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INTERNATIONAL CENTRE FOR ENVIRONMENTAL AND INDUSTRIAL TOXICOLOGY (ICEIT)

CRI's ICEIT has been designated as a
"UNEP Centre of Excellence for Environmental and Industrial Toxicology".

Manganese and Related Neurotoxic Pathways

Neurodegenerative diseases comprise a group of disorders characterized by progressive loss of neurons over a period of time due to various factors such as oxidative stress, inflammation, accumulation of toxic proteins, excitotoxicity, and metal overexposure.

Among those, acute overexposure of manganese (Mn) causes manganism and its chronic overexposure causes extrapyramidal effects characteristically similar to Parkinson's disease (PD), including hypokinesia, rigidity, and tremor.

The present review typically focuses on how overexposure to- and excessive accumulation of Mn can lead to the activation of various neurotoxic pathways such as oxidative stress, apoptosis, excitotoxicity, protein misfolding, and inflammation which are the causative factors of various neurodegenerative diseases.

Further, the source of Mn exposure, various transporters, and its kinetics inside the human body is compiled.

Mn is found mainly in fruits, nuts, green leafy vegetables, brown rice, soybean, whole wheat bread, tofu, sweet potato, beans and drinking water. It is not produced by the human body.

Mn^{2+} and Mn^{3+} are mainly found in living bodies and it is the 4th most widely used heavy metal in the world. It is physiologically required to perform various functions. However, its excessive accumulation in the body can cause toxicity.

Mn can enter the human body mainly via two routes: the oral route and the inhalation route. There are various transporters known to transport Mn. Mn^{3+} is transported via transferrin receptors (Tf R) localized on the neuronal cells, that are common transporters for Mn and iron. Mn^{2+} utilizes a divalent metal transporters1 (DMT1) to cross the blood-brain barrier which is encoded by the SLC11A2 gene and regulates the transport of metal ions. DMT1 transporters are also present on nasal epithelial tissues that allow Mn to enter brain cells via the olfactory nerve. Mn transport also occurs through capillary endothelial cells of blood-brain barrier (BBB) and olfactory epithelium which leads to its accumulation in the basal ganglia of the brain.

The deleterious effect of manganism in humans is mostly dependent on physiological variations between sexes, ages, and health issues. Toddlers and children are the most vulnerable to manganism as their excretion mechanisms are less effective and their gastrointestinal tract is more capable of absorbing the metal. Additionally, their BBB is highly permeable to Mn, which adds to the vulnerability of manganism to them.

Mn is used in a wide range of industrial processes and commercial products. Mn is also incorporated into fungicides, such as maneb and mancozeb. Occupational exposure to Mn is the primary cause of human Mn intoxication.

Chronic exposure to Mn is highly linked with neurodegeneration characterized by motor defects and verbal and cognitive impairment. Mn can easily cross the BBB, enter neurons, and disrupt normal homeostasis by causing oxidative stress and inflammation.

Mn overexposure leads to mitochondrial dysfunction by inhibiting the

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Manganese and Related Neurotoxic Pathways

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complexes of electron transport chains, thus generating oxidative stress. It also alters calcium homeostasis, dysregulate enzyme activity, and an imbalance in neurotransmitters level like dopamine and serotonin.

Mn overaccumulation causes glutamate-mediated excitotoxicity by impairing the glutamate aspartate transporter (GLAST) receptor, which is responsible for the uptake of extracellular glutamate into the astrocytes.

Mn in excess converts the monomer form of α-synuclein into oligomers that are toxic to neurons. Furthermore, it increases the exocytosis of misfolded α-synuclein, which activates microglia, chemokines, and proinflammatory cytokines.

The relationship between Mn overexposure and pathogenesis of PD, Huntington's disease (HD), and Alzheimer's disease (AD) has been discussed.

The symptoms of manganesemia are similar to those of other neurological disorders like PD, HD, AD, and amyotrophic lateral sclerosis (ALS), which suggest that the aetiology of all these diseases shares a common mechanism at cellular and molecular levels, such as an increase in oxidative stress, mitochondrial impairment, and inflammation.

Despite the critical research and investment, no preventive or disease-modifying treatment has been found because of diverse pathological factors.

The emerging treatment approaches for Mn toxicity utilizing bioinformatics tools, chelation therapy with calcium ethylenediamine tetra-acetic acid (Ca^{2+}EDTA), para-aminosalicylic acid (PAS), and phytochemicals like flavonoids that are known to rescue neurons from oxidative stress and inflammation are enveloped in the compilation.

Future research should concentrate on better ways to achieve Mn homeostasis in the body, understanding Mn-induced neurotoxicity, and treating hypermagnesemia.

Source: Neurotoxicology and Teratology, Vol. 94, Article 107124, November 2022.

Children Exposure to Environmental Organic Pollutants and the Autism Spectrum Disorder Risk

Autism Spectrum Disorder (ASD) is a group of neurodevelopmental ailments categorized based on impaired social and verbal communication and restrictive and/or repetitive behavioral patterns. The causative factors of ASD are diverse, which may be caused by interplay between genes and environmental factors through the epigenetic modification and/or other toxic action on the neurodevelopmental process.

Organic pollutants (OPs) including organochlorine pesticides (OCPs), polychlorinated biphenyls (PCBs), polybrominated diphenyl ethers (PBDEs) and polycyclic aromatic hydrocarbons (PAHs) have showed neuro-damaging effects, but studies concerning the autism spectrum disorder (ASD) risk are limited.

These organic pollutants have long half-lives and persist in the environment for very long periods, this leads to direct or indirect human exposure through various pathways such as dermal contact, ingestion of contaminated food and water, and inhalation of aerosols and dust. Young children and pregnant women are particularly vulnerable to such environmental pollutants.

Glutathione S-transferase (GST) enzyme system plays a key role as an antioxidant for the detoxification of toxic compounds generated due to xenobiotics (heavy metals, OCPs, PCBs, PBDEs).

Studies have shown that GSTM1 (Glutathione S-transferase Mu 1) and GSTT1 (Glutathione S-transferase Tau 1) null genotypes, alone and/or in combination with GSTP1 (Glutathione S-transferase Pi 1) polymorphism, may have associated with the risk of ASD by increasing and/or decreasing the enzyme capacity to detoxify the toxic compounds generated due to various environmental contaminants.

A case-control study with ASD children was conducted on the different land use settings across Punjab, Pakistan. Serum concentrations of 26 OCPs, 29 PCB congeners, 11 PBDEs and 32 PAHs were measured. The relation between null polymorphisms in GSTT1 and GSTM1 genes and levels of target pollutants in serum were also highlighted.

The results demonstrated the significant associations of ASD with selected studied PCBs, OCPs and PAHs in children from Pakistan.

Serum PCB77, PCB118, PCB128, PCB153 were significantly higher, but PCB187 was significantly lower in the ASD cases when compared to the controls.

Serum BDE99 was significantly higher in the healthy controls than in the ASD cases. Among the analyzed OCPs, p,p′-DDE was significantly elevated in the ASD cases with comparison in the controls.

For PAHs, serum dibenzothiophene was significantly higher in the ASD, while perylene and fluorene were significantly higher in the controls.

In addition, many of the serum pollutants were significantly associated with GSTT1, GSTM1 (null/present polymorphism) and presented the genotypic variation to respond xenobiotics in children.

The children living in proximity to urban and industrial areas had a greater exposure to most of the studied pollutants when compared to the rural children, however children residing in rural areas showed higher exposure to OCPs. For

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Telomere Length in Buccal or Salivary Cells as a Biomarker of Exposure to Air Pollution

Air pollution is a toxic mixture of volatile organic components, metals, oxides, ozone, biological agents, and particulate matter (PM) responsible for worldwide morbidity and mortality in humans.

Many studies reported the association between exposure to air pollution and molecular changes such as the formation of micronuclei, microRNA dysregulation, DNA methylation, and telomeric shortening.

Telomeres are repetitive DNA-protein sequences located at the end of chromosomes and play an essential role in preserving information in our genome by protecting against end-to-end fusion, nucleolytic degradation, breakage, and inappropriate recombination.

Telomeres shorten with each cell replication approximately 50–100 bp to a critical length that makes the telomeric DNA unable to replicate. Telomere erosion also stops cell division resulting in senescence and acting as an epigenetic indicator of biological age.

Exposure to environmental and occupational factors that cause oxidative stress and inflammation can lead to a modification of telomere length (TL) which might determine the onset of many environmental diseases. Therefore, TL was suggested as a marker of disease risk.

Several types of human tissues and cells were used for TL assessment: leucocytes, placenta, cord blood, sperm, buccal cells, and saliva.

Leukocytes are widely used for TL measurement due to the ease of extraction from blood samples. Placental tissue and cord blood are limited to studies focusing on pregnant women and newborns and sperm to study male reproductive health.

Buccal and salivary cells represent the first barrier that airborne particles meet and can metabolize possible carcinogens coming from the outside into reactive products. Moreover, their sampling is the least invasive and the cheapest methodology commonly used for research on children or adolescents.

Several molecular epidemiology studies used this biological matrix for investigating the early biological effect due to environmental pollution.

Studying the association between environmental pollution and TL buccal or salivary cells could lead to a better understanding of the processes by which exposure to pollutants can cause damage to health.

The review aimed to summarize published studies on the effects of exposure to air pollution on TL in salivary or buccal cells to identify whether TL can be a useful marker of pollutant-induced damage to health.

The reviewed studies investigated the association between TL and occupational exposure (genotoxic substances in mechanical workers, and pesticides in pesticides applicators), residential traffic exposure (NOx, NO_2, $PM_{2.5}$, PM_{10}, and black carbon), and household air pollution ($PM_{2.5}$ and black carbon from biomass stoves).

The studies involved adults and children. Although few studies have yet been carried out, almost all reported a negative association between salivary or buccal TL and exposure to air pollutants stating that it could be a good indicator of occupational or airborne pollution exposure.

However, further research is needed to evaluate the effect of acute versus long-term exposure on salivary or buccal TL as well as the role of confounding factors.

Moreover, most of the reviewed studies were conducted on healthy adults, so it is important to deeply investigate how TL is associated with all-cause mortality such as cancer, diabetes, cardiovascular disease, and respiratory disease, how it can be affected during childhood, and which changes over time can be associated with diseases' onset in adulthood.

Finally, because TL maintenance is a dynamic process, longitudinal studies aimed to examine the effect of prenatal exposure on TL at birth and TL attrition rate with increasing age in response to environmental exposures will provide information on the dynamics of TL throughout life and aging.

Source: Mutation Research/Genetic Toxicology and Environmental Mutagenesis, Vol. 883-884, Article 503561, November-December 2022.

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the first time, the exposure-hazard correlations were traced to the children's inhabited land settings, which is characterized on the basis of the indigenous environmental polluted samples including water, indoor dust, and food.

Importantly, the exposure pathway analysis showed that water was more critical in the semiarid areas where water needs to be efficiently used.

It is interesting to note that the ASD related OPs are mostly exposure factor traceable for some scenarios, which is useful for the primary prevention to against OPs-related ASD risk.

The present study adds relevant information that would be helpful to associate the distal risk aspects of urban expansion, industrial and agronomic activities with the susceptibility to health outcome by conducting the exposure pathway analysis of toxicants.

Source: Environmental Pollution, Vol. 315, Article 120381, December 2022.

Environmental Risk Factors and Etiopathogenesis of Parkinson's Disease

Parkinson's disease (PD) is a prevalent progressive neurodegenerative disorder that predominantly affects elderly populations. The overall incidence rate of PD is expected to significantly increase over time. PD's burden is substantially increasing due to a longer life expectancy and the consequent increasing number of elderly people, longer disease duration in individuals, as well as the contribution from environmental factors.

PD is characterized by the neuropathological hallmark of the loss of nigrostriatal dopaminergic (DAergic) innervation in the substantia nigra pars compacta (SNpc) and the appearance of Lewy bodies with aggregated α-synuclein.

Although several familial forms of PD have been reported to be associated with several gene variants, most cases in nature are sporadic, triggered by a complex interplay of genetic and environmental risk factors.

Evidence from meta-analyses of mechanistic research and epidemiological studies confirms that the risk for sporadic PD is modulated by environmental factors, including exposure to neurotoxic pesticides/herbicides, solvents, and heavy metals as well as traumatic brain injury.

Other environmental factors implicated as potential risk factors for PD include industrial chemicals, wood pulp mills, farming, well-water consumption, and rural residence.

The present review summarizes the environmental toxicology of PD with the focus on the elaboration of chemical toxicity and the underlying pathogenic mechanisms associated with exposure to several neurotoxic chemicals, specifically 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), paraquat (PQ), rotenone, dichlorodiphenyl-trichloroethane (DDT), dieldrin, manganese (Mn), and vanadium (V).

MPTP has been widely used to mimic the pathophysiological features of PD in multiple organisms, including mice, cats, guinea pigs, and nonhuman primates.

PQ, a neurotoxic pesticide, shares similarities in structure with MPTP and is known to increase oxidative derivatives.

Rotenone can induce loss of nigral DAergic neurons and behavioral changes in humans. However, unlike PQ, rotenone directly inhibits mitochondrial complex I and results in mitochondria deficits.

DDT induces the formation of extracellular vesicles; and disrupts DA transport by inhibiting the vesicular monoamine transporter (VMAT2) and the plasma membrane DA transporter (DAT).

Dieldrin triggers epigenetic modification, perturb proteasomal homeostasis, and activates the apoptotic protein kinase C delta (PKCδ) signaling pathway.

Excessive exposure to Mn leads to its accumulation in the human brain and triggers neurotoxicity, even resulting in the development of manganism, a PD-like movement disorder.

Vanadium (V), which easily crosses the blood-brain barrier (BBB), generates iron-mediated reactive oxygen species (ROS) and therefore induces neurotoxic damage to the brain.

Interestingly, exposure to environmental neurotoxins not only impacts motor symptoms but also influences the host gut microbiome.

Traumatic brain injury (TBI) has also been linked as a risk factor for several neurodegenerative diseases, but the strongest emerging evidence is associated with the development of PD. Inflammation, metabolic dysregulation, and protein accumulation have been implicated as potential mechanisms through which TBI can initiate or accelerate PD.

The evidence regarding their molecular and cellular signaling on neurodegeneration from various mechanistic perspectives: mitochondrial dysfunction, neuroinflammation, oxidative stress, histone modification, and protein misfolding/aggregation is described.

The pesticides tend to share certain actions, including inhibition of the mitochondrial respiratory chain and production of oxidative stress. Antioxidants can be applied to attenuate the toxicity.

In addition to mitochondrial dysfunction, recent studies link microRNAs and pesticide neurotoxicity, revealing that microRNA dysregulation could be a novel mechanism underlying pesticide-induced neurotoxicity based on two conditions: microRNAs sharing similar dysregulation functions with other types of epigenetic modification, and the differential expression of microRNAs occurring in patients with PD .

Furthermore, exosomes are importantly involved in trafficking and cell-to-cell communication. This may have broad implications in the environmental stress response as exosomes can cross the blood-brain-barrier (BBB) and communicate across various organs.

The significance of toxicants entering the brain via the olfactory nerve, which bypasses the BBB, remains an exciting topic to explore intervention strategies.

The cellular responses to chemical exposure following the inhalation of environmental pollutants will depend on their different oxidation states and solubility, yet such parameters have not been adequately accounted for in existing human dose-response studies.

Epidemiology studies incorporating good tracing and management combined with complete occupational exposure histories with both behavioral and biochemical endpoints of neurotoxicity tailored to specific subgroups of PD patients are needed.

Considering the high societal cost of PD, advancing the environmental exposure assessment science and its integration with other approaches, including the epigenomic disease model toolbox, would help fill an unmet need.

An overview of the current findings from cellular, animal, and human studies of PD provides information for possible intervention strategies aimed at halting the initiation and exacerbation of environmentally linked PD.

Source: International Journal of Molecular Sciences, Vol. 23, Issue 18, Article 10808, September 2022.

Effect of Phorate on the Development of Hyperglycemia in Mouse

Phorate is a systemic, broad-spectrum organophosphorus insecticide and is commonly used in the agricultural sector to control sucking and chewing pests, leaf hoppers, and mites. Like other pesticides, phorate not only causes environmental pollution but also poses serious threats to human and animal health.

In humans and animals, the gut is the key reservoir of microbial communities, comprising both commensal and pathogenic bacteria. Many studies have found that because the gut microbiota is frequently exposed to exogenous antibiotics from drugs or from the food chain, it possesses multiple drug-resistance genes. Moreover, long-term exposure of humans and animals to antibiotics enriches intestinal drug-resistance genes.

A recent review on intestinal microbiota and antibiotic resistance conducted in a large human cohort in China found that the antibiotic resistance of the intestinal microbiota is closely associated with faecal metabolites and the host's metabolic health. Antibiotic-resistance gene diversity is associated with a higher risk of type 2 diabetes (T2D). However, to date, no studies have assessed the effects of phorate on glucose metabolism.

Phorate is a potential risk factor for human health, and the acceptable daily intake recommended by the WHO is 0.0005 mg/kg bw/day. Occupational exposure of farmers to phorate increases their daily intake of pesticides, with a median exposure of 0.69 μg/kg bw/day, the equivalent to 0.006279 mg/kg bw/day in mice.

The present study was conducted to explore the hazards of pesticide residues with respect to host metabolic health and the correlation between the production of resistance genes and glucose metabolism.

The study measured the blood glucose concentrations and assessed the distribution characteristics of antibiotic-resistance genes in the intestinal microbiota of high-fat-diet-fed mice exposed to various concentrations of phorate.

The present study found, for the first time, that phorate has a hyperglycaemic effect on high-fat-diet-fed mice. The results clearly demonstrated a dose-dependent relationship between phorate and hyperglycaemia which showed that 0.005 and 0.5 mg/kg of phorate induced obvious hyperglycemia in the high-fat-diet-fed mice.

Upon entry through oral gavage, phorate inevitably affects the intestinal microbiota of mice. The gut microbiota engages in symbiotic relationships and regulates various metabolic functions, including intestinal barrier homeostasis and glucose homeostasis.

Akkermansia muciniphila secretes a glucagon-like peptide-1-inducing protein to improve glucose homeostasis and regulate metabolic diseases in mice. Exposure to phorate markedly reduced the abundance of *Akkermansia muciniphila* in the mouse intestine, and this may have led to the observed increases in blood glucose concentrations.

Interestingly, researchers found that phorate may also contribute to the development of resistance genes in the intestinal microbiota as well as the development of hyperglycemia in mice.

The results showed that hyperglycemic mice carried the vancomycin-resistance gene *vanRG*, the tetracycline-resistance gene *tetW/N/W,* and the multidrug-resistance genes *acrD* and *evgS*; these genes have not been previously reported in mice. The increase in the abundance of these resistance genes is attributable to the use of phorate.

Efflux pumping was the primary mechanism of drug resistance in the Firmicutes, Proteobacteria, Bacteroidetes, Verrucomicrobia, Synergistetes, Spirochaetes, and Actinobacteria found in the mouse intestine. Therefore, phorate causes hyperglycemia in mice primarily by causing the dominant bacteria in the intestine to produce efflux pumps.

In conclusion, phorate can cause hyperglycaemia in mice by influencing the abundance of the intestinal microbiota and by modulating or altering the expression of drug-resistance genes. Changes in the abundance of the intestinal microbiota are closely related to the presence of antibiotic-resistant bacteria in the intestinal tract and the host's metabolic health.

Source: Antibiotics, Vol. 11, Issue 11, Article 1584, November 2022.

Use of Straighteners and Uterine Cancer

Uterine cancer is one of the most common gynecologic cancer. The incidence and mortality rates have increased in the United States in the past 2 decades, with more than 65,950 new cases and 12,550 deaths expected in 2022, according to the National Cancer Institute.

Exposure to excess estrogen and a hormonal imbalance of estrogen and progesterone have been identified as key risk factors for uterine cancer. Thus, it has been hypothesized that synthetic estrogenic compounds such as endocrine-disrupting chemicals (EDCs) could contribute to uterine cancer risk because of their ability to alter hormonal actions.

Hair product use is common among women in the United States and Europe with more than 50% reporting using permanent hair dyes. Hair products may contain hazardous chemicals with endocrine-disrupting and carcinogenic properties.

Hair product constituents, including formaldehyde and formaldehyde-releasing chemicals in some straighteners, and oxidized para-phenylenediamine and 4-aminobiphenyl in hair dyes, have also played a potential role in carcinogenesis, supporting an association between hair product use and cancer development.

Previous studies have found hair product use to be associated with a higher risk of hormone-sensitive cancers including breast and ovarian cancer; however, no previous study has investigated the relationship with uterine cancer.

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WHO-UNICEF: Children and E-Waste - Key Messages

Electronic and electrical waste (e-waste) is the world's fastest growing waste stream, increasing three times faster than the world's population.

The escalating consumption of newer electrical and electronic equipment every year has been likened to a tsunami of e-waste. In 2019, the world produced 53.6 million tonnes of e-waste, but less than 20% was documented as appropriately disposed of or recycled.

Unmanaged and improperly managed e-waste is polluting soil, water and air, harming the health of communities, especially children. E-waste includes items such as refrigerators, washing machines, computers, cellphones and other consumer electronics.

As many as 18 million children and adolescents, and about 13 million women, are working in the informal sector, of which e-waste is a sub-sector.

With millions of children's lives at stake, we must take urgent action to end child labour and protect children's health from the effects of e-waste.

The e-waste problem is growing because of higher consumption, shorter product life cycles and few repair options, coupled with low recycling capacity.

E-waste contains valuable elements such as gold, silver, copper, palladium and platinum that makes it attractive to recycle. E-waste also contains highly toxic materials, such as lead and cadmium, which are released into the environment through informal recycling activities. When this is done in an unsound manner, it harms the environment and children's health.

Children's developing bodies and brains make them uniquely vulnerable to the hazardous substances in e-waste. Therefore, effective action is urgently required to ensure environmentally sound management of e-waste and elimination of child labour. There must be measures to prevent exposure, detect evidence of harm and provide care and treatment for children and pregnant women affected by e-waste-related contamination.

Source: WHO Technical Document, Children and E-Waste. 7 November 2022.

Use of Straighteners and Uterine Cancer

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Therefore, the present study aims to examine associations between hair product use and the age-specific hazard of uterine cancer in a large, racially and ethnically diverse cohort in the United States.

Over an average of 10.9 years of follow-up, 378 uterine cancer cases were identified. The findings showed a higher incident uterine cancer rate for women who self-reported either ever or frequent hair straightener use in the prior 12 months, relative to those who did not.

Negligible associations were observed for other hair products used including permanent dyes, semi-permanent dyes, temporary dyes, bleach, highlights, and hair permanents with uterine cancer.

This is the first epidemiologic study investigating the relationship between straightener use and uterine cancer.

Chemical exposure through the pathway of hair product use, especially straighteners, could be more concerning than other personal care products. Higher percutaneous absorption of chemicals has been observed in scalp compared with other skin such as on the forearm, palm, and abdomen. Straightener use may cause scalp lesions and burns, which facilitates the permeability of chemicals through the scalp.

Researchers observed stronger associations with straightener use among women with low physical activity. Because physical activity has been associated with decreased sex steroid hormones and less chronic inflammation, women with higher physical activity might be less susceptible to other risk factors for uterine cancer. However, more studies are warranted to understand the interrelationship between physical activity, hair product use, and uterine cancer.

Although no differences in the hazard ratios between racial and ethnic groups were observed, the adverse health effects associated with straightener use could be more consequential for African American women because of the higher prevalence and frequency of hair product use, younger age of initiating use, and harsher chemical formulations than other races and ethnicities.

Brands or ingredients of hair products were not collected in this study; thus, the specific chemicals contributing to incident uterine cancer were not identified. Future efforts are needed to identify the chemical ingredients, which might result in the elevated rates.

Given the widespread use of hair products and the rising incidence of uterine cancer, the findings which identify hair straightener use as a potential target for intervention are particularly relevant for public health approaches to reduce uterine cancer incidence.

Source: Journal of the National Cancer Institute, Vol. 114, Issue 12, Pages 1636–1645, December 2022.

Mercury Exposures from Skin-Lightening Products

Mercury is a global pollutant of concern to human health. Several inorganic and organic forms of mercury exist naturally in the environment (metallic or elemental), and although there are differences in their toxicity, all forms can adversely impact human health including the nervous, cardiovascular, and immune systems.

Human exposures to mercury outside of occupational settings are largely realized through the consumption of mercury-contaminated seafood and contact with certain products that contain mercury, including dental amalgam, pesticides, broken fluorescent light bulbs, and batteries.

Skin-lightening cosmetics also contain mercury, and there are increasing concerns about the dangers posed by frequent usage of such products. In certain cosmetic products, organic mercury compounds, including ethylmercury, methylmercury, and phenyl mercuric salts, may be used as preservatives. Further, inorganic mercury salts (mercurous chloride (calomel), mercuric chloride, mercurous oxide, ammoniated mercuric chloride and mercuric iodide, and ammoniated mercury), may be purposefully added as they interfere with the tyrosinase enzyme inhibiting the skin from producing melanin, resulting in lighter skin pigmentation.

Because mercury is absorbed through the skin, mercury poisoning may arise after use of a skin-lightening product. Exposure to inorganic mercury has been associated with renal toxicity, neurological abnormalities, and dermal rashes.

Skin-lightening products exist in various forms (most commonly creams and soaps), and they are used without medical supervision. Use of skin-lightening products is practiced worldwide, particularly in African, Asian, and Caribbean nations, as well as in darker-skinned communities in Europe and North America. The market for skin-lightening products is increasing as the demographics of users continues to expand, making it one of the fastest-growing beauty industries globally.

The entry into force of the Minamata Convention on Mercury on 16 August 2017 was a global environmental agreement by governments set in place to reduce emissions and releases of mercury and mercury compounds to protect human health and the environment (Article 1). Article 4 of the Minamata Convention mandated that parties must ban the manufacture, import, and export of products that include creams and soaps with a mercury content higher than 1 µg/g after 2020.

The objective of the present study was to increase understanding of worldwide human mercury exposure from skin-lightening products. The researchers organized peer-review studies into 4 groups: mercury in products, usage, human biomarkers of exposure, and health impacts.

This is the first systematic literature review characterizing the amount of mercury that human populations worldwide may be exposed to through the use of mercury-added skin-lightening products.

The findings conclude that mercury is still prevalent in many skin-lightening products in many countries worldwide and that some people and populations worldwide experience relatively high exposures to mercury from the use of such skin-lightening products.

A total of 787 skin-lightening products were identified from 25 studies that included creams (70.1%), soaps (19.3%), facial cream (4.6%), and other products (6.0%). the maximum reported values varied with the highest amount found in cream (314,387 µg/g), followed by facial cream (35,824 µg/g), soap (8,665 µg/g), and an item from the other products group (2,700 µg/g). The overall pooled central median mercury concentration in skin-lightening products was 0.49 µg/g. The results showed that mercury was an active ingredient with concentration greater than 1 µg/g in approximately 25% of products tested.

Mercury concentrations in skin-lightening products varied across geographic regions, with the highest median concentrations found in products purchased from countries in the WHO Eastern Mediterranean, South-East Asia, and Western Pacific regions.

In terms of usage, mercury was the second most popular bleaching agent globally after topical corticosteroids. The study found great variability in skin-lightening product usage patterns across populations. In general researchers conclude that most individuals who use these products apply skin-lightening items primarily on their face, typically from <1 to 3 times per day, for less than a year, and in quantities of 11-50 g per month.

The estimate mercury exposure for 1 year to be 150 µg mercury through the following calculation: 0.05 µg/g mercury, which was the overall pooled median concentration ×25g product/month × 12 months. This estimate can vary significantly, based on factors including product type, application, and skin characteristics and with the recognition of the great variances in frequency, duration, and quantity of product used, as illustrated by our data.

From the 2018 UN Global Mercury Assessment, it was determined that in populations with background exposures to mercury, levels of the chemical in blood, hair, and urine are generally <5 µg/L, 2 µg/g, and 3 µg/L, respectively. In the current study, the highest biomarker concentrations in these studies were well above their respective reference values.

Most individual biomarker concentrations in studies were either not stated or grouped together based on reference values set out by various agencies and health departments. Aside from the case series studies, biomarker studies generally sampled small groups of individuals likely due to the difficulty in isolating individual users and the negative stigma surrounding use of skin-lightening products.

Mercury in urine reflects exposure to inorganic and elemental forms of mercury, and as a noninvasive and relatively inexpensive biomarker to sample, this may be particularly attractive

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CALENDAR OF EVENTS

International Training Courses at Chulabhorn Research Institute, Year 2023

	Training Course	Date	Duration	Closing Date
1	Environmental Toxicology and Health	June 29 - July 5, 2023	5 work days	May 5, 2023
2	Environmental and Health Risk Assessment and Management of Toxic Chemicals	November - December 2023	10 work days	October 2023

Course Coordinator: *Khunying* Mathuros Ruchirawat, Ph.D.

Course Description:

Environmental Toxicology and Health (June 29 - July 5, 2023)

This course provides students and participants with a background of the major groups of toxic substances encountered by man and animals through food and the environment, as well as through exposure at the workplace. These toxicants include toxic substances in air, water and soil; solvents; gases; pesticides; hazardous wastes and other pollutants. The course focuses on the chemistry, fate and distribution in the environment, mechanisms of their action, toxic manifestation in living organisms, as well as toxic syndrome in human beings. The course also provides information on the latest technologies used to study changes and effects in biological systems, e.g. biomarkers, the omics technologies, gene-environment interactions, epigenetics and transgenic models, and covers environmental health issues such as climate change, and their adverse health effects in humans.

Requirement: Participants should have some basic knowledge in chemistry and the biological/biomedical sciences.

Fellowships:

A limited number of fellowships are available that will cover round-trip airfare, accommodation (on site) and meals, training materials, and health insurance.

Contact: Chulabhorn Research Institute (CRI)
54 Kamphaeng Phet 6 Rd.,
Lak Si, Bangkok 10210, Thailand
Tel: +66 2 553 8535
Fax: +66 2 553 8536
E-mail: envtox@cri.or.th

More information and application:
Please visit - http://www.cri.or.th/en/ac_actcalendar.php

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in exposure assessment studies. Finally, mercury in whole blood can provide information on recent exposures to both organic and inorganic mercury.

In conclusion, mercury widely exists as an active ingredient in skin-lightening products and that there is large variability in human exposures. Although knowledge gaps and limitations exist (e.g., nonrandom selection bias, geographic regions with no data), these synthesized findings help increase our understanding of potential exposures worldwide to mercury through the use of these products.

In addition, the information in this study will be critical in helping regulatory agencies and intergovernmental organizations better understand the global prevalence of mercury-added skin-lightening products to better promote actions that can help eliminate the production and use of such products.

Source: Environmental Health Perspectives, Vol. 130, No. 11, November 2022.

The ICEIT NEWSLETTER is published quarterly by the International Centre for Environmental and Industrial Toxicology of the Chulabhorn Research Institute. It is intended to be a source of information to create awareness of the problems caused by chemicals. However, the contents and views expressed in this newsletter do not necessarily represent the policies of ICEIT.

Correspondence should be addressed to:

ICEIT NEWSLETTER
Chulabhorn Research Institute
Office of Academic Affairs
54 Kamphaeng Phet 6 Road
Lak Si, Bangkok 10210, Thailand
Tel: +66 2 553 8535
Fax: +66 2 553 8536
CRI Homepage: <http://www.cri.or.th>

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