PHARMACEUTICAL TOXICOLOGY-II PRACTICE

PURPOSE AND GENERAL INFORMATION

A) ANALYTICAL TOXICOLOGY

Analytical toxicology is a science that deals with the qualitative and quantitative recognition of poisoning-causing compounds and isolation of poisons from biological material.As a result of environmental pollution and the development of the industry, many toxic substances are exposed.It is a fact that drugs used in treatment cause intoxication due to overdose or genetic features.In this type of poisoning, it is important to determine the presence and level of the poison in the body's fluid and tissues in order to make the treatment in a healthy way or to illuminate the forensic institutions in the case of death.As a biological material in poisoning, urine, blood, vomit can be taken as an example.In cases of death due to poisoning, it is possible to take samples from appropriate tissues.In cases of acute intoxication, the food container, cups, their contents (eg, nutrients, water) or drug bottles which are considered to contain the substance that may cause poisoning can be used for toxicological analysis.In chronic poisonings, for example, workplace air is also considered to be the material to be analyzed.

When selecting samples from tissues to investigate the poisoning factor in death events, it should be taken into consideration that the distribution in the organism is not equal.The distribution of substances in tissues varies according to physical properties, chemical structure and metabolism.For example, lead in bones, arsenic in hair and nails, fat-soluble substances in the brain are collected, ethyl alcohol distributes evenly in all body fluids.If there is information about the cause of poisoning, the selection of biological material is facilitated, and when this information is not available, enough samples are taken from various tissues and toxicological analysis is required.

For toxicological analysis, it is necessary to have knowledge about the metabolism of poisons, because the metabolites of some substances are more likely to be found in biological material than the actual substance. For example;

- benzene poisoning → phenol in urine,
- trichlorethylene poisoning→trichloroacetic acid in blood and urine,
- heroin poisoning → morphine in urine.

In addition, the diagnosis of some poisoning cases can also be achieved by detecting changes in the level of some substances naturally present in the body, other than the poison itself and its metabolites. For example, the level of coproporfirin increases in lead poisoning.

Table 1. Selection of analysis material according to poisonings

Materiel	Poisoning agent
Urine	Arsenic, fluorine, zinc, sleeping drugs, other drugs.
Stomach contents, gastric lavage	Poisons taken shortly before oral poisoning
Intestinal content	Poisons taken 1-2 days before death
Blood	Nitrite, nitrate, chlorate, carbon monoxide, barbiturates
Brain	Essential poisons, alkaloids, barbiturates, boric acid, thallium
Liver	Heavy metals (As, Pb, Sb, Hg, Zn, Tl), fluorine, barbiturates, cyanide, alkaloids
Kidney	Mercury, lead, copper, molybdenum
Bone	Fluorine, arsenic, lead
Hair, nail	Arsenic, lead
Lungs	Respiratory poisons
Muscle	Cyanide, thallium
Fat	Chlorinated hydrocarbons

Samples taken for toxicological analysis are placed in clean containers, sealed, labeled and sealed if necessary. In general, no preservatives should be added to prevent disruption.

Classification of poisons according to isolation methods:

In toxicological analysis, various chemical and physicochemical methods are used to identify the substance causing poisoning. In order to apply these methods, it is necessary to separate the causative agent from the biological material. In analytical toxicology, to facilitate analysis; poisons are classified according to this separation process.

I- **Volatile poisons:** They are sought by general methods such as water vapor distillation, microdifusion, or special devices developed for volatile substances such as ethyl alcohol and cyanide. Alcohols, ketones, aldehydes, cyanide, halogenated hydrocarbons, carbons, carbon sulfide, phosphorus, aromatic hydrocarbons are the main examples.

II- **Non-volatile organic poisons:** The substances in this group are separated from the biological material by liquid-liquid extraction. Barbiturates, salicylates, alkaloids and some other drug groups are important toxicological examples.

III- **Metallic poisons:** They are isolated from the biological material as a result of the destruction process. Arsenic, lead, mercury, bismuth, antimony, cadmium are the main examples in terms of toxicology.

IV- **Toxic anions:** They are separated from the biological environment by dialysis or ion exchange methods. Chlorate, phosphate, thiocyanate are among the anions that can be counted in this group.

V- **Gases:** Carbon monoxide, methane, hydrogen sulfide are examples of this group.

VI- **Various poisons:** These are the substances which should not be separated by general extraction methods such as insecticides, toxins and glycosides, but a special extraction method should be applied for each.

VOLATILE POISONS

Volatile poisons are separated from the biological material by distillation or microdifusion methods. The microdifusion method will be discussed in Experiment 2; distillation can be summarized as follows:

Distillation Method: Distillation is to vaporize a liquid substance by boiling it to its boiling point and concentrate the vapor in a separate container. Distillation of volatile poisons is done in two ways: normal distillation and water vapor distillation.

Water vapor distillation: Each liquid substance has a certain vapor pressure depending on the temperature. If a gas stream and vapor are removed from the liquid, the substance evaporates to provide the balance. In practice, water vapor is used for this purpose. Generally, when water vapor is sent to the substances which are quite high from the boiling point of the water, these substances evaporate in the evaporation pressure ratio in response to that temperature. These vapors, together with water vapor, are condensed through the cooler.Poisons drifting with water vapor; they are divided into two groups: poisons drifting with water vapor in acid medium and basic medium.

The pH of the medium is adjusted to 5 with dilute sulfuric acid or tartaric acid in order to isolate the water vapor drifting poisons in the acid medium. Benzene, acetone, phenol and formaldehyde are examples of volatile poisons that can be drained by water vapor in the acid medium. In case of looking for poisons that can be entrained with water vapor in the basic environment, the pH of the medium is

adjusted to 8 with dilute sodium hydroxide or magnesium oxide. Examples of this group include aniline, amphetamine, chloral, chloroform and nicotine.

Recognition of Volatile Poisons:

The product obtained by distillation is called distillate. For the purpose of defining the volatile poison present in the distillate, the following operations are performed:

1. The smell of distillate is checked. Certain compounds, such as phenol, benzene, and carbon sulfide, can be identified by their characteristic odor.
2. It is controlled by the litmus paper whether the distillate is acid or basic.
3. After experiments performed in order to find the functional groups of the substance in the distillate, special experiments are carried out according to the results of this reaction.

Table 2. Some general and specific recognition reactions for alcohol and aldehydes

	On the distillate			**On the oxidized distillate**		
	($K_2Cr_2O_7 + H_2SO_4$) reactive	Schiff reactive	Chromotropic acid reagent	($K_2Cr_2O_7 + H_2SO_4$) reactive	Schiff reactive	Chromotropic acid reagent
Formaldehyde	**+**	–	**+**	**+**	**+**	**+**
Acetaldehyde	**+**	**+**	–	**+**	**+**	–
Methyl alcohol	**+**	–	–	–	**+**	**+**
Ethyl alcohol	**+**	**+**	–	**+**	**+**	–