Al-Mustaqbal University College
Department of Pharmacy
4th stage
Practical General Toxicology
Lab: 1

TOXICOLOGY & CHEMICAL INTERACTION

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Chemical Interaction

- ✓Throughout the day, an individual may come **in contact** with **many chemicals** at any given **time** (in the workplace, cosmetics, medications, diet, hobbies, etc.).
- ✓As a result, it is necessary to consider **how** various chemicals may **interact** with each other.

Chemical Interaction

- ✓ Interactions may impact a number of physiologic processes including:
    1. Absorption
    2. Protein binding
    3. Receptor signalling
    4. Biotransformation
    5. Excretion of one or both of the interacting toxicants.
- ✓ As a consequence, the cumulative response(s) of an individual to combinations of toxicants may be increased or decreased.

Chemical Interaction

- ✓The study of chemical interactions often provides a better understanding of key mechanisms of toxicity.
- ✓A number of terms have been used to describe pharmacological and toxicological interactions:

1. The additive effect
2. Synergistic effect
3. Potentiation effect
4. Antagonism effect

Additive Effect

- ✓ **It occurs when the combined responses of two chemicals is equal to the sum of the responses to each chemical given alone (e.g., 2 + 3 = 5).**
- ✓ **For example, when two organophosphorus insecticides are given together, inhibition of acetylcholinesterase enzymes (AChE) is usually additive, based on the relative ability of each one to inhibit AChE.**

Synergistic Effect

- ✓It is observed when the combined responses of two chemicals are much greater than the sum of the response to each chemical when given alone (e.g., 2 + 2 = 20).
- ✓For example, both carbon tetrachloride and ethanol are hepatotoxic compounds, but together they produce much more liver injury than expected based on the extent of damage at a given dose when administered alone.

Potentiation Effect

- ✓ **It occurs when one substance does not produce/ or produce slight toxicity on a particular tissue or system but when added to another chemical makes that chemical much more toxic (e.g., 0 + 2 = 10).**
- ✓ **Isopropanol, for example, is not hepatotoxic on its own, but when it is administered in combination with carbon tetrachloride, the hepatotoxicity of carbon tetrachloride is much greater than when it is given alone.**

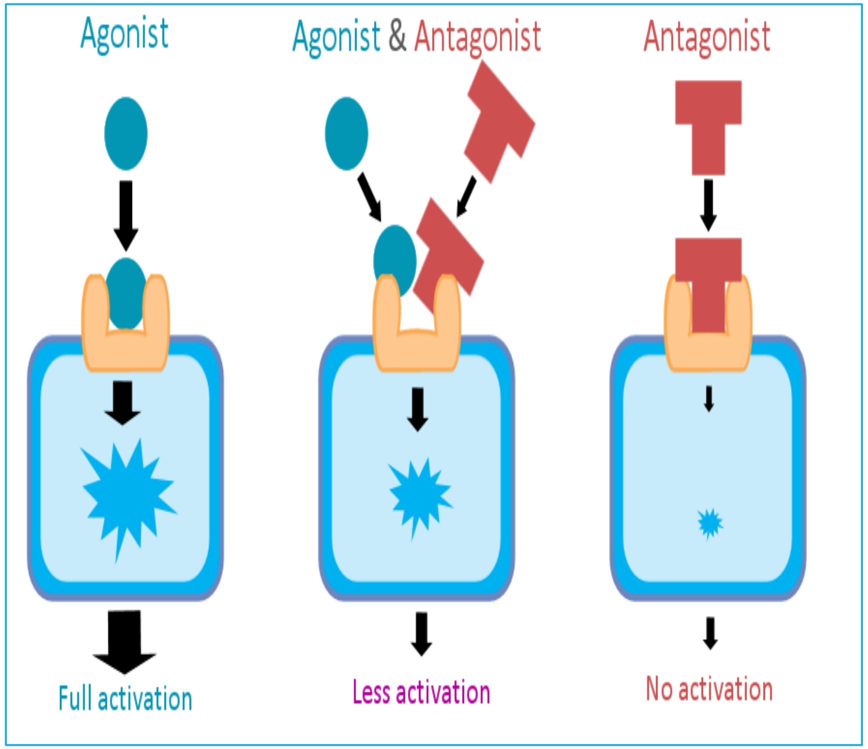
Antagonism Effect

- ✓It occurs when two chemicals administered together interfere with each other's actions or one interferes with the action of the other (e.g., 4 + 6 = 8).
- ✓Antagonism of the toxic effects of chemicals is often desirable in identifying important mechanisms of toxicity as well as in developing antidotes.
- ✓There are four major types of antagonism: receptor, chemical, dispositional, and functional

Receptor Antagonism

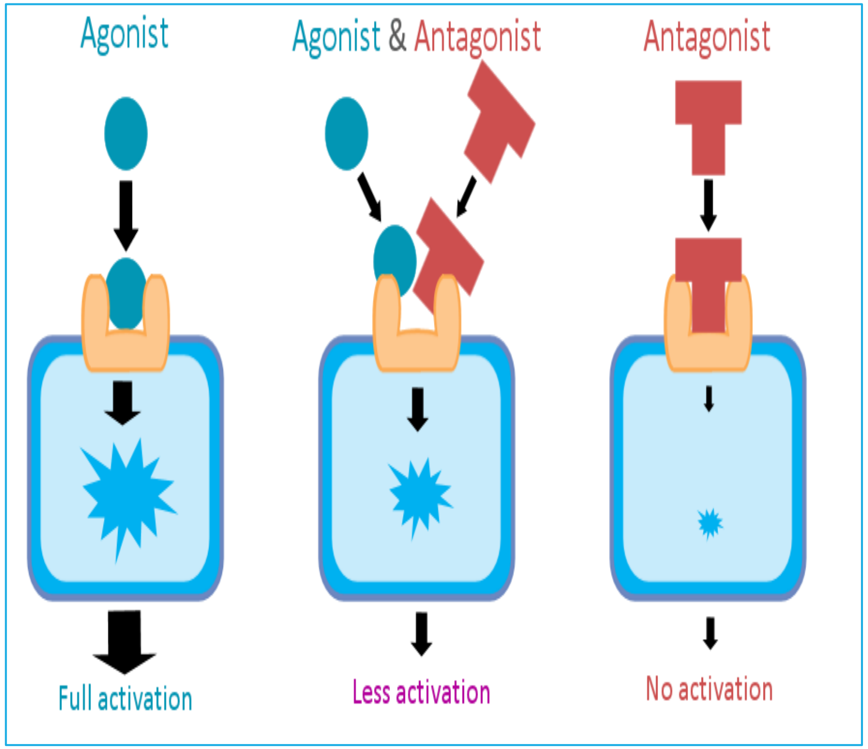
- ✓It occurs when two chemicals that bind to the same receptor produce less of an effect when given together relative to the addition of their separate effects (e.g., 4 + 6 = 8) or when one chemical antagonizes the effect of the second chemical (e.g., 0 + 4 = 1).

- ✓Receptor antagonists are often termed blockers.



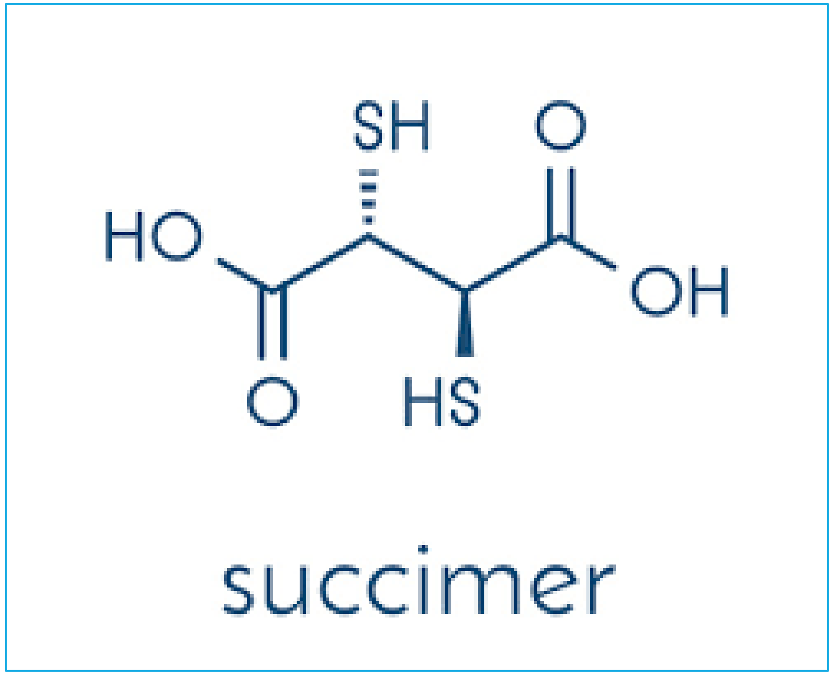
Receptor Antagonism

- ✓For example, the receptor antagonist **naloxone** treats the respiratory depressive effects of **morphine** by **competitively binding** to the same receptor.
- ✓Thus, **rapid** administration of naloxone can be **life-saving** for someone who has overdosed on **morphine**.



Chemical Antagonism

- ✓It is simply a direct chemical reaction between two compounds that produces a less toxic product.
- ✓For example, dimercaptosuccinic acid (succimer) chelates or binds to metal ions, such as arsenic, mercury, and lead, leading to decreases in their toxicity.



Dispositional Antagonism

- ✓If the parent compound is responsible for the toxicity of the chemical (such as the anticoagulant warfarin) and its metabolic breakdown products are less toxic than the parent compound, increasing the compound's biotransformation by administering a drug that increases the activity of the metabolizing enzymes (e.g., a "microsomal enzyme inducer" such as phenobarbital) will decrease its toxicity.
- ✓However, if the chemical's toxicity is largely due to a metabolic product (as in the case of the organophosphate insecticide parathion), inhibiting its biotransformation by an inhibitor of microsomal enzyme activity (e.g., piperonyl butoxide) will decrease its toxicity.

Functional Antagonism

- ✓It occurs when **two** chemicals **counterbalance** each other by producing **opposing effects** on the **same** physiological function, often through **different** signalling pathways.
- ✓For example, **blood pressure** can markedly **fall** during severe intoxication with a **barbiturate**, which can be effectively **antagonized** by the intravenous administration of a **vasopressor** such as **norepinephrine**.
- ✓In this case, the **barbiturate** works through **GABAA** receptors and **norepinephrine** activates **α-adrenergic receptors** to produce **opposing** effects on vascular tone.

THANK YOU FOR YOUR ATTENTION