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Phytochemicals, Antioxidant Activity, and Antimicrobial Effects of the Fractions of *Corrigiola telephiifolia* Pourr.

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ABSTRACT

This study aimed to provide new data on the chemical composition and biological properties of *Corrigiola. telephiifolia* Pourr., demonstrating the influence of different extraction solvents and geographic locations on these properties. It presents novel findings on the phytochemical contents, antioxidant activity, and antimicrobial effects of various fractions of *Corrigiola telephiifolia* Pourr. roots collected from three distinct regions in Morocco. The obtained results reveal significant variations in TPC, TFC, and antioxidant activity depending on the extraction fraction and geographic origin. Notably, the fraction of raw extract exhibited the highest TPC values in all sampled sites (44.76 ± 0.05 in Agouray, 35.89±0.02 in Sefrou, and 14.99 ± 0.03 mg·GAE/g·dw in Azrou). The peak values of TFC were recorded in the fraction of raw extracts for all sampling sites (20.80 ± 0.01 in Agouray, 18.62 ± 0.01 in Sefrou, and 11.54 ± 0.01 mg QAE/g dw in Azrou). The highest values of FRAP were recorded in the fraction of raw extract of Agouray (2.00±0.00). Furthermore, the hexane fraction showed the highest DPPH and Chelating power with IC_{50} equal to 0.46 ± 0.02 mg·mL^{-1} and 0.10 ± 0.00 mg·mL^{-1}, respectively. All fractions showed significant and variable antibacterial activities. The highest anti-microbial activity was recorded in in ethyl acetate fraction of the sample from Agouray against *E. coli* (MIC = 0.039). The highest anti-microbial effect was recorded also in ethyl acetate fraction against *E. coli* and *P. aeruginosa*, and raw fraction against *B. subtilis* and *P. aeruginosa* (MBC = 0.313 against both microorganisms). Agouray consistently demonstrated superior results across multiple parameters, indicating it as the best region for the highest phytochemical and bioactive properties. This study evaluated the chemical compounds and biological properties of *Corrigiola. telephiifolia* Pourr. and demonstrated the effect of the sampled area and solvent.

Keywords: *Corrigiola telephiifolia*, polyphenols, flavonoids, antioxidant activity, antimicrobial activity.

INTRODUCTION

Since prehistoric times, medicinal plants have been utilized in traditional medicine due to their numerous beneficial qualities (Süntar, 2020). These plants contain various bioactive components that contribute to their medicinal benefits, such as alkaloids, flavonoids, terpenoids, and phenolic compounds (Balunas and Kinghorn, 2005; Chaudhari et al., 2021). The diverse chemical elements found in medicinal plants provide a wide range of pharmacological actions, including antioxidant, immunomodulatory, analgesic, anti-inflammatory, and antibacterial properties (Sun and Shahrajabian, 2023). For instance, plants like Turmeric (*Curcuma longa*) possess curcumin, a polyphenolic compound, which contributes to its biological properties, such as antioxidant and anti-inflammatory effects (Jurenka, 2009). Other studies have shown a significant relationship between antioxidant properties and phenolic compounds in grains of *Sorghum bicolor* L. Moench (Punia et al., 2021), Eureka lemon (*Citrus limon* L. Burm. *f.*) (Dong

et al., 2019), as well as leaves and berries of Raspberry genotypes (Lebedev et al., 2022).

Currently, many investigations have focused on the phytochemical compounds in medicinal plants and their relationship with extraction methods (Chen et al., 2022; Rébufa et al., 2022), solvents (Akinmoladun et al., 2022; Mehmood et al., 2022), and conditions (Sirichan et al., 2022). For example, Mohammed et al. (2022) studied the impacts of extraction solvents on bioactive compounds in the aerial and root parts of plants, demonstrating that the quantity of flavonoids and polyphenols varied depending on the type and percentage of solvents used. Adam et al. (2019) examined the impact of solvents and extraction techniques on the yield and antioxidant properties of five extracts from medicinal plants in Sudan, finding variability among methanol, chloroform, and n-hexane solvents. Generally, the variation in the yield of bioactive compounds according to extraction solvents is governed by the chemical composition of the plant material and the polarity of the extraction solvents. However, this type of investigation needs to be extended to other medicinal species, especially those with diverse chemical compositions or those lacking data on their chemical properties.

Corrigiola telephiifolia Pourr. is a glabrous perennial plant from the Caryophyllaceae family, known for its fragrant and developed roots (Doudach et al., 2022). This plant grows in sandy soils of the Mediterranean region, including areas such as Switzerland, Germany, France, as well as North African countries like the Atlas and Rif mountains of Morocco (Hebi and Eddouks, 2020). *Corrigiola telephiifolia* has been widely used in traditional North African medicine to treat various ailments, including inflammation, flu, ulcers, cough, dermatological conditions, and jaundice. It is also used as a diuretic and anesthetic (Zakariya et al., 2020; Benkhnigue et al., 2023). Traditional healers often use a small amount of root powder with honey to treat abdominal pain. Despite its widespread use, there is a need for more detailed investigations into the extraction and utilization of its bioactive compounds, such as polyphenols, flavonoids, and tannins, to support its medicinal applications (Amine et al., 2017).

This study sought to provide new insights into the chemical compounds and biological properties of *Corrigiola telephiifolia* and to demonstrate how different extraction solvents and geographic locations impact these properties.

A scientifically rigorous evaluation of the phytochemical contents, antioxidant activity, and inhibitory effects of various fractions of *Corrigiola telephiifolia* Pourr. roots from three different regions in Morocco was conducted. The total flavonoid content (TFC) and total phenolic content (TPC) wee investigated, the antioxidant activity was assessed using DPPH scavenging activity, and the antimicrobial activity against two fungi and four bacteria was evaluated by determining the minimum bactericidal concentrations (MBC) and minimum inhibitory concentrations (MIC).

MATERIALS AND METHODS

Plant material

Samples of *Corrigiola telephiifolia* Pourr. were gathered in April 2018 in three provinces, namely Agouray (near Meknes province), Azrou (West Middle Atlas), and Sefrou (near Fez). Once brought back to the laboratory, the roots of the plant were dried in the shadow in a dry place. The sample of roots was then ground into a fine powder and stored in dark pillboxes for further analysis.

Plant extraction

The samples from various regions were arranged in triplicate by combining 1 ml of used solvent (pure solvents and mixtures) with 50 mg of powdered roots. The mixture was then subjected to sonication for half an hour in an ultrasonic immersion at room heat. Subsequently, the extract was obtained by centrifuging the mixture for 10 minutes at 10,000 rpm. Finally, the extract was stockpiled in a dark environment at a temperature fixed at 4 °C. The first step of extraction consists of a screening using solvents with different polarities viz. water, ethanol, di-ethyl ether, acetone, methanol, ethyl acetate, chloroform, hexane, petroleum ether, dichloromethane, butanol in order to choose the best solvent to use for the next step. The second step consists of extracting the pure selected solvent and their mixtures.

Fractionation

The powdered root (20 g) was extracted by sonication with an optimized mixture of water-methanol-ethanol (60.8; 8.9; 30.3) for half an hour. The resulting extract was cleaned via the Whatman filter paper.

Then, the obtained filtrate was concentrated in vacuo at 40 °C using a rotary evaporator and was then adjourned in 200 ml of distilled water. The ready extract was therefore shared with dichloromethane (200 mL × 3), n-hexane (200 mL × 3), chloroform (200 mL × 3), and ethyl acetate (200 mL × 3) using the separating funnel. Three extracts of each solvent were combined and evaporated under lessened pressure employing a rotary evaporator and suspended in ethanol. Finally, AQF (aqueous fraction), CHF (chloroform fraction), HF (hexane fraction), EAF (ethyl acetate fraction), and DCMF (dichloromethane fraction) fractions were obtained (Fig. 1).

Total phenolic content

The total phenolic content (TPC) content was assessed spectrophotometrically, based on the colorimetric method using the Folin-Ciocalteu reagent (Ma et al., 2010) with modification. A volume of 50 µL from the obtained trial was added to a volume of 450 µL of a solution of the Folin-Ciocalteu reagent diluted 10 times. Following a 5-minute incubation period at ambient temperature, a solution of sodium carbonate with a volume of 450 µL (concentration: 75 $g \cdot L^{-1}$) was introduced. Following cultivation in the absence of light for 2 hours at air temperature, the absorbance of all samples was assessed at a wavelength of 760 nm via a spectrophotometer. The calibration curve exhibited a concentration range of 0.062 to 1 $mg \cdot mL^{-1}$ in a solution of ethanol (gallic acid), as shown by the equation $y = 2.8388x + 0.0556$ and a coefficient of determination (R^2) value of 0.9994. The experimentation was directed in three assays, and the findings are shown in terms of milligrams of gallic acid equivalent (GAE) per gram of the plant material in its dry state.

Total flavonoid compounds

The aluminum chloride colorimetric technique was employed to quantify the total flavonoid compounds (TFC) of studied extracts (with some adjustments) (Pourmorad et al., 2006). Further, 0.5 mL of each extract was assorted with 5% $NaNO_2$ (0.3 ml), and after 5 min, 0.3 ml of $AlCl_3$ (10%) and 1 ml of 1M NaOH were added to the combination. The tubes were accustomed to 5 ml via extracted water (distillation). Then, the optical density (absorbance) of the extract was quantified at 415 nm and quercetin was adopted to prepare the curve of standard calibration ($y = 3.8762x - 0.044$, $R^2 = 0.9993$). The obtained results were presented as milligrams of quercetin corresponding to a gram of dried sample (plant) (mg·Qu/g·dw) and three replicates were used for each experiment.

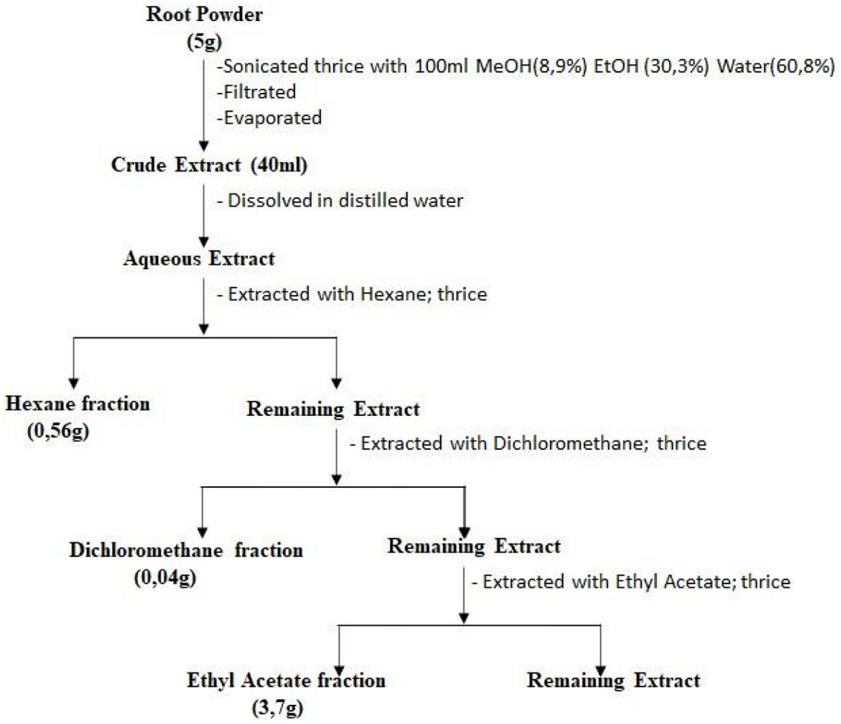

Figure 1. Fractionation of *Corrigiola telephiifolia* extract

Antioxidant activity

Ferric Reducing-Antioxidant Power (FRAP)

The procedure for determining reducing power followed the methodology outlined by (Chavan et al., 2013) In this method, each extract trial or standard was united with 2.5 ml of potassium ferricyanide (formula; $[K_3Fe(CN)_6]$ solution (1%) and 2.5 ml of phosphate buffer (concentration of 0.2 M and pH of 6.6) The solution was subjected to incubation at a temperature of 50 °C for 20 min. A volume of 2.5 milliliters of trichloroacetic acid solution with a concentration of 10% was introduced into the combination. Subsequently, the mixture underwent centrifugation for 10 minutes at a rapidity of 3000 rpm. A mixture was prepared by combining the distilled water (2.5 ml) with the uppermost coating of the solution (with a concentration of 2.5 ml) and 0.5 ml of $FeCl_3$ (0.1% concentration). The resulting mixture was then subjected to spectrophotometric analysis, with the absorbance being assessed at a wavelength of 700 nm.

Free radical scavenging activity: DPPH

DPPH (2.2-diphenyl-1-picrylhydrazyl) was produced as defined by (DiCiaulaa et al., 2014). Further, a 25 µl volume of different concentrations of samples or standards was introduced into a 1 mL ethanolic solution of DPPH at 60 µM concentration. Moreover, the optical density (absorbance) readings were documented at a wavelength of 517 nm following a 60-minute incubation period at ambient temperature. A negative control was employed by measuring the absorption of a blank sample consisting of an equivalent quantity of methanol and DPPH solution. The experiment was conducted in triplicate, and the inhibition percentage of the free radical scavenging properties for each extract was determined employing the following calculation method:

$$\% \text{ inhibition} = [(Abs_{control} - Abs_{sample}/Abs_{control}) \times 100] \quad (1)$$

The percent inhibition was plotted against the content of the sample or standard and the IC50 was determined (concentration of the extract or standard capable of trapping 50% of the free radical of DPPH).

Chelation of metal ions

The assessment of the chelation degree of ferrous ions by fraction was conducted following the study conducted (Miguel, 2010). In summary, the samples were subjected to incubation with a 0.05 ml solution of $FeCl_2 \cdot 4\ H_2O$ at a concentration of 2 mM. Further, the beginning of the reaction occurred upon the introduction of 0.2 ml of a 5 mM ferrozine solution. Subsequently, the absorbance at a wavelength of 562 nm was measured after 10 minutes. A control was used in the experiment, consisting of an untreated sample. The calculation of the chelating power % was performed following Equation 1.

Antimicrobial activity

Microbial strains

The study investigated the in vitro inhibitory effects of crude extracts and their fractions (DCM, Hexane, ET AC, and Aqueous) against four bacteria and two pathogenic fungal strains (Gonelimali et al., 2018). The bacterial cells assayed included two Gram-negative germs of bacteria *(Pseudomonas aeruginosa* and *E. coli)* and two Gram-positive germs (*Bacillus Subtilis* and *Staphylococcus aureus*). Further, the fungi strains used were *Candida tropicalis* and *Saccharomyces*. Microorganisms were obtained from the Laboratory of Functional Ecology and Environmental Engineering, FST-USMBA, Fez. All microorganisms were maintained at 4 °C on nutrient agar slopes. The identification of the chosen microorganisms involved a comprehensive set of morphological, physiological, and standard biochemical testing. The identification of the fungus was conducted by observing its development on suitable media and analyzing its morphological as well as microscopic features, as described in other studies (Khan et al., 2009; Gonelimali et al., 2018). The modified Kirby Bauer disc diffusion technique, as drawn in the Clinical and Laboratory Standards Institute (CLSI) guideline, was utilized to conduct the antimicrobial susceptibility test for all microbiological isolates. The term "multidrug-resistant (MDR) isolates" refers to the isolates that exhibit resistance to three distinct classes of antibiotics, as described by preceding studies directed by (Khan et al., 2009; Gonelimali et al., 2018).

Antimicrobial assay of extract fractions

Mueller Hinton Agar (MHA) plates were used to assess the antibacterial activity of plant fractions (extracts) based on the agar well diffusion technique. To reach a turbidity level equal to 0.5 McFarland standards, the tested strains

were added to the nutrient broth and gestated for one night at 37 °C. As a consequence, 1.5 × 108 CFU/ml was the ultimate inoculum concentration. With the use of a standardized microbial culture broth, grass culture was applied to the MHA plate. Plant extracts were made in dimethyl sulfoxide (DMSO) at 50 mg/ml concentration. Using a sterile cork borer with a 6 mm diameter, six wells, each measuring 6 mm in diameter, were made in the contaminated medium. Fifty microliters of extracts derived from different plants were added to each well. Nitrofurantoin (300 mcg) and Amikacin (30 mcg) were the positive controls for bacteria germs, while cyclohexylamine (1 mg/ml) was the positive control for fungal isolates. DMSO served as the solvent control or negative control. The prepared mixture was then allowed to diffuse for about half an hour at chamber temperature, and before it was incubated at 37 °C for 18–24 hours. Further, after the cultivation time, the dishes were inspected to understand whether there was a clean region around the well that was free of growth. This would indicate that the chemicals being studied were effective against microorganisms. The inhibition region (ZOI) was detected and estimated in millimeters by (Gonelimali et al., 2018).

Calculating the MIC and MBC of fractions

The researchers employed the potage microdilution procedure to ascertain the minutest inhibitory concentration (MIC) based on the procedures defined by the Clinical and Laboratory Standards Institute (CLSI). To get various concentrations, extracts were serially diluted using Mueller Hinton broth on a microtiter plate. To attain a final concentration of $10^5 \times 5$ colony founding units per milliliter (CFU/mL), the bacterial inoculum was added to the wells. The experimental setup included the utilization of positive control, which consisted of amikacin as a typical pharmaceutical agent. A sterile sealer was applied on the plate, which was then raised at 37 °C for 24 hours. Resazurin was introduced into every well of the microtiter plate and incubated at 37 degrees Celsius for 30 minutes. The wells that showed signs of bacterial development became pink, whereas the wells that showed no signs of bacterial growth stayed blue. The smallest concentration of the sample (fractions or extracts) that successfully stops bacteriological growth is known as the minutest inhibitory concentration, or MIC (Gonelimali et al., 2018; Witasari et al., 2022).

Statistical analysis

All experiments selecting the solvent proportion were accomplished in triplicate and the recorded results were stated as a medium ± standard error and IC_{50} values have been determined. Statistical tests for the comparison of studied parameters were made with a one-way ANOVA followed by the Tukey multiple comparison test. The tests were considered significant at $p \leq 0.05$. Principal component multivariate analysis (PCA) was employed to analyze the principal Phyto compounds (polyphenols and flavonoids) characterizing the fractions of *Corrigiola telephiifolia*. The statistical calculation was achieved based on the free version (version 10) of STATISTICA software (StatSoft, INC., 2011).

RESULTS

Total phenolic content

Results of TPC in fractions of *Corrigiola telephiifolia* Pourr. from Azrou, Agouray, and Sefrou regions (central Morocco) are offered in Figure 2. On the basis of the obtained results, the values of TPC were variable depending on fractions and sampled areas. The raw fraction exhibited the highest TPC values across all regions, 44.76 ± 0.05 mg GAE/g dw in samples of Agouray, 35.89 ± 0.02 mg GAE/g dw in samples from Sefrou, and 14.99 ± 0.03 mg GAE/g dw in samples from Azrou. In organic solvents, the fraction of dichloromethane showed the highest values of TPC compared to the other fractions, principally in samples from Agouray, followed by Sefrou and Azrou (15.80 ± 0.03, 12.94 ± 0.01 and 6.99 ± 0.02 mg GAE/g dw). Fractions of ethyl acetate demonstrated medium TPC values with superior quantities in samples from Agouray and Sefrou. The lowest values of TPC in organic solvents were obtained in the fraction of hexane. In the aqueous fraction, the value of TPC was medium with significantly superior values in samples from Agouray and Sefrou compared to samples from Azrou.

Total flavonoid content

Figure 3 presents the results of TFC in fractions of *Corrigiola telephiifolia* Pourr. from the Azrou, Agouray, and Sefrou regions (Central Morocco). The obtained results confirmed the variability of TFC depending on fractions of

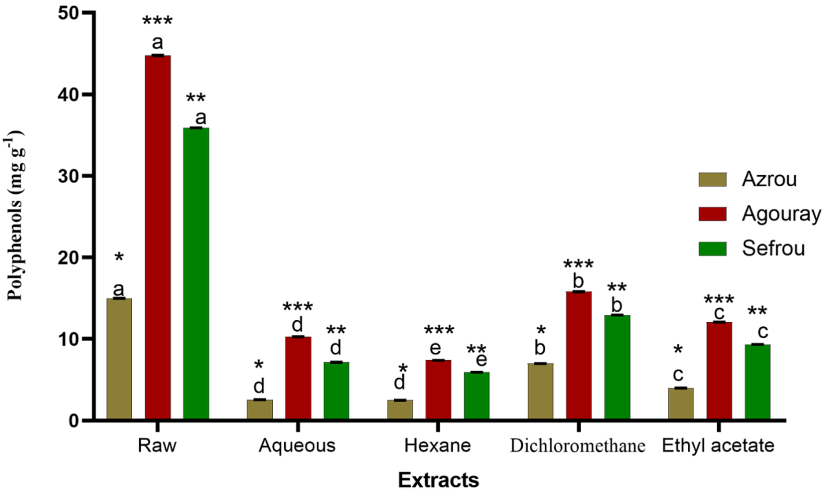

Figure 2. Comparison of total phenolic content in fractions of *Corrigiola telephiifolia* Pourr. sampled from Azrou, Agouray, and Sefrou in central Morocco (*denote comparison of sampled sites from the same fraction (***>**>*); letters denote comparison among the fractions of the same sampled site (a>b>c>d>e))

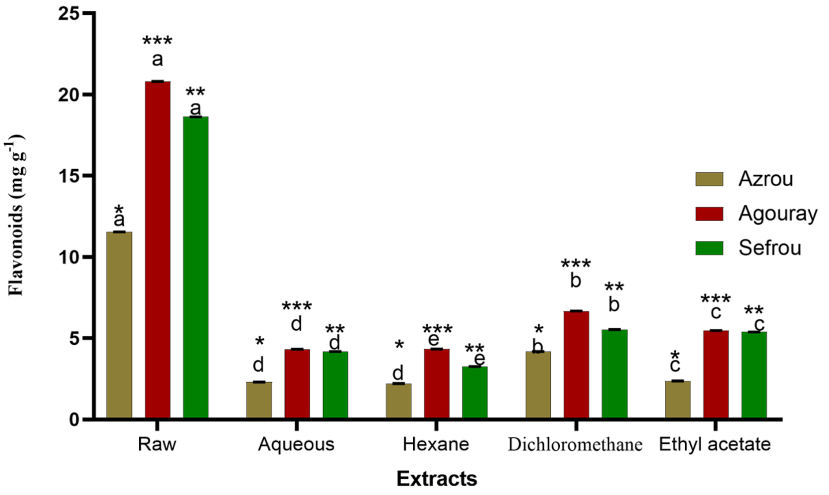

Figure 3. Comparison of total flavonoid content (TFC) in fractions of *Corrigiola telephiifolia* Pourr. from the Azrou, Agouray, and Sefrou regions (central Morocco) (*Denote comparison of sampled sites from the same fraction (***>**>*); letters denote comparison among the fractions of the same sampled site (a>b>c>d>e))

extraction solvents and sampling site. As in the case of TPC, the maximum values of TFC were recorded in raw extracts for all sampling sites. The sample from Agouray showed the highest value of TFC, followed by the sample of Sefrou and Azrou (11.54 ± 0.01, 20.80 ± 0.01, and 18.62 ± 0.01 mg·QAE/g·dw, respectively). In organic solvents, the fraction of dichloromethane showed the highest values of TFC compared to the other fractions, principally in the samples from Agouray, followed by Sefrou and Azrou (6.67 ± 0.01, 5.53 ± 0.00, and 4.18 ± 0.01 mg·QAE/g·dw, respectively). Medium quantities of TFC were recorded in fractions of ethyl acetate and hexane, principally in the samples from Agouray and Sefrou, respectively. Fractions of ethyl acetate demonstrated medium TFC values with superior quantities in the samples from Agouray and Sefrou (respectively, 5.47 ± 0.01 and 5.38 ± 0.01 mg·QAE/g·dw). The lowest values of TFC in organic solvents were obtained in the fraction of hexane (respectively, 2.21 ± 0.01, 4.33 ± 0.01, and 3.26 ± 0.01 mg·QAE/g·dw). In the aqueous fraction, the value of TFC was medium with significantly superior values in the samples from Agouray and Sefrou (respectively, 4.32 ± 0.01 and 4.18 ± 0.01·mg·QAE/g·dw) compared to the samples from Azrou (2.30 ± 0.01 mg·QAE/g·dw).

Multivariate analysis

Figure 4 presents the principal component analysis of chemical compounds in fractions of *Corrigiola telephiifolia Pourr*. from the Azrou, Agouray, and Sefrou regions (Central Morocco). The chemical compounds (TPC and TFC) from studied fractions are presented in two axes with a total inertia of 99.96%. The raw fraction from Azrou was principally characterized by higher TPC and TFC, while the raw fraction from Agouray was dominated by TPC. The other fractions were far from the sampled sites.

Ferric reducing antioxidant power

Results of ferric reducing antioxidant power (FRAP) in fractions of *Corrigiola telephiifolia* Pourr. from the Azrou, Agouray, and Sefrou regions (Central Morocco) are presented in Figure 5. Recorded results demonstrated that the values of FRAP were variable depending on the sampling site and fraction of each solvent. The highest values were recorded in the fraction of raw extract, principally in the samples of Agouray, followed by Azrou, and Sefrou ($p > 0.05$) (respectively, 2.00 ± 0.00, 1.94 ± 0.00 and 1.80 ± 0.00). In the fraction of aqueous extract, the values of FRAP were statistically similar among sampling sites. In organic solvents, the fraction of dichloromethane presented the highest value of FRAP in all sampled sites (respectively, 1.64 ± 0.00, 1.53 ± 0.00 and 1.54 ± 0.06) followed by the fraction of ethyl acetate (respectively, 1.54 ± 0.00, 1.10 ± 0.01, and 1.25 ± 0.00). The fraction of hexane presented the lowest ferric reducing antioxidant power (FRAP) in all sampled areas (respectively, 1.09 ± 0.00, 1.01 ± 0.00, and 1.11 ± 0.00).

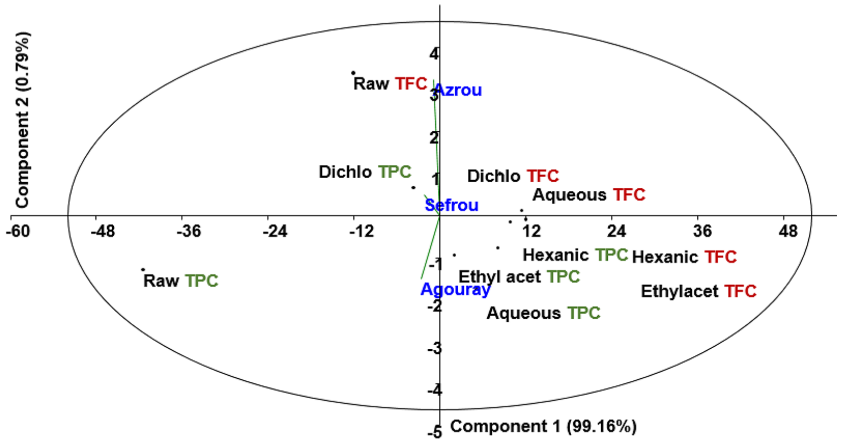

Figure 4. Principal component analysis of chemical compounds in fractions of *Corrigiola telephiifolia Pourr*. from the Azrou, Agouray, and Sefrou regions (Central Morocco)

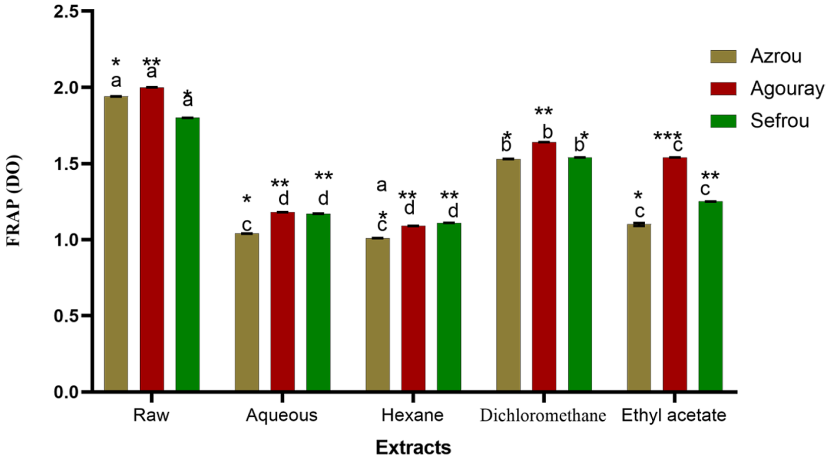

Figure 5. Ferric reducing antioxidant power (FRAP) in fractions of *Corrigiola telephiifolia Pourr*. sampled from Agouray, Azrou, and Sefrou (Central Morocco) (*Denote comparison of sampled sites from the same fraction (***>**>*); letters denote comparison among the fractions of the same sampled site (a>b>c>d>e))

DPPH radical scavenging activity and chelating power

Figure 6 presents the results of chelating power (CP) and DPPH radical scavenging activity in fractions of *Corrigiola telephiifolia* pour. sampled from Agouray, Azrou, and Sefrou (Central Morocco). The recorded results revealed a significant variation of DPPH radical scavenging activity in *Corrigiola telephiifolia Pourr.* depending on the sampled site and fraction of extracts. The fraction of raw extract showed the lowest DPPH radical scavenging activity, mainly in Azrou, followed by Sefrou and Agouray (respectively, 0.29 ± 0.00, 0.30 ± 0.02, and 0.46 ± 0.02 mg·mL^{-1}). In contrast, the highest value of DPPH was recorded in the fraction of hexane (organic extracts), mainly in the samples from Agouray, followed by Azrou and Sefrou (2.07 ± 0.04, 1.53 ± 0.02, and 0.65 ± 0.00 mg·mL^{-1}, respectively). Fractions of dichloromethane and ethyl acetate showed inferior values of DPPH in all sampled regions. Fraction of aqueous extracts showed superior DPPH activities in the samples from Agouray and Azrou compared to the samples from Sefrou (1.44 ± 0.01, 1.49 ± 0.10, and 0.40 ± 0.01 mg·mL^{-1}, respectively).

Results of chelating power demonstrated variable values depending on the sampling site and fraction of *Corrigiola telephiifolia Pourr*. In organic extracts, the highest values were recorded in the fraction of hexane extract from Agouray, followed by Sefrou and Azrou (respectively, 0.16 ±

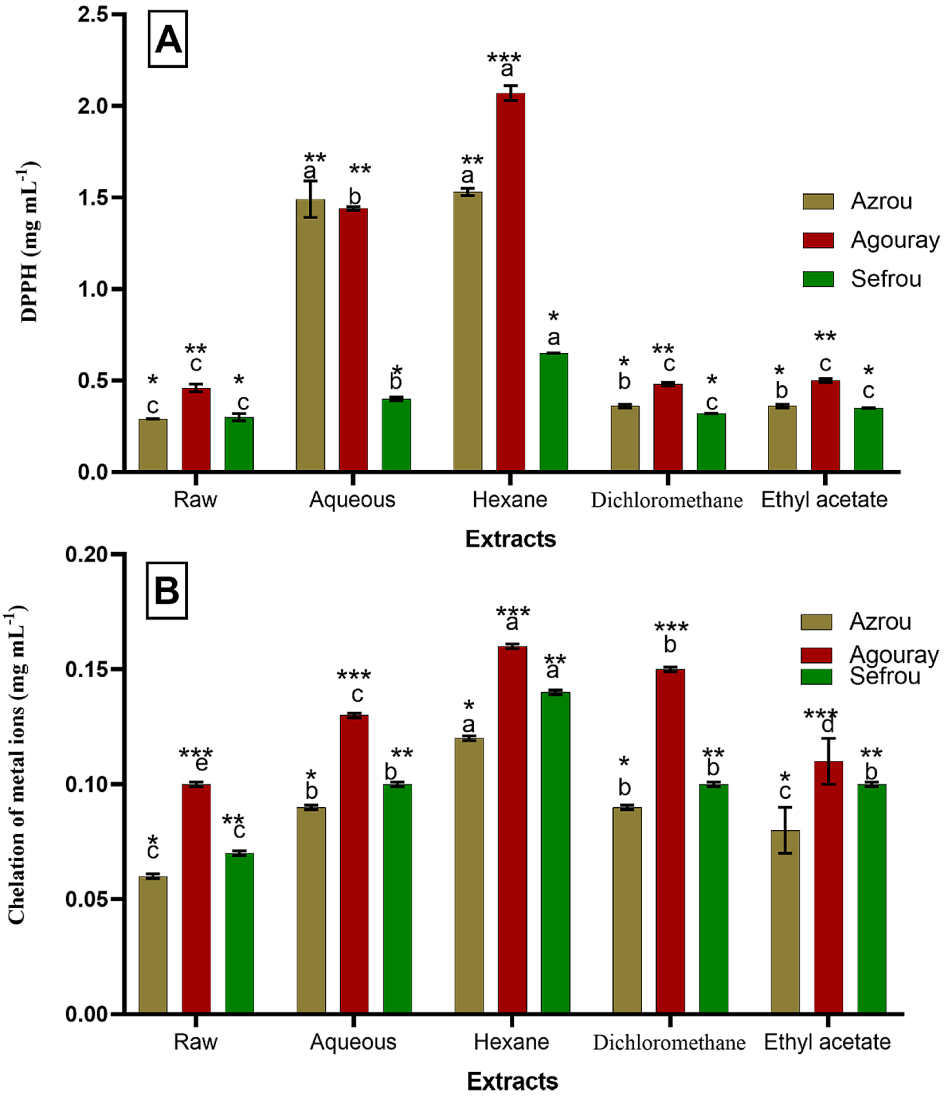

Figure 6. DPPH radical scavenging activity (A) and chelating power (B) in the fractions of *Corrigiola telephiifolia Pourr*. sampled from Agouray, Azrou, and Sefrou (Central Morocco) (*Denote comparison of sampled sites from the same fraction (***>**>*); letters denote comparison among the fractions of the same sampled site (a>b>c>d>e))

0.00, 0.14 ± 0.00, and 0.12 ± 0.00 mg·mL^{-1}). Compared to the fraction of dichloromethane and ethyl acetate. The lowest values of chelating power were recorded in the fraction of raw extracts of *Corrigiola telephiifolia* Pourr. from all sampled sites.

Antimicrobial activity

The results of antimicrobial activity from the fractions of *Corrigiola telephiifolia* Pourr. are presented in Table 1. All tested fractions showed significant inhibitory effects against tested bacteria and fungi. The obtained results showed variable anti-microbial activities depending on the type of fraction, tested microorganism, and origin of the plant. In Agouray, the highest anti-microbial activity was recorded in ethyl acetate against *E. coli* (0.039), followed by hexane against *P. aeruginosa*, dichloromethane against *P. aeruginosa* and *E. coli* (0.078), ethyl acetate against *P. aeruginosa*, and raw against *P. aeruginosa* with MIC estimated at 0.078 each. In contrast, the lowest inhibitory effects were recorded in aqueous fraction against *Saccharomyces*, followed by *C. tropicalis*, *B. subtilis*, *S. aureus* (2.5 each). In Azrou, the highest anti-microbial effect was recorded in hexane against *S. aureus*, dichloromethane against both *E. coli* and *P. aeruginosa*, ethyl acetate against *S. aureus*, *B. subtilis*, *E. coli*, and *P. aeruginosa*, and raw fraction against *B. subtilis* and P. *aeruginosa* (MIC estimated at 0.078 each). In contrast, the lowest inhibitory effects were recorded in the aqueous fraction against *B. subtilis*, *C. tropicalis*, *S. aureus*, and *Saccharomyces* with MIC estimated at 5. In Sefrou, the highest antibacterial activity was recorded in hexane against *S. aureus*, *E. coli*, *P. aeruginosa*, dichloromethane against *B. subtilis*, *S. aureus*, *E. coli*, ethyl acetate against *S. aureus* and *B. subtilis*, raw *E. coli*. and *S. aureus*. In contrast, the lowest inhibitory effect was recorded in the aqueous fraction against *Saccharomyces* with a MIC value estimated at 5.

MBC was also variable depending on the type of fraction, tested microorganism, and the sampled site. In the samples from Agouray, the aqueous fraction showed negative inhibitory

Table 1. Minimal inhibitory concentration (MIC) and minimal bactericide concentration (MBC) in fractions of *Corrigiola telephiifolia* Pourr. from Azrou, Agouray, and Sefrou (Central Morocco) (DCM: dichloromethane, ET AC: ethyl acetate)

AGOURAY																				
FRACTIONS			HEXANE			DCM			ET AC			RAW			AQUEOUS			Gentamicin/ Amphotericin		
			MIC	MBC	MBC/ MIC	MIC	MBC	MBC/ MIC	MIC	MBC	MBC/ MIC	MIC	MBC	MBC/ MIC	MIC	MBC	MBC/ MIC	MFC	MBC	MBC/ MFC
Bacteria	Gram-positive	*S. aureus*	0.156	1.25	8.01	0.156	0.625	4.01	0.078	0.625	8.01	0.156	0.625	4.01	2.5	-	ND	0.32	0.20	0.64
		B. subtilis	0.313	0.625	2.00	0.156	0.625	4.01	0.156	0.625	4.01	0.078	0.313	4.01	2.5	-	ND	0.35	0.24	0.69
	Gram-negative	*E. Coli*	0.156	0.625	4.01	0.078	0.625	8.01	0.039	0.313	8.03	0.078	0.625	8.01	0.625	2.5	4.00	0.37	0.26	0.7
		P. aeruginosa	0.078	0.625	8.01	0.078	0.625	8.01	0.078	0.313	4.01	0.078	0.313	4.01	0.625	2.5	4.00	0.35	0.24	0.69
Fungi		*C. tropicalis*	0.625	5	8.00	0.625	2.5	4.00	0.625	2.5	4.00	0.313	1.25	3.99	2.5	-	ND	2.08	2.16	1.04
		Saccharomyces	1.25	2.5	2.00	0.313	1.25	3.99	0.313	1.25	3.99	0.625	-	ND	5	-	ND	2.12	5.62	2.65
AZROU																				
Bacteria	Gram-positive	*S. aureus*	0.313	2.5	7.99	0.625	2.5	4.00	0.313	2.5	7.99	0.625	2.5	4.00	5	-	ND	0.32	0.20	0.64
		B. subtilis	1.25	5	4.00	0.625	2.5	4.00	0.313	2.5	7.99	0.313	1.25	3.99	5	-	ND	0.35	0.24	0.69
	Gram-negative	*E. Coli*	0.625	2.5	4.00	0.313	2.5	7.99	0.313	2.5	7.99	0.625	2.5	4.00	1.25	-	ND	0.37	0.26	0.7
		P. aeruginosa	0.625	2.5	4.00	0.313	2.5	7.99	0.313	2.5	7.99	0.313	1.25	3.99	1.25	-	ND	0.35	0.24	0.69
Fungi		*C. tropicalis*	2.5	-	ND	2.5	-	ND	2.5	-	ND	1.25	5	4.00	5	-	ND	2.08	2.16	1.04
		Saccharomyces	2.5	-	ND	1.25	5	4.00	1.25	5	4.00	1.25	-	ND	5	-	ND	2.12	5.62	2.65
SEFROU																				
Bacteria	Gram-positive	*S. aureus*	0.313	1.25	3.99	0.313	1.25	3.99	0.313	1.25	3.99	0.313	1.25	3.99	2.5	-	ND	0.32	0.20	0.64
		B. subtilis	0.625	2.5	4.00	0.313	1.25	3.99	0.313	1.25	3.99	1.156	0.625	0.54	2.5	-	ND	0.35	0.24	0.69
	Gram-negative	*E. coli*	0.313	1.25	3.99	0.313	1.25	3.99	1.156	0.625	0.54	0.313	1.25	3.99	1.25	5	4.00	0.37	0.26	0.7
		P. aeruginosa	0.313	1.25	3.99	1.156	0.625	0.54	1.156	0.625	0.54	1.156	0.625	0.54	1.25	5	4.00	0.35	0.24	0.69
Fungi		C. tropicalis	1.25	5	4.00	1.25	5	4.00	1.25	5	4.00	0.625	2.5	4.00	2.5	-	ND	2.08	2.16	1.04
		Saccharomyces	1.25	5	4.00	0.625	2.5	4.00	0.625	2.5	4.00	1.25	5	4.00	5	-	ND	2.12	5.62	2.65

effects against *B. subtilis*, *C. tropicalis*, *S. aureus*, and *Saccharomyces*, while raw extract showed a negative effect against *Saccharomyces* only. The highest antimicrobial effects were recorded in ET AC fraction against *P. aeruginosa* and *E. coli*, and raw fraction against *P. aeruginosa* and *B. subtilis*. In contrast, the lowest inhibitory was recorded in hexane fraction against *C. tropicalis*. In samples of *Corrigiola telephiifolia* Pourr. from Azrou, the fractions showed different MBC values. The aqueous fraction showed negative activity against all tested microorganisms, while hexane, dichloromethane, and ethyl acetate demonstrated negative effects against *C. tropicalis*. Similarly, raw and hexane showed a negative effect against *Saccharomyces*. The highest anti-microbial activity was recorded in raw extract against both *B. subtilis* and *P. aeruginosa*, while the lowest activity was recorded in raw fraction against *C. tropicalis*. The lowest activity was recorded against *C. tropicalis* and *Saccharomyces* by raw, ethyl acetate, and dichloromethane fractions, respectively. In the samples from Sefrou, the fractions showed variable anti-microbial activities depending on the tested microorganisms and type of fraction. The aqueous fraction showed a negative effect against *S. aureus*, *B. subtilis*, *C. tropicalis*, and *Saccharomyces*. The highest inhibitory effect was recorded in dichloromethane against *P. aeruginosa*, ethyl acetate against *P. aeruginosa and E. coli*, and raw against *P. aeruginosa* and *B. subtilis*. In contrast, the lowest inhibitory effect was recorded in the aqueous fraction against both *E. coli* and *P. aeruginosa*, raw against Saccharomyces, ethyl acetate and dichloromethane against *C. tropicalis*, and hexane against both *C. tropicalis* and *Saccharomyces*.

DISCUSSION

This study presents new data on the phytochemical properties of *Corrigiola telephiifolia* Pourr. collected from Morocco. The TPC, TFC, and antioxidant activity of various fractions derived from three distinct regions of *Corrigiola telephiifolia* were compared. The obtained results showed variable chemical properties depending on the fraction type and the sample's origin. These results are important for pharmacopeia and medicine in Morocco and the Mediterranean basin.

This study revealed an important quantity of total phenolic compounds in samples and fractions of *Corrigiola telephiifolia.* The raw fraction exhibited the highest TPC values across all regions, while the aqueous fraction displayed significantly lower TPC values in all sampled sites. Similarly, decreasing TPC values were observed for thetraction methods, sampling areas, used parts of the plant, and extraction solvents (Lakmichi et al., 2010; Oualcadi et al., 2021; Doudach et al., 2022). Daoudi et al., (2017) investigated total polyphenols from samples of *Corrigiola telephiifolia* Pourr. collected from the Middle Atlas. The researchers employed three conventional methods of extraction, namely infusion, decoction, and maceration at ambient temperature. In the results, the highest value of TPC was recorded in the maceration method (58.51 eq Ag mg/g extract), followed by infusion with (51.46 eq Ag mg/g extract), and decoction (49.85 eq Ag mg/g extract). In another study, Miguel et al. (2014) assessed the antioxidant and chemical properties in eleven extracts of Moroccan plants including *Corrigiola telephiifolia* Pourr. In the results, the total polyphenols in extracts of *Corrigiola tolephiifolia* were estimated at 14.593 ± 0.942 mg GAE compared to 31.386 ± 0.942 mg GAE in the extract of *Equisetum arvense*. In a recent study, (Oualcadi et al., 2021) aimed to discover the appropriate method for measuring the antioxidant capacity of the primary bioactive components found in five medicinal plants, including *Corrigiola telephiifolia* Pourr. microwave assisted Soxhlet extraction (MASE) and response surface methodology (RSM) modeling were used for the projecting assessment of TPC, TTC, and concentrations of flavonoid (TFC). In the results, TPC was estimated at 6.47 ± 0.10 mg·GAE/g·dw, while the predicted value was at 6.17 ± 0.70 mg ·GAE/g·dw. All these findings of the bibliography confirm the variation of polyphenols in the extracts of *Corrigiola telephiifolia* Pourr. depending on the used extraction method, solvents, and sample site, which is in agreement with the results obtained in this paper. In the considered case, the significant difference in the TPC of the fraction could be attributed to the used solvents and the pedoclimatic conditions of the sampled area. In fact, the samples from Azrou were under the humid climate of the central Middle Atlas, while the samples of Sefrou were under the semi-arid climate of the eastern Middle Atlas. In contrast, the samples from Agouray were under the degraded Mediterranean climate, subject to continental influences during the summer and winter seasons. Equally, the

altitude was higher in Sefrou (1600) and Azrou (1300) compared to Agouray (560 m). In terms of extract solvent, row extracts contain all chemical elements compared to fractions that contain only fractions of bioactive compounds. The difference in TPC among the studied extracts is due to the polarity of each solvent. Similar results were recorded in organic and aqueous extracts from the aerial portions of *Haloxylon scoparium* (Lachkar et al., 2021). Further, ethyl acetate, methanol, petroleum ether and chloroform and by maceration in cold with methanol were the used solvents to evaluate the quantity of TPC. In aqueous extracts, TPC was 6.83 ± 0.04 (µg·GAE·mg^{-1}·E) with decoction, 3.81 ± 0.21 (µg·GAE·mg^{-1}·E) in infusion and 3.96 ± 0.07 (µg·GAE·mg^{-1}E) with maceration. In organic extracts, the TPC was variable from 161.65 ± 1.52 (µg·GAE mg^{-1}·E) in methanol, 147.11 ± 6.11 (µg GAE mg^{-1}·E) in macerated methanol, 49.42 ± 1.02 (µg·GAE ·mg^{-1}·E) in chloroform and 11.30 ± 1.58 (µg·GAE ·mg^{-1}·E) in petroleum ether. Similar findings were currently recorded in various extracts from seeds of *Peganum harmala* L. (Souad) (Senhaji et al., 2022). The extract obtained via maceration in methanol has the highest concentration of polyphenols (94.37 ± 0.62 µg·GAE/mg·E), while the extract of ethyl acetate comprises the uppermost levels of flavonoids (366.13 ± 1.88 µg·QE/mg·E).

This experiment demonstrated for the first time the variation of flavonoids in extracts of *Corrigiola telephiifolia Pourr.* depending on the type of solvents, fractions, and origin of samples. Concerning the effect of the sampled area, TFC was 8.67 ± 1.50 mg·RE/g·dw in the samples of *Corrigiola telephiifolia* from the South of Morocco (Oualcadi et al., 2021) compared to 3.843 ± 0.215 (mg/g, dry weight) in the samples from Fes-Meknes region (Miguel et al., 2014). Concerning the effect of extraction solvent, (Do et al., 2014; Bui et al., 2021; Khalili et al., 2022) demonstrated that the used extraction solvent affects directly the quantity of flavonoids in various plants counting *Limnophila aromatic*, *Avicennia officinalis*, and *Allium cepa*. For instance, different percentages of methanol, followed by both ethanol and acetone in aquatic (50%, 75%, and 100%) were utilized as solvents in the extraction of *L. aromatic*, and in a result, and the 100% ethanol extract (31.11) has the greatest rate (29.34–31.11 mg·QCE/g·DFLA) with the uppermost value, followed by the 100% acetone extract (30.86 mg·QCE/g·DFLA) and the 75% aqueous and acetone extract (29.36 mg·QCE/g·DFLA) (Do et al., 2014). In one more study (Mehmood et al., 2022) examined the fluctuation of flavonoids within three medicinal plants native to Azad Jammu and Kashmir, namely *Aloe vera*, *Bergenia ciliata*, and *Achillea millefolium*. This examination was conducted by subjecting the plants to several solvent systems, including water, ethanol, and methanol. The findings revealed that the ethanol extract of *A. millefolium* exhibited a high flavonoid content of 27.13 ± 0.64 mg·QE/g·dry weight. Similarly, the methanol extract of *B. ciliata* had a significant flavonoid content of 17.44 ± 0.44 mg·QE/g·dry weight. Additionally, the methanol extract of *Aloe vera* displayed a noteworthy flavonoid content of 14.68 ± 0.67 mg·QE/g·dry weight. The variation of total flavonoids in the results of the presented study and those of previous investigations is suggested to be governed by the polarity of each solvent and its affinity toward flavonoids. Comparable results were confirmed by Dong et al. (2023) who elucidated the correlation and molecular interface mechanism of several flavonoids in different molecular diluents. Similarly, Palaiogiannis et al. (2023) examined the process of succeeding solvent extraction of flavonoids and polyphenols from leaves of *Cistus creticus* L. The findings of the study demonstrated that sequentially employing a series of solvents proves to be a more effective approach for extracting greater quantities of antioxidant compounds. This method also allows for the extraction of phyto-compounds with diverse antioxidant properties, which can be attributed to the synergistic interactions between the combined solvents and flavonoids.

In this paper, the antioxidant capacity of used solvents and their fraction in the extracts of *Corrigiola telephiifolia* Pourr. and the effect of origin of samples were assessed. Ferric reducing-antioxidant power, followed by free radical scavenging activity and chelation of metal ions in hexane, dichloromethane, chloroform, ethyl acetate, and aqueous (fractions of *Corrigiola telephiifolia* Pourr. sampled from Agouray, Azrou, and Sefrou were recorded. The obtained results showed that the antioxidant activities were variable among fractions and sampled areas. The uppermost values of DPPH radical scavenging activity were detected in the hexane fraction for all sampled sites. The maximum values of chelating power were also observed in the hexane fraction. The highest ferric reducing antioxidant power was recorded in the raw extracts from Agouray, followed by Azrou

and Sefrou. In comparison with previous studies, Oualcadi et al. (2021) evaluated from five folk medicinal plants including *Corrigiola telephiifolia* Pourr. and recorded variable values ranging from 0.69 ± 0.03 (g·AAE/g·dw) for DPPH (IC50 = 3701.17 ± 78.05 µg/mL) to 0.0040 ± 0.0002 (g·AAE/g·dw) for FRAP (IC50 = 10265.0 ± 361.9 µg/mL). This variation is suggested to be related to the chemical constituents of the sampled plants and the fraction of bioactive compounds in each extract (Maisuthisakul et al., 2008; Prado et al., 2013). Ahmed et al. (2019) investigated the total phenolic content and antioxidant properties in the extracts and essential from sweet basil *(O. basilicum* L.) and demonstrated an advanced relationship between antioxidant properties and phenolic contents in extracts of basil. Similarly, Muflihah et al. (2021) demonstrated a significant relationship between antioxidant properties and bioactive compounds counting polyphenols and flavonoids in 12 Indonesian indigenous herbs.

All tested fractions showed significant inhibitory activities against tested bacteria and fungi. In Agouray, the highest anti-microbial activity was recorded in ethyl acetate against *E. coli* (0.039), In Azrou, the highest anti-microbial effect was recorded in hexane against *S. aureus*, dichloromethane against both *E. coli* and *P. aeruginosa*, ethyl acetate against *B. subtilis*, *P. aeruginosa, S. aureus*, and *E. coli*, as well as raw fraction against *B. subtilis* and *P. aeruginosa*, In Sefrou, the uppermost inhibitory activity was recorded in hexane against *E. coli*, *S. aureus*, *P. aeruginosa*, dichloromethane against *B. subtilis*, *S. aureus*, *E. coli*, ethyl acetate against *S. aureus*, and *B. subtilis* while raw against *E. coli* and *S. aureus*.

In another study (Doudach et al., 2012), conducted an assessment of the antibacterial properties exhibited by aqueous and methanolic extracts derived from *Corrigiola telephiifolia* Pourr. The evaluation specifically targeted the impact on both Gram-negative strains of bacteria (*K. pneumonia*, *E. coli* and *P. aeruginosa)* as well as Gram-positive germs like *Bacillus subtilis*, *S. aureus,* and *Micrococcus luteus.* As a consequence, the methanol extracts exhibited noteworthy antibacterial properties against the majority of the pathogens tested. The methanol extracts of *Corrigiola telephiifolia* Pourr. exhibited the highest level of effectiveness against *K. pneumoniae*, *P. aeriginosa*, *M. luteus*, and *E. coli*, as evidenced by MIC levels reaching between 3.12 and 6.25 mg/ml. further, the observed inhibitory activity of the water extract was found to be lower than that of the methanolic extract, with minutest inhibitory concentrations of 3.12 mg/ml and 12.5 mg/ml, respectively, against all experienced strains of bacteria. In another study, Amine et al. (2017) conducted an assessment on the antibacterial properties of aqueous extracts derived from *Corrigiola telephiifolia* Pourr., which were gathered from the Middle Atlas section in central Morocco. Further, the investigation aimed to assess the efficiency of these extracts against three distinct bacterial germs. The findings indicate that the aqueous extract of *Corrigiola telephiifolia* Pourr. exhibits a modest level of activity against *E. coli*. at a dose of 100 $\mu g \cdot mL^{-1}$, the inhibition zone had a size of 9 ± 0.06 mm. In contrast, the strains of *K. pneumoniae*, *S. aureus,* and *E. coli*, exhibited vulnerability to the macerate from *A. pyrethrum* at 100 $\mu g \cdot mL^{-1}$ concentration, resulting in inhibition zones estimated at 16.55 ± 0.6 mm, followed by 14.95 ± 1.25 mm and 10.83 ± 0.96 mm, correspondingly. This paper is an investigation into the antimicrobial properties of several fractions derived from extracts of *Corrigiola telephiifolia*. The difference in inhibitory effects among used fractions is governed by the variety of chemical compounds in each fraction and solvent. Similar results were currently recorded in fraction of *Z. montanum, Z. officinale Roscoe,* and *Z. zerumbet* against *Propionibacterium* (Aji et al., 2022).

CONCLUSIONS

This study presented new data on the bioactive constituents and antioxidant activity in raw and fractions of organic and aqueous extracts of roots from *Corrigiola telephiifolia* Pourr. sampled from three sites in Morocco. The obtained data showed that the contents of total phenols and flavonoids varied depending on fractions of extracts and sampling site. The raw fraction exhibited the highest TPC values in all sampled sites, while the lowest values were recorded in hexane fraction. The raw extracts showed the highest TFC with a supreme value in samples from Agouray, while the other extracts showed lower TFC values. Similarly, the antioxidant activities were variable depending on extracts and sampling site. The highest value of ferric-reducing antioxidant power (FRAP) was recorded in a fraction of raw extract, followed by dichloroform, while in the fractions of the other extracts, the values of FRAP

were similar. The uppermost DPPH radical scavenging activity was observed in the hexane fraction for all sampled sites. The chelating power was significantly superior in the hexane fractions of all sampled sites. The antioxidant activities were related to the quantity of total polyphenols and flavonoids in the fractions of the extracts, while the quantity of bioactive compounds was connected to various factors counting origin of samples, pedoclimatic conditions of the plants, and used solvents during the extraction. This research highlighted the potential of *C. telephiifolia* as a source of valuable phytochemicals and supports its traditional medicinal uses. However, further research is needed to understand the underlying mechanisms of these variations and to explore the potential therapeutic applications of this plant.

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