

High-Dilutions as Mercury's Chelating Agent

Abstract

Background: Mercury (Hg) is one of most relevant toxic metals. High Hg concentrations in professional environments are detected. During years they have been searching forms to decrease heavy metals toxicity in vivo using chelating agents or other competitive substances. The same toxic metal high-dilutions, shows its effectiveness, even pre or post treated poisonings. Homeopathy can act controlling metal poisoning levels in leaving organism.

Objectives: This work proposal was to evaluate the homeopathic medication action during Hg contaminated patients' treatment, observing mercury concentration in different tissues.

Methods: 52 patients were evaluated clinical and laboratorial. They had been selected and distributed blindly and at random in 2 groups Placebo and Mercurius solubilis. The choice of the homeopathic medication was made from the similitude homeopathic principle. Those patients had been submitted to the Hg blood, urine and in the hair analyses and life quality questionnaire (SF36) before the beginning of the treatment, in 30 and 60 days also.

Results: By the end of the treatment it had a significant Hg hair level reduction in those individuals treated with homeopathic medication, beyond the presence of indications of the increase Hg urinary elimination and improvement of aspects of the quality of life as functional capacity, vitality and reduction of painful sensation.

Conclusion: This study showed that Hg high-dilution was effective in treating mercury contamination, without collateral effects as chemical agents. Further studies with a bigger population are necessary to a greater comprehension about the effectiveness of the homeopathic treatment.

Keywords: Homeopathy; High-dilutions; Mercury poisoning; Occupational contamination

Research Article

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Introduction

Metals are probably the toxic elements that human beings have known longer than any other. We have used mercury (Hg) since ancient times [1]. In 370 A.D. Hippocrates described abdominal cramps in workers who extracted metals and Pliny the Elder (23-79) refers to mercury and arsenic poisoning [2]. In fact, Hippocrates was concerned with environmental contamination in his medical practice. Some of his principles of epidemiology and therapeutics influenced Hahnemann's work and were discussed by Paracelsus and later by Robert Boyle, who focused on "emanations" as the cause of illness (Hunter & Davis, 2000). In 1830 Hahnemann listed approximately 1,260 different symptoms related to mercurial intoxication [3]. Literature has shown the risks of excessive Hg-occupational exposure. In Brazil, industrialisation spread the use of the metal in urban centres. High mercurial concentrations have lately been detected in work environments, particularly dental surgeries [2].

Mercury is a non-essential, toxic and cumulative element, and mercury compounds' toxicity varies according to chemical form, means of intoxication, dosage and time of exposure [4]. Urban workers may become Hg-contaminated through the use of agro-toxic substances containing *chlorine-alkalis*, the industrial

production of Hg-lamps and medical equipment, and the sterilisation of surgical equipments with mercury tensiometres and the handling of dental mixtures containing Hg [5]. Mercury is a potent enzyme inhibitor, with high affinity for -SH groups, high-molecular-weight proteins with membrane structural function [6].

It has recently been observed that early nephro and neurotoxicity may develop as a result of Hg poisoning depending on the sensitivity and susceptibility of each subject [7]. Studies have established a protocol to evaluate the neuro-toxic effects of dental workers' exposure to Hg amalgam [8]. These studies have shown neuropsychological and behavioural alterations, including under low, but prolonged exposure [1].

Blood, urine and hair are available biological materials and provide reliable indicators for evaluating the extension of Hg contamination [2]. Due to its biochemical constitution as tissue, hair is exposed to the organism's internal metabolic environment, including blood, lymph and extracellular fluids [9]. It is assumed that Hg concentration in the hair is proportionate to that in the bloodstream, reflecting the general organic contamination of this metal. Hair mineralogram is an examination of human tissue that tends to accumulate biological minerals and toxic elements

in its protein structure. It is considered to be a reliable biological indicator of contamination by toxic metals because it enables study physicians to evaluate Hg concentration over time [2] via such techniques as cold vapour atomic absorption spectrophotometry, which causes the mercury contained in the biological material to be released. Hg hair concentrations compatible with the appearance of symptoms vary between 50-125µg/kg, reflecting plasmatic concentrations compatible with the initial effects of the intoxication, such as paresthesia [9].

Mercurial blood concentration tests indicate exposure to organic and inorganic Hg, which may have been caused by the consumption of contaminated food products. This test should be conducted early because mercury remains in the bloodstream for only a few days after exposure [10].

Mercury can be removed from the organism by chelating agents via the formation of a chemical complex which includes the metallic atom. This compound is eliminated by renal excretion. Initial chelation was accomplished using BAL (2,3-dimercaptopropanol or dimercaprol - British Antilewisite), CaNa₂-EDTA (calcium disodium edentate) and penicillamine with toxic allergy-like reactions, renal damage and haematological alterations. In recent years DMSA (dimercaptosuccinic acid) and DMPS (sodium dimercaptopropanesulfonate) have been used in hastening removal of mercury compounds [1], but they have caused side effects in approximately 42% of patients [11].

A promising strategy to prevent harmful effects is the use of ultra dilutions of these substances, which induces tolerance and cellular recovery. This phenomenon is known as "protective hormesis" (stimulant effect of ultra dilutions) and occurs in several organic systems and with various chemical components [12]. The same substance that caused an imbalance in organic homeostasis or pathology will help in the recovery of such processes. In French and Brazilian studies, low centesimal potencies (such as 7CH, 15CH, 30CH) of toxic metals are used as chelating agents [13,14]. Patients usually respond well to therapeutic testing when administered low decimal doses such as 3D, 5D, and up to 60D in some cases [15].

The study of ultra dilutions in experimental toxicology initially assessed the *in vivo* effect of using dynamised Hg to protect Hg-induced intoxication. Studies with mice submitted to HgCl₂ in high dilutions (10⁻¹⁸ and 10⁻³⁰) showed an ultra dilution protective effect against induced acute mercury intoxication [16-18]. The different dilutions studied have a particular action in chronic tissue metal deposit. This phenomenon was observed even in those animals whose urinary elimination had ceased weeks before during the intoxication process [13]. An ultra diluted dose of HgCl₂ used as pre-treatment in fibroblast cellular culture showed a significant protective cellular response to an intoxication caused by the substance itself [19,20]. Pre-treatment with infinitesimal doses administered intraperitoneally, subcutaneously and orally reduced mice mortality. The tolerance these animals acquired after being preventively treated with high dilutions of such metals as Hg, Cd, As and Pb proved to be not a local but a systemic reaction [21].

Objectives

General objective

To evaluate the effectiveness of ultra dilutions as toxic metal mobilising agents.

Specific objectives

- To evaluate the effectiveness of ultra-diluted *Mercurius solubilis* in the treatment of mercury contaminations.
- To study the behaviour of two ultra-diluted *Mercurius solubilis* potencies (7CH and 12CH) in the treatment of occupational mercury contaminations.

Methodologies

Casuistic methodology

The study was conducted with 52 patients presenting mercurial contamination, randomly selected and blindly distributed into two different groups: one receiving homeopathic medication *Mercurius solubilis* (7 CH and 12 CH) and the other a placebo. Sampling was heterogeneous regarding age (over 18), gender and race.

The study lasted for 60 days, with two returns (every 30 days) to evaluate the evolution of Hg blood, urine and hair concentrations concurrently with the patient's general state of health. It included occupationally exposed Hg-contaminated patients in good clinical conditions and with initial Hg urinary dosage lower than the maximum biological index allowed in Brazil (which, according to its Ministry of Labour, is 35µg/ml of urinary creatinine for dental professionals and workers).

The following patients were excluded: those who had, during the six months preceding the study, taken any medication that might have affected their tissue Hg content, such as EDTA, BAL, DMSA, etc; and those who did not comply with the protocol, either for not taking the medication as instructed or for not returning to the following appointment.

Collection and analysis of biological materials

Blood, urine and hair samples were collected before the beginning of treatment (T1). After the 30 first days (T2) new blood, urine and hair analyses were performed. Patients continued the treatment for another 30 days (T3) using the same dosing and administration, i.e: 7 days taking medication, 14 days of interruption, then another 7 days of medication. A clinical and laboratory re-evaluation of the patients was conducted subsequently.

The methodology applied to read blood, hair and urine samples was that proposed by Laszlo Magos and Thomas W Clarkson [22], modified for hair analysis. Determination of hair Hg concentration was obtained via cold vapour atomic absorption spectrophotometry (CV-AAS). The equipment used was a model-1255 LDC Analytical Mercury Monitor (LDC, Riviera Beach, FL) connected to a model-3435 HP multimeter (Hewlett Packard, Palo Alto, CA) and a Neptune Dyna bomb (Magnetek Universal

Electric, USA). HG measurement accuracy was ensured by the use of hair international standards provided by Hair Mercury Comparison Program (Ottawa, Ontario, Canada). The analyses were conducted in the Environmental Chemistry Laboratory of the University of Brasília (Brazil). Urine and hair were analysed in Hg monitor via cold vapour atomic absorption spectrophotometry (CV-AAS) and evaluated by different types of spectrographic equipment, given the different Hg levels in the samples. Blood was analysed in a cold vapour fluorescence device in a flux injection system.

The study physician did not know that part of the patients had been assigned ultra diluted *Mercurius solubilis* (7CH and 12CH) and that the control group had been administered with the inert medium. Both homeopathic remedies and placebo doses were initially given to patients during 7 consecutive days, 7 drops, twice a day. Medication was interrupted for 14 days (during the homeopathic aggravation phase according to Kent's dynamic clinical prognosis [23, this therapy being repeated for a further 7 days).

The medications used in this protocol were in accordance with the prevailing regulations of Decree 57.477/65, which provides for the handling, pharmacopoeia, industrialisation and sale of homeopathy-related products, administrative rule 1180 dated August 1997, concerning the 2nd edition of the Brazilian Homeopathic Pharmacopoeia and resolution 23, dated 6 of December, 1999 and issued by the Brazilian Bureau of Sanitation Surveillance.

Therapeutic methodology

Mercurius solubilis was prepared in potencies 7CH (10^{-16} M) and 12CH (10^{-24} M), diluted and dynamised according to the Hahnemanian centesimal scale method and the Brazilian Homeopathic Pharmacopoeia.

Highly-diluted $HgCl_2$ solutions were prepared and provided by the homeopathic pharmacist in charge. The homeopathic medication was prepared by grinding 1g of $HgCl_2$ with 99g of lactose for one hour in a porcelain mortar. The first dilution (10^{-2} or 1CH) was obtained at the end of this hour. The second potentisation/trituration (10^{-4} or 2CH) was obtained by taking 1g from the first potentisation (or first trituration) and once more adding 99g of lactose. The same procedure was repeated to obtain the third potentisation/trituration (10^{-6} or 3CH). Next, to obtain the fourth dilution (10^{-8} or 4CH) in the fluid phase, 1g from the third potentisation/trituration was taken and diluted in a 20% aqueous alcohol solution, after which it was strongly shaken 100 times (this process is also known as "succession" in homeopathy). To obtain the desired dilutions and potentisations from the fifth dilution on, 1g from the previous fluid was taken and 99g of a 70% aqueous alcohol solution was added, after which each solution was shaken 100 times [24].

Statistical methodology

The study's interest lay in the comparison of the data obtained from the three different groups at three different moments (pre-treatment, and at 30 and 60 days). Therefore, the statistical

method chosen was a Linear Model with Repeated Measures, using the structure of adequate variances according to the data. Two groups were taken into consideration: placebo and homeopathic medication. The patients treated with *Mercurius solubilis* were analysed ensemble, regardless of the homeopathic potency they were taking (7CH or 12CH). This method allowed comparisons both between the groups and among the different moments of the study [25].

Results

The study was conducted with 52 Hg-contaminated patients: 22 males and 30 females. Blood, urine and hair analyses were performed for diagnostic confirmation of the contamination symptoms and were repeated 30 and 60 days after the medication was administered. The subjects were divided into two different groups:

Group I: Placebo (n = 28)

Group II: Homeopathic medication *Mercurius solubilis* (n = 26)

Identification and clinical data

The subjects presented very similar heights and ages: the majority were approximately 1.7 metres tall and aged around 40 (Table 1). On average, the intoxication period of the patients in the placebo group (12 years) was slightly longer than that of the group taking medication (9.2 years). However, in the former group the percentage of patients who had previously received treatment (8%) was lower than that in the medicated group (15.4%), which also showed a higher percentage of patients with lesions (22.7%) than the placebo group (16.7%) (Table 1).

Table 1: Sample characteristics.

Variable	Group		P
	Placebo	Medication	
Age (years; average \pm SD)	40.2 \pm 10.1	41.6 \pm 12.5	0.653
Height (meters; average \pm SD)	1.70 \pm 0.09	1.67 \pm 0.06	0.319
Period of intoxication (years; average \pm SD)	12 \pm 12.8	9.2 \pm 8.0	0.370
Gender (% of males)	46.2	38.5	0.575
Previous treatment (% yes)	8.0	15.4	0.686
Presence of lesion (% yes)	16.7	22.7	0.605

Comparison of variables related to identification and qualitative clinical data

The T-student test was used for the comparison of the variables (age, height and time of intoxication) between the two groups. Since for all the situations observed the significance level had values greater than 0.05 ($p > 0.05$), it can be concluded that there is not a statistically significant difference among averages of age, height, period of intoxication, presence of previous treatment and presence of lesion between the two groups. The Qui-square

testing was used for the qualitative variables in order to study any likely association between the classes of characteristics and the groups. There were no such associations between the variables and the groups, which indicate that the percentages for the placebo and medication groups were similar.

Comparison of laboratory parameters

The repeated measure variance analysis technique was applied to the following comparisons since they were made between the groups at different moments. The test characteristics were the same as those previously described.

Statistical evaluation of mercurial urinary concentration

There was no statistically significant difference between average Hg urinary concentration values between the groups, not even between the rate standard deviations ($p > 0.05$). However, there is evidence of increased Hg urinary excretion in the medication group around the 30th day of treatment, a tendency which decreased subsequently.

Statistical evaluation of blood mercury concentration

There was no statistically significant difference between average Hg blood concentration values between the groups, nor between the moments. Hg serum concentration in the studied period of time did not prove to be a reliable indicator for assessing the treatment, since it does not distinguish between the groups.

Statistical evaluation of hair mercury concentration

The significant differences ($p < 0.05$) of hair rate averages above were among the moments studied and between the groups. Concerning the groups, in all samples the average value was smaller in the medication group. Multiple comparisons between main effects were performed in order to identify at which moment values differed from one another. There is no difference only between the values at 30 and 60 days, and the initial value is different from that obtained from the two other samples (30 and 60 days).

Discussion

High concentrations of both essential and non-essential metabolic elements can accumulate in the body until toxic levels are reached. Out of non-essential elements Hg is one of the most harmful to human health.

Mercurial intoxication can be analysed from two basic sides, both directly related to health: one is the environmental destruction and the other is the genetic damage caused to human beings, particularly those socially and economically involved in some type of professional activity subject to clastogenic and mutagenic substances and agents [25].

This paper wanted to study the therapeutic use of ultra-dilutions not only taking into account the various parameters of mercurial contamination evaluation but also prioritising treatment in a systemic manner, i.e. observing the validity of its application as mercury's mobilising agent in the tissues.

The fact that individual sensitivity and susceptibility vary in the population should not be disregarded. Damages to health arising from Hg occupational contamination are aggravated by exposure to environmental and other sources of contamination. Intervening variables such as dietary and social habits, hydric contamination, medications, cosmetics, dental amalgam, geographic location and mercury's chemical interaction with other environment components add to the toxic load caused by mercury [26].

Human exposure to Hg can be evaluated by its concentration in tissues and biological fluids. Hg hair level is a parameter for chronic contamination [27].

Early diagnosis and treatment are important to control poisoning evolution in either household or professional environments and prevent such irreversible damages as neurological sequelae [28]. It was observed that the use of ultra dilutions can significantly contribute not only to the biological control of environmental exposure to Hg but also the early treatment of mercurial intoxications.

An effective metal intoxication treatment depends on the therapeutic agent's ability to penetrate intracellular spaces and mobilise the metal deposited there. This study assessed the toxic metal tissue mobilisation caused by the use of ultra diluted medication.

When ultra diluted remedies follow the principle of similitude they may trigger certain phenomena that accompany the dynamic process of cure. These reactive variants, such as the positive excretory response to Hg, which was observed around the 30th day of treatment, may have diverse origins. Patients taking *Mercurius solubilis* presented increased Hg urinary excretion followed by decreased mental symptoms.

Infinitesimal doses of toxic metals can trigger the elimination of the same toxin from the organism. Patients rapidly present improved clinical conditions and quality of life without classic chelation's inconvenience of depleting essential minerals from the organism. Orally-administrated infinitesimal doses have proven to be efficient, rapid and risk-free [13,29,30].

In his study on the relation between infinitesimal doses and the kinetics of elimination, Wurmser [13] showed in experiments with mice that ultra dilutions of a given toxic substance can trigger the elimination of the same toxin from the organism. The toxic element becomes "motile" and is eliminated by the action of these low doses. The tissue cells that had been previously sensitised by the toxin during the intoxication process begin to be desensitised by the homoeopathic medication [30]. This study observed biological signs of this desensitisation in the group of patients treated with the ultra diluted homoeopathic medications *Mercurius solubilis* 7 CH and *Mercurius solubilis* 12 CH.

Under a cellular-level isopathic point of view, self-recovery may be triggered by the use of ultra dilutions of the same substance that led to imbalance in the organism. This stimulant effect will manifest in a growing activity of the cellular expression of protective proteins' genetic program, supplementing their cellular production with subsequently increased resistance to the aggressive agent [31].

The residual elimination caused by the homeopathic medication represents from 5 to 10% of the toxic metal in the organism [13,30] and favours the likelihood of ultra diluted solutions being used in challenge testing. This study observed increased Hg urinary elimination, thereby suggesting this type of residual elimination.

In the last decades, reports on the action of ultra diluted chemical, biological and physical agents have become increasingly common. Ultra dilutions of substances coming from cytokines, hormones, minerals and biological tissues have been used to influence the immune system by inducing a protective and restorative response of cells [32]. This study evaluated the efficacy of ultra diluted quantities of the toxic metal itself in the treatment of Hg poisoning.

Patients usually responded well to therapeutic testing with low potencies of ultra diluted remedies, such as D3 and D5, but ultra dilutions may reach D60 in some cases. This study observed the effect of ultra diluted homeopathic medications *Mercurius solubilis* 7 CH and *Mercurius solubilis* 12 CH on the reduction of Hg tissue concentrations.

Hormesis is the stimulant effect of subinhibitory concentrations of toxic substances on a living organism, a non-specific phenomenon that enhances the latter's resistance and growth. This 'action v. reaction' model suggests the efficacy of vital force activity in combating intoxications [33]. *Hormesis* refers to the observation of those phenomena occurring on a living organism when they are exposed to high doses [32]. This study observed decreased concentration of Hg hair contamination followed by increased Hg urinary elimination (Figures 1-3).

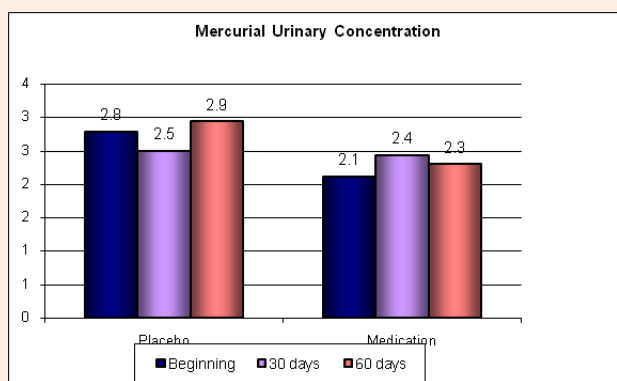


Figure 1: Hg Urinary Concentration in the control group and in the group receiving homeopathic medication.

The dynamic nature of ultra diluted medications can be interpreted as an informative action between similar structures. The medication carries a fraction of the information that has affinity with the organism. It is a real process of communication, in which the biological system interprets the information it receives. The medication thus informs the organism about its intrinsic organisation and triggers the organic response seeking *homoestasis*.

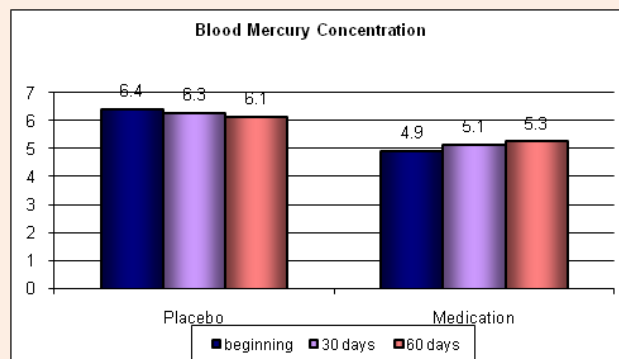


Figure 2: Hg Blood Concentration in the placebo group and in the group receiving homeopathic medication.

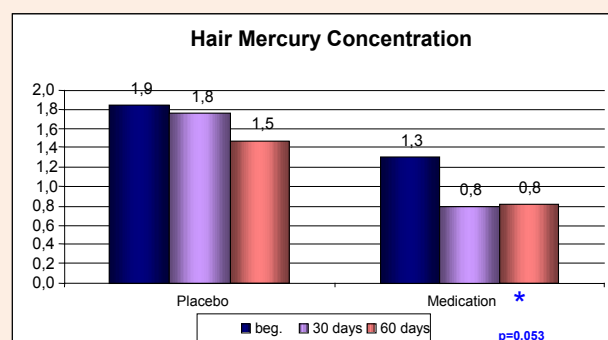


Figure 3: Hg concentration in the hair of the patients in the control group and in the group receiving homeopathic medication. *ANOVA with repeated measures. P<0.05 for the difference between the groups at the beginning and at 30 and 60 days of treatment.

To search for high dilutions' action mechanism requires an approach of physical, molecular and biological nature. Physical and molecular aspects intervene in the solvent via the potentiation, which justifies the specific action of potentised medications. Biological aspects suggest the pharmacodynamic interaction between medication and biological receptor. Several research models have been developed based on this physical-molecular, biological and clinical view, but none of them has been able to include all the integrated mechanisms of these diverse areas in a single paradigm that explains the complex interaction between biological the phenomenon and the medication potentised in a high dilution. Even though there are still many questions to be answered by following papers on this matter, this clinical essay observed this interaction of physical aspects (potentised medication), molecular aspects (use of same poisoning substance) and the impact of these aspects on the biological material (reduced Hg concentration in the hair).

Metal dilutions' protective effects on the treatment of poisoning with the same metal were shown by the law of identity [13]. In theory, the most sophisticated concept used in association with ultra dilutions is related with the identity law, which governs the stimulant and/or intoxicating nature of substances.

This concept is utilised to explain in the both theory and the homeopathic principle of similitude, based on the assumption that a living organism can reach an 'Organiser Response' capable of stimulating metabolism at various levels. This is the reason why increased Hg urinary elimination (Figure 1) was observed during the study when the last *Mercurius solubilis* (7 CH and 12 CH) ultra dilutions were administered, followed by reduced Hg concentration in the hair of patients after treatment.

Apart from showing significant signs of homeopathic medications' real therapeutic usage in individual toxic situations, the results obtained in this study suggest that Homeopathy can be used in large scale in public health helping in the prevention and treatment of populations exposed to environmental contamination. This concept can also be applied to labour medicine minimising either preventively or therapeutically the impact of likely workers' intoxications.

Conclusion

The results suggest that homeopathic medications are effective as toxic metals' chelating agents by which mobilise Hg-contaminated tissues. The study observed reduced Hg concentration in the hair of patients and increased Hg urinary elimination.

Homeopathic solutions *Mercurius solubilis* proved its efficacy in the treatment of mercurial contamination. Both *Mercurius solubilis* potencies (7 CH and 12 CH) observed during the study were effective in the mobilising the toxic metal. At the end of the treatment, there was a reduction of Hg pathogenesis-related symptoms reported by those patients receiving ultra diluted medication in comparison with the placebo group. The group treated with the homeopathic medication showed improved quality of life, thus suggesting its efficacy.

The use of ultra dilutions in the treatment of intoxications causes a residual elimination of the toxic material. Homeopathic medication can be used in challenge testing for the diagnosis of metal poisoning, which opens new fields of application for homeopathy in toxicology and epidemiology.

References

- Faria Mde A (2003) Chronic Occupational Metallic Mercurialism. *Rev Saude Publica* 37(1): 116-127.
- Pascalichio AAE (2002) Dialogo Between public health and orthomolecular medicine: a case study of the contamination by heavy metals, in the human perspective, through the capillary mineral gram. Doctoral Thesis USP, Faculdade Pública, São Paulo, Brazil, p. 90.
- Bonnivair G (1971) Read intoxications. *Homoeo France* 59 (6): 323-333.
- World Health Organization (WHO) (2003) Elemental Mercury and inorganic Mercury Compounds: Human Health Aspects. Concise International Chemical Assessment Document 50, WHO, Geneva, p. 1-68.
- Rossini SR, Reimão R, Lefèvre BH, Medrado-Faria MA (2000) Chronic insomnia in workers poisoned by inorganic mercury: psychological and adaptive aspects. *Arq Neuropsiquiatr* 58(1): 32-38.
- Olszewer E, Smith B, Laganá S (1998) Manual of interpretation of the mineralogram: examination of the hair. Tecnopress Sao Paulo, Brazil.
- Viveiros M (2002) *Jornal a Folha de. Sao Paulo, Brazil.*
- Aposhian HV (1983) DMSA and DSP- Water soluble antidotes for heavy metal poisoning *Ann Rev Pharmacol Toxicol* 23: 193-215.
- Watts DL (2003) *Trace Elements and Other Essential Nutrients.* Dallas, USA.
- NRC (2000) Toxicological effects of methylmercury. National Research Council, Washington, USA.
- Schuurs A, Exterkate R, ten Cate JM (2000) Biological mercury measurements before and after administration of chelator (DMPS) and subjective symptoms allegedly due to amalgam. *Eur J Oral Sci* 108(6): 511-522.
- Gaddipati JP, Rajeshkumar NV, Grove JC, Maharaj SV, Centeno JA, et al. (2003) Low-dose cadmium exposure reduces human prostate cell transformation in culture and up-regulates metallothionein and MT-1G mRNA. *Nonlinearity Biol Toxicol Med* 1(2): 199-212.
- Wurmser L (1957) Influence des doses infinitesimales sur la cinétique des eliminations. *Les laboratoires homeopathiques de France, France, p. 1-17.*
- Leite LB (1998) Study on patients intoxicated by lead and treated with homeopathic preparation. Institute of Biosciences, Botucatu, Brazil.
- <http://www.naturmednet.de/Studien?detox.htm>
- Delbancut A, Barouillet MP, Cambar J (1993) Evidence and mechanistic approach of the protective effects of heavy metal high dilutions in rodents and renal cell cultures. *Montpellier, France, p. 71-82.*
- Laure F, Cal JC, Guillemain, Cambar J (1985) Influence of the diluting factor on the protective effect of *Mercurius corrosivus* on the toxicity induced by mercuric chloride in mice. *French Homeopathy* 73: 375-380.
- Bastide M, Boudard F (1994) Scientific research in homeopathy. *Ver Port farm* 44(3): 1994
- Boiron J, Abecassis J, Citte J, Bernard AM (1981) L'étude de l'action de dilutions hahnemanniennes de chlorure mercurique sur l'index mitotique de cultures de cellules animales. *Ann Homeo Franç* 23(3): 43-49.
- Cotte J, Bernard A (1983) Effects de Hahnemannian Dilutions of *Mercurius Corrosivus* on the Multiplication in Culture of Fobroblasts Entangled by Mercuric Chloride. *Aspects of Homeopathy Research* 1: 1983.
- Yoshikawa H (1970) Preventive effect of pretreatment with low dose of metals on acute toxicity of metals in mice. *Ind Health* 8: 184-191.
- Clarkson TW (1989) Mercury. *J Am Coll Toxicol* 8: 1291-1296.
- Kent JT (2002) *Lições de Filosofia Homeopática. (2nd edn), Organon, Sao Paulo, Brazil.*
- Atheneu (1997) *Pharmacopeia Homeopática Brasileira. (2nd edn), General Methods. São Paulo, Brazil.*

25. Gonçalves A, Ferrari I, Barbosa A, Serra O, Padovani CR (1998) Maternal-infant evolution of mercury contamination: study in two Brazilian indigenous populations. *R bras Med* 55: 612-620.
26. Glina Débora MR, Satut Blanca TG, Andrade Esther MO (1997) A exposição ocupacional ao mercúrio metálico no módulo odontológico de uma unidade básica de saúde localizada na cidade de São Paulo. *Saúde Pública*.
27. World Health Organization (1993) National Institute for Minamata disease, WHO Collaborating Center for Studies on Health Effects of Organic Mercury- Proceedings of the International Symposium on "Assessment of Environmental Pollution and Health Effects from Methylmercury". Convention Hall, Kumamoto National Hospital, Japan.
28. Clarkson TW, Strain JJ (2003) Nutritional factors may modify the toxic action of methylmercury in fish-eating populations. *J Nutr* 133(5 Suppl 1): 1539S-1543S.
29. Sukul A, Sinhabau SP, Sukul NC (1999) Reduction of alcohol induced sleep time in albino mice by potentized *Nux vomica* prepared with 90% ethanol - *British Homeopathic Journal* 88(2): 58-61.
30. Moreira HM (1999) Als Efeitos do acetato de chumbo diluído e dinamizado (preparação homeopática) no tratamento do Saturnismo. *Revista de Homeopatia APH* 64(4).
31. <http://www.giriweb.com/wiegant.htm>
32. Jonas WB, Dillner DK (2000) Protection of mice from tularemia infection with ultra-low, serial agitated dilutions prepared from *Francisella tularensis* - infected tissue. *J Sci Explor* 14(1): 35-52.
33. Cal JC, Larue F, Guillemain J, Cambar J (1986) Chronobiological approach of protective effects of *Mercurius corrosivus* against mercury-induced nephrotoxicity. *Ann Rev Chronopharmacol* 3: 99-102.