

## **Environmental Toxicology**

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**Dose response relationship:** The characteristics of exposure and the spectrum of effects come together in a correlative relationship usually referred to as the dose response relationship. This relationship is most fundamental concept in toxicology and its understanding is necessary for the study of toxicity of chemicals.

A better understanding of dose response relationship can be developed with the help of following three assumption.

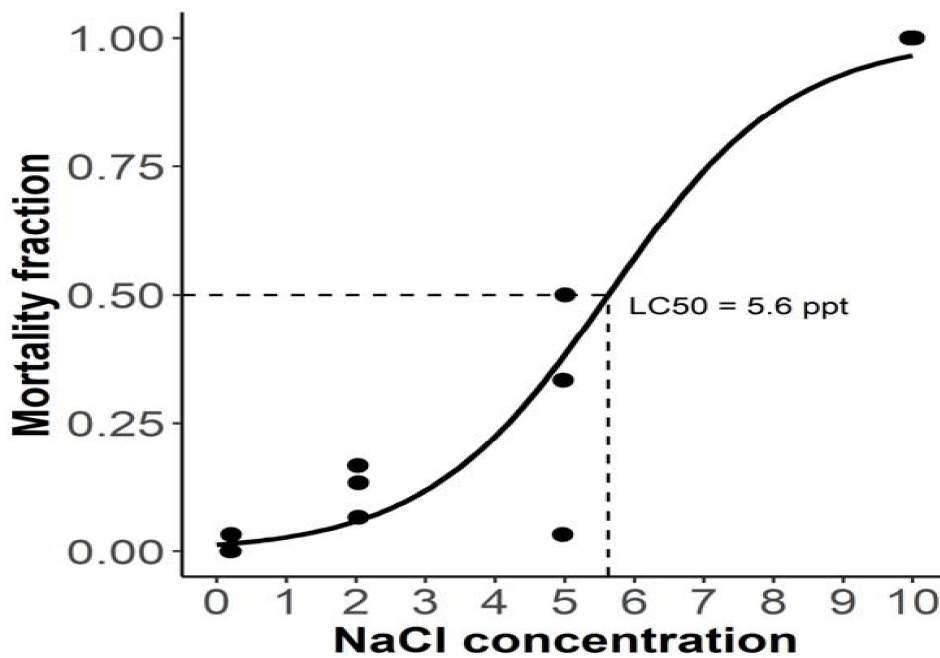
- a) The toxic response is a function of concentration of the chemical at the site of action.
- b) The concentration at the site of action is related to the dose of chemical to which the organisms are exposed
- c) The response is causally related to the chemical i.e. the response is obtained only due to the exposure of the chemical.

**1. Toxic response is a function of concentration of the xenobiotics at the site of action:** The xenobiotics (chemical) induced adverse effects as a result of their interaction with the suitable receptors. The receptor may be an enzyme, the interaction of toxicants with receptor may be reversible or irreversible, and such interaction is assumed to initiate a proportional response. The reversible and irreversible may give rise to different types of response. The response may be very short as it depends on the concentration at the site of action, which may only be transient in case of reversible interaction. But, with irreversible interaction, a single interaction will theoretically be sufficient to cause adverse effect.

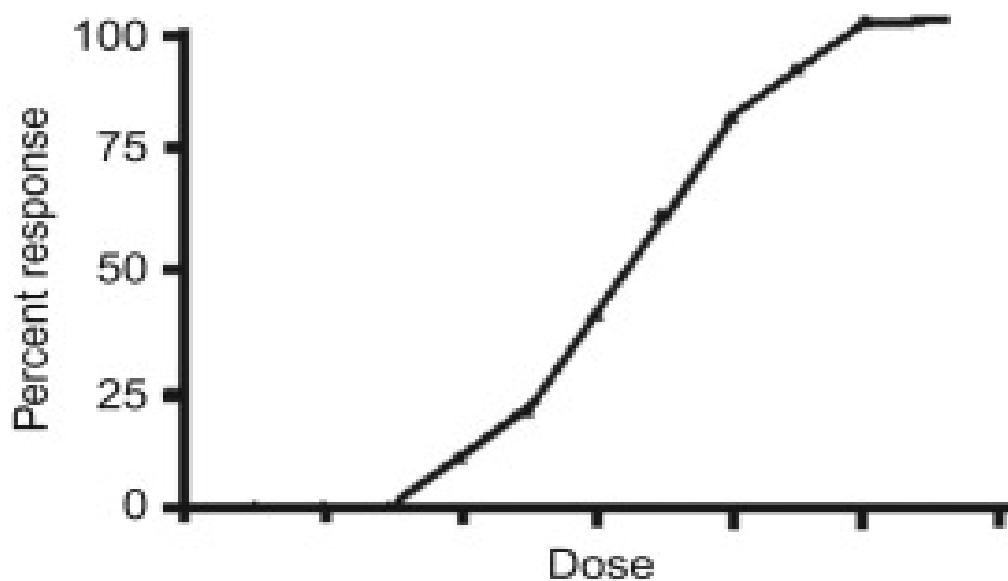
**2. Concentration at the site may be related to the dose of toxicant administered:** Although the concentration in tissues is generally related to the dose of xenobiotics compounds to which organisms are exposed. There are various factors, which affect this concentration. Thus, the absorption from the site of exposure, distribution in tissues, biotransformation and excretion, all determine the concentration of toxicant at the target site.

**3. The response is causally related to the chemical:** The study of dose response relationship is to know with reasonable certainty that the obtained response is only due to the application of the chemical. Because in certain cases, when a response is obtained the influence of more variables. The true dose to which organism has been exposed, the site and relative specificity of the response. Thus dose response relationship is based on the knowledge that the observed response is a result of exposure to known toxicant.

**Measurement of dose response relationship:** Whatever response is selected for the measurement the relation between the degree of response of the biological system and the amount of toxicant administered assumes a form that occurs so consistently as to be considered as classic and fundamental and is referred to as the dose response relationship. Determination of medium lethal concentration ( $LC_{50}$ ) / medium lethal dose ( $LD_{50}$ ) on animal models are exposed to different dose of toxicants and cause death in 50 percent of animals. The graph so obtained is termed as dose response curve.



**Dose Response Curves:** The mechanism by which a toxicant produces an adverse effect is an important determinant of the dose-toxicity relationship. In many cases toxicity can be directly related to the concentration of active agent at specific receptor sites and irrespective of the biochemical mechanisms. The dose response relation is to determine the percentage of animals in a particular dose group, which show the response.



**Therapeutic Index:** The therapeutic index is defined as the ratio of dose required to produce a toxic effect and the dose needed to obtain the desired therapeutic response. Therapeutic index is used as an index of comparative toxicity of two different toxicants is an approximate statement of the relative safety of a drug or toxicants expressed as the ratio of lethal or toxic dose to the therapeutic dose:

$$TI = LD_{50}/ED_{50}$$

The  $ED_{50}$  is approximately 20, and the  $LD_{50}$  is about 200, thus the therapeutic index is 10, a number indicative of a relatively safe toxicant or drug.