

Current Findings on the Heavy Metal Content in Herbal Drugs

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ABSTRACT

In this contribution, an overview on the current legal requirements regarding limits for heavy metals in plant material is given, drawing particular attention to the limits for lead, cadmium and mercury in herbal drugs proposed for the European Pharmacopoeia (Ph. Eur.). A new set of data resulting from about 7100 samples of herbal drugs (fresh and dried) tested for lead and cadmium and about 2500 samples tested for mercury between 2002 and 2007 is presented. Based on this evaluation the proposed limits for the Ph. Eur. can in principle be regarded as acceptable provided that exemptions are included for several herbal drugs, e.g. those accumulating cadmium. Such exemptions might be included either in the general monograph Herbal drugs or in individual Ph. Eur. monographs. For these herbal drugs, respective limits are proposed based on recent experiences from daily practice.

KEYWORDS

Heavy metals, lead, cadmium, mercury, herbal drugs.

1. INTRODUCTION

Heavy metals such as lead (Pb), cadmium (Cd) and mercury (Hg) are natural constituents of the environment like air, water and soil. Furthermore, they are produced by technical and industrial processes and thus have gained importance as contaminants. Medicinal plants growing in nature can accumulate heavy metals to a certain extent depending on their individual properties and the concentration of heavy metals in soil, air and water [1-13]. An overview on the soil contamination e.g. with heavy metals has been published by a working group of German authorities [14].

As heavy metals pose a hazard to human and animal health, their content in plants used for consumption or medicinal purposes must be limited. For this reason limits for heavy metals have been set for foodstuffs and medicinal products by health authorities.

In addition to previous reports [3,15] a new set of data originating from quality control analysis of manufacturers of herbal products is now presented. Acceptable limits are proposed for some species showing a tendency to accumulate certain heavy metals.

1.1. Regulatory framework

In 1991, the German Ministry of Health published a 'draft recommendation for limits of heavy metals in medicinal products of plant and animal origin' [16], which included the following limits for plants, parts of plants, oils, fats and waxes of plant origin and products thereof as well as for other products of plant origin, each with reference to the dried matter: lead 5 mg/kg, cadmium 0.2 mg/kg, mercury 0.1 mg/kg, with some exemptions for cadmium of 0.3 mg/kg for linseed, hawthorn and yarrow and of 0.5 mg/kg for birch leaf, St. John's wort, willow bark and mate. This draft recommendation has never been finally adopted but, nonetheless, the current practice of the health authority is still to use it in the assessment of the quality of herbal medicinal products. As no binding limits for heavy metals currently exist, the German Federal Institute for Drugs and Medical Devices (BfArM) accepts tabular listing of the results that have been found.

The European Pharmacopoeia (Ph. Eur.) describes a method for determination of heavy metals in herbal drugs and fatty oils [17]. This method covers lead, cadmium and mercury as well as arsenic, copper, iron, nickel and zinc. Limits for heavy metals in herbal drugs do not exist except in the individual monograph *Kelp* for arsenic (90 mg/kg), lead (5 mg/kg), cadmium (4 mg/kg) and mercury (0.1 mg/kg) [18].

Maximum values for heavy metals in herbal drugs and extracts have been discussed by several authors. For medicinal plants used for infusions, limits of 10.0 mg/kg Pb and 0.5 mg/kg Cd calculated on dry weight were proposed by Schilcher and Peters in 1990 [19]. The World Health Organisation (WHO) recommends limits for various medicinal plants of not more than 10 mg/kg Pb and 0.3 mg/kg Cd in the final dosage form of the plant material [20]. For the Ph. Eur. monograph *Herbal drugs* [21], the following limits were drafted: lead 5 mg/kg, cadmium 0.5 mg/kg, mercury 0.1 mg/kg, "unless otherwise stated in an individual monograph or unless otherwise justified and authorised". Furthermore, the draft proposes the definition of suitable limits for the contents of arsenic, copper, iron, nickel and zinc if required by the relevant authority or by the nature or origin of the herbal drug. According to the proposed revision of the monograph *Extracts* [22], herbal drugs used for the preparation of extracts may exceed the limits set for heavy metals, provided the finished extract complies with the above-mentioned requirements for herbal drugs.

In 2007, the European Commission started to discuss the need for setting maximum levels for lead, cadmium and mercury in food supplements in order to amend Commission Regulation (EC) No. 1881/2006 [23], taking into account that high levels of these metals were found in some food supplements during monitoring activities. After discussion with interested parties and evaluation of data gained from practical experiences, the following limits have been set and will become effective on 1 July 2009: lead 3.0 mg/kg, cadmium 1.0 mg/kg, mercury 0.10 mg/kg (for seaweed products, a limit of 3.0 mg/kg is set for cadmium) [24].

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Table 1. – Limits for lead, cadmium and mercury set or proposed in different regulatory frameworks and scientific contributions

Reference (year)	Lead (mg/kg)	Cadmium (mg/kg)	Mercury (mg/kg)	Comments
Schilcher and Peters (1990) [19]	10.0	0.5		
German Ministry of Health (1991) [16]	5	0.2	0.1	with exemptions
Kabelitz (1998) [15]	10	0.5		
WHO (1999) [20]	10	0.3		
Ph. Eur. monograph <i>Kelp</i> (2007) [18]	5	4	0.1	
WHO (2007) [28]	10	0.3		
Regulation (EC) 396/2005 (2008) [25,26]			0.020	for herbal infusions and spices
Ph. Eur. draft monograph <i>Herbal drugs</i> (2008) [21]	5	0.5	0.1	
Regulation (EC) 1881/2006 (2008) [24]	3.0	1.0	0.10	cadmium 3.0 for seaweed products

The annexes of Regulation (EC) 396/2005 include a limit for mercury of 0.020 mg/kg in herbal infusions and spices and varying from 5 mg/kg (berries and small fruits) to 1000 mg/kg (hops) for copper [25,26]. According to the existing German regulation on pesticides (RHmV), however, the limit for mercury is not applicable if the contamination is caused by environmental influence [27].

An overview on maximum values for toxic metals set by countries in different regions of the world has recently been published by the WHO [28]. In this context, the WHO again proposes a limit of 10 mg/kg for lead and 0.3 mg/kg for cadmium in dried herbs [28]. Table 1 compiles limits for lead, cadmium and mercury set or proposed so far in different regulatory frameworks and scientific contributions.

1.2. Industries' initiatives

The BAH, the German Medicines Manufacturers' Association, founded a working group on contaminants in the year 2000. This working group maintains a large database on heavy metals that includes data from several companies. The database provides a detailed and extensive overview on the actual situation regarding the heavy metal content of herbal drugs. By specific evaluation of the database, the content of heavy metals can be demonstrated for each individual herbal drug, as well as the occurrence of a particular metal in different herbal drugs. Additionally, various percentiles, e.g. the 90th percentiles [14,15], can be calculated and the results can be assessed according to different legal frameworks. Such data has also been used to provide health authorities with current information on the actual occurrence of heavy metals in material used for medicinal or food purposes. In this context, proposals for maximum levels for heavy metals in herbal drugs have been submitted to the Ph. Eur., as well as to the European Commission, in order to support their activities to control metal contamination in herbal medicinal products and food supplements, respectively.

In 1998, Kabelitz published a detailed evaluation of a database on heavy metals [15], which included more than 12 000 samples originating from quality control analyses by several pharmaceutical companies. On this basis, maximum levels for lead of 10 mg/kg and for cadmium of 0.5 mg/kg were proposed.

In the following, the authors of this publication on behalf of the BAH working group on contaminants present an updated data-set and propose limits for some species based on recent experiences from daily practice.

2. MATERIALS AND METHODS

A total of about 7100 samples of herbal drugs (fresh and dried) of various origin were tested for lead and cadmium in

the present study period of 2002-2007. Mercury data was gathered from about 2500 samples in the same observation period.

Determination of these heavy metals was performed using validated methods such as atomic absorption spectrometry (AAS) according to Ph. Eur. chapter 2.4.27 [18], inductively coupled plasma mass spectrometry (ICP-MS) according to Ph. Eur. chapter 2.2.58 [29], or inductively coupled plasma optical emission spectrometry (ICP-OES). Some other publications reported alternative determinations using ICP-AES, ICP-OES and voltametric methods [30-32].

The following limits of quantification (LOQ) were set by the working group: 0.4 mg/kg for Pb, 0.07 mg/kg for Cd and 0.02 mg/kg for Hg. Due to different validation data from various laboratories with respect to the LOQ, the highest value obtained with the respective method was taken as harmonised LOQ. Thus a unique basis for an appropriate evaluation was established. Fresh plant material was dried prior to analysis. A certain variability might arise due to the different methods used, and should be taken into consideration in the assessment of heavy metals and the proposed limits.

Usually, knowledge of the number of samples (n) and the existence of a normal distribution according to Gauss are required for statistical evaluation. However, heavy metal contents in herbal drugs normally do not show such a distribution. For this reason, calculation of percentiles has been established [14,15]. In addition to the minimum and maximum values shown in Table 2, the 90th percentile has been utilised for assessment of the heavy metal content. This approach to establish limits, which should not be exceeded, was also used by Kabelitz [15].

For evaluation of the 90th percentile of each heavy metal and each herbal drug the obtained values were sorted by size. For calculation of the 90th percentiles a number of samples of at least $n = 20$ is required, e.g. in the case of 20 values the 90th percentile corresponds to the value of the 18th sample. The 90th percentile can be interpreted as the value for which any sample of the population shows a smaller value with a probability of 90 per cent. A more precise correlation with regard to the population can be achieved with an increasing number of samples.

For each individual herbal drug with a number of analysed samples of $n \geq 20$, Table 2 shows the calculated 90th percentiles (mg/kg) for lead, cadmium and mercury occurring in 109 different herbal drugs. In cases where the number of analysed samples was less than 20, the 90th percentiles have not been calculated (n.c.). Furthermore, the lowest and highest values found (mg/kg) are listed. The 90th

percentiles (mg/kg) exceeding the limits proposed for the Ph. Eur. are indicated in bold.

Apart from the evaluation presented here, in 214 cases (66.3 per cent) of all 323 herbal drugs included in the

BAH database, fewer than 20 values for all heavy metals are available. For this reason, these herbal drugs have not been evaluated.

Table 2. - Heavy metal content in herbal drugs

Herbal drug	Metal	n	Min (mg/kg)	Max (mg/kg)	90 th Percentile (mg/kg)*
Almond nut	Cd	22	< 0.07	< 0.07	< 0.07
	Pb	22	< 0.4	< 0.4	< 0.4
	Hg	9	< 0.02	0.02	n.c.
Angelica root	Cd	21	< 0.07	1.16	0.76
	Pb	17	< 0.4	2.37	n.c.
	Hg	2	< 0.02	< 0.02	n.c.
Aniseed	Cd	57	< 0.07	0.19	0.11
	Pb	57	< 0.4	1.26	< 0.4
	Hg	21	< 0.02	< 0.02	< 0.02
Apple fruit	Cd	38	< 0.07	< 0.07	< 0.07
	Pb	39	< 0.4	108.1	0.46
	Hg	18	< 0.02	< 0.02	n.c.
Arnica flower	Cd	75	< 0.07	1.69	0.78
	Pb	69	< 0.4	4.04	1.21
	Hg	18	< 0.02	0.05	n.c.
Artichoke leaf	Cd	210	< 0.07	0.74	0.43
	Pb	209	< 0.4	32.16	2.2
	Hg	40	< 0.02	0.12	0.02
Bermuda grass rhizome (ital.)	Cd	30	< 0.07	0.26	0.18
	Pb	31	< 0.4	1.42	1.02
	Hg	7	< 0.02	< 0.02	n.c.
Birch leaf	Cd	88	< 0.07	0.93	0.66
	Pb	83	< 0.4	3.93	1.87
	Hg	29	< 0.02	0.2	0.03
Bitter-orange peel	Cd	29	< 0.07	0.08	< 0.07
	Pb	29	< 0.4	1.45	< 0.4
	Hg	12	< 0.02	< 0.02	n.c.
Blackberry leaf	Cd	22	< 0.07	0.32	0.26
	Pb	22	< 0.4	2.8	1.76
	Hg	7	< 0.02	0.04	n.c.
Blackcurrant leaf	Cd	37	< 0.07	0.09	< 0.07
	Pb	37	< 0.4	10.43	1.09
	Hg	12	< 0.02	0.02	n.c.
Blond psyllium husk	Cd	68	< 0.07	0.07	< 0.07
	Pb	68	< 0.4	2.3	0.5
	Hg	39	< 0.02	0.04	< 0.02
Buckwheat herb	Cd	26	< 0.07	0.78	0.34
	Pb	25	< 0.4	1.69	0.74
	Hg	12	< 0.02	< 0.02	n.c.
Burdock root	Cd	32	< 0.07	0.42	0.36
	Pb	30	< 0.4	5.88	3.09
	Hg	17	< 0.02	0.02	n.c.
Camomile flower	Cd	109	< 0.07	0.76	0.5
	Pb	97	< 0.4	3.12	1.2
	Hg	50	< 0.02	0.02	< 0.02
Caraway seed	Cd	45	< 0.07	0.15	0.1
	Pb	45	< 0.4	1.56	< 0.4
	Hg	18	< 0.02	0.03	n.c.
Cardamon fruit	Cd	25	< 0.07	0.44	0.3
	Pb	25	< 0.4	1.22	0.41
	Hg	9	< 0.02	< 0.02	n.c.
Cayenne pepper fruit	Cd	20	< 0.07	0.32	0.09
	Pb	19	< 0.4	0.5	n.c.
	Hg	4	< 0.02	< 0.02	n.c.
Cinnamon bark	Cd	81	< 0.07	0.64	0.36
	Pb	82	< 0.4	11.89	2.61
	Hg	24	< 0.02	0.02	< 0.02

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Herbal drug	Metal	n	Min (mg/kg)	Max (mg/kg)	90 th Percentile (mg/kg)*
Clove bud	Cd	30	< 0.07	< 0.07	< 0.07
	Pb	30	< 0.4	0.59	< 0.4
	Hg	10	< 0.02	< 0.02	n.c.
Coltsfoot leaf	Cd	20	0.09	0.33	0.31
	Pb	20	< 0.4	2.48	1.44
	Hg	2	< 0.02	< 0.02	n.c.
Common ivy herb	Cd	25	< 0.07	0.5	0.3
	Pb	24	< 0.4	1.91	1.5
	Hg	17	< 0.02	0.03	n.c.
Coriander seed	Cd	20	< 0.07	0.57	0.16
	Pb	20	< 0.4	< 0.4	< 0.4
	Hg	3	< 0.02	< 0.02	n.c.
Cowslip, oxslip flower	Cd	36	< 0.07	0.18	0.07
	Pb	36	< 0.4	2.95	1.82
	Hg	16	< 0.02	0.03	n.c.
Daisy flower	Cd	28	0.101	0.98	0.56
	Pb	27	< 0.4	10.81	4.99
	Hg	3	< 0.02	0.04	n.c.
Dandelion herb	Cd	46	0.22	1.04	0.55
	Pb	45	< 0.4	7.44	2.57
	Hg	10	< 0.02	< 0.02	n.c.
Dandelion herb, flower	Cd	25	0.1	1	0.4
	Pb	25	< 0.4	3.28	1.08
	Hg	7	< 0.02	< 0.02	n.c.
Devil's claw root	Cd	99	< 0.07	0.21	0.12
	Pb	100	< 0.4	2.73	0.6
	Hg	26	< 0.02	< 0.02	< 0.02
Echinacea herb	Cd	19	< 0.07	0.07	n.c.
	Pb	20	< 0.4	0.53	0.43
	Hg	5	< 0.02	< 0.02	n.c.
Echinacea root	Cd	83	< 0.07	2.54	0.36
	Pb	85	< 0.4	3.44	1.76
	Hg	17	< 0.02	0.02	n.c.
Elder flower	Cd	47	< 0.07	< 0.07	< 0.07
	Pb	47	< 0.4	3.25	1.26
	Hg	27	< 0.02	0.021	< 0.02
Eyebright herb	Cd	31	< 0.07	1.4	1.14
	Pb	39	< 0.4	47.37	2.7
	Hg	8	< 0.02	< 0.02	n.c.
Fennel seed	Cd	114	< 0.07	0.37	0.09
	Pb	116	< 0.4	0.65	< 0.4
	Hg	63	< 0.02	0.04	< 0.02
Frangula bark	Cd	27	< 0.07	0.1	0.08
	Pb	28	< 0.4	4.42	2.02
	Hg	9	< 0.02	< 0.02	n.c.
Garlic bulb	Cd	22	< 0.07	0.11	0.07
	Pb	22	< 0.4	0.64	< 0.4
	Hg	5	< 0.02	0.02	n.c.
Giant goldenrod herb	Cd	20	< 0.07	0.57	0.41
	Pb	18	< 0.4	0.67	n.c.
	Hg	7	< 0.02	0.02	n.c.
Ginger rhizome	Cd	107	< 0.07	0.64	0.35
	Pb	101	< 0.4	4.12	1.28
	Hg	26	< 0.02	0.3	0.08
Ginkgo leaf	Cd	25	< 0.07	0.201	0.07
	Pb	25	< 0.4	5.4	4.69
	Hg	14	0.037	0.09	n.c.
Ginseng root	Cd	81	< 0.07	0.35	0.19
	Pb	83	< 0.4	1.62	0.45
	Hg	38	< 0.02	< 0.02	< 0.02
Goldenrod herb	Cd	73	< 0.07	1.05	0.84
	Pb	71	< 0.4	2.5	0.75
	Hg	22	< 0.02	0.02	< 0.02

Herbal drug	Metal	n	Min (mg/kg)	Max (mg/kg)	90 th Percentile (mg/kg)*
Hamamelis leaf	Cd	25	< 0.07	0.09	0.08
	Pb	22	< 0.4	1.22	0.68
	Hg	13	< 0.02	0.04	n.c.
Hawthorn fruit	Cd	56	< 0.07	0.16	< 0.07
	Pb	57	< 0.4	4.41	< 0.4
	Hg	25	< 0.02	0.06	< 0.02
Hawthorn leaf and fruit	Cd	117	< 0.07	0.35	0.21
	Pb	200	< 0.4	98.3	4.21
	Hg	41	< 0.02	0.06	0.02
Hibiscus flower	Cd	44	< 0.07	0.37	0.14
	Pb	32	< 0.4	2.33	0.41
	Hg	12	< 0.02	< 0.02	n.c.
Hop strobile	Cd	85	< 0.07	< 0.07	< 0.07
	Pb	85	< 0.4	3.53	0.51
	Hg	35	< 0.02	0.04	0.02
Horse-chestnut seed	Cd	22	< 0.07	< 0.07	< 0.07
	Pb	22	< 0.4	1.12	< 0.4
	Hg	4	< 0.02	< 0.02	n.c.
Horsetail herb	Cd	70	< 0.07	0.63	0.26
	Pb	68	< 0.4	21.45	0.92
	Hg	31	< 0.02	0.1	0.02
Iceland moss herb	Cd	38	< 0.07	0.61	0.44
	Pb	39	1.32	15.39	11.06
	Hg	21	< 0.02	0.05	0.03
Java tea leaf	Cd	23	< 0.07	0.09	0.07
	Pb	24	1.03	4.02	3.67
	Hg	10	< 0.02	< 0.02	n.c.
Juniper fruit	Cd	39	< 0.07	0.2	0.12
	Pb	39	< 0.4	0.89	< 0.4
	Hg	14	< 0.02	0.02	n.c.
Kelp	Cd	25	0.07	1.45	1.11
	Pb	25	< 0.4	3.58	0.87
	Hg	8	< 0.02	0.05	n.c.
Ladies mantle herb	Cd	26	< 0.07	0.48	0.17
	Pb	26	< 0.4	1.1	0.66
	Hg	10	< 0.02	0.026	n.c.
Lapacho bark	Cd	24	< 0.07	< 0.07	< 0.07
	Pb	24	< 0.4	1.28	0.47
	Hg	9	< 0.02	0.02	n.c.
Lavender flower	Cd	33	< 0.07	0.16	0.08
	Pb	33	< 0.4	7.53	4.08
	Hg	18	< 0.02	0.04	n.c.
Lemon balm leaf	Cd	84	< 0.07	0.18	< 0.07
	Pb	84	< 0.4	10.4	1.53
	Hg	42	< 0.02	0.05	0.04
Lemon verbena herb	Cd	24	< 0.07	0.57	< 0.07
	Pb	23	< 0.4	2.57	0.66
	Hg	5	< 0.02	< 0.02	n.c.
Lemongrass leaf	Cd	44	< 0.07	0.44	0.26
	Pb	46	< 0.4	1.01	< 0.4
	Hg	18	< 0.02	0.02	< 0.02
Lime flower	Cd	38	< 0.07	0.12	0.11
	Pb	38	< 0.4	9.21	3.24
	Hg	19	< 0.02	0.02	n.c.
Linseed	Cd	29	< 0.07	0.5	0.42
	Pb	19	< 0.4	< 0.4	n.c.
	Hg	8	< 0.02	< 0.02	n.c.
Liquorice root	Cd	61	< 0.07	0.18	< 0.07
	Pb	62	< 0.4	1.45	0.56
	Hg	26	< 0.02	0.02	< 0.02
Lovage root	Cd	29	< 0.07	0.61	0.52
	Pb	25	< 0.4	1.15	0.88
	Hg	10	< 0.02	0.03	n.c.

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Herbal drug	Metal	n	Min (mg/kg)	Max (mg/kg)	90 th Percentile (mg/kg)*
Mallow flower, blue	Cd	26	0.11	0.92	0.41
	Pb	27	< 0.4	1.78	0.97
	Hg	5	< 0.02	0.06	n.c.
Mallow leaf	Cd	103	< 0.07	3.61	0.4
	Pb	103	< 0.4	57.42	3.36
	Hg	66	< 0.02	0.04	0.02
Marigold flowers	Cd	122	< 0.07	1.09	0.44
	Pb	121	< 0.4	2.05	0.92
	Hg	55	< 0.02	0.04	< 0.02
Marshmallow root	Cd	28	0.09	0.95	0.62
	Pb	30	< 0.4	5	1.17
	Hg	11	< 0.02	< 0.02	n.c.
Maté leaf	Cd	27	< 0.07	0.78	0.41
	Pb	27	< 0.4	0.97	0.72
	Hg	12	< 0.02	0.02	n.c.
Melilot herb	Cd	20	< 0.07	0.23	0.17
	Pb	20	< 0.4	0.72	0.48
	Hg	5	< 0.02	0.02	n.c.
Milk thistle fruit	Cd	33	0.09	0.51	0.37
	Pb	32	< 0.4	< 0.4	< 0.4
	Hg	3	< 0.02	< 0.02	n.c.
Millet seed	Cd	12	< 0.07	< 0.07	n.c.
	Pb	20	< 0.4	60.78	2.32
	Hg	2	< 0.02	< 0.02	n.c.
Mistletoe herb, apple tree	Cd	13	< 0.07	< 0.07	n.c.
	Pb	13	< 0.4	< 0.4	n.c.
	Hg	6	< 0.02	0.06	n.c.
Mistletoe herb, fir	Cd	8	0.28	0.62	n.c.
	Pb	8	< 0.4	2.89	n.c.
	Hg	3	< 0.02	0.02	n.c.
Mistletoe herb, hawthorn	Cd	7	< 0.07	0.08	n.c.
	Pb	7	< 0.4	< 0.4	n.c.
	Hg	2	0.02	0.02	n.c.
Mistletoe herb, lime tree	Cd	9	< 0.07	0.34	n.c.
	Pb	9	< 0.4	< 0.4	n.c.
	Hg	2	< 0.02	0.02	n.c.
Mistletoe herb, oak	Cd	12	< 0.07	0.39	n.c.
	Pb	12	< 0.4	0.41	n.c.
	Hg	4	< 0.02	0.03	n.c.
Mistletoe herb, pine	Cd	6	0.51	1.06	n.c.
	Pb	6	< 0.4	< 0.4	n.c.
	Hg	1	< 0.02	< 0.02	n.c.
Mistletoe herb, poplar	Cd	10	< 0.07	1.81	n.c.
	Pb	10	< 0.4	< 0.4	n.c.
	Hg	3	< 0.02	0.02	n.c.
Mistletoe herb, total	Cd	248	< 0.07	3.16	0.78
	Pb	225	< 0.4	2.89	1.2
	Hg	53	< 0.02	0.06	0.04
Mistletoe herb, unknown	Cd	176	< 0.07	3.16	0.64
	Pb	153	< 0.4	2.83	1.33
	Hg	31	< 0.02	0.05	0.04
Mistletoe herb, willow	Cd	7	0.38	1.15	n.c.
	Pb	7	< 0.4	< 0.4	n.c.
	Hg	1	< 0.02	< 0.02	n.c.
Nettle herb	Cd	123	< 0.07	0.09	< 0.07
	Pb	129	< 0.4	6.81	1.5
	Hg	64	< 0.02	0.17	0.02
Nettle root	Cd	34	< 0.07	0.2	0.12
	Pb	43	< 0.4	4249.6	7.06
	Hg	11	< 0.02	0.021	n.c.
Oats bran	Cd	25	< 0.07	< 0.07	< 0.07
	Pb	25	< 0.4	< 0.4	< 0.4
	Hg	0	-	-	-

Herbal drug	Metal	n	Min (mg/kg)	Max (mg/kg)	90 th Percentile (mg/kg)*
Oats straw, green	Cd	30	< 0.07	0.12	< 0.07
	Pb	31	< 0.4	< 0.4	< 0.4
	Hg	18	< 0.02	0.05	n.c.
Passionflower herb	Cd	45	< 0.07	0.66	0.43
	Pb	45	< 0.4	1.98	0.48
	Hg	22	< 0.02	0.03	0.02
Peppermint leaf	Cd	109	< 0.07	0.42	0.08
	Pb	110	< 0.4	65	1.21
	Hg	51	< 0.02	0.06	0.03
Pumpkin seed	Cd	47	< 0.07	0.1	< 0.07
	Pb	47	< 0.4	0.56	< 0.4
	Hg	16	< 0.02	< 0.02	n.c.
Raspberry leaf	Cd	65	0.08	0.87	0.41
	Pb	66	< 0.4	3.46	1.59
	Hg	17	< 0.02	0.03	n.c.
Red clover flower	Cd	10	< 0.07	0.15	n.c.
	Pb	23	< 0.4	3.12	1.28
	Hg	4	< 0.02	< 0.02	n.c.
Red vine leaf	Cd	54	< 0.07	< 0.07	< 0.07
	Pb	54	< 0.4	3.4	2.1
	Hg	29	< 0.02	0.06	0.04
Restharrow root	Cd	40	< 0.07	0.19	0.12
	Pb	38	< 0.4	3.18	1.3
	Hg	17	< 0.02	0.02	n.c.
Ribwort herb, leaf	Cd	73	< 0.07	0.5	0.36
	Pb	71	< 0.4	5.24	1.18
	Hg	44	< 0.02	0.03	< 0.02
Rooibos leaf, organic	Cd	48	< 0.07	0.11	< 0.07
	Pb	48	< 0.4	0.46	< 0.4
	Hg	11	< 0.02	< 0.02	n.c.
Rose-hip shell	Cd	26	< 0.07	< 0.07	< 0.07
	Pb	27	< 0.4	1.14	< 0.4
	Hg	7	< 0.02	< 0.02	n.c.
Rose petal	Cd	24	< 0.07	0.12	< 0.07
	Pb	24	< 0.4	2.36	1.24
	Hg	6	< 0.02	0.02	n.c.
Rosemary leaf	Cd	32	< 0.07	< 0.07	< 0.07
	Pb	31	< 0.4	2.23	1.91
	Hg	14	< 0.02	0.06	n.c.
Safflower flower	Cd	20	< 0.07	0.11	0.1
	Pb	31	< 0.4	258.9	53.12
	Hg	12	< 0.02	0.05	n.c.
Sage leaf (<i>S. officinalis</i>)	Cd	94	< 0.07	0.14	< 0.07
	Pb	97	< 0.4	6.47	2.39
	Hg	35	< 0.02	0.06	0.03
Saw palmetto fruit	Cd	29	< 0.07	< 0.07	< 0.07
	Pb	30	< 0.4	< 0.4	< 0.4
	Hg	5	< 0.02	< 0.02	n.c.
Seaweed	Cd	21	0.55	6.6	5.71
	Pb	21	< 0.4	1.75	< 0.4
	Hg	6	< 0.02	< 0.02	n.c.
Senna leaf (<i>C. acutifolia</i>)	Cd	30	< 0.07	< 0.07	< 0.07
	Pb	30	< 0.4	0.93	0.58
	Hg	8	< 0.02	0.02	n.c.
Senna leaf (<i>C. angustifolia</i>)	Cd	20	< 0.07	< 0.07	< 0.07
	Pb	20	< 0.4	0.72	0.44
	Hg	9	< 0.02	0.02	n.c.
Senna pod (<i>C. angustifolia</i>)	Cd	22	< 0.07	< 0.07	< 0.07
	Pb	22	< 0.4	0.65	0.45
	Hg	5	< 0.02	< 0.02	n.c.
Silver lime leaves	Cd	42	< 0.07	0.21	0.11
	Pb	42	< 0.4	15.15	2.99
	Hg	42	< 0.02	0.02	< 0.02

Herbal drug	Metal	n	Min (mg/kg)	Max (mg/kg)	90 th Percentile (mg/kg)*
Spinach leaves	Cd	53	0.29	3.25	1.57
	Pb	52	< 0.4	6.8	0.9
	Hg	9	< 0.02	0.05	n.c.
St. John's wort herb	Cd	188	< 0.07	2.51	0.95
	Pb	181	< 0.4	14.51	1.63
	Hg	72	< 0.02	0.1	0.02
Strawberry leaf	Cd	56	< 0.07	1.46	0.54
	Pb	56	< 0.4	5.05	2.1
	Hg	6	< 0.02	0.05	n.c.
Sweet-orange peel	Cd	25	< 0.07	0.11	< 0.07
	Pb	28	< 0.4	< 0.4	< 0.4
	Hg	4	< 0.02	< 0.02	n.c.
Tea (black, green), organic	Cd	129	< 0.07	0.21	0.09
	Pb	131	< 0.4	6.32	2.55
	Hg	22	< 0.02	< 0.02	< 0.02
Tea (C. sinensis)	Cd	25	< 0.07	0.61	< 0.07
	Pb	27	< 0.4	5.66	1.05
	Hg	13	< 0.02	< 0.02	n.c.
Thyme herb	Cd	92	< 0.07	0.7	0.55
	Pb	76	< 0.4	4.73	1.81
	Hg	32	< 0.02	0.06	0.04
Turmeric rhizome	Cd	20	< 0.07	0.21	0.08
	Pb	20	< 0.4	0.8	0.45
	Hg	12	< 0.02	< 0.02	n.c.
Valerian root	Cd	132	< 0.07	0.54	0.27
	Pb	132	< 0.4	8.81	2.4
	Hg	70	< 0.02	0.06	0.03
Watercress herb	Cd	37	< 0.07	6.53	0.98
	Pb	36	< 0.4	311.91	6.5
	Hg	10	< 0.02	0.03	n.c.
Willow bark	Cd	61	0.13	3.53	1.7
	Pb	43	< 0.4	6.92	0.75
	Hg	22	< 0.02	< 0.02	< 0.02
Wormwood herb	Cd	56	< 0.07	1.1	0.85
	Pb	35	< 0.4	1.82	0.63
	Hg	18	< 0.02	0.02	n.c.
Woundwort flower	Cd	27	< 0.07	0.58	0.43
	Pb	26	< 0.4	0.94	0.67
	Hg	9	< 0.02	0.02	n.c.
Yarrow herb	Cd	52	< 0.07	0.98	0.55
	Pb	51	< 0.4	1.48	0.85
	Hg	18	< 0.02	0.02	n.c.
Yellow gentian root	Cd	114	< 0.07	0.98	0.35
	Pb	112	< 0.4	19.23	2.16
	Hg	36	< 0.02	0.25	< 0.02

* n.c.: not calculated

3. RESULTS AND DISCUSSION

Taking into consideration the limits proposed for the Ph. Eur. and the 90th percentiles of the samples evaluated, in total 4 herbal drugs out of 109 exceed the limits for lead, 20 out of 109 exceed the limits for cadmium, and none exceed the limits for mercury. The herbal drugs exceeding the limits for lead and cadmium are listed in Table 3; those exceeding the limits for cadmium are additionally presented in Figure 1. The 90th percentiles calculated in this current study have been compared with those obtained by Kabelitz in 1998 [15].

In addition, for mistletoe herb a closer examination is made because the plant grows on different host trees like apple tree, fir, hawthorn, lime tree, oak, pine, poplar and willow. As can be seen from Table 2, for mistletoe herb the 90th percentiles were calculated for all samples examined. Additionally, data is presented for material from every single host tree (Table 4). It can be observed that the cadmium accumulation depends on the host tree, e.g. in the cases of fir, pine, poplar and willow, apparently higher values

were obtained. For mistletoe herb from single host trees, calculation of individual 90th percentiles was not possible due to the low amounts determined.

A 90th percentile of more than 5 mg/kg lead was found for Iceland moss herb, nettle root, safflower flower and watercress herb. For these herbal drugs, more values are available in this evaluation compared to Kabelitz. In the cases of nettle root and watercress herb, higher values have been found in this evaluation; for Iceland moss herb the 90th percentile was lower. Safflower flower showed remarkably higher values than other herbal drugs and was not listed by Kabelitz. Frangula bark and ginkgo leaf exceeded the limits in the publication of Kabelitz but not in the present evaluation. Sundew herb was not assessed in the present study because only 7 values were available, of which 5 were below and 2 were above 5 mg/kg (maximum 21.5 mg/kg).

For 20 herbal drugs listed in Table 3, a 90th percentile of more than 0.5 mg/kg cadmium was found, indicated in bold. Kabelitz found higher values in 17 cases. For 13 out of the

mentioned 20 herbal drugs, higher values were found in this evaluation compared to Kabelitz, for 2 herbal drugs (birch leaf, goldenrod herb) the values were comparable, for 3 herbal drugs (dandelion herb, St. John's wort herb, willow bark) the 90th percentile was lower in this publication, and 2 herbal drugs (eyebright herb, seaweed) were not assessed by Kabelitz. Except for kelp, spinach and willow bark the 90th percentiles were between 0.5 and 1 mg/kg as shown in Figure 1. Other herbal drugs not exceeding the limits in the present evaluation, but mentioned by Kabelitz, were mallow leaf and lemongrass leaf. Dandelion herb and root, fumitory herb, kava kava rhizome, lungwort herb, sandy immortelles flower, tormentill rhizome and wild pansy herb were not assessed in the present publication because fewer than 20 samples were available.

The comparison of the results of the former and the present evaluation of herbal drugs exceeding the proposed Ph. Eur. limits (Table 3) shows in some cases considerably high differences in the 90th percentiles. A possible reason for the observed deviations might be the different numbers of samples analysed.

4. CONCLUSION

The limits for lead (10 mg/kg), cadmium (1.0 mg/kg) and mercury (0.1 mg/kg) that have been proposed so far by the

BAH are based on the evaluation published by Kabelitz in 1998 [15]. According to the recent evaluation, the limits proposed for the Ph. Eur. are in principle acceptable provided that exemptions are included for several plants, e.g. those accumulating cadmium. Such exemptions might be included either in the general monograph *Herbal drugs*, stating that for these herbal drugs higher limits are acceptable, or within individual Ph. Eur. monographs, mentioning the specific limits under Tests. Table 5 contains a list of herbal drugs for which exemptions for lead and cadmium levels are justified based on the recent evaluation and previous reports [15].

In this context, the limits for food supplements agreed upon within the European Commission (lead 3.0 mg/kg; cadmium 1.0 mg/kg and 3 mg/kg for seaweed products; mercury 0.10 mg/kg) have to be regarded critically, particularly with regard to the limit for lead. As can be seen from Table 2, in 12 cases of the recent evaluation the limit for lead, and in 3 cases the limit for cadmium, is exceeded.

4.1. Perspectives

The working group will continue collecting and evaluating data on heavy metals occurring in herbal drugs. Publication of the evaluation is planned on a regular basis in order to keep the overview up-to-date.

Table 3. – Comparison of evaluations of heavy metals in herbal drugs

Herbal drug	Metal	n	90 th Percentile (mg/kg)*	n	90 th Percentile Kabelitz 1998 (mg/kg)*
Angelica root	Cd	21	0.76	49	0.58
Arnica flower	Cd	75	0.78	56	0.35
Birch leaf	Cd	88	0.66	245	0.67
Daisy flower	Cd	28	0.56	25	0.42
Dandelion herb	Cd	46	0.55	161	0.69
Dandelion herb and root	Cd	16	n.c.	50	0.64
Eyebright herb	Cd	31	1.14	9	n.c.
Fumitory herb	Cd	15	n.c.	12	1.05
Goldenrod herb	Cd	73	0.84	19	0.86
Kava kava rhizome	Cd	1	n.c.	17	0.63
Kelp**	Cd	25	1.11	63	1.05
Lemongrass leaf	Cd	44	0.26	25	0.64
Lovage root	Cd	29	0.52	23	0.26
Lungwort herb	Cd	2	n.c.	10	0.79
Mallow leaf	Cd	103	0.40	18	1.17
Marshmallow root	Cd	28	0.62	32	0.45
Misteltoe herb	Cd	248	0.78	210	0.48
Sandy immortelles flower	Cd	8	n.c.	37	0.69
Seaweed	Cd	21	5.71	-	-
Spinach leaf	Cd	53	1.57	57	0.93
St. John's wort herb	Cd	188	0.95	496	1.30
Strawberry leaf	Cd	56	0.54	37	0.27
Thyme herb	Cd	92	0.55	157	0.48
Tormentill rhizome	Cd	2	n.c.	12	2.13
Watercress herb	Cd	37	0.98	24	0.46
Wild pansy herb	Cd	17	n.c.	47	1.00
Willow bark	Cd	61	1.70	120	1.80
Wormwood herb	Cd	56	0.85	49	0.42
Yarrow herb	Cd	52	0.55	109	0.49
Frangula bark	Pb	28	2.02	80	7.04
Ginkgo leaf	Pb	25	4.69	15	10.52
Island moss herb	Pb	39	11.06	35	14.35
Nettle root	Pb	43	7.06	34	3.86
Safflower flower	Pb	31	53.12	-	-
Sundew herb	Pb	7	n.c.	16	6.60
Watercress herb	Pb	36	6.5	24	2.27

* n.c.: not calculated
** individual limits in [17]

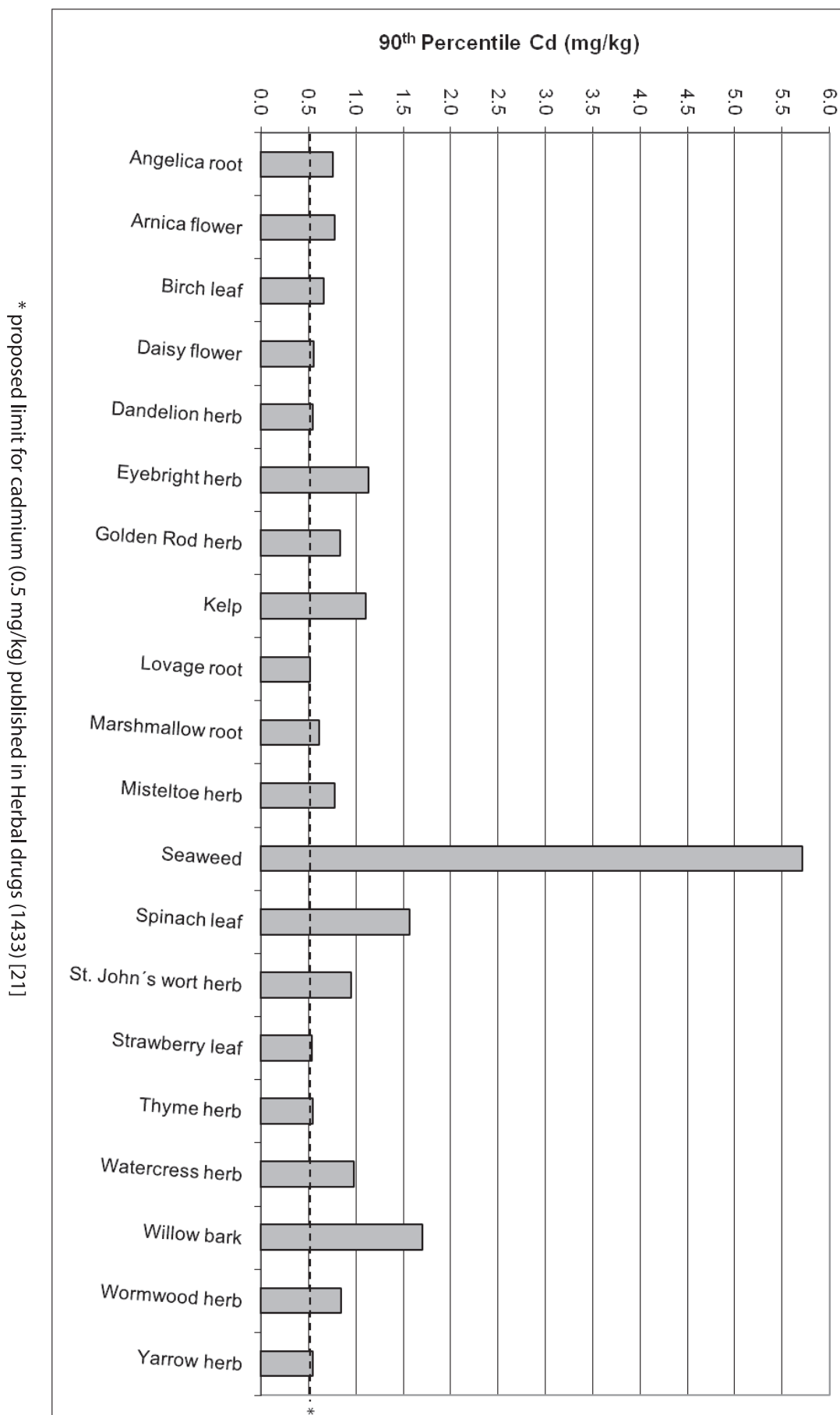


Figure 1. Herbal drugs exceeding the limits for cadmium as compared to the limit proposed for the European Pharmacopoeia

Table 5. – Proposed exemptions for cadmium and lead in herbal drugs as compared to the proposals for Cd (0.5 mg/kg) and Pb (5 mg/kg), published in Herbal drugs (1433) [21]

Metal	Herbal drug	Limit (mg/kg)
Cd	Angelica root	0.8
	Arnica flower	0.8
	Birch leaf	0.7
	Daisy flower	0.6
	Dandelion herb	0.6
	Eyebright herb	1.1
	Fumitory herb*	1.5
	Goldenrod herb	0.8
	Kava rhizome**	0.6
	Lungwort herb**	0.8
	Marshmallow root	0.6
	Mistletoe herb	0.8
	Sandy immortelles flower**	0.7
	Seaweed	5.7
	Spinach leaf	1.6
	St. John's wort herb	1.0
	Thyme herb	0.6
	Tormentill rhizome**	2.1
	Watercress herb	1.0
Wild pansy herb**	1.0	
Willow bark	1.7	
Wormwood herb	0.9	
Yarrow herb	0.6	
Pb	Iceland moss herb	11
	Nettle root	7
	Safflower flower***	10
	Sundew herb**	7
	Watercress herb	7

* the 90th percentile was calculated from 15 values
 ** due to the low amount of values, the 90th percentile from Kabelitz [15] was taken
 *** a lower limit than the 90th percentile is proposed

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