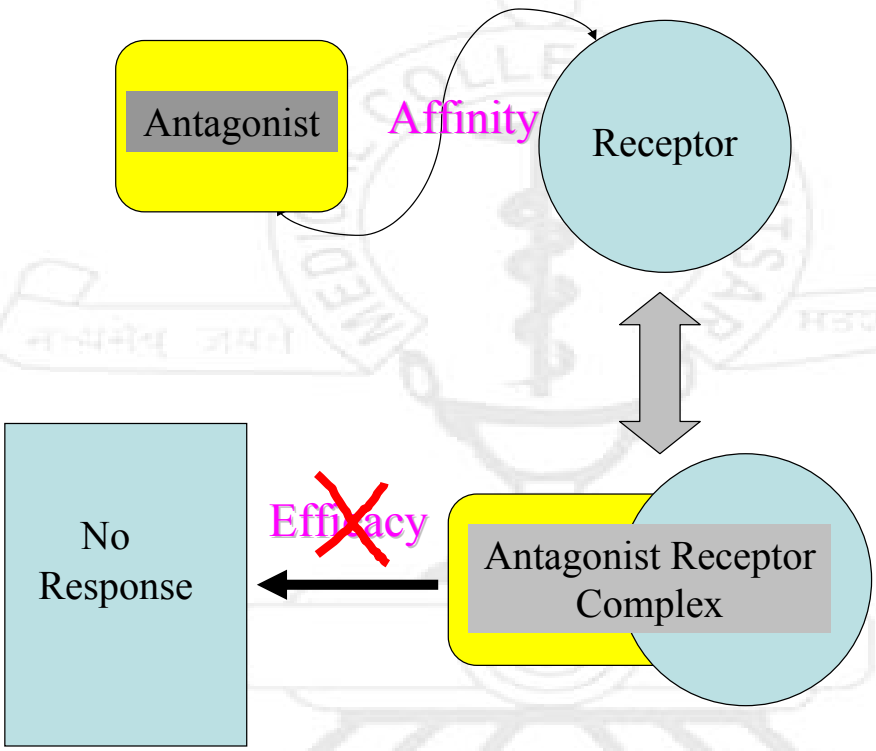
Dose Response Relationship

Drug Receptor Interaction

- Occupation of a Receptor by a drug may or may not result in activation of the receptor.
- **D + R = DR > pharmacological effect**
- The active complex (DR) leads to a cellular response that is proportional to the number of receptors occupied
- A drug has a maximal effect when all receptors are occupied

Affinity/ Efficacy

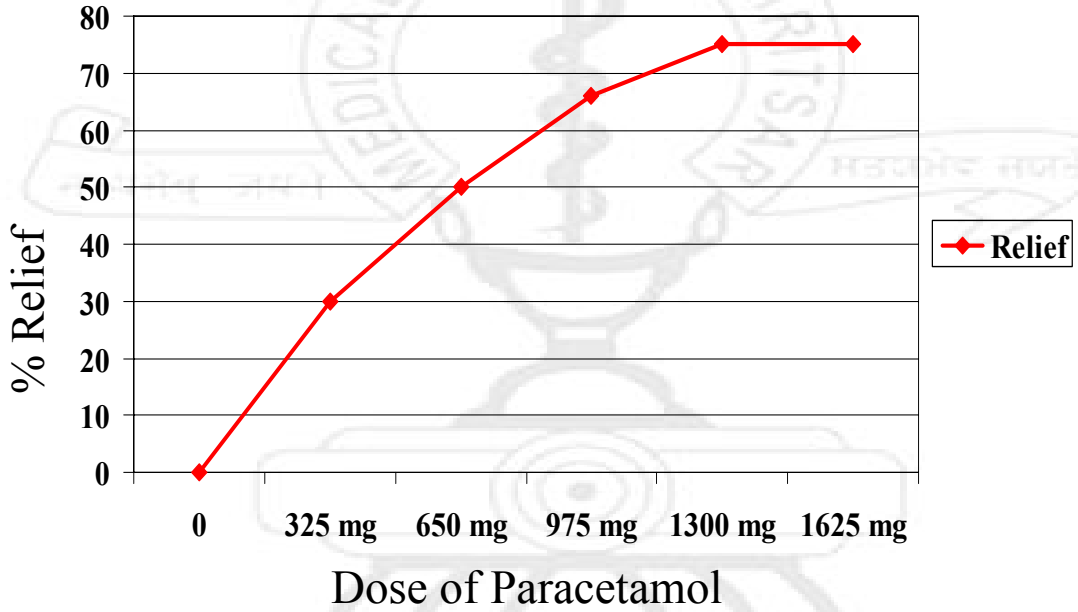
- The property of a drug to bind to receptors is Affinity.
- Once it is bound the property to evoke a response is Efficacy- Intrinsic Activity.



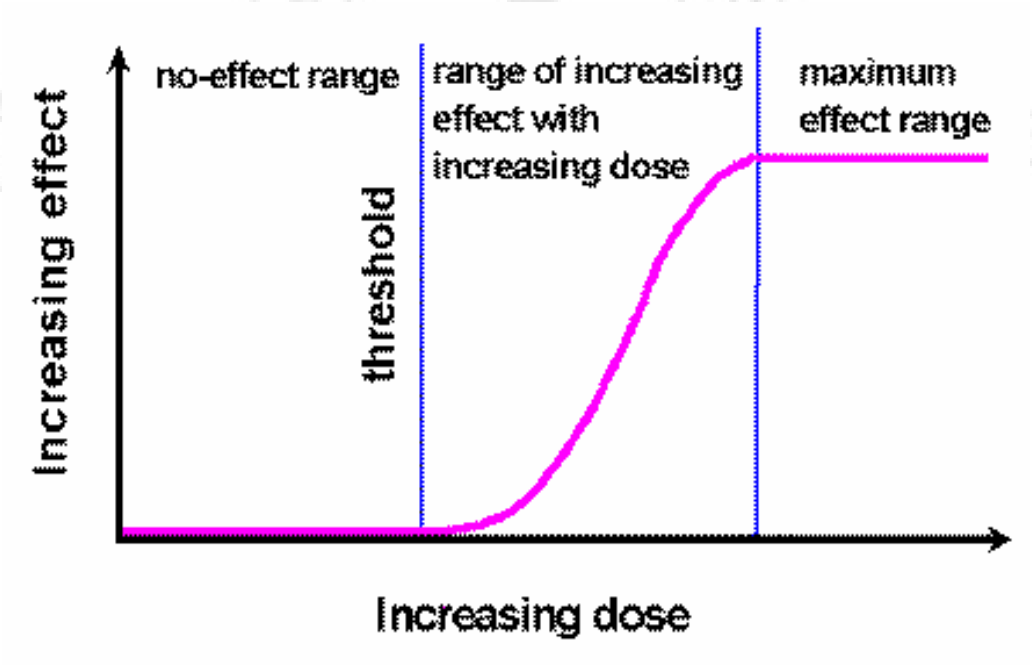
Quantification of Effects

- Drugs exhibit a characteristic relationship between the dose and the pharmacologic effect.
- Represented by the Dose Response Curve

Dose Response Curve



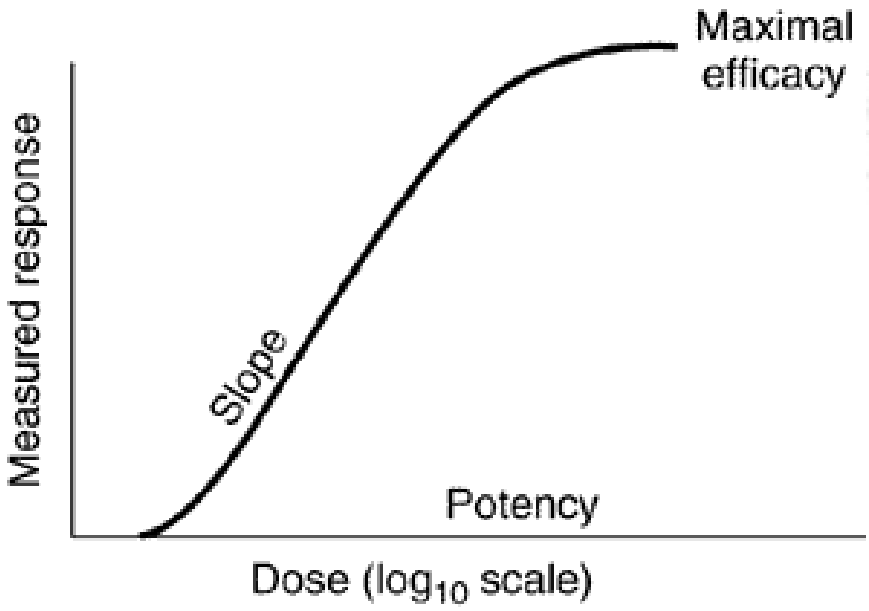
Log dose response curve- Sigmoid



Slope

- The mid-portion of DRC
- Varies from drug to drug
- Steepness of slope denotes that a small increase in drug dose leads to large change in response.

Slope/ Efficacy/ Potency



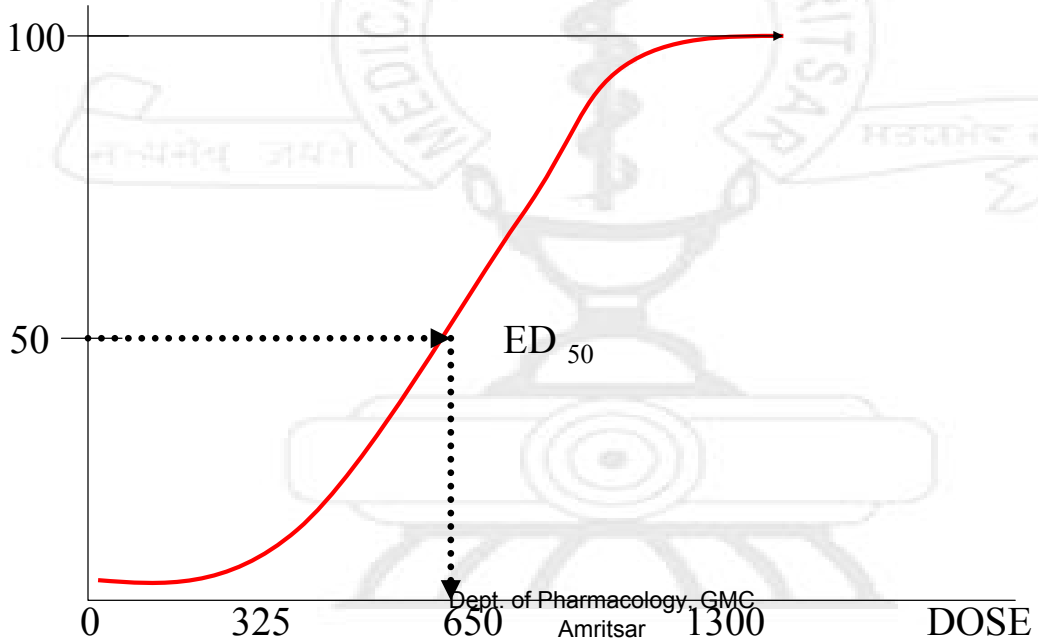
Efficacy

- Maximal response produced by a drug
- Depends on the number of Drug Receptor Complexes (DRC) formed
- Efficiency with which the DRC elicits a cellular response
- A compound may bind to a receptor without eliciting a response – zero efficacy

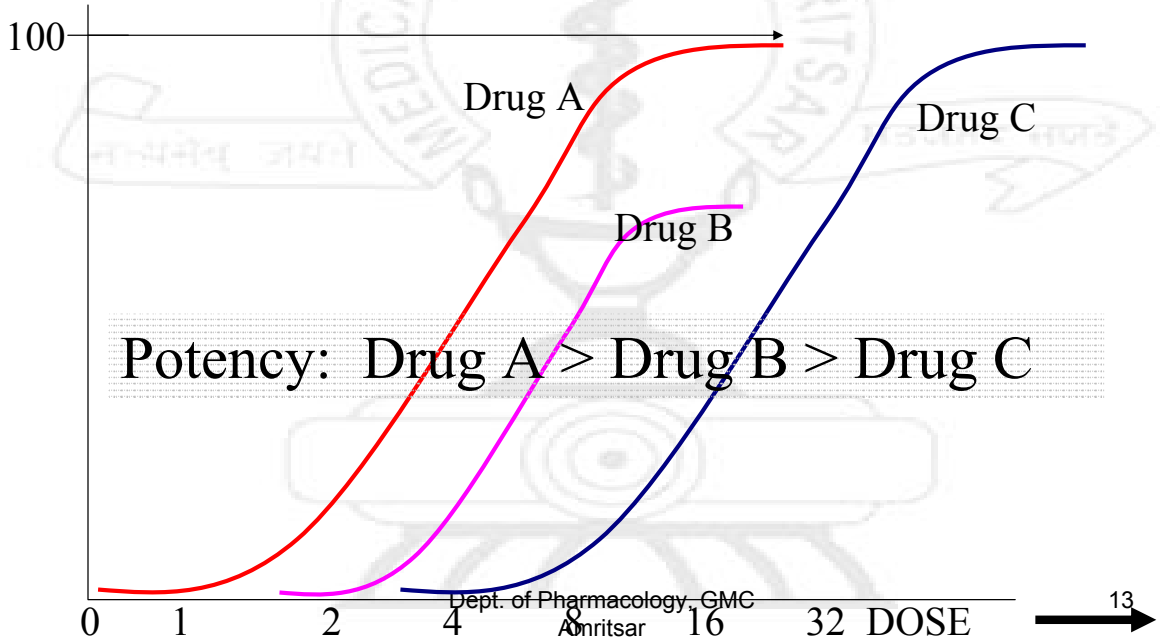
Potency

- The amount of drug needed for evoking a given response depends on its Potency.
- Lower the dose required the more potent the drug.
- In clinical use the dose needed for eliciting 50% response – Effective Dose 50 -ED_{50}.
- In experiments as Lethal Dose 50 – LD_{50}.

ED_{50}



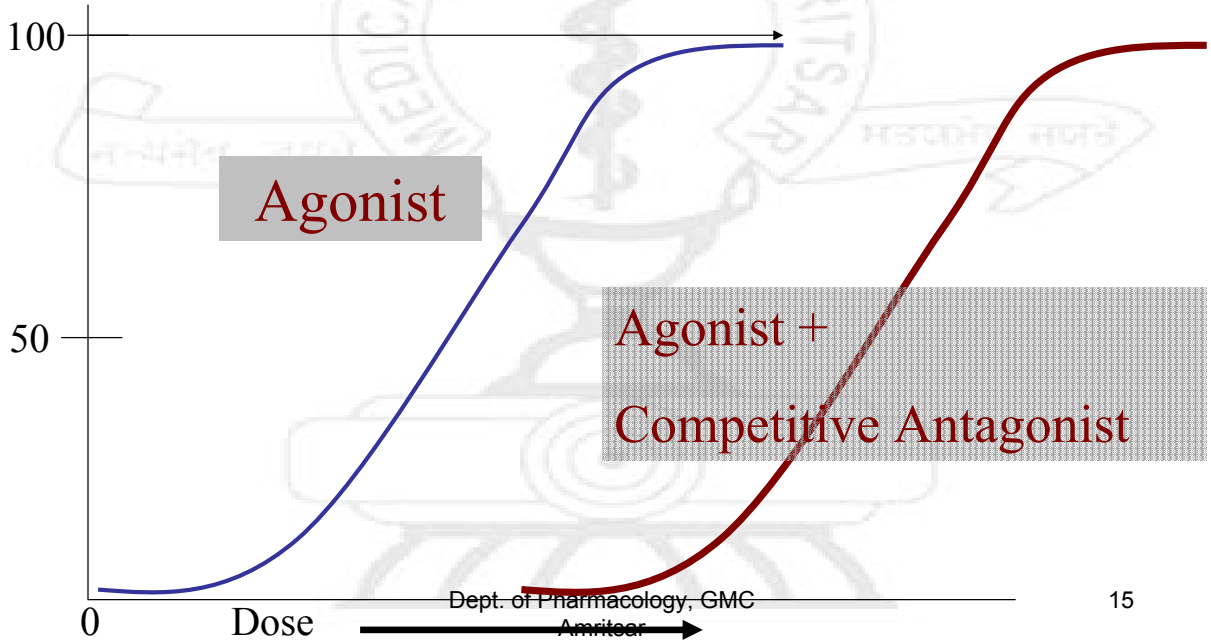
Efficacy : Drug A = Drug C
Drug B - has least efficacy



Competitive Antagonists

- Compete for a site on receptor already occupied by an agonist.
- The duration of action of a reversible antagonist is closely correlated with its rate of elimination.
- As it gets eliminated, the concentration at its site of action falls, and there is less of it to compete with the agonist.
- Shifts the DR curve to the right thus making the combination less potent.

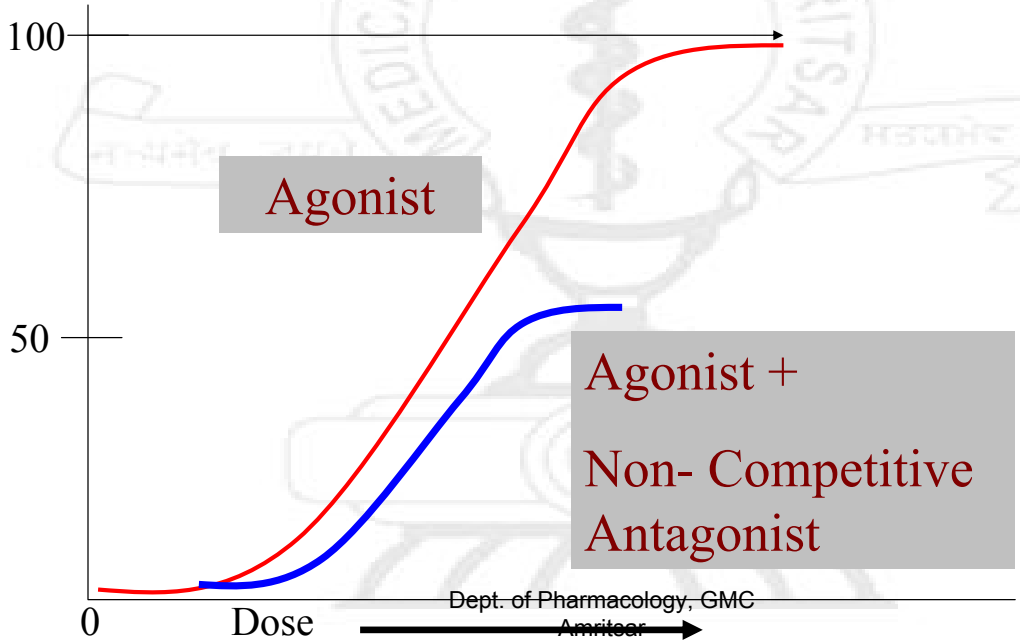
Competitive Antagonist



Non-competitive antagonist

- Prevent the binding of an agonist or prevent agonist from activating the receptor.
- The duration of action of an irreversible antagonist is determined by the rate of synthesis of new receptors.
- The effects of irreversible antagonists can often be seen long after the final dose is administered.
- Decreases the maximal response obtained with an agonist alone.

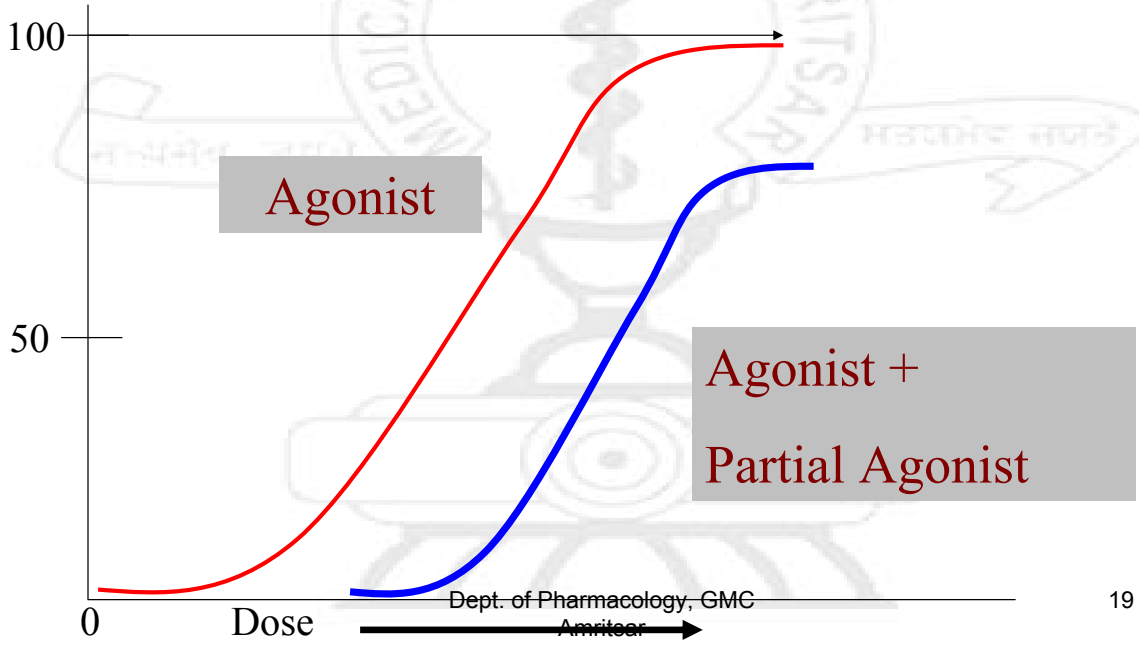
Non-Competitive Antagonist



Partial agonist

- Blocks the agonist binding site but cause less response than a full agonist.
- Partial agonist has an affinity that is increased/ decreased or equal to that of an agonist.

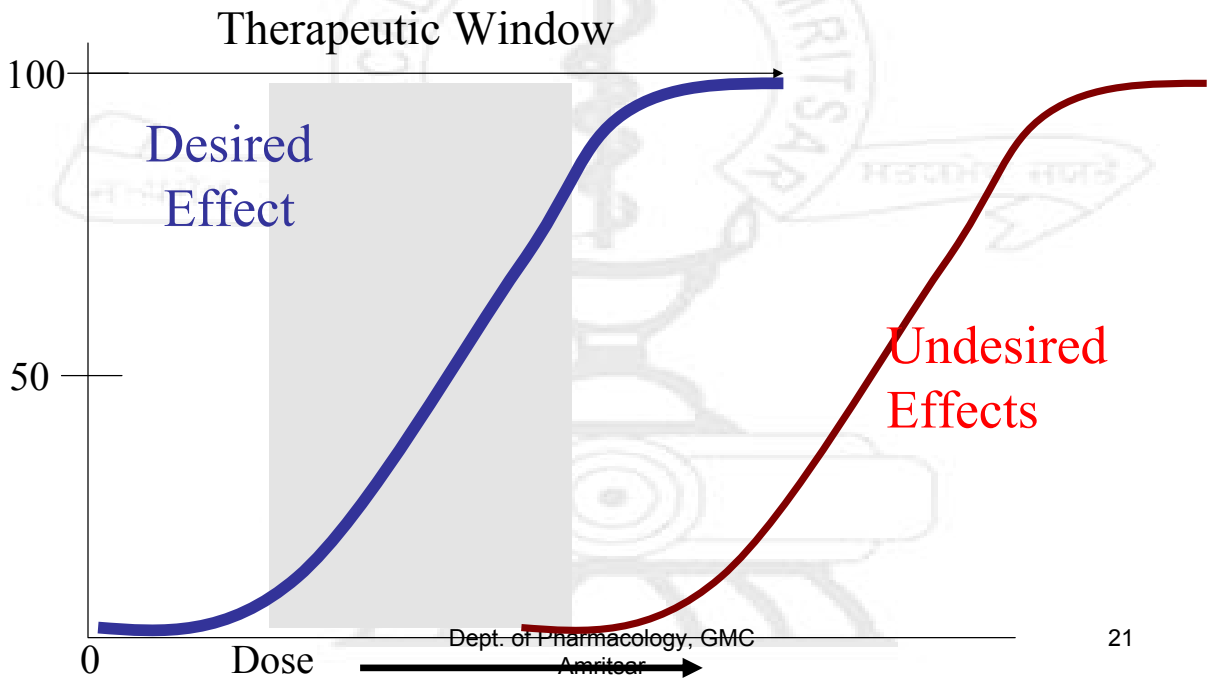
Partial Agonist



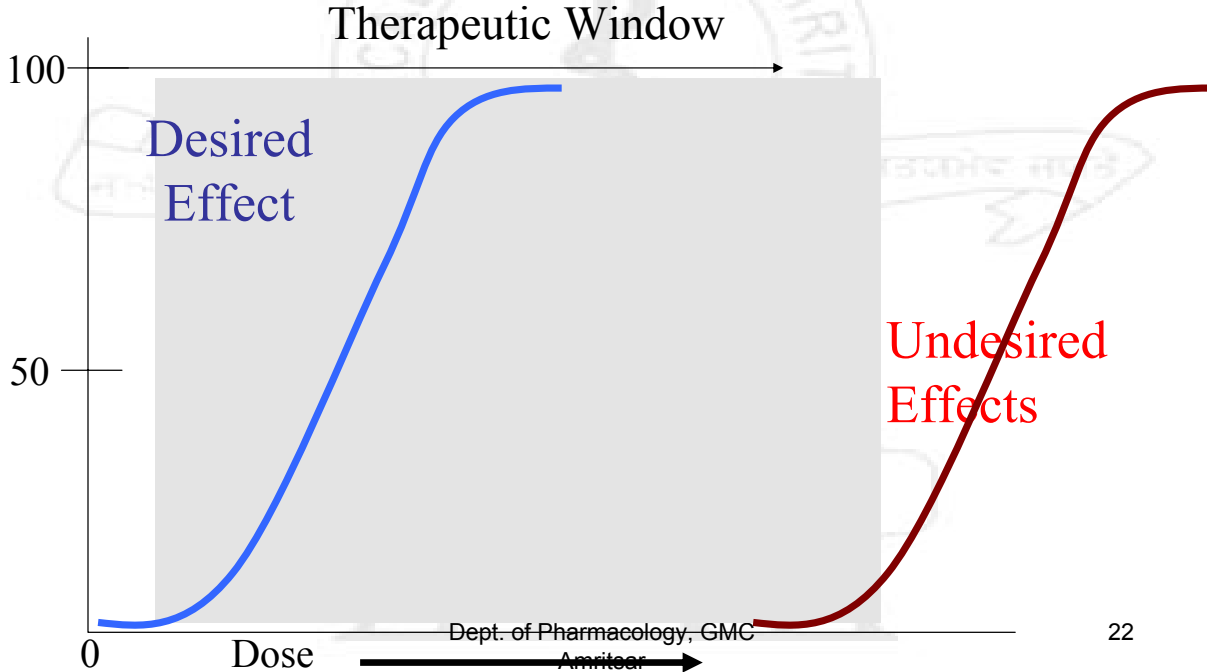
Therapeutic index

- Ratio of the drug that produces toxicity to the dose that produces the desired clinical effect.
- TI=Toxic dose/effective dose
- Drugs that have small TI are important in leading to toxicity.
- Drugs with large TI are safe.

Narrow Therapeutic Index



Large Therapeutic Index



Uses of Dose Response Curves

- Predict the effects of changing the dose.
- Correlate between efficacy and adverse effects.
- Facilitate comparisons of alternative medications for the same indication.
- Enhance understanding of how best to use receptor blockers