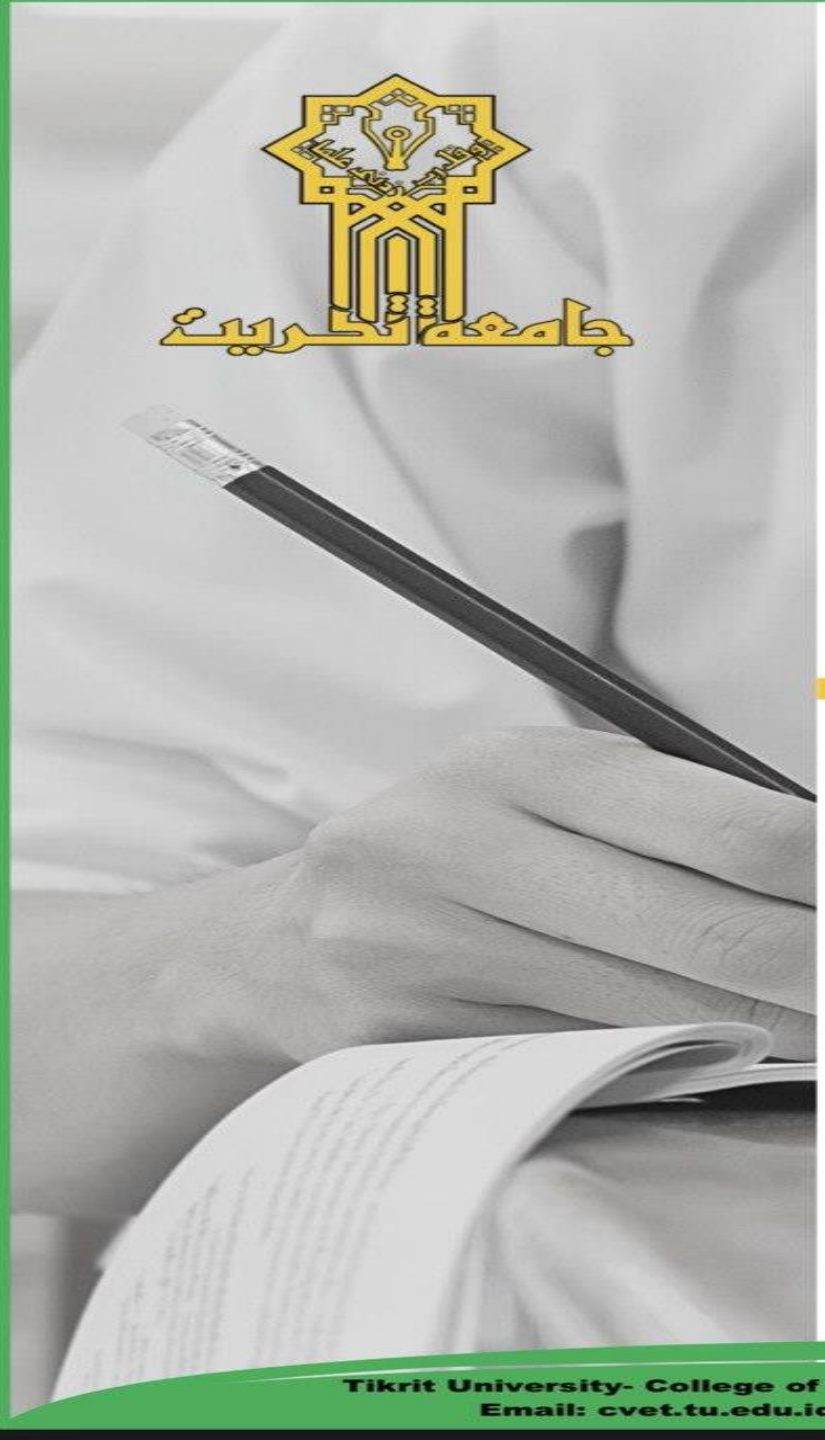
Dose Response Relationship: Determination of the ED_{50} and LD_{50}



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Dose Response Relationship

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Subject year:2024

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Font type (times new roman)

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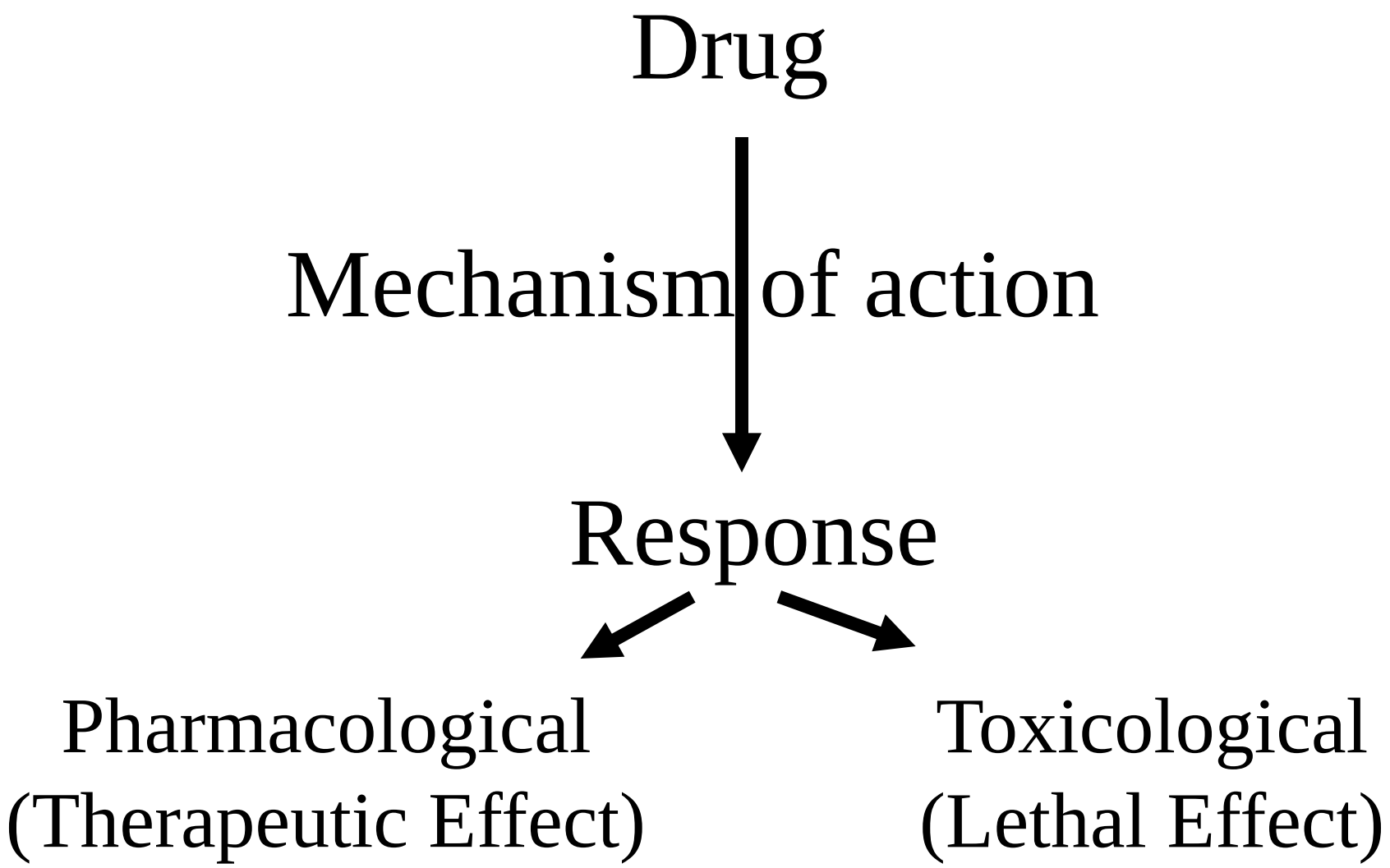
Lecturers link


Drug
Mechanism of action
Response
Pharmacological
(Therapeutic Effect)
Toxicological
(Lethal Effect)

Types of Response

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:

***M**edian **E**ffective **D**ose (**ED_{50}**):
The dose of the drug that produce **therapeutic response** in 50 % of the animals.

***M**edian **L**ethal **D**ose (**LD_{50}**):
The dose of the drug that produce **Lethal response** in 50 % of the animals.

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

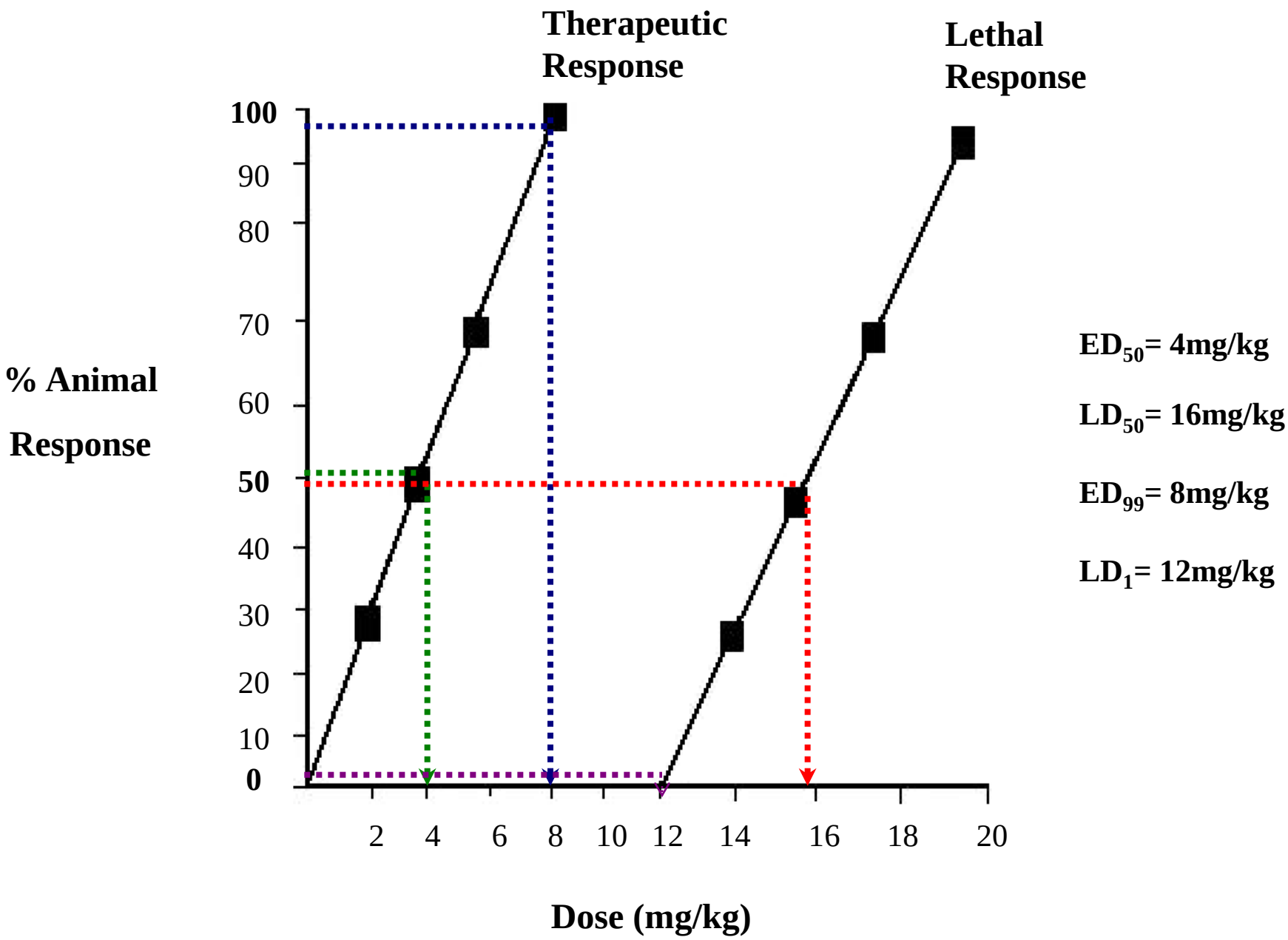
1. Used in calculation of the drug safety.

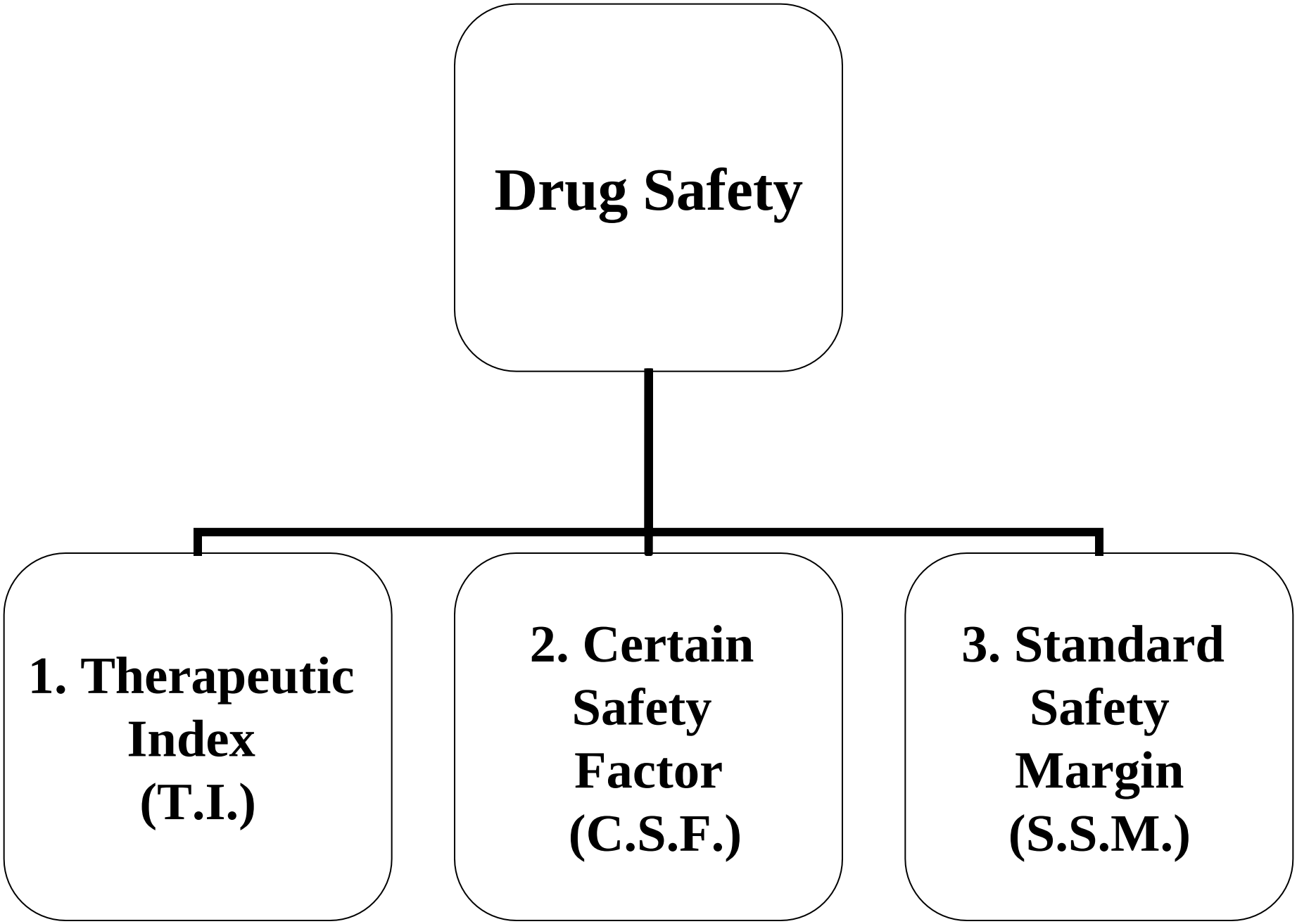
2. Used as first step in researches for unknown drug.

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

1. Time consuming.

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


Therapeutic Response
Lethal Response
100
90
80
70
60
50
40
30
20
10
0
% Animal Response
2
4
6
8
10
12
14
16
18
20
Dose (mg/kg)
ED50= 4mg/kg
LD50= 16mg/kg
ED99= 8mg/kg
LD1= 12mg/kg


Drug Safety
1. Therapeutic Index (T.I.)
2. Certain Safety Factor (C.S.F.)
3. Standard Safety Margin (S.S.M.)

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.) =

$(LD_1 / ED_{99} - 1) \times 100 =$

$(12\ mg / 8\ mg - 1) \times 100 =$

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 SAFER 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 **Toxic** 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 SAFER, A or B?