HERBICIDES

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Contents

Summary

A herbicide is defined as any chemical that is used to kill or regulate, typically adversely, the growth of unwanted plants.

There is a broad range of herbicides with hundreds of different active ingredients used worldwide. Herbicides can be classified according to their method of application, mechanism of action, selectivity or most any other criteria. For example, contact or post-emergence herbicides are sprayed directly onto the plant, and their effect is restricted to the parts of the plant to which they were applied. Herbicides designated as translocated herbicides can be applied either to the soil or to the plant. In the former case, application is before emergence, and active residues in the soil are translocated to the plant during germination and growth. When applied directly to the plant, translocated herbicides are absorbed and distributed within the plant to their site of action. Non-selective herbicides kill all vegetation, whereas the herbicidal effects of selective agents is ideally restricted to unwanted plants, with minimal adverse effects on crops or other desirable vegetation. Relative selectivity can be achieved through the mechanism of action of the herbicide, differences in inactivation of the herbicide between plant species, as well as through the mode and timing of herbicide application.

The use of crops that have been genetically engineered to be herbicide-resistant also enhances the selectivity of herbicides toward non-resistant, unwanted plants. Selectivity toward plants, as opposed to humans and other non-target organisms, is also afforded by the fact that many herbicides are inactivated by microbes within the soil. At least in the case of those herbicides, risks for dispersion within the environment and exposure to humans is low when they are used properly.

The mechanisms of action of the commonly used classes of herbicides include the inhibition of photosynthesis and, consequently, the generation of energy with the plant cell. Phenylurea- and glyphosate-based herbicides act through this general mechanism. Glyphosate-based agents, however, target a photosynthetic enzyme that is exclusive to plants. Other classes of herbicides mimic plant chemicals that suppress growth (e.g., chlorophenoxy herbicides), or they act to inhibit metabolic processes such as lipid and protein synthesis (e.g., acetamide herbicides). In the case of acetamide herbicides, some selectivity is achieved against plants (e.g., some broad-leaf weeds) that lack the enzyme necessary for the degradation of the herbicide. The bipyridilium herbicides diquat and paraquat initiate a nonselective oxidative process that results in damage to photosynthetic cells of the plant, resulting in loss of respiration and desiccation.

In the United States, registration of a herbicide is contingent on a body of evidence that indicates it can be used in a manner that does not pose an undue risk to humans or the environment. In general, herbicides are less toxic than are other types of pesticides (e.g., insecticides and rodenticides), and when used as directed they pose little risk to humans. Invariably, however, exposure to herbicides will occur because of intentional ingestion, an accident with handling, misidentification, or inappropriate use. Under these circumstances, some classes of herbicides are associated with significant toxicity.

Paraquat poisoning, for instance, is associated with selective, potentially severe, lung toxicity and is often fatal. Poisoning with chlorophenoxy herbicides, in contrast, affects most major organ systems. Symptoms range from increased respiratory rate, myotonia, anorexia, tremors, ataxia to coma; death, if it occurs, results from ventricular fibrillation. Arochlor, a chloroacetamide herbicide, exhibits low acute toxicity, but it can be metabolized to an active carcinogen.

The potential risk for toxicity to humans and non-plant species from exposure to commercially available herbicide formulations is compounded by inclusion of various adjuvants, surfactants, or solvents. These agents are added to facilitate application, dispersion, solubility or absorption of the herbicide. Yet, they may be toxic in their own right or augment the toxicity of the herbicide. Solvents or dispersing agents may increase volatility and augment the risk for inhalational exposure. They also may extend the persistence of a herbicide on and increase its rate of absorption through the skin. These considerations, the fact that herbicides account for the majority of pesticide use, and the potential for long-term exposure make the evaluation of the adverse health effects of herbicides particularly important.

An overview of the mechanisms and the symptoms of toxicities for the major classes of herbicides are presented in this paper. There are numerous references related to the pharmacodynamics of herbicides within the scientific literature, and they, as well as

other resources, should be used to obtain a more complete description of the actions and adverse effects of each class of herbicides as well as the clinical management of herbicide poisonings.

1. Introduction

Herbicides represent a diverse class of chemicals used to control unwanted, fast-growing broad-leaf weeds in agricultural, recreational and urban settings as well as to control woody, deciduous plants in right-of-ways for roads, utilities and other commercial enterprises. Currently, the amount of herbicides used exceeds the amounts of insecticides and other pesticides. Despite their ready availability and widespread use, herbicides account for only about 0.7% of total non-pharmacological human exposures reported annually to poison control centers in the U.S.

By definition, herbicides are intended to be selectively toxic to plants without having an effect on mammalian cells. With some exceptions, this intent has been largely met, as most herbicides exhibit low toxicity in mammals including humans. Nonetheless, the widespread and increasing use of herbicides together with the potential for low-dose, persistent exposure (for example, as a result of agricultural run-off and contamination of ground water) raises concern about the health effects of herbicides. The diversity in the mechanisms of action – particularly those related to regulation of growth, inhibition of cell division, blockade of key metabolic processes or disruption of membrane integrity – between the various classes of herbicides adds to the concern about potential long-term consequences in humans. These concerns are particularly acute in the light of epidemiological studies suggesting associations between exposure to herbicides and the occurrence of certain types of cancers, including leukemia, Hodgkin's disease, non-Hodgkin's lymphoma, soft-tissue sarcoma and cancer of the colon, breast, ovary and prostate. Moreover, contaminants introduced during the manufacturing process or adjuncts used to aid solubilization or application may cause toxicities with time- and dose-dependencies different from and independent of those of the actual herbicide. Such agents may also have effects when the herbicide does not. Dermal absorption is considered to be the primary route of exposure to herbicides, although ingestion is an important means of accidental and intentional exposure.

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Robert E. Kramer received a Doctor of Philosophy Degree from The University of West Virginia (Department of Physiology) in 1976. His dissertation research focused on endocrine regulation of hepatic and adrenocortical mixed function oxidases. His postdoctoral training was related to intracellular signaling within the adrenal cortex, with emphasis on the regulation and expression of steroidogenic cytochrome P450 enzymes. His research focuses on the mechanisms of action of steroidogenic agonists

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Rodney C. Baker received a Master of Science Degree (nutrition) from Utah State University in 1970. His thesis addressed the interaction between diet protein quantity or quality and the metabolism of organochlorine pesticides. He received a Doctor of Philosophy Degree in 1974 from North Carolina State University (physiology/toxicology). His research project was directed toward elucidating the mechanism of piperonyl butoxide action. Dr. Baker's postdoctoral training was in the area of lipid biochemistry. His research activities have centered on the interaction of various classes of drugs and xenobiotics on lipid metabolism and disruption of phospholipid dependent intracellular signal transduction processes. Dr. Baker is currently a Professor of Pharmacology and Toxicology at The University of Mississippi Medical Center, Jackson, Mississippi.