Inverse agonist :

It has full affinity towards the receptor but produces effect completely opposite to that produced by an agonist.

e.g, benzodiazepines (agonist)

ß carboline (inverse agonist)

Antagonist:

Antagonist have only

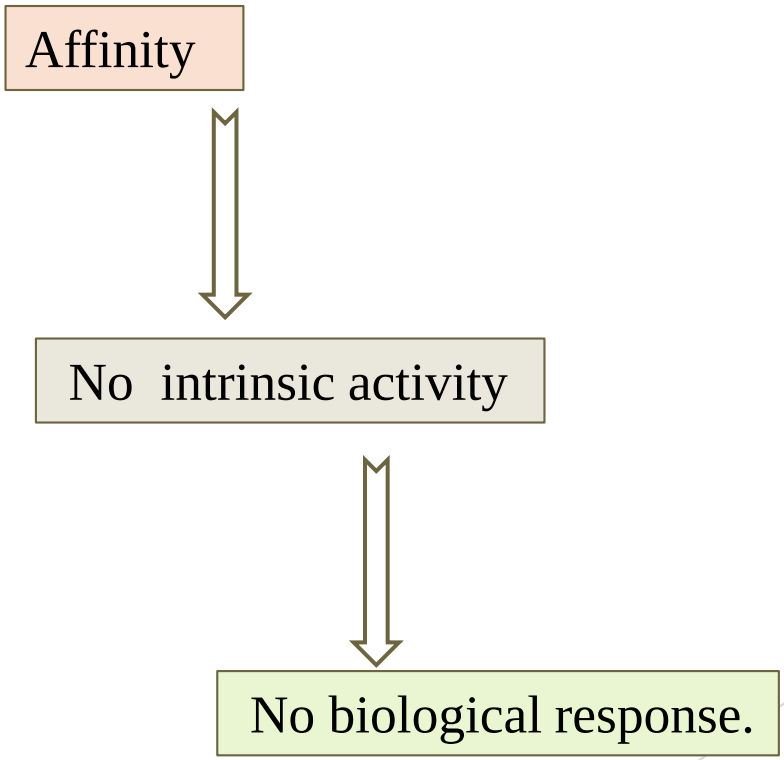
Affinity

No intrinsic activity.

They block the receptor (e.g., naloxone, atropine).

Antagonist:

Antagonist have only affinity no intrinsic activity



Types of antagonisms

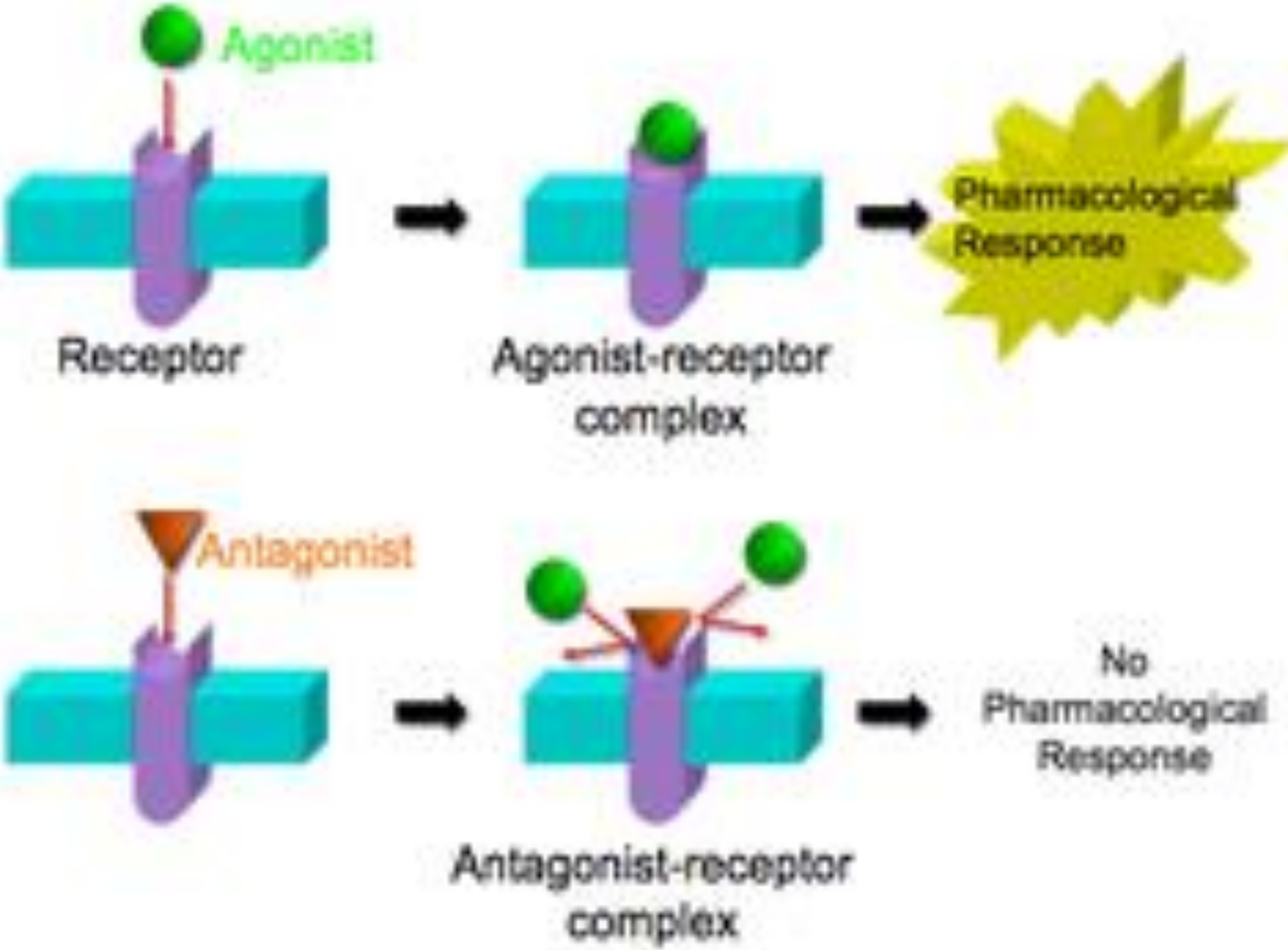
- Receptor block (pharmacological antagonism)

a) Competitive antagonism (reversible)

b) Non-competitive antagonism (irreversible)

- Chemical antagonism
- Physical antagonism
- Physiological antagonism
- Pharmacokinetic antagonism(dispositional)

Pharmacological antagonism


Agonist
Receptor
Agonist-receptor complex
Pharmacological Response
Antagonist
Antagonist-receptor complex
No Pharmacological Response

Competitive – antagonism (1)

In this type of antagonism the drug selectively binds to the receptor without activating it but in turn inhibits the binding of an agonist to the receptor.

Surrmountable Block

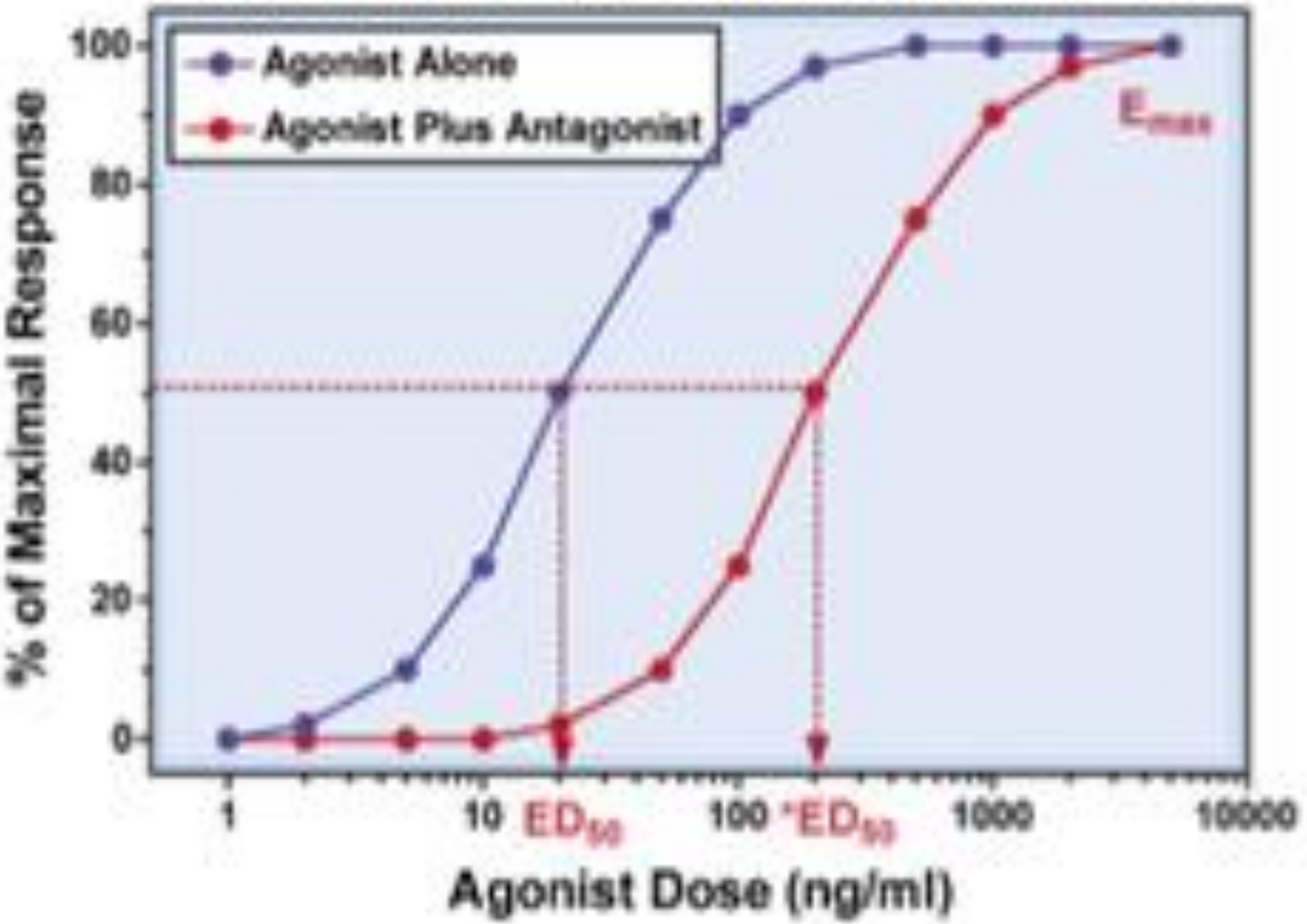
(Weak hydrostatic bonds)

Acetylcholine → **MUSCRINIC receptor** ← ***Atropine***

Morphine → **Opioid receptor** ← ***Nalaxone***

(agonists) **(antagonists)**

Reversible Competitive Antagonism



non-Competitive – antagonism

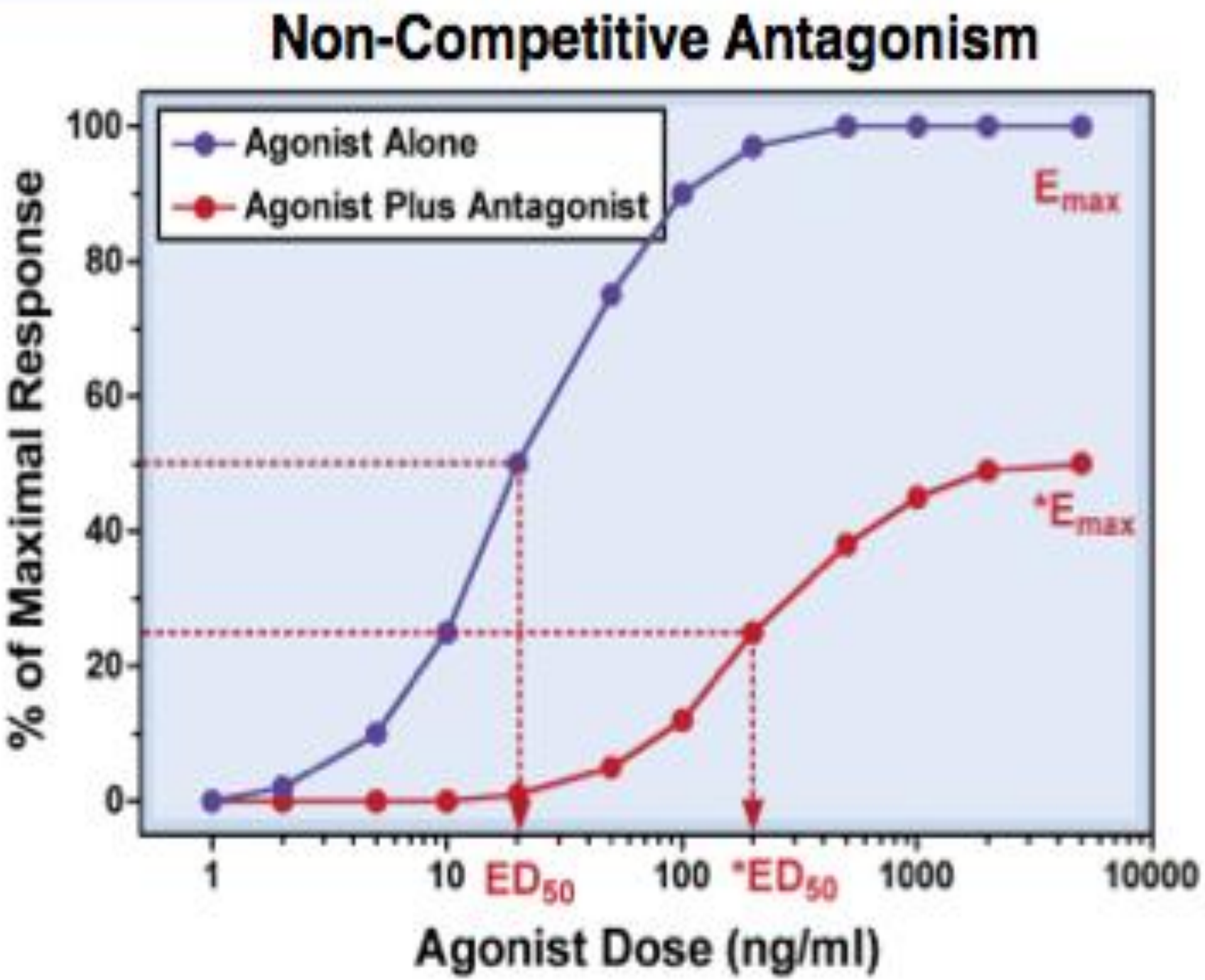
The antagonist binds to the receptor with a high affinity so that the agonist cannot displace it from the binding site.

(covalent bonds)

example

Adrenaline ***alpha receptor*** ***Phenoxybenzamine***

(Agonist) **(receptor)** ***(Antagonist)***


Non-Competitive Antagonism
Agonist Alone
Agonist Plus Antagonist
E_{max}
$^*E_{max}$
% of Maximal Response
100
80
60
40
20
0
1
10
100
1000
10000
ED_{50}
$^*ED_{50}$
Agonist Dose (ng/ml)

CHEMICAL ANTAGONISM

In this type, the agonist and the antagonist are combined in a solution and the effect of the agonist is lost.

or

The opposing effect of the two drugs is due to their chemical property.

example

Dimercaprol (chelating agent) form insoluble complexes with metals in metal poisoning

Physiological - Antagonism

In this type of antagonism, a drug produces an effect opposite to that produced by another drug by acting on different receptor or on the same receptor.

example

Adrenaline and Histamine in Anaphylactic shock.

Pharmacokinetic antagonism

In this type of antagonism, any drug altering the absorption, distribution, metabolism or excretion of another drug can alter the concentration of the drug at its receptor site.

example

$NaHCO_3$ increases the excretion of aspirin and thus decreases its concentration.

PHYSICAL ANTAGONISM

The opposing action of two drugs is due to their physical property.

example

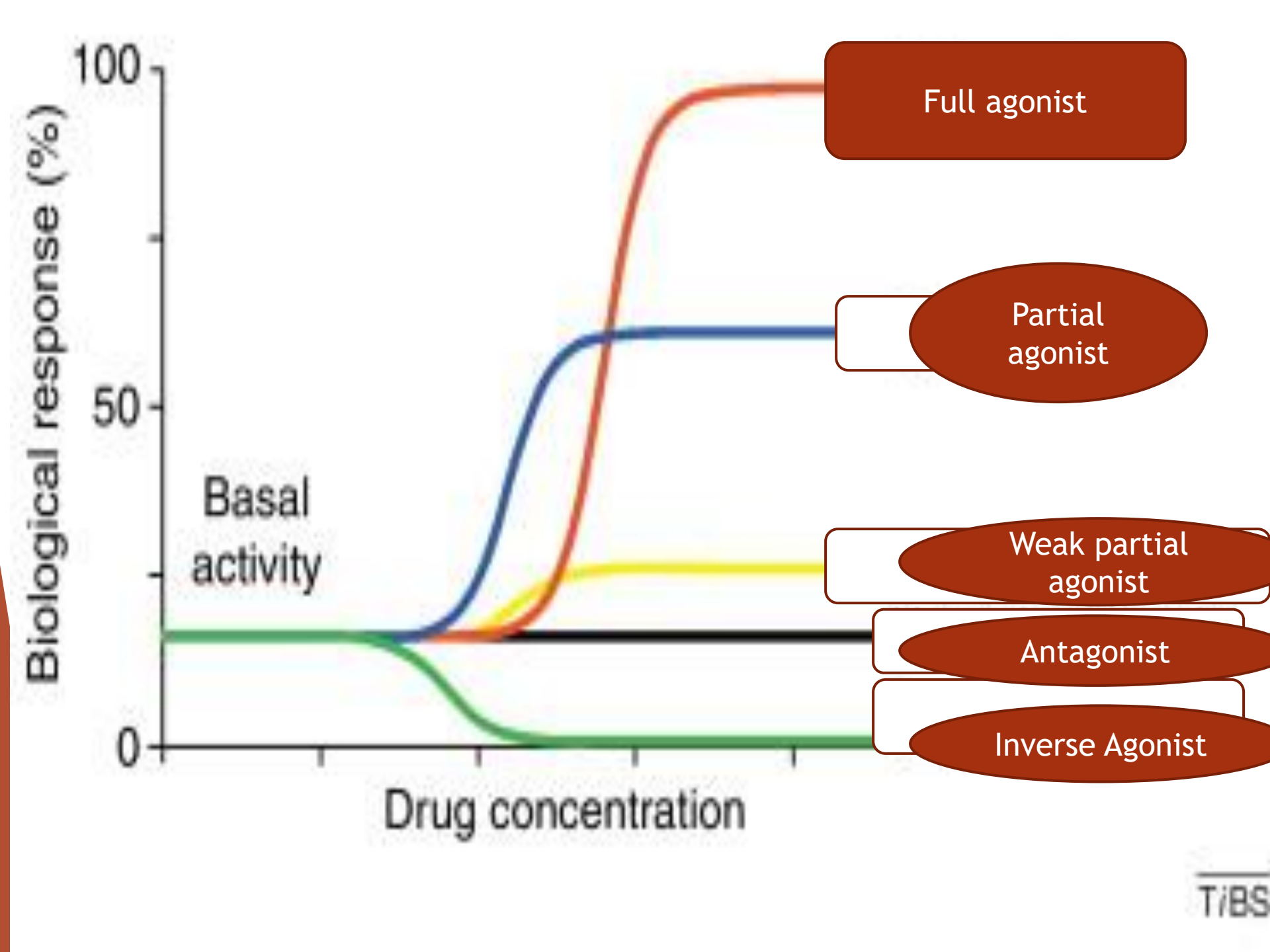
Activated charcoal adsorbs toxic substances in case of poisoning.


Poison is Swallowed
Charcoal Absorbs up to 60% of the Toxic Substance
Stops the Poison From Leaving the Stomach
Activated Charcoal

References

- 12th edition, by Bertram G. Katzung, Susan B. Masters, and Anthony J. Trevor
- Lippincott Illustrated Reviews: Pharmacology 6th edition (Lippincott Illustrated Reviews Series) Sixth, North American Edition
- **Pharmacology Principles and Applications** Paperback – April 1, 2016 by Abdul Jalil Popalzai (Author).

Quiz

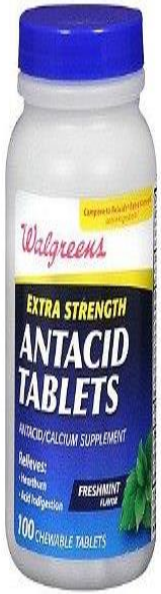

100
50
0
Biological response (%)
Basal activity
Drug concentration
Full agonist
Partial agonist
Weak partial agonist
Antagonist
Inverse Agonist
TiBS

+

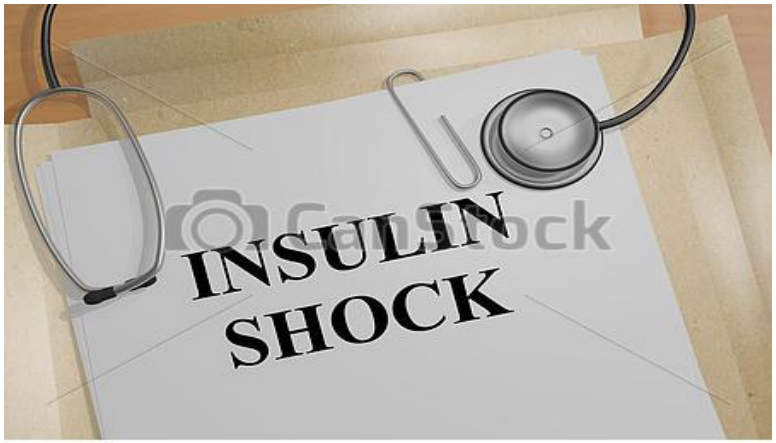
=

Chemical Antagonism

Physphysiological-antagonism



Chemical antagonism



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Physiological Antagonism

- Phenobarbitone increasing the metabolism of warfarin

- **Warfarin effect being reduced by in its increased metabolism**

Pharmacokinetic antagonism


Thank You