2.4 Assessment of Toxicity

2.4.1The dose-response relationship

Thus a dose-response relationship is used to measure the impact of various concentrations of a pollutant on a population. The aim is to specify a threshold concentration at which some effect is observed. The dose of a poison is the product of its concentration and the duration of its exposure to an organism. A dose is described as acute if a large concentration is administered in a short time, whereas a chronic dose is a small concentration applied over a long period of time. Both however, ultimately lead to the same exposure level over different periods of time. An acute toxic effect is a rapid response to the poison, while chronic toxic effects are those that appear over a prolonged period of exposure. This might eventually lead to death, but also includes sublethal effects, such as reduction in the reproductive potential, changes in behaviour, physiology or morphology (Sheehan, 1984)

The potential toxicity (harmful action) inherent in a substance is exhibited only when that substance comes in contact with a biological system. A chemical normally thought of as "harmless" may evoke a toxic response if added to a biological system in sufficient amount. The toxic potency of a chemical is thus defined by the response that is produced in a biological system. The impact of a toxic agent is proportional to the dose administered. Small doses produce a mild effect while larger doses have a severe effect. In general two types of dose-response relationship are used in toxicological studies:

(a) Graded response: Variations in the intensity of toxic response in relation to the dose is termed as graded response. It is generally studied in relation to chronic effects. When exposed to gradually rising levels of a toxicant, individuals show no apparent response till a certain concentration is reached, which is followed by the onset and a gradual rise in the severity of the effect. A point is finally reached at which the intensity of toxic response is maximum. This is similar to biotic response due to the influence of a particular factor that we have studied earlier. However, in the case of toxicant the situation is complicated because they have multiple sites and mechanism of action.

(b) Quantal response: When it is necessary to specify a toxic threshold, it is more appropriate to measure a quantal response, which the organism either does or does not show. It generally measures the dose-related variations in the distribution of toxic response in a natural population. The end point selected in such studies is quantal in nature (mortality for instance). Up to a certain dose, none of the members of the population show any effect. As the dose is increased susceptible members are first affected. A gradual rise in the number of individuals affected rises with the increase in the concentration of the toxicant. Eventually at a particular concentration maximum number of individuals is affected. In environmental toxicology, quantal responses are measured in an acute test, the **LD_{50}** toxicity test. This measures the dose at which 50% of the population is killed within a specified period. Other quantifications are shown in table 2.1.

Such a type of test is termed as bioassay. A bioassay is a procedure in which the responses of organisms are used to measure or detect the presence or effect of one or more substances, wastes, or environmental factors, alone or in combination. Bioassay is used for a variety of purposes such as simulation studies in microcosms and mesocosms, toxicity, effect of various factors singly or on combination, and effect of various pollutants. The prerequisite for bioassay is to first acclimatize the organism to the test environmental conditions before the start of the experiment, and to use controls in order to identify the response under test conditions.

Bioassay may be short term (usually 24 hours but may be extended to about 8 days), intermediate (8-90 days), and long term using the full life cycle (for more details see Environmental management- Mukherjee 2000).

Table 2.1 Quantal response values

LD_{50}	= lethal median dose: dose resulting in 50 % mortality
LC_{50}	= lethal median concentration: the concentration in the surrounding medium resulting in 50 % mortality
LT_{50}	= median lethal time: the time taken to kill half the population at a particular level of exposure
ED_{50}	= median ecological dose: the environmental level of exposure causing 50 % mortality
TL_m	= median tolerance limit: the concentration where 50 % survival is observed.
NEC	= no effect concentration: the highest concentration at which a known effect of a pollutant is not observed.

For different substances the doses needed to produce an adverse effect varies widely. LD50 values are used to compare acute toxicity. The test substance or preparation may be applied to the animal orally, under the skin, by inhalation, into the abdomen or into the vein. LD50 and LC50 are the parameters used to quantify the results of different tests so that they may be compared. LD50 is the abbreviation used for the dose, which kills 50% of the test population. LC50 is the abbreviation used for the exposure concentration of a toxic substance lethal to half of the test animals. LD50 is expressed in milligrams per kilogram of body weight of the test animal (which must be mentioned). LC50 is expressed in millilitres per kilogram of body weight of the test animal (which must be mentioned), exposed to the substance by inhalation during a specified period. The variation in the numerical values of LD50 and LC50 is wide. Table 2.2 describes the variation in LD50 values measured in ingestion studies on the rat.

It is important to mention the species on which the test was conducted because the numerical values of LD50 and LC50 depend on several factors, such as the biological system or animal, strain, sex, age and diet. The LD50 of DDT insecticide administered orally is 87 mg/kg of body weight for a rat but 150 mg/kg of body weight for a dog. The LD50 for dioxin is 0.02 mg/kg of body weight for a rat and 0.001 mg/kg of body weight for a dog, i.e. the rat is twenty times more tolerant than the dog. The assessment of how a human system would react is not a straightforward estimation from the animal tests. However, the animal test gives an idea of the level of the toxic effects.

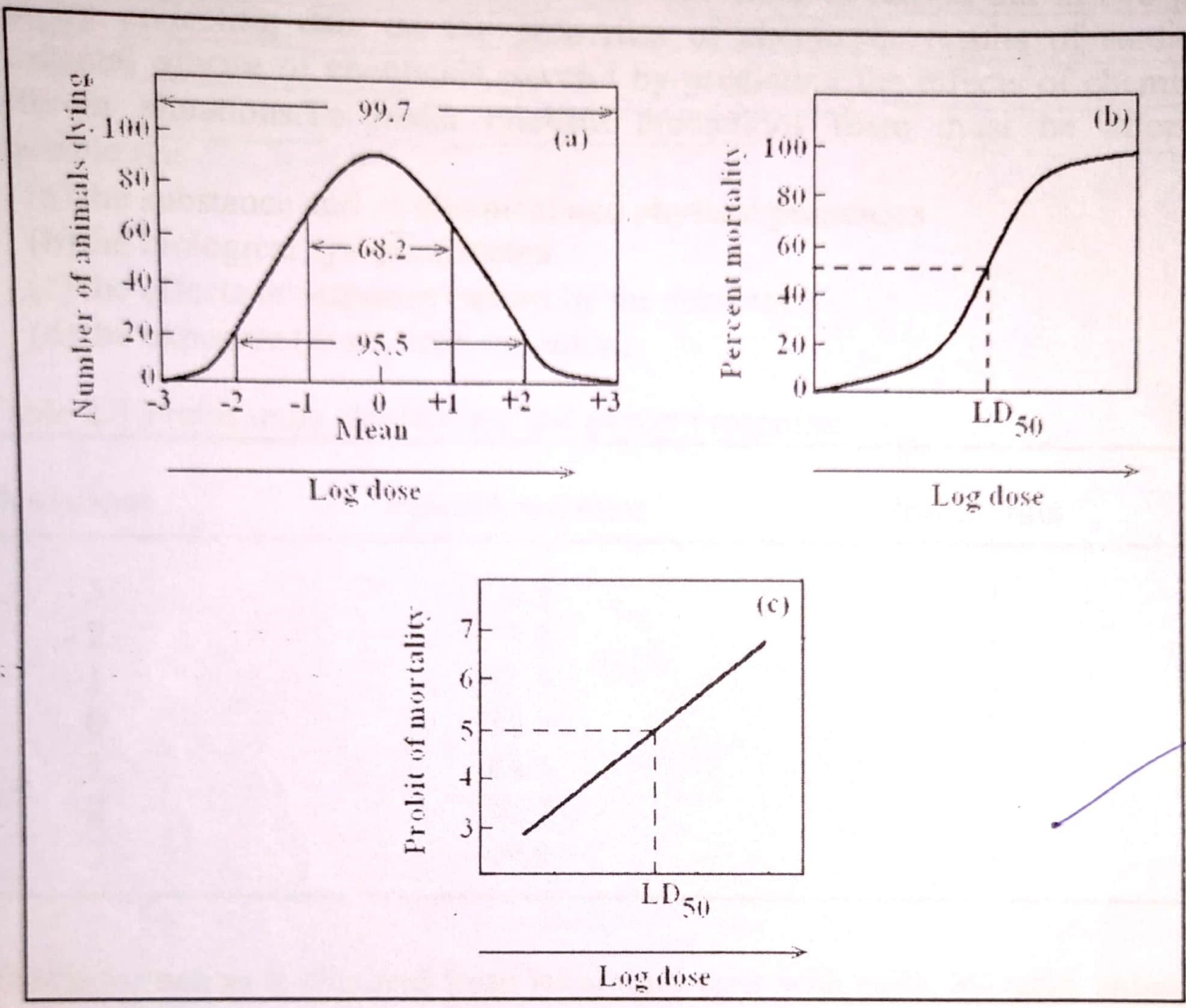

Figure 2.1 The derivation of the probit scale and LD $_{50}$ – the dose that is lethal to 50 percent of the population. A number of animals are exposed to the pollutant over a range of concentrations, usually expressed as log dose for convenience. If this range is properly selected, a more or less normal distribution of responses will occur (a) with few animals responding at very low or very high doses. Most die at some intermediate levels. If this data is redrawn by plotting the proportion of individuals at each dose (the percentage response at each dose), a sigmoidal dose – response curve results (b). The final step is to straighten the line. This can be done by expressing the deviation as a probit. A probit scale scores each successive standars deviation from the mean as one. The mean is set to 5, so one SD above the mean is 6 and two SD below the mean is 3 (c). Modified and redrawn from Beeby, 1993.