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Research Article

Elemental Profile of *Achillea millefolium* L. from Wild Populations in Albania

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Abstract

Achillea millefolium L. is a medicinal plant widely harvested for traditional and official use across the Balkan region, yet its elemental composition and safety profile remain uncharacterized for Albanian localities. This study evaluated the concentrations of macro elements (N, P, K, Ca, Mg) and microelements (Fe, Zn, Mn, Cd) in the aerial parts of A. millefolium collected from five regions of Albania (Kukësi, Kruja, Përmeti, Korça, and Pogradeci). Plant material was subjected to microwave-assisted acid digestion and elemental concentrations were determined by atomic absorption spectrometry (AAS 800D, Analytic Jena). The dominant macroelement order K > Ca > N > P > Mg was consistent across all five regions. Potassium ranged from 26.78 to 32.17 g/kg dry weight, calcium from 21.19 to 29.70 g/kg, nitrogen from 4.53 to 9.65 g/kg, phosphorus from 5.34 to 9.32 g/kg, and magnesium from 5.40 to 9.89 g/kg. Among microelements, iron ranged from 15.43 to 67.35 mg/kg, zinc from 53.57 to 60.50 mg/kg, and manganese from 25.74 to 92.99 mg/kg. Cadmium concentrations ranged from 0.020 mg/kg in Kukësi to 0.497 mg/kg in Pogradeci. In Kukësi, Kruja and Përmeti, cadmium concentrations were below the WHO maximum permissible limit of 0.3 mg/kg for raw medicinal plant material, while those from Korça and Pogradeci exceeded this limit. These results indicate that geographic origin plays a significant role in the elemental composition and safety profile of wild-harvested *A. millefolium* in Albania.

Keywords: Achillea *millefolium*, Macroelements, Microelements, Cadmium, Medicinal Plants, Elemental Analysis.

1. Introduction

Achillea millefolium L., commonly known as yarrow, is a member of the Asteraceae family. It has been used in traditional medicine by European, Asian, and North American populations [1-5]. Its therapeutic effects have been documented for this species for improving wound closure, alleviating digestive system disturbances such as dyspeptic symptoms and intestinal cramping, managing gynecological conditions including menstrual cycle abnormalities, reducing inflammatory responses, lowering body temperature, and providing gentle sedative effects [3, 6-11]. The plant is prepared through

several methods, including water-based decoctions consumed as therapeutic beverages, alcohol extracts, dermatological preparations for topical administration, and concentrated volatile oil formulations [3, 12-18]. Each preparation method selectively extracts distinct chemical constituents appropriate for targeted therapeutic effects [19-25].

The broad therapeutic effects of *A. millefolium* are attributed to its secondary metabolites. Chemical analyses have identified several classes of active compounds, such as volatile terpenes and hydrocarbons classified as monoterpenes and sesquiterpenes, glycosylated flavonoids such as apigenin, luteolin, and quercetin, and phenolic carboxylic acids represented by caffeoylquinic acid, and proazulene precursors of the blue-pigmented anti-inflammatory agent chamazulene [1]. In animal models, these compounds were shown to suppress inflammatory cascades, relax smooth muscle tissues, stimulate bile secretion, inhibit microbial proliferation, neutralize oxidative stress, protect hepatic tissues, and accelerate wound repair [1]. Most studies have focused on characterizing organic bioactive metabolites; however, the inorganic mineral composition of medicinal plants also has an important role in plant physiology and in their effects on human health after consumption [2].

Mineral nutrients are classified as macronutrients and micronutrients according to their tissue concentration and physiological importance. Macroelements, such as calcium (Ca), magnesium (Mg), potassium (K), nitrogen (N), and phosphorus (P), are present at relatively high levels. Calcium stabilizes cell walls and is a secondary messenger in signal transduction pathways that regulate responses to environmental stimuli and development [44]. Magnesium is an element of chlorophyll and plays a role as a cofactor for numerous enzymes that catalyse reactions in carbohydrate metabolism, nucleic acid synthesis, and protein assembly pathways [7, 14]. Potassium serves as a regulator of osmotic pressure within the plant cytoplasm, activates enzyme systems, controls stomatal aperture dynamics, and facilitates the long-distance transport of photosynthetic products through phloem tissues [15]. Nitrogen is a component of amino acids, proteins, chlorophyll, and nucleic acids, and its availability directly influences both plant growth and secondary metabolite production [26-31]. Phosphorus is fundamental for energy transfer, nucleic acid synthesis, and maintenance of cellular membrane integrity [24, 32].

Microelement nutrients, including iron (Fe), manganese (Mn), and zinc (Zn), are found at lower concentrations in the tissue, but are indispensable for plant growth and development. Iron is essential for photosynthetic and respiratory electron transport and chlorophyll biosynthesis, but its biological availability becomes severely restricted under aerobic alkaline soil conditions due to precipitation as insoluble ferric hydroxide complexes [5, 22]. Manganese plays a critical role in the oxygen-evolving complex of photosystem II and antioxidant defence [28, 33-38]. Zinc is a structural and a catalytic cofactor for numerous enzymes involved in gene expression and hormone metabolism [6]. These elements contribute to both plant physiological performance and the nutritional value of medicinal plant materials.

These essential elements are beneficial for the medicinal plant and for human health, but the potential for accumulation of toxic heavy metals represents a significant safety concern. Metals such as lead (Pb), cadmium (Cd), and mercury (Hg) are toxic even at low concentrations. Lead affects the nervous system causing neurodevelopmental deficits in children, causes cognitive impairment, hypertension and renal dysfunction in adults [34, 39-43]. Toxicological studies have demonstrated that there is no safe threshold for lead exposure, with adverse effects even at levels considered safe previously [23, 33]. Cadmium accumulates primarily in the kidneys and liver, causing renal tubular dysfunction (proteinuria), bone demineralization and is classified as a Group 1 human carcinogen by the International Agency for Research on Cancer [19, 37]. Recent surveys have documented concerning levels of heavy metal contamination in medicinal plant products from various geographical regions [34, 42]. Recognizing these risks, international regulatory bodies have established or updated maximum permissible limits for toxic elements in medicinal plant materials. The World Health Organization (WHO) has published guidelines recommending maximum limits of 10 mg/kg for lead and 0.3 mg/kg for cadmium in medicinal plant materials by [45]. The European Pharmacopoeia has incorporated similar limits and requires testing for heavy metals in herbal drugs.

This study aimed to evaluate the macro elements such as potassium (K), nitrogen (N), calcium (Ca), magnesium (Mg), phosphorus (P), and micro elements iron (Fe), zinc (Zn), manganese (Mn), cadmium (Cd) in Achillea millefolium. The plant was collected from 5 geographical locations across Albania (Kukësi, Kruja, Përmeti, Korca and Pogradeci). The evaluation was carried out using microwave-assisted acid digestion. Elemental analysis was performed using an AAS 800 D atomic absorption spectrometer (Analytik Jena, Germany) at the Scientific Laboratory of Agro-Environment and Ecology, Agricultural University of Tirana. To our knowledge, no data on the elemental composition of *A. millefolium* collected from Albanian localities have been previously reported.

Given the importance of macro- and micronutrients in plant growth, and the widespread use of *Achillea millefolium* in Albania and worldwide, analysis of these elements is needed to understand its contribution to nutritional value. In addition, the assessment of toxic elements is critical to ensure safety in herbal remedies and dietary preparations. Elemental profiling supports quality control, risk assessment, and the safe standardization of *A. millefolium* for pharmaceutical and nutraceutical use.

2. Materials and Methods

2.1 Collection and Preparation of Plant Material

Plant material of *Achillea millefolium* was collected from May to July 2024 during its peak flowering. The botanical identity of the collected material was confirmed by botanist L. Kupe. Samples were collected from five different regions in Albania: Kukësi, Kruja, Përmeti, Korca, and Pogradeci, to capture potential variations under different environmental conditions [21]. The collection sites were: Bicaj village, Kukës (41.9943°N, 20.4128°E, 460 m a.s.l.), a site lying in close proximity to Gjallica mountain,

Qafë Shtamë, Kruja (41.5207°N, 19.8922°E, 1,230 m a.s.l.), Mali i Thatë, Korça (40.8808°N, 20.8405°E, 1,300 m a.s.l.); Bredhi i Hotovës National Park, Permeti (40.3675°N, 20.4280°E, 1,100 m a.s.l.); and Mali i Valamarës, Pogradeci (40.7933°N, 20.4648°E, 1,600 m a.s.l.). The sites represent a range of altitudes and geological settings across Albania, from lowland valleys in the northeast to high-altitude massifs in the southeast. At each site, aerial parts were collected from a minimum of 30 individual plants and pooled to form a representative composite sample for each region. In each region, the aerial parts of the plants were collected randomly from natural populations in the early morning. Upon collection, the plant material was washed with tap water and subsequently rinsed with deionized water to remove surface dust and adhering soil particles. After collection, the samples were placed in paper bags to prevent moisture condensation and sent to the Scientific Laboratory of Agro-Environment and Ecology at the Agricultural University of Tirana. Plant material from each region was processed separately. The samples were spread in single layers and dried in the shade at room temperature (approximately 25°C) until constant weight was achieved. The dried samples were ground into fine powder using a stainless-steel mill to avoid metal contamination. The powdered material was sieved through a 0.5 mm mesh sieve to ensure homogeneity of particle size. The sieved material was stored in airtight containers at room temperature for further analysis.

2.2 Sample Digestion Procedure

For mineral analysis, approximately 0.3 g of each sample was weighed and transferred to Teflon digestion vessels. The samples were treated with 9 ml of nitric acid (HNO_3, 65%) and 1 ml of hydrogen peroxide (H_2O_2, 30%). Microwave-assisted digestion was performed in an ETHOS ONE microwave digestion system. The digestion program was set at a temperature of 180°C for 30 min. After digestion and cooling to room temperature, the digest was filtered and diluted to 100 ml with deionized water. All reagents used were of analytical grade, and procedural blanks were prepared under identical conditions to monitor potential contamination. Elemental concentrations were determined by atomic absorption spectrometry using an AAS 800 D instrument (Analytic Jena, Germany). Each sample was analysed in triplicate and results are expressed as mean ± standard deviation.

3. Results and Discussion

The concentrations of macroelements (N, P, K, Ca, and Mg) in the aerial parts of *Achillea millefolium* collected from five Albanian regions are presented in Table 1 and illustrated in Figure 1. The concentrations of microelements (Fe, Zn, Mn) are presented in Table 3 and illustrated in Figure 2. Cadmium (Cd) concentrations are presented in Table 4 and illustrated in Figure 3. One-way ANOVA revealed statistically significant differences among regions for all elements ($p < 0.001$ for all). The dominant macroelement order across all five regions was K > Ca > N > P > Mg. Among microelements, the order was Fe > Zn > Mn at Kukësi and Kruja, where iron accumulation was highest, while Mn > Zn > Fe was observed at Përmeti, Korça, and Pogradeci, where manganese

concentrations were elevated. The regional distribution of macroelement concentrations is shown comparatively in Figure 1.

Table 1. Concentrations of macroelements (g/kg dry weight) in aerial parts of *Achillea millefolium* collected from five regions in Albania (mean ± SD, n = 3)

Region	N (g/kg) *Mean ± SD*	P (g/kg) *Mean ± SD*	K (g/kg) *Mean ± SD*	Ca (g/kg) *Mean ± SD*	Mg (g/kg) *Mean ± SD*
Kukës	5.503±0.015^{d}	9.317±0.015^{a}	30.940±0.010^{b}	22.340±0.010^{d}	5.397±0.015^{e}
Krujë	6.530±0.010^{c}	8.743±0.006^{b}	32.166±0.006^{a}	24.327±0.006^{c}	5.993±0.001^{b}
Përmet	9.650±0.010^{a}	6.280±0.010^{d}	26.780±0.026^{e}	21.193±0.006^{e}	9.888±0.002^{a}
Korcë	7.670±0.010^{b}	6.750±0.001^{c}	27.390±0.010^{d}	25.297±0.006^{b}	5.611±0.001^{c}
Pogradec	4.526±0.006^{e}	5.337±0.006^{e}	28.797±0.006^{c}	29.697±0.006^{a}	5.493±0.001^{d}

Different superscript letters within the same column indicate statistically significant differences between regions (one-way ANOVA followed by Tukey's HSD post-hoc test, α = 0.05). All elements showed significant regional variation (p < 0.001).

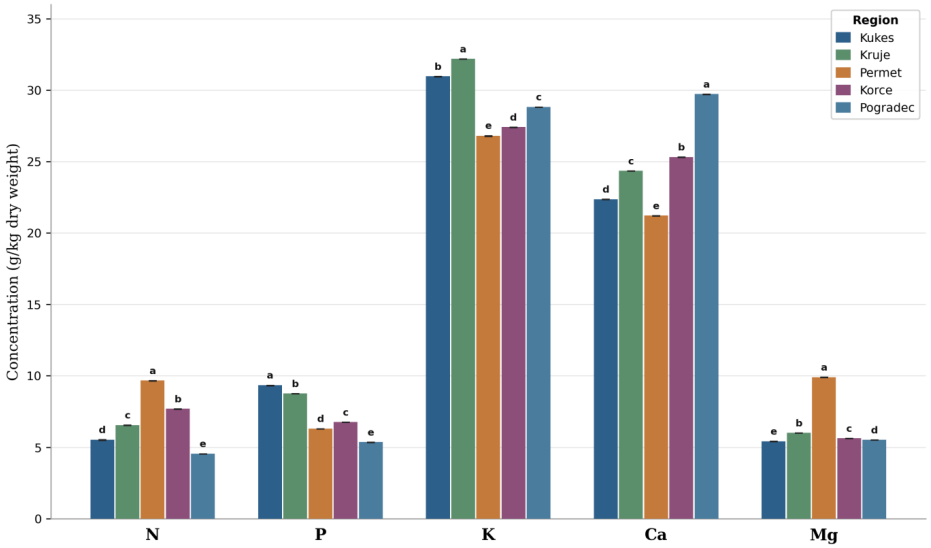


Figure 1. Concentrations of macroelements (g/kg dry weight) in aerial parts of Achillea millefolium collected from five regions in Albania. Values are mean ± SD (n = 3). Different letters above bars indicate statistically significant differences between regions for each element (Tukey's HSD, p < 0.05).

The macroelement order K > Ca > N > P > Mg observed in this study is consistent with that reported for *A. millefolium* from Kosovo (K > Ca > N > Mg > P; [11] and with mineral profiles documented across three *Achillea* species from Iran, where K > Ca dominance was confirmed across 25 accessions regardless of geographic origin [12]. A similar elemental order was also observed in *A. collina* from the flora of Bulgaria [9] confirming that potassium and calcium dominance is a consistent genus-level characteristic of *Achillea.* Compared to the adequate ranges for plant dry matter established by Marschner, 2012, [26] all macroelements except N were at or above the upper end of the adequate range, suggesting active accumulation of these elements in wild *A. millefolium* from Albanian mountain habitats. Nitrogen concentrations, by contrast, were below the typical adequate range across all sites, consistent with collection from

unmanaged, low-fertility habitats [26]. The element-by-element discussion is presented in the following sections.

3.1 Potassium

Potassium was the dominant microelement in all five regions, ranging from 26.78±0.026 g/kg in Përmeti to 32.17±0.006 g/kg in Krujë, with regional differences being statistically significant ($p < 0.001$). These values exceed those reported for *A. millefolium* from Kosovo (23.85 g/kg) and surpass the upper end of the adequate range for plant dry matter (10-25 g/kg). The K > Ca dominance is consistent across *A. collina* from Bulgaria [9] and three *Achillea* species from Iran [12], confirming this as a genus-level characteristic. Potassium plays a central role in enzyme activation, osmotic regulation, stomatal function, and photosynthesis, and has been associated with the biosynthesis of essential oils and secondary metabolites in *A. millefolium* [20; 29]. The consistently high K concentrations across all Albanian sites suggest active potassium accumulation regardless of altitude or geographic location.

3.2 Calcium

Calcium concentrations ranged from 21.19±0.006 g/kg in Përmeti to 29.70±0.006 g/kg in Pogradeci, with regional differences statistically significant. Values were comparable to Kosovo (21.98 g/kg; [11] but considerably higher than the highest Ca reported for *Achillea millefolium* in Moldova (14.2 g/kg, the highest among 15 Asteraceae species studied), and well above the typical range for plant aerial tissues (1-10 g/kg; [26]. The elevated Ca values are consistent with the known capacity of *Achillea* species to accumulate calcium, confirmed across multiple geographies [9, 12]. Calcium acts as an essential secondary messenger in plant stress signalling [43] and activates enzymes involved in the biosynthesis of phenolic compounds, flavonoids, and antioxidant molecules [39]. The elevated calcium concentrations across all Albanian populations may positively contribute to the pharmacological activity of this species. The absence of concurrent soil data precludes a definitive explanation for the regional variation; future work should include soil sampling to establish plant-soil relationships.

3.3 Nitrogen

Nitrogen was highest in Përmeti (9.65±0.010 g/kg) and lowest in Pogradeci (4.53±0.006 g/kg), all regional differences being statistically significant. All values fall below the typical adequate range (15-40 g/kg). The Përmeti value (9.65 g/kg) is comparable to Kosovo (9.95 g/kg; [11] while the lower values at Pogradec and Kukës reflect greater nitrogen limitation at those sites. This is characteristic of wild plants growing in unmanaged, low-fertility habitats, where nitrogen availability is typically limited compared to cultivated sites [26, 41]. Nitrogen limitation is known to redirect carbon flow toward the accumulation of nitrogen-independent secondary metabolites such as phenolics, flavonoids, and terpenoids [40, 41], which are the principal bioactive compounds of *A. millefolium.* The low N concentrations across Albanian populations may therefore be associated with enhanced accumulation of these pharmacologically relevant metabolites.

3.4 Magnesium

Magnesium was highest in Përmeti (9.888±0.002 g/kg) and lowest in Kukësi (5.40±0.015 g/kg), with all regions differing significantly except Kukësi and Pogradeci. All values exceed the typical adequate range (1.5–3.5 g/kg; [26] and are broadly consistent with Kosovo (6.95 g/kg; [11], though Përmeti shows notably higher accumulation. In *A. wilhelmsii* from Iran, Mg concentrations up to 5.9 g/kg were reported [12], within the range of our Albanian values. Magnesium is the central atom of the chlorophyll molecule, indispensable for photosynthesis and carbon fixation, and functions as a cofactor for enzymes involved in carbohydrate metabolism [26]. Enhanced photosynthetic capacity from higher Mg availability increases carbon skeleton availability for phenolic and terpenoid biosynthesis [41].

3.5 Phosphorus

Phosphorus ranged from 5.34±0.006 g/kg in Pogradeci to 9.32±0.015 g/kg in Kukësi, all regional differences statistically significant. Values exceed the typical adequate range (2-5 g/kg [26] and are higher than Kosovo (6.15 g/kg; [11]. High P content was noted in *A. filipendulina* and *A. vermicularis* from Iran [12], suggesting that phosphorus accumulation varies among *Achillea* species and populations. Phosphorus is a fundamental component of ATP, nucleic acids, and phospholipids, essential for energy transfer and metabolic regulation; its availability influences the production of terpenoids and phenolic compounds in medicinal plants [26, 40]. A summary comparison of macroelement concentrations recorded in this study with published data for *Achillea millefolium* and related *Achillea* species, alongside adequate ranges for plant dry matter [26], is presented in Table 2."

Table 2. Comparison of macroelement concentrations (g/kg dry weight) in *Achillea millefolium* from Albanian populations with published data for this species and related *Achillea* taxa, and adequate ranges for plant dry matter

Element (g/kg DW)	This study (Albania) Range	Kosovo [11]	Turkey [36]	Moldova† [18]	Adequate range Marschner 2012
N	4.53–9.65	9.95	10.10	n.r.	15–40
P	5.34–9.32	6.15	6.30	n.r.	2–5
K	26.78–32.17	23.85	24.30	n.r.	10–25
Ca	21.19–29.70	21.98	22.20	14.2*	1–10
Mg	5.40–9.89	6.95	7.00	n.r.	1.5–3.5

n.r. = not reported. ¹ . † Ivanova et al. (2024): range across 15 Asteraceae species including A. millefolium from Moldova; Ca 14.2 g/kg was the highest value, recorded in A. millefolium specifically. Adequate range: typical adequate concentrations in plant aerial dry matter (Marschner, 2012).

3.6 Microelements

The concentrations of microelements (Fe, Zn, Mn) and the toxic element cadmium (Cd) in the aerial parts of *Achillea millefolium* across the five Albanian regions are presented in Table 3. One-way ANOVA confirmed statistically significant differences between regions for all four elements ($p < 0.001$). The regional distribution of microelement concentrations is illustrated in Figure 2.

Table 3. Concentrations of microelements (mg/kg dry weight) in aerial parts of *Achillea millefolium* collected from five regions in Albania (mean ± SD, n = 3).

Region	Fe (mg/kg) *Mean ± SD*	Zn (mg/kg) *Mean ± SD*	Mn (mg/kg) *Mean ± SD*
Kukës	67.350±0.050[a]	60.500±0.010[a]	25.738±0.003[e]
Krujë	65.650±0.050[b]	53.570±0.020[e]	33.647±0.021[d]
Përmet	18.337±0.015[d]	57.920±0.026[c]	70.217±0.006[c]
Korcë	29.300±0.010[c]	56.723±0.012[d]	79.227±0.006[b]
Pogradec	15.433±0.006[e]	58.693±0.012[b]	92.993±0.012[a]

Values are expressed as mean ± SD (n = 3). Statistical differences among regions were evaluated by one-way analysis of variance (ANOVA) followed by Tukey's Honestly Significant Difference (HSD) post-hoc test (α = 0.05). All elements showed statistically significant regional variation (p < 0.001). Different superscript letters within the same column indicate statistically significant differences between regions for that element. Regions sharing the same superscript letter are not significantly different from each other (p > 0.05). The letter 'a' denotes the highest mean concentration.

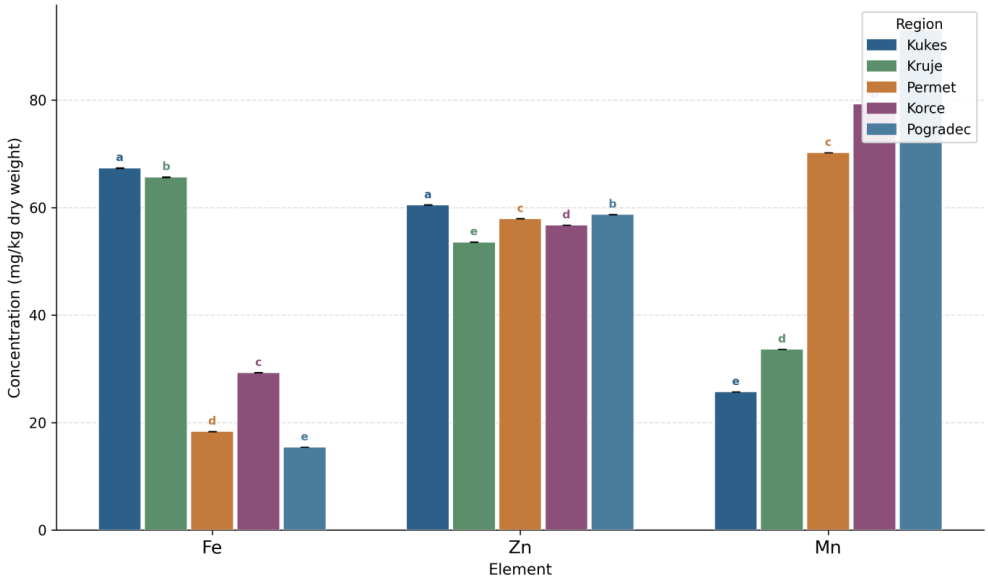


Figure 2. Concentrations of microelements (mg/kg dry weight) in aerial parts of Achillea millefolium collected from five regions in Albania. Values are mean ± SD (n = 3). Different letters above bars indicate statistically significant differences between regions for each element (Tukey's HSD, p < 0.05).

3.7 Iron

Iron concentrations differed significantly among regions ($p < 0.001$), ranging from 15.433±0.006 mg/kg in Pogradeci to 67.350±0.050 mg/kg in Kukësi, with all pairwise regional differences being statistically significant. The range recorded (15.43-67.35 mg/kg) is comparable to Kosovo (59.85 mg/kg; [11] and considerably lower than Turkish populations (360.4 mg/kg [36] the latter likely reflecting proximity to anthropogenic contamination. Very low values from Bosnia (1.81-5.67 mg/kg; [27] reflect leaf-only analysis, whereas the present study analyzed whole aerial parts. In Serbian plantation material, Fe was below EU maximum allowable concentrations [34], consistent with our values from uncontaminated mountain sites. There is no WHO/FAO permissible limit for Fe as it is an essential nutrient. As a dicotyledonous species, *A. millefolium* acquires iron through the demand-driven Strategy I mechanism (FRO2/IRT1 system), which is

downregulated when iron status is sufficient [5, 30], explaining the greater site-specific variation compared to Zn. Based on RDA analysis of *A. millefolium* from Iran, this species can contribute approximately 54% of the adult Fe RDA per serving [16].

3.8 Zinc

Zinc concentrations differed significantly among regions ($p < 0.001$), ranging narrowly from 53.570±0.020 mg/kg in Krujë to 60.500±0.010 mg/kg in Kukësi, with all pairwise regional differences statistically significant despite the narrow numerical range. Albanian values are higher than Kosovo (35.42 mg/kg; [11], Turkey (47.6 mg/kg; [36] and the Asteraceae range in Moldova (27-76 mg/kg; [18]. The Bulgarian study reported higher Zn in urban versus rural sites [13] our remote mountain populations show elevated Zn without anthropogenic influence, confirming high Zn accumulation as an intrinsic characteristic of *A. millefolium*. All Albanian values marginally exceed the FAO/WHO reference value of 50 mg/kg [45] which warrants consideration in quality control assessments, though this does not represent a toxicological concern at typical herbal preparation doses. The low regional variability is consistent with the known tight physiological regulation of zinc homeostasis via the ZIP transporter family [30]. Zinc is an essential cofactor for enzymes involved in gene expression, protein synthesis, and biosynthesis of flavonoids and phenolic compounds that are among the principal bioactive constituents of *A. millefolium* [6, 26].

3.9 Manganese

Manganese showed the greatest regional variation of all measured elements ($p < 0.001$), ranging from 25.738±0.003 mg/kg in Kukësi to 92.993±0.012 mg/kg in Pogradeci a 3.6-fold difference with a clear ascending gradient Kukës < Krujë < Përmet < Korçë < Pogradeci and all pairwise differences statistically significant. Albanian values are considerably higher than Kosovo (31.87 mg/kg [11] and comparable at the highest sites to Turkey (85.5 mg/kg [37] all values fall within the Asteraceae range reported in Moldova (23-150 mg/kg [18]. In *A. collina* from Bulgaria, Mn ranked third in the elemental order after K and Ca [9] consistent with our findings. The wider regional variation of Mn compared to Zn reflects the less strictly regulated Mn uptake in Strategy I plants, which is more sensitive to soil availability and pH [26, 38]. All Albanian values remain well below the WHO maximum permissible limit of 200 mg/kg [45] indicating no safety concern. Manganese is a key component of the oxygen-evolving complex of Photosystem II and participates in antioxidant defense as a cofactor of Mn-superoxide dismutase [28, 38].

3.10 Cadmium-Safety Assessment

Cadmium concentrations ranged from 0.020 mg/kg in Kukësi to 0.497 mg/kg in Pogradeci, with all regional differences statistically significant ($p < 0.001$). The WHO maximum permissible limit for Cd in raw herbal plant material is 0.3 mg/kg (WHO, 2007). Kukësi (0.020 mg/kg), Kruja (0.080 mg/kg), and Përmeti (0.038 mg/kg) were well within this limit. However, Korça (0.443 mg/kg) and Pogradeci (0.497 mg/kg) exceeded the WHO limit by 1.48- and 1.66-fold respectively. For comparison, Kosovo reported

0.035 mg/kg [11]. Bulgarian populations were below the WHO limit in both urban and rural settings [13] with Cd ranging 0.015-0.268 mg/kg across 12 samples of *A. millefolium* [4]. Bosnian populations were below threshold [27] and Serbian plantation material was below EU maximum allowable concentrations [35]. The elevated Cd at Korça and Pogradeci is therefore unusual among European populations and raises an important safety concern.

Table 4. Cadmium (Cd) concentrations (mg/kg dry weight) in aerial parts of *Achillea millefolium* from five regions in Albania (mean ± SD, n = 3), compared to the WHO permissible limit.

Region	Cd (mg/kg) Mean ± SD	WHO limit (mg/kg)
Kukës	0.020±0.001^{e}	0.3
Krujë	0.080±0.001^{c}	0.3
Përmet	0.038±0.003^{d}	0.3
Korcë	0.443±0.012^{b}	0.3
Pogradec	0.497±0.006^{a}	0.3

Values are expressed as mean ± SD (n = 3). All regional differences: $p < 0.001$ (one-way ANOVA, Tukey's HSD, $\alpha = 0.05$). The letter 'a' denotes the highest mean. WHO maximum permissible limit for Cd in raw medicinal plant material: 0.3 mg/kg (WHO, 2007). Rows in red indicate regions exceeding the WHO limit.

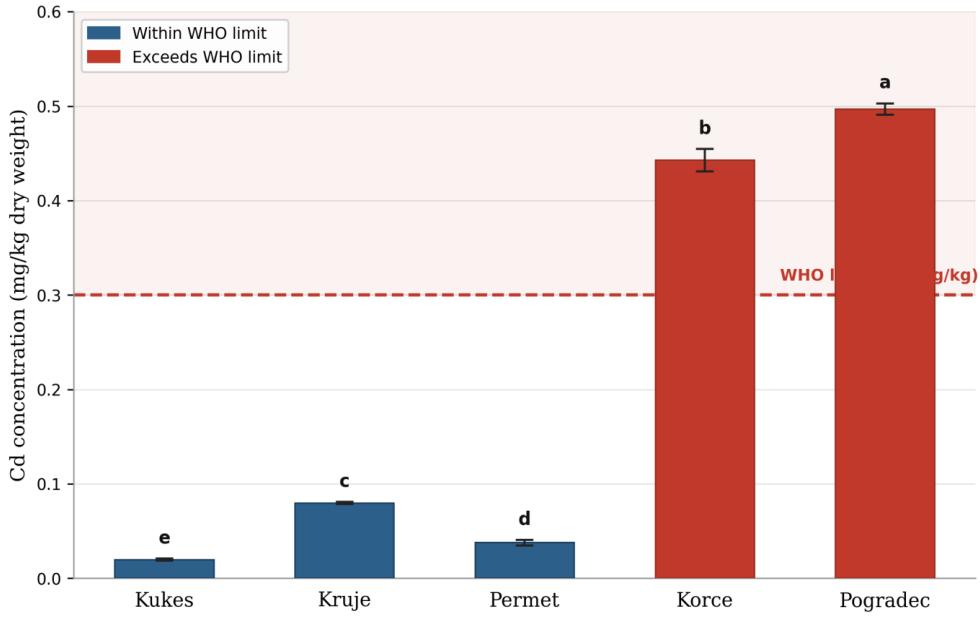


Figure 3. Cadmium (Cd) concentrations (mg/kg dry weight) in aerial parts of Achillea millefolium from five Albanian regions. Values are mean ± SD (n = 3). Different letters indicate significant differences between regions (Tukey's HSD, $p < 0.05$). The red dashed line indicates the WHO maximum permissible limit (0.3 mg/kg; WHO, 2007). Blue bars = within WHO limit; red bars = exceeds WHO limit.

The capacity of *A. millefolium* to accumulate Cd has been demonstrated experimentally: plant Cd reached up to 10 mg/kg when soil Cd supply was 3 mg/kg, characterising this species as a ready cadmium accumulator [8]. Similarly, *Achillea* plants from anthropogenically disturbed habitats in Dagestan exceeded the maximum permissible Cd level by 1.2-1.7 times [39] a magnitude comparable to the exceedances

recorded at Korça and Pogradeci in the present study. Cadmium is a non-essential element; chronic exposure is associated with renal tubular dysfunction, bone demineralisation, and carcinogenicity [19, 37]. Concurrent soil Cd analysis is essential to determine whether the elevated values reflect natural geochemical enrichment or anthropogenic inputs. A summary comparison of microelement and cadmium concentrations with published data for *Achillea millefolium* and related Asteraceae species is presented below.

Table 5. Comparison of microelement and cadmium concentrations with published data for *Achillea millefolium* and related Asteraceae species

Element	This study (Albania)	Kosovo [11]	Turkey [36]	Bulgaria [13]	Bosnia† [27]	WHO/FAO limit
Fe (mg/kg)	15.43–67.35	59.85	360.4	urban>rural	1.81–5.67†	No limit
Zn (mg/kg)	53.57–60.50	35.42	47.6	urban>rural	1.58–4.75†	50 mg/kg
Mn (mg/kg)	25.74–93.00	31.87	85.5	urban>rural	7.90–34.68†	200 mg/kg
Cd (mg/kg)	0.020–0.497	0.035	n.d.	Below WHO	below WHO	0.3 mg/kg

† Leaf samples only. WHO/FAO limits: Cd 0.3, Zn 50, Mn 200 mg/kg (WHO, 2007). No limit for Fe. n.d. = not determined.

3.11 Herbal Safety Assessment

From an herbal safety perspective, the macroelement concentrations recorded in Albanian populations of *A. millefolium* do not raise toxicological concerns. Potassium, calcium, magnesium, and phosphorus were all elevated relative to the adequate range for plant dry matter [26] consistent with active accumulation in wild mountain habitats, and no maximum permissible limits for these elements in medicinal plant materials have been established by WHO or FAO. Nitrogen was below the adequate range at all sites, reflecting the low-fertility conditions of the collection habitats, and does not represent a safety concern. The elevated Ca and Mg concentrations may in fact contribute positively to the nutritional value of herbal preparations derived from this species [16]. Among microelements, manganese and iron were within safety limits at all sites. Zinc marginally exceeded the FAO/WHO reference value of 50 mg/kg at all five sites (53.57-60.50 mg/kg), though this is unlikely to represent a health risk at typical herbal preparation doses. The most significant safety concern is the cadmium concentration at Korça (0.443 mg/kg) and Pogradeci (0.497 mg/kg), which exceeded the WHO maximum permissible limit of 0.3 mg/kg for raw medicinal plant material [45]. *A. millefolium* from these two regions should not be used in herbal preparations without further quality control and source verification. Populations from Kukësi, Kruja and Përmeti satisfied all WHO and FAO/WHO elemental safety criteria for both macro- and microelements and may be considered suitable for herbal use. Monitoring of cadmium levels in medicinal plants from the Korça and Pogradeci areas is recommended, given that chronic cadmium exposure is associated with renal dysfunction and carcinogenicity [19, 37].

3.12 Study Limitations and Future Perspectives

This study provides a multi-site elemental characterisation of *Achillea millefolium* from Albanian wild populations in five regions. Concurrent soil elemental analysis was not

performed; the relationship between local soil chemistry and the observed regional variation remains to be established. Future work should include soil sampling to calculate bioconcentration factors.

4. Summary and Conclusion

This study provides an evaluation of macro- and microelement composition in *Achillea millefolium* collected from five regions of Albania, filling a gap in the elemental characterisation of this species from the central Balkan region. The dominant macroelement order K > Ca > N > P > Mg was consistent across all regions, in agreement with published data for this species from Kosovo, Iran, and Bulgaria, confirming this hierarchy as a genus-level characteristic of Achillea independent of geographic origin. Absolute concentrations of K, Ca, Mg, and P exceeded the adequate ranges for plant dry matter at all sites, suggesting active accumulation of these macroelements in wild Albanian populations. Nitrogen concentrations were consistently below the adequate range at all sites, consistent with growth in unmanaged, low-fertility mountain habitats. Among microelements, zinc showed narrow regional variation (53.57-60.50 mg/kg), reflecting tight physiological regulation, while manganese displayed the greatest variability (25.74-92.99 mg/kg), with a clear ascending gradient from Kukësi to Pogradeci, and iron showed pronounced site-specific differences (15.43-67.35 mg/kg). All microelement concentrations remained below WHO maximum permissible limits for medicinal plants, except for zinc, which marginally exceeded the FAO/WHO reference value of 50 mg/kg at all sites. This exceedance is unlikely to represent a toxicological concern at typical herbal preparation doses. The most significant finding from a public health perspective is the cadmium concentration recorded at Korça (0.443 mg/kg) and Pogradeci (0.497 mg/kg), which exceeded the WHO maximum permissible limit of 0.3 mg/kg by 1.48- and 1.66-fold respectively. This represents a safety concern for herbal preparations derived from these two regions and is unusual relative to other European populations of this species, where Cd is consistently reported below the WHO threshold.

The source of this cadmium accumulation, whether reflecting local geochemical conditions or anthropogenic inputs, could not be determined in the absence of concurrent soil analysis, which represents the primary limitation of this study. The findings demonstrate that elemental composition in wild A. millefolium is highly sensitive to geographic origin and cannot be assumed to be uniform across collection sites. From a quality control perspective, populations from Kukësi, Kruja and Përmeti meet WHO safety criteria and may be considered suitable for use in herbal preparations, while collection from Korça and Pogradeci requires further quality assessment and cadmium monitoring before pharmaceutical or nutraceutical use. Future research should integrate soil elemental analysis, longitudinal monitoring, and phytochemical profiling to establish a mechanistic link between environmental conditions, mineral nutrition, and secondary metabolite production in this species.

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Conflict of Interests

The authors would like to confirm that there is no conflict of interests associated with this publication and there is no financial fund for this work that can affect the research outcomes.

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