

Toxic Effects Arsenic and Dieldrin Mixtures

**Tuskegee University
College of Veterinary Medicine**

Dissemination Project

**WHY SHOULD ANYONE CARE
ABOUT CHEMICAL
MIXTURES SUCH AS
ARSENIC AND DIELDRIN?**

**Arsenic and Dieldrin are
Toxic
Environmental
Contaminants!!**



What is Arsenic ???



- **Arsenic** - semi-metallic naturally-occurring chemical. It is all around us in the environment and we are all exposed to small doses on a regular basis.
- It is difficult to detect as it is generally odorless and flavorless, meaning people have little idea when it is around.
- **How is arsenic used?**
Many uses including pesticide, treated wood, feed additive, old medicinal agent, treatment for promyoleucytic leukemia in children

Why is arsenic Important?

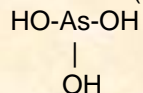
- Arsenic is very toxic
 - ❑ FDA; It causes many forms of cancer
 - ❑ Classified as human carcinogen by EPA
 - ❑ Arsenic binds to many proteins (sulfhydryl enzymes) in the cells

What is the risk?

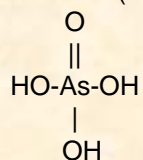
- Arsenic can kill humans quickly if consumed in large amounts, although small, long-term exposure can lead to a much slower death or other illness.
- Studies have linked prolonged exposure to arsenic with cancer, diabetes, thickening of the skin, liver disease and problems with the digestive system.
- It has also been associated with nervous system disorders - feeling tingling or losing sensation in the limbs - and hearing difficulties

Chemical diversity(forms) of Arsenic

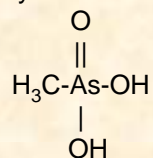
Arsenious Acid (As^{+3})



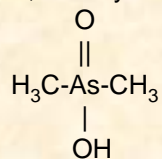
Arsenic Acid (As^{+5})



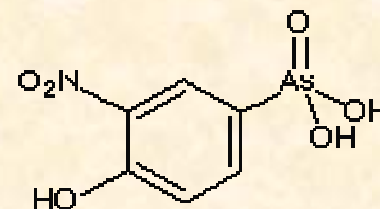
Monomethylarsonic Acid (MMA)



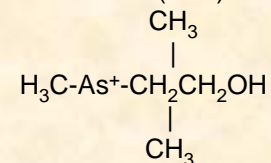
Dimethylarsenic Acid
(DMA, cacodylic acid)



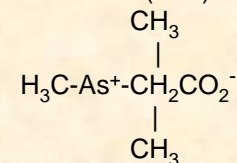
Roxarsone



Arsenocholine (AsC)



Arsenobetaine (AsB)



Arsenic

Arsenic (As) is found in earth's crust as arsenopyrite (FeAsS) and other sulfur and metallic containing minerals

Used in a variety of forms: electronic solid state devices (GaAs), pigments, pyrotechnics (As_4S_4), pesticides, metallurgy, wood preservative (chromated copper arsenate, CCA), chicken feed supplement (roxarsone), herbicide (cacodylic acid).

Arsenic trioxide (As_2O_3 or As_4O_6) {one of the primary intermediates used to make other forms of arsenic} forms arsenous acid when dissolved in water

Salts are called arsenites [represents the +3 oxidation state of arsenic, As(III)]
Arsenates (AsO_4^{-3}) are salts of arsenic acid (orthoarsenic acid) [+5 oxidation state of arsenic]

Arsenite can be easily oxidized to arsenate
arsenate can also be reduced to arsenite

Arsenite is highly poisonous (thought to either cause or promote cancer)
Other forms, such as AsB found primarily in shellfish, are relatively nontoxic because it is rapidly excreted unchanged in urine
Thus, there is a big emphasis today on speciating the forms of arsenic.

Arsenic in water

- Major route of exposure
- Artesian wells
- Maximal contamination limit (MCL) arsenite or arsenate as regulated by EPA 10 ug/L total arsenic in drinking water for biological systems



Arsenic exceeds EPA levels in water

- Where is Arsenic Most Prevalent in Drinking Water in the U.S.? Compared to the rest of the United States, western states have higher arsenic levels (levels greater than 10 ppb).
- Parts of the Midwest and New England have some areas where arsenic levels are greater than 10 ppb. While many areas may not have detected arsenic in their drinking water above 10 ppb, there may be geographic "hot spots" with higher levels of arsenic than in surrounding areas

What happens if you are poisoned?

- A person exposed to large amounts of arsenic - either through eating or drinking it - will usually die, and symptoms will appear within 30 minutes of exposure.
- There is a similar outlook for people who breathe large amounts of it, although the onset of symptoms may be delayed as the concentration is likely to be lower.
- Physical contact with arsenic can cause, initially, the skin to thicken and, with prolonged contact, blood flow to the heart to become decreased.

What are the symptoms?

- The first sensations include a metallic taste in the mouth, excessive saliva production and problems swallowing.
- The next stage is to suffer vomiting and diarrhea coupled with garlic-like breath, stomach cramps and excessive sweating.
- As the poison's effects progress, the patient will suffer seizures and go into shock, dying within a few hours. If death does not occur at this stage, it will happen a few days when the kidney fails.

What is the treatment?

- Arsenic poisoning can be treated if it is caught early enough, through a series of injections into muscles.
- The patient needs 2.5mg to 5mg per kilogram of body weight of a drug called dimercaporal every four hours for the first two days followed by two injections on the third day then one a day for the next five days.

Arsenic Exposure of Children



Occupational Exposures of Arsenic

- Coal miners
- Industrial workers in microelectronic
- Agricultural workers
- Workers who are exposed to wood



Arsenic toxicosis in Bangladesh

**Arsenic is found in
groundwater
of many countries:
particularly South
East Asia
&/esp. Bangladesh**



**A community meeting discussing
how to get pure water**



TOXIC

EFFECTS



Arsenic

- Experimental studies of arsenic on a rat cell line, confirmed their earlier report that arsenic can act as an endocrine disruptor
- These toxic effects occur at extremely small concentrations - as low as 20 times below the new standard of 10 ppb.
- Endocrine-disrupting chemicals disturb hormone signaling and regulation in the body, causing reproductive problems and other abnormalities

Endocrine disruption

- An important contributor to arsenic's ability to increase risk of a host of diseases including several forms of cancer, heart disease, diabetes, and reproductive or developmental problems.

Hyperpigmentation in Arsenic toxicosis

Condition in which patches of skin become darker in color than the normal surrounding skin



Arsenic contaminated water

Keratosis of the foot



Arsenic exposure Multiple skin cancers



Skin cancers



Benefits of Arsenic

- Small doses of arsenic have been shown to send some forms of cancer into remission, and it can also help thin blood.
- Homoeopathists have also used undetectable amounts of it to cure stomach cramps. However, therapies involving the chemical are still in the experimental stages.

Ferns remove arsenic

- Ferns naturally take up arsenic in high concentrations.
 - Edenspace, a Virginia-based company that now licenses the patent for the ferns and sells (4.95/plant) them commercially under the name “edenfern.”
 - Ferns now planted to remove arsenic from ground water by Army Core of Engineers and in Washington DC, New Mexico, Florida and other states
- *Brake fern (Pteris vittata)*



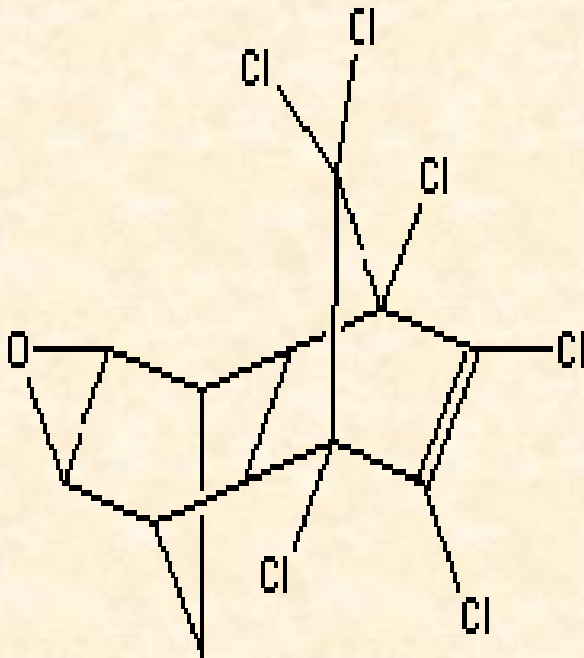
What is Dieldrin???

- DDT like Pesticide
- Endocrine disruptor

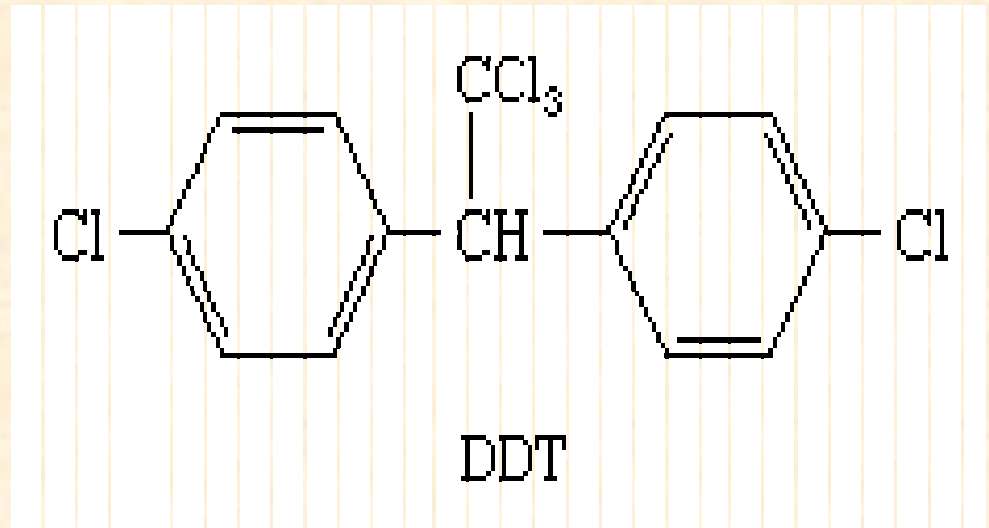
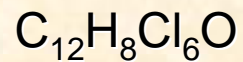
Why is dieldrin important?

- Long half-life
- Persistent in the environment
- Accumulates in environment/body (body fat)

CHEMICAL STRUCTURES OF DIELDRIN and DICHLORODIPHENYLTRICHLOROETHANE (DDT)



DIELDRIN



DDT



How is/was Dieldrin used?

Pesticidal effectiveness

- Fruit farming
- Cotton farming
- Termite control

How are you Exposed to toxins such as arsenic and dieldrin?

- Inhalation
- Oral exposure
- Dermal
- Others routes (eyes, ears...etc.)

Research objectives at Tuskegee University

- Determine toxic/adverse effects of low levels of arsenic, dieldrin, and their mixtures on target organs(e.g, liver, kidney), reproduction, biochemical enzymes(oxidation), hormones, hematology, pathology.
- To determine if the mixtures cause additive (increased), no difference, or antagonistic(oppose) effects after exposure.

Research Results

Decreased pup weight

Initial decrease in feed consumption

Decreased maternal body weight at the higher doses

Decreased implantation sites

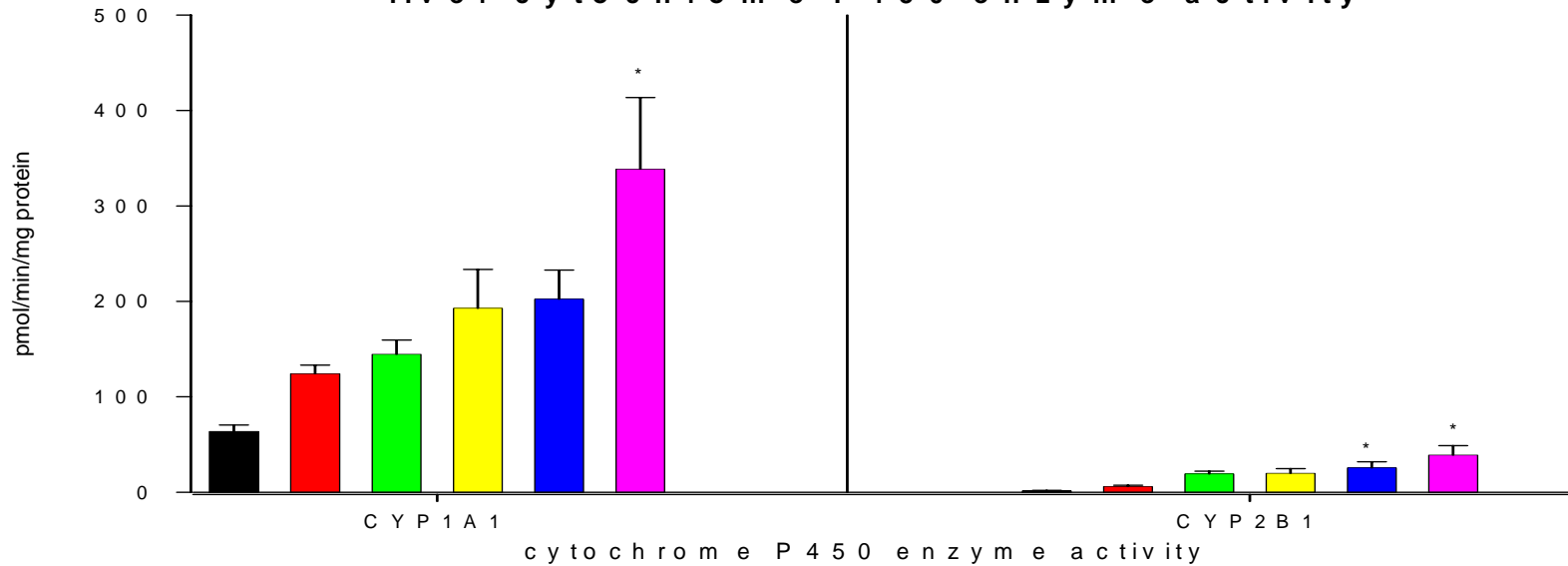
Abnormal behavior such as avoidance and aggressiveness

Decrease in thyroid (T3) hormone levels

Increased drug metabolizing enzymes
(cytochrome P450)

Arsenic-diieldrin mixture induced drug metabolizing enzymes

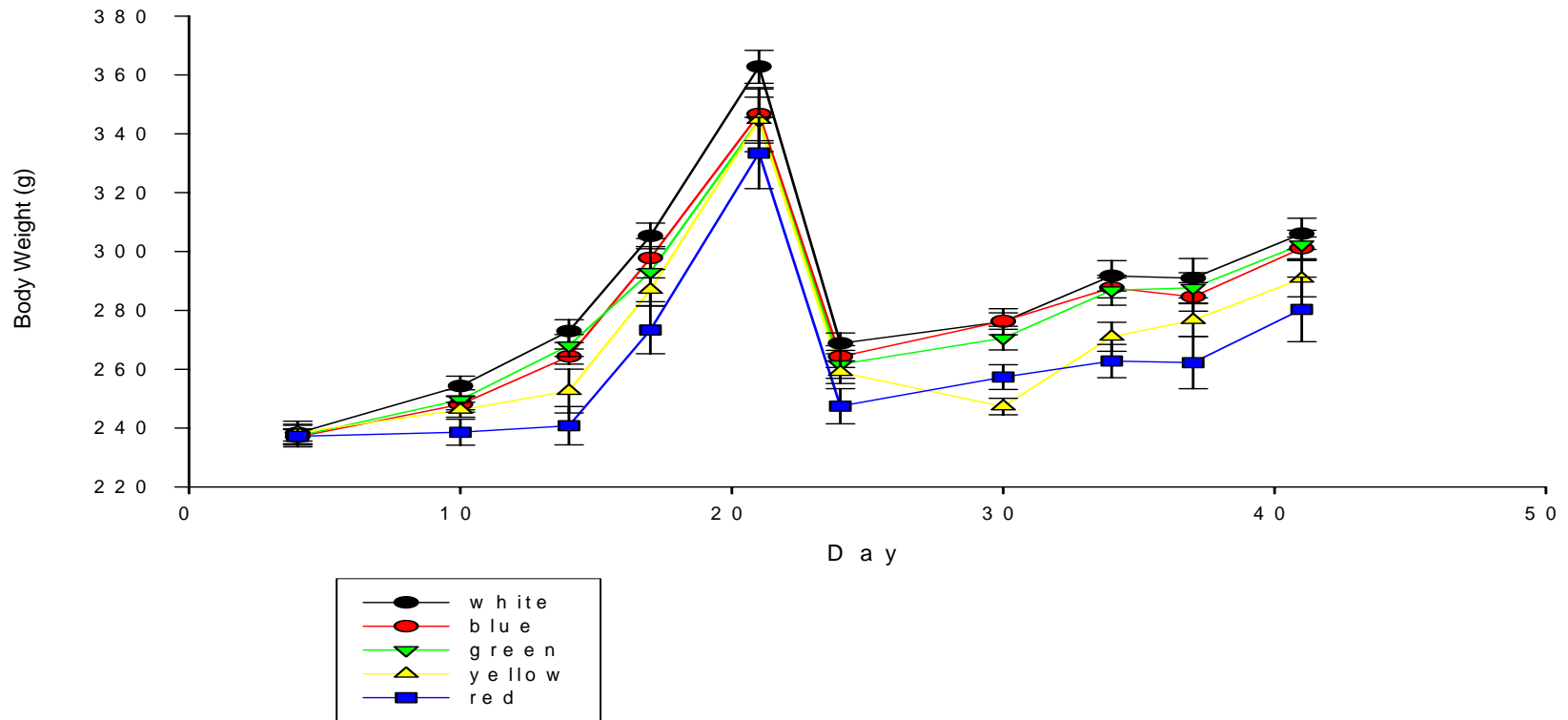
Figure 3. Effect of arsenic-diieldrin mixtures on liver cytochrome P 450 enzyme activity



- Group 1 (Arsenic-Dieldrin: 0-0)
- Group 2 (Arsenic-Dieldrin: 0.25-0.187)
- Group 3 (Arsenic-Dieldrin: 0.5-0.35)
- Group 4 (Arsenic-Dieldrin: 1-.075)
- Group 5 (Arsenic-Dieldrin: 2-1.5)
- Group 6 (Arsenic-Dieldrin: 4-3)

Arsenic-diieldrin mixture decreased body weight

Figure 4. Body weight of female rats



arsenic-diieldrin mixture increased liver weight

	Arsenic-Dieldrin Mixture (mg/kg/day)					
	0-0	0.25-0.187	0.5-0.35	1-0.75	2-1.5	4-3
Liver	8.56±0.17	8.57±0.17	8.363±0.15	8.21±0.33	9.81±0.3*	10.44±0.4*

Significance of research results

- Arsenic dieldrin mixtures increased liver toxicity
- Decreased thyroid hormone levels(t3)
- Importance of assessing the risks of chemical mixtures at a hazardous site
- People living or working near hazardous waste sites where arsenic and dieldrin mixtures are present have increased risk of liver toxicosis

Risk Assessment

- Risks
- Hazard
- Toxicity testing and evaluations
- Doses and adverse effects
- Statistical significance
- Modeling scenarios
- Usefulness of risk assessment: Public health issues and concerns
- Provides guidelines for safety

Safety



Read label

MSDS Sheet

Follow directions

Safety: Proper management of chemicals

- Handle chemicals safely
- Hold chemicals away from the body to decrease the risk of contact
- Wash hands after using chemicals
- **If exposed, follow necessary directions for emergency**
Report possible exposure to Poison Control Center
If you have a poisoning emergency, call 1-800-222-1222.
If the victim has collapsed or is not breathing, call 911.

Wear safety garments

- Mask to protect the nose
- Goggles for eye protection
- Gloves
- Apron
- Hat
- Boots



Safety Guidelines

- Proper Storage of chemicals and pesticides
 - Store in lock proof area to prevent access of children and pets
 - Monitor environmental temperatures
 - Maintain proper labels



References

- **Ogden, Graham, Datiri, Mansour etl al Effects of Arsenic and Dieldrin and their mixtures.. The Toxicologist; Vol 41; 2005**
- **[www. ATSDR.gov](http://www.ATSDR.gov)**
- **www.epa.gov/superfund/accomp/success/rma.htm**

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Ms. Harrison

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The Students

ATSDR

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