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Toxicology and the environment: An IUPAC teaching program for chemists*,†

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Abstract: Increasingly, chemists are faced with legislation requiring assessment of hazard and risk associated with the production, use, and disposal of chemicals. In addition, the general public are concerned about the dangers that they hear may result from the widespread use of chemicals. They look to the chemist for explanations and assume that chemists understand such matters. When they discover that chemists are often ignorant of the potential of chemicals to cause harm, their confidence in the profession is lost and chemophobia may result. In 1993, IUPAC agreed on a joint project between the Toxicology Commission and the Committee on Teaching of Chemistry to address the issue of the teaching of toxicology in the chemistry curriculum. Part of the project was a distance learning program, which is available through the Internet and on CD. The program currently consists of seven modules, one of which deals specifically with environmental toxicology. The contents of each unit will be explained as each has some input into environmental matters and green/sustainable chemistry. The program is aimed at teacher and student alike, and each module has self-assessment exercises at the end of the module. Additionally, there is material on health and safety, ethical matters, and a case study of the use of dichlorodiphenyltrichloroethane (DDT).

Keywords: toxicology; environment; distance learning; fundamental toxicology; environmental toxicology.

INTRODUCTION

Toxicology is the science of the assessment of how substances, whether natural or synthetic, can harm life by physicochemical reactions with living cells. Inevitably, such a definition implies an interaction with the environment and therefore has implications for the application to green/sustainable chemistry.

Chemicals are used increasingly in domestic and nontechnical environments, where their safe handling is no longer solely the concern of qualified chemists. For instance, consider the use of domestic cleaners; solvents and detergents; weed killers and pesticides; and proprietary medicines. The question is asked, therefore, who is the person to whom the public might turn to seek help and advice in the safe handling of these chemicals? As like as not, the answer that comes back is, the chemist. It is not unreasonable that the chemist is seen as the person who can give help and advice on the handling of chemicals, on the toxic effects associated with them, and on how to deal with an incident when and if it occurs. However, this need may not recognized in the curricula for the training of the chemist, and indeed, apart from what he or she may pick up indirectly as part of the general educational process,

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†This paper is not a critical review of a teaching program, but a description of the program. For this reason, it may depart from the prescribed publication policy for a conference-based paper.

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there may not be a formal training in toxicology. That makes the chemist very vulnerable. The public's perception of chemicals and the chemical industry is not favorable. It sees both as threats to health and the environment, and this has had an adverse effect on chemistry and on the use of its products. Despite this, globally, very few college or university chemistry courses incorporate toxicology.

IUPAC, through its Commission on Toxicology, recognized this and, with the support of the Committee on the Teaching of Chemistry, has used the IUPAC Web site to promote a distance learning program in toxicology for chemists. The program consists of a series of modules that are freely downloadable in Adobe Acrobat PDF format and are designed to be used both by educators and by students [1]. Educators are asked to select whatever is appropriate to their students and to use the material as they wish, adding content specifically relevant to their circumstances. In addition, the program contains material related to health and safety, ethical considerations, and a case study of the use of dichlorodiphenyltrichloroethane (DDT), its successes and failures; this is a good example of an application to environmental chemistry. For self-study, the modules have self-assessment questions and model answers. The Commission on Toxicology has other publications relevant to the teaching of toxicology to which the educator and student are referred [2–4].

Much of toxicology has a direct impact on green/sustainable chemistry, which is where the emphasis of this presentation lies. Indeed, one of the modules of "Essential Toxicology" is devoted specifically to environmental toxicology, but in fact, the whole of the program has relevance to sustainable chemistry. It emphasizes factors affecting living organisms and particularly human effects, recognizing that organisms, especially humans, constitute a component of the environment.

LEARNING PROGRAM

The program consists of seven modules:

- General considerations
- Factors affecting risk of poisoning
- Environmental toxicology
- Hazard and risk
- Management of potentially toxic substances
- Risk assessment and risk management
- Common types of chemical that cause health risks

These modules are intended for the educator and student alike. They may be treated as independent modules in that each deals with a different aspect of toxicology and, therefore, they do not follow on one from the other. It is advisable however, to work through the first section before embarking upon the others as this is a general introduction. Each module is accompanied by a self-assessment exercise at the end of the module.

Although only one of these sections refers specifically to the environment, there is an environmental aspect to each section. In addition, there is material on health and safety, ethical considerations, and a case study on the use of DDT.

General consideration

This module describes the fundamental principles of toxicology, and for this reason it is important that the student studies this section before embarking on any of the others. It considers the relationship between toxicity and dose, and the fact that some substances are essential for life as well as toxic, while others are very toxic. Many metals and their salts are essential for good health in trace amounts (e.g., copper, zinc, and iron), but are toxic in larger amounts. Other compounds, (e.g., insecticides, organic solvents, etc.) are toxic with no known requirement to support life. In both cases, the toxicity is dose-related. The smaller the dose needed to produce an adverse effect, the greater the toxicity. There is, however, a difference in the dose/response curve. Substances that are essential for life show an adverse effect at low and high concentrations due to deficiency and excess, respectively, whereas those that are not essential show a simple relationship throughout, between increasing dose and adverse effect.

There are some myths about toxicology which are laid to rest in this module; it is important that the student understands these myths are often embedded in public misconceptions. There is a belief that chemicals that are man made are injurious to health, whereas substances that are natural are beneficial. Clearly, this is not the case, and, indeed, one of the most toxic substances known is the toxin produced by the bacterium *Clostridium botulinum*. Substances that are essential for health are equally beneficial whether produced from a natural source or manufactured by the chemical industry. Vitamin C is a good example.

Factors affecting risk of poisoning

This module looks at the routes and mechanisms by which toxic materials are distributed throughout the environment and the body. A substance entering the environment is distributed in the air, water, soil, sediments, and living organisms. The interrelationship between these in terms of the partitioning of a given substance is complex and variable. For example, a volatile compound is likely to have a higher concentration in the air than one that is less volatile, whereas a more water-soluble compound is likely to have a higher concentration in water. Similarly, a substance may bind to soil or sediments and be retained there.

Substances may enter the body through several routes, by inhalation or ingestion, skin absorption, and eye exposure. In pregnancy, substances entering the body by any of these routes may also reach the fetus via the maternal blood stream and the placenta. The distribution of different substances within the body varies considerably, and so therefore does the toxic effect. Most substances will not be distributed evenly between different body compartments and organs. For example, iron is stored in the liver and in abnormally high amounts is hepatotoxic; many salts of metals (e.g., cadmium, mercury, and lead) and some drugs (e.g., gentamycin, cyclosporin, and lithium carbonate) are particularly nephrotoxic. A substance may have an acute or chronic effect (or both) on a particular organ or organs. In order to understand this in detail, it is necessary to understand the toxicokinetic and toxicodynamic behavior of the substance, and what controls its absorption, distribution, metabolism, and excretion. These concepts are introduced in this module.

The situation is further complicated by the fact that there may be interactions between different substances. These may be simply additive, but they may also be synergistic where the overall effect is greater than the sum, or antagonistic where the effect is less than the sum.

Environmental toxicology

Large exposures to chemicals can affect human health, directly or indirectly, by disrupting ecological systems that exist in rivers, lakes, oceans, streams, wetlands, forests, and fields. The release of chemicals into the environment knows no political boundaries and can have a global impact. Many examples of global impact can be cited. One is the detection of DDT and its derivatives in both the Arctic and Antarctic. It has never been used in either place but is now present in the bodies of polar bears and penguins. Another example is the consequences of the nuclear power station disaster at Chernobyl in the Ukraine in 1986. The effects of this disaster are still being noted in the excessive presence of radioactive cesium in lambs in some parts of Britain.

There are many sources of air pollution, but the most significant comes from the burning of fossil fuels with the production of sulfur and nitrogen oxides, volatile organic compounds, and carbon dioxide, resulting in acid rain and global warming. There are other side effects, less well known. For example, if acid precipitation reduces the pH of waterways to below 6.0, aluminum ions become soluble and bioavailable and toxic to marine life. (At a pH above 6.0, aluminum is mostly in the insoluble hydroxide form that is not biologically available.) The release of carbon dioxide and water vapor into the atmosphere from the burning of fossil fuels does not prevent solar radiation from reaching the Earth, but it does prevent the loss of infrared radiation, hence the phenomenon of global warming. This results in climatic and ecological changes. Most starkly, climate changes result in the reduction of the polar ice caps, with all that follows from that. Ecological changes result in increased microbiological activity converting more chemicals, more quickly, into volatile organic compounds, which are released into the atmosphere.

The depletion of ozone in the upper stratosphere has been another consequence of environmental pollution through the burning of fossil fuels and the release of other volatile organic compounds into the atmosphere, the most notable being chlorofluorocarbons (CFCs), which were used extensively as refrigerants. This consequence reached public prominence when it was noted that there were "holes" in the ozone layer over the poles. Ozone reduces the amount of solar UV radiation that reaches the Earth's surface. Thus, its depletion results in increases in radiation-related afflictions, most particularly skin cancers and cataracts. The recognition of the role of CFCs in ozone depletion resulted in the Montreal Protocol in 1987. This was an international agreement signed by many countries with a commitment to reduce the release of CFCs into the environment [5].

The concept of risk assessment is introduced in this module, but is dealt with in more detail in the following module. It has already been indicated that as substances enter the environment by a diversity of routes, they may become more concentrated and have a more toxic effect in different parts of the environment and in different parts of the body. These effects will be very different from one substance to another. Risk assessment requires understanding this complex process and calculating the probability of adverse effects resulting from a given exposure. If this indicates a high probability of harm, high priority must be given to reducing or eliminating the exposure. The Montreal Protocol is a good example of the outcome of a risk assessment.

Hazard and risk

Hazard is defined as the potential of a substance to cause damage, while toxicity is the assessment of its ability to poison. Risk is a measure of the probability that harm may result from exposure to a chemical. Thus, if there is no exposure, there is no risk regardless of the magnitude of the hazard. Similarly, a chemical with a small hazard becomes toxic if the exposure is excessive. In this module, terms such as no-observed-adverse-effect level (NOAEL), lowest-observed-adverse-effect level (LOAEL), and tolerable daily intake (TDI) are defined and dose/response curves are introduced. A dose/response curve is a graphical assessment of the quantitated effect of a chemical measured against its dose. The shape of such a curve is different if the chemical has a threshold below which it is not hazardous or if it is hazardous at all concentrations, i.e., whether its NOAEL is zero or not. The curve is different again for a chemical that is a nutrient at physiological concentrations but is toxic at higher concentrations.

Management of toxic substances

In industrial terms, the management of chemicals is referred to as the "life cycle" of the chemical and is the management of the chemical throughout its processing from "cradle to grave". This is illustrated by reviewing the chloralkali process from "cradle to grave". The chloralkali process is the industrial manufacture of sodium hydroxide, chlorine, and hydrogen from sodium chloride by the electrolysis of brine. It is a manufacturing process on a large scale, and therefore these chemicals are referred to as heavy chemicals. Sodium chloride has a low level of hazard for humans (unless ingested in large amounts), but high risk may be associated with handling it in large amounts as part of an industrial process. It should be noted here that sodium chloride may be highly toxic for some organisms such as freshwater fish or terrestrial plants.

The chloralkali process is a good example as it illustrates many of the hazards of industrial processes as indicated in Table 1.

Table 1 Hazards of the chloroalkali process.

Process	Hazard
Mining of NaCl	Hazardous for miners and environment Loss of farmland Waste disposal (see below)
Transportation	Combustion of fossil fuels Risk of accidents and spillage
Manufacture of NaOH, Cl_2, H_2	High temperature (100 °C) High electrical input Highly hazardous products
Waste disposal	Major problem with heavy chemicals Subject to legislation
Transport of NaOH, Cl_2, H_2	See above Highly hazardous materials
Manufacture of derivatives	Highly hazardous starting materials Dependent on product properties
Transportation	See above
Waste disposal	See above

It is clear that managing the process of prevention is much easier, safer, and less costly than coping with the consequences of exposure to a major industrial hazard. In recent years, there have been a number of initiatives to try to control the handling of chemicals, for example, prior informed consent (PIC), a United Nations procedure which bans or restricts the movement of chemicals from one country to another without prior consent; the Joint Meeting on Pesticide Residues (JMPR) which operates under the auspices of the World Health Organisation (WHO) and establishes levels of pesticide residues which may be tolerated for consumption on a daily basis; the publication of international chemical safety cards prepared by the International Program on Chemical Safety in collaboration with the Commission of the European Communities [6].

Risk assessment and management

Risk assessment has been mentioned in the module on environmental toxicology, but is dealt with here in more detail. Risk assessment is defined as the identification and quantification of risk resulting from the specific use of a chemical and risk management as the decision-making process to select the optimal steps for reducing a risk to an acceptable level.

No chemical, natural or manufactured, can be said to be totally without risk, and so the perception of risk is very important. This perception may be influenced by social need and understanding of the nature of toxicity. At one time, tetraethyllead was regarded as an essential ingredient of motor fuel but now is regarded as unacceptable because of epidemiological evidence that it damages the brain and the nervous system in children [7].

In manufacturing, risk management must include the siting of factories, giving cognizance to chemical containment and waste disposal. At the domestic level, the labeling of products must give sufficient hazard warning in a way that can be understood by all, but at the same time must not overstate the hazard. Domestic products may need additives to reduce the risk of the product, for example, the addition of a damping agent to chlorate(VII) preparations sold as domestic weed killer.

Risk may be accidental or anticipatable, and the management of the two may be different simply because the latter is predictable and the former is not. There is an interrelationship between the law, the science, and the technical process. This is becoming an increasingly difficult part of risk management as the legal requirements become more complex. There is a similar interrelationship between the workplace, the product, and the environment. Risk management systems have to take into account chemical considerations (the chemical and physical properties of reagents and products), toxicological considerations (dose/effect, dose/response curves), legislation, physical considerations (plant design and siting, prevailing weather), etc. Risk has to be reviewed; whether it is acceptable, tolerable, or unacceptable. The first and last of these are easy risk management decisions, but the second may be difficult and must offset the advantages against risk and disability both in terms of health and the environment.

Common types of chemicals that cause health risks

In this section, chemicals are subdivided into six common groups, and some examples in each group are considered for their toxicity and health risk. These are summarized in Table 2.

Table 2 Some common types of chemicals and their health risks.

Chemical	Specific example	Health risk
Dust/fume	Small particles (10 μm or less)	Lung damage, cancer
	Nanoparticles (100 nm or less)	Lung and heart damage
Gases	Sulfur/nitrogen oxides	Lung/nose irritants
	Carbon monoxide	De-oxygenated hemoglobin
	Hydrogen cyanide	Cellular respiration
Solvents	Volatile organic solvents	Effect many organs
Metals	Lead	Anemia, brain/nerve function
	Mercury	Nervous system
	Nickel/chromium	Dermatitis, lung cancer
Acid/bases	Mineral acids	Corrosive, lung damage
	Strong bases	Corrosive, deep skin sores
Pesticides	Most pesticides	WHO classification defines severity

Other considerations

As indicated above, there are other considerations in this program apart from the main modules. The first of these is health and safety, which specifically considers health and safety procedures within the laboratory. Laboratory safety is the responsibility of all laboratory workers. This requirement is laid down in law in many countries, and even the most junior member of a laboratory team must be familiar with basic safety requirements. Good health and safety procedures are a requirement of good laboratory practice. In this context, good practice encompasses the following: the handling and storage of chemicals and reagents; the handling of samples (in an analytical laboratory) with particular requirements for biological samples, both tissue and fluids; the safe use of equipment. All routine procedures must have a written protocol, and in a hospital laboratory, this is extended to procedures carried out with patients. In addition, there must be a laboratory health and safety manual, a procedure for fire precautions and an accident report protocol. Much of this has always been in place in well-organized laboratories, but in many countries it is now a legal requirement.

Every practicing scientist, as in all other aspects of life, has to work within his or her own code of ethics. There can be no sub-specialty of chemistry where this is more important than the application of toxicology to the environment. A brief section is therefore included in which a definition of ethics is considered; a code of conduct and a consequent code of ethics is presented; and a teaching program is reviewed.

A case study of the use of DDT is included, which is of interest to both toxicologists and environmentalists. DDT was first synthesized in 1874, but was not recognized as an insecticide until 1939, when it was widely used to reduce malaria, which it did successfully. It is long lasting, cheap, and has no apparent effect on humans. However, its chemical persistence and fat solubility caused bio-accumulation, and it was found to be very transferable (detected in both polar regions). It destroyed other insects, not just mosquitoes, and this had enormous ecological effects, including the spread of bubonic plague. As a consequence, it was banned by international agencies, but by 2000 the level of malaria in parts of Africa was higher than ever before. WHO and other organizations now recommend the reintroduction of DDT in certain malarial areas under well-controlled conditions.

The use of DDT has been both an enormous success and disaster from which lessons should be learnt. The harmful consequences of widespread use of any substance in the environment may not be predictable, and thus well-planned monitoring is essential. Even where environmental damage is possible, benefits may be sufficient to justify careful and limited use of a chemical.

Finally, each of the seven modules finishes with a self-assessment exercise. This exercise consists of a series of statements which the student is invited to say are true or false. Subsequent pages repeat the statements indicating whether they are true or false.

CONCLUSIONS

This distance learning program is freely available through the IUPAC Web site and in CD form, and is suitable for teachers and students alike. It demonstrates how the practice of toxicology and protection of the environment are closely linked, as environmental issues are raised in virtually every section. It is not intended that the program should be limited to the sections presented here; in the longer term, it will be expanded to cover other aspects of toxicology. It is part of a wider IUPAC program in toxicology that already includes a number of publications [8–12], in addition to those already mentioned above [1–4]. Currently, the "Explanatory Dictionary of Key Terms in Toxicology" is in preparation and should be available toward the end of 2006.

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