

Is mercury really toxic? The way forward for its judicious medicinal applications based on the therapeutic doctrines of Ayurveda

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Mercury-based formulations have been extensively used in Indian and Chinese systems of medicine with high therapeutic index. However, at present mercury is considered as a global pollutant having potent neurotoxic effects. Also, it has been proposed to ban the export, import and manufacture of a range of products containing mercury from 2021. This situation compels one to ponder how mercury-based formulations were safe during ancient times, but are now considered to be toxic. Naturally mercury occurs in three forms, viz. elemental (Hg), inorganic (HgS, HgCl₂) and organic (MeHg). Organic mercury is completely absorbed by gastrointestinal tract, and elemental mercury is 75–80% absorbed by the lungs only in vapour state, while 10% of inorganic mercury is absorbed by the gastrointestinal tract. Additionally, organic mercury crosses the blood brain barrier and placenta, producing neurotoxic symptoms and foetal toxicity. In Ayurvedic science, mercury is converted only into inorganic form with special stabilization technology and this stabilized mercury is converted to mercuric polysulphides under gastrointestinal conditions, whereas elemental mercury is converted to organic form by specific bacteria. Thus mercury available in the atmosphere is converted into organic form that is highly toxic, while using Ayurvedic methods it is converted to inorganic form having potent therapeutic activity. Judicious and injudicious application of mercury has advantageous and disadvantageous effect respectively.

Keywords: Ayurveda, mercury, neurotoxic effects, pharmacokinetic profile, stabilization.

MERCURY is a hazardous metal causing serious health problems¹, especially in children and during embryonic development². A study showed that more than 2265 individuals had died and infants were born with severe developmental disabilities due consumption of fish contaminated by mercury³. The United States Environmental Protection Agency reported that mercury is a potent neurotoxic that negatively impacts human health and envi-

ronment around the world⁴. The agency has also started mercury policy project (MPP) to eliminate its use, reduce its export and trafficking, and significantly reduce mercury exposure at the local, national and international levels⁵. The European Commission estimates current mercury demand at 260–400 tonnes/year and projects that it will be reduced up to 40–220 tonnes/year in 2025–2030. It is proposed to ban the use of new products containing mercury in manufacturing processes from 2018, restricted use in certain manufacturing processes in dental amalgam from 2019, and ban the export, import and manufacturing of a range of products containing mercury from 2021 (ref. 6).

Ancient Ayurvedic scholars were attracted to mercury for its positive characters; they were also aware of its negative impacts (toxicological profile)⁷. In *Samhita* period (800 BC–200 AD) mercury (or its compounds) was rarely used for the benefit of mankind, in spite of its therapeutic value. However, with the development of *Rasa Shastra* procedures like *Shodhan*, *Maran*, etc. it was frequently used for therapeutics. In the medieval period, mercury (or its compounds) was used for the treatment of common disorders such as *jwara* (fever), *kasa* (cough), etc. to critical situation. It is also used in the Chinese system of medicine for therapeutic purposes⁸.

The herbomineral compound containing silver, mercury, sulphur and arsenic trisulphide has been used for the treatment of leukaemia, without any side effects^{9–11}. After critical analysis of ancient and contemporary document on mercury, there is a state of dilemma that mercury is blessing for mankind or not, so a hypothesis is assumed that mercury is boon for human.

Materials and methods

To find out if mercury is a boon or bane, we searched various domains of knowledge such as Ayurvedic science, contemporary medical science, environmental science, etc. along with World Health Organization (WHO) documents, reputed national/international publications and other available resources. After obtaining data we critically analysed mercury and its compounds and their potential role, both positive and negative.

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Table 1. Pharmacokinetic profile of mercury

Mercury	Elemental (metallic)	Inorganic (mercuric chloride)	Organic (methyl, ethyl)
Sources of exposure	Environmental: volcanic explosions, weathering of rocks, degassing; anthropogenic inadvertent combustion: fossil fuels (coal), waste incineration; industrial gold/silver mining, batteries, switches, fluorescent lights, thermometers, sphygmomanometers; anthropogenic intentional; dental amalgams; ritual and folk medicine.	Environmental none; industrial products disinfectants, antimicrobials alternative; medicines, cosmetics vapour lamps, embalming photography latex paint (pre-1990s). Example: mercuric chloride.	Environmental conversion fish and shellfish (e.g. methyl mercury); Industrial production fungicides, bactericides (e.g. phenyl mercury); vaccine preservatives (e.g. thiomersal).
Routes of exposure	Inhalation (volatile at room temp): 75–85% absorption; ingestion and skin: almost no absorption.	Ingestion: 10% absorbed; skin: can be high and fatal.	Gastrointestinal: rapid and complete absorption; parenteral: 100% absorbed; transplacental: concentrated in cord blood.
Elimination	Urine and faeces	Renal	Faeces: $T_{1/2}$ 45 to 70 hours
Toxicity	Lungs, eyes, gingival, skin, central nervous system, kidneys, immune system.	Primary: kidneys, gastrointestinal tract; secondary: central nervous system.	Primary: central nervous system; secondary: cardiovascular system.

Source: World Health Organization. Mercury: children's health and the environment. 2008; available from: <http://www.who.int/ceh/capacity/Mercury.pdf>.

Pharmacokinetic profile of mercury

Among the three forms of mercury, viz. elemental, inorganic and organic, 75–85% of elemental mercury is absorbed by the lungs in the form of mercury vapour, organic mercury is completely absorbed by the gastrointestinal tract, while only 10% of inorganic mercury is absorbed by gastrointestinal tract (Table 1)¹².

Observations

From Tables 2 to 4, it can be seen that inorganic mercury (sulphide form) is extensively used in Ayurvedic science; some references for the use of elemental mercury are available, but none for organic mercury^{13–47}.

Discussion

In Africa, artisanal small-scale gold mining (ASGM) is a common practice; it is used for the extraction of gold from its ore through 'amalgamation'. This process is responsible for 37% global mercury emissions⁴⁸; ASGM workers and their families are directly exposed to mercury vapours. In addition, dental amalgam is the main source of mercury toxicity because individuals with amalgam have 2–12 times more mercury in their body tissues compared to those without amalgam. Mercury, particularly mercury vapour, is known to be the most toxic even in very low doses and is non-radioactive⁴⁹. It is reported that approximately 80% of inhaled mercury vapour is absorbed via the lungs⁵⁰; so individuals living in or near an ASGM community and those with dental amalgam suffer from neurologic disorders, kidney and toxic to immune system and autoimmune dysfunction. It

might be possible that these abnormalities occur due to inhalation of elemental mercury vapour. In Ayurveda, only few references are available where mercury (elemental) is used externally (in the form of *lepa*) for therapeutics⁵¹. From Table 1, it is clear that absorption of mercury (elemental) through skin is almost negligible¹². Thus, almost negligible amount of mercury may be entering the body system when it is used externally in the form of *lepa*; this is also supported by contemporary science⁵².

In Ayurveda, mercury is subjected to specific procedures like *Shodhan*, *Samskar*, etc.⁵³, where it is either subjected to triturating by specified liquid medium with specified plant material, or fomentation process. It has been reported that boiling and frying reduced Hg bioaccessibility by 40% and 60% respectively, rendering Hg-protein complexes less available for solubilization during digestion, due to strong affinity for proteins⁵⁴. It might be possible that during the processing of mercury using decoction of plants, it forms Hg-protein complex which is poorly absorbed by gastrointestinal tract⁵⁵ before use of mercury as medicine it is converted into suitable dosages with herbs, metals and minerals and animal product.

Furthermore, before therapeutic use, mercury is converted into sulphide form by mixing solid sulphur with liquid mercury to form *Kajjali* (black powder of mercury sulphide)⁵⁶, or by dissolving mercury in liquid sulphur by applying specific process to form *Parpati*⁵⁷, or in a gas-phase reaction between gaseous mercury and gaseous sulphur with unique equipment (*Kupi pakwa*)⁵⁸. Mercury is converted into a black-coloured mercurial compound (non-stoichiometry mixture of elemental mercury and sulphur permits the formation of meta-cinnabar) in the presence of sulphur through mechanical pressure⁵⁹ and

Table 2. Properties of mercury and mercury-based formulations

Formulation	Form of mercury	Properties
<i>Lelitik prayog</i>	Elemental	<i>Kushtha</i> (skin disorders) ¹³ .
<i>Savarnikaran lepa</i>	Elemental	<i>Savarnikaran</i> (enhancement of skin completion) ¹⁴ .
<i>Lepa</i>	Elemental	<i>Nilika, sphota on mukha roga</i> ¹⁵ .
<i>Poorna chandrodayam</i>	Inorganic	Particle size in the range 60–70 nm; irregular size ¹⁶ .
Mercury preparations	Inorganic	Vital in <i>Siddha</i> medicine for debilitating disease ¹⁷ .
Ayurvedic and Chinese traditional medicines	Inorganic	Mercurial medicine may not pose a problem, unless due to misuse, abuse, over dosage and improper storage ¹⁸ .
Cinnabar	Inorganic	Used as a sedative in traditional Chinese medicine ¹⁹ .
Anxiolytic	Inorganic	High-dose HgS (1.0 g/kg/day) intoxication reduced the activity of Na(+)/K(+)-ATPase in the brainstem neurotoxicity, but toxicity by HgS completely disappears after cessation of its administration ²⁰ .
<i>Garbha chintamani rasa</i>	Inorganic	Improved liver synthetic activity, reduced lipids level and increased kidney function parameters used to improve the complications in diabetic condition ²¹ .
<i>Sidh Makardhwaj</i>	Inorganic	Neurotoxic potency of mercuric sulphide (HgS) is about 1000 times less than soluble methyl mercury (MeHg) ²² .
<i>Hridayarnava Rasa</i>	Inorganic	Safe from genotoxic hazards ²³ .
<i>Swasa kuthara rasa and smriti sagara rasa</i>	Inorganic	Free from genotoxicity abnormality ²⁴ .
<i>Kajjali</i>	Inorganic	Does not have genotoxic potential ²⁵ .
<i>Makaradhwaaja</i>	Inorganic	Attributed to anti-stress activity. Improves the quality of life ²⁶ .
<i>Mahamrutyunjaya rasa</i>	Inorganic	Cardiotonic property ²⁷ .
<i>Rasa sindur</i>	Inorganic	Human gut flora does not convert mercury sulphide into toxic derivatives like methyl mercury ²⁸ .
Mercury in Indian and Chinese systems of medicine	Inorganic	Chronic ailments like syphilis, high fever, pneumonia, insomnia, nervous disorders, deafness and paralysis of the tongue ²⁹ .
<i>Arogyavardhini vati</i>	Inorganic	Does not produce toxicological effects on brain, liver and kidney up to 10 times higher dose ³⁰ .
<i>Rasa sindhura</i>	Inorganic	Increases lifespan and fecundity ³¹ .
<i>Arogyavardhini vati</i>	Herbomineral	Reduces oxidative stress (decreasing MDA and increasing GSH), increases serum HDL level, efficacious in dyslipidemia ³² . Reduces the risk factors of CVD ³⁰ .
<i>Sidh makardhwaj</i>	Inorganic	Does not show toxic effect on brain (cerebrum), liver and kidney ³³ , effective in the treatment of rheumatoid arthritis ³⁴ .
<i>Mahamrutyunjaya rasa</i>	Inorganic	Cardiotonic property ²⁷ .

indicated as single therapeutic agent as well as used in various herbomineral formulations for the treatment of different disorders. Pharmaceutical process of *Kupi pakwa* involves four steps (*Shodhan*, *Kajjali* preparation, *Bhavana* and *Kupi pakwa*). Before the preparation of *Kajjali*, *Shodhan* (purification and potentiation) of mercury, sulphur, etc. is done as mentioned in the Ayurvedic literature. The prepared *Kajjali* is levigated by specified liquid media for a certain period and then filled in glass bottles (*Kachkupi*) followed by indirect and homogenous heating for a certain period⁶⁰. Mercury is then converted into non-toxic, stabilized form and used in therapeutics⁶¹. In Ayurvedic science, compounds of mercury are used along with specified organic liquid media in the form of *Anupana*. It has been reported that foodstuff like green tea, black tea and coffee simultaneously ingested with fish meal (containing mercury) decreased fish mercury bioaccessibility. Thus one can ensure that before the administration of mercury as medicine, it is converted into a form which is least toxic and absorbed to some extent by gastrointestinal tract, so that only small amounts enter the biological fluid that may not show toxic effect.

Three inorganic mercurial compounds are used for therapeutic purposes in Ayurveda, namely chloride (*Rasa*

Pushap, *Rasa Karpura*), sulphide (*Parpati*, *Rasa Sindur*, etc.) and oxide form (*Mridarsing*)⁶². Among them, sulphide form is frequently used. The chloride form is not used because of accumulation and also since it acts as poison when used in excess dose⁵⁸. It is supported by contemporary science that cinnabar (mercuric sulphide) is less nephrotoxic and hepatotoxic than HgCl₂ (*Rasa Pushap*, *Rasa Karpur*)⁶³; this may be due to strong affinity of mercury for the thiol (SH) groups (such as GSH, cysteine), which provide the major intracellular defence mechanism against mercury-induced toxicity. Mercury is useful in many cosmetic preparations in its inorganic form for skin lightening by suppression of melanin production by the skin⁶⁴. Furthermore, inorganic mercury does not pass the blood brain barrier and placenta⁶⁵. Inorganic mercury used in Ayurveda does not enter the brain and does not go into foetal circulation, hence it does not produce any adverse effects on the brain and foetus. It is reported that only 10% of inorganic mercurial compounds are absorbed through the gastrointestinal tract⁶⁶ and therapeutic dose mentioned for sulphide of mercury (inorganic form) is less⁵⁸. So small amount of mercury is available for therapeutic action and it may not show any negative effects.

Table 3. Hazardous effects of mercury

Use of mercury	Form	Hazardous effects
Mercury	Inorganic and methyl mercury	Disrupts the endocrine system ³⁵
Mercury	Elemental	Inhibits the production of neurotransmitters ³⁶
Mercury toxicity	Elemental	Causes damage to the immune system ³⁷
Mercury	Elemental	Damage to kidney ³⁸
Mercury (Hg)	Inorganic mercury	Causes adverse effects on nervous system ³⁹
Mercury	Elemental	Cognitive deficits, liability, fatigue, decreased stress tolerance ⁴⁰
Mercury	Organic	Mental retardation, cerebellar ataxia deformed limbs, hyper-salivation growth disorders ⁴¹
Methyl mercury	Organic	Increase blood pressure ⁴²
Methyl mercury	Organic	Neurotoxic ⁴³
Methyl mercury	Organic	Induces oxidative stress and mitochondrial dysfunction ⁴⁴ , inhibits cardio-protective activity of paraoxonase ⁴⁵ , kidney injuries ⁴⁶ , immune, neurological and behavioural dysfunctions ⁴⁷

Table 4. Indications of mercury based formulations

Formulation	Dosages form	Indications
<i>Rasa sindur</i>	Powder	Bronchial asthma, pleurisy with effusion.
<i>Rasraj rasa</i>	Liquid	Stroke, hypertension, diabetes, erectile dysfunction, oligospermia, kidney disorders, vata disorders.
<i>Rasraj raas</i>	Tablet	Paralysis, hemiplegia, lockjaw.
Destone	Capsule	Urinary tract infections, kidney stones, prostate gland inflammation and leucorrhoea.
<i>Ekanvir ras</i>	Capsule	Paralysis, Bell's palsy, hemiplegia, brachial palsy and sciatica.
<i>Carwin</i>	Capsule	Deep-seated wounds; tumours; loss of appetite, diminished growth, strength and vital elements along with haematopoiesis; physical and general ill-health due to radiation and chemotherapy.
<i>Addyzoa</i>	Capsule	Increases sperm count and motility; improves sperm morphology (prevents DNA damage to sperms); increases sexual desire.
<i>Rasa sindur</i>	Powder	HIV-AIDS.
<i>Brento</i>	Tablet	Impaired cognitive function, improves overall mental, performance, memory, concentration and learning abilities.
<i>Mahayograj guggul</i>	Tablet	Used in muscular-skeletal disorders; maha yogaraj <i>guggul</i> is not only anti-inflammatory and safe in the long run, but it medicinal herbs strengthen the system and extend remission.
<i>Rhumayog</i>	Tablet	Coronary insufficiency and ischaemic heart disease; the oleoresin of guggul has a cholesterol-lowering effect. It also has hypolipidaemic and anti-inflammatory effects.
<i>Vrihat Vatchintamani rasa</i>	Tablet	Improves sensory and motor performance in chronic neurological conditions such as hysteria, insomnia and paralysis.
<i>Purnachandra rasa</i>	Tablet	Rejuvenator; improves strength, stamina and energy.
<i>Vasanti Kusumakar rasa</i>	Tablet	Diabetes, diabetic carbuncle, diabetic neuropathy, diabetic retinopathy.
<i>Trailokya chintamani rasa</i>	Tablet	Chronic and recurrent respiratory tract infections such as influenza, pneumonia, cachexia, emaciation associated with fever.

Source: ref. 76.

Ingested mercury on the effect of gastrointestinal tract

It has been reported that MeHg is not formed in human intestinal flora under anaerobic conditions because of the low redox potential from cinnabar, HgS or HgCl₂ (ref. 67). The intestinal bacteria may produce soluble mercuric polysulphides from HgS instead of methylmercury⁶⁸. It was found that cinnabar is most likely converted into mercuric polysulphides under simulating gastrointestinal tract condition and that the latter exhibited relatively high membrane permeability as well as high affinity to plasma protein, but low cytotoxicity in HK-2 cells²⁸.

The Minimata disaster in Japan was due to the release of industrial wastewater containing mercury into the Minimata Bay, where it was converted to methyl mercury (MeHg) by bottom sediment microorganisms in the aquatic environment and entered the ecosystem through the food chain⁴³. The methyl mercury can be biomagni-

fied rapidly, leading to high concentration in top predators in the aquatic ecosystems⁶⁹; i.e. higher concentration of MeHg is present in humans because, they are usually the top predatory in many food webs⁷⁰. When people of particular region consumed contaminated fishes, they exhibited signs of neurological damage; their offspring were also severely affected by such disorders, because this form of mercury is completely absorbed by gastrointestinal tract and higher mercury levels are available in the biological fluid that may be responsible for such adverse effects. MeHg causes imbalance in calcium homeostasis due to dysregulation of intracellular calcium stores and/or increased permeability of the biomembranes to this ion⁷¹. It preferentially accumulates in astrocytes and inhibits glutamate uptake causing neuronal dysfunction⁷². MeHg and glutamate concentrations lead to the typical appearance of neuronal lesions associated with toxic stimulation⁷³. MeHg causes neurotoxicity induced by the formation of reactive radicals. It also causes oxidative stress, resulting in

CNS damage by several interacting mechanisms, including mitochondrial damage with increase in intracellular free calcium ion, activation and inhibition of enzymes, release of excitatory amino acids, metallothioneins expression, and microtubule disassembly⁷⁴. It inhibits mitochondrial enzyme and subsequently depolarizes mitochondrial membrane, thus reducing ATP production⁷⁵.

Conclusion

Thus, the rational use of mercury in its inorganic form (HgS, HgCl₂) will be beneficial for humans and wildlife, whereas irrational use in the organic form (MeHg) will produce hazardous effects.

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