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Research article

Diversity and biological activities of medicinal plants of Santiago island (Cabo Verde)

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ABSTRACT

Plants continue to constitute key elements of medical practice in West African countries. The Cabo Verde archipelago hosts a great diversity of medicinal plants and local markets are considered important sites for trading plants harvested by rural communities. This study has two main goals: (i) to assess the medicinal uses of native species in Santiago, the biggest island of the archipelago, and (ii) to evaluate the antioxidant, antimicrobial and antidiabetic/anti-hyperglycemic activities of two native trees (*Tamarix senegalensis* and *Sideroxylon marginatum*) used in traditional medicine and traded in local markets. Our results revealed that on Santiago Island, 24 native plants are used in traditional medicine. The main uses of these species (*e.g.*, forage, timber, food and fibres), their medicinal applications, the plant parts used, their mode of administration and conservation status are presented here for the first time. Moreover, the pharmacological characterization of two native tree species revealed that hydroethanolic extracts were richer in phenolic compounds and more active than their aqueous counterparts. All the studied extracts revealed significant antioxidant properties (DPPH and FRAP assays) and were generally moderately active against Gram-positive bacteria. All the extracts inhibited the activities of the carbohydrate digestive enzymes α-glucosidase and α-amylase in a dose-dependent manner. For α-glucosidase, the detected inhibitory activity (IC_{50} values from 2.0 ± 0.2 μg/mL

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to 9.9 ± 1.2 μg/mL) was significantly higher than that of acarbose, suggesting that extracts of both species can delay glucose absorption, thereby assisting in slowing down the progression of diabetes. Our findings highlight the crucial importance that medicinal plants have for the Cabo Verdean population, while also raising awareness on the need for sustainable use and conservation of native flora, and of tree species traded in local markets in particular.

1. Introduction

Over the last decades, numerous novel medicines were developed from plants, demonstrating that pharmacological screening is instrumental to the development of new agents [1]. Therefore, isolation and profiling of secondary metabolites produced by plants used in traditional medicine may reveal interesting bioactivities and disclose sources of new drugs to treat many diseases (*e.g.*, diabetes mellitus [2] or bacterial infections [3]). In the literature, recent reports account for the presence of several valuable bioactive compounds in plant materials possessing remarkable biological, pharmaceutical and medicinal activities (*e.g. Bunium* L. (Apiaceae): native in Mediterranean to Central Asia and India [4]; *Siparuna* Aubl. (Siparunaceae) native in Tropical America [5]; *Aloysia* Paláu (Verbenaceae) native in Subtropical America [6]; *Zingiber officinale* Roscoe (Zingiberaceae) native in India to China and *Allium sativum* L. (Amaryllidaceae) native in Central Asia to Iran [7]). Notwithstanding the tremendous potential for product development, much work still needs to be done, particularly regarding indigenous African medicinal plants [8]. According to Van Wyk [9], more than 5400 plant species are used in traditional medicine in Africa, but only 10% have been commercially developed to some extent.

Scientifically, knowledge of most African medicinal plants remains limited [10]. Their sustainable use and conservation makes the development of cultivation protocols imperative to preserve their remarkable diversity [11]. Not in the least because traditional medicine is a significant element of African culture and a key resource for dealing with health problems, most particularly in rural areas [12].

The archipelago of Cabo Verde is located in West Africa (ca. 500 km off Senegal). Since its colonization in the late sixteenth century, the flora of these islands has been a source of materials used in folk medicine [13]. Overall, the rural population retains good knowledge of plants and their properties, and uses natural resources to meet some of their needs [14]. Nevertheless, the long-established body of knowledge on their medicinal properties is at risk of disappearing owing to the social changes the country has experienced over the last decades, above all in terms of land use and the conversion of natural ecosystems into agricultural land and urbanised areas [15]. Hence, calls to raise awareness and implement measures to conserve the archipelago's native plant species, given that most of them are threatened with extinction from overharvesting and habitat destruction [16].

Despite some recent botanical studies enriching our knowledge of Cabo Verdean flora and vegetation (*e.g.* Refs. [17–19]) and some fruitful approaches to phytogenetic resources (*e.g.* Refs. [20,21]), few available studies concern themselves with the uses of medicinal plants in this archipelago [13]. In fact, only a few endemic species have so far been phytochemically investigated, namely *Artemisia gorgonum* Webb ([22–27]), *Echium hypertropicum* Webb, *Echium stenosiphon* Webb subsp. *stenosiphon* [28], and *Micromeria forbesii* Benth [29].

In Cabo Verde, many people still rely on plants to treat health conditions, which are commonly sold in local markets, rooted in local insular culture [13]. Nevertheless, as yet, little information on medicinal plants traded in Cabo Verde's traditional markets is available to the scientific community. Of particular concern are the traded native endangered tree species which would benefit from conservation measures to prevent their unsustainable use and overexploitation. In fact, there are very few native tree species in Cabo Verde; *Sideroxylon marginatum* (Decne. ex Webb) Cout. is one of the three endemics, and *Tamarix senegalensis* DC. is one of the four non-endemics [30].

The genus *Sideroxylon* L. which includes 81 species is found in America, Asia and Africa [31]; different species have been used in traditional medicine to treat several disorders, including bacterial infections and diabetes (*e.g.* Refs. [32–34]). With 73 species [35], *Tamarix* L. (tamarisk) is the largest genus in the Tamaricaceae family and occurs in a wide variety of environments, including arid areas. It is traditionally used in Asian and African countries to treat various ailments, including bacterial infections and diabetes [36]. Although other species of these two genera are widely used in traditional medicine and have been subjected to phytochemical analyses, only one recent study has evaluated the phenolic profile and some bioactive properties of *Sideroxylon marginatum* and *Tamarix senegalensis* from Cabo Verde [27]. A more in-depth assessment of the biological activities and therapeutic potential of these two native tree species would be relevant to support the empirical recognition of their medicinal value by the Cabo Verdean population.

This study aims to assess the medicinal uses and pharmacological potential of plants traded in local markets and used on the island of Santiago, and specifically to: (1) retrieve the ethnobotanical information from the most important herbarium collections and literature, complemented by field surveys; and (2) enhance available knowledge on the potential medicinal properties of two of such plants – *Sideroxylon marginatum* (endemic) and *Tamarix senegalensis* (non-endemic native), by assessing their i) *in vitro* antioxidant activities; ii) antidiabetic/antihyperglycemic potential (α-glucosidase and α-amylase inhibitory activities); and iii) antimicrobial activities. Hopefully, our results will raise awareness on the need for the sustainable use and conservation of endemic flora, especially the native trees traded in the local markets of Cabo Verde Islands.

2. Material and methods

2.1. Studied area

The Cabo Verde archipelago is located in the north-eastern Atlantic Ocean, about 500 km off Africa's west coast and 1500 km south of the Canary Islands [37]. This archipelago has ten islands, being Santiago (Fig. 1A), with an area of 991 km^2, the largest island, both in size and population, and hosts the nation's capital, Praia. Santa Catarina is the second most populated municipality in Santiago Island, playing an important commercial role and has a combination of fields and urban areas, with Assomada city as the center. Assomada lies near the midpoint of the main road that crosses the island from Praia in the south to the northern port of Tarrafal.

The vascular flora of the archipelago is currently thought to comprise about 740 species, with 92 endemics [38]. Anthropogenic activities have placed considerable pressure on the natural ecosystems, and agricultural activities are more evident in elevated areas, benefiting from rainfall and humidity [15]. However, these areas still have patches of natural vegetation, which, due to their enormous value, have been the target of conservation actions and are included in the Protected Areas Network of Cabo Verde [16].

2.2. Diversity of medicinal plants in Santiago

2.2.1. Data collection

The data on the native plant species used in traditional medicine in Santiago Island was obtained through field surveys made by some of the authors (MMR, MCD, IG). To complement the information collected in the surveys, bibliographic research, online databases, and the study of herbarium material were also conducted, namely from:

1. A comprehensive literature search was conducted in June–July 2022, on Google scholar, PubMed, Scopus and BioMed Central, using different keywords like "Cape Verde", "Cabo Verde", "Medicinal Plants", "Ethnobotany", "Traditional medicine". In addition to the outlined searching strategy, bibliographic sources, including literature in Portuguese ([39–45,45–52]), with information on uses and common names of Cabo Verde's medicinal species were consulted.
2. Online databases: (i) PROTA - The Plant Resources of Tropical Africa [53], which provides detailed information on the uses of many African plants, including their medicinal applications; (ii) African Plant Database [][55], which provides information on the habit and ecology of species occurring in Africa; (iii) Plants of the World Online [35], which provides up-to-date information on species taxonomy and distribution; and (iv) IUCN - Red List of Threatened Species [54] providing information on conservation status, and major threats of each evaluated species;
3. Herbarium specimens of endemic and non-endemic native species from Santiago Island deposited in the herbarium LISC of the University of Lisbon; the medicinal information available on the labels of each specimen was collected.

2.2.2. Database construction

Based on the best available knowledge, a database including the taxonomic family, scientific and common names, distribution and

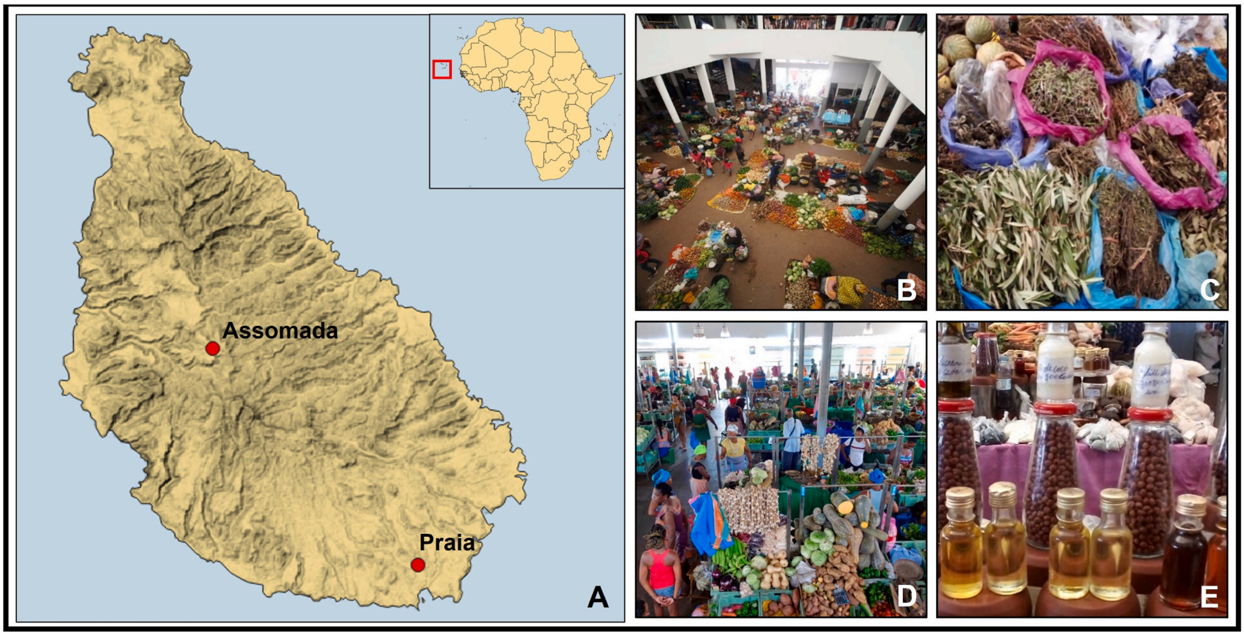

Fig. 1. Location of the two studied markets within Santiago Island (A). Assomada market (B, C) and Praia market (D, E).

native status in Santiago Island, species habit (herb, shrub or tree), main uses, medicinal applications, part(s) used in medicine, and administration mode. The conservation status of each species was also assigned, according to IUCN Red List [54] and Romeiras et al. [16].

2.2.3. Prospection and sampling of marketed species

We conducted surveys in the two major markets of Santiago, *i.e.*, Assomada market (Fig. 1 B, C) and Praia market (Fig. 1 D, E). These markets were chosen because: (1) medicinal plants are sold singularly (dried parts of each species) for a particular treatment and with no processing; and (2) the medicinal plant traders occupy permanent booths, which have allowed us to perform multiple visits over the past four years (since June/2019). To obtain updated information on Santiago medicinal plants, ethnobotanical questionnaires were carried out in these two markets and after being informed about the objectives of the study, the vendors were interviewed according to mutually agreed conditions (Please see more details in Supplementary file). Recorded uses, prices and local names of the medicinal plants were registered.

Among the medicinal plants sold in these markets, two emblematic native trees of Cabo Verde were recorded during the different surveys and selected for laboratory analysis, because they were reported by the sellers as two highly traded medicinal plants with great importance in the treatment of infections and pains.

Samples of dry leaves and stems of *Sideroxylon marginatum* and of *Tamarix senegalensis* were analyzed in FCT laboratory facilities. The botanical identification and assignment of the scientific name of the species were made by the authors (MCD and MMR). A voucher specimen of each species was deposited at the herbarium LISC/University of Lisbon (see details in Table 1 [42], [16,17,40,42–44,46], [16,39,42], [16,44,53], [16,39,40,42,45], [16,17,39–43], [16,17,42,47], [16,17,42,48–50], [16,40,53], [16,42], [16,42,52], [16,42, 45], [16,17,42,47], [16,40,43], [16,39,41–43,49], [16,17,42,43,47], [16,42,43], [16,39,42,46], [16,41–43,45], [,53–55], [16,17,42, 43,47,51] [16,16,17,39–45,45–54]).

2.3. Pharmacological characterization of plants

2.3.1. Hydroethanolic and aqueous extracts preparation

After botanical identification, aerial parts (leaves and stems) of *Tamarix senegalensis* and *Sideroxylon marginatum*, were grounded (Moulinex, coffee mill) and stored in the dark. To prepare the hydroethanolic extracts (HEE), powdered aerial parts (2.5 g) were extracted with 25 mL of a 70% hydroethanolic solution in an ultra-sonic bath (P-Selecta ULTRASONS), for 60 min, and after left for 24 h under agitation, at room temperature and protected from light. Subsequently, extracts were centrifuged (11000 g, 30 min, 4 °C, Centrifuge 4K–15C, Sigma, Osterode am Harz, Germany) and the supernatants were collected. The extraction yield was determined gravimetrically, after evaporating 2.0 mL of each extract to dryness, using a rotary evaporator at 40 °C, under reduced pressure. Both plants were also extracted by infusion (aqueous extracts (AE)). In brief, powdered aerial parts (5 g) were boiled with 100 mL of ultrapure water for 3 min, and then filtered (Whatman No. 1) and centrifuged (11000 g, 30 min, 4 °C, Centrifuge 4K–15C, Sigma, Osterode am Harz, Germany). The supernatants were collected and lyophilized (ScanVac CoolSafe110-4, Labogene, Lillerød, Denmark). The extracts were kept at −80 °C until analysis.

2.3.2. Reagents used in the laboratory analyses

α-Amylase from porcine pancreas, α-glucosidase from *Sacharomyces cerevisiae*, (+)-catechin, 3,5-dinitrosalicylic acid, 2,2-diphenyl-1-picrylhydrazyl (DPPH), 4-nitrophenyl-α-D- glucopyranoside (NPG), soluble potato starch, 2,4,6-tris(2-pyridyl)-*s*-triazine (TPTZ) were purchased from Sigma-Aldrich (St. Louis, MO, USA). Folin-Ciocalteu reagent was purchased from Merck (Darmstadt, Germany). Acarbose and gallic acid were purchased from AlfaAesar (Karlsruhe, Germany). All the culture media were purchased from Biokar diagnostics (Allonne, France).

2.3.3. Determination of total phenolic contents (Folin-Ciocalteu)

The total phenolic contents of different plant extracts were determined by the Folin-Ciocalteu method, according to Loebler et al. [56]. Briefly, 6.0 mL of H_2O, 100 μL of the different extracts and 500 μL of undiluted Folin-Ciocalteu reagent were mixed in a 10.0 volumetric flask. The mixture was maintained at room temperature for 1 min followed by the addition of 1500 μL of Na_2CO_3 (20% w/v) and H_2O up to 10.0 mL. The reaction mixtures were incubated for 120 min at room temperature in the dark. Increasing gallic acid concentrations (50–500 mg/L) were used to obtain a standard curve and the absorbances of samples and standards were measured at 765 nm (SPEKOL 1500, Analytik Jena, Germany). Values were assessed in triplicate and the results were expressed as milligrams of gallic acid equivalents (GAE) per gram of dried extract (mg GAE/g dried extract). Data are presented as means ± standard deviations.

2.3.4. Quantification of flavonoids by ultraviolet–visible spectrophotometry

The flavonoid contents were determined according to Barros et al. [57]. In short, 500 μL of extracts were mixed with 2 mL of H_2O and 150 μL of $NaNO_2$ (5% w/v). After 6 min, 150 μL of $AlCl_3$ (10% w/v) were added and allowed to stand further 6 min. Finally, 2 mL of NaOH (4% w/v) and H_2O up to 5 mL were added and the mixtures were incubated at room temperature in darkness for 15 min. Increasing (+)-catechin concentrations (0.125–1 mM) were used to obtain a standard curve. The intensity of the pink colour was measured at 510 nm (SPEKOL 1500, Analytik Jena, Germany). Values were assessed in triplicate and the results were expressed as μmol of catechin equivalents (CE) per gram of dried extract (μmol CE/g dried extract). Data are presented as means ± standard deviations.

2.3.5. Determination of antioxidant activities

2.3.5.1. DPPH free radical scavenging assay. The antioxidant activities of the plant extracts against the DPPH free radical ($DPPH^{\bullet}$) were determined based on the procedure described by Miceli et al. [58]. $DPPH^{\bullet}$ solution (24 mg/L in ethanol) was mixed with 500 μL of each extract at different concentrations, or with 500 μL of the extract solvent (control). After 20 min of incubation at room temperature and in the dark, the intensity of the purple colour at 517 nm was recorded (SPEKOL 1500, Analytik Jena, Germany). The radical scavenging activity (Inhibition (%)) was measured as the decrease in absorbance of the samples versus $DPPH^{\bullet}$ solution according to the following formula:

$$Inhibition\ (\%) = [(Abs_0 - Abs_1)/(Abs_0)] \times 100 \tag{1}$$

Where Abs_0 is the absorbance of the control and Abs_1 is the absorbance in the presence of the extracts. All determinations were performed in triplicate. Data are presented as means ± standard deviations.

2.3.5.2. Ferric reducing antioxidant power (FRAP assay). The FRAP assay was carried out according to the procedure described by Lima et al. [26]. Briefly, 3 mL of a freshly prepared FRAP reagent [sodium acetate buffer (0.25 M, pH 3.6), TPTZ (2,4,6-tripyridyl-*s*-triazine) 10 mM in 40 mM HCl and $FeCl_3 \cdot 6H_2O$ (20 mM) mixed at the ratio of 10:1:1 and warmed at 37 °C], were mixed with 400 μL of the different extracts and left for 20 min at 37 °C. Afterwards, the absorbance was read at 593 nm (SPEKOL 1500, Analytik Jena, Germany). Increasing ferrous sulphate ($FeSO_4$) concentrations (0–1.25 mM) were used to obtain the standard curve and the results were expressed as mmol Fe^{2+}/g of dried extract. All determinations were performed in triplicate. Data are presented as means ± standard deviations.

2.3.6. Determination of antidiabetic/antihyperglycemic activities

2.3.6.1. α-Glucosidase inhibitory assay. The inhibition of the α-glucosidase enzyme was determined according to the chromogenic method described by Rouzbehan et al. [59], with some modifications. Reaction mixtures containing 5 μL of α -glucosidase (6.25 U/mL in phosphate buffer (pH 6.9, 0.1 M)), 125 μL of phosphate buffer (pH 6.9, 0.1 M), and 20 μL of the plant extracts at different concentrations (up to 0.2 mg/mL) were prepared in a 96 wells microplate (Greiner Bio-One, Rainbach im Mühlkreis, Austria) and incubated for 15 min at 37 °C. The reaction was started by adding 20 μL of substrate solution (*p*-Nitrophenyl-α-D-glucopyranoside, 2.75 mM in phosphate buffer (pH 6.9, 0.1 M)) and the plates were incubated for an additional 15 min, at 37 °C. The reaction was stopped by the addition of 80 μL of 0.2 M Na_2CO_3. The absorbance of the wells was measured in a microplate reader (FLUOstar® Omega Plate Reader, BMG Labtech, Ortenberg, Germany) at 405 nm. The reaction mixture without the plant extracts was used as negative control and reaction mixtures without α-glucosidase were used as samples' blanks. Increasing concentrations of acarbose (80–980 μg/mL) were used as positive controls. The enzyme inhibitory rate was calculated as follows:

$$Inhibition\ (\%) = [(Abs_{negative\ control} - (Abs_{sample} - Abs_{sample\ blank})\ x\ 100/\ (Abs_{\ negative\ control})] \tag{2}$$

Values were assessed in quadruplicate and the results were expressed as the final concentration (μg/mL) in the reaction mixture, which reduces the enzyme activity by 50% (IC_{50}). Data are presented as means ± standard deviations.

2.3.6.2. α-Amylase inhibitory assay. The inhibition of the α-amylase enzyme was determined according to the method described by Ferron et al. [60]. Briefly, reaction mixtures containing 100 μL of Type VI-B porcine pancreatic α-amylase (0.5 mg/mL in 100 mM sodium phosphate buffer, containing 6.7 mM sodium chloride, pH 6.7) and 100 μL of each extract at different concentrations (up to 6.0 mg/mL) were preincubated in test tubes at 37 °C for 10 min. Then, 100 μL of 1% starch (w/v, previously suspended in 100 mM sodium phosphate buffer, containing 6.7 mM sodium chloride, pH 6.7, and boiled for 10 min) was added. After 10 min at 37 °C, 200 μL of DNS reagent (consisting of 20 mL of 96 mM DNS, 8 mL of 5.315 M sodium potassium tartrate tetrahydrate in 2 M NaOH and 12 mL of distilled water) was added. The reaction mixtures were heated at 100 °C for 15 min, to stop the reaction, cooled until room temperature and diluted with 2 mL of distilled water. The intensity of the red colour was measured at 520 nm (SPEKOL 1500, Analytik Jena, Germany).

The reaction mixture without the plant extracts was used as negative control and the reaction mixtures without α-amylase were used as samples' blanks. Increasing concentrations of acarbose (5.0–100.0 μg/mL) were used as positive controls. The enzyme inhibitory rate was calculated as follows:

$$Inhibition\ (\%) = [(Abs_{negative\ control} - (Abs_{sample} - Abs_{sample\ blank})\ x\ 100/\ (Abs_{\ negative\ control})] \tag{3}$$

Values were assessed in triplicate and the results were expressed as the final concentration (μg/mL), in the reaction mixture, which reduces the enzyme activity by 50% (IC_{50}). Data are presented as means ± standard deviations.

2.3.7. Determination of antimicrobial activities

The antimicrobial activities of hydroethanolic and aqueous extracts was assayed against Gram-negative bacteria (*Escherichia coli* ATCC® 8739™, *Pseudomonas aeruginosa* ATCC® 9027™ and *Salmonella enterica* subsp. *enterica* serovar Choleraesuis ATCC® 10708™), Gram-positive bacteria (*Staphylococcus aureus* ATCC® 6538™, methicillin resistant *Staphylococcus aureus* (MRSA) ATCC® 33591™, *Enterococcus faecalis* ATCC® 29212™, *Listeria monocytogenes* ATCC®15313™ and *Bacillus cereus* ATCC®11778™) and a yeast (*Candida albicans* ATCC® 10231™). All microorganisms were kept at −70 °C in a broth containing glycerol (15% v/v). Microorganisms were subcultured on TSA (*Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella enterica* subsp. *enterica* serovar Choleraesuis, *Staphylococcus aureus*, MRSA, *Enterococcus faecalis* and *Bacillus cereus*), Brain Heart Infusion agar (*Listeria monocytogenes*) or Sabouraud Dextrose agar (*Candida albicans*) and incubated at 30 ± 2 °C (*Bacillus cereus* and *Candida albicans*) or at 35 ± 2 °C (remaining microorganisms). Isolated colonies were transferred to saline medium (NaCl, 0.85% w/v) and the turbidity of the suspension (DEN-1B McFarland Grant Bio Densiometer, Grant Instruments, Cambridge, United Kingdom) was adjusted to 0.5 on the McFarland scale (approx. 1-2 × 10^8 CFU/mL for bacteria and 1-5 × 10^6 CFU/mL for yeasts) [61,62].

2.3.7.1. Well diffusion assay. The antimicrobial potential of the extracts was assessed by the well diffusion assay [63]. With a sterile swab, microbial suspensions were spread on the surface of Mueller-Hinton agar Petri dishes (bacteria). Then, wells (6 mm in diameter) were punched aseptically and 50 μL of plant extracts (20 mg/mL) were poured into the wells. The plates were incubated in the dark for 24 h, at 30 ± 2 °C (*Bacillus cereus* and *Candida albicans*) or at 35 ± 2 °C (remaining microorganisms). Antimicrobial activity was evaluated by measuring the diameter of the growth inhibition zone (in mm) around the well. Paper disks impregnated with 5 μg of vancomycin (Gram-positive bacteria), 5 μg of ofloxacin (Gram-negative bacteria) and 2.5 μg of ketoconazole (*Candida albicans*) were used as positive controls. Water and a 70% hydroethanolic solution were used as negative controls for assays with aqueous or hydroethanolic extracts, respectively. Data are presented as means ± standard deviation. All the determinations were performed in triplicate.

2.3.7.2. Broth microdilution assay. The antimicrobial activity of the different extracts was subsequently evaluated by the broth microdilution assay in 96-well microplates [63]. Briefly, two-fold serial dilutions of each sample and controls were prepared in sterile Mueller-Hinton broth to a final volume of 100 μL per well. Then, each well was inoculated with a 1:10 dilution of the previously prepared microbial suspensions (to achieve 10^6 CFU/mL in each well for bacteria and 10^4 CFU/mL for yeasts in each well). The microplates were incubated in the dark for 24 h, at 30 ± 2 °C (*Bacillus cereus* and *Candida albicans*) or at 35 ± 2 °C (remaining microorganisms). Vancomycin (1 mg/mL, Gram-positive bacteria), ofloxacin (1 mg/mL, Gram-negative bacteria) and ketoconazole (0.1 mg/mL, for *C. albicans*) were used as positive controls. Water and a 70% hydroethanolic solution were used as negative controls for assays with aqueous or hydroethanolic extracts, respectively. At the end of the incubation period, the plates were observed and the lowest concentration that inhibited the visible growth of the tested microorganisms (MIC) was recorded. All the determinations were performed in triplicates.

2.3.8. Statistical analysis

After verifying the assumption of normality and variance homogeneity, factorial analysis of variance (ANOVA) followed by the Tukey's test was used to identify statistical significance between *Tamarix senegalensis* and *Sideroxylon marginatum*, and/or extraction procedure (hydroethanolic and aqueous extracts). All statistical analyses were performed at 0.05 level of probability with the software STATISTICA™ 7.0 (StatSoft, Tulsa, OK, USA).

3. RESULTS

3.1. Diversity of medicinal plants in Santiago island

Our results identified 24 native taxa (19 endemics and 5 native non-endemics) recognized as medicinal plants used in Santiago's traditional medicine (Table 1). Their common name, main uses (*e.g.*, forage, timber, food and fibres), medicinal applications, plant parts used, administration mode and conservation status are presented in Table 1. Many of these taxa are endemic, representing 79% of the total. The identified species belong to 20 families; Apocynaceae, Asteraceae, Lamiaceae and Plantaginaceae are the most represented families, each with two taxa.

All the taxa are found in other islands of Cabo Verde, except *Tornabenea annua* (synonym of *Daucus carota* subsp. *annuus*), a single-endemic species of Santiago. Most of them occur in Santo Antão (21 taxa), São Nicolau (18 taxa), Fogo (18 taxa), Brava (18 taxa) and São Vicente (17 taxa). More than half (13 taxa) are shrubs, 7 are herbaceous plants, and 4 are trees.

The most frequent conditions treated are cough and respiratory diseases (12 taxa, 50%), fever (9 taxa, 37.5%), stomach problems (7 taxa, 29.2%) and pains (6 taxa, 25%). Most species used for these purposes are classified as threatened species (Fig. 2). Four taxa stand out for their high number of medicinal applications: *Artemisia gorgonum* is used for 10 of the 23 established categories, *Lavandula rotundifolia* is used for 9 categories, *Campylanthus glaber* has 8 medicinal applications, and *Micromeria forbesii* has 6 applications. These species were mentioned as medicinal plants by different sources, and they were also found in the markets during the fieldwork (Table 1). Among these species*,* *Campylanthus glaber* and *Micromeria forbesii* are highly threatened in Cabo Verde and are classified as Endangered [16].

Different plant parts are used in traditional medicine; the most common are leaves (35%), sap (15%) and the whole plant (15%) (Fig. 3).

Many medicinal plants are also used for other purposes. Among the 24 medicinal taxa, 11 are used for forage (46%), 8 are used for fuel (33%), 3 are used for food (13%), 2 are used for fibres (8%), and 2 are used for timber (8%). Some of these taxa are used for several purposes simultaneously; for instance, *Calotropis procera* and *Tamarix senegalensis* are used for traditional medicine, fibre, forage, fuel,

Table 1
Identification of native taxa recognized as medicinal plants used in Santiago's traditional medicine.

Family	Scientific names	Common names	Native status	Distribution CV[a]	Habit	Main uses	Medicinal applications[b]	Parts used[c]	Preparation and administration	Conservation status[d]	Markets and Voucher[e]	Other Herbarium recorder	References[f]
Apiaceae	*Daucus carota* subsp. *annuus* (Bég.) Mart. Flores, D.M. Spooner & M.B. Crespo [*Tornabenea annua* Bég]	Funtxo, aipo	E	St	Herb	Medicinal, Forage	E	Lv, Fr	Infusion	EN*	Ass Silva 1	Barbosa 5673	[42], MS
Apocynaceae	*Periploca chevalieri* Browicz	Lantisco, curacabra, curtecabra, corcabra, curcabra	E	SA, SN, St, F, Br	Shrub	Medicinal, Forage, Fuel	E, F, I, M, N	Lv, St, Rt	Infusion, oral administration	EN	Ass Silva 7	M.C. Duarte, L. Catarino & I. Gomes, sn	[16,17,40, 42–44,46], MS
	Cynanchum daltonii (Decne.) Liede & Meve [*Sarcostemma daltonii* Decne.]	Gestiba, ervatão, alvatão, alcatrão	E	SA, SV, SN, Bv, St, F, Br	Shrub	Medicinal	Q	Sa	Directly applied to tooth	LC		Barbosa, 5824	[16,39,42]
Asclepiadaceae	*Calotropis procera* (Aiton) W.T. Aiton [*Asclepias procera* Aiton]	Bombardeiro	N	All islands	Tree	Medicinal, Fibre, Forage, Fuel, Timber	D, O, Q	Lv, Sa	Leaves infusion and sap directly applied	NE	Ass Silva 6	Barbosa, 5899	[16,44,53], MS
Asparagaceae	*Dracaena caboverdeana* (Marrero Rodr. & R.S.Almeida) Rivas Mart., Lousã, J.C.Costa & Maria C. Duarte [*Dracaena draco* subsp. *caboverdeana* Marrero Rodr. & R.S.Almeida]	Dragoeiro	E	SA, SV, SN, St, F, Br	Tree	Medicinal	A, D, E, F, H	Sa	Syrup, oral administration	CR*			[16,39,40, 42,45]
Asteraceae	*Artemisia gorgonum* Webb	Losna, lorna, absinto	E	SA, St, F	Shrub	Medicinal, Forage, Fuel	B, C, E, F, G, H, J, R, T, Others	Wp	Infusion, vaporization and smoked as a cigarette	VU	Pra; Ass Silva 2	Veiga, 22	[16,17, 39–43], MS
	Nidorella nobrei A.Chev. [*Conyza feae* (Bég.) Wild]	Losna-brabo, losna-bravo	E	SA, SV, SN, St, F, Br	Shrub	Medicinal	R	Wp	Infusion, bath	EN		Barbosa, 6176	[16,17,42, 47]
Boraginaceae	*Echium hypertropicum* Webb	Língua-de-vaca	E	St, Br	Shrub	Medicinal, Forage, Fuel	C, F, S Others	Se	Seeds oil, oral administration	EN		Barbosa, 6026	[16,17,42, 48–50]

(*continued on next page*)

Table 1 (*continued*)

Family	Scientific names	Common names	Native status	Distribution CV[a]	Habit	Main uses	Medicinal applications[b]	Parts used[c]	Preparation and administration	Conservation status[d]	Markets and Voucher[e]	Other Herbarium recorder	References[f]
Brassicaceae	*Nasturtium officinale* W.T. Aiton	Agrião	N	SA, SV, SN, St, F, Br	Herb	Medicinal, Food, Forage	C, E, O, Others	Ae	Syrup, oral administration	LC	Ass Silva 12	M.C. Duarte & S. Gomes, 176	[16,40,53], MS
Campanulaceae	*Campanula jacobaea* C.Sm. ex Webb	Contra-bruxas-azul, dedal	E	SA, SV, SN, St	Shrub	Medicinal	E	Wp	Infusion, bath and oral administration	VU		Veiga, 19	[16,42]
Caryophyllaceae	*Paronychia illecebroides* Webb [*Herniaria illecebroides* C. Sm.]	Agrião-de-rocha, palha-de-formiga, mato-de-engodo	E	SA, SV, SL, SN, Bv, M, St, F, Br	Herb	Medicinal, Forage	E	Wp	Syrup, oral administration	NT		Barbosa, 5757	[16,42,52]
Cleomaceae	*Cleome brachycarpa* Vahl ex DC.	Palha-minhoto, erva-de-santo-antónio	N	SA, SV, SL, S, Bv, M, St	Herb	Medicinal, Forage	A	Se	Maceration, dermal administration	NE	Ass Silva 11	Barbosa, 5739	MS
Euphorbiaceae	*Euphorbia tuckeyana* Steud. ex Webb	Tortolho, tira-olho, tortilho	E	SA, SV, SL, SN, S, Bv, St, F, Br	Shrub	Medicinal, Fuel	U, D	Sa	Unknown	NT		Barbosa, 6150	[16,42,45]
Gentianaceae	*Centaurium tenuiflorum* subsp. *viridense* (Bolle) O.Eriks., A.Hansen & Sunding [*Erythraea viridensis* Bolle]	Fel-da-terra	E	St, F, Br	Herb	Medicinal	C, Others	Ae	Infusion, oral administration	CR*		Barbosa, 6065	[16,17,42, 47]
Lamiaceae	*Lavandula rotundifolia* Benth.	Aipo, elisbon, gilbon, alfazema-brava, alpo-rotcha	E	SA, SV, SN, St, F	Shrub	Medicinal	A, C, E, F, G, H, L, R, Others	Lv, Fl	Infusion, bath and oral administration	NT	Pra; Ass Silva 9	Barbosa, 6061	[16,40,43], MS
	Micromeria forbesii Benth.	Erva-cidreira, cidreirinha	E	SA, St, F, Br	Shrub	Medicinal	B, C, E, F, V, Others	Lv	Infusion, oral administration	EN	Ass Silva 5	Barbosa, 6066	[16,39, 41–43,49], MS
Leguminosae	*Lotus purpureus* Webb	Piorno, cabritagem, cafetagem	E	SA, SV, SN, Bv, St, F, Br	Herb	Medicinal	A, F, P	Lv	Infusion, bath and oral administration	DD		M. Romeiras, 946	[16,17,42, 43,47]
Plantaginaceae	*Campylanthus glaber* Benth.	Alecrim-brabo, alecrim-bravo	E	SA, SV, SN, St, F, Br	Shrub	Medicinal	A, D, E, F, I, P, R, Others	Wp	Infusion and directly applied, oral and dermal administration	EN	Ass Silva 3	Matos, 6180	[16,42,43], MS
Plantaginaceae	*Globularia amygdalifolia* Webb	Mato-botão	E	SA, SN, St, F, Br	Shrub	Medicinal, Fuel	Q	Lv	Infusion and maceration, chew	EN			[16,39,42, 46]
Sapotaceae	*Sideroxylon marginatum* (Decne. ex	Marmulano	E	SA, SV, SN, Bv, St, F, Br	Tree	Medicinal, Food, Fuel	A, D, N, O	Lv, Bk	Infusion, maceration,	EN	Ass Silva 8	Barbosa, 6082	1, 6, 7, 10, 12

(*continued on next page*)

Table 1 (*continued*)

Family	Scientific names	Common names	Native status	Distribution CV[a]	Habit	Main uses	Medicinal applications[b]	Parts used[c]	Preparation and administration	Conservation status[d]	Markets and Voucher[e]	Other Herbarium recorder	References[f]
	Webb) Cout. [*Sapota marginata* Decne. ex Webb]								oral and dermal administration				
Scrophulariaceae	*Verbascum capitis-viridis* Hub.-Mor. [*Celsia insularis* Murb.]	Sabão-de-feiticeira, sabão-de-lagartixa, sabugo	E	SA, SV, SN, Bv, M, St	Herb	Medicinal	C, F, K, T	Lv, Fr, Rt, Sa	Infusion, bath and oral administration	VU		Veiga, 21	[16,41–43,45]
Solanaceae	*Withania somnifera* (L.) Dunal [*Physalis somnifera* L.]	Podoreira	N	SA, SV, SN, Bv, St, F, Br	Shrub	Medicinal, Forage, Food	I, U, Others	Lv	Infusion	DD	Ass Silva 4	Barbosa, Matos & I. Silva 14423	[53], MS
Tamaricaceae	*Tamarix senegalensis* DC.	Tarrafe, tarafe, tamargueira	N	SA, SV, SN, S, Bv, M, St, Br	Tree	Medicinal, Fibre, Forage, Fuel, Timber	D, E	Lv, Fr	Infusion, bath and oral administration	NE	Ass Silva 10	Matos, 5702	[53], MS
Urticaceae	*Forsskaolea procridifolia* Webb	Urtiga, artiga, língua-de-vaca-branca, rafa-saia	E	SA, SV, SL, SN, S, M, St, F, Br	Shrub	Medicinal, Forage	E, Q	Lv	Infusion and smoked as a cigarette	NT		Barbosa, 6177	[16,17,42,43,47,51]

[a] **Distribution in Cabo Verde islands**: SA, Santo Antão; SV, São Vicente; SL, Santa Luzia; SN, São Nicolau; S, Sal; Bv, Boavista; M, Maio; St, Santiago; F, Fogo; Br, Brava.
[b] **Medicinal applications**: A, pains; B, intestinal problems; C, stomach problems; D, skin inflammations, wounds and burns; E, cough and respiratory diseases (including flu and cold); F, fever; G, malaria; H, dysentery and diarrhea; I, thrombosis and blood problems; J, stings, bites and poisoning; K, diseases of the liver and gallbladder; L, diseases of the kidney; M, diabetes; N, rheumatism and arthritis; O, bones and joints; P, headaches; Q, tooth and mouth diseases; R, menstrual problems and uterine disorders; S, hemorrhoids; T, internal parasites; U, sexually transmitted diseases; V, pregnancy, childbirth, breastfeeding and diseases of the new-born; Others (*i.e.*, cancer prevention, diuretic, soothing properties, appetite disorders, memory disorders, measles, dizziness, and cholesterol).
[c] **Parts used in medicine:** Ae, aerial parts of plant; Bk, bark; Fl, flowers; Fr, fruits; Lv, leaves; Rt, roots; Sa, sap; Se, seeds; St, stem; Wp, whole plant.
[d] **Conservation status:** Conservation status according to the IUCN Red List [54]. The taxa marked with * were classified according to Romeiras et al. [16].
[e] Vouchers of studied species are housed in LISC Herbarium.
[f] **References**: [16,17,39–45,45–53]. References to medicinal uses referred during field research in the markets of Santiago are also highlighted: MS.

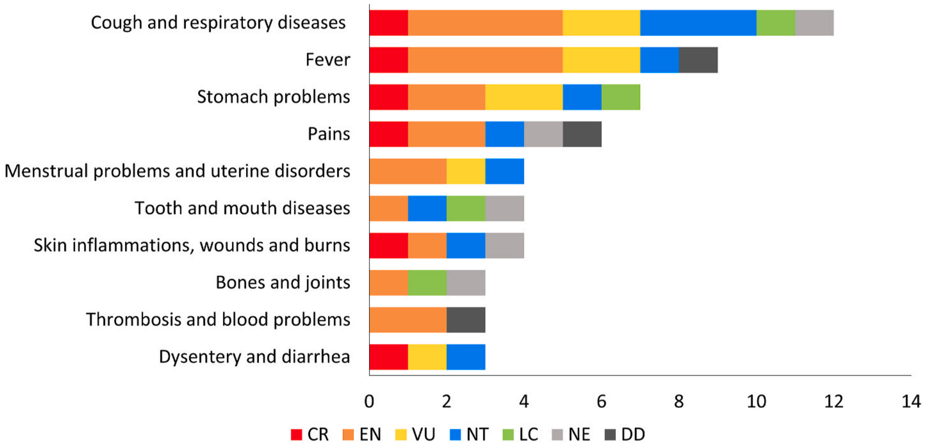

Fig. 2. Health conditions treated with three or more medicinal plant taxa in Santiago Island (Cabo Verde) (see more details in Table 1). The colours of the bars represent the IUCN Red List categories in which medicinal species are classified. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

and timber.

Our study reveals that 13 (54%) of the 24 medicinal taxa are classified in threatened categories according to the IUCN criteria [16, 54]. Two endemic species (*i.e.*, *Centaurium tenuiflorum* subsp. *viridense* and *Dracaena caboverdeana*) with 5 medicinal applications are classified as Critically Endangered. Moreover, 8 taxa are classified as Endangered, 3 as Vulnerable, and 4 as Near Threatened; only 2 taxa are classified as Least Concern. *Lotus purpureus* is classified as Data Deficient, and the widespread native non-endemic species, *Calotropis procera*, *Cleome brachycarpa*, *Tamarix senegalensis*, and *Withania somnifera* are still not evaluated.

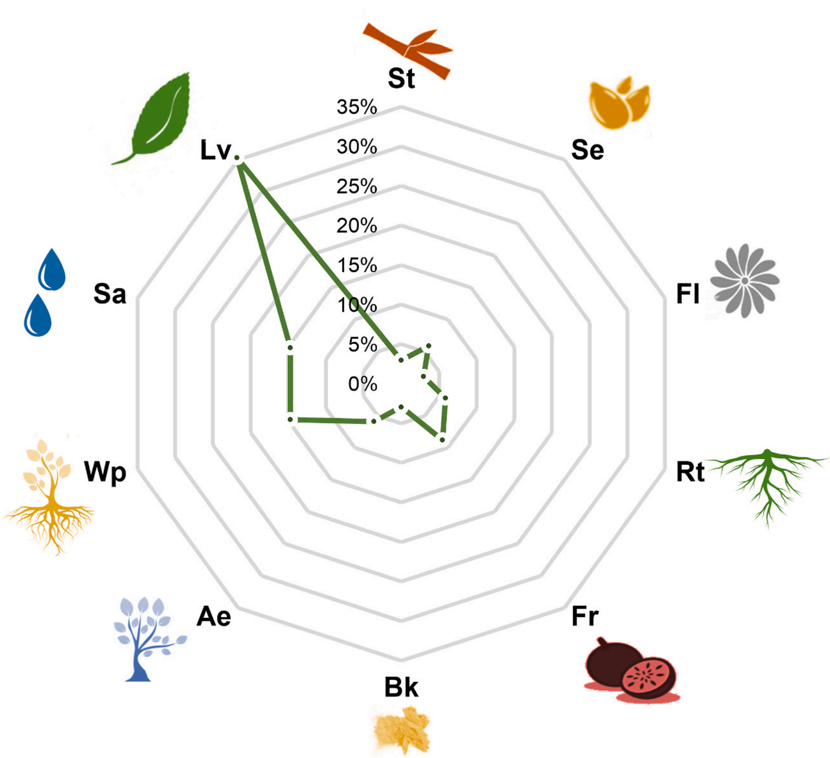

Fig. 3. Plant parts used in traditional medicine in Santiago. Lv (leaves), 35%; Sa (sap), 15%; Wp (whole plant), 15%; Ae (aerial part), 6%; Bk (bark), 3%; Fr (fruits), 9%; Rt (roots), 6%; Fl (flowers), 3%; Se (seeds), 6%; St (stems), 3%.

3.2. Markets' characterization

Fourteen sellers were found at the two traditional markets (7 sellers in Praia and 7 in Assomada). Throughout the visits and questionaries made from 2019 to 2022 (see Supplementary file), these 14 sellers continued to sell on the same market, and only in 2022, we found new sellers of medicinal plants. Our results show that most medicinal plant vendors in Santiago markets are 35–45 years-old women. It was possible to verify that there were specialized vendors who sold only medicinal related items, mineral ingredients, plants and ready to use preparations. All of them were able to provide information about the medicinal uses of the plants. Most of them received knowledge of traditional medicinal practices from their forefathers and local elders, although some said that they learned it by themselves. All the vendors were from rural zones since traditional medicine practices are more common in rural areas. Regarding medicinal plant harvesting, it is not done by the vendors, who buy the products from collectors; the interviews indicated that anyone can make such harvests, although caution is recommended not to harm the plants.

The diversity of plants sold at the market in Praia is less than at the market in Assomada, which is probably due to the market's location in a rural area in the interior of Santiago Island, where it is easier to collect plants. In both markets, the prices of plants vary between 50 and 1000 Cabo Verdean Escudos (CVE) (the exchange rate on November 13, 2022 was: USD 1 equivalent to 106.53 CVE, https://www.xe.com/currencyconverter/). Prices vary according to the availability of the plants, with annuals (which grow only during the rainy season) and those found in hard to reach places, such as mountainous areas, with higher prices.

3.3. Pharmacological characterization of *Sideroxylon marginatum* and *Tamarix senegalensis*

3.3.1. Total phenolic and flavonoids contents and antioxidant capacities

The total phenol and flavonoid contents and the antioxidant activities (DPPH$^\bullet$ and FRAP assays) of *Sideroxylon marginatum* and *Tamarix senegalensis* extracts are presented in Table 2. The total phenolic contents ranged from 189.2 ± 4.3 mg GAE/g in *Sideroxylon marginatum* aqueous extract (AE) to 535.5 ± 4.5 mg GAE/g in *Tamarix senegalensis* hydroethanolic extract (HEE). The total phenolic content of *Tamarix senegalensis* HEE and AE were significantly higher than the HEE and AE of *Sideroxylon marginatum*, respectively. The total flavonoid contents ranged from 90.5 ± 2.7 μmol CE/g in *Tamarix senegalensis* AE to 290.4 ± 8.6 μmol CE/g in *Sideroxylon marginatum* HEE. *Tamarix senegalensis* HEE had the highest content in total phenolic compounds and *Sideroxylon marginatum* HEE had the highest content in flavonoids.

The antioxidant capacity of the different extracts was evaluated by their reducing power (FRAP assays) and radical scavenging capacity (DPPH$^\bullet$ scavenging assay). The FRAP assay measures the ability of the extracts to reduce the Fe^{3+}-TPTZ complex to Fe^{2+}. For both species, the hydroethanolic extracts presented a reducing capacity higher than the aqueous extracts (Table 2). The reducing capacity of *Tamarix senegalensis* HEE was significantly higher than that of *Sideroxylon marginatum*, while both AE extracts exhibited lower and similar reducing activity ($p < 0.05$).

The stable radical DPPH$^\bullet$ was used to screen the plant extracts potential to scavenge free radicals. Both aqueous and hydroethanolic extracts of *Sideroxylon marginatum* and *Tamarix senegalensis* presented scavenging capacity against the free radical DPPH.

3.3.2. Antimicrobial activities of plant extracts

The antimicrobial activity of the four different plant extracts was determined against different microorganisms frequently responsible for infectious diseases and foodborne diseases. The zones of inhibition (mm) exhibited by plant extracts are listed in Table 3. Under the assayed conditions, the negative controls (water and 70% ethanol) did not show zones of inhibition.

Hydroethanolic and aqueous extracts of both plant species were able to inhibit the growth of Gram-positive bacteria. Conversely, none of the extracts showed activity against Gram-negative bacteria. The antibacterial activities of the hydroethanolic extracts were higher than those of their aqueous counterparts. Among the investigated extracts, the *Sideroxylon marginatum* HEE presented the most pronounced activity against all the Gram-positive bacteria tested. On the other hand, the *Tamarix senegalensis* AE presented the lowest activity. *Sideroxylon marginatum* extracts were the only ones showing antifungal activity by inhibiting the growth of the yeast *Candida albicans*.

Table 4 shows the MIC values obtained from the microdilution test. Several authors have been classifying the antimicrobial activity of natural extracts as strong inhibitors (MIC up to 500 μg/mL), moderate inhibitors (MIC between 600 and 1500 μg/mL) and weak inhibitors (MIC above 1600 μg/mL) [64,65]. Therefore, the extracts exhibited strong activity against *B. cereus*, moderate activity against the remaining Gram-positive bacteria and weak or no activity against *C. albicans* and Gram-negative bacteria.

Table 2
Total phenols and flavonoids contents, DPPH• scavenging activities and ferric reducing antioxidant powers (FRAP) of the two studied species.

Plant extracts	Phenolic content (mg GAE/g)	Flavonoids content (μmol CE/g)	FRAP (mmol Fe^{2+}/g)	DPPH[a] Inhibition %
Sideroxylon marginatum HEE	$338.4^{b} \pm 7.4$	$290.4^{a} \pm 8.6$	$5.43^{b} \pm 0.26$	$90.2^{a} \pm 0.1$
Sideroxylon marginatum AE	$189.2^{d} \pm 4.3$	$114.8^{b} \pm 3.9$	$3.13^{c} \pm 0.06$	$90.5^{a} \pm 1.1$
Tamarix senegalensis HEE	$535.5^{a} \pm 4.5$	$122.8^{b} \pm 2.6$	$8.75^{a} \pm 0.15$	$88.0^{a} \pm 0.5$
Tamarix senegalensis AE	$268.8^{c} \pm 7.9$	$90.5^{c} \pm 2.7$	$3.37^{c} \pm 0.03$	$89.6^{a} \pm 0.2$

[a] Extract concentration 50 μg/mL; HEE, hydroethanolic extract; AE, aqueous extract, GAE, gallic acid equivalents, CE, catechin equivalents. In each column, different letters denote significant differences ($p < 0.05$).

Table 3
Antimicrobial activities of hydroethanolic (HEE) and aqueous (AE) extracts (20 mg/mL) of the two studied plant species in terms of growth inhibition zone (mm).

Microorganisms	*S. marginatum* HEE	*S. marginatum* AE	*T. senegalensis* HEE	*T. senegalensis* AE
Staphylococcus aureus	$13.8^{a} \pm 0.7$	$11.1^{b} \pm 0.8$	$14.0^{a} \pm 0.1$	$11.5^{b} \pm 0.5$
MRSA	$13.0^{a} \pm 0.5$	$10.5^{b} \pm 0.5$	$12.6^{a} \pm 0.5$	$11.0^{b} \pm 0.9$
Enterococcus faecalis	$12.0^{a} \pm 0.1$	$9.3^{b} \pm 0.5$	$11.3^{a} \pm 0.5$	$7.5^{c} \pm 0.6$
Listeria monocytogenes	$11.0^{a} \pm 0.1$	$8.8^{c} \pm 0.5$	$10.0^{b} \pm 0.1$	$7.3^{d} \pm 0.5$
Bacillus cereus	$14.5^{a} \pm 0.8$	$12.1^{c} \pm 0.4$	$13.5^{b} \pm 0.5$	$11.9^{c} \pm 0.6$
Escherichia coli	nd	nd	nd	nd
Pseudomonas aeruginosa	nd	nd	nd	nd
Salmonella enterica subsp. *enterica* serovar Choleraesuis	nd	nd	nd	nd
Candida albicans	$12.5^{a} \pm 0.5$	$9.5^{b} \pm 0.6$	nd	nd

MRSA: Methicillin resistant *Staphylococcus aureus*; nd: not detected. In each row, different letters denote significant differences ($p < 0.05$).

Table 4
Minimum inhibitory concentration (μg/mL) of hydroethanolic (HEE) and aqueous (AE) extracts of the two studied plant species.

Microorganisms	*S. marginatum* HEE	*S. marginatum* AE	*T. senegalensis* HEE	*T. senegalensis* AE
Staphylococcus aureus	1000	1000	1000	1000
MRSA	500	1000	500	1000
Enterococcus faecalis	1000	1000	1000	1000
Listeria monocytogenes	1000	1000	1000	1000
Bacillus cereus	250	250	250	250
Escherichia coli	>2000	>2000	>2000	>2000
Pseudomonas aeruginosa	>2000	>2000	>2000	>2000
Salmonella enterica subsp. *enterica* serovar Choleraesuis	>2000	>2000	>2000	>2000
Candida albicans	2000	>2000	>2000	>2000

MRSA: Methicillin resistant *Staphylococcus aureus*.

3.4. *In vitro α-glucosidase and α-amylase inhibitory activities*

Hydroethanolic and aqueous extracts of *Sideroxylon marginatum* and *Tamarix senegalensis* were tested for their α-glucosidase and α-amylase inhibitory capacities through colorimetric methods. The inhibitory potential of the extracts was compared on the basis of their IC_{50} values, which are the concentrations that inhibit 50% of the enzyme activity under the specific set of assay conditions (Table 5). Acarbose, an antidiabetic drug that acts by inhibiting carbohydrate digestive enzymes was used as positive control.

All the extracts inhibited the α-glucosidase activity in a dose-dependent manner. IC_{50} values ranged from 2.0 ± 0.2 μg/mL for *Tamarix senegalensis* HEE to 9.9 ± 1.2 μg/mL for *Sideroxylon marginatum* AE. The α-glucosidase inhibitory capacities of the hydroethanolic extracts were higher than those of their aqueous counterparts. *Tamarix senegalensis* extracts had a greater ability to inhibit the α-glucosidase activity than *Sideroxylon marginatum* extracts. The four extracts exhibited an inhibitory activity higher than the positive control (acarbose).

The extracts also inhibited α-amylase activity in a dose-dependent manner. Nevertheless, in this case, all the extracts were less effective than acarbose. As previously observed, the inhibitory capacities of the hydroethanolic extracts were higher than those of their aqueous counterparts. However, for α-amylase, *Sideroxylon marginatum* extracts exerted a more powerful inhibitory activity than *Tamarix senegalensis* extracts (Table 5).

4. Discussion

The medicinal plants reported for Santiago Island and traded in local markets are highly diverse. The people of Cabo Verde still use traditional plants for disease prevention, but our study revealed that several of the used species are endemic and threatened, their area of occurrence is small, and harvesting for medicinal purposes is a major threat to their conservation [16]. In order to raise awareness

Table 5
IC_{50} values (μg/mL) of hydroethanolic (HEE) and aqueous (AE) extracts from the two studied species against α-glucosidase and α-amylase.

Plant extracts	α-Glucosidase	α-Amylase
Sideroxylon marginatum HEE	$3.9^{b} \pm 0.5$	$16.4^{c} \pm 0.1$
Sideroxylon marginatum AE	$9.9^{a} \pm 1.2$	$99.8^{b} \pm 1.2$
Tamarix senegalensis HEE	$2.0^{c} \pm 0.\ 2$	$112.0^{b} \pm 5.8$
Tamarix senegalensis AE	$4.2^{b} \pm 0.6$	$630.8^{a} \pm 7.6$
Acarbose	336.3 ± 14.7	11.6 ± 1.0

In each column, different letters denote significant differences ($p < 0.05$).

about the need for sustainable use and conservation of endemic flora, especially medicinal plants, WHO (World Health Organization) carried out surveys between 2005 and 2018 to identify global trends and the current situation in Traditional and Complementary Medicine, covering not only policy and regulation, but also products, practices and practitioners [][66]. However, Cabo Verde did not participate in any of the three surveys promoted by WHO.

Cabo Verde lacks official legislative or regulatory texts governing the practice of traditional medicine, as well as licensing procedures for traditional medicine practitioners, and procedures for the official approval of traditional medical practices and remedies. Medicine practitioners are not involved in Cabo Verde's primary health care program at either the local or national level [67]. However, recently, the Government of Cabo Verde has expressed its intention to change this situation and regulate traditional and complementary medicine, as a complement to conventional medicine, with the aim of promoting and improving the National Health System. In this context, future actions are planned to study the therapeutic effects of medicinal plants, as well as the training and qualification of practitioners [68].

4.1. Use of native medicinal plants in Santiago

Based on recent surveys and bibliographic research, the present study updated information about the medicinal native plants of Santiago Island. It highlights the importance that native species have for Cabo Verdean populations as a medicinal resource. The market surveys indicated that the knowledge of medicinal plants in Santiago is traditionally kept by local healers and rural populations. Moreover, our study underlines the great importance of endemic species for traditional medicine, some of them have high ethnopharmacological importance and are classified as threatened species. ***Artemisia gorgonum***, for instance, is indicated in the treatment of 10 medical conditions and is classified as Vulnerable; ***Campylanthus glaber***, used for 8 medical conditions, and ***Micromeria forbesii***, applied in 6 medical conditions, are both classified as Endangered; ***Dracaena caboverdeana***, with 5 medicinal applications, is classified as Critically Endangered; ***Periploca chevalieri*** also has 5 applications and is classified as Endangered.

It was noted that the health conditions for which more species are applied are respiratory problems and fevers, which are still some of the most widespread health problems in Africa ([69,70]). Due to their small distribution area, restricted to Cabo Verde, the endemic medicinal plants remain poorly studied, but they might be a source of new compounds of interest for many industries. Currently, the conservation of local knowledge and the conservation of native biodiversity is of major importance in the development of African countries [71]. However, significant gaps in available data on the therapeutic applications and conservation status of most African medicinal plants are yet to be solved.

The Red List of endemic plants of Cabo Verde [16], together with studies on the uses and applications of native plants, provides an important tool to identify and prioritize overexploited and threatened species.

For medicinal plants with limited abundance and slow growth, as is the case for most perennial endemics in Cabo Verde, overharvesting often results in population decline and may lead to extinction. The impact of harvesting for medicinal purposes depends on the parts of the plants used and how they are collected. For example, harvesting the whole plant is more destructive than the collection of fruits and flowers ([72,73]). In this sense, if traditional medicine preparations can be done using leaves, flowers or fruits, instead of the whole plant, the damaging effects would be much less. Wang et al. [74], for instance, concluded that ginseng (*Panax ginseng* C.A. Mey.) leaf-stem and root extracts have similar pharmacological properties, but leaf-stem has the advantage of being a more sustainable resource. Scientific research is, once again, very important in this process, not only to validate the therapeutic effect of the plant, but to detect what parts of the plant can be used to produce the effect with minimum damage.

Studies that relate the use of species with their conservation status may represent a major contribution to the science, pharmaceutical industries, and the economy of the country.

Recently, Varela et al. [30] highlighted the need to implement a strategic plan to protect the Cabo Verde native trees (*e.g.*, *Sideroxylon marginatum*), and it was proposed to expand the Network of Protected Areas, as the best way to face climate changes in this very vulnerable archipelago. These conservation measures will contribute to protect the endemic medicinal plants and prevent the dramatic loss of plant genetic diversity. However, further measures should be considered to achieve an effective conservation of endemic species, both within and outside the network of protected areas, while enabling their sustainable use as valuable resources for local populations. *Ex situ* cultivation, together with the use of biotechnological tools to propagate wild plant material (such as *in vitro* micropropagation), could represent a suitable strategy. This approach was already implemented in similar situations (*e.g.* Ref. [75]) and can be a sustainable alternative to halt the continuous loss of plant diversity in native habitats especially relevant in the case of wild species traditionally used.

In addition, complementary *ex situ* conservation actions, targeted towards the recovery of native plant populations, should be implemented. Botanical gardens play an important role in *ex situ* conservation, but other methods can be used, such as seed banks. To play an effective role in conserving wild plant diversity, these actions must be implemented in a way that prevents the genetic composition of *ex situ* populations from changing from that of wild populations through random genetic drift, artificial selection, and mutation accumulation [76].

Altogether, the *in situ* and *ex situ* conservation measures of the species, together with good harvesting practices, should be promoted by local authorities. In these, as in all conservation efforts, the involvement of local communities is pivotal and traditional knowledge and practices should be considered [77].

4.2. Bioactive properties

The emergence of microbial strains resistant to multiple antibiotics is increasing, and it is urgent to find effective and affordable alternatives to treat microbial infections. Therefore, there is a need for medicinal plants being exploited as a source of an alternative to conventional antibiotics [3]. On the other hand, it is foretold that there will be at least 350 million people in the world with type 2 diabetes by the year 2030, if suitable prevention measures are not taken. Postprandial hyperglycemia is a major problem in type 2 diabetes, therefore delaying glucose absorption is one of the therapeutic approaches proposed for diabetes control [59]. Two important digestive enzymes involved in postprandial hyperglycemia are α-amylase and α-glucosidase, which are involved in the degradation of starch. So, inhibiting these two enzymes could potentially prevent type 2 diabetes and its complications [78]. Some currently available antidiabetic drugs, such as acarbose, act by inhibiting the activity of α-glucosidase and α-amylase [79]. However, these drugs are associated with gastrointestinal side effects such as abdominal pain and diarrhea ([79,80]) and also with hepatotoxicity [81]. Many studies have been directed towards the discovery of plant extracts able to inhibit these digestive enzymes due to their low cost, safety and low incidence of undesirable side effects [80].

Several scientific reports showed that members of the genus *Tamarix* and *Sideroxylon* are valuable plants, rich in polyphenols and other phytochemicals, and have several pharmacological properties, including antioxidant, anti-inflammatory, antidiabetic and antimicrobial activities (*e.g.* Refs. [33,34,36,82]). Recently, Essoh et al. [27] showed that extracts from *Tamarix senegalensis* and *Sideroxylon marginatum* from Cabo Verde were able to prevent the nitric oxide production in the mouse macrophage cell line (RAW264.7) (anti-inflammatory activity) and to inhibit lipid peroxidation in porcine cell homogenates and the *in vitro* oxidative hemolysis of sheep red blood cells (antioxidant activity). However, to our knowledge, no studies were performed to evaluate neither the antimicrobial potential of *Tamarix senegalensis* and *Sideroxylon marginatum* from Cabo Verde nor their potential for the management of diabetes.

The bioactive properties of medicinal plants have been related to their composition in phenolic compounds, particularly in flavonoids (*e.g.* Refs. [36,83,84]). Therefore, the quantification of total phenolic and flavonoid compounds when evaluating the bioactive potential of plant extracts is highly relevant since they are among their most effective bioactive constituents [26].

When extracting bioactive compounds from plant materials, the resulting extracts are always a combination of different classes of compounds that are selectively soluble in different types of solvents. The use of alcoholic solutions provides satisfactory results for the extraction of bioactive compounds and the use of a mixture of alcohol and water has the advantage of modulating the polarity of the alcohol solvents, enabling a higher extraction yield of bioactive compounds such as polyphenols [85] while water extracts are only able to extract water soluble compounds. For this reason, in the present work, for each plant species, two extracts were performed: an hydroethanolic extract, aiming to maximize the extraction of phenolic compounds, and an infusion (aqueous extract) to simulate the preparation used in traditional medicine.

Tamarix senegalensis HEE showed higher total phenolic content and antioxidant activity when compared with extracts from other species of *Tamarix*, for example, methanolic leaf extracts of *Tamarix gallica* L. and *Tamarix articulata* Wall. [86], or water-acetone leaves extracts of *Tamarix ramosissima* Ledeb. [87].

Sideroxylon marginatum extracts also exhibited high phenolic and flavonoid contents and antioxidant capacity. However, bark extracts from *Sideroxylon obtusifolium* (Roem. & Schult.) T.D.Penn., a Brazilian species, presented a free radical scavenging capacity higher to those obtained in the present study [33].

The DPPH of both *Tamarix senegalensis* and *Sideroxylon marginatum* extracts makes them both very powerful antioxidant agents. Similarly, the FRAP activity of hydroethanolic and aqueous extracts from both plants are classified as very high, according to the FRAP classification described by Katalinic et al. [88]. However, even widely used as fast and reliable methods to evaluate the general antioxidant capacity of plant extracts, *in vitro* assays lack biological relevance, which must be established through *in vivo* studies [2].

In what concerns the *in vitro* carbohydrate digestive enzymes inhibitory assays, both hydroethanolic and aqueous extracts of *Tamarix senegalensis* and *Sideroxylon marginatum* from Cabo Verde showed α-amylase and specially α-glucosidase inhibitory activity. In fact, the four extracts showed an α-glucosidase inhibitory activity higher than acarbose. Different *Tamarix* species, such as *Tamarix articulata* [89,90] or *Tamarix gallica* [91,92], have shown antidiabetic activities both in *in vitro* and *in vivo* studies. *Sideroxylon obtusifolium* has been used in traditional Brazilian medicine for centuries also due to its antidiabetic properties [33]. Extracts from *Tamarix senegalensis* and *Sideroxylon marginatum* from Cabo Verde showed inhibitory activities higher than the aqueous extract from the leaves of *Morinda lucida* A.Gray, a medicinal plant used in West Africa to treat diabetes [93]. Other studies carried out with extracts of other plants considered as antidiabetic [80] also showed an α-glucosidase inhibitory activity higher than acarbose.

Results obtained suggest that hydroethanolic and aqueous extracts of both *Tamarix senegalensis* and *Sideroxylon marginatum* from Cabo Verde can delay the glucose absorption, thereby reducing postprandial glucose and insulin peaks, helping to slow down the progression of diabetes. The antioxidant activity of these extracts may also contribute to the prevention or treatment of this disease, as oxidative damage has been identified as a risk factor for the development of diabetes [94] and for the tissues damage caused by this disease [95].

As previously indicated, the extracts were more active against α-glucosidase than against α-amylase. According to Haile et al. [2], a more effective carbohydrate digestive enzymes inhibitor is expected when it has strong α-glucosidase and mild α-amylase inhibitory activities, as observed with the extracts of both *Tamarix senegalensis* and *Sideroxylon marginatum* of Cabo Verde, because intestinal disorders are associated with the fermentation of the undigested starch by the gut microbiota.

The ability to inhibit α-glucosidase and α-amylase enzymes need to be further validated using *in vivo* experimental models. However, Andrade-Cetto et al. [96], when analysing the antidiabetic activity of some Mexican medicinal plants, found good correlations between the results obtained with diabetic rats and the *in vitro* assay of α-glucosidase.

Some flavonoids, such as kaempferol, quercetin, apigenin, morin, luteolin, rhamnetin, rhamnazin or tamarixetin, are able to inhibit both α-glucosidase and α-amylase, being the flavonoid structure and the position and number of OH groups determining factors for a better or worse ability to inhibit carbohydrate digestive enzymes (*e.g.* Ref. [36]). Recently we identified some flavonoids in ethanolic

Table 6
Phenolic compounds identified in ethanolic and aqueous extracts from *Sideroxylon marginatum* and *Tamarix senegalensis* from Cabo Verde.

Species	Phenolic compounds identified[a]
Sideroxylon marginatum	Quercetin-*O*-hexosyl-deoxyhexosyl-pentoside, quercetin-*O*-hexosyl-pentoside, quercetin-*O*-hexosyl-deoxyhexoside, isorhamnetin derivative, quercetin-*O*-deoxyhexoside
Tamarix senegalensis	Ferulic acid sulphate derivative, methylquercetin-sulphate (tamarixetin sulphate), methylquercetin hexoside (tamarixetin-3-*O*-hexoside), methylkaempferol (kaempferide), kaempferol methyl ether sulphate, kaempferol-*O*-hexurunoside

[a] According to [27].

and aqueous extracts of both *Tamarix senegalensis* and *Sideroxylon marginatum* from Cabo Verde [27]. Two quercetin derivatives and three kaempferol derivatives were identified in *Tamarix senegalensis* extracts (Table 6 [27]). Quercetin-*O*-hexosyl-deoxyhexosyl-pentoside was the major compound found in *Sideroxylon marginatum* extracts. Beside this compound, other quercetin derivatives as well as an isorhamnetin derivative were also identified (Table 6). The inhibitory activities detected could be related to these flavonoids. For instance, the biological activity of quercetin includes also antioxidant, anti-inflammatory activity, antitumor properties and have been reported to have antiviral activity [97].

The assayed extracts of *Tamarix senegalensis* and *Sideroxylon marginatum* from Cabo Verde demonstrated antibacterial activity against different opportunistic Gram-positive bacteria. *Sideroxylon marginatum* extracts were also active against *Candida albicans*. This activity may be related to the higher content of flavonoids presented by *Sideroxylon marginatum* than by *Tamarix senegalensis* extracts. Several reports suggest that flavonoids are important antimicrobials in plant life, serving as phytoalexins, protecting plants from different types of microorganisms, as well as allelochemicals inhibiting the growth of microorganisms around the plant [98]. Different mechanisms by which bioactive compounds can exert their antimicrobial activity have already been identified. These mechanisms include membrane disruption, inhibition of cell envelope synthesis, inhibition of nucleic acid synthesis, inhibition of electron transport chain and ATP synthesis, among others [98].

The antimicrobial activity of plant extracts of several species of *Tamarix* has been previously evaluated against bacterial and fungal species. However, results showed that the antibacterial properties of *Tamarix* spp. dramatically depend on the species and geographical origin, as well as on the method/solvent used for the extraction of active compounds [36]. In the *Sideroxylon* genus, *Sideroxylon obtusifolium* ethanolic bark extracts were able to inhibit the growth of Gram-positive bacteria and *Candida albicans* [99]. Also, fractions and subfractions prepared from leaf extracts of *Sideroxylon mascatense* (A.DC.) T.D.Penn. were able to inhibit the growth of different Gram-positive and Gram-negative bacteria, and of fungi [34].

Despite the antimicrobial activity presented by the extracts of both *Tamarix senegalensis* and *Sideroxylon marginatum* from Cabo Verde, results obtained do not suggest these plants as potential antimicrobial agents as the extracts were inactive against Gram-negative bacteria and were only moderately active against most of the Gram-positive bacteria tested.

5. Conclusions

Medicinal plants are used worldwide for the treatment of different pathologies and form an important basis for the development of new medicines. In developing countries, medicinal plants and traditional medicine often serve as key resources for treating health problems, whether for economic or cultural reasons. In Cabo Verde traditional medicine and (consequently) medicinal plants are recognized as important health resources, especially by rural populations. On Santiago Island, medicinal plants are frequently used by local populations and traded in local markets. Most of these medicinal plants have not been the subject of detailed studies on their quality, safety and effectiveness, and have therefore not yet been validated as herbal drugs. Studies on the active principles, biological activity, or even the economic impact of medicinal plants on the Cabo Verdean society are rare. To our knowledge, this study is the first to present a preliminary assessment of the antidiabetic and antimicrobial activities of *Tamarix senegalensis* and *Sideroxylon marginatum*, which showed relevant antioxidant, and antidiabetic activities. These properties may be related to the presence of phenolic compounds, particularly some flavonoids, as the literature shows a clear link between polyphenols and antioxidant and antidiabetic activities of herbal extracts. The present study was restricted to a preliminary screening of the bioactive properties of the selected plant extracts; therefore, further investigations will be necessary to gather detailed evidence on their chemical composition and safety, and to identify and isolate the active components. In addition, the *in vitro* antioxidant capacity of the extracts, as well as their ability to inhibit α-glucosidase and α-amylase enzymes, need to be further validated using *in vivo* experimental models.

Medicinal plant species from Cabo Verde, could face a local extinction of some populations, due to their unsustainable use and overexploitation. There are international policies to promote the conservation of rare and endangered species, namely those established by the CBD (Convention on Biological Diversity), and conventions that regulate the overexploitation of valuable biodiversity, such as CITES (the Convention on International Trade in Endangered Species of Wild Fauna and Flora). Thus, it is urgent that mechanisms are put in place to ensure their conservation, while providing alternatives for local communities, highly dependent on these natural resources for their well-being. In particular, high priority should be given to *in situ* conservation of native medicinal plants traded in local markets. For example, reforestation actions implemented in Cabo Verde should include native trees, such as the studied species (*i.e., Tamarix senegalensis* and *Sideroxylon marginatum*), ensuring their conservation in natural habitats, in order to promote their sustainable use and preservation of the wealth of traditional knowledge that indigenous peoples still possess regarding the native medicinal flora in the archipelago.

Author contribution Statement

Maria M. Romeiras: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Anyse P. Essoh: Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Sílvia Catarino: Analyzed and interpreted the data; Wrote the paper.

Joceline Silva: Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data.

Katelene Lima: Performed the experiments;

Eromise Varela: Performed the experiments;

Mónica Moura: Contributed reagents, materials, analysis tools or data.

Isildo Gomes: Contributed reagents, materials, analysis tools or data.

Maria Cristina Duarte: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Maria Paula Duarte: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

All authors have reviewed and approved the submitted version of this manuscript.

6. Ethical Issues

This work was developed under a collaboration protocol between Cabo Verdean institutions (Universidade de Cabo Verde (Uni-CV), Escola Superior de Ciências Agrárias e Ambientais (ECAA), Instituto Nacional de Investigação e Desenvolvimento Agrário (INIDA) and Direção Nacional do Ambiente (DNA)) and Portuguese (Instituto Superior de Agronomia (ISA) and Faculdade de Ciências (FC) of the Universidade de Lisboa and Faculdade de Ciências e Tecnologia of the Universidade dos Açores) under the project "Climatic changes and plant genetic resources: the overlooked potential of Cabo Verde's endemic flora" CVAgrobiodiversity/333111699, funded by the "Aga Khan Development Network" (AKDN) and the "Fundação para a Ciência e Tecnologia" (FCT). The team includes senior researchers and post-graduate students from Cabo Verde (APE, EV, IG JS, KL) and Portuguese researchers (MCD, MM, MMR, MPD, SC). The study is strictly of a scientific nature, not including any development component, and the necessary licences were obtained under the collaboration protocol above mentioned.

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Declaration of Competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e14651.

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