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TIN Toxicity with Analytical Aspects and its Management

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Abstract

Tin is a silvery-white metal, naturally occurring as cassiterite. It is denoted by symbol Sn, has an atomic number 50 and atomic weight 118.71u. The two commonly found oxidation states of tin are Sn (IV) called stannic and Sn (II) called stannous with approximately equal stabilities. Tin has been extensively used for storing food and beverages, transportation, construction industries, in paints, as heat stabilizers, and biocides. Several anthropogenic and natural processes release tin and its compounds into the environment posing a severe toxicological threat to living beings. Several studies prove absorption and accumulation of tin in the various parts of the body such as lungs, kidney, and spleen resulting in impairment of respiratory system, degenerative changes in kidney, central nervous system and reproductive system. The clinical features of tin poisoning along with appropriate diagnosis has been discussed in this paper. The identification of tin and its compounds using various advanced analytical techniques will help in better dealing with the toxic effects of the same. Also, the hospitalization and post-hospitalization management will help to understand the proper care and treatment required by the patient.

Keywords: Tin toxicity; Poisoning; Tin; Biocides; Analytical techniques etc.

Introduction

Tin is a chemical element that belongs to group 14 in the periodic Table. It is represented as Sn, which stands for the Latin word 'stannum'. Tin is a silvery metal that occurs in two stable oxidation states +2 and +4 and is also 49th most abundant element on earth, which is mainly obtained from mineral cassiterite. Tin is globally used to preserve the canned food and beverages; other well-known uses of tin are in the transportation sector and various electrical appliances. Industries use both organic and inorganic forms of tin common examples of organotin includes agrochemicals, biocides, Polyvinyl chloride and some catalysts.[1,2]

Studies suggest no biological significance of tin in the living organisms, however, various research establish the toxic aspects of the tin if consumed regularly. Dosage of tin more than 130 mg/kg is known to get accumulated in kidneys, bones, and spleen. The inorganic form of tin and certain salts are known to cause severe effects on the gastrointestinal system, respiratory system, reproductive and renal system.[3] Symptoms of mild toxicity includes nausea, vomiting, diarrhea and irritation of the upper respiratory tract. Severe effects include irreversible damage to renal tubules and various neurodegenerative changes leading to disorientation, confusion, memory loss with severe epileptic seizures in many cases. Therefore, proper

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management is required in case of Sn poisoning along with proper treatment in order to avoid further damage.

Sources of TIN

The concentration of the tin in earth crust is approximately 0.0006%, the main sources of tin exposure to humans are anthropogenic in nature. Some of the common sources of tin exposure are discussed below.[4]

1. Tin present in the soil is released to the atmosphere due to the process of weathering.
2. Certain biocides and antifouling paints contain compounds of tin such as Tributyltin and triphenyltin.
3. Canned food and beverages are a major source of tin.
4. Disposal of products made of tin leads to its leaching in the ground.
5. Industries dealing with manufacturing and processing any form of tin are a source of occupational exposure.
6. The process of mining is known to release metallic tin in the environment, which is further converted into the inorganic compounds of tin.[5]
7. Tin also gets accumulated in various fishes and plants which grow near high in concentration.

Human Exposure of TIN

There are three commonly known methods of the exposure of tin, most common being ingestion followed by inhalation and dermal absorption. Some of these are discussed in detail below.[6]

1. Consumption of canned food and beverages is known to administer tin in the body. The actual concentration of tin in canned food is governed by various factors such as storing temperature, the acidity of the food, the presence of oxidizing agents, lacquered or unlacquered can, etc.
2. Inhalation of the tin particles near landfills or industries dealing with the manufacturing of tin products.
3. Eating seafood which has high levels of tributyltin and triphenyltin.
4. Dermal absorption is a common occupational exposure and is commonly seen in the case of organotin compounds.
5. Regions, where polyvinyl compounds are used for water distribution, are known to have a high concentration of mono-and dibutyltin and Mono-and dimethyltin.

Pharmacokinetics and Metabolism

Absorption

Studies suggest organic tin compounds are absorbed much faster as compared to inorganic tin compounds in the body. It is observed, with an increase in the dosage of tin in the body the gastrointestinal absorption decreases. Tin incorporated in the food naturally is readily absorbed than stannous chloride present in some food. Although there is very poor absorption of tin in the body, some compounds such as dibutyltin and trimethyltin were detected in post-mortem blood and liver suggesting their absorption in the body.[7]

Distribution

After absorption in the intestine, tin reaches various body parts via blood. Less than 17 mg of tin is found in the human body, and various experimental studies suggested the highest concentration of tin in kidneys and liver. A trace amount of inorganic tin is known to cross the placental barrier.

Excretion

Most of the ingested inorganic tin remains unabsorbed and is readily excreted in urine and feces and a small amount in bile. Organotin compounds generally degrade via dealkylation and de-arylation through the liver and finally discharged from the kidney, saliva, digestive tract, respiratory tract.[8]

Mechanism of Toxicity

There are few studies stating the possible bioalkylation of tin via reductive Cobalt-Carbon bond cleavage of alkyl cobalamines. Although there is no direct experimental study present on the topic. Some salts of tin such as stannous chloride are shown to cause genotoxicity by damaging the DNA and causing chromosomal aberrations. Stannous ions are known to reduce hydrogen peroxide and produce reactive oxygen species.

Onset and Duration of Action

In the case of tin poisoning appearance of symptoms depends upon the dose of exposure. The occurrence of symptoms appears depending upon the form of the tin compound and its mode of exposure. Usually in case of acute poisoning symptoms may appear within hours, however, in chronic poisoning, the appearance of symptoms may take several months or years.

Fatal Dose / Fatal Period

The fatal dosage of tin varies greatly depending upon the compound of tin and its mode of exposure. According to the World Health Organization, the intake of 200 mg/kg in salt is fatal in humans.[9] The fatal period varies a lot depending upon several factors, in general, it can be estimated as an incubation period of 15 minutes to 14 hours. Triphenyltin acetate if consumed orally in dosage 260 mg/kg is fatal in humans. Triethyltin if consumed about 90 mg/day for 7–8 days is highly toxic and lethal.[10]

Normal and Reference Values

Table 1: Showing normal and toxic levels of tin.

Biological Matrixes	Normal level	Toxic level
Blood	Less than 0.005 µg /mL	More than 0.009 µg/ml
Urine	1 – 20 µg/L	More than 30 µg/ml
Hair	Less than 0.30 µg/g	More than 0.32 µg/g

Systemic Effects on Body

Studies suggest that the metallic form of tin is not very toxic due to its poor absorption by the body. However acute intake of inorganic compounds of tin has some adverse effects like nausea, vomiting, irritation in skin or eyes and various gastrointestinal issues. Organic compounds of tin such as $(CH_3)_3Sn$ (trimethyltin) and $(C_2H_5)_3Sn$ (triethyltin) are known to interfere with the nervous system and immune system in certain animals.[11,12] Very few experimental data available regarding the effect of tin and its compound on human health, the majority of the studies were carried out in animals.

Respiratory effects

Prolong exposure to dust of stannic oxide gets deposited in the lungs and is known to cause stannosis in humans. Tributyltin oxide is known to produce irritation of the upper respiratory tract with symptoms of pain and tightness in the chest, further exposure can lead to difficulty in breathing and coughing. Certain inflammatory changes such as bronchitis, lung edema, and hyperemia were observed in some animals such as rats and rabbits.

Gastrointestinal effects

Studies suggest that ingestion of trimethyltin chloride and tributyltin oxide produce severe nausea, vomiting, diarrhea followed by substernal and epigastric burning. Continuous pain and burning can persist even after 2–3 months of exposure.

Renal effects

Several experimental studies conducted on animals reveals proximal tubule degeneration and high level of tin in the urine. Further necropsy studies suggested damage to glomeruli, as well as collecting tubules. Extensive congestion in the kidney along with swelling in the renal tubular epithelium was also observed.

Neurological effects

Several studies suggest neurobehavioral changes in humans due to long-term exposure to organotin compounds, common effects include headache, impaired memory, deafness, cognitive dysfunction, and neuropsychiatric behavior, in some of the serious cases, epileptic seizures were also observed. Swelling in the brain and spinal cord along with degeneration of myelin can be seen in some cases.[13]

Reproductive effects

Experimental studies done on rat suggests, acute and intermediate exposure of compounds such as tributyltin bromide and dibutyltin dibromide reduce pregnancy rates. Some impairment was also seen in the female reproductive function, but these changes looked reversible once the exposure was reduced.

Analysis

There are several analytical techniques available in order to detect tin and its compounds, some of these commonly used techniques are listed below.

Qualitative test

1. *Cacotheline test:* A Whatman filter paper is moistened with a saturated solution of cacotheline and dried at room temperature. A drop of test solution containing tin is put on the above filter paper. Development of violet colour indicates the presence of tin.[14]
2. *Meissner's flame test:* the sample containing tin is mixed with zinc and HCl, then a test tube containing water is dipped in the above solution and immediately held over a flame of Bunsen burner. The appearance of blue coloured flame proves the presence of tin. Production of this flame is due to $SnCl_4$ (which is volatile in nature) and its reduction to SnH_4.[15]

Quantitative analysis

1. *Polarography or Voltammetry method:* Voltammetry method for analyzing tin uses the varying degree of the electric potential in the solution containing metal, this method is very sensitive detecting 1 to 1000 parts per million.
2. *Potentiometric titration:* This method measures the variations in the redox potential when the solution containing tin is titrated against the potassium iodate solution. Such a method is generally used for estimating stannous (tin II) present in radiopharmaceutical vials sealed in inert gases or nitrogen. Stannous estimation by potentiometric titration is not possible in vials with antioxidants such as ascorbic acid.
3. *Flame atomic absorption:* Determination of tin in biological materials such as blood, urine, fecal matter, etc. requires a series of extraction processes followed by separation and detection.[16] Commonly used techniques in the case of biological material are spectrophotometry and photometry. It is seen that the determination of tin is usually done both as total metal and organotin analysis. Flame atomic absorption is the direct method for determining tin in any sample, this method uses the absorption of optical radiation by the free gaseous atoms of the tin in any given sample.
4. *Gas Chromatography (GC):* Determination of the organotin compound is preferentially done by gas chromatography (GC) due to its high resolution. This process requires some preparatory steps such as extraction, derivatization, separation, and detection. Extraction is carried out using organic solvent or various ion-exchange methods. Extraction is followed by derivatization, which includes the formation of alkyl, ethyl or hydride derivatives using respective chemical agents. The next step in the series is separation using variations in the boiling point of the compounds, once the atoms are separated identification is done using MS (mass spectrometry) and AAS (atomic absorption spectrometry).[17]
5. *Inductively Coupled Plasma-Atomic Emission Spectroscopy (ICP- AES)*: Multielement analysis of tin in drinking water, canned food, air, and waste is done using this method. This method requires dilution of the test sample with HCl, which is then pumped to a nebulizer in order to produce an aerosol. Very fine aerosol particles are then allowed to pass the plasma using the cyclonic spray chamber. This method is considered one of the most precise methods to analyze tin using a quantitative approach.[18]

Clinical Appearances/Symptoms in Tin Poisoning

Clinical appearances and symptoms in case of tin poisoning depends upon the amount of substance, form of tin (organic/inorganic), mode of exposure and duration of the exposure.[19]

A. In case of acute toxicity

i. *Gastrointestinal effects*
- Nausea
- Abdominal pain and burning
- Vomiting
- Diarrhea
- Irritation in esophagus

ii. *Systemic effects*
- Lacrimation and severe conjunctivitis
- Upper respiratory tract irritation
- Irritants to the skin and mucous membranes
- Headache
- Subacute lesions

B. In case of chronic toxicity

- Proximal tubule degeneration
- Congestion of kidney and
- Swelling of renal tubules
- Memory loss
- Cognitive dysfunction
- Epileptic seizures

Diagnostic Investigation

- It is necessary to know and record the medical history of the patient, exposed to any form of tin poisoning.
- The physical examination is equally important where forced vital capacity (FVC) posteroanterior chest roentgenogram, and forced expiratory volume per sec (FEV1) is performed. Patients are also subjected to eye examination which includes various tests for visual activity and pupillary reaction.
- For the detailed investigation, kidney function test, urine albumin, glutamate-oxaloacetate transaminase test is also performed for a hepatic function test.
- X-ray of chest and blood tests are common in the case of organotin compounds.

Management and Treatment

All kinds of tin exposure should be taken seriously and treated as soon as possible. Delay in the identification of the symptoms and treatment can cause severe irreversible damage. Criteria for management of tin poisoning are

1. ***Observation at home:*** Ingestion of a very small amount of tin or its compound is unlikely to cause any systemic toxicity, an asymptomatic patient can be observed at home.
2. ***Observation in hospital:*** Intake of a large amounts of tin in any form should be evaluated in the hospital. A person with any acute or chronic symptoms of poisoning should be referred to a healthcare facility.
3. ***Criteria for toxicological consultation:*** If any systemic toxicity of tin is observed in the patient, then the physician should consult a medical toxicologist or nearby poison control center.

4. Hospital management

1. The history of exposure of a patient to tin or its compound is noted to get a clear idea about the type and mode of poisoning.
2. Signs and symptoms of the patient, along with liver function, urine test, blood potassium and ammonia levels, MRI, CT scans are closely monitored.
3. In the case of mild poisoning symptomatic treatment is preferred.
4. In very severe patients few dosages of glucocorticoids are administered. Potassium glutamate and sodium glutamate is given intravenously in order to reduce blood ammonia. Oral administration of potassium is also helpful in order to normalize intractable hypokalemia and sodium bicarbonate is administered for metabolic acidosis; some sedatives are also helpful in controlling twitches and spasm.[20]
5. In some cases, gastrointestinal decontamination is carried out, patient with a confirmed significant amount of inorganic tin exposure is made to undergo whole bowel irrigation until the effluent is cleared. Decontamination is done by subjecting patients to electrolyte solution of polyethylene at a rate of 2L/h for normal adults.
6. Chelation therapy using EDTA- Patients with severe tin poisoning are intravenously administered with EDTA diluted with physiological saline solution (0.9% NaCl) at a very slow rate; this method is very effective for removing the tin and its compounds from the body. It is the property of EDTA to bind with toxic metals and in turn form, the stable complexes, later these complexes are eliminated from the body via urine.[21]

Conclusion

Tin and its compounds are known to show toxic effects in case of acute and chronic exposure to the body. People working in industries dealing with tin should take special care and should be subjected to periodic testing of blood, renal function test, urine albumin and another test to monitor levels of tin in the body. Consumption of canned food and beverages is a very common mode of tin exposure that should be taken care of.

Any symptom mild or severe in patients, must not be ignored and should rush for immediate medical help for symptomatic treatment.

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