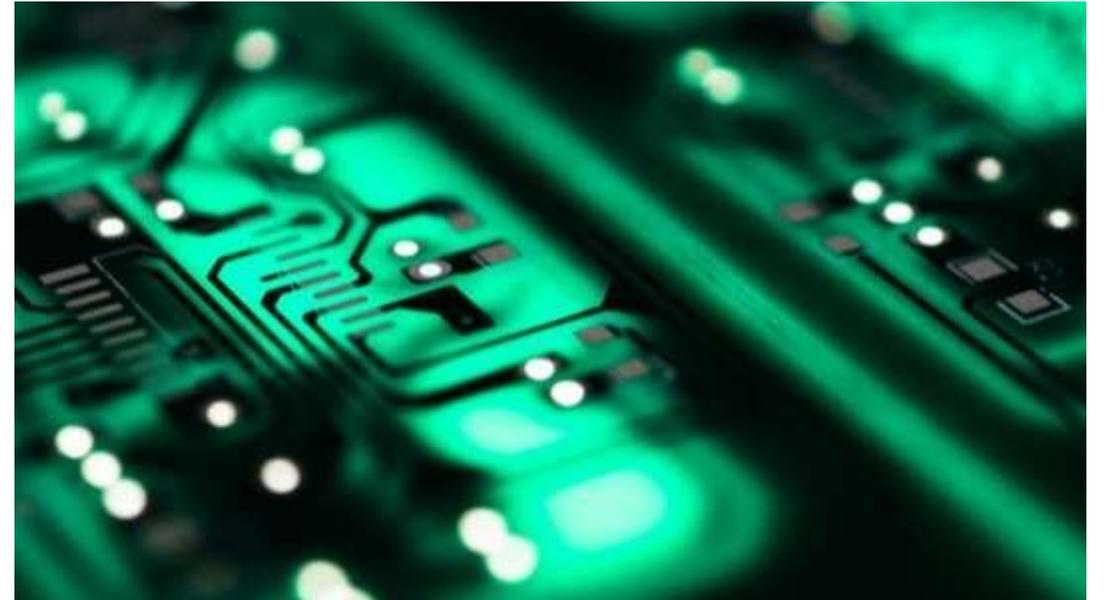




THERAPEUTIC INDEX

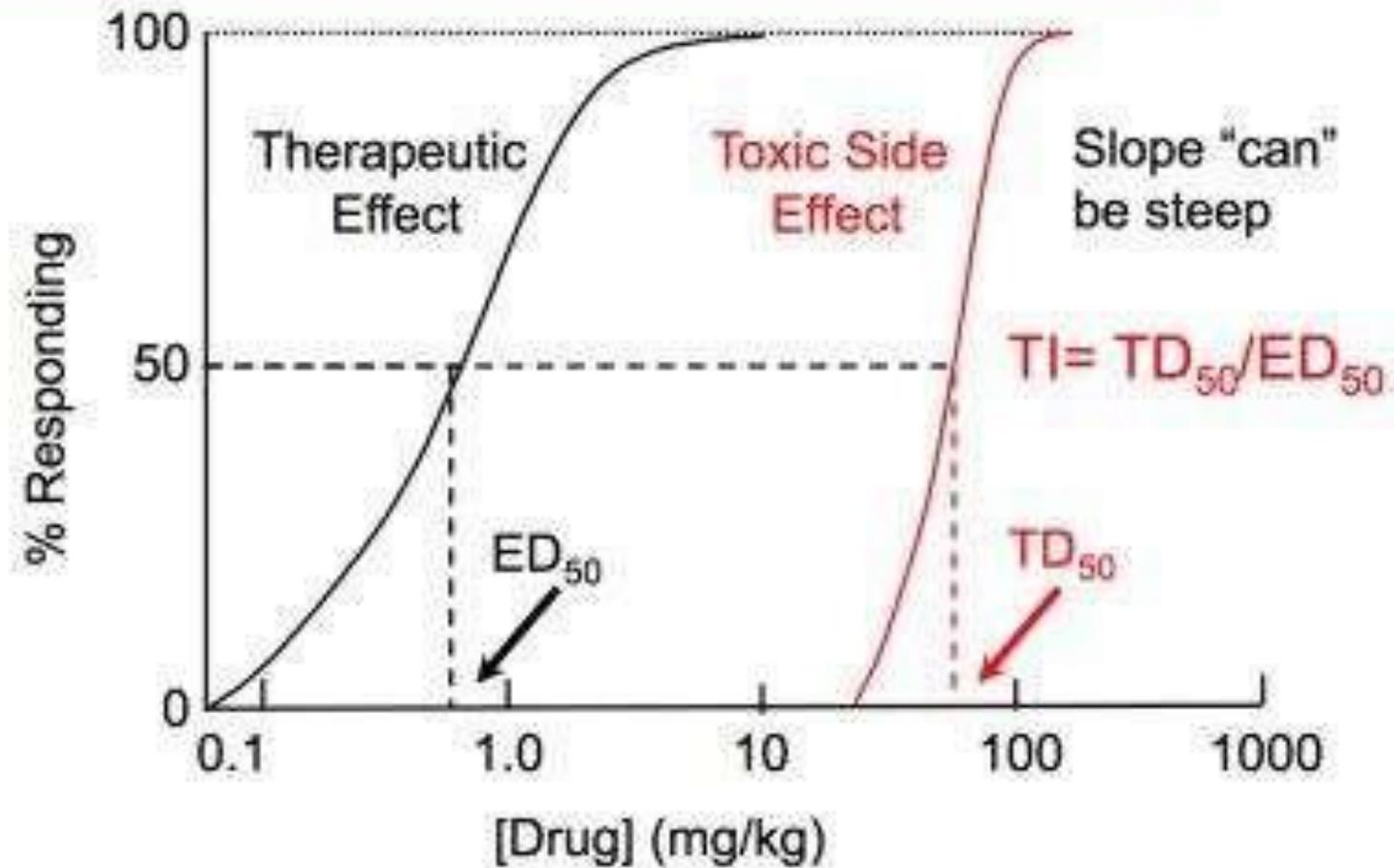
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- A ratio that compares the blood concentration at which a drug becomes toxic and the concentration at which the drug is effective.
- The ratio between the dosage of a drug that causes a lethal effect and the dosage that causes a therapeutic effect.
- The larger the therapeutic index (TI), the safer the drug is.
- If the TI is small (the difference between the two concentrations is very small), the drug must be dosed carefully and the person receiving the drug should be monitored closely for any signs of drug toxicity.



Drug Safety - Therapeutic Index



- ❑ The **Therapeutic Index (TI)** is used to compare the therapeutically effective dose to the toxic dose of a pharmaceutical agent.
- ❑ The TI is a statement of relative safety of a drug.
- ❑ It is the ratio of the dose that produces toxicity to the dose needed to produce the desired therapeutic response.
- ❑ The common method used to derive the TI is to use the 50% dose-response points, including TD50 (toxic dose) and ED50 (effective dose).

$$TI = \frac{\textit{toxic dose}}{\textit{dose for therapeutic response}} = \frac{TD50}{ED50}$$

DOSE RESPONSE

- ❖ The dose-response relationship is an essential concept in toxicology. It correlates exposures with changes in body functions or health.
- ❖ In general, the higher the dose, the more severe the response. The dose-response relationship is based on observed data from experimental animal, human clinical, or cell studies.
- ❖ Knowledge of the dose-response relationship establishes:
 - ✓ **Causality** — that the chemical has induced the observed effects.
 - ✓ The **threshold effect** — the lowest dose where an induced effect occurs.
 - ✓ The **slope** for the dose response — the *rate* at which injury builds up.

LETHAL DOSES/CONCENTRATIONS



Lethal Dose 0% (LD0) — represents the dose at which no individuals are expected to die. This is just below the threshold for lethality.



Lethal Dose 10% (LD10) — refers to the dose at which 10% of the individuals will die.

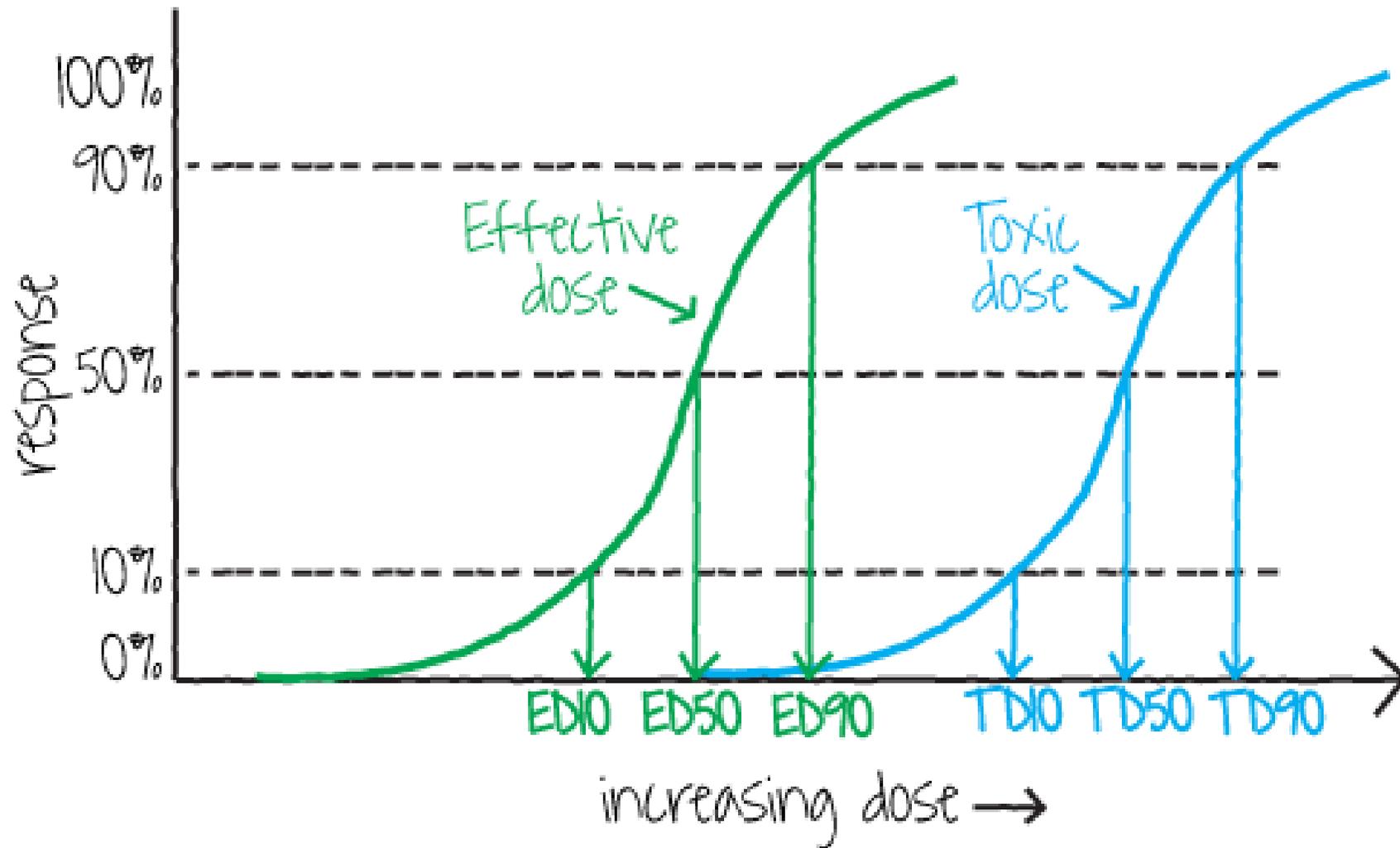


Lethal Concentration 50% (LC50) — for inhalation toxicity, air concentrations are used for exposure values. The LC50 refers to the calculated concentration of a gas lethal to 50% of a group. Occasionally LC0 and LC10 are also used.

EFFECTIVE DOSES (EDS)

- ❑ **Effective Doses (EDs)** are used to indicate the effectiveness of a substance.
- ❑ Normally, effective dose refers to a beneficial effect such as relief of pain. It may also stand for a harmful effect such as paralysis.
- ❑ Thus, the specific endpoint must be indicated.

| Term | Effective for this percentage of the population |
|------|---|
| ED0 | 0% |
| ED10 | 10% |
| ED50 | 50% |
| ED90 | 90% |



Dose-response curves representing effective dose and toxic dose for the same drug

Thank

You!