4.1: Interactions

Interactions

As noted in "**Factors Influencing Toxicity**," the presence of other chemicals, at the same time, earlier, or later may:

- Decrease toxicity (**antagonism**).
- Add to toxicity (**additivity**).
- Increase toxicity (**synergism** or **potentiation**) of some chemicals.

For example, interactions between two or more toxic agents can produce lung damage by interactions:

- Between chemicals.
- Between chemicals and receptors.
- In which a first agent modifies the cell and tissue response to a second agent.

Interactions may occur by:

- Simultaneous exposure to two or more agents.
- Exposure to two or more agents at different times.

Figure 4.1.1. Interactions between two or more substances often impact toxicity
(Image Source: iStock Photos, ©)

Sources of Interactions

Humans are normally exposed to many chemicals at one time. For example, the use of consumer products, medical treatments, and exposures from the diet and environment (such as from soil, air, and water) can consist of exposures to hundreds, if not thousands, of chemicals. Other examples include:

- Hospital patients receive an average of six drugs daily.
- Consumers may use five or more consumer products before breakfast (for example, soap, shampoo, conditioner, toothpaste, and deodorant).
- Home influenza treatment consists of aspirin, antihistamines, and cough syrup taken simultaneously.
- Drinking water may contain small amounts of pesticides, heavy metals, solvents, and other organic chemicals.
- Air often contains mixtures of hundreds of chemicals such as automobile exhaust and cigarette smoke.
- Gasoline vapor at service stations is a mixture of 40-50 chemicals.

Figure 4.1.2. The use of personal care products can result in expsoures to hundreds of chemicals
(Image Source: iStock Photos, ©)

Figure 4.1.3. *Cold and flu remedies are another source of chemical exposure*
(Image Source: iStock Photos, ©)

Toxicology studies and human health risk assessments have traditionally focused primarily on a single chemical. However, as noted above, people are exposed to many chemicals every day. They are also exposed to non-chemical stressors every day and throughout a lifetime.

In addition, non-chemical stressors include infectious agents, diet, and psychosocial stress, all of which have potential roles in contributing to the health effects associated with chemical exposures.

Approaches for Assessing Interactions

Development of methods to assess the health effects associated with complex exposures is underway at **various organizations**.

Non-animal tools and approaches are demonstrating high potential for use in assessing combined effects of chemicals on humans and the environment. These tools and approaches may help uncover information about new mixture components or entire mixtures,

which can promote understanding of the underlying mechanisms of their combined effects. The strategies for assessing interactions rely less on *in vivo* testing and more on non-animal studies and computational tools and incorporate emerging approaches such as:

- The adverse outcome pathway (AOP) concept.
- *In vitro* methods.
- "Omics" techniques.
- *In silico* approaches such as quantitative structure activity relationships (QSARs).
- Read-across.
- Toxicokinetic modeling.
- Integrated approaches to testing and assessment (IATA).

The goals include the ability to development more effective and comprehensive regulatory assessments while reducing the reliance on animal testing.

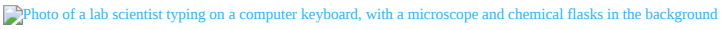

Figure 4.1.4 *Modern testing methods rely heavily on computational toxicology*
(Image Source: iStock Photos, ©)

Knowledge Check

The presence of one chemical decreasing toxicity of another chemical is called:

- ◯ Additivity
- ◯ Antagonism
- ◯ Synergism

Answer

Antagonism - **This is the correct answer.**

When the presence of another chemical decreases toxicity of a chemical, this is called antagonism.

Additivity is when the combined toxic effect of two chemicals when given together is less than the sum of their individually measured toxic effects.

- ◯ True
- ◯ False

Answer

False - **This is the correct answer.**
An additive effect occurs when the combined effects of two or more chemicals is equal to the sum of the effects of each chemical given alone.

Piperonyl butoxide is not an insecticide; however, it can greatly increase the effects of a pyrethrum insecticide. Thus, piperonyl butoxide can be called a synergist and this interaction can be called synergism.

- ◯ True
- ◯ False

Answer

True - **This is the correct answer.**
The interaction of this combination is synergism. Synergists are used to enhance the toxicity of several commonly used insecticides.