ODOMENE JUSTICE

17/SCI03/006

BCH306

1. Write short note on the toxicological effect of food additives and preservatives.

The toxicological effect of food additives and preservatives maybe immediate or may be harmful in the long run if one has constant exposure or accumulations. Immediate effects may include headaches, change in energy level and alterations in mental concentration, behaviour or immune response. Long term effects may increase one's risk of cancer, cardiovascular diseaseand other degenerative conditions. Some modern synthetic preservatives have become controversial because they have been shown to cause respiratory or other other health problems. Some studies point to some synthetic preservatives and artiificial coloring agents aggravating ADD & ADHD symptoms in those affected. There are many ways food additives & preservatives can have toxicological effects in the body. an example is:

Aluminum toxicity in the premature infant:

Premature infants are fed intravenously, because they do not tolerate oral feeding. The calcium gluconate and phosphates which are used as components of the feeding solution given intravenously contain significant amount of aluminum. In premature infants kidneys are not fully matured and therefore their ability to excrete the aluminum is very less. Consequently premature infants are at risk of sufficient aluminum accumulation as these may develop metabolic bone disease, cholestatic hepatitis, and reduction of mental development.

Aluminium-induced bone disease:

Aluminium is used in most food additives & preservatives. Osteomalacia is the manifestation of Aluminum-induced low-turnover bone disease. In a dialysis patient Aluminum-induced bone disease is seen when serum Al is greater than thirty microgram per litre[6-8].

2. Describe various categories by which toxicity testing studies can be performed. Hence write on various tests for assessing the toxicity of any two major organ in the body.

Categories which toxicity testing studies can be carried out are:

Acute Toxicity Studies: Acute toxicity studies provide information on the potential for health hazards that may arise as result of short-term exposure. Determination of acute oral, dermal, and inhalation toxicity is usually the initial step in evaluating the toxic characteristics of a pesticide. **Subchronic Toxicity Studies:** Subchronic exposures do not elicit effects that have a long latency period (e.g., carcinogenicity). However, they do provide information on health hazards that may result from repeated exposures to a pesticide over a period up to approximately 30% of the lifetime of a rodent. **Chronic Toxicity Studies:** Information derived from chronic studies is used to assess potential hazards resulting from prolonged and repeated exposure to a pesticide over a large portion of the human life span. These studies usually last 12 to 24 months. **Developmental Toxicity Studies:** Developmental toxicity studies are designed to assess the potential of developmental effects in offspring resulting from the mother's exposure to the test substance during pregnancy. These effects include death of the developing organism, structural abnormalities, altered growth, and functional deficiencies.

3. Discuss the various routes by which the body can be exposed to foreign substances

There are four routes by which the body can be exposed to foreign substances: inhalation, skin (or eye) absorption, ingestion, and injection.

• **Inhalation**: For most substances in the form of vapors, gases, mists, or particulates, inhalation is the major route of entry. Once inhaled, substances are either exhaled or deposited in the respiratory tract. If deposited, damage can occur through direct contact with tissue or may diffuse into the blood through the lung-blood interface. Upon contact with tissue in the upper respiratory tract or lungs, it may cause health effects ranging from simple irritation to severe tissue destruction. Substances absorbed into the blood are circulated and distributed to organs that have an affinity for that particular substance. Health effects can then occur in the organs, which are sensitive to the toxicant.

• **Skin (or eye) absorption**: Skin (dermal) contact can cause effects that are relatively innocuous such as redness or mild dermatitis; more severe effects include destruction of skin tissue or other debilitating conditions. Many chemicals can also cross the skin barrier and be absorbed into the blood system. Once absorbed, they may produce systemic damage to internal organs. The eyes are particularly sensitive to chemicals. Even a short exposure can cause severe effects to the eyes or the substance can be absorbed through the eyes and be transported to other parts of the body causing harmful effects.

• **Ingestion**: Chemicals that inadvertently get into the mouth and are swallowed do not generally harm the gastrointestinal tract itself unless they are irritating or corrosive. Chemicals that are insoluble in the fluids of the gastrointestinal tract (stomach, small, and large intestines) are generally excreted. Others that are soluble are absorbed through the lining of the gastrointestinal tract. They are then transported by the blood to internal organs where they can cause damage.

• **Injection**: Substances may enter the body if the skin is penetrated or punctured by contaminated objects. Effects can then occur as the substance is circulated in the blood and deposited in the target organs.

4. Bioavailability of any toxicant is influenced majorly by lipid barrier, discuss.

5. Explain the concept of molecular targets of toxicants.

The toxic action of a chemical is a consequence of the physical/chemical interaction of the active form of that chemical with a molecular target within the living organism.Examples of molecular targets are:

- Proteins -Arylhydrocarbon(Ah) receptor-dioxin
  -Hemoglobin-CO
- Lipids- Carbon tetrachloride
- DNA- Aflatoxin

6. Write on the toxicological effect of a named food preservative.

Nitrates & Nitrites:

The salts of nitrite and nitrate are commonly used for curing meat and other perishable produce. They are added to food to preserve it and also help hinder the growth of harmful microorganisms, in particular *Clostridium botulinum*, the bacterium responsible for life-threatening botulism. Nitrites, together with nitrates, are also added to meat to keep it red and give flavour, while nitrates are used to prevent certain cheeses from bloating during fermentation. Nitrate is found naturally in vegetables, with the highest concentrations occurring in leafy vegetables like spinach and lettuce. It can also enter the food chain as an environmental contaminant in water, due to its use in intensive farming methods, livestock

production and sewage discharge. In humans, nitrite and nitrate from food are rapidly absorbed by the body and, for the most part, excreted as nitrate. Some of the nitrate absorbed by the body is recirculated through salivary glands and part of it is converted by mouth bacteria into nitrite. Absorbed nitrite can oxidise haemoglobin to methaemoglobin, an excess of which reduces the ability of red blood cells to bind and transport oxygen through the body. Nitrite in food (and nitrate converted to nitrite in the body) may also contribute to the formation of a group of compounds known as nitrosamines, some of which are carcinogenic. Exposure to nitrites poses the highest risk to infants and pregnant women. In pregnant women, the harmful byproduct of nitrites known as methemoglobin accumulates in the body and deprives the cells of oxygen. Nitrate exposure during pregnancy can cause birth defects, according to a study published in 2004 in "Epidemiology," and high amounts in infants can lead to a serious respiratory condition known as blue-baby syndrome.

7. Carcinogenesis could result from toxicant exposure, discuss.

8. Describe the various excretory pathways of toxicants.

When a toxic xenobiotic (or its metabolites) is rapidly eliminated from the body, it is less likely that they will be able to concentrate in and damage critical cells. Except for the lung, polar (hydrophilic or water-soluble) substances have a definite advantage over lipid-soluble toxicants as regards elimination from the body. Chemicals must again pass through membranes in order to leave the body, and the same chemical and physical properties that governed passage across other membranes applies to excretory organs as well.

Toxicants or their metabolites can be eliminated from the body by several routes. The main routes of excretion are via urine, feces, and exhaled air. Thus, the primary organ systems involved in excretion are the urinary system, gastrointestinal system and respiratory system. A few other avenues for elimination also exist.

Urinary Excretion: Elimination of substances by the kidneys into the urine is the primary route of excretion of toxicants. The primary function of the kidney is the excretion of body wastes and harmful chemicals. The functional unit of the kidney responsible for excretion is the nephron. Each kidney contains about one million nephrons. The nephron has three primary regions that function in the renal excretion process, the glomerulus, proximal tubule, and the distal tubule. These are identified in the illustrations.

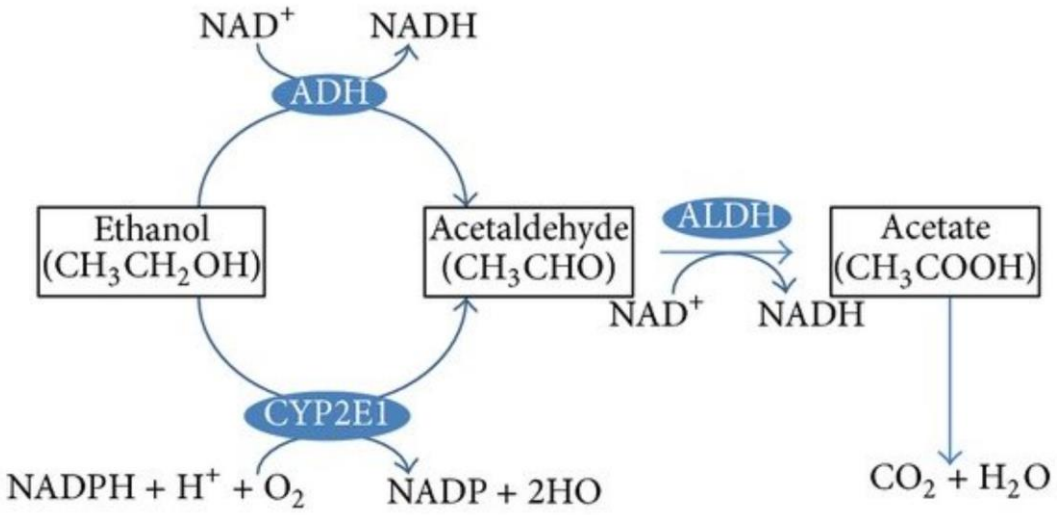
Fecal Excretion: Elimination of toxicants in the feces occurs from two processes: excretion in bile, which then enters the intestine, and direct excretion into the lumen of the gastrointestinal tract. The biliary route is an important mechanism for fecal excretion of xenobiotics and is even more important for the excretion of their metabolites. This route generally involves active secretion rather than passive diffusion. Some heavy metals are excreted in the bile, e.g., arsenic, lead, and mercury. However, the most likely substances to be excreted via the bile are comparatively large, ionized molecules, such as large molecular weight (greater than 300) conjugates. Once a substance has been excreted by the liver into the bile, and subsequently into the intestinal tract, it can then be eliminated from the body in the feces, or it may be reabsorbed. Another way that xenobiotics can be eliminated via the feces is by direct intestinal excretion. While this is not a major route of elimination, a large number of substances can be excreted into the intestinal tract and eliminated via feces. Some substances, especially those which are poorly ionized in plasma (such as weak bases), may passively diffuse through the walls of the capillaries, through the intestinal submucosa, and into the intestinal lumen to be eliminated in feces. Intestinal excretion is a relatively slow process and is therefore an important elimination route only for those xenobiotics that have slow biotransformation, or slow urinary or biliary excretion. Increasing the lipid content of the intestinal tract can enhance intestinal excretion of some lipophilic substances.

Several minor routes of excretion exist, primarily via mother's milk, exhaled air, sweat, saliva, tears, and semen.

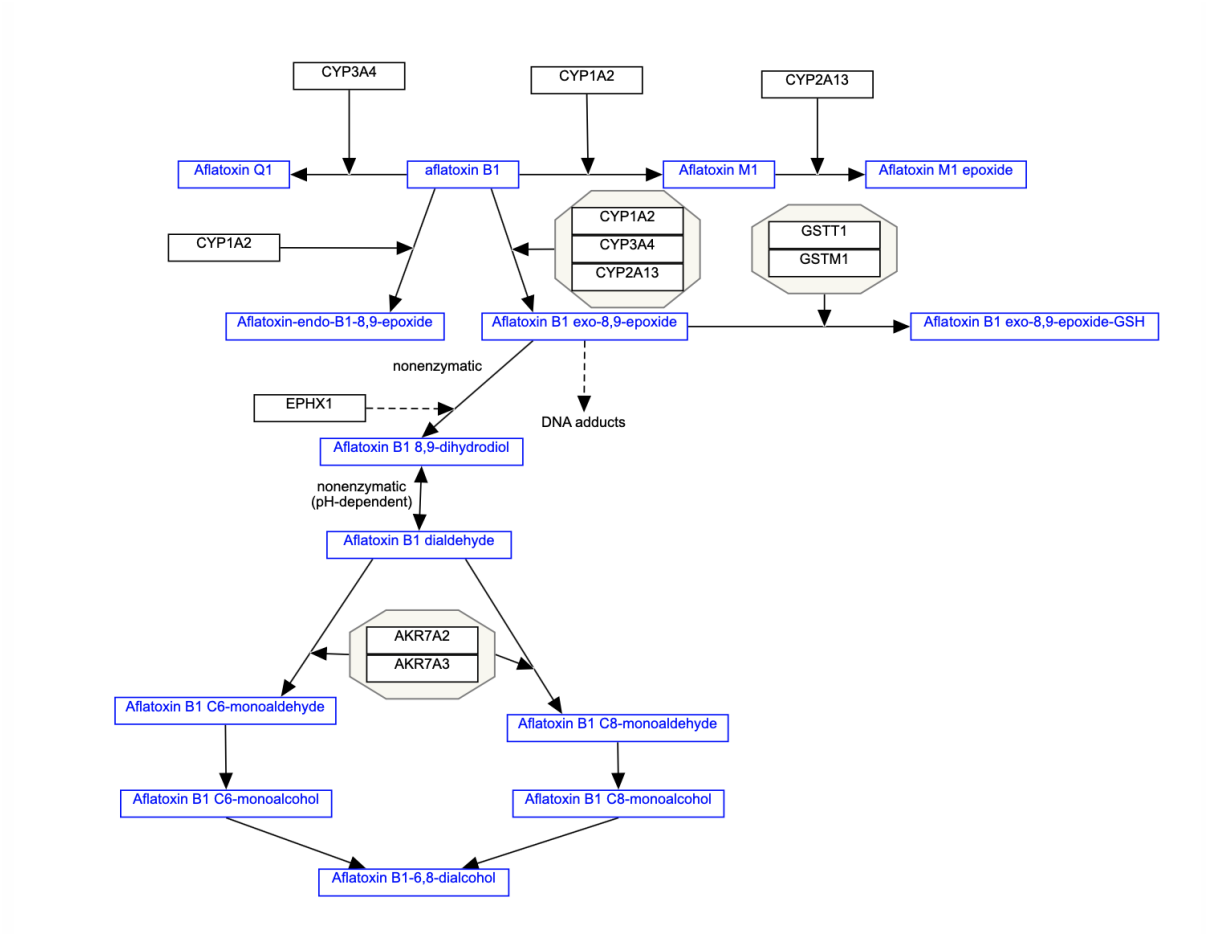
9. With the aid of schematic diagram, describe the toxicological process in mammal.

10. With the aid of an adequate pathway, discuss phase I and II metabolism of:

- **Ethanol:**Ethanol is metabolized into acetaldehyde by alcohol dehydrogenase (ADH) and the microsomal enzyme cytochrome P450 2E1 (CYP2E1). The ADH enzyme reaction is the main ethanol metabolic pathway involving an intermediate carrier of electrons, namely, nicotinamide adenine dinucleotide (NAD+). Acetaldehyde is rapidly metabolized by aldehyde dehydrogenase (ALDH) in the mitochondria to acetate and NADH. And acetate is eventually metabolized in the muscle to carbon dioxide and water.



- **Aflatoxin B1:**



11. Write on:

Toxicokinetics: Toxicokinetics refers to the quantitation and determination of the time course of the disposition or ADME(absorption, distribution, metabolism & excretion) for a given toxic xenobiotic.

Toxicodynamics: The term "toxicodynamics" describes what a toxicant does physiologically, biochemically, and molecularly to an animal's body following exposure.