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Dose Response Relationship: Determination of the ED_{50} and LD_{50}

Drug

Mechanism of action

↓

Response

↙ ↘

Pharmacological (Therapeutic Effect) **Toxicological (Lethal Effect)**

Types of Respons

↙ ↘

1. Graded Response
Duration of Sedation which depend on plasma concentration of the drug e.g: **Diazepam**
5mg 10 min.
10mg 20 min.

2. Quantal Response
All or none response
Yes or No response
+ve or –ve response
e.g: **Ketamine**
1mg No Anesthesia
5mg Anesthesia

Quantal Response:

***Median Effective Dose (ED_{50}):**
The dose of the drug that produce **therapeutic response** in 50 % of the animals.

***Median Lethal Dose (LD_{50}):**
The dose of the drug that produce **Lethal response** in 50 % of the animals.

Advantages of ED_{50} and LD_{50}:

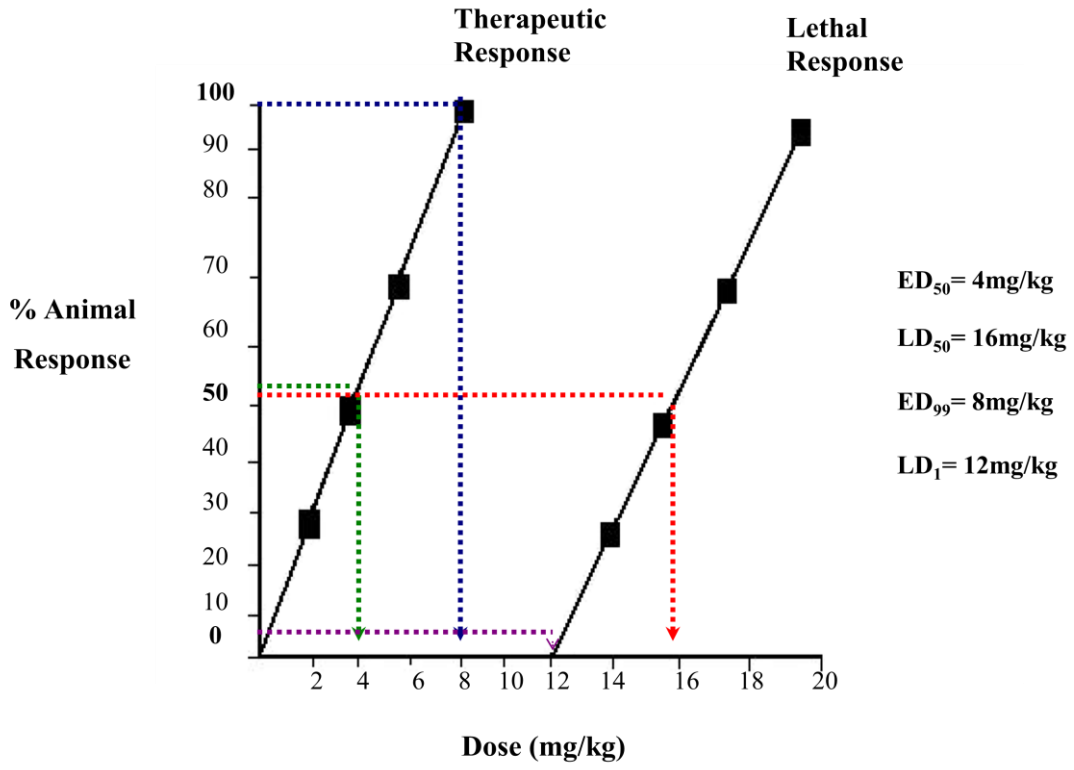
1. Used in calculation of the drug safety.

2. Used as first step in researches for unknown drug.

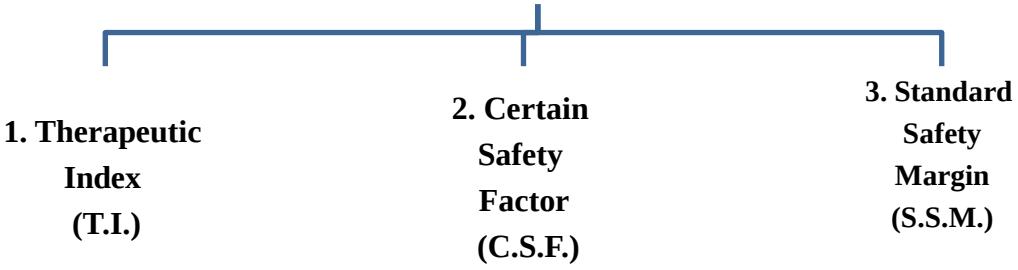
Disadvantages of ED_{50} and LD_{50}:

1. Time consuming.

2. Using of large numbers of animals to calculate it.



Drug Safety



1-Therapeutic Index (T.I.) =LD_{50} / ED_{50} =
16 mg / 4 mg =4

Multiplication of the **Effective Dose** 4 times to kill 50% of the animals

Note:
The higher T.I. . → Safer drug

e.g.:
Drug A (T.I.)= 5
Drug B (T.I.)= 10
Drug B is more SAFER than drug A

2. Certain Safety Factor (C.S.F.) =LD_1 / ED_{99} =
12 mg / 8 mg =
1.5

Multiplication of the **Effective Dose** 1.5 times to kill 1% of the animals

Note:
The higher C.S.F. → Safer drug

e.g.:
Drug A (C.S.F.)= 2.5
Drug B (C.S.F.)= 0.5

Drug A is more SAFER than drug B

3-Standard Safety Margin (S.S.M.) =(LD_1 / ED_{99} – 1) × 100 =
(12 mg / 8 mg – 1) × 100 =50 %

Multiplication of the **Effective Dose** 50% to kill 1% of the animals

Note:
The higher S.S.M. → Safer drug

e.g.:
Drug A (S.S.M.)= 100 %
Drug B (S.S.M.)= 30 %

Drug A is more <u>SAFER</u> than drug B

Question

Drug A:
LD_1= 3 mg/kg
ED_{99}= 1 mg/kg

Drug B:
LD_1= 160 mg/kg
ED_{99}= 100 mg/kg

Calculate S.S.M.? Which Drug is more **<u>Toxic</u>** than other?

Drug A

Dose Mg/kg	No. used	No. anesthetized	% anesthesia	No. died	% death
1	10	2	20	0	0
2	10	6	60	0	0
3	10	8	80	0	0
4	10	10	100	0	0
5	10	0	0	0	0
6	10	0	0	1	10
7	10	0	0	2	20
8	10	0	0	4	40
9	10	0	0	8	80
10	10	0	0	10	100

Drug B

Dose Mg/kg	No. used	No. anesthetized	% anesthesia	No. died	% death
10	10	0	0	0	0
20	10	2	20	0	0
40	10	4	40	0	0
80	10	6	60	0	0
120	10	10	100	0	0
140	10	0	0	2	20
160	10	0	0	4	40
180	10	0	0	6	60
200	10	0	0	8	80
220	10	0	0	10	100

1. Find: ED_{50}, LD_{50}, ED_{99} and LD_1? 2. Calculate: T.I., C.S.F. and S.S.M.? 3. Which drug is <u>SAFER</u>, A or B?