

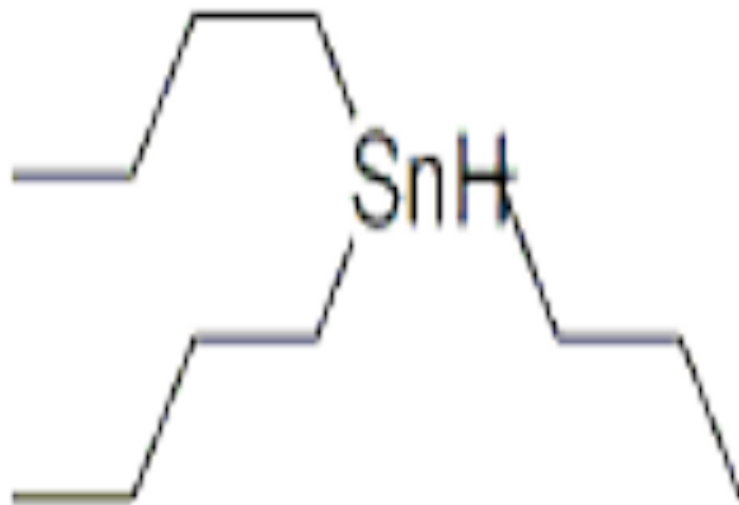
# COMPOUND TOXICITY

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BIOL 564

# TRIBUTYLSTANNANE

- \* STRUCTURE: Source: [http://us.chemicalbook.com/ChemicalProductProperty\\_US\\_CB6736950.aspx](http://us.chemicalbook.com/ChemicalProductProperty_US_CB6736950.aspx)



# PHYSICAL AND CHEMICAL PROPERTIES:

- \* Part of the aromatic hydrocarbon family.
- \* Considered an organotin
- \*  $K_{ow}$  values range from 3.2 to 4.1
- \* TBT's bioaccumulation within an organism will depend on its uptake and its capacity to eliminate it
- \* It has been shown to bioamplify

# Uses, History

- \* Acts as a biocide
- \* It is used as an antifouling agent in paints of boats, on fishnets, buoys and docks
- \* Also used as a disinfectant for various uses, also as a fungicidal wood preservative and used to stabilize PVC resins.
- \* Used in other industries as well: breweries, pulp and paper mills, etc.

# Restriction on use

- \* Due to its high aquatic toxicity, its uses has been very limited
- \* In many countries, its use in antifouling paints on boats has been limited to boats over 25m(82 feet) and vessels with aluminum hulls
- \* Standards have been set for the amount that can be leached in the water (4ug/cm<sup>2</sup>/day)

# Mode of entry in Aquatic Environment

- \* Leaches from the paint and usually stays within the area where it has been applied.
- \* Runoff from industry

# Chemical reactivity, Speciation, Half-Life

- \* In seawater, it is found as TBT hydroxide, TBT chloride and TBT carbonate.
- \* pH affects it
- \* Its physical half-life varies depending on medium:  
water: approx. 3months, Sediment: more than 2 years

# Toxicity to aquatic life

- \* TBT concentrations seem to affect growth of marine algae
- \* In oysters (*Crassostrea gigas*, *C. glulata* and *Saccrostrea glomerata*), it has been shown that larvae development is affected by low levels of TBT as well as problems in the shell development.

# Toxicity cont'd

- \* Imposex, or the development of male characteristics in females has been associated to exposure of low levels of TBT in snails, dogwhelks and mollusks.
- \* An increase in the response of cytochrome p450 caused by TBT exposure in Atlantic salmon *Salmo salar* as well as endocrine disruption has been studied.
- \* In a genetically female Japanese Flounder *Paralichthys olivaceus*, it looks like TBT might have caused masculinization

# Toxicity cont'd

- \* TBT seems to have an effect on the release of AGPWamide and acts as a neurotoxicant.
- \* AGPWamide is an important neuropeptide for the reproductive behavior and penile eversion and is a Penis Morphogenic Factor or PMF in Gastropod Mollusks.
- \* AGPWamide seems to play an important role when it comes to imposex however, further studies are needed.

# Toxicity cont'd

- \* In some Sea otters found dead off of the coast of California, high concentrations of TBT have been found. They are specially at risk because of their diet (Benthic and mostly invertebrates).
- \* Sea otters that died from infectious disease seemed to have a higher concentration than the sea otters that died from trauma or other causes. There might be a link between TBT and immunosuppression however, needs further investigation

# Mode of entry into the organisms

- \* Biosorption in algae
- \* Uptake from the gills
- \* Through the diet

# Molecular mode of toxic interaction

- \* In algae: Biosorption on the cell membrane and entrance within the cell through passive or active transport. The ability to degrade TBT to DBT and MBT will dictate the tolerance of the algae to TBT
- \* In mollusks, the toxicity will depend on the rate of uptake versus elimination. Imposex is due to the TBT's effect on male steroid hormone and the fact that the organism cannot excrete it so readily.

# Molecular mode of toxic interaction

- \* In fish, TBT has been shown to inhibit the cytochrome p450 system and the inhibition of EROD activity therefore diminishing the capability of eliminating the xenobiotic.
- \* In Marine Mammals, TBT leads to a reduction of cytochrome p450 and that may be due either by the damage to the heme moiety of the p450 or by binding to the active site (competing).

# Degradation

- \* Through a debutylation process TBT → DBT → MBT → organic tin. Less toxic forms
- \* In algae *C. vulgaris* and *Chlorella sp.* binds to extracellular membrane. Goes in the cell through either passive diffusion or transport mechanism. Eliminated by degrading to DBT and MBT (*c.vulgaris*) and DBT (*Chlorella sp.*) with a TBT-metabolizing enzyme and then excreted. High capacity to degrade them to less toxic forms gives them a high tolerance to TBT

# Degradation cont'd

- \* By active transport outside the organism by ABC multidrug transporters
- \* Degradation by cytochrome p450 activity

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# Chromium Structure

- \* Has symbol Cr and atomic number 24
- \* Is steel grey in color
- \* Chromium III or trivalent chromium is less toxic because it is less mobile
- \* In water, it associates with water molecules and anions and forms chromium III chloride hydrate
- \* Chromium VI or hexavalent chromium is a strong oxidant at pH 7 or less and is the most common form found in groundwater
- \* Can also be found as Chromium (II), (IV), (V)

# Physical and Chemical Properties

- \*  $\text{Cr}^{3+}$  is water insoluble however  $\text{Cr}^{6+}$  is more soluble
- \* pH affects the structure. Gives it a wide range of chemical speciation
- \* Hexavalent chromium is 500 times more toxic than chromium III which precipitates at pH 5 or higher exiting the solution
- \* Physical half-life depends on the Isotope and can range from days to millions of years
- \* In presence of high oxygen content  $\text{Cr}^{3+}$  oxidizes into  $\text{Cr}^{6+}$

# Uses, Application, Production history

- \* It is often used as an alloy in stainless steel. Has a strong resistance to corrosion
- \* Used in dyes and pigments
- \* Used in tanneries
- \* Good for high temperature refractory applications (furnaces, kilns, etc.)
- \* Chromium (III) helps in the lipid and sugar metabolism in humans

# Mode of entry in the aquatic environment

- \* Leached in the ground water at industrial contaminated sites
- \* Through waste water

# Toxicity to aquatic life

- \* Hexavalent chromium can go through the membrane with a transporter
- \* In alga *Chlamydomonas reinhardtii*, phytotoxycity can cause the degradation of pigment status, the nutrient balance and an increase in the antioxidant enzyme activity as well as oxidative stress, affects the chloroplast and the membrane ultrastructure.
- \* In Mussels, it can cause DNA damage and modifications of genes involved in the stress response in gills

# Toxicity to aquatic life

- \* In fish, hexavalent chromium has been known to cause various changes in the fish morphology such as affect the epithelial cells (Hyperplasia and lifting), the gills (degeneration of the lamellae), lamelar cells (hyperplasia) and the central axis tissues (atrophy).
- \* In mammals, causes cancers in humans and might cause reproductive issues in mammals such as the North Atlantic right whale

# Mode of entry into the organisms

- \* In algae, enters the cell either through diffusion or active transport
- \* In mussels,  $\text{Cr}6+$  is absorbed through an anion-exchange carrier or by reduction to  $\text{Cr}3+$  which then gets trapped within the cell
- \* In fish, enters through the cell membrane using active transport

# Mode of entry into the organisms

- \* In mammals, exposure routes are through inhalation or contaminated water supply orally, or through skin
- \* The transport mechanism through the membrane seems to be done by anion transport system or membranes

# Molecular mode of toxic interaction

- \* In algae, *causes oxidative damage as it can increase the amount of reactive oxygen species as well as by diminishing the capacity of the cell to have antioxidant reactions.*
- \* In Mussels, *M. galloprovincialis*, the effect on the digestive gland has been studied and showed an increase in the concentration of chromium. Affects lipid metabolism, changes the activity of the antioxidant enzyme catalase and the GST

# Molecular mode of toxic interaction

- \* In Fish, may affect the ATP-ase enzymes and the transport of ions in and out of the cell.
- \* Reduction of Cr<sup>6+</sup> to Cr<sup>3+</sup>. The reduction creates an increase in the production of reactive oxygen species which, once inside the cell, interacts with various structures and may cause DNA damage

# Molecular mode of toxic interaction

- \* In Mammals, degradation of hexavalent chromium into Cr(V), Cr (IV) and Cr (III). The Cr (III) and a combination of the intermediates that are produced interact with cell components and cause toxicity

# Breakdown/Defense

- \* In mammals, breakdown of Cr 6+ to Cr (V), Cr(IV) and Cr (III) by antioxidant enzymes and excreted in urine

# Breakdown/Defense

- \* In algae, the activation of antioxidant mechanisms such as carotenoids help reduce metals toxicity
- \* In mussels, *M. galloprovincialis*, breakdown of Cr6+ is done with the GSR enzyme which recycles oxidative glutathione. It breaks it down mostly to the more stable trivalent chromium
- \* In fish, usually have an antioxidant response involving superoxide dismutase and glutathione reductase

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