

Use of Obese Zucker Rats in the Study of Diabetes

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Arsenic is a metalloid similar to phosphorous, and is very toxic. At sub toxic doses it was once used as a stimulant, and can also treat ailments such as certain types of leukemia. At toxic doses, Arsenic disrupts the production of ATP, and can lead to organ failure. As it occurs in the environment, arsenic is an inorganic element, which becomes organic when absorbed by plants and animals, and combines with Hydrogen and Carbon. Exposure can come from oral intake with trace amounts in food and water, or breathing in arsenic from dust, smoke, or air. This usually occurs in areas where levels are naturally high, or near areas where arsenic is used in production.

Arsenic intoxication can cause severe damage to the liver, resulting in toxic hepatitis, which can be associated with hepatic necrosis and elevated liver enzyme levels. High level arsenic has also been linked to hepatic angiosarcoma, a rare form of cancer in the liver. Ingestion of arsenic has also been strongly associated with an increased risk of skin cancer for humans. Thus far, there has been no direct link between arsenic poisoning and the development of cancer forms following the onset of contact.

Dieldrin is a large hydrocarbon originally used as a pesticide, designed to kill insects. This insecticide however, is one of high molecular weight, and has a tendency to accumulate in the tissues of animals. It has been linked to issues such as Parkinson's, Breast Cancer, and damage to other organ systems of the body such as the immune, reproductive, and nervous systems.

Dieldrin can be found everywhere in the environment, though it is only found in trace amounts. Higher levels of exposure occur from the consumption of aquatic animals such as fish and shellfish, which have been contaminated from chemical exposure, or from other contaminated food sources. Long term exposure to smaller amounts of Dieldrin; also indicate a serious problem, as the accumulation in the tissues produces a major carcinogenic health risks, ranging from enlarged liver and lesions to hepatomas, depending on the animal type, dosage and the duration of exposure. Laboratory rats, when exposed to three different doses showed a consistent increase in tumors, though result showed only that of benign tumors, with no signs of malignancy. When exposed to higher doses of Dieldrin, there appears to be no dose related increase in tumors or malignancy.

In order to assess the effects of Arsenic and Dieldrin mixtures on the rats, we will be taking a look at the test results particularly for enzymes present, as well as gross lab data including liver weights obtained from necropsy. Emphasis will be placed on the

Cytochrome P450 complex, as well as Oxidative enzymes, and Liver enzymes. This will show how the mixtures affect the metabolic processes at large, and will also if the rats are suffering from oxidative stress, or exhibit any depression in liver function. Large emphasis is placed on the enzymes dealing with the liver, because of growing interest with enzymes including aspartate aminotransferase (AST) and alanine aminotransferase (ALT) and their correlation to Type II Diabetes. This is because individuals with type 2 diabetes mellitus have a higher incidence of liver function test abnormalities than individuals who do not have diabetes.

Aspartate aminotransferase (AST) is an enzyme found in the bloodstream and in many vital organ tissues such as the heart, liver, kidneys, and lungs, among others. (BCH) Though it is not specific to liver tissue only, it is an enzyme designated to the determination of liver disease. (BCH) This is done by observing the extent to which AST responds as a result of tissue damage. Levels between ten and twenty times the normal amount can be indicative of cirrhosis of the liver, while twenty times or more can be caused by severe viral hepatitis. (YHP)

Alanine Aminotransferase (ALT) is also an enzyme used to indicate liver functioning capability. It is slightly more focused with the liver as the production site, though it can also be found in other parts of the body including skeletal and cardiac muscle cells. In animals, ALT is considered to be relatively specific to hepatocytes, thus making it the ideal test for indication of liver disease.