

Corrigiola Litoralis Subsp. Telephiifolia (Pourr.) Briq. – An Extensive Review of Geographical Distribution, Phytochemical Content, Functionality, and Guidelines for Prospect Investigations

Wissal El Yaagoubi^{1,2*}, Meriem Soussi¹, Saadia Belmalha², Ismail Mansouri³,
Wafae Squalli¹, Lahsen El Ghadraoui¹

¹ Laboratory of Functional Ecology and Environmental Engineering, Faculty of Sciences and Technology, Sidi Mohamed Ben Abdellah University, Fez, 30000, Morocco

² Department of Plant Protection and Environment National School of Agriculture BP S/40 50 000 Meknes, Morocco

³ Research Team “Biology, Environment and Health”, Department of Biology, Faculty of Sciences and Technologies Errachidia, Moulay Ismail University of Meknes, 5(2000) Errachidia, Morocco

* Corresponding author’s e-mail: wissalelya@gmail.com

ABSTRACT

Corrigiola telephiifolia is an aromatic and medicinal herb whose constituents hold worldwide interest for its various ethnopharmacological properties in the pharmaceutical field. This review provides a comprehensive analysis of the geographical distribution, phytochemical contents, traditional uses, and pharmacological properties of *Corrigiola telephiifolia* Pourr. Through an exhaustive search of primary databases, literature from 1950 to 2022 was examined, focusing on keywords to ensure inclusivity. The plant exhibits diverse physiological functions, potentially aiding in the prevention of diabetes, dyslipidemia, oxidative stress, and microbial infections while enhancing immunity. Similarly, we outlined recommendations for future research aimed at addressing existing gaps, and additional comprehensive studies are necessary to investigate the influence of climate change and other factors on the variability of chemical constituents. These endeavors would provide fresh perspectives on the biological characteristics of this species and offer guidance for future research initiatives.

Keywords: bioactive compounds, traditional medicine, pharmacological properties, *Corrigiola telephiifolia* Pourr.

INTRODUCTION

Before the development of the pharmaceutical industry, medicinal plants were used as the first treatment line to relieve different health disorders throughout the long human history (Elahee et al., 2019; Ren et al., 2021). The search for efficacious herbs and appropriate formulations that might be safe without inducing adverse effects leads to the conduction of different investigations *in vitro* and *in vivo* of natural products extracted from wild or cultivated plants (Kifle et al., 2022; Ulriksen et al., 2022). In parallel, different ethnopharmacological and survey studies were conducted on different traditional uses of different herbs or their derivatives to provide knowledge

and insights into their beneficial properties as a framework for the experimental studies (Bellakhdar, 1989; Bellakhdar et al., 1991; Bellakhdar, 1997; Lekouch et al., 2001; Bnouham et al., 2006; Bnouham, 2010; Sana et al., 2010). However, despite the scientific progression and development of modern medication, natural remedies are still used to treat or limit the evolution of many health disorders particularly in rural areas of developing countries (Bellakhdar, 1989).

The Moroccan pharmacopeia is rich in medicinal herbs knowledge inherited from ancestral generations and transferred to other the next ones, and a lot of this knowledge is not yet well documented (Elachouri, 2018; El-Ghazouani et al., 2021; Bouyahya et al., 2022). It has been

documented that 231 medicinal plants have been identified and listed in Moroccan pharmacopeia (Bellakhdar et al., 1991; Hachlafi et al., 2020; Bouyahya et al., 2022; Mohamed et al., 2022). One of the most used plants in traditional medicine is *Corrigiola litoralis* subsp. *telephiifolia* (Pourr.) Briq. or Serghina as commonly named in Moroccan culture (Mouhajir et al., 2001). This plant belongs to the Caryophyllaceae family and grows in different soils accounting for rocky and sandy soils (Lakmichi et al., 2010a). In Morocco, the plant is distributed in mountainous areas of the central Middle Atlas and Northern regions of the Rif close to the Mediterranean coasts (Lakmichi et al., 2010a). The species has also been seen in coastal regions around the Mediterranean in Spain and Italy (Doudach et al., 2022). The plant occupies different sorts the stony substrate, preferring humid conditions over well-drained sandy soils. Equally, it can arise in brown soils and acidic poor clay substrates principally with low abundance, and avoids soil salinity (Lakmichi et al., 2010b). In addition, Morocco is well known for its wealth and a long list of medicinal plants used in the treatment of different ailments.

Corrigiola telephiifolia Pourr. has been widely used in North Africa countries including Morocco, Algeria, and Tunisia as traditional herb to treat delicate health conditions and various ailments such as dermatological diseases, ulcers, and inflammation (Al Faiz et al., 2006; Lakmichi et al., 2010a; Kabbaj et al., 2012; Zakariya et al., 2020). Different parts of this plant such as roots that release sweet odors when burned, while their powder is used to treat dermatological disorders, diuretics, and inflammation (Al Faiz et al., 2006). In addition, the root extracts of the aforementioned plant exhibited a powerful protective effect against histopathological damages induced by carbon tetrachloride (Doudach et al., 2022). Other studies have proved that the *Corrigiola telephiifolia* Pourr. roots extracts acted as a cytotoxic agent against murine colon adenocarcinoma CT-26 and melanoma cell lines WM-266 (Doudach et al., 2013). Research conducted by (Hebi and Eddouks, 2019) showed that the administration of aqueous extracts of areal parts of *Corrigiola telephiifolia* pour attenuates metabolic disorders in streptozotocin-intoxicated rats. The antioxidant profile of *Corrigiola telephiifolia* Pourr. makes it an excellent vegetable matrix to counteract the deleterious effects of reactive oxygen species which amerce different pathological

processes, such as Parkinson's disease (Tieu et al., 2003) and cardiovascular diseases (Gao et al., 2008). Within this frame, numerous studies have shown that the *Corrigiola telephiifolia* exhibits an interesting inhibition lipid peroxidation effect, scavenging free radicals, inhibiting lipoxygenase, and acetylcholinesterase activities (Doudach et al., 2013; Miguel et al., 2013; Hebi and Eddouks, 2019; Zakariya et al., 2020).

In this paper, we presented a review to summarize the existing knowledge on the medicinal uses of *Corrigiola telephiifolia* Pourr., chemical compounds, and to itemize its therapeutic effects scientifically. In detail, we reviewed data on geographical distribution, chemical compounds, medicinal uses, and biological properties. The utilization of reviews is crucial in effectively incorporating pre-existing literature and facilitating the accessibility of data for the purpose of informed decision-making. In this particular review the most relevant features that need further research to fill the gap in the knowledge of this unique and multi-use plant are documented. All information documented in this review will be of real importance in enriching the Moroccan and the Mediterranean databases on *Corrigiola telephiifolia* Pourr. as a natural agent widely used to treat different ailments.

METHODOLOGY

Search approach and collection criteria

All information sources used to prepare the current review were obtained and collected using search engines including Google Scholar, Science Direct, PubMed, MDPI, and Web of Science. During our research, we used the following keywords: *Corrigiola telephiifolia* Pourr, pharmacological properties of *Corrigiola telephiifolia* Pourr., the phytochemical profile of *Corrigiola telephiifolia* Pourr. and the geographical distribution of *Corrigiola telephiifolia* Pourr. The articles were searched from 1950 to 2022 and a total of 287 papers including 230 peer-reviewed articles and 57 non-peer-reviewed papers aided the compilation of this article. The non-peer-reviewed papers inserted to avoid any low-quality information since this is the first review paper concerning *Corrigiola telephiifolia* Pourr. geographical distribution, phytochemical content, functionality, and guidelines for prospect investigations. Only 115 articles were selected for their scientific

quality and relevance to prepare the current work. These articles include clear data on targeted topics. Equally, we prepared a map of geographical distribution based on the selected articles.

According to (Rivera et al., 2014; Dauncey et al., 2016), the International Plant Names Index (IPNI) and The Plant List (www.plantlist.org) were used to verify the accuracy of the botanical names of the plants. Quattrocchi (2012) provided the names that are commonly used in English. Only plants that have historically been used to treat DM were considered. The search on the aforementioned databases included the plant's name together with various combinations of the phrases “traditional,” “ethnomedicinal,” and “ethnobotanical”.

Study selection

A total of 287 papers including 230 peer-reviewed articles and 57 non-peer-reviewed papers were selected. Furthermore, the selected papers were divided as follows: 30 from PubMed, 60 from ScienceDirect, and 27 from Google Scholar. The non-peer-reviewed papers to avoid any low-quality information since this is the first review paper to concerning *Corrigiola telephiifolia* Pourr geographical distribution, phytochemical content, functionality, and guidelines for prospect investigations. Only 115 articles were selected for their scientific quality and relevance to prepare the current work. These articles include clear data on targeted topics. The selection method adhered to the Preferred Reporting Items for Reviews and

Meta-Analyses (Figure 1). Equally, a map of geographical distribution based on the selected articles was prepared.

RESULTS AND DISCUSSION

Taxonomy

Corrigiola telephiifolia Pourr. is member of the family Caryophyllaceae, Order Caryophyllales, which is composed of 80 genera of flowering plants and approximately 2.000 species. It is distinguished by its fleshy, closely spaced leaves (Nowicke, 1975; Klak et al., 2003). The majority of these plants are herbaceous, with stems bearing simple leaves that are typically arranged in opposition to one another and linked to the stem at the level of a swelling node, like in real carnations or catchflies (Bittrich, 1993). Phylogenetic categorization, which is based on genetic traits, primarily plastid DNA sections, replaced the traditional Cronquist classification that was introduced in 1981 (Candau, 1978; Bittrich, 1993; Klak et al., 2003).

Doudach et al. (2022) presented a new description of the plant and mentioned that *Corrigiola telephiifolia* Pourr. is a perennial plant with nearly 60 cm in height (Figure 2), and a thick stem. Similarly, the mature plant is characterized with higher leaves, which are slightly fleshy, close together, sub spatulate, obovate, or oblong, while lower ones are narrower. Furthermore, flowering branches are entirely leafless and flowers are pedicellate with a rounded green

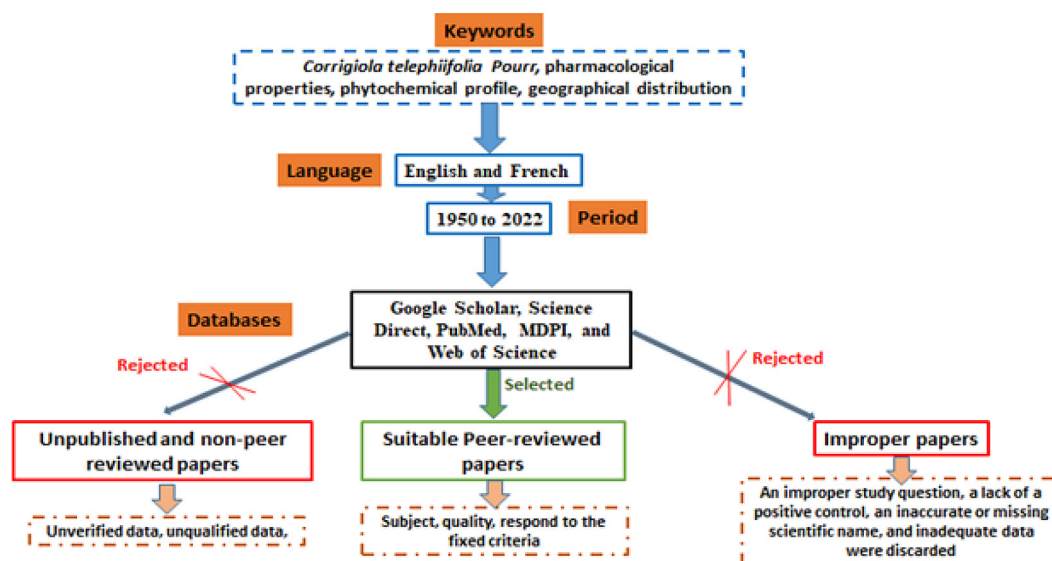


Figure 1. Followed research method to complete this review

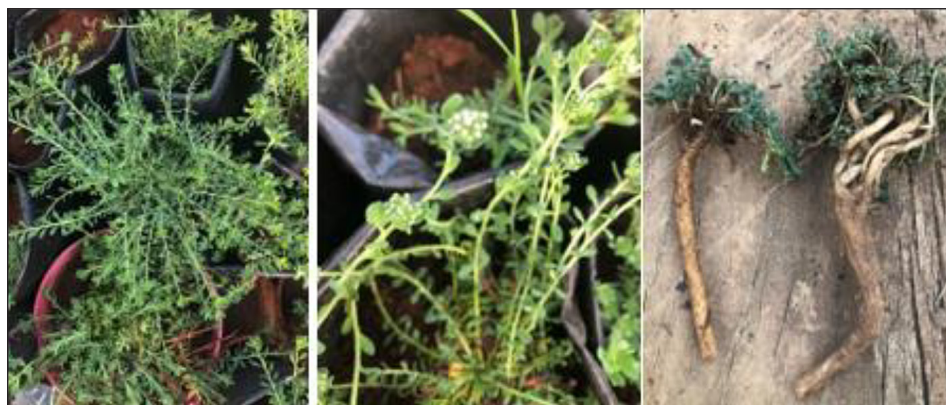


Figure 2. *Corrigiola telephifolia* Pourr.

part and produce tuberos seeds (Bittrich, 1993). *Corrigiola telephifolia* Pourr. flowers during two seasons per year, from mid-January in winter and spring in the Mediterranean area (Doudach et al., 2022). However, more studies based on the latest advances in molecular technologies are needed to classify this species and to understand the map and functions of its genome (Yu et al., 2021; Lapierre et al., 2023). The use of new technologies is suggested to separate between subspecies and varieties depending on sampled areas as mentioned currently for subspecies of *Musa* (Dhivya et al., 2020). Equally, the biology and phytosociology of this species need further updates principally in accordance with current climate change. Because many plants have shifted their entire cycle in a response to adverse climatic conditions counting hot temperatures (Davis and Shaw, 2001), which is the case in Morocco and North Africa (Carneiro et al., 2010; Schilling et al., 2012).

Geographical distribution

A sub-Atlantic mediterranean species, *Corrigiola telephifolia* Pourr. is found in mediterranean regions of North Africa (Morocco and Algeria) and West and Central Europe (Spain, France, Italy, and Portugal) (Figure 3) (Bittrich, 1993; Güntsch et al., 2002; Castroviejo, 2020, 2020). The plant is common in most parts of Spain's regions and provinces (Blanca et al., 2009; Castroviejo, 2020; VALDÉS,). It is known to occur in most of the northern and eastern regions of Portugal, but it is rare in the southern regions and nonexistent in most of the western regions (Sequeira et al., 2011; Açores, 2014). It exists in Corsica and a few provinces in the southern part of the French mainland (Tutin et al., 1972). Records

come from a few locations in the Tuscany region and Sardinia, Italy (Tutin et al., 1972).

The species is also known to exist in Algeria (Maire, 1952) and primarily in Morocco in northern Africa. It can be found in multiple important floristic divisions, including the Rif (which includes the Loukkos, Tazeka, Oued Laou, Targuist, and Tazeka Peninsula south to Larache), Maamoura, Oued Cherrat, Kenitra, between Casablanca and Rabat, between Romani and Rabat, Sidi Allal El Bahraoui, Ain Harrouda Forest, Tiflet, and Timeksouine which are located in Morocco's North Atlantic. It is also native to Middle Atlantic of Morocco (From Cape Beddouza to Casablanca, Nouasser Abda, Oudjan, Berrechid, Meknès, Middle of Sebou, Jebel Izzou, Mechra Benabbou, Oum-Rabie, Bni-Abid, Fès, Zaer, Ben Slimane, Khouribga, Sidi Zouine, Merzouga, Skhour Rhamna, Kella Serrahna, Zaouia Cheikh, and Marrakech), and the Atlas (Seksoua Parc, Ida-ou-Tanane, Jbel Ayachi, and Siroua) (Maire, 1952; Benabid, 2000; Ibn-Tattou and Fennane, 2008; Blanca et al., 2009). The plant can be located as high as 3.000 meters. More than 20.000 km² is the area of occupancy (AOO) and 2.000 km² is the extent of occurrence (EOO). Currently, many ethnobotany studies reported the distribution of *Corrigiola telephifolia* Pourr. in rural areas of Middle Atlas, Saiss plain (Yaagoubi et al., 2023), and Al-Haouz Rehamna (Benkhniqie et al., 2023), which indicate that the geographical distribution is not yet limited. Therefore, the geographical assessment of this plant needs more attention, principally in the Northern slope of the mediterranean basin, where data from analyzed papers is fragmentary and limited.

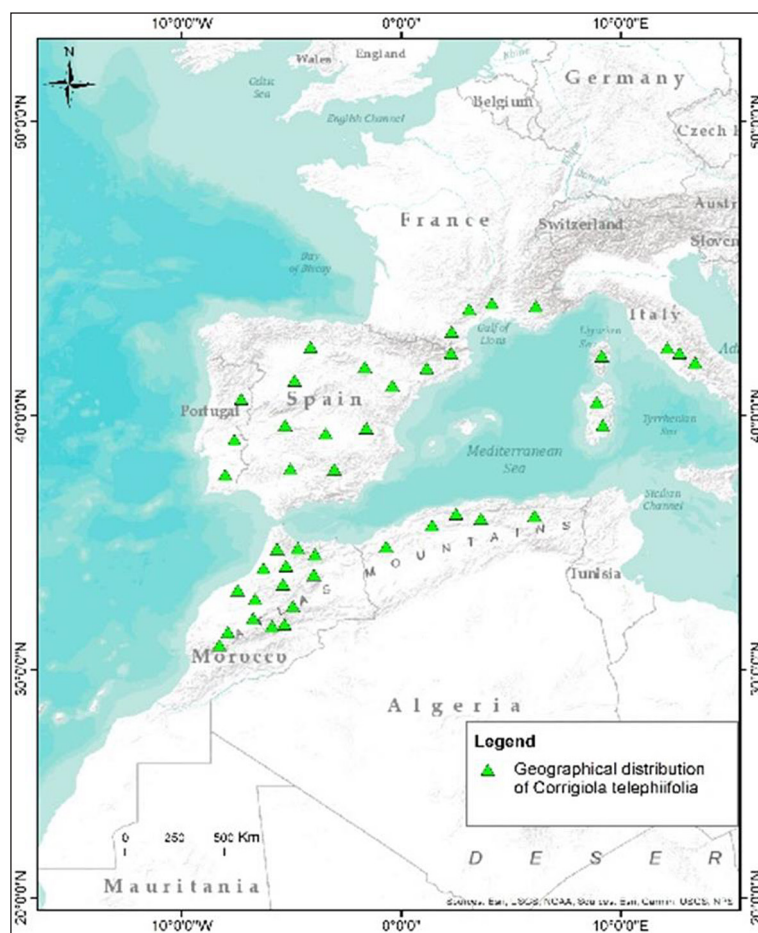


Figure 3. Geographical distribution of *Corrigiola telephiiifolia* Pourr

Chemical characteristics

Corrigiola telephiiifolia Pourr. Has been the subject of several studies in the last decade, due to the wide range of beneficial effects of its components (Doudach et al., 2012, 2013; Daoudi et al., 2017; Doudach et al., 2022). However, by screening scientific databases, it was realized that the chemical characterization of *Corrigiola telephiiifolia* pour. was concentrated on phenolic content from aqueous extracts (Mouhajib et al., 2001; Lakmichi et al., 2010a). These chemical components were extracted from the areal and underground parts of the plants.

The phytochemical analysis of methanolic extracts from roots and aerial parts of the plant has revealed the presence of a diversity of chemical compounds including alkaloids, tannins, saponins, terpenes, flavonoids, and quinones (Table 1, Figure 2). However, the composition and concentrations of chemical compounds were variable among analyzed studies depending on sampling areas, used materials, and extraction

methods. For instance samples (methanolic extracts from roots) collected near Ben Slimane city (Atlantic Morocco), the saponins were the most dominant compounds, followed by Steroids, quinones, and terpenes with moderate concentrations, and low concentrations of flavonoids and tannins (Doudach et al., 2022). In contrast, Water and aqueous-alcoholic (70%) extracts of root and areal parts showed high concentrations of Polyphenols (33.05 mg to 58.5 ± 0.76 mg). (Oualcadi et al., 2021) reported that the *C. telephiiifolia* contained total phenolic content (TPC) amounting to 6.47 ± 0.10 mg GAE/g, while Miguel et al., (2013) found that the Total Polyphenol Compounds of *C. telephiiifolia* was 14.593 ± 0.942 mg GAE/g. Another study reported that the TPC of the plant aqueous extract had a content of 33.05 mg GAE/ml (Hebi and Eddouks, 2019). These variations suggest the interference of environmental and biogeographical conditions since these have shown direct and indirect effects on the chemical composition of plants (Kleinwächter and Selmar,

Table 1. Chemical composition, extraction methods of different parts of *Corrigiola telephiifolia* Pourr.

Part used	Extracts	Compounds/Antioxidant activity	Concentration	References
Root Aerial part	Water Aqueous alcoholic (70%) Water	Polyphenols	58.5 ± 0.76 mg 14.593 ± 0.942 mg 33.05 mg	(Amine et al., 2017) (Miguel et al., 2014) (Hebi and Eddouks, 2019)
Root Aerial part	- Aqueous alcoholic (70%) Water	Flavonoids	- 3.843 ± 0.215 mg 14.87 mg -	(Amine et al., 2017) (Miguel et al., 2014) (Hebi and Eddouks, 2019) (Doudach et al., 2022)
Root	-	Tannins	-	(Amine et al., 2017) (Doudach et al., 2022)
Root	-	Alkaloids	-	(Amine et al., 2017) (Doudach et al., 2022)
Root	-	Saponins	-	(Amine et al., 2017) (Doudach et al., 2022)
Root	-	Steroids	-	(Amine et al., 2017)
Aerial part	Aqueous-alcoholic (70%)	Thiobarbituric acid reactive species (TBARS)	1.154 ± 0.120	(Miguel et al., 2014)
Aerial part	Aqueous-alcoholic (70%)	free radical-scavenging activity (ABTS)	0.737 ± 0.079	(Miguel et al., 2014)
Aerial part	Aqueous-alcoholic (70%) Methanolic extract	Free radical scavenging activity (DPPH)	0.673 ± 0.061 82.07 ± 0.31%	(Miguel et al., 2014) (Doudach et al., 2022)
Aerial part	Aqueous-alcoholic (70%)	Chelating metal ions	0.1792 ± 0.040	(Miguel et al., 2014)
Aerial part	Aqueous-alcoholic (70%)	Hydroxyl radical scavenging activity	0.287 ± 0.013	(Miguel et al., 2014)
Aerial part	Aqueous-alcoholic (70%)	5-Lipoxygenase assay	1.523 ± 0.030	(Miguel et al., 2014)
Root	-	Terpenes	-	(Doudach et al., 2022)
Root	-	Quinones	-	(Doudach et al., 2022)

2014). For example, *Gentiana rigescens* (one of the most important medicinal plants in Asia) has adjusted its geographical distribution to respond to climate change, and this has impacted on its chemical compounds (Pan et al., 2015; Shen et al., 2021). Furthermore, Szakiel et al. (2011) have proved the effects of biotic stressors such as herbivorous and pathogens on the saponins in many plant species because of their roles in the defence system (Hussain et al., 2019). Fouedjou et al. (2021) have reported new monodesmoside triterpene saponins named telephiifoliosides A and B, which exhibited high antiproliferative effects on human malignant epithelial cells (Figure 4). These polyphenolic compounds or secondary metabolites were the results of the biotic and abiotic stress exposure of the plant (Dicko et al., 2005) and are well known for their antioxidant potential to act pleiotropically (Laaroussi et al., 2020). Furthermore, other studies principally on areal parts counting leaves and stems are required to determine the phenolic profile of *Corrigiola telephiifolia* Pourr., which is suggested to valorize this poorly investigated plant.

Traditional uses across of the plant Moroccan territories

In Morocco, *Corrigiola telephiifolia* is harvested for both private and commercial purposes (El-Hilaly et al., 2003; Lakmichi et al., 2010a). Commercial basis, 370 tons of this plant are exported annually (Etablissement Autonome de Controle et de Coordination des, 2006; Lakmichi et al., 2010a). Dried roots of *C. telephiifolia* are used in fumigation candles to ward off bad spirits and scent clothing and homes. The root's fragrant qualities are also utilized in cosmetics, fragrances, and other beauty care items (such as powders, blushes, and dry scents) (Bellakhdar, 1989, 1997a, 1997b; Bellakhdar et al., 1991; Benchaâbane and Abbad, 1997). Health problems, such as coughs, migraines, and illnesses of the lungs, liver, and skin, are treated with the root. utilized as a diuretic as well (Zakariya et al., 2020). In addition, tonic, fortifier, and aphrodisiac preparations are made with it (Lakmichi et al., 2010a). Inhaled fumes are used to treat respiratory conditions like colds, rheumatism, coryza,

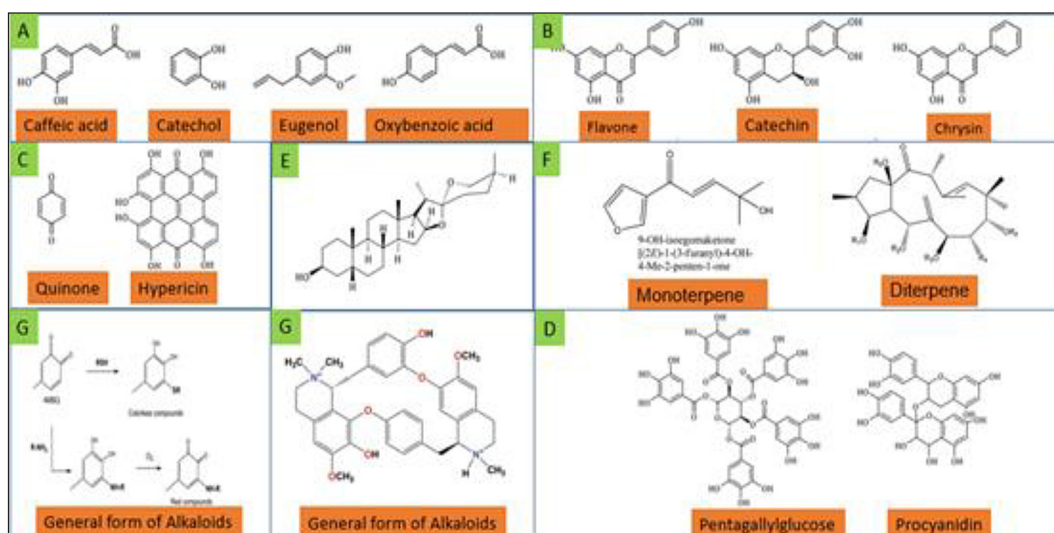


Figure 4. Structures representing of polyphenols (a), flavones and flavonoids, (b), quinones (c), tannins (d), saponins (e), terpenes (f), alkaloids (g), and quinones (h)

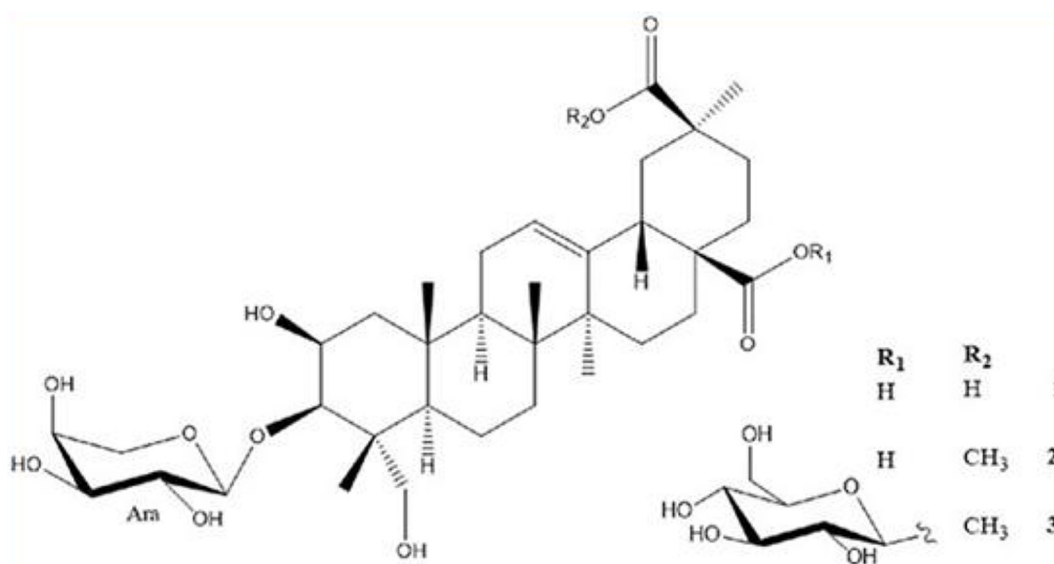


Figure 5. Structure of newly recorded triterpenoid saponins (telephiifoliosides) from the roots of *Corrigiola litoralis*

influenza, headaches, and dizziness (Bellakhdar, 1997; Kabbaj et al., 2012; Eddouks et al., 2017; Bencheikh et al., 2021; Beniaich et al., 2022). Due to the tonic and restorative properties of the dried ground root, it is sometimes added to food, particularly bread or couscous (Bellakhdar, 1997; Lakmichi et al., 2010a). Average cytotoxic and inhibitory values demonstrate the potential action of *Corrigiola telephiifolia* (CT) root extracts, making them highly interesting in the emerging field of anticancer drug research (Doudach et al., 2013). Table 2 summarizes different traditional uses of CT across Moroccan territories.

Agronomic uses

In agriculture, many phytopathogens affect crops and cause heavy economic losses (Chen, 2020; Fones et al., 2020), but with advances in pesticide control technologies, farmers are capable of reducing losses to acceptable levels (Rabiey et al., 2019; Razaq et al., 2019). However, the intensity of chemical treatments induce resistance in many phytopathogens, mainly fungi, and bacteria, which widely impacted on the environment (Hendrickson et al., 2019; Mira et al., 2021). Therefore, scientists have turned to

Table 2. Traditional preparation methods, administration, and uses of areal and root parts of *Corrigiola*

Region	Used part	Preparation	Administration	Uses	Reference
–	Roots	Decoction	Oral	Digestive and liver disorders	(Merrouni and Elachouri, 2021)
–	Roots	Powder	Oral	Diabetes	(Idm'hand et al., 2020)
Aguelmous khenifra	Roots	Decoction	Oral	Influenza, Cough, Respiratory, Urogenital, gastric, neurological, microbial, typhoid, rheumatologic, and ENT pathologies	(Mouhajir et al., 2001; Najem et al., 2021)
Agourai	Roots	Decoction, infusion, fumigation	Oral, Inhalation	Cold, Lung disorders	(Chaachouay et al., 2020)
Morrocan Rif	Whole plants	Decoction	Oral	Kidney stones	(El-Hilaly et al., 2003)
	Roots	Decoction, Burnt	Oral, Washing, Fume	Lung disorders, hair care, magic, and bad spirit	(El-Hilaly et al., 2003)
Central Middle Atlas	- Roots	- Decoction	- Oral	Respiratory disorders, Digestive tract disorders, Cosmetic, urogenital, gastric and dermatological, neurological, respiratory, and typhoid pathologies	(Daoudi et al., 2017; Najem et al., 2019)
–	Roots	–	–	Used as an analgesic, diuretic, flu treatment, dermatological conditions, inflammation, ulcers, coughs, and jaundice	(Chandra & Rawat, 2015)
El Haouz Rhamna	Roots	Powder	Cooked with bread	Antidiabetic	(Benkhniqne et al., 2014)
Middle Moulouya	Whole plant	Decoction Cataplasm	Oral, Cataplasm	Against colds, constipation bloody diarrhea intestinal pain and hair loss	(HassaniM et al., 2013)
Agadir	Roots	Powder	Mixed with black cumin, gingers rhizome, <i>Alpinia officinarum</i> rhizome, pure honey, and goat butter are used for forty days	Allergy	(El Hafian et al., 2014)
Moroccan Central plateau	Roots Leaves	Powder	Oral Local application with Henné	Respiratory diseases Digestive disorders, Hepatic diseases and Hair treatment	(El Hafian et al., 2014; Makbli et al., 2016)
Casablanca	Roots	Powder	Apply to skin with henna powder	Skin infections	(Makbli et al., 2016)
Zaer	Roots	Powder	Mixed with honey Incorporate into bread Associated with <i>Rubia peregrina</i>	Digestive disorders, lung diseases, rheumatic affections, fortifying and aperitif, and haircare	(DANS & LA REGION, 2009)
Rif	Roots	Powder	Alone or mixed with black cumin, Cataplasm, Oral	Treatment of wounds and burns and against allergy	(Bachar et al., 2016, 2021)
Kenitra	Roots	Powder	Oral	Diarrhea, rheumatological disorders, and gastrointestinal diseases	(Salhi et al., 2010)
–	Roots	The whole roots	Burning some part of the body with the root	Bumezwi, heart palpitations, anxiety, and abdominal pain	(Bellakhdar, 1997a)
–	Roots	–	–	Cosmetic, hair care, magic, liver diseases, spleen, and lung disorders	(Bellakhdar et al., 1991)
–	–	–	–	Digestive disorders (stomachache), respiratory and rheumatic diseases. As a tonic and aperitif	(Bellakhdar et al., 1991)

–	Roots, Whole plant	Powder, fume, root	Decoction, fume, fresh root	Flu and migraines, dermatological diseases, inflammation, ulcer, cough, jaundice, antispasmodic, aphrodisiac, antiasthenic given to parturient women, cancer digestive wound treatment, and diabetes.	(Zakariya et al., 2020)
–	Roots, EO	–	–	Dermatological diseases and cough, antiasthenic, antispasmodic, diuretic, aphrodisiac, stomach aches, chills, lung diseases, and rheumatic diseases	(Doudach et al., 2013)
–	Roots	Powder	Decoction	Flu, dermatological diseases, inflammation, ulcer, cough, jaundice, diuretics, and cancer (digestive and liver)	(Miguel et al., 2013)
–	Roots	Powder	–	Stomach-aches, chills, lung diseases, rheumatic diseases, fortifying and appetizer, inflammation, ulcer, cough, jaundice, aesthetic and diuretic	(Doudach et al., 2012)
North African	Root	Powder	–	Flu, skin conditions, soreness, ulcer, cough, jaundice, anesthetic, diuretic, chills, fever, lung conditions, rheumatism, fortifying, and appetizer	(Doudach et al., 2022)
–	–	–	–	Illnesses of the respiratory, digestive, skin, urogenital, neurological, and typhoid systems. Additionally fragrant, corrigiola roots are frequently employed in fumigations, have a reputation for warding off bad geniuses, and can also be used to treat allergies.	(Amine et al., 2017)
–	Roots, fume	Powder, fume	–	Aromatic fume, flu, dermatological diseases, inflammation, ulcer, cough, and jaundice	(Lakmichi et al., 2010a)
–	–	–	–	An anti-asthenic, antispasmodic, diuretic, aphrodisiac, influenza, and headaches	(Oualcadi et al., 2021)

biological materials, including extracts, essential oils, and other derivatives to manage the severity of phytopathogens on crops and during storage (Amoabeng et al., 2019; González-Castro et al., 2019; Isman, 2020).

In a study conducted in Morocco, extracts of *Corrigiola telephiifolia* were applied to the most devastating fungi of Moroccan crops, *Fusarium oxysporum albedinis* and *Sclerotium rolfsii* that cause bayoud and sugar beet root rot diseases respectively (Lakmichi et al., 2010a). For this test, five organic extracts of CT were added to dishes containing hyphal of *Sclerotium rolfsii* and *Fusarium oxysporum albedinis*, and the incubation was realized *in vitro*. As result, all extracts showed significant inhibition of both fungi in a concentration-dependent manner (Lakmichi et al., 2010a). These successful tests can be used as the basis for bio-based controls of these devastating fungi.

Beneficial properties

Antioxidant effect

Considering progress of scientific research in pharmaceutical industries (Nayyereh et al., 2020), medicinal and aromatic plants are still excellent sources of a wide range of bioactive compounds with unexpected therapeutic effects (Christaki et al., 2012; Choudhary et al., 2021). The antioxidant potential of different herbs is a good tool to predict their actions *in vivo* and is examined by numerous complementary assays including the phosphomolybdenum test, free radical scavenging activity test, radical cation decolorization, ferric reducing antioxidant power (Moon and Shibamoto, 2009; Xiao et al., 2020). In fact, numerous studies have shown that natural products act pleiotropically through their powerful antioxidant ability, improving the antioxidant defense system and reducing oxidative stress (Lakmichi et al.,

2010a; Doudach et al., 2013; Miguel et al., 2013; Hebi and Eddouks, 2019). The antioxidant abilities of *C. telephiifolia* pour, were tested via different methods including DPPH, TBARS, ABTS, Chelating metal ion, Hydroxyl radical scavenging activity, and Lipooxygenase assay, on diverse extracts, including aqueous, aqueous ethanolic, and methanolic extracts (Table 3) (Doudach et al., 2013, 2022; Miguel et al., 2013). The obtained results showed high antioxidant potential when compared with antioxidant standards such as Trolox and Butylhydroxytoluene (BHT) (Miguel et al., 2013; Doudach et al., 2022). For example, (Doudach et al., 2022) evaluated the antioxidant ability of *C. telephiifolia in vivo*, using carbon tetrachloride as a toxic agent that induces oxidative stress and histopathological damage. Results of this experiment showed that the administration of methanolic extract of CT at doses of 5 and 10 mg/kg/day sustained for 60 days counteracts the perturbations observed in CCl₄-intoxicated mice, inducing less biliary deposits and suppressing necrosis foci. The authors reported also that the methanolic extract of CT exhibited a remarkable cytoprotective effect on the translated liver by lowering the haptic enzyme releases (Table 3) (Doudach et al., 2022). Similarly, aqueous extract (5 mg/kg) of *C. telephiifolia* have demonstrated significant antioxidant activity using oral administration in the DPPH and BHT assays conducted *in vitro* on Diabetic Rats (Hebi and Eddouks, 2019). This potent antioxidant capability was supported by the higher concentration of phenolic compounds (33.05 mg EAG/g) that ensure the scavenging of oxidative species (Mathew

et al., 2015; Skrypnik et al., 2019), either through sequential proton loss electron transfer, hydrogen atom transfer, transition metal chelation, or single electron transfer (Zeb, 2020).

Antidiabetic effect

The management of metabolic disorders using medicinal plants started since ancient times, and the determination of the exact time of the first cases using herbs as multifaceted drugs remains very difficult (Petrovska, 2012; Jamshidi-Kia et al., 2018). As antidiabetic agents, many plant species and their derivatives, such as *Argania spinosa* (L.) Skeels, *Cladanthus mixtus* (L.) Oberpr. and Vogt, and *Pulicaria mauritanica* Batt. are commonly used to treat different diabetic cases (Arumugam et al., 2013; Hebi et al., 2018; Ouhaddou et al., 2020). Similarly, *Corrigiola telephiifolia* Pourr. has been incorporated among medicinal plants used for the treatment of diabetes (Benkhniue et al., 2014). However, used parts, biogeography, and administration ways are variables.

In Morocco, *Corrigiola telephiifolia* Pourr. is widely used in traditional medicine to treat various health disorders including diabetes. In the southern provinces surrounding Agadir, root powder of *Corrigiola telephiifolia* Pourr. is mixed with seeds of *Nigella sativa*, the rhizome of *Zingiber officinale*, the rhizome of *Alpinia officinarum* Hance, pure honey, and goat butter and used orally to treat diabetes (El Hafian et al., 2014). In central areas around Marrakech and Haouz-Rhamna regions fresh roots are pulverized and mixed with flour to prepare bread, then used as a treatment for

Table 3. Pharmacological properties of *Corrigiola telephiifolia* Pourr.

Effect	Used part	Extraction solvent	References
Hypolipidemic	Arial parts	Aqueous	(Hebi and Eddouks, 2019)
Antioxidant	Arial parts Roots	Aqueous, Cyclohexane, Dichloromethane, MeOH EtOH Water-EtOH	(Miguel et al., 2013; Hebi and Eddouks, 2019; Oualcadi et al., 2021)
Cytotoxic	Roots	Dichloromethane	(Doudach et al., 2013)
Diuretic	Roots	EtOH-water (75 :25)	(Zakariya et al., 2020)
Antiviral	Roots	MeOH	(Mouhajir et al., 2001)
Lipoxygenase	Aerial parts	EtOH, MeOH	(Miguel et al., 2013)
Antibacterial	Roots	Aqueous, MeOH	(Doudach et al., 2012; Amine et al., 2017)
Hepatoprotective	Roots	MeOH	(Doudach et al., 2022)
Anti-inflammatory	Roots	Aqueous EtOH Chloroform	(Miguel et al., 2013)
Non-toxic	Roots	Aqueous EtOH	(Doudach et al., 2013)

diabetes (Benkhniqie et al., 2014). Similarly, the root powder of CT is incorporated into bread and administrated to diabetic persons in the Middle Atlas areas (Hachi et al., 2016). At the laboratory level, only two studies have investigated the beneficial effects of CT on diabetic cases; the application of aqueous extract on plasma total cholesterol in diabetic rats by (Hebi and Eddouks, 2019), and on glycemia of STZ-induced diabetic rats by (Hebi and Eddouks, 2020). In the first case, the aqueous extract of aerial parts of CT was examined in a type 1 diabetic animal model with the extract administered orally for 15 days at a dose of 5 mg/kg/day. The obtained results revealed that the aqueous extract has no significant modification of blood glucose level, while the daily administration of the aqueous extract was effective in reducing glycemia in streptozotocin-intoxicated rats (Hebi and Eddouks, 2019). Persistent hyperglycemia raises the coronary risk index, metabolic disorders, cardiovascular index, and atherogenic index (Laaroussi et al., 2020, 2020; Bakour et al., 2021). In the second study (Hebi and Eddouks, 2020), the aqueous extract of the CT was evaluated against the hyperglycemia induced by STZ in Wistar rats. According to the obtained results of the oral glucose tolerance test, the authors found that the administration of an aqueous extract of CT prevents significantly the elevation of glycemia within 30 min after glucose administration. Current data suggest that *Corrigiola telephiifolia* Pourr. could be used as a promising natural product for more original investigations due to the restricted number of articles published.

Antihyperlipidemic effect

Corrigiola telephiifolia Pourr. is widely used in Moroccan folk medicine to treat dyslipidemia which is highly related to the development of cardiovascular diseases (Table 3). It is traditionally used to treat numerous human ailments (Kabbaj et al., 2012; Eddouks et al., 2017). However, only one study has investigated the effects of *Corrigiola Telephiifolia* Pourr. at the laboratory. The administration of an aqueous extract of *Corrigiola Telephiifolia* Pourr. for two weeks improves lipid profile via decreasing triglyceride and cholesterol in STZ-intoxicated Wistar rats (Hebi and Eddouks, 2019). However, other investigations of the effect of *Corrigiola Telephiifolia* Pourr. on metabolic disorders are needed to explore more beneficial properties of this plant.

Diuretic effect

Ethnopharmacological studies are keystones in numerous experimental investigations. In fact, *Corrigiola telephiifolia* Pourr. appears in several ethnomedicinal studies as a natural product widely used to treat kidney disorders (Table 3) (Bellakhdar, 1997a; Kabbaj et al., 2012; Eddouks et al., 2017; Zakariya et al., 2020; Bencheikh et al., 2021). However, the first report to confirm the diuretic utility of CT is only published currently by (Zakariya et al., 2020). Authors found that the administration of different doses of aqueous ethanolic extracts of CT roots (200 mg/kg, 400 mg/kg, and 700 mg/kg) affected positively diuresis increasing urine flow in a dose-dependent and shows a significant increase in sodium, potassium, chloride excretion without any sign of dehydration (Zakariya et al., 2020). The diuretic effect of CT could be due to its phenolic compounds which act differently in the way they affected diuresis and electrolyte excretion (Jadhav et al., 2010; Schlickmann et al., 2018). It has been proved that CT roots contain numerous phytochemical compounds, particularly telephiifoliosides A and B, new triterpenoid saponins identified for the first time (Fouedjou et al., 2021). Triterpene saponins are well known for their diuretic effects as previously reported (Diniz et al., 2009; Tiwari et al., 2012). The mechanism of action is still unclear and scientific research is going on to discover other new molecules of CT implicated in beneficial Diuretic effects.

Antimicrobial effect

Pathogenic bacteria afflict both humans and animals leading to serious health problems. The widespread of infectious diseases is in high association with the misuse of antimicrobial chemical agents such as antibiotics through acquiring resistance (Ousaaïd et al., 2021). Medicinal plants are excellent biorationals and effective agents against pathogenic bacteria than chemical drugs often accompanied by adverse effects (Veeresham, 2012). A comparative study was conducted to investigate the antibacterial property of two extracts (methanolic and aqueous extracts) of two medicinal plants including *Corrigiola telephiifolia* Pourr. and *Mesembryanthemum nodiflorum* L. against numerous pathogenic bacteria including Gram-positive (*Staphylococcus aureus*, *Bacillus subtilis*, and *Micrococcus luteus*) and Gram-negative (*Pseudomonas aeruginosa* *Klebsiella pneumonia*

and *Escherichia coli*) (Table 2). The authors found that the methanolic extract of *Corrigiola telephiifolia* Pourr was more effective than the aqueous extract with minimal inhibitory concentration (MIC) ranging from 3.12 to 12.5 mg/ml (Doudach et al., 2012). The study conducted by (Daoudi et al., 2017) on three two gram-negative bacillus strains (*Escherichia coli* and *Klebsiella pneumonia*) and a gram-positive strain (*Staphylococcus aureus*) found that the aqueous extract was less effective against three pathogenic bacteria and showed a diameter of inhibition of 09 ± 0.06 mm at a dose of 100 µg/ml. The same authors revealed that the aqueous extract of CT contains a considerable amount of phenolic compounds which could explain the beneficial properties of CT (Daoudi et al., 2017). Experimental evidences have shown that phenolic compounds affect the microbes growth process and disturb the membrane stability translating into the modification of its permeability leading microbes death (Carvalho et al., 2018; Ousaaïd et al., 2021). In addition, bioactive compounds sabotage the energy process and macromolecular synthesis of pathogens, leading to their inhibition (Botton et al., 1990; Carvalho et al., 2018). However, more advanced investigations are required on different pathogens, because natural products extract contains more active compounds that can act through synergistic effects with fewer adverse effects.

Cytotoxic effect

Numerous medicinal plants have recently received considerable attention from scientific communities due to their less toxic effect, effectiveness, lower costs, and great availability in nature (Bencheikh et al., 2021). Many critical health conditions, such as cancer requires special healthcare and expensive drugs. Medicinal plants are still used for their multifaceted purposes as a potential source of different bioactive compounds which could be integrated into the therapeutic chemical drugs well known for their anticancer effects (Milner et al., 2010; Afrin et al., 2020). Several medicinal plants are well known for their chemo preventive and suppressive effects on cancer cells. Such plants include *Artemisia annua* L., *Coptis chinensis* L., *Curcuma longa* L., *Fagonia indica* Burm. f., *Garcinia oblongifolia* Champ. ex Benth., *Garcinia indica* (Thouars) Choisy, *Hedyotis diffusa* Willd., *Loranthus parasiticus* L., *Scurrula parasitica* (L.) Blume, *Morus*

alba L., *Paris polyphylla* Sm., *Perilla frutescens* (L.) Britt., *Platycodon grandiflorus* (Jacq.) A. DC., *Prunus armeniaca* L., *Rabdosia rubescens* (Hemsl.) Hara, *Scutellaria baicalensis* Georgi, *Scutellaria barbata* D. Don, *Tripterygium wilfordii* Hook. f., *Tussilago farfara* L., *Wedelia chinensis* (Osbeck) Merr. Khan et al. (2020).

Ethnobotanical studies on Moroccan traditional medicine has revealed that *Corrigiola telephiifolia* Pourr., which is in the list of plants with anticancer properties possess anticancer activity (Table 2) (Kabbaj et al., 2012; Doudach et al., 2013). From this background, Doudach et al (2020) conducted the first *in vitro* study on the anticancer activity of CT, in which different extracts (cyclohexane, dichloromethane, methanol, and aqueous extracts) of plants collected from the Ben Slimane region, Morocco, were examined for the viability to human melanoma cell lines (WV-266) and murine colon adenocarcinoma (CT-26) (Doudach et al., 2013). The authors found that all studied extracts exhibited dose-dependent cytotoxicity against both cancer cells (WM-2066 and CT-26). They also found that the cyclohexane extract was the most cytotoxic agent against CT-26 and WM-266 with an IC_{50} of 70 µ/ml and 120 µg/ml respectively (Doudach et al., 2013). The remarked difference between all studied extracts could be explained by the polarity of solvents and their ability to extract the most effective phytochemicals.

Guidelines for future investigations

Geographical distribution and climate change

No information is available on the spatial trends of this plant in Northern Africa and the Northern slope of the Mediterranean (Benkhni-gue et al., 2014; Hachi et al., 2016). Therefore, determining spatiotemporal distribution would be of vital importance to improving our understanding of the dynamics of vegetation cover dominated by *Corrigiola telephiifolia* Pourr. Establishing maps of distribution vis-à-vis climatic conditions, edaphic characteristics, and human activities could help clarify the factors governing this species' distribution. Equally, the investigation of the impact of climate change (precipitation and temperature) on CT is also suggested to explain the direct impacts of hot temperatures on biological and physiological traits and consequently the chemical properties of our focal plant.

Identification of chemical response to biotic factors

Secondary metabolites such as saponins recorded in *Corrigiola telephiifolia* Pourr. occur frequently in many medicinal plant species as part of their defense system (insert literature to support statement”. Metabolite content in plants appears to be dynamic, answering to many external factors including biotic stimuli associated with pathogenic infection and herbivory attack, as well as involved in plant mutualistic symbioses with mycorrhizal fungi and rhizobial bacteria. Thus, the identification of the impacts of biotic factors on biochemical compounds in *Corrigiola telephiifolia* Pourr. is suggested to clarify how the beneficial bioactive molecules react against the biotic stimuli. This would help in the cultivation and industrial trends of this plant.

Bioactive molecules and biological activities

The number of studies that investigated bioactive molecules in *Corrigiola telephiifolia* Pourr. is limited to four papers (Doudach et al., 2013, 2022b; Hebi and Eddouks, 2019; Oualcadi et al., 2021). Thus, the screening of bioactive molecules must be in the first line, because this is suggested to reveal new interesting biomolecules such as the newly recorded telephiifoliosides A and B (Fouedjou et al., 2021). Equally, the phytochemical screening of samples from different areas is suggested to complete the chemical map of the *Corrigiola telephiifolia* Pourr. in the Mediterranean area. Then the application of these molecules to other metabolic and health disorders would help fill the gap in data around this species. Consequently, if new therapeutic features will be discovered the conservation of the species is suggested to be easy for the local population by focusing on the economic incomes in a sustainable development manner.

CONCLUSION

Corrigiola telephiifolia Pourr. is one of the most medicinal plants commonly used to treat different health-critical conditions. It is a plant limited studied despite its remarkable place in the Moroccan pharmacopeia as a natural product with multiple functional activities accounting for antioxidant, antidiabetic, anti-dyslipidemia,

antimicrobial, anti-inflammatory, and anticancer effects. These pharmacological properties could be attributed to its saponins content, which contains two monodesmoside triterpene saponins named telephiifoliosides A and B, known for their biological effects generated by the synergistic effect between different bioactive compounds of *Corrigiola telephiifolia* Pourr. However, more comparative studies are needed to investigate new chemical constituents, their biological properties, and the impact of environmental conditions on their synthesis in *Corrigiola telephiifolia* Pourr. Equally, the impact of climate change on geographical distribution, adaptation, and chemical composition needs to be investigated in order to select suitable conservation measures.

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