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Evaluation of macro and microminerals in crude drugs and infusions of five herbs widely used as sedatives

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Abstract: It has been determined the concentration of fourteen micro and macrominerals (Al, Ca, Co, Cr, Cu, Fe, K, Li, Mg, Mn, Na, P, Se, and Zn) in both crude drugs and infusions of *Melissa officinalis* L., Lamiaceae, *Nepeta cataria* L., Lamiaceae, *Passiflora caerulea* L., Passifloraceae, *Tilia x moltkei* Späth ex C.K. Schneid., Tiliaceae, and *Valeriana officinalis* L., Caprifoliaceae. These herbs are widely consumed by its sedative properties, either alone or in herb mixtures. All measurements were performed using an inductively coupled plasma optical emission spectrometer (ICP-OES). The products were obtained from regional markets, mainly in San Luis province (Argentina). The estimated daily intake was compared with current recommendations. All products and its infusions were included within the upper tolerable limits for minerals, in trace elements such as toxic elements present at low levels.

Introduction

In recent years the nervous (mainly stress and anxiety) and sleep disorders increased considerably, becoming prevalent diseases affecting a high percentage of the population (Pollak et al., 2009). Often these conditions are treated with long-term use of benzodiazepine analogues, although these drugs show limited benefits with obvious side-effects, such as impaired cognitive function, memory and general daytime performance. In addition, long-term administration can results in tolerance and dependence.

Herbal drugs have been gradually accepted as remedies all around the world because of their safety and efficacy (Roth & Drake, 2004), and many herbal sedative products widely available can perform the same therapeutic action with fewer side effects, dependence or tolerance than synthetic pharmaceuticals (Cass, 2004). Some herbal remedies have become increasingly popular treatments for stress, anxiety, dementia, and forgetfulness (Carlini, 2003; Kinrys et al., 2009), used mostly in the form of herbal infusion.

Although many of these herbs or supplements appear to be safe, World Health Organization (WHO) has stressed the need to set up quality standards for medicinal drugs of plant origin, given the marked increase in consumption that has taken place in recent decades (Yeh et al., 2002), the large number of species involved, and the potential side effects or interact both with standard pharmaceuticals and other supplements (Carrasco et al., 2009; Ernst, 2002; Murphy et al., 2005; WHO, 2004). The consumers are not informed about the possible toxicity of these products, and toxicity itself depends on the level of product contamination, as well as on the route of administration, quantity, frequency and duration of intake. Considering the complexity of these drugs and their inherent biological variation, it is necessary to evaluate their quality, safety and efficacy (WHO, 2007). Of course, this is applicable to natural medicines used in treating central nervous system disorders (Coleta et al., 2001; Kinrys et al., 2009).

Mineral elements can cause a therapeutic effect by themselves, or contribute to the daily intake, since some 25 elements have been identified as essential for keeping human health. Therefore, the essential and trace elements in food and medicinal plants have been studied by several research groups worldwide (*i.e.* Chizzola et al., 2008; Del Vitto et al., 2009; Kara, 2009; Martins et al., 2009; Nookabkaew et al., 2006). Moreover, determining the level of minerals can contribute both to an effective quality control and traceability of herbal medicines, and even to establish the safety of its use in terms of levels of toxic elements.

The objective of this study was to evaluate and describe the mineral contents (Al, Ca, Co, Cr, Cu, Fe, K, Li, Mg, Mn, Na, P, Se and Zn) in crude drugs and infusion obtained by ICP-OES from five medicinal herbs characterized by their mild sedative effects: *Melissa officinalis* L., Lamiaceae, *Nepeta cataria* L., Lamiaceae, *Passiflora caerulea* L., Passifloraceae, *Tilia x moltkei* Späth ex C.K. Schneid., Tiliaceae, and *Valeriana officinalis* L., Caprifoliaceae. The results were compared to weighted values found in plants as well as previously settled limits for herbal medicines and derived products.

Materials and Methods

Plant material

Ten samples of each plant species were harvested in the field or acquired in regional markets, as suitable, in the summer 2006-2007. Plant specimens were authenticated by vouchers preserved at Herbarium, Universidad Nacional de San Luis (acronym: UNSL) and identified by the botanists co-authors of this study, as follows: *Melissa officinalis* L., Lamiaceae (Argentina, San Luis city herbal market, UNSL-H #830); *Nepeta cataria* L., Lamiaceae (Argentina, San Luis province, Pringles dept., Río Grande, March 23, 2007, L.A. Del Vitto & E.M. Petenatti #9432, UNSL); *Passiflora caerulea* L., Passifloraceae (Argentina, San Luis province, La Capital dept., vicinity of Juana Koslay city, March 21, 2007, L.A. Del Vitto & E.M. Petenatti #9431, UNSL); *Tilia x moltkei* Späth ex C.K. Schneid., Tiliaceae (Argentina, San Luis city herbal market, UNSL-H #832); and *Valeriana officinalis* L., Caprifoliaceae (Argentina, San Luis city herbal market, UNSL-H #831).

Assays

Sample preparation and extraction

Botanical drugs were dried in an oven at 75 °C during 24 h until constant weight. Afterwards the material was ground using a Wiley 3379 series grinder and passed through a sieve (0.50 mm diameter). The powder (2.0 g) was transferred to a porcelain crucible and 5 mL of indium solution (500 mg L^{-1}) was added as internal standard to evaluate the degree of recovery. One gram of each of the samples was dry-ashed in a crucible in furnace at 550 °C for about 7 h. The ash was dissolved in 10.0 mL of HCl in a conical flask. The solution was filtered into a 100 mL standard flask and made up to the mark with distilled water, to determine micro and macroelements.

Infusions were made according to the Argentinian Pharmacopoeia (FNA, 1978), *i.e.* to 5 g of raw drug were added 100 mL of deionized water at 90 °C, and then allowed to stand for 20 min. The obtained infusions were filtered and evaporated to dryness. The residue was ashed in a muffle furnace for a minimum of 4 h at 480 °C and handled as above for the dry material. All chemicals used were of analytical grade.

Analytical procedure

Fourteen elements were determined in each sample by direct nebulization using an ICP-OES instrument (Varian Vista Pro, Melbourne, Australia). Working conditions for ICP-OES instrument were: forward power 1.4 kW, coolant gas flow rate 15 L min^{-1}, auxiliary gas flow rate 1.5 L min^{-1}; nebulizer gas flow rate 0.68 L min^{-1}; the viewing height was 8 mm above the load coil. This instrument is equipped with a Czerny-Turner monochromator, holographic diffraction grid and a VistaChip charge coupled device (CCD) array detector. The analytical quality was checked through analysis of a plant reference material (V-10 hay powder; International Atomic Energy Agency, Vienna, Austria).

Statistical analysis

A standard statistical procedure was adopted to obtain the final values of the elemental concentrations: for each sample, four independent measurements were carried out. Statistical analysis was performed using R software version 2.8.1 (R Development Core Team, 2008).

Results and Discussion

Mineral contents of raw samples

The overall compositions of five different herbal sedative species were evaluated through the ICP-OES technique. Elements such as Al, Ca, Co, Cr, Cu, Fe, K, Li, Mg, Mn, Na, P, Se and Zn were simultaneously determined in samples of raw drugs and infusions.

The composition in macrominerals of the five medicinal herbs under study is detailed in Table 1.

Similar mineral abundance profiles were observed among samples under study. Series of K, Ca and Mg appeared in decreasing order of concentration in all samples, except the concentration of Ca in *Passiflora caerulea* and *Tilia x moltkei*, where this element was the richest relatively. The highest value of Ca was established in *Passiflora caerulea* (19.8 mg g^{-1}), while *Melissa officinalis* was richest in Mg and K (4.03 and 16.90 mg g^{-1}, respectively). *M. officinalis* and *Valeriana officinalis* showed the highest contents of Fe (0.90 and 0.97 mg g^{-1} respectively). Al, Na, and P, were present at levels under 5 mg g^{-1}.

The compositions in microminerals founded in crude drug are listed in Table 2.

To summarize, microminerals were present in the same sequence in all species, with significant quantities of Mn (104.3 to 55 µg g^{-1}), Zn (39.4 to 23.2 µg g^{-1}), Cu (13.5 to 4.8 µg g^{-1}), Li (15.4 to 4.4 µg g^{-1}), and minor contents (under 10 µg g^{-1}) of Cr (4.9 to 1.8 µg g^{-1}), Co (0.5 to 0.2 µg g^{-1}), and Se (0.5 to 0.3 µg g^{-1}). *Passiflora caerulea* showed the highest values of Mn (followed by *Valeriana officinalis* with a close ratio), but the lower rates of Cu. The highest contents of Zn, Cr, and Co were found in *V. officinalis*, while *Melissa officinalis* had the highest values of Cu and Li; the last element reached more than twice the values of the other species. Finally, similar concentrations of Se were observed in the plants under study.

Mineral contents of the infusions

The concentration of macromineral elements determined in infusions is shown in Table 3.

Generally, there were large differences in the major nutrient input to the infusion by the five species; the differences ranging from close levels to more than 20 times higher. High contributions of K, Mg, and Na were observed on the infusions obtained from *Melissa officinalis* (852.3, 80.0, and 16.2 mg L^{-1}, respectively), as expected according their highest concentrations on raw materials; but it is striking the highest transference of Ca in this species (572.1 mg L^{-1}), because *Passiflora caerulea* had greater content of Ca in raw drug (19.8 mg g^{-1}, Table 1). On the other hand, *Valeriana officinalis* release important levels of Al (1.9 mg L^{-1}), Fe (2.5 mg L^{-1}), and P (111.4 mg L^{-1}) as we expect according to highest concentrations on raw materials.

Seven microminerals were determined on infusions (Table 4). No significant variations were found for Se, while Zn ranged from 5.3 to 0.4 mg L^{-1}.

In infusions of *Melissa officinalis*, highest

Table 1. Concentrations of macroelements in raw material (dry weight basis, mean and %RSD).

Plant species	Parameters	Al	Ca	Fe	K	Mg	Na	P
Melissa officinalis	Mean [mg g^{-1}]	0.92	14.8	0.90	16.90	4.05	0.49	2.76
	RSD [%]	10.5	7.4	6.5	1.7	4.3	1.5	2.2
Nepeta cataria	Mean [mg g^{-1}]	0.45	10.2	0.47	11.85	2.10	0.12	2.12
	RSD [%]	10.0	7.3	4.7	0.9	0.11	1.0	1.7
Passiflora caerulea	Mean [mg g^{-1}]	0.64	19.8	0.65	16.10	2.00	0.42	2.60
	RSD [%]	6.0	2.2	5.6	1.2	3.1	8.0	2.0
Tilia x moltkei	Mean [mg g^{-1}]	0.31	13.9	0.22	9.95	2.30	0.12	2.30
	RSD [%]	10.0	2.9	2.8	1.1	11.2	1.0	1.6
Valeriana officinalis	Mean [mg g^{-1}]	1.00	3.2	0.98	8.25	1.32	0.19	3.06
	RSD [%]	7.0	1.1	8.0	3.1	3.2	2.6	2.7
Ponderate values in plants[a]	[mg g^{-1}]	0.5-2.0	2.0-35.0	0.025-0.3	5.0-60.0	1.0-8.0	trace	1.0-8.0

[a]Duke et al., 2002.

Table 2. Concentrations of microelements in raw material (dry weight basis, mean and %RSD).

Plant species	Parameters	Co	Cr	Cu	Li	Mn	Se	Zn
Melissa officinalis	Mean [mg g^{-1}]	0.45	1.96	13.50	15.40	63.50	0.49	30.00
	RSD [%]	0.9	5.4	11.8	2.5	5.17	2.7	3.5
Nepeta cataria	Mean [mg g^{-1}]	0.35	2.40	10.22	6.37	59.60	0.32	36.10
	RSD [%]	0.7	3.4	10.2	8.9	2.36	11.0	5.7
Passiflora caerulea	Mean [mg g^{-1}]	0.35	1.82	4.80	5.50	104.27	0.50	33.35
	RSD [%]	0.9	6.1	6.4	1.9	5.75	4.1	4.3
Tilia x moltkei	Mean [mg g^{-1}]	0.25	2.05	10.23	4.52	54.90	0.48	23.20
	RSD [%]	1.7	8.3	8.0	8.1	4.95	6.0	4.3
Valeriana officinalis	Mean [mg g^{-1}]	0.50	4.87	5.80	4.40	91.30	0.31	39.40
	RSD [%]	0.4	9.9	3.1	10.2	10.41	6.1	6.8
Ponderate values in plants	[mg g^{-1}]	0.02-1[a]	0.1-0.5[a]	4-30[b]	3-5[a]	15-800[b]	0.01-2[a]	15-800[b]

[a]Kabata-Pendias & Mukherjee, 2007; [b]Duke et al., 2002.

concentration of Cu (0.25 mg L^{-1}) and Li (0.30 mg L^{-1}) was transferred, in correlation with the high content in raw drug. Turn, *Passiflora caerulea* gave the highest levels of Mn (2.35 mg L^{-1}), while *Tilia x moltkei* provided highest concentration of Zn (5.3 mg L^{-1}). To infusions of *Passiflora caerulea* and *Valeriana officinalis* was transferred the highest level of Co (0.06 mg L^{-1}).

As seen, the transport rate of different chemical species to infusion has varied greatly, not only among the minerals, but taking account different plant species. Average extraction rate varied from about 99% (K) to 0.51% (Fe). The extractabilities for P, Na, Mg and Ca were ranged from 31% to 47%, while Zn, Co and Se varied from 10% to 16%. Finally, extractabilities of Cu, Li, Mn, Cr, and Al were from 1.8% to 3%. Summarizing, higher variations were observed in the macro and micromineral inputs to the infusion especially for Zinc, such as in *Melissa officinalis* (2.7%) compared with *Tilia x moltkei* (46.0%).

Contribution to the dietary intake

A typical treatment with any of these drugs, as herbal infusion, consists in the daily intake of three to four teacups, which can vary from 150 to 250 mL each one. Thus arises the following table about the average daily intakes (ADI) of minerals, based on the concentration of elements transferred by the crude drug to the infusion, that were compared to the recommended daily allowance (RDA) settled by international health authorities (Table 5).

Among the infusions of the studied species, *Melissa officinalis* has supplied the highest percentages of RDA in Ca, K, Mg, Na, Cu, and Li; *Valeriana officinalis* has provided the highest levels of Al, Fe, P, and Cr (the last in the same proportion as *Nepeta cataria*); *Passiflora caerulea* showed the highest contributions of Mn and Se, while *Tilia x moltkei* provided the highest giving of Zn (note: the RDA for Co is not known).

It is remarkable that the minimum rates of contribution to RDA apply to *Tilia x moltkei*, mainly for Al, Fe, K, Mg, P, Cr, Mn, and Se; this same condition was seen in *Passiflora caerulea* for Cu and Li, in *Melissa officinalis* for Zn, in *Valeriana officinalis* for Ca, and finally, in *Nepeta cataria* for Na.

Table 3. Concentrations of macroelements released to infusions (mean and %RSD).

Plant species	Parameters	Al	Ca	Fe	K	Mg	Na	P
Melissa officinalis	Mean [mg g^{-1}]	0.31	572.14	0.23	852.32	80.05	16.23	70.15
	RSD [%]	0.01	86.44	0.05	37.76	10.20	1.78	6.83
Nepeta cataria	Mean [mg g^{-1}]	0.34	114.66	0.27	509.41	39.70	1.40	35.30
	RSD [%]	0.03	8.97	0.03	23.70	3.89	0.01	0.66
Passiflora caerulea	Mean [mg g^{-1}]	0.43	311.43	0.30	741.14	54.60	10.50	68.90
	RSD [%]	0.01	26.15	0.04	24.79	3.43	1.44	3.56
Tilia x moltkei	Mean [mg g^{-1}]	0.25	57.62	0.16	225.30	19.78	1.95	31.58
	RSD [%]	0.06	5.52	0.01	8.32	0.98	0.05	1.37
Valeriana officinalis	Mean [mg g^{-1}]	1.90	25.82	2.50	422.60	24.83	3.85	111.42
	RSD [%]	0.05	3.62	0.15	6.91	3.19	0.48	7.88

Table 4. Concentrations of microminerals released to infusions (mean and %RSD).

Plant species	Parameters	Mn	Co	Cr	Cu	Li	Se	Zn
Melissa officinalis	Mean [mg g^{-1}]	0.45	0.01	0.02	0.25	0.30	0.02	0.40
	RSD [%]	0.06	0.00	0.01	0.05	0.11	0.01	0.09
Nepeta cataria	Mean [mg g^{-1}]	0.60	0.01	0.03	0.17	0.05	0.02	1.62
	RSD [%]	0.03	0.00	0.02	0.04	0.01	0.01	0.32
Passiflora caerulea	Mean [mg g^{-1}]	2.35	0.06	0.03	0.06	0.03	0.02	3.40
	RSD [%]	0.18	0.09	0.02	0.01	0.05	0.01	0.93
Tilia x moltkei	Mean [mg g^{-1}]	0.32	0.01	0.01	0.07	0.06	0.02	5.30
	RSD [%]	0.04	0.00	0.00	0.02	0.01	0.01	0.30
Valeriana officinalis	Mean [mg g^{-1}]	1.24	0.06	0.03	0.14	0.07	0.02	0.80
	RSD [%]	0.04	0.05	0.02	0.05	0.02	0.01	0.31

Table 5. Contribution of mineral elements from herbal infusions to average daily intake of minerals and comparison with recommended values of allowance.

Element	*Melissa officinalis*		*Nepeta cataria*		*Passiflora caerulea*		*Tilia x moltkei*		*Valeriana officinalis*		RDA mg day^{-1}
	ADI [mg day^{-1}]	CDI [%]	ADI [mg day^{-1}]	CDI [%]	ADI [mg day^{-1}]	CDI [%]	ADI [mg day^{-1}]	CDI [%]	ADI [mg day^{-1}]	CDI [%]	
Al	0.14	1.66	0.15	1.78	0.19	2.28	0.11	1.31	0.85	10.05	2-10
Ca	257.47	25.75	51.60	5.16	140.15	14.01	25.93	2.59	11.62	1.16	1,000-1,200
Fe	0.10	0.70	0.12	0.81	0.14	0.90	0.07	0.47	1.12	7.48	8-18
K	383.54	8.16	274.23	5.83	333.51	7.10	101.38	2.16	190.04	4.04	4,700
Mg	36.02	11.26	17.87	5.58	24.57	7.68	8.90	2.78	11.17	3.49	310-320
Na	7.31	0.49	0.64	0.04	4.73	0.32	0.88	0.06	1.73	0.12	1,500
P	31.56	3.16	15.88	1.59	31.01	3.10	14.21	1.40	50.11	5.01	700
Co	0.005	nc	0.005	nc	0.026	nc	0.005	nc	0.025	nc	unk
Cr	0.007	27.00	0.014	54.00	0.012	46.80	0.006	22.50	0.014	54.00	0.025
Cu	0.113	1.13	0.077	0.77	0.029	0.29	0.031	0.31	0.065	0.65	0.9
Li	0.137	27.30	0.024	4.73	0.014	2.80	0.025	4.95	0.030	6.00	0.2-0.6
Mn	0.203	10.14	0.269	13.46	1.058	52.90	0.143	7.13	0.556	27.79	1.8-2.3
Se	0.008	15.75	0.008	15.75	0.009	18.00	0.007	14.40	0.008	15.75	0.055
Zn	0.180	1.80	0.726	7.26	1.590	15.90	2.400	24.00	0.359	3.59	8-11

ADI: Average daily intake. CDI: Contribution to daily intake. RDA: Recommended Dietary Allowance; nd: non determined yet; nc: non calculated; unk: unknown.

Discussion

As a whole, the mineral profile obtained for the five medicinal herbs studied is comparable to the levels that usually found in different anatomical parts of plants (Duke et al., 2002). Samples of crude drug of *Melissa officinalis, Nepeta cataria, Passiflora caerulea, Tilia x moltkei* and *Valeriana officinalis* were rich in essential macrominerals, especially K, Ca, Mg, and P (mostly in that descending order), with low contents of Fe and Na. Mineral content on *Melissa officinalis* and *Tilia x moltkei* is agree with those obtained by other authors in similar studies (Başgel & Erdemoğlu, 2006; Özcan et al., 2008; Raczuk et al., 2008). In addition, microminerals were present in relative large quantities in Mn, Zn, and Cu, and to a lesser extent for Li, and even lower values for Cr, Se, and Co, always in that sequence in all studied species. These values varied widely depending on the different plant species.

According to the Dietary Recommended Intakes (DRI) for minerals settled by reference health authorities (Food & Nutrition Board, 2009), their content in the infusions set in this study were much lower than the limits. Although none of the infusions is in itself a complete source of minerals, highlight the contribution of Ca, Mg, K, Li (from *Melissa officinalis* tea), Zn (from *Tilia x moltkei*) and Se (from *Passiflora caerulea*), in contrast with the other studied herbs. Taking in mind that Ca, Mg, K, Zn and Se are actively involved in the synthesis of neurotransmitters and receptors as well as in the transmission of nerve impulses (Black, 2003; Tepper, 2006), and lithium salts are useful in the treatment of some nervous illness, the intake of infusions of the studied herbs (containing these minerals in an interesting level) may contribute in an indirect way to the therapeutic effects (mainly psycholeptic, Carlini, 2003) of these drugs.

Besides the case of possible punctual contamination with toxic elements, especial attention should be considered, when these herbs are used in phytomedicine. Despite of low levels of some minerals in these products, even trace amounts of metals may control, trigger or stop the biochemical reactions in the living organisms and modulate pharmacological activity of these herbs. This study could be contribute to the future investigations on the interactions between macro and microminerals in these herbs and the rest of its biologically active components. Therefore, it is necessary to reach a wide knowledge about mineral content in these herbs, contributing to design a best quality control of plant materials.

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