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SHORT COMMUNICATION

Comparative metabolome and metallomic analyses of three organs from *Cistus creticus*

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Abstract

Main conclusion **There is a noted variation in metabolomic and metallomic content between the different organs of *Cistus creticus*, which might inform future research and nutritional or medicinal use of the plant.**

Abstract *Cistus creticus* L. (Cistaceae), known by the common name rock rose, is a garden flower and an emerging medicinal plant. *C. creticus* extracts have analgesic, anti-inflammatory, antioxidant effects, and potent antimicrobial power. Extracts or essential oil from *Cistus* promote reduction in triglyceride levels, repress diabetes biomarkers and promote reduction of UV-B damage. All this collectively indicates possible beneficial effects for treatments of infections, diabetes, and skin aging. While several studies reported a number of metabolites in *C. creticus*, there is no comprehensive metabolome and elemental analyses of its different organs. We performed GC–MS, UHPLC–MS and ICP-MS analyses of flowers, leaves, and stems of *C. creticus* and report known, as well as new, metabolites in the three different organs, as well as essential elements. Leaves were richest in primary metabolites such as essential amino acids, sugars, and organic acids, with some exceptions. They were also richest in myricitrin, myricetin-3-*O*-glucoside, and myricetin-3-*O*-pentoside, which have potent antioxidant, anti-inflammatory, and antidiabetic activities, as well as azelaic acid, quinic acid, kaempferol and its derivatives, and other secondary metabolites. Stems were richest in asterbatanoside. Other secondary metabolites, such as cistusin, chlorogenic acid, nicotinic acid, and punicalin, were most abundant in the flowers. We have identified metabolites with different beneficial activities in *C. creticus* and demonstrated that their levels greatly vary depending on the type of organ they are present in. These findings indicate that organ-specific enrichment of bioactive metabolites could inform targeted therapeutic development for diabetes, infections, and inflammatory disorders.

Keywords *Cistus creticus* · Essential minerals · Metabolome analysis · Nutritional qualities · Primary metabolites · Secondary metabolites

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Introduction

Cistus creticus L. (common name rock rose) is an herb from the family Cistaceae, used as a garden flower for decades. It is widely distributed in the Mediterranean ecosystems, e.g., the maquis plant communities. In recent years, it has attracted attention as a medicinal plant because of its antioxidant, analgesic, anti-inflammatory, antimicrobial, and antioxidant power (Kielar et al. 2025). Extracts of *C. creticus* protected against oxidative DNA damage in vitro by reducing H_2O_2-induced plasmid DNA strand breaks (Kilic et al. 2019). Extracts from *C. creticus* also exhibited anti-inflammatory activity and reduced IL-6 levels in a concentration-dependent manner (Guzelmeric et al. 2023), suggesting their possible use for preparation of medications against inflammation. *Cistus* species are traditionally used to treat diabetes in the Mediterranean. Extracts from *C. creticus* inhibited acetylcholinesterase and butyrylcholinesterase, two biomarkers for diabetes (Kahraman 2026). In Turkish folk medicine, tea from the leaves of *C. creticus* is used, whereas in Morocco, the leaves of *C. creticus* are used by patients after decoction or as a powder (Barkaoui et al. 2017; Boutaj 2024). Furthermore, extracts from *C. creticus* exhibited activity against human oral bacteria fungal microorganisms (Hickl et al. 2024). Additionally, the extracts from *C. creticus* exhibited activity against MIA PaCa-2 human pancreatic cancer cells (Guzelmeric et al. 2023). In humans with mild dyslipidemia (elevated triglyceride levels), supplements containing standardized formulation including *C. creticus* led to a significant decrease in triglyceride levels (Tsolakou et al. 2023). Finally, the essential oil of *C. creticus* increased the expression of the anti-aging gene SIRT1 in the HaCaT human keratinocyte cells and reduce their damage and senescence under UV-B light, indicating possible inhibition of skin aging (Ledrhem et al. 2022).

Because of these therapeutic properties of *C. creticus*, its biochemical composition was intensively investigated in recent years. Secondary metabolites, including various phenolics, were identified and their biological activity assessed (Nur Onal et al. 2023; Papanikolaou et al. 2024; Aouiffat et al. 2025; Guelifet et al. 2025). Recently, a non-targeted metabolome profiling by GC–MS and LC–qTOF-MS identified a number of primary and secondary metabolites from the aerial parts of *C. creticus* (Kahraman et al. 2026). However, no investigations into the metabolome compositions of the different areal parts (e.g., leaves, stems, flowers) have been performed so far. The elemental composition of these parts is also unexplored.

Here, we perform comprehensive metabolome and metallome analyses of leaves, stems, and flowers of *C. creticus* in order to determine their nutritional properties, the presence of metabolites with health promoting properties, and their relative abundances in the different plant organs.

Materials and methods

Plant material

Plant material from *C. creticus* (Fig. 1) was collected from Nature Park "Strandja", Bulgaria, during the vegetative period in 2024 and separated in three distinctive groups (organs)—leaves, stems, and flowers. Five replicates for each organ were prepared, comprised of material from multiple plants. The plant material was cleaned and subsequentially dried by air in darkness at room temperature. All dry samples were ground to a coarse powder with electric laboratory mill (GRINDOMIX GM 200; Retsch, Haan, Germany), followed by an additional homogenization to fine powder using a bead mill (VWR, Darmstadt, Germany) at 30 Hz for 60 s. Subsequently, this material was freeze-dried at − 40 °C.

Metabolome analysis

Each sample (20 mg freeze-dried material) underwent a standard two-phase (methanol–chloroform) extraction (Perez De Souza et al. 2021). Briefly, 750 µL of 100% MeOH (LC–MS grade; Chromasolv; Honeywell, Charlotte, NC, USA) with isovitexin (CAS: 29702-25-8; Sigma) internal standard was added to the plant material and the samples were homogenized thoroughly, after which 400 µL of chloroform (HPLC grade; Chromasolv, Honeywell) was added. After homogenization on a shaker at 1200 rpm for 2 min, 800 µL of water (LC–MS grade; LiChrosolv, Merck) was added to the samples and vortexed well. Finally, samples were centrifuged for 10 min at 15 000 g. The aqueous phase was then analyzed on a UHPLC-MS (ACQUITY UPLC I-Class PLUS, SYNAPT XS; Waters).

Fig. 1 *Cistus creticus* in natural conditions

Chromatographic conditions: BEH C18 column (1.7 µm, 2.1 mm × 100 mm; Waters), kept at 40 °C. Sampler temperature set at 15 °C. Mobile phase A 0.1% formic acid (LiChropur, Merck)–water (LiChrosolv, Merck), phase B 0.1% formic acid–acetonitrile (Chromasolv, Honeywell). Flow rate at 0.4 mL/min. Gradient as follows: 0–1 min, 1% B; 1–11 min, 1–40% B; 11–13 min, 40–70% B; 13–15 min, 70–99% B; 15–16 min, 99% B; 16–17 min, 99-1% B; 17–20 min, 1% B. Injection volume 2 µL. Q-TOF mass spectrum conditions: an electrospray ion source (ESI) was used. Capillary voltage 2.5 kV, sampling cone voltage 40 V, source temperature 120 °C, desolvation temperature 250 °C. Cone gas flow of 50 L/h, desolvation gas flow of 600 L/h, and nebuliser gas flow of 6.5 bar. The detector was set in negative mode, resolution analyzer mode, continuum survey with a range of 50–1500 Da and scan time of 0.3 s. For MS/MS, a gradient fragmentation energy of 20 to 30 V was used. Post-acquisition, data were imported in Progenesis QI (Waters/Non-Linear Dynamics) and processed using default parameters. In brief, all runs were assessed for suitability as an alignment reference, performing automatic alignment. Peak picking was performed at automatic sensitivity (default setting), no retention time limits, fragment sensitivity of 0.2% base peak, and with all available adducts. Abundances were normalized to sample mass. Compound data were exported and annotated using the metabolite database, available at the Center of Plant Systems Biology and Biotechnology in Plovdiv, Golm Metabolome Database, and referenced to publicly available fragmentation spectra databases (Kopka et al. 2005; Horai et al. 2010). Chromatographs are available as Supplementary material.

Derivatization was carried out as in Lisec et al. (2006) on 100 µL of dried extract using 20 mg/mL methoxyamine hydrochloride (Sigma-Aldrich) in pyridine (Emsure; Merck) and trimethylsilyl-*N-methyl* trifluoroacetamide (Restec). Derivatized extracts were analyzed on a TSQ9000 GCMS (Thermo Fisher Scientific) following a 1 µL injection. Helium was used as carrier gas at a constant flow rate of 2 mL/s and gas chromatography was performed on a 30-m DB-35 column with 0.32 mm inner diameter and 0.25 µm film thickness (Agilent Technologies). The injection temperature was 230 °C, and the transfer line and ion source temperatures were set to 250 °C. The initial temperature of the oven (85 °C) increased at a rate of 15 °C/min up to a final temperature of 360 °C. After a solvent delay of 180 s, mass spectra were recorded at 20 scans/s with a 70–600 m/z scanning range. The chromatograms were processed in Xcalibur v.4.1.31, and peaks were annotated to an internal library of over 100 standards recently analyzed on the same instrument. In addition, prominent peaks not present in the internal library were manually annotated by matching spectra to publicly available databases (e.g., Fiehn Spectral library; Kind et al. 2009).

Metallomic analysis

Sample preparation was done with the help of a MARS 6 microwave digestion system (CEM Corporation, Matthews, NC, USA). The digestion was performed in PTFE vessels by adding 0.5 mL trace metal grade concentrated HNO_3 (Suprapur; Merck) and 2 mL 30% H_2O_2 (Emsure; Merck) to 0.25 g homogenized and lyophilized samples. The samples were left for 30 min before being placed in the microwave and digested in closed vessels. Samples and method blanks were prepared and digested in a single batch and later diluted to 15 mL with reagent water (Arium Comfort I – H2O-I-1-TOC-T; Sartorius). Measurements were performed using an inductively coupled plasma mass-spectrometer (7850 ICP-MS, Agilent Technologies). The system was fitted with a glass nebulizer, quartz spray chamber, nickel cones, and a torch with a 2.5 mm injector, as well as an Ultra High Matrix Introduction system and ORS4 cell operating in helium (He) mode. The optimized ICP-MS operation conditions for the analysis were as follows: RF power of 1600 W, plasma argon flow rate of 15.0 L/min, and nebulizer gas flow rate of 0.9 L/min. Data acquisition was performed using Mass Hunter software. ICP-MS data were imported into Microsoft Excel, and each of the detected elements was calculated using standards and a first-order (linear) calibration curve.

Results and discussion

Metabolome analysis

The combined analysis of both GC–MS and UPLC-MS identified 99 metabolites in total: 50 for GC–MS and 49 for UPLC-MS, respectively, with most major phytochemical classes being represented (Supplementary Table S1). The principal component analysis (PCA) of the samples from the leaves, stems, and flowers showed a clear separation between the different organs, confirming the differences and the specificity of their metabolomes (Fig. 2). The biological replicates from each of the three different organs clustered together very clearly, demonstrating low variability and robustness of the analysis. A heatmap, which displays the distribution of these compounds between the three analyzed organs, is presented in Fig. 3.

Primary metabolites

The combined GC–MS and UHPLC-MS have annotated amino acids, as well as the major sugars, organic acids, and other primary metabolites (Fig. 3). The amino acids, identified in all samples, were most abundant in the leaves, followed by the flowers. Few exceptions were ornithine, arginine and glutamic acid, which showed diminished presence

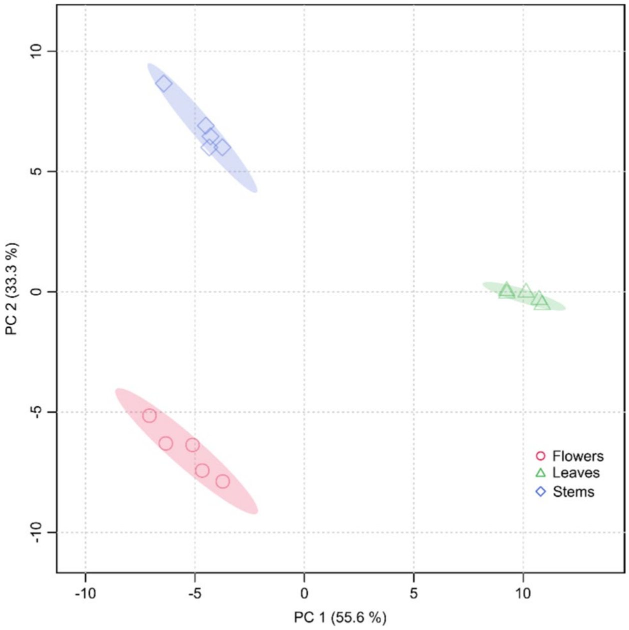

Fig. 2 Principal component analysis of metabolome samples from leaves, stems, and flowers of *Cistus creticus*

in leaves, and tryptophan, represented mostly in stems. Organic acids were also mostly highest abundant in leaves, with some exceptions like uric and methyl-maleic acids, present mostly in flowers, and malic acid, being highest in stems. Saccharides followed similar pattern, with leaves having the richest profile, with few exceptions, for example, sucrose and trehalose dihydrate being highest in stems, while raffinose was very pronounced in the flowers. Altogether, these results collectively demonstrate that the leaves have the highest nutritional values as sources of both energy-rich sugars and essential amino acids and can be used for food like fresh salads or in cooked dishes.

Secondary metabolites

Given the known complex polyphenolic profile of the well-studied relative species *Cistus incanus*, these compounds were given most attention during the analysis. Many of the expected compounds were successfully annotated in all three organs. The organ-specific distribution analysis showed variations in polyphenolic levels, with leaves demonstrating the highest abundance, followed by flowers, and finally stems.

One of the groups of compounds which *Cistus* is noted for are ellagitannins, with these hydrolysable tannins representing the dominant polyphenolic class (Starzec et al. 2023; De Filippis et al. 2025). They are present in some berries (blackberry, raspberry, strawberry), as well as in grapes and pomegranate (De Filippis et al. 2025). Through multiple mechanisms, ellagitannins show a plethora of beneficial properties. Of note are the hypoglycemic effects of these compounds, through their very effective α-glucosidase inhibitory activity, which reaches almost 100% for cistusin, punicalagin and terflavin A (Starzec et al. 2023). They also have antiviral and antibacterial properties. While total extracts have a more pronounced effect, punicalin shows almost similar antiviral activity, which could be explained by its high affinity for some viral spike proteins (De Filippis et al. 2025). Punicalin also can suppress the replication of some bacterial species, such as *Staphylococcus aureus* through interaction with sulfhydryl groups in bacterial cell wall proteins and downregulation of biofilm formation genes (De Filippis et al. 2025). In the analyzed samples, punicalin, punicalagin and cistusin showed highest levels in the flowers, with punicalagin found in the leaves in almost comparable amount; terflavin A had highest abundance in leaves.

Another polyphenol sub-class, commonly detected in *Cistus*, are phenolic acids, of which a number were annotated. They are known for their potent antioxidant, anti-inflammatory, antimicrobial, and neuroprotective properties, which contribute to their beneficial effects in prevention and management of chronic diseases (Kumar and Goel 2019). Gallic acid has numerous beneficial effects. It has potent free radical scavenging capabilities, neutralizing reactive oxygen species (ROS) and reducing oxidative stress at the cellular level by increasing the activity of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), and elevating levels of glutathione (GSH), vitamin C, and vitamin E (Kahkeshani et al. 2019; Hadidi et al. 2024). Shikimic acid, a key plant metabolite with antimicrobial and antiviral properties, serves as the starting material for pharmaceutical synthesis of the antiviral product oseltamivir (Tamiflu). In an in vitro model, compared with the product, the pure compound causes similar modulation of the interleukin cytokines IL-6 and IL-8, responsible for the activation and recruitment of lymphocytes (Bertelli et al. 2008). Of note is that if shikimic acid is combined with quercetin, the effects are significantly higher, showing that synergistic effects should be taken note of and considered, when working with full extracts. The relative abundance of gallic acid was similar in leaves and flowers. Shikimic acid was mostly present in leaves.

The hydroxycinnamic acids—caffeic acid, *p*-coumaric acid, chlorogenic acid (5-CQA), neochlorogenic acid (3-CQA)—are recognized as potent antioxidants acting through multiple mechanisms (Taofiq et al. 2017; Sova and Saso 2020). It is assumed that their primary mode of action involves radical scavenging through hydrogen or electron donation, with the resulting phenoxyl radicals stabilized by delocalization within their aromatic structure. Additional mechanisms include chelation of transition metals (copper and iron) that catalyze oxidative stress, inhibition of ROS-generating enzymes, and modulation of gene expression

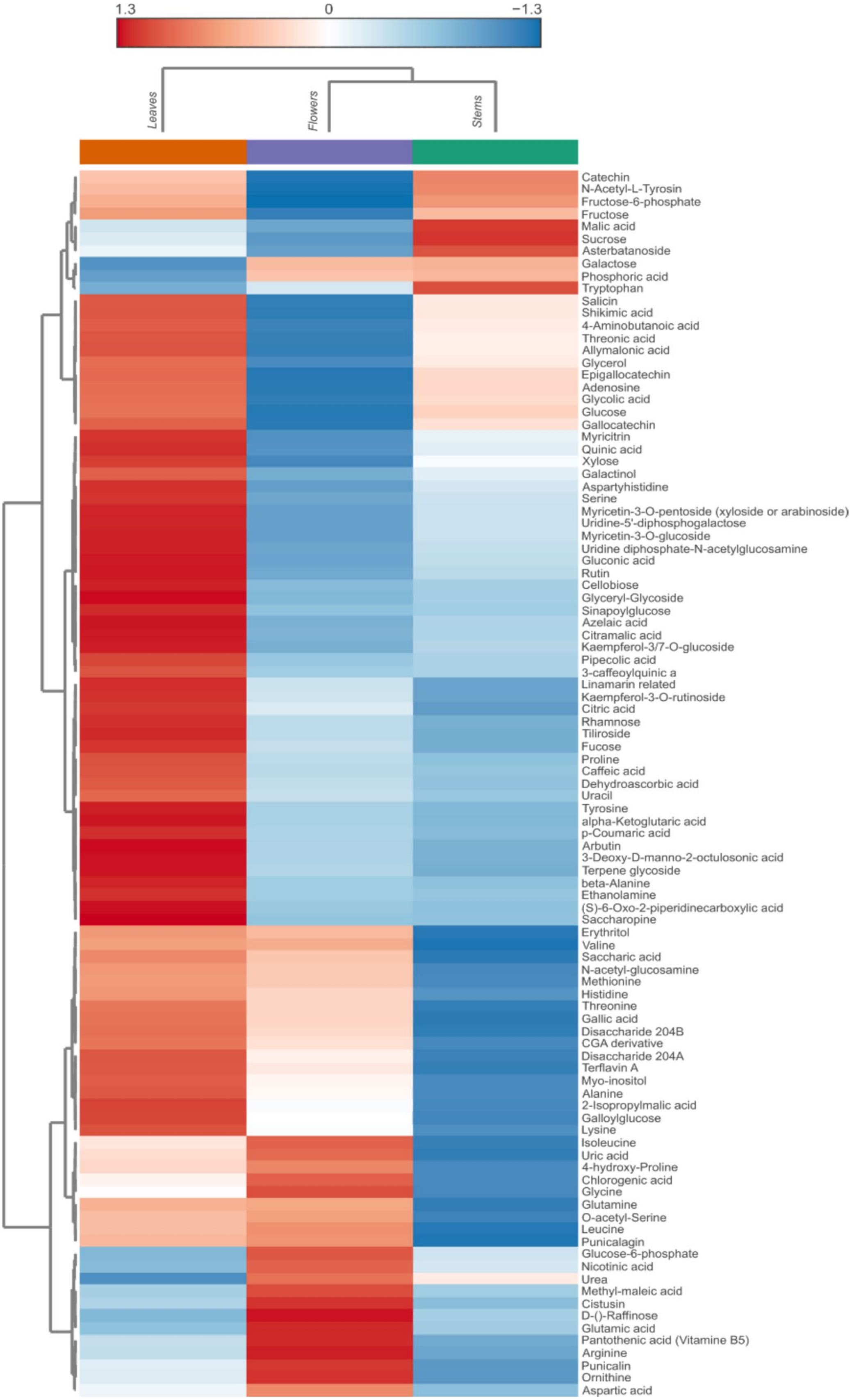

Fig. 3 Heatmap, comparing the abundances of the annotated compounds between the three analyzed *C. creticus* organs—leaves, flowers, and stems

through the ARE/Nrf-2 pathway (Teixeira et al. 2013). Caffeic acid, *p*-coumaric acid and neochlorogenic acid were detected in high amounts in leaves. In contrast, chlorogenic acid had highest abundance in the flowers.

Cistus contains a diverse array of flavonoid compounds that represent distinct metabolic pathways within the phenylpropanoid biosynthetic network (Pielorz et al. 2022; Starzec et al. 2023). The flavonol glycosides appear in various forms, including myricetin-3-O-glucoside, myricetin-3-O-rhamnoside (myricitrin), and quercetin-3-O-rutinoside (rutin). The presence of acylated flavonoids, as tiliroside, adds further complexity to the profile. Catechin, gallocatechin and epigallocatechin are represented as well. This diverse flavonoid composition, encompassing flavonols, their glycosides, and flavan-3-ols, has the potential for synergism with the plant's abundant ellagitannin content to produce potent antioxidant effects and enzyme inhibitory activities and enhances the plant's bioactive potential.

A recent comparative metabolome study of essential oils from nine plant species revealed that *C. creticus* is highly abundant in secondary metabolites, compared with the other species, and is particularly rich in α-pinene, carvacrol, p-cymene, and γ-terpinene (Türkmen et al. 2025). The essential oil of *C. creticus* had high anticancer activity, especially against breast adenocarcinoma (MCF-7), gastric carcinoma (NCI-N87), human prostate carcinoma (LNCaP clone FGC-Luc2), and hepatocellular carcinoma (HepG2) cancer cell lines (Türkmen et al. 2025). In another study, essential oil from *C. creticus* was shown to induce the anti-aging gene *SIRT1* expression in human keratinocytes, leading to senescence inhibition (Ledrhem et al. 2022). Leaf trichomes of *C. creticus* are also known to secrete various labdane-related diterpenoids, which have antimicrobial, anti-inflammatory, and cytotoxic effects (Papanikolaou et al. 2024).

Myricetin derivatives including myricitrin, myricetin-3-*O*-glucoside, and myricetin-3-*O*-pentoside exhibit potent antioxidant, anti-inflammatory, and antidiabetic activities, with myricitrin specifically demonstrating strong antiglycation effects that inhibit advanced glycation end-product formation (Imran et al. 2021; Bernacka et al. 2022; Niisato and Marunaka 2023). Catechin, gallocatechin and epigallocatechin demonstrate complementary cardiovascular and metabolic benefits including blood pressure reduction, prevention of atherosclerosis, enhanced insulin secretion, potent free radical scavenging that protects against lipid peroxidation, and anti-inflammatory activities through modulation of oxidative stress pathways (Bernatoniene and Kopustinskiene 2018; He et al. 2018). Kaempferol glycosides, including kaempferol-3-*O*-rutinoside and kaempferol-3/7-*O*-glucoside, provide cardio- and neuroprotective effects through the modulation of several proinflammatory signaling pathways (Silva Dos Santos et al. 2021). Rutin also has comprehensive cardiovascular and neuroprotective properties, while also providing antidiabetic effects through improved insulin signaling, antiarthritic relief, antimicrobial activity, and multi-organ protective effects through reduced lipid peroxidation and enhanced antioxidant enzyme activities (Semwal et al. 2021; Bazyar et al. 2023). Tiliroside exhibits potent anti-inflammatory and antioxidant properties, along with antidiabetic, anti-obesity, lipid-lowering, and hepatoprotective effects, through modulation of key pathways (Jin et al. 2016; Zhuang et al. 2021; Adachi et al. 2025). Most detected flavonoids were mostly present in leaves, with an exception being catechin, found in a slightly higher amount in the stems.

It should be noted that the extraction methods are extremely important for the metabolite compositions of the respective extracts, and this can be a limitation of a particular study. There are no universal extraction methods and hence there may be variability in determining the metabolomes of plant tissues and organs. Different extraction methods were utilized for the biological studies employing *C. creticus.* For example, Kahraman et al. (2026) used methanolic extracts from *C. creticus* to study the inhibitory activity of the extracts on acetylcholinesterase and butyrylcholinesterase. A hydro-distillation method was used to explore the anticancer potential of *C. creticus* essential oil on human cancer cell lines (Türkmen et al. 2025). Steam distillation followed by liquid–liquid extraction using n-hexane was used to obtain the *C. creticus* essential oil, used in a subsequent study of mitochondrial development and SIRT1 activation in human keratinocytes (Ledrhem et al. 2022). To study the antimicrobial activity of *C. creticus* on bacterial and fungal oral pathogens, ethyl acetate was used as extraction solvent (Hickl et al. 2024).

Metallomic analysis

Given the high content of phytochemical compounds in *Cistus*, it is also important to assess not only the minerals which are needed for growth of the higher plants, but also the trace elements that are essential both to plants and humans. The samples were investigated for the presence of 18 elements, eight of which (Bi, Cd, Cr, Co, Ni, Pb, Sr, Tl) were below the limit of detection. The mean values of five replicates ($n = 5$) with the relative standard deviation of the rest of the elements (Ca, K, Mg, Zn, Mn, Fe, B, Cu, Na, Al) found in the samples under investigation are listed in Table 1. Many metals and metalloid elements, especially several very important for the human health elements (Ca, Mg, Mn, B), were present at higher levels in the leaves (Table 1). These elements are either important signals like Ca^{2+} and/or serve as co-factors of hundreds of essential human proteins, including hydrolases, transferases, lyases, DNA/RNA polymerases, and others. Examples of such enzymes include glutamine synthetase (uses either Mg^{2+} or

Table 1 Levels of essential elements in *C. creticus* samples from three different organs (leaves, stems, and flowers), presented as mg kg^{-1} DW

Sample	Ca	K	Mg	Zn	Mn
Cistus creticus (leaves)	**77.4 ± 6.8**	2248 ± 263.0	**1284.4 ± 196.7**	26.4 ± 3.2	**17.9 ± 1.4**
Cistus creticus (stems)	25.1 ± 1.8	2297.6 ± 224.5	209.6 ± 28.7	17.4 ± 4.2	8.2 ± 1.0
Cistus creticus (flowers)	20.3 ± 2.8	1639.0 ± 147.4	331.9 ± 72.8	**47.7 ± 9.3**	4.6 ± 0.9
Sample	**Fe**	**B**	**Cu**	**Na**	**Al**
Cistus creticus (leaves)	192.9 ± 33.7	**1.85 ± 1.3**	0.28 ± 0.04	27.5 ± 2.4	23.9 ± 4.0
Cistus creticus (stems)	150.5 ± 21.4	0.67 ± 0.4	0.15 ± 0.01	19.9 ± 2.2	14.3 ± 0.9
Cistus creticus (flowers)	180.4 ± 32.6	0.49 ± 0.08	0.21 ± 0.05	22.2 ± 1.8	14.6 ± 2.2

Data are means of five biological replicates ± SE. Bold indicates the samples with significantly more abundant elements

Mn^{2+} in its active site), which controls and converts toxic levels of glutamate to the less toxic glutamine, pyruvate carboxylase, arginase, and MnSOD, to name a few (Jomova et al. 2022). The highest levels of Mg and Mn in the leaves are expected, as both elements participate in photosynthesis-related processes (e.g., Mg is part of the chlorophyll and Mn is part of the oxygen-evolving complex) (Çakmak et al. 2023; Hawkesford et al. 2023). Mn is essential for the activities of enzymes of the shikimic acid and subsequent pathways, leading to the biosynthesis of aromatic amino acids (such as tyrosine), secondary metabolites (lignin, flavonoids), and the phytohormone indole acetic acid (Çakmak et al. 2023). Two other elements essential to human health, Fe and Cu, were most abundant in both leaves and flowers. These elements are essential for other key enzymes, e.g., the Fe-containing hemoglobin, the electron transfer Fe–S proteins, the cytochromes, the superoxide radicals-detoxifying enzyme Cu/Zn SOD, Cu-containing cytochrome C oxidase and tyrosinase (Jomova et al. 2022). Zn is predominant in the flowers of *C. creticus*. The highest levels of Zn in the flowers were not foreseen, although data about mineral composition of flowers are rather limited. In addition to the above-mentioned Cu/Zn SOD, Zn is an important constituent of more than 300 enzymes (e.g., histone deacetylases, carbonic anhydrases (CAs), matrix metalloproteinases, RNA polymerases, carboxypeptidase A, protein kinase C, alcohol dehydrogenase, carbonic anhydrase, and nitric oxide synthase) and the Zn finger transcription factors (McCall 2000). K is distributed similarly in all organs (Table 1). The ICP-MS raw data are available in Supplementary Table S2.

Compared with other species, the leaves of *C. creticus* contain very high amounts of K, Mg, and Mn. Recent comparative analysis of essential elements in fruits from ten different crop species identified banana as the richest in K (326–524 mg kg^{-1}) and Mg (270–540 mg kg^{-1}) and berry crops such as blueberry, raspberry, and strawberry being richest in Mn (4.3–5.8 mg kg^{-1}) (Wittenberg et al. 2026). The leaves and the stems of *C. creticus* have fourfold higher K than banana, and the leaves of *C. creticus* have more than twofold higher levels of Mg than banana and more than threefold higher levels of Mn than the berry crops.

Conclusion

Leaves of *C. creticus* presented themselves as the richest source of most metabolites, followed by flowers and then stems. Nutritionally, the abundance of essential amino acids and minerals in the leaves makes them an excellent supplement for fresh salads or herbs for cooked meals. From a phytochemical standardization perspective, the increased abundance of polyphenolic compounds in leaves—particularly ellagitannins, flavonoids, and phenolic acids—suggests that leaf-based extracts can deliver more consistent and potent antioxidant activity compared to preparations that incorporate stems or mixed aerial parts. This distribution of bioactive compounds across the plant organs can have impact on both scientific research and commercial applications of *C. creticus*.

The variability of metabolites and essential elements in the different plant organs highlights the need for continuous quality control, especially when sourcing new material in order to ensure batch-to-batch reproducibility. Along with that, it could also enable manufacturers to optimize their raw material selection and processing protocols, to achieve target concentrations of bioactive metabolites. Another important issue is the known geographical (Starzec et al. 2023) and seasonal (Valares Masa et al. 2016; Dimcheva et al. 2019) variation of bioactives, thus further calling attention to the process of quality control.

The presented data, while exploratory in nature, could be of valuable insight for further detailed studies on the distribution of specific metabolites in different *C. creticus* organs. For future research applications, understanding organ-specific metabolite accumulation patterns could enable more targeted investigations into biosynthetic pathways, gene expression profiles, and environmental factors that influence secondary metabolite production in *C. creticus*. A more detailed metabolic map can be assembled, including quantitative data, or data on seasonal variation or stress-induced metabolite accumulation.

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Author contribution TG, PS, RM and KT conceived the research. TG, MA, VI and MW designed the research. MA, VI, MW, TM, DG and TR conducted experiments and/or analyzed data. TG, MA, VI and MW wrote the manuscript. All authors read and approved the manuscript.

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Data availability In addition to the published Supplementary Tables and chromatograms, all data will be made available upon request by users.

Declarations

Competing interest The authors declare no conflict of interest regarding this manuscript.

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