Original Article

Elemental Composition of the Medicinal Plants *Hypericum perforatum, Urtica dioica* and *Matricaria chamomilla* Grown in Ukraine: A Comparative Study

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ABSTRACT

Objective: To determine concentrations of essential microelements Fe, Cu, Mn and Zn, as well as toxic metals Pb, Cd, Cr and Co, in three herbal remedies and compare the experimental data obtained with available literature data. **Materials and Methods:** Elemental compositions of three herbal remedies, Chamomile flowers, Urtica folia (nettle) and Hyperichi herba (St John's wort), grown and produced in Ukraine, were studied by flame atomic absorption spectroscopy. **Results:** The Fe concentration decreases, as well as the Zn and Mn concentrations, increase in going from nettle through chamomile to St John's wort. The Cu content is virtually independent of the plant type. Statistically significant negative correlations between the element concentrations were found in Fe-Mn and Fe-Zn pairs. The studied samples of St John's wort are more contaminated with Cd than other plants, while the highest Pb content is observed in some samples of nettle. **Conclusion:** The measured levels of both Pb and Cd still secure against overuse of toxic metals with herbal remedies.

Key words: Medicinal plants, Atomic absorption spectroscopy, Elemental composition, Pb, Cd contamination.

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INTRODUCTION

Last decades the use of medicinal plants for the prevention and treatment of various sicknesses has increased remarkably in line with the global trend of people returning to natural therapies. Herbal medicines are often considered to be less toxic compared to chemical substances and with reduced adverse effects on the human organism.[1] However, it is not entirely correct to consider them a priori safe products.[2,3]

Conventional medicines consist of a limited number of purified compounds. Their safe doses are well-established. Ingress of any organic or elemental impurities is controlled on all stages of the pharmaceutical production. On the contrary, medicinal plants may contain a mixture of chemical compounds and elements. In the quality assessment of medicinal plants, the primary focus lies, generally, on active pharmaceutical ingredients. But herbs always contain a broad spectrum of both metals and metalloids. Their concentrations vary in a wide range depending on various botanical, environmental and agricultural factors.[4,5,6]

Some heavy metals such as Pb, Cd, and Hg are natural constituents of the environment or generated by industrial processes. Medicinal plants, which grow in nature, can accumulate heavy metals. As heavy metals threaten human and animal health, their content in plants used for consumption or medicinal purposes is limited. However, many studies report abnormally high levels of certain toxic elements compared to their safe/tolerable exposures in medicinal plants.[6,7,8] Some other microelements participate in biochemical processes and are known as essential elements.[9] Many essential elements may also be toxic to human health depending on dose.[10] However, their content is not controlled and restricted in herbal medicines.

Summing up, the elemental composition of commercial medicinal herbs may vary in a wide concentration range, including both toxic and essential trace elements. The lack of regulation on the manufacturing of herbal medicines allows potentially harmful quantities of these elements to penetrate the products. Therefore, determining elemental compositions of medicinal plants is crucial. Three herbs widely distributed in Ukraine and many other countries are studied in the given work. They are nettle, chamomile, and St John's wort. The paper goal is to study elemental composition of the plants mentioned above, including the study of possible correlations between element concentrations and comparative analysis of compositional differences between plants.

MATERIALS AND METHODS

The specimens of herbal remedies, Herba Hyperici (commonly known as St John's wort), Flores *Chamomilla* (chamomile) and Folia Urtica (nettle), were bought at local pharmacies in Kiev, Ukraine. Before analysis, the samples were ground in a high-speed rotor mill to obtain a homogeneous sample and stored in polyethylene containers.

All chemicals purchased from commercial sources were of analytical grade. Accurately weighed 2 g-in-weight plant samples were placed into a Teflon reaction crucible and treated with 10 ml of 30% H_2O_2 / concentrated 65% HNO_3 (1:4, v/v). Decomposition of the samples was carried out in a closed-vessel microwave digestion system. The digestion program consisted of three stages and was as follows: 80% power for 15 min, 100% for 5 min and 80% for 20 min. After cooling, the clear digested solutions were transferred quantitatively into clean volumetric flasks and made up to 50 ml with twice distilled water. Blank experiments were carried out in the same way. Three independent digestions were performed for each plant specimen. The digests were used to determine concentrations of Cu, Zn, Fe, Mn, Pb, Cd, Co and Cr by flame atomic absorption spectroscopy (FAAS). A double-beam Solaar S4 AA Spectrometer (Thermo Electron Co., USA) was used, applying standard conditions in air/acetylene flame and D_2 correction. The quantitative determinations were carried out by external calibration with the use of certified reference materials produced by Bogatsky Physics-Chemistry Institute (Odessa, Ukraine). The working range for each element was within a linear range of the method. Calibration intervals were adjusted according to the expected concentrations of elements. Measurement of each sample was repeated three times, and the mean value was calculated.

Both own experimental results and available literature data for individual plants under study were analysed by statistical methods using IBM SPSS 20 software. The results were expressed either as the means ($C_m(exp)$) with standard errors of the mean (SEM) for data with a normal distribution or medians (C_{med}) and quartiles for asymmetric distributions. All data were tested for normal distribution with the Shapiro–Wilks model and variance homogeneity with the Levene's test. Any correlations between microelement contents were examined with the use of Pearson correlation coefficients (rij).

One-way analysis of variance (ANOVA) was used to analyse possible differences among the mean concentrations. The significance level α was set at or below 5% (α ≤ 0.05). If the significant differences were found to exist among the means, then post hoc pairwise multiple comparisons were applied to determine which means differ. Depending on the results of Levene's tests, either the least significant difference or Tamhane's T2 methods were used in post hoc comparisons for equal or unequal variances respectively.

RESULTS

For convenience, eight studied chemical elements were divided into two equal groups. Four elements, Cu, Zn, Mn and Fe, participate in biochemical processes and are known as essential elements in plants.[9] Other elements, Pb, Cd, Co and Cr, were reckoned among toxic metals. Modern pharmacopoeias attribute Cd and Pb to Class 1, Co to Class 2A, and Cr to Class 3.[11]

The mean concentrations $C_m(exp)$ for essential and toxic elements are shown in Figure 1a and Figure 1b respectively. The studied plants are arranged in order of increasing or falling concentration of a element. In going from nettle through chamomile to SJW (Figure 1a), the $C_m(exp)$ value decreases from 90 to 40 µg/g for Fe, and it simultaneously increases from 5 to 27 µg/g for Zn and from 45 to 100 µg/g for Mn. The Cu concentration is rather stable and almost independent of the plant type, fluctuating between 6 and 8 µg/g. Toxic metals are detected in a
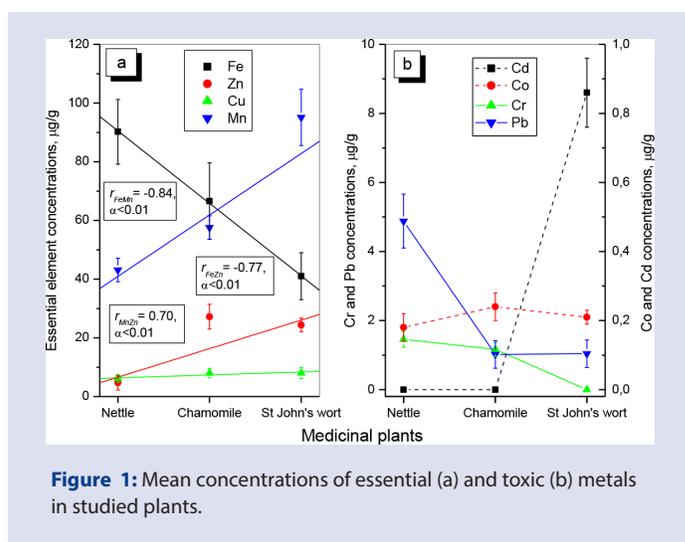
Figure 1: Mean concentrations of essential (a) and toxic (b) metals in studied plants.
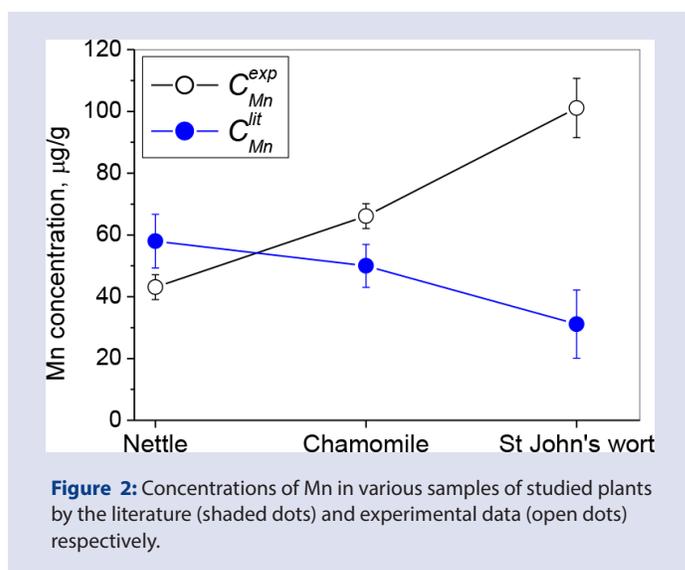
Figure 2: Concentrations of Mn in various samples of studied plants by the literature (shaded dots) and experimental data (open dots) respectively.

limited number of samples (Figure 1b). For example, Cr is observed in nettle and chamomile but is below the detection limit in all SJW samples. Cadmium is detected in samples of SJW only. All studied samples contain Co and Pb.

The results obtained demonstrate the presence of statistically significant pair correlations in elemental concentrations between plants. The significant values of Pearson coefficients rij were found only for three pairs of essential elements labelled in Figure 1a. Iron demonstrates very high anti-correlations with Mn and Zn while Mn also correlates with Zn. No significant correlations were revealed between toxic-toxic or toxic-essential pairs.

The average microelement concentrations in different plants were compared between each other to find significant differences between the compared plants. Running an ANOVA test at first, we have got significant results for Fe, Mn, Zn, Cd, and Cr. For these elements, therefore, at least one of the groups tested differs from the other groups. Then the procedure of post hoc multiple comparisons was applied to know which group differentiates. The results for Fe, Mn, Zn, Cd, Pb and Cr are shown in Table 1. The significant differences in Mn and Fe are detected for all three plant pairs. The Zn concentrations are similar in SJW and chamo-

Table 1: ANOVA post hoc multiple comparisons of elemental concentrations.

Variables	Plant 1	Plant 2	Mean difference	Standard error	α
Fe	SJW	Nettle	-50.446*	8.049	0.000
	SJW	Chamomile	-26.792*	8.049	0.006
	Nettle	Chamomile	23.654*	9.858	0.034
Mn	SJW	Nettle	57.926*	10.289	0.001
	SJW	Chamomile	34.928*	10.498	0.027
	Nettle	Chamomile	-22.997*	2.803	0.010
Zn	SJW	Nettle	20.322*	3.502	0.000
	SJW	Chamomile	-2.198	3.502	0.542
	Nettle	Chamomile	-22.520*	4.289	0.000
Cd	SJW	Nettle	0.859*	0.017	0.001
	SJW	Chamomile	0.859*	0.017	0.001
	Nettle	Chamomile	0	0	.
Pb	SJW	Nettle	-4.483	0.781	0.084
	SJW	Chamomile	-0.300	0.093	0.157
	Nettle	Chamomile	4.183	0.785	0.092
Cr	SJW	Nettle	-1.456	0.229	0.070
	SJW	Chamomile	-1.165*	0.153	0.050
	Nettle	Chamomile	0.291	0.275	0.735

* Differences are significant at the 0.05 level (2-tailed)

mile, but they both are significantly higher than in nettle. No concentration difference is observed between plants with detectable levels of Pb, Cd and Cr.

DISCUSSION

There are known many published works which are devoted to the study of elemental composition of nettle,[12-18] chamomile.[12-24] and SJW.[13,15,16,25-29] For brevity, all above-cited 18 papers are hereinafter referred to as the literature data. Their results were averaged to either $C_m(lit)$ or $C_{med}(lit)$ and compared with $C_m(exp)$.

The $C_m(lit)$ values for Zn and Cu in all plants are similar in magnitude to the $C_m(exp)$ values. The $C_m(exp)$ values for Cu vary from 6 to 8 μg/g (Figure 1a) while the Cu concentrations derived from the literature range from 2 to 25 μg/g with the mean values 7, 9 and 12 μg/g for nettle, chamomile and SJW respectively. Two samples with anomalously high Cu content (83 и 120 μg/g) were reported in.[29] The minimal $C_m(exp)$ of Zn (4.6 μg/g) was measured in nettle while the $C_m(exp)$ values were 27 and 25 μg/g for chamomile and SJW respectively (Figure 1a). The calculated $C_m(lit)$ values are approximately 34, 55 and 46 μg/g for nettle, chamomile and SJW respectively. A spread between individual data is not large except for anomalously high (>100 μg/g) Zn content observed in some samples of chamomile.[13,19] and SJW.[13,15,28]

The mean Fe concentrations derived from the literature are much higher than the experimental averages: $C_m(lit)$ varies between 180 and 300 μg/g while $C_m(exp)$ changes from 40 to 90 μg/g. However, for Fe, both $C_m(lit)$ and $C_m(exp)$ decrease from nettle to St John's wort. A rather high scatter of individual results follows from the literature: in all plants differences between minimal and maximal Fe concentrations are of two orders of magnitude. For example, the minimal and maximal Fe concentrations amount to 14-22 μg/g.[16] and 3456 μg/g.[18] in nettle, 15-16 μg/g.[16] and 3125 μg/g.[21] in chamomile, and 7-9 μg/g.[27] and 1177 μg/g.[18] in SJW respectively. Evidently, the presence of highly contaminated samples elevates $C_m(lit)$ while no abnormal amount of Fe was detected in our experiments.

An apparent discrepancy between experimental and literature data is observed for Mn (Figure 2). The $C_m(lit)$ value for Mn decreases from nettle to SJW while $C_m(exp)$ demonstrates an opposite tendency. The minimal Mn concentrations reported in the literature is practically independent of plant type fluctuating between 7 and 8 μg/g.[16,25] The maximal reported values are 150 μg/g,[21] 200 μg/g.[18] and 240-260 μg/g.[29] for nettle, chamomile and SJW respectively. Despite the presence of samples with higher Mn contents in SJW compared to other plants, the average $C_m(lit)$ (72 μg/g) is lower than the average $C_m(exp)$ value (101 μg/g). In turn, the difference between $C_m(exp)$ and $C_m(lit)$ is rather small for nettle and chamomile. Therefore, the studied samples of SJW seem to be contaminated with Mn above the average level.

The concentration distributions of toxic metals by the literature data are characterised by significant non-zero (positive) skewness and kurtosis and do not obey the normal law. To describe the probability of asymmetric datasets, we used medians $C_{med}(lit)$, quartiles (Q_{25}, Q_{50} and Q_{75}) and concentration minimum $C_{min}(lit)$ and maximum $C_{max}(lit)$ (Table 2).

For all three toxic metals in chamomile (Cd was not detected), the $C_m(exp)$ values (Figure 1b) are rather close to $C_{med}(lit)$ (Table 2) and located within Q_{25} or Q_{50} of the published distributions. In other words, the studied chamomile samples are among half samples with the lowest concentrations. The measured concentrations of Co and Pb in SJW and Co and Cr in nettle demonstrate similar behaviour: the $C_m(exp)$ values (Figure 1b) are lower than $C_{med}(lit)$ (comparable for Cr in nettle) and located within Q_{25} (Q_{50} for Cr in nettle) of the published datasets. Therefore, the measured concentrations of these elements are among the lowest values observed in the literature (Table 2).

The experimental concentrations of Pb in nettle are higher than the median value (1.59 μg/g) of published data: the measured $C_m(exp)$ (4.9 μg/g) is comparable with the highest Pb concentration (4.8 μg/g) detected in nettle.[12]

Since SJW is known as an accumulator of Cd, the highest concentrations of Cd (~20 μg/g) published by[29] are still much larger than the measured $C_m(exp)$ (0.86 μg/g).

Table 2: Descriptive statistics for toxic metals in plants by the literature data in comparison with $C_m(exp)$ ±SEM.

	SJW				Chamomile				Nettle			
Parameter	Cd	Co	Pb	Cr	Cd	Co	Pb	Cr	Cd	Co	Pb	Cr
$C_m(exp)$	0.86	0.21	1.04	0.00	0.00	0.24	1.02	1.17	0.00	0.18	4.88	1.46
SEM	0.10	0.03	0.40			0.04	0.40	0.20		0.04	0.78	0.23
$C_m(lit)$	0.74	0.46	1.97	1.07	0.56	0.39	0.90	2.87	0.10	0.61	2.42	2.67
$C_{med}(lit)$	0.61	0.42	1.60	0.49	0.22	0.24	0.72	1.70	0.10	0.48	1.59	1.20
$C_{min}(lit)$	0.05	0.03	0.01	0.04	0.09	0.01	0.06	0.07	0.06	0.08	0.88	0.66
$C_{max}(lit)$	13.00	2.60	9.00	5.00	1.70	1.40	2.73	11.19	0.14	2.35	4.80	8.71
Skewness	7.15	3.92	2.30	1.47	1.50	2.16	1.53	1.95	1.29	2.38	1.51	2.16
Kurtosis	54.78	20.95	5.73	1.98	1.36	5.10	2.51	4.44		5.95		4.72
Quartile Q_{25}	0.11	0.31	0.62	0.27	0.20	0.15	0.28	0.43	0.08	0.18	1.24	1.00
Quartile Q_{50}	0.61	0.42	1.60	0.49	0.22	0.24	0.72	1.70	0.10	0.48	1.59	1.20
Quartile Q_{75}	0.80	0.51	2.38	1.70	0.75	0.38	1.13	3.50	0.12	0.49	3.20	1.77

Table 3: LOC and ULSC ranges[30-35] in comparison with $C_m(exp)$ and safe daily intakes.

	LOC, mg	ULSC, mg	Range of $C_m(exp)$, mg/kg	Most contaminated plant	Safe intake, g/day
Cu	0,6-10	10-12	5-12	SJW	1000
Fe	8-40	45	26-100	Nettle	440
Mn	0,3-8	11	40-138	Nettle	80
Zn	8-18	40-50	2-34	Chamomile	1500
Co	0.02-0.04	0,6	0.2-0.4	SJW	1500
Cr	0.025-0.035	1	0.9-1.8	Nettle	560
Cd		0.006	0.4-0.89	SJW	22
Pb		0.012	1.0-6.2	Nettle	16

Since Pb and Cd are not involved in the metabolic activity, the presence of these elements can be considered as an indication of the environmental contamination of a plant.

Although an active pharmaceutical ingredient in medicinal plants is mainly associated with organic compounds, microelements can give an additional effect. Many organisations in the world, involved in the study of the influence of various elements on human health, specify recommendations and restrictions on their daily consumption. Two aggregated characteristic exposures, entitled Level of Optimal Consumption (LOC) and Upper Limit of Safe Consumption (ULSC), are constructed on the basis of the universally recognised norms.[30-32,34,35] The LOC, ULSC and measured $C_m(exp)$ are shown in Table 3. The ratios of ULSC to the maximal measured concentrations estimate safe limits of daily intakes of the most contaminated herbs from the viewpoint of possible side effect of the microelements (Table 3). The most severe situation concerns possible abuse of Pb and Cd. For some most contaminated samples, oral daily intake of 22 g SJW or 16 g nettle is equivalent to the ULSC for Cd or Pb respectively. The measured concentrations of Pb and Cd may become restrictive factors for a more intensive safe consumption of the most contaminated samples of nettle and SJW.

CONCLUSION

The concentrations of essential elements Fe, Cu, Mn and Zn and toxic metals Pb, Cd, Co and Cr were studied by FAAS in samples of herbal medicines nettle, chamomile and SJW grown in Ukraine. The Cu content varies between 5.7 and 9.6 μg/g and is weakly dependent on the plant type. The Fe concentration decreases from 90 to 40 μg/g while Zn and Mn increase from 5 to 27 μg/g and 45 to 100 μg/g, respectively, in going from nettle through chamomile to SJW. Statistically significant negative

correlations in Fe-Mn and Fe-Zn pairs, as well as a positive Zn-Mn relationship, follow from the results obtained.

The Cr concentrations are below the detection limits in all studied samples. Cobalt was detected in all plants, and its levels (0.2-0.25 μg/g) are comparable with those published in the literature. Lead is detected in all plants; its highest-level amounts to 4.9 μg/g in nettle and is an order of magnitude lower in other plants. Cadmium (~0.85 μg/g) is detected in some samples of SJW while this element is below the detection limit in other plants. The measured levels of both Pb and Cd still secure against overuse of toxic metals with herbal remedies. However, the limits of tolerable daily intakes are not so far from the doses which can be accumulated during very intensive consumption of the considered remedies.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS USED

SJW: St John's wort; **ANOVA:** one-way analysis of variance; F**AAS:** flame atomic absorption spectroscopy; **LOC:** level of optimal consumption; **ULSC:** upper limit of safe consumption.

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GRAPHICAL ABSTRACT
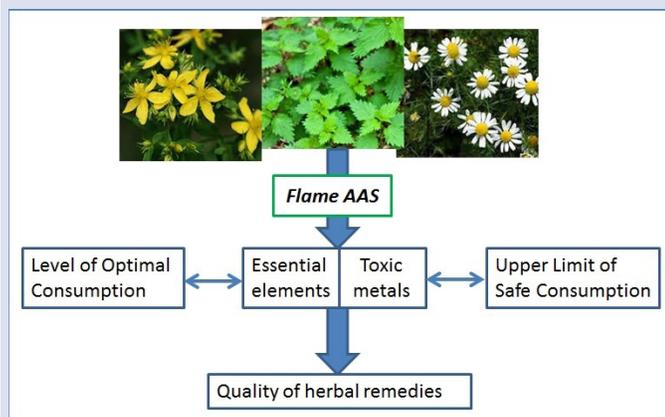
SUMMARY

- Statistically significant correlations were found between element concentrations. They are negative for Fe-Mn and Fe-Zn pairs and positive for Zn-Mn.
- The studied samples of St John's wort are more contaminated with Cd (up to 0.85 μg/g) than other plants, while the highest Pb content (4.9 μg/g) is observed in some samples of nettle
- The measured levels of both Pb and Cd secure against overuse of toxic metals with herbal remedies.

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