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Abstract

20 000 subjects were enrolled in a large-scale field study to determine the concentration of total mercury in saliva. A statistical relationship was found between the mercury concentration in the pre-chewing saliva and chewing saliva, and the number of amalgam fillings. The mean number of amalgam fillings was 9 and the median mercury concentration was 11.6 µg/l in the pre-chewing saliva and 29.3 µg/l in the chewing saliva, which is considerably higher than reported in most previous publications. Extrapolation to the uptake of total mercury per week has shown that the provisional tolerable weekly intake (PTWI) value of the WHO is exceeded in at least 30% of the subjects.

Keywords

amalgam, mercury, saliva, chewing, binding form

1. Introduction

In the second half of the last century, the "first amalgam war" was fought in the USA for various reasons [1]. The aim was to prevent charlatans also using this simple technique. The amalgams used at the time released very high quantities of mercury and "miracle cures" in patients with chronic diseases after removal of the amalgam fillings raised doubts about the material. A short "second amalgam war" was then started by the German chemist *Alfred Stock* [2], who drew attention to the fact that mercury is continuously released from fillings and may possibly be associated with a

number of disease symptoms [3]. The discussion of amalgam was renewed in the 80s when manifestations of the corrosion of amalgam were investigated [4-12]. Ionic binding forms (Hg^{2+}, Hg_2^{2+}) and mercury complexes with natural substances were of prime interest. Attention has been paid primarily since the end of the 80s to the release of mercury vapour Hg^0[13-22]. In recent years, saliva in its property as solutizer and transport medium for mercury in its various binding forms has been increasingly taken into account [23-29, 42].

Gerhard [30, 31] has drawn attention to the relationship between infertility, polycystic ovaries, hormone disorders, loss of hair in women and heavy metal burden. Investigations at the Laboratory for Reproduction Toxicology at the Tübingen Women's Hospital on the influence of heavy metals on humans reproduction have shown that female patients with amalgam fillings have a considerably higher mercury concentration in the follicular fluid than in those without amalgam fillings [32]. To test the possible toxic actions of mercury on hormone producing cells, human granulosa cells were cultured. It was found that the hormone synthesis was significantly reduced already at a relatively low mercury concentration, while the cell vitality was almost unaffected [33, 34]. For further insight into the relationships between amalgam fillings, mercury concentration in the saliva and fertility, a large-scale field study using saliva analyses was carried out. In the present report, the results of mercury concentrations are presented. In a second publication correlations between symptoms of health and amalgam fillings will be shown.

2. Materials and methods

2.1 Group selection and sampling

People were asked to participate in the field study via an article in number 12/95 of the parenting magazine ELTERN as well as through a concerted publicity campaign in January 1996, which found widespread resonance in the German media. On sending a contribution to cover costs to the MOMO-Stiftung, Radolfzell, participants were supplied with a test kit consisting of 2 tubes (each packed in a shock-resistant transport tube) with

precise instructions for filling and in addition a questionnaire for entering, amongst other things, body weight, number of amalgam fillings and symptoms of health.

The test kit consisted of two tubes. About 5 ml of pre-chewing saliva was to be collected in the first tube. The instructions were that nothing should be eaten or drunk for 2 h before taking the sample. A line on the tube helped the estimation of 5 ml pre-chewing saliva.

In the second tube the total quantity of chewing saliva was collected that was obtained through chewing sugar-free chewing gum for precisely 10 min. This was generally 15 - 20 ml.

The test kit was sent to the Organic Chemistry Institute, where it was immediately recorded and analysed on receipt.

Up to the end of April 1996, somewhat more than 20000 subjects had submitted their samples. In the present report only the 17 351 individual results are analysed with respect to mercury for which complete data sets were available.

2.2 Reagents

The chemicals used were all of analytical quality from E. Merck, Darmstadt, FRG. Deionised water was produced with a Millipore device. Argon was used as the transporting gas and preparation of the solutions was based on the instructions of *Guo et al.* [35].

Oxidation reagents: 2 g KBr and 0.56g $KBrO_3$ dissolved in 50 ml of deionised water.

HCl solution: 30 ml HCl (32 - 36%) diluted to 2.5 l with water.

$KMnO_4$ solution: 5 g of $KMnO_4$ dissolved in 2.5 l of water.

Reduction solution: Eight pellets of NaOH dissolved in 2.5 l of water. Subsequent addition of 8 g of $NaBH_4$

Standard solutions: All reference solutions were prepared in glass volumetric flasks. Before preparing the reference solutions, the flasks were rinsed 3 times with HNO_3 (65%) and three times with deionised water. To prevent fluctuations in the reference solutions by vaporisation of the mercury, the reference solutions were not used for more than 2 days.

The stock solution contained mercury at a concentration of 1000 mg Hg/l. The reference solution contained 5000 µg Hg/l. It was prepared by diluting the stock solution with the addition of 1 ml of HNO_3 (65%) to 100 ml. Calibration solutions with the following concentrations were prepared from the reference solution: 1.00 µg Hg/l, 5.00 µg Hg/l, 10.00 µg Hg/l, 20.00 µg Hg/l and 30.00 µg Hg/l. 2 ml of HNO_3 (65%) to 500 ml of solution were added to the calibration solutions to assist stabilisation. For the blank solution, 1 ml of HNO_3 (65%) was diluted to 250 ml with deionised water. As the solutions decompose with time, they were freshly prepared for each series of measurements.

2.3 Sample preparation

Before adding any reagents, the volume of chewing saliva was measured. Samples of pre-chewing saliva and chewing saliva were subsequently mixed with 1 ml of HCl (32 - 36%). 500 µl $KBr/KBrO_3$ solution was pipetted to aliquots of both types of saliva and then diluted with deionised water to final dilutions of 1:20 for pre-chewing saliva samples and 1:10 for chewing samples.

If there were irregular measuring signals or the reference concentrations were outside the calibration range, samples in the autosampler tubes were again diluted 1:5.

2.4 Measurement

Measurement of the Hg concentrations was carried out with a newly developed cold-vapour flow-injection mercury system with cold-vapour atomic absorption from the PERKIN-ELMER Bodenseewerk. Both the FIMS 100 (see diagram in Fig. 1) and the FIMS 400 were used.

Fig. 1: Scheme of the FIMS 100 for analysis of Hg in saliva.

The calibration repeatedly gave correlation coefficients of < 0.995. This was specified for the apparatus, as were also the consequences for deviations of individual values for the calibration solutions. The following deviations were defined as permissible:

5 µg Hg/l ð 4.5 - 5.5 µg Hg/l

10 µg Hg/l ð 9.5 - 10.5 µg Hg/l

20 µg Hg/l ð 19.0 - 21.0 µg Hg/l

30 µg Hg/l ð 28.5 - 31.5 µg Hg/l

If the correlation coefficient of the standard solutions deviated even after repeated recalibration, new calibration solutions were prepared.

At the beginning of each measuring day, 2 calibrations were carried out after warming up of the lamp. A standard of 10 µg Hg/l was measured after every 15 samples as a quality control sample. The measured concentrations had to lie between 9.0 µg Hg/l and 11.0 µg Hg/l. Otherwise completely new calibration was carried out and the samples since the last successful quality control sample were measured again. A complete new calibration was carried out after every 55 samples.

Complete recalibration was also carried out after the following breakdowns or interventions in the measuring system:

Analytical solution got into the cuvette

Cleaning of the cuvettes or of the cuvette window

Change in the argon input pressure

Exchange of the filter membrane of the separator.

The filter membrane of the separator was exchanged before each new rack

series in order to ensure higher operation reliability during the measurements. The samples were measured in duplicate. The result is the mean of the two determinations.

Detailed investigations by *Guo et al.* [35] have confirmed that with the pre-treatment of the samples used and the reagents that are used bound forms of mercury such as CH_3HgCl, $Hg(CH_3COO)_2$, or C_6H_5HgCl in the saliva are detected with yields of > 96%.

The limit of detection is about 0.01 µg Hg/l. We were able to confirm the statements made by *Guo et al.* [35] with regard to the precision of the measurements (2% relative standard deviation of the signal for 1 µg Hg^{2+}/l in 1:10 diluted saliva).

3. Results

Considerably more women (59.3%) than men (40.7%) participated in this field study. This applied especially in the group of women in child-bearing age (up to > 65%). This may be attributable to the announcement of the field study in the parenting magazine ELTERN, which is read predominantly by women, to occasional publications on the possible relationship between heavy metal burden and fertility and a generally higher health consciousness of women.

Fig. 2: Composition of the group according to age and sex (n = 18000)

The age groups above 50 years and below 25 years were clearly under-represented in comparison with the composition of the population of the Federal Republic of Germany (FRG). (Fig. 3).

Fig. 3: Population of the FRG according to age and sex (1993)

The age group 6 - 9 years was represented with 28 subjects, the age group of 10 - 14 years with 60 subjects and the 15 - 19 year-olds with 169 subjects. Because of the quite small groups, statements about these age groups are only possible to a limited extent.

Fig. 4 shows the distribution of the number of amalgam fillings for a group of 17 351 subjects. 245 subjects reported either to have no amalgam fillings or to have undergone a complete removal of them. The distribution resembles a Gaussian normal distribution curve, with a maximum at 8 - 10 fillings.

Fig. 4: No of amalgam fillings in the subjects (n = 17 351)

The mean for the total group of 17 351 subjects used for statistical analysis was 9.1 fillings. The results of the intermediate analyses that were carried out after each 500 received and measured samples were within a very narrow range about this value. The means for the respective cohorts of 500 ranged from 8.4 to 9.4 fillings.

Fig. 5: Number of fillings according to age groups (n = 18000)

The dependence of the number of fillings on age is very marked. The group of 6 - 9 year-olds had about 3 fillings. The group of 30 - 34 year-olds had the highest number with a mean of 11 fillings. In the older age groups the number of fillings fell continuously to about 5.

Fig. 6: Percentage distribution of the mercury concentrations in pre-chewing saliva and chewing saliva (n = 17 351)

About a quarter of the total group had Hg concentrations in the pre-chewing saliva of up to 5 µg/l and 96% of the values were less than 100 µg/l. In one percent of the subjects Hg concentrations > 200 µg Hg/l were measured, in 37 subjects the values were over 400 µg/l and in 11 subjects over 1000 µg/l.

The distribution curve for mercury in the chewing saliva clearly shifted to higher Hg concentrations. Values of less than 5 µg/l were found in only 11% of the group and 90% of the values were less than 100 µg Hg/l. In 1.7% of the subjects Hg concentrations of >200 µg Hg/l were measured, in 60 subjects the values were over 400 µg/l and in 15 subjects over 1000 µg/l.

There was a direct relationship between the number of amalgam fillings and the mercury concentration. Fig. 7 shows a plot of the median Hg concentrations against the number of fillings. It was found that about 1.3 µg Hg/l was present per amalgam filling for pre-chewing saliva and about 3.4 µg Hg/l for the chewing saliva. That individual values can of course deviate considerably is seen clearly in the comparison of the means and the medians for the total group (Table 1).

Fig. 7: Statistical dependence of mercury concentration in the saliva on the number of fillings (n = 17 351)

Table 1: Means and medians for pre-chewing saliva and chewing saliva

	Pre-chewing saliva	Chewing saliva
Mean	27.3 µg Hg/l	47.1 µg Hg/l
Median	11.6 µg Hg/l	29.3 µg Hg/l

Whilst all the extreme values are taken into account in the means, these are largely eliminated in the calculation of the median.

To make this effect clear, Figs 8 and 9 show the concentration distributions for a subgroup with 9 amalgam fillings as well as the central 66% range in accordance with *Ott et al.* [23]. For pre-chewing saliva, the 66% range is 4.7 to 40 µg Hg/l and for chewing saliva 14.5 to 73.6 µg Hg/l (see also Table 2, which lists the 66% range for 1 - 16 fillings).

Fig. 8: 66% range for 9 amalgam fillings in Fig. 9: 66% range for 9 amalgam
pre-chewing saliva (n = 1478) fillings in chewing saliva (n = 1478)

Table 2: Dependence of the 66% range on the number of fillings.

Fillings	66% range pre-chewing	66% range chewing saliva	n

	saliva (µg Hg/l)	(µg Hg/l)	
1	0.2 - 7.9	0.1 - 10.1	208
2	0.5 - 8.6	0.6 - 16.7	414
3	1.1 - 12.9	2.2 - 26.2	588
4	1.8 - 19.1	3.9 - 33.8	880
5	2.0 - 22.8	4.8 - 40.2	1077
6	2.8 - 24.7	6.6 - 49.7	1314
7	3.2 - 29.3	8.1 - 54.7	1364
8	4.1 - 33.6	10.6 - 63.3	1681
9	4.7 - 40.0	14.5 - 73.6	1478
10	5.0 - 42.0	14.2 - 80.5	1788
11	5.7 - 46.6	16.4 - 89.1	1449
12	5.7 - 48.1	18.7 - 94.4	1467
13	6.6 - 43.7	20.3 - 97.6	926
14	7.1 - 54.4	21.3 - 103.1	873
15	7.6 - 59.1	22.5 - 109.8	629
16	6.7 - 62.2	21.4 - 113.6	430

4. Discussion

4.1 Composition of the study population

The composition of the study population does not correspond to that of the population distribution in the Federal Republic of Germany and cannot therefore be directly extrapolated. Comparison of Fig. 2 and Fig. 5 shows that the age group of 25 - 40 years is over-represented, i.e. the age group in which there are the most fillings (on average more than 9). This must be taken into account on comparison with previous investigations such as that of *Ott et al.* [23], which included 54 subjects aged 15 - 39 years with amalgam fillings and 15 subjects aged 20 to 55 years without amalgam fillings or that of *Mayer et al.* [29] which covered 56 amalgam carriers and 7 subjects without amalgam fillings aged between 18 and 46 years.

The average number of fillings or the number of fillings with the greatest frequency is 9 (8 - 10) fillings for the study population, which is somewhat higher than that found in previous investigations. In the paper by *Mayer et al.* [29] the maximum was 7 - 9 fillings and in *Ott et al.* [23] 7. The number of amalgam fillings for the 6 - 9 year-olds corresponds to the results in a study population of *Engin-Deniz et al.* [28] with 32 primary school children aged 10 years (2.5 fillings with a range of 1 - 8 fillings).

4.2 The mercury concentrations in saliva

At first sight, there is, in view of about 35,000 analyses, no uniform picture of a relationship between the number of amalgam fillings and the mercury concentrations in pre-chewing and chewing saliva. We found Hg concentrations in the saliva of between 0.0 µg/l and several 100 µg/l for each individual number of fillings. Only on statistical analysis of the data a relationship was brought to light.

A correlation of Hg concentration and number of fillings can be shown both for the means of the concentrations for the individual groups per number of fillings and the corresponding medians (Fig. 7). The 66% range for pre-chewing saliva and chewing saliva are also dependent on the number of amalgam fillings (Table 2).

The absolute concentrations in the field study are generally higher than those in previous publications. *Ott et al.* [23] found a concentration range in

pre-chewing saliva of 54 subjects with an average of 7 fillings of 0.60 to 143 µg Hg/l, a central 66% range of 1.32 to 18.5 µg Hg/l and a median of 4.90 µg/l. The range for chewing saliva was 0.30 to 193.8 µg Hg/l, the central 66% range 2.25 to 37.27 µg Hg/l and the median 12.95 µg Hg/l (Fig. 10).

Fig. 10: Mercury concentrations in the saliva. Comparison of the values given by the BGA and the results of the field study.

Engin-Deniz et al. [28] found in the investigation in children mentioned above mercury concentrations in the pre-chewing saliva of between 0.06 and 6.10 µg Hg/l and in the chewing saliva 0.05 to 20.6 µg Hg/l. The means and medians for pre-chewing saliva were 0.07 and 0.7 µg Hg/l respectively and for chewing saliva 0.44 and 4.4 µg Hg/l.

Schiwara et al. [36] reported concentrations > 250 µg Hg/l after chewing gum. *Gradl* and *Gebhardt*[44] found on examination of 56 amalgam carriers (mean number of fillings 8) a mean for pre-chewing saliva 8.1 ± 9.7 µg/l and for chewing saliva 26.6 ± 31.3 µg Hg/l (first chewing phase) or 30.2 ± 39.0 µg Hg/l (2nd chewing phase).

In a study on 120 women, *Gerhard et al.* [30] determined mean values in the pre-chewing saliva and chewing saliva according to number of fillings of 24 and 54 µg Hg/l respectively (0-5 fillings), 74 and 68 µg Hg/l respectively (6 - 10 fillings) and 101 or 173 µg Hg/l respectively (>11 fillings).

Mayer et al. [29] found in subjects with more than 12 fillings median values for pre-chewing saliva of 32.7 µg Hg/l and for chewing saliva 53.8 µg Hg/l (phase 2) or 58.8 µg Hg/l (phase 3). In this investigation a relationship between the number of fillings and the mercury concentration in the pre-chewing saliva and chewing saliva is shown, as is also in the paper by *Schiwara et al.*[36].

The results of the field study are largely in accordance with the results of *Mayer et al.* [29] with respect to both a statement about dependence of Hg concentration in the pre-chewing and chewing saliva as well as in the median values according to the number of amalgam fillings.

4.3 Calculation of the daily and weekly burden

We approached the calculation of the weekly intake of total mercury - independently of the respective binding form - in two stages. In the first stage, we took into account the partial burdens from food, beverages, air and saliva. In the second stage we also tried to take into account the additional load of Hg⁰ which vaporises from the amalgam fillings.

The uptake of total mercury from the food amounts, according to *Schelenz* and *Diehl* [37, 38] to about 7.6 μg/day. *Schiele* [39] reported daily quantities of 13 - 53 μg Hg from canteen meals with a median of 22 μg total mercury. It is interesting to note from *Schiele's* results that he could not find any difference between canteen meals and a fish-rich diet.

The *International Commission for Radiological Protection*[40] assumes a daily Hg uptake from food of 20 μg. *Bowen*[41] calculated on the basis of seven literature reports values of 4 - 20 μg per day. *Brune* [42] took into account in his consideration of metal release from dental biomaterials a total mercury intake per day of 20 μg from food and beverages.

The *WHO* [43] estimates the daily intake of total mercury from food to be 3.6 μg and that from the air to be 0.04 μg and from water 0.05 μg.

Taking into account the literature data, we assumed in this investigation a daily intake with the food of 10 μg total mercury. In addition we took into account on the basis of *Schiele's* report [39] an estimated uptake of 1 μg Hg from inspired air and a further μg Hg from drinking water and beverages.

To calculate the Hg burden via pre-chewing saliva, we have experimentally determined a saliva flow rate of 13.5 ml/20 min (n = 35). With 22 h production of pre-chewing saliva, this means a total quantity of 891 ml. The rate that we have assumed agrees very well with that of *Gradl* and *Gebhardt* [44] (3.2 ml in 5 min) and that of *Mayer et al.* [29] (0.7 ml/min). The assignment of a saliva flow with the same flow rate over 22 h appears to be justified as we were able to find in a series of individual subjects that the pre-chewing saliva has a higher mercury burden before the first food and

beverage intake than during the day (Fig. 11). The somewhat lower saliva flow rate during the night is therefore balanced out by a higher mercury concentration in the saliva.

Fig. 11: Mercury concentrations in the saliva at different times of day (n =1)

To calculate the load from chewing saliva, the individually determined saliva volumes were used as a basis and equated to a period of 2 h. *Gradl* and *Gebhardt*[44] carried out their extrapolation to determine the daily Hg burden from mercury on the assumption of 1 h chewing saliva (90 ml) and 23 h basal saliva (880 ml).

To take the mercury vapour released from amalgam fillings into account, a mean value of 1.31 µg Hg⁰ per filling and day was calculated on the basis of the values given by *Skare* and *Engqvist* [45] and *Vimy* and *Lorscheider*[17] and other values given in the literature.

On the basis of the first assumptions we obtained a distribution of daily mercury burden as shown in Fig. 12.

About 30% of the subjects lie, according to this method of extrapolation, within the assumed range of the WHO for the uptake of total mercury of up to 21 µg. For a further 40%, burdens that are still below the PTWI values of the WHO (300 µg total mercury per week) are found. About 30% of the subjects take up more mercury per week than the PTWI value. 3.5% of the subjects are more than 3 times higher than the PTWI value and 1.9% are 4 times higher.

Fig. 12: Calculated Hg burden from food, air, beverages and saliva (without taking into account the uptake from the gas phase).

Original assumptions that most of the samples examined that lead to a decisive excess above the PTWI value were samples containing coarse amalgam particles have not been confirmed, apart from a few exceptions

(mercury content in the saliva more than 1000 µg/l).

Repeated sampling at different times of day showed deviations of less than 20% in subjects with high Hg concentrations both in the pre-chewing and in the chewing saliva. If particulate matter was causally responsible for the high analytical values, then the differences would be considerably larger.

The investigations by *Mayer et al.* [29] show that 17% of the subjects examined exceeded the ADI value for mercury of 45 µg/day, taking into account a total of 22 µg Hg from food, respired air and drinking water. *Gradl* and *Gebhardt*[44] have shown in their subjects that at least 17% of those examined had an Hg burden that was equivalent to or higher than that of the food intake.

Fig. 13 shows what the additional effect can be on taking into account the gas phase in the oral cavity. While there is scarcely any change of distribution in the range high above the PTWI values, there are clear effects around the PTWI value, so that according to this basis for calculation, about 43% of the subjects have an individual daily burden above the PTWI value. *Brune* and *Evje* [24] calculate a daily burden of 20 µg from the ionised mercury from the amalgam fillings alone.

Fig. 13: Distribution of values above and below the PTWI values of the WHO (including the burden from the gas phase).

Schiele [46] also found that amalgam fillings could lead to an additional Hg burden in humans which in many cases may even be several times the basal load from foodstuffs with a maximum that is about 20-fold.

Fig. 14: Proportion of subjects with total mercury loads above the PTWI values according to age groups.

In contrast to the present field study as well as the results of *Mayer et al.* [29], *Gradl* and *Gebhardt*[44] and *Brune* and *Evje*[24], the WHO assumes a daily mercury uptake by the body of only 10.61 to 27.71 µg. The Advisory

Committee on Toxicology of the German Society for Pharmacology and Toxicology has also assumed according to *Drasch et al.* [47] in 1989 that the uptake of mercury from tooth amalgam can be a maximum of 8 µg mercury per day.

To us it seems to be primarily of note that in the burden-oriented results from the field study several age groups exceed the PTWI values particularly frequently (Fig. 14). The group of 20 - 39 year-olds is particularly striking, i.e. including women of child-bearing age. A comparison with Fig. 5 supplies the explanation, since the number of amalgam fillings in this group is particularly high at 9 - 11 fillings. In the age group of 6 - 9 year-olds and in the 10 - 14 year-olds, apparently the lower number of fillings is just sufficient to exceed the PTWI frequently, not least because of the lower body weight.

4.4 Binding forms of mercury

The fact that mercury is taken up in its various binding forms does not, of course, mean that it is subsequently absorbed by the body. Hg^0 vapour in the lungs is absorbed to about 80%, whereas Hg^{2+} in the intestines is taken up to only about 7 - 10%. Methylated mercury is absorbed from the intestines to about 80%, but amalgam particles and mercury droplets are virtually not absorbed at all.

According to investigations by *Knappwost*[48] mercury vapour (Hg^0) in the air is not oxidised as the oxygen pressure of mercuric oxide increases with decreasing size of the particles of mercury oxide and accordingly tends to infinity with infinitely small particles. Mercury vapour is thus stable in air. Probably for this reason a number of investigators assume that Hg^0 vapour which occurs especially after mechanical loading of amalgam fillings remains in this oxidation state even when the Hg^0 is incorporated in the saliva.

This postulate of stability is, however, no longer automatic in biological fluids. Hg^0 is rapidly oxidised enzymatically in blood and oxidation complexing procedures also take place rapidly in saliva. Thus *Brune* and

Evje have already pointed out in 1985 [24] and *Brune* again in 1988 [42] that minute mercury droplets and Hg^0 vapour that are released from amalgam fillings are rapidly dissolved in the oxygen-rich environment with the formation of Hg^{2+} ions [49]. Hg^{2+} ions can thus be formed in the saliva both by electrochemical corrosion and by subsequent oxidation of Hg^0 ð Hg^{2+} + 2e. Complexing of Hg^{2+}, e.g. with SH-groups of the saliva proteins, redox reactions between Hg^0 and sulphur-containing proteins, but also methylations may occur as subsequent reactions in the body. All organisms contain enzymes for methylation. Methyl corrinoid derivatives, such as methyl-vitamin B_{12} can function as methylating agents.

Reaction routes of this type do not, of course, apply to microscopically detectable fragments of amalgam fillings. These pass almost unchanged through the gastro-intestinal tract.

In the further research and assessment of the role played by amalgam fillings for human health, the different binding forms of mercury and its transformation possibilities must be taken into account in addition to closer monitoring of the input routes (such as, for example, saliva).

Acknowledgements

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