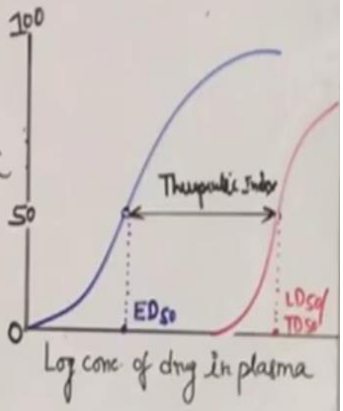
Therapeutic Index (TI)

In toxicology a similar relationship exists between toxic dose and the therapeutic response.

- ✓ The therapeutic index of a drug is the ratio of the dose that produces toxicity to the dose that produces a therapeutic effect.
- ✓ LD 50 is the median lethal dose which is expected to cause mortality in 50% of animals belonging to the same species and strain
- ✓ ED 50 is the median effective dose that produce the desired effect in 50% of population/ animals tested

✓ Therapeutic Index

Therapeutic Index = $\frac{\text{Dose that produce toxicity in 50\%}}{\text{Dose that produce clinical effect in 50\% of patient}}$



Equation – Therapeutic Index = $\frac{LD_{50}\ (Animal)}{ED_{50}} / \frac{TD_{50}\ (Human)}{ED_{50}}$

point – ① This may also calculated as – Distance between - benificial effect DRC and unwanted effect DRC.

② T. Index give idea about drug safety margine.

③ Higher the Therapeutic Index = Greater the safety of drug – eg. $\frac{LD_{50}}{ED_{50}} = \frac{100}{10} = ⑩$ = Safer. $\frac{20}{10} = ②$ = Unsafe

④ Reasonably safe drug must have Therapeutic Index more than 1 (>1)

⑤ High T.I = ① Penicillin ② Diazepam ③ Atenolol.

⑥ Low T.I = ① Lithium ② Warfarin ③ Digoxin ④ Barbiturates

⑦ Therapeutic Index may be different for each use of drug.

Exa:- Therapeutic Index of Aspirin is different for – Headach & Inflammation.

Limitation – ① Not

Therapeutic Index

$$\text{Therapeutic Index} = \frac{LD_{50}}{ED_{50}} \quad \text{OR}$$

$$\text{Therapeutic Index} = \frac{\text{Median toxic dose}}{\text{Median effective dose}}$$

$$\text{Therapeutic Index} = \frac{\text{Tachycardia due to salbutamol in 50\% test subjects}}{\text{Specified reduction in airway resistance in 50\% test subjects}}$$

Importance of therapeutic index:

- ✓ To determine the dose at which drug is safe and toxic

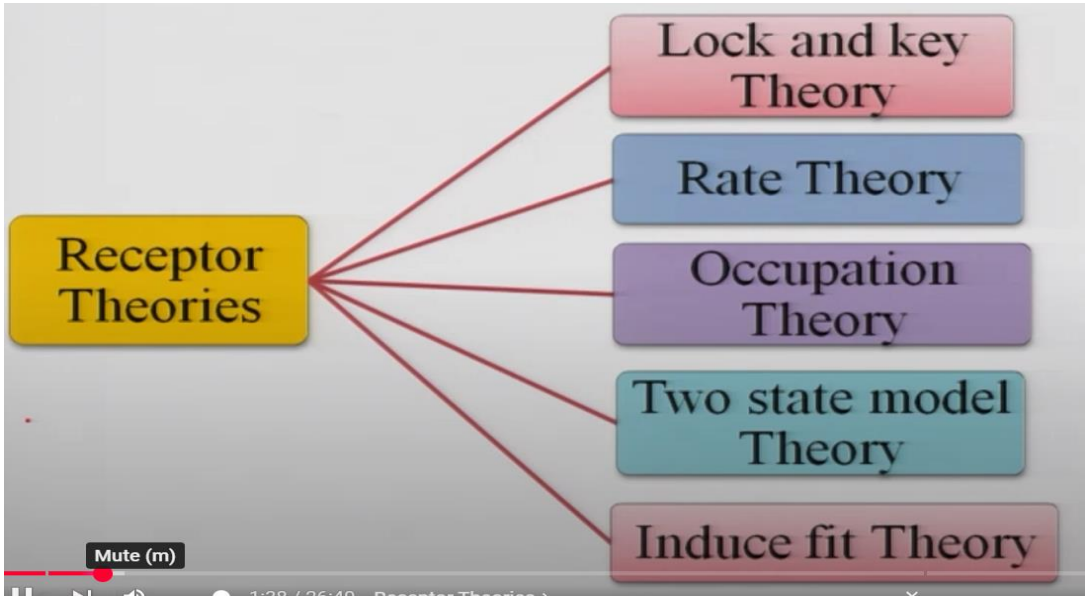
Determination of therapeutic index:

In humans the TI of drug is determined using drug trails

- ✓ The gap between the therapeutic effect dose response curve and adverse effect dose response curve defines safety of margin or therapeutic index of drug
- ✓ Lowest level of dose is called effective level/ ED_{50}
- ✓ Highest level of dose is called toxic level/ LD_{50}

Receptor Theories

There are several theories has been used to explain the pharmacology of receptor which includes



Receptor Theories

1. Lock and Key Theory:

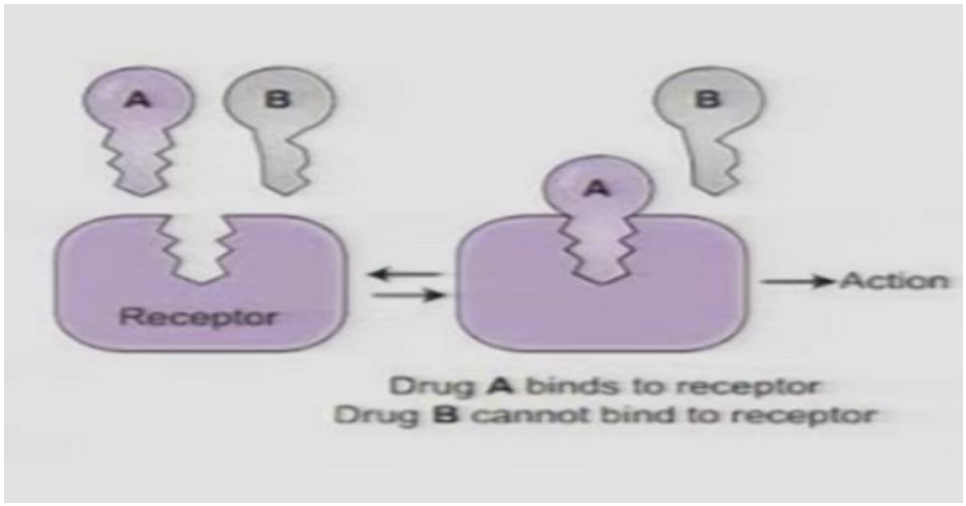
✓In lock and key theory receptor act as lock and drug act as key

✓Imagine every lock has its key in the same way every drug has its own receptor to bind and produce pharmacological action.

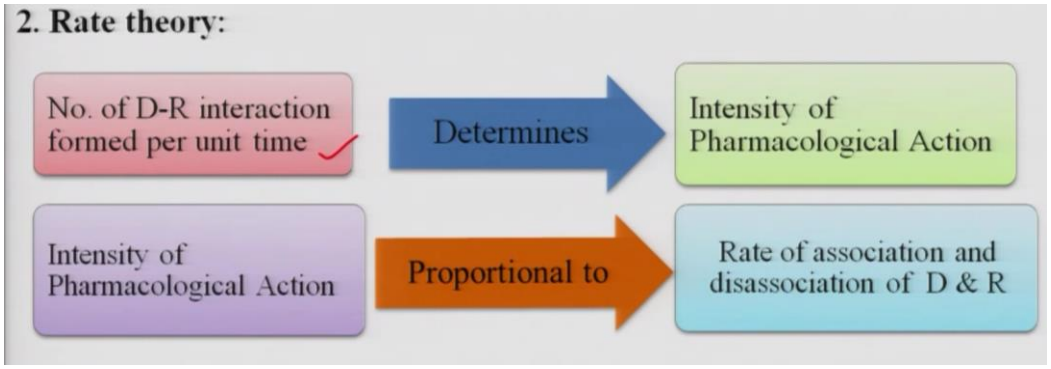
✓The drug molecule must fit into the receptor and produce its action like key fits into the lock

✓This is known as Intrinsic Activity(IA)

✓False drug to false receptor don't show any biological action


A
B
B
A
Receptor
Action
Drug A binds to receptor
Drug B cannot bind to receptor

2. Rate theory:



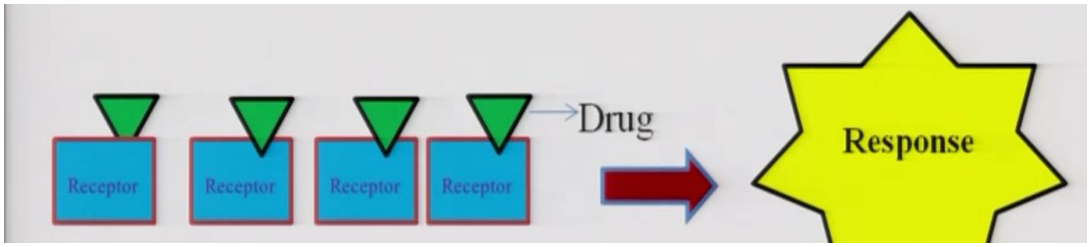
2. Rate Theory (Contd..)

- ✓ The activation of receptor is directly proportional to the number of encounters of drug with its receptor per unit time
- ✓ In rate theory agonist is drug with fast association and dissociation
- ✓ Partial agonist is drug with intermediate association and intermediate dissociation
- ✓ Antagonist is drug with fast association and slow dissociation

3. Occupation theory:

Intensity of Pharmacological Response → Proportional to → Number of receptors occupied by the drug

Number of receptors occupied by the drug → Depends on → 1. Dose of drug 2. Total No. of receptors available

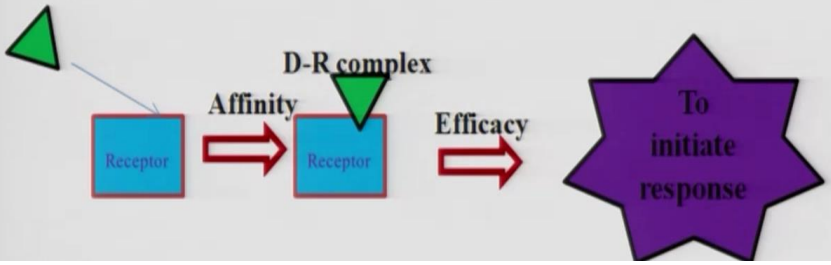


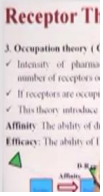
3. Occupation theory (Contd..)

- ✓ Intensity of pharmacological response directly proportional to number of receptors occupied by the drug
- ✓ If receptors are occupied by drug, maximum effect is obtained
- ✓ This theory introduce (i) Affinity (ii) Efficacy/ Intrinsic activity

Affinity: The ability of drug bind with receptor to create D-R Complex

Efficacy: The ability of D-R complex to initiate response





4. Two- state model: