Chemicals and Materials

Synergism and related terms

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What is meant by the term "synergism"?

Synergism comes from the Greek word "synergos" meaning working together. It refers to the interaction between two or more "things" when the combined effect is greater than if you added the "things" on their own (a type of "when is one plus one is greater than two" effect).

In toxicology, synergism refers to the effect caused when exposure to two or more chemicals at one time results in health effects that are greater than the sum of the effects of the individual chemicals.

When chemicals are synergistic, the potential hazards of the chemicals should be re-evaluated, taking their synergistic properties into consideration.

What are related terms?

In addition to synergism, other terms are used to define toxicologic interactions.

Additive Effect - This action occurs when the combined effect of two or more chemicals is equal to the sum of the effect of each agents given alone (they do not interact in a direct way); for example:

2 + 2 = 4

This effect is the most common when two chemicals are given together.

Potentiation - This effect results when one substance that does not normally have a toxic effect is added to another chemical, making the second chemical much more toxic; for example:

0 + 2 > 2, not just 2

Antagonism - Antagonism is the opposite of synergism. It is the situation where the combined effect of two or more compounds is less toxic than the individual effects; for example:

4 + 6 < 10

Antagonistic effects are the basis of many antidotes for poisonings or for medical treatments. For example, ethyl alcohol (ethanol) can antagonize the toxic effects of methyl alcohol (methanol) by displacing it from the enzyme that oxidizes the methanol.

In comparison, a **synergistic effect** is the situation where the combined effect of two chemicals is much greater than the sum of the effects of each agent given alone, for example:

2 + 2 >> 4 (maybe 10 times or more)

Why does synergism occur?

While the mechanisms of synergism can change from situation to situation, most of the time there appears to be an effect on the enzymes that regulate or influence the way our bodies work.

Our bodies have enzymes that are designed to do specific "jobs". For example, there is an enzyme that helps break down alcohol - this is why we do not stay intoxicated "forever" after consuming alcohol. These enzymes normally transform (metabolize) the foreign substances (alcohol in this example) into less toxic or non-toxic substances which are eliminated out of the body.

With synergism, an enzyme function could either be inhibited (restricted) or accelerated in some way. Either way, the result is that the chemicals are either "free" or "enhanced" to cause a greater biologic effect in the body.

What are examples of synergism?

There are various examples including:

(a) Carbon tetrachloride and ethanol (ethyl alcohol) are individually toxic to the liver, but together they produce much more liver injury than the sum of their individual effects on the liver.

(b) The much higher incidence of lung cancer resulting from occupational exposure to asbestos in smokers (compared to exposed non-smokers).

(c) The toxicity of some insecticides notably pyrethrin (from chrysanthemums) and synthetic pyrethrins (pyrethroids) can be increased many times by the addition of compounds which themselves are not insecticides. These synergists are sesamin, sesamolin, piperonyl butoxide, MGK-264 (bicycloheptenedicarboximide) and sesamex. Piperonyl butoxide is perhaps the most widely used synthetic pyrethrin synergist. The insecticide activity of pyrethrins increases tenfold when 1 part piperonyl butoxide is mixed with 9 parts pyrethrin. There are no reports available on toxic effects on humans resulting from the exposure to piperonyl butoxide.

(d) Barbiturate drugs have a greater effect on the central nervous system (CNS) by causing CNS depression when taken with general anesthetics, alcohol (acute consumption) narcotic analgesic (pain reliever) and other sedative hypnotic drugs.

(Adapted from: Klaassen, C., 2007. "Casarett and Doull's Toxicology: The Basic Science of Poisons. 7 th Edition")

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