PURPOSE OF THE PHARMACEUTICAL TOXICOLOGY LABORATORY AND GENERAL INFORMATION

Biochemical and Molecular Toxicology

Following the industrialization, it is getting important to investigate the possible toxic effects of the drugs, chemicals and their metabolites on human and environment at molecular levels. After entering into the body via entry routes (orally, dermal, inhalation), chemicals are absorbed and they go to their target organs to show their effects. The alterations occurred on the chemicals by several enzymes in the organism is called biotransformation or metabolism. After biotransformation, the effect of the chemical can increase or decrease. The exposure route, dose of the xenobiotic are some of the factors affecting the change of the toxicity. Lipophilic substances turn to hydrophilic forms during the metabolism in order to excrete easily. If they stay same as before, they cannot be excreted and start to accumulate in the organism so there are some enzyme systems located in the organism to turn the lipophilic substances to their hydrophilic metabolites. These enzyme systems are classified into two topics called as Phase I and Phase II reactions. In Phase I reactions, it is aimed to add some polar groups to the chemical to enhance its polarity for easy excretion. Oxidation, reduction and hydrolysis reactions are the Phase I reactions. Generally without some exceptions, Phase I reactions result in detoxification. In some reactions, chemicals turn more toxic metabolites during Phase I reactions and this is called activation or toxication. In Phase II reactions; sulphate, glucuronic acid or glutation groups are added to the substances that make them more polar. After Phase I and II reactions, the formed polar metabolites lost their toxic features are excreted easily from the body.

With enhanced industrialization and pollution, humans and the environment are exposed to much more harmful chemicals so the investigations aiming to protect the environment and the human health are getting more important. Today, it is easier to get knowledge about the functions of the cell by molecular researches. For example, the recent techniques make the isolated DNA molecule more refined. After isolation, with PCR method DNA molecule can be multiplied easily. Furthermore, after the development of SCE (Sister Chromatid Exchange)

and MN (Micronuclei) methods, it gets easier to obtain the genotoxic potentials of the exposed chemicals and the evaluation of the risk that can be occurred.

Similarly, a lot of compounds used in daily life turns prooxidant-antioxidant balance into prooxidation and cause oxidative stress. Prooxidant mechanism is known as the enzymatic and nonenzymatic eradication of free radicals. However, this mechanism can be inadequate when the body exposed to high level of toxic chemicals causing cell death and illness. The indicators of oxidative damage are the measurements of MDA (malondialdehyde) and GSH (glutathione) levels. The main risk group for chemical exposure is pregnant women. Excess exposure to chemicals in pregnancy causes the death of fetus or malformations in the fetus. Thus, teratogenity tests in toxicology are very important.

The acute toxicity of a chemical is important in the toxicity investigation of a chemical. In acute toxicity studies, response to one dose is assessed. Firstly, LD50 value of the chemical is determined. LD50 is the dose of the chemical that kills the 50% of animals tested. Species difference and the exposure route are the factors affecting LD50 value. Therefore, it is not constant for a chemical. It is a statistical term that indicates dose-lethality relationship specific for a species in given conditions. Determination of toxicities resulted in long term/repeated exposure to a chemical needs subacute, subchronic and chronic toxicity tests.

The examples described above can be increased; however the examples are given related to the planned laboratory practice lessons.