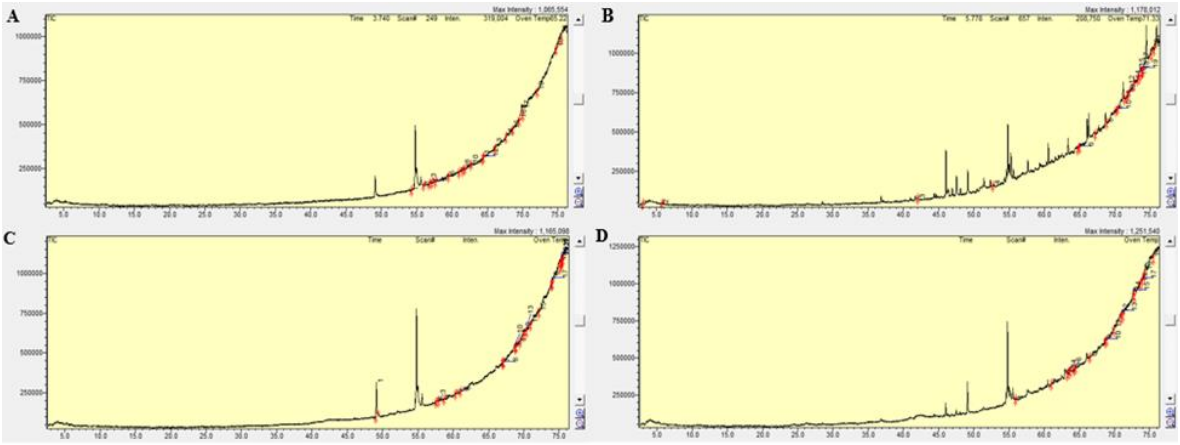


Figure 3. GC-MS analysis of *Cyperus fuscus* species. (A) Water extract of the underground part, (B) methanol extract of the underground part, (C) water extract of the aerial part, and (D) methanol extract of the aerial part of *C. fuscus*.

Table 6. Medicinally important phytochemicals in the *Cyperus fuscus* extract.

Chemical compound	Uses	Reference
1. Lanosta-7,9(11)-dien-18-oic acid, 22,25-epoxy-3,17,20-trihydroxy-,γ-lactone, (3β)-	Antioxidant	Akter *et al.*, 2022
2. İsolongifolan-8-ol	Anticancer	Manimaran *et al*., 2022
3. 6-Hexadecenoic acid, 7-methyl, methyl ester (E)	Antifungal and antitumor	Xu *et al*., 2009
4. Quercetin 7,3',4'-trİmethoxy	Antimicrobial, anticancer, and antitrematodal	Marrez *et al*., 2019; Rajesh *et al*., 2020
5. 12-hydroxy-3-keto-bisnor-4-cholenic acid	Anticancer	Alamri, 2023
6. Benzoic acid, 3-methyl-2-trimethylsilyloxy-, trimethylsilyl ester	Anti-inflammatory, antifungal, and antibacterial	Amrati *et al*., 2021
7. Ginsenol	Antiviral	Volobueva *et al.*, 2021
8. 2-Bromopropionic acid, 6-ethyl-3-octyl ester	Antioxidant	Matthew *et al*., 2021
9. Geranyl isovalerate	Anticancer, antimicrobial, and antioxidant	Sayed *et al*., 2022; Resul *et al*., 2021; Qudah, 2013
10. Isochiapin b	Antidiabetic, antioxidant, antimicrobial, antiviral, and antibacterial	Kuranayati et al., 2022; Qanash *et al*., 2022; Değirmenci *et al*., 2020;
11. Quassin	Immunomodulatory	Bhattacharjee *et al*., 2009
12. Dasycarpidan-1-methanol, acetate (ester)	Antibacterial	Moni *et al*., 2023
13. 2,4-Di-tert-butylthiophenol	Antimicrobial and antifungal	Goa *et al*., 2018; Meshram *et al*., 2013
14. Myrtanol, 2-mercapto-	Antioxidant	Gyrdymova *et al*., 2017
15. Hexadecanoic acid, methyl ester(CAS)	Cytotoxic effect	Atasever-Arslan *et al*., 2015
16. Cytidine, 2'-deoxy-(CAS)	A new model for base-specific inhibition of G and C on DNA and RNA level	Buck, 2018
17. N-Methyl-1-adamantaneacetamide	Larval toxicity, anti-inflammatory, and antioxidant	Chellappandian *et al*., 2022; Kakarla *et al*., 2014
18. Taraxasterol	Anticancer, anti-inflammatory, cardiovascular aging, and antiapoptotic ability	Sang *et al*., 2023; Li *et al*., 2022; Bao *et al*., 2018; Zheng *et al*., 2018; Zhang *et al*., 2012
19. Megastrol asetate	Hormonal therapy agents and anti-obesity	Wagner *et al*., 2023; Ferdous *et al*., 2022;
20. Picrotoxinin	Antileukemic, neuroprotective activity,	Sarkar *et al*., 2020; Ma *et al*., 2019; Mansikkamäki *et*

	anti-inflammatory, and angiogenesis effect	*al*., 2019; Wang Meng *et al*., 2017
21. 1-Monolinoleoylglycerol trimethylsilyl ether	Antioxidant, antitumor, antibacterial, anticancer, and antimicrobial	Farhat *et al*., 2023

DISCUSSION and CONCLUSION

Aging is an inevitable process for all living organisms during which the production of ROS increases, causing skin aging by promoting the activation of collagenase and elastase. In this context, the anti-elastase and anti-collagenase effects of *C. fuscus* were investigated to evaluate their anti-aging properties. Elastin is a protein found in the connective tissue that is responsible for the elasticity of the skin and lungs and is catalyzed by the elastase (Fulop *et al*., 2012). When the water and methanol extracts from *C. fuscus* were compared, the methanol extracts inhibited elastase at a higher rate than the water extracts. Additionally, the extracts obtained from the underground parts of the plant showed significantly higher activity compared with extracts from the aerial parts. Among the methanol extracts, the underground parts exhibited considerably higher activity on elastase. Collagen is the most abundant component of the ECM, constituting 80% of the dry weight of skin. Collagens also contribute to skin physiology by maintaining structure, retaining water, and supporting skin integrity (Prabhu *et al*., 2021). As a person ages, collagen synthesis in the skin decreases while collagenase enzyme levels increase (Thring *et al*., 2009). Considering this fundamental aspect of our study, the effect of *C. fuscus* on collagenase was evaluated. The inhibitory activity of *C. fuscus* extracts (both aerial and underground parts) on collagenase was tested at different concentrations (Figure 1). Methanol extracts of *C. fuscus* strong showed anti-collagenase activity, which was higher in extracts from the underground parts of the plant compared with the aerial parts. As the extract concentration increased, a significant increase in activity was observed in both the aerial and underground extracts.

Our results highlight that extracts obtained from *C. fuscus* have significant anti-collagenase activity. Caniklioğlu *et al*. (2018) investigated the antioxidative activity of ethanol and chloroform extracts of three different endemic taxa (*Tanacetum heterotomum*, *Tanacetum densum* subsp. *eginense*, and *Tanacetum alyssifolium*) found in Erzincan. The antioxidative activity of the extracts were tested using methods, such as DPPH radical activity, reducing power, total phenolic content, total flavonoid content, ABTS radical activity, metal chelation activity, and total antioxidant capacity. Of the studied species, *Tanacetum heterotomum* extracts had the highest antioxidant activity for many of the tested parameters. In another study by Mau *et al*. (2004), the antioxidative activities of methanol extracts prepared with the mycelia of commercially available *Grifola frondosa*, *Morchella esculenta*, and *Termitomyces albuminosus* in Taiwan were investigated. In the study, the methanolic extracts of all three species showed high antioxidant activity (ranging 85.4–94.7%) at a concentration of 25 mg/mL. The reducing power activities of the extracts at 25 mg/mL ranged between 0.97 and 1.02. The DPPH radical scavenging activities of the extracts at 10 mg/mL were in the range of 78.8% to 94.1%. Based on the literature, we can conclude that the observed DPPH radical scavenging effect for *C. fuscus* was significant in our study. Moreover, when compared with ascorbic acid samples, *C. fuscus* has a significant DPPH radical scavenging activity suggesting its use as a potential antioxidant. The total phenolic content and enzyme inhibitory activity of *C. fuscus* extracts indicate that they might help restore the skin's elasticity, thus, slow down the aging process and reduce wrinkles. Further detailed studies are planned to identify the active compounds and potential senolytic agents associated with the properties of *C. fuscus*. In a similar study, Şey *et al*. (2009) evaluated the anti-aging and antioxidant properties and anti-elastase and anti-collagenase activities of 23 plant extracts (from 21 plant species), along with selected antioxidant analyses, including phenolic content. Şey *et al*. (2009) observed the highest anti-collagenase activity in white tea (~89%), followed by cleavers (~58%), burdock root (~51%), bladder wrack (~50%), anise and angelica (~32%), green tea (~47%), rose tincture (~41%), and

lavender (~31%). From the panel of tested plant extracts, they reported that around a dozen showed high or satisfactory anti-collagenase or anti-elastase activities, with nine having inhibitory activity against both enzymes. Their study highlighted that products and treatments derived from plants that do not contain synthetic substances can be considered in this context. Phenolic compounds are one of the most common and widespread groups of plant secondary metabolites. The health-promoting effects of phenolic compounds are based on their antioxidant and anti-aging properties. Phenolic compounds with high levels are used in cosmetic products to combat environmental free radicals known to cause certain skin-damaging conditions (Petruk *et al*, 2018).

GC-MS analysis was used in our study to identify the chemicals in water and methanol extracts from the underground and aerial parts of *C. fuscus* (Tables 4 and 5). When compared with previous literature studies, our study detected phytochemical compounds. GC-MS was used to explore essential oils found in *C. fuscus*. The main components were dehydroaromadendrene, azulenone, a-selinene, a-ylangene, and b-caryophyllene. The volatile oil derived from *C. fuscus* has been reported to have various biological effects, such as antioxidative, antibacterial, analgesic, cytotoxic, apoptotic, anti-inflammatory, and antifungal properties (Erdem *et al*., 2018). Comparing our GC-MS results with the literature, it is evident that the extracts contain molecules with known activities, such as antioxidants and anti-enzymatic effects, and compounds with anticancer, antitumor, antitrematodal, anti-inflammatory, antifungal, antidiabetic, antiviral, cytotoxic, apoptotic, neuroprotective activity, antibacterial, and antileukemic properties (Table 6).

Our study has shown the major potential of *C. fuscus* as a natural anti-aging agent that acts by its inhibitory effects on elastase and collagenase, which are key contributors to skin aging. The methanol extracts of *C. fuscus*, particularly from the underground parts, exhibited higher inhibitory activity against these enzymes compared with water extracts. The presence of phenolic compounds and the observed DPPH radical scavenging activity further imply the antioxidative properties of the plant, suggesting its potential use in skincare and anti-aging products.

The GC-MS analysis revealed a variety of bioactive compounds within the extracts, including antioxidants, anti-inflammatory agents, and other compounds with therapeutic properties, such as anticancer and antiviral activities. These findings indicate that *C. fuscus* could be a valuable source of natural compounds for the development of cosmetics and pharmaceuticals aimed at reducing the effects of aging and promoting skin health.

In conclusion, *C. fuscus* shows promise as a multifunctional plant with applications in anti-aging, antioxidative, and anti-inflammatory treatments. However, no direct clinical studies on this plant have been reported in the current literature. Therefore, further research, including clinical trials, is warranted to fully explore and validate its therapeutic potential in skincare and other related areas.

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Declaration of Conflicting Interests and Ethics

The authors declare no conflict of interest. This research study complies with research and publishing ethics. The scientific and legal responsibility for manuscripts published in IJSM belongs to the authors.

Data Availability Statement

Research data is available and can be sent with e-mail upon request.

Authorship Contribution Statement

Handan Şapcı Selamoğlu: investigation, methodology, resources, data curation, visualization, writing (original draft); **Begüm Birgül**: investigation, methodology, data curation, visualization; **Cem Vural**:

formal analysis (statistical analysis and interpretation), validation, writing (review and editing); **Hatice Bekci**: writing (review and editing); and **Nihat Yılmaz**: writing (review and editing).

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