Indian Journal of Chemistry
Vol. 45B, October 2006, pp. 2346-2352

Green Education

Toxicology and the environment — An IUPAC teaching programme for chemists

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Received 12 June 2006

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 a joint project between the Toxicology Commission and the Committee on Teaching of Chemistry to produce a multi-author book, 'Fundamental Toxicology for Chemists'. This book has been published in 1996. A second, expanded edition has been published early in 2006 by the Royal Society of Chemistry. The textbook is associated with an ongoing distance learning programme which is available through the internet and on CD. The distance learning programme currently consists of seven units one of which deals specifically with environmental toxicology. The contents of each unit are explained as each has some input into environmental matters. In addition the programme includes a case study of dichlorodiphenyltrichloroethane (DDT) and a paper on toxicology and ethics, both of which are presented. Each unit includes assessment exercises, some of which are demonstrated.

Keywords: Toxicology, environment, DDT, air pollution, ozone, global warming, green chemistry

IPC Code: Int. Cl.[8] C07C25/20

Chemicals are used increasingly in domestic and non-technical 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 recognised 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, 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 favourable. 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 distance learning in toxicology for chemists. IUPAC's activities in toxicology education started with the preparation of a thoroughly refereed consensus "Glossary for chemists of terms used in toxicology"[1], followed by the textbook "Fundamental Toxicology for Chemists"[2]. This textbook was well received and a second edition will soon be published by the Royal Society of Chemistry. The textbook was written to support a suggested curriculum and this in turn provided the basis for a set of educational modules entitled "Essential Toxicology—A Resource for Educators"[3]. The modules were compiled and taken through the thorough review procedure of IUPAC before being approved by the organization. These modules are freely downloadable in Adobe PDF format and are designed to be used both by educators and by students. 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. For self-study, the web modules have self-assessment questions and model answers. There is now an additional "Glossary of terms used in toxicokinetics"[4]. An "Explanatory Dictionary of Key Terms in Toxicology" is approaching publication. The original glossary for chemists is being revised and it is expected that this will lead to further developments. In particular, it is likely that new distance learning modules will be prepared corresponding to the new textbook content.

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 programme has relevance to sustainable chemistry. However, these cannot be reviewed in isolation without taking into account ethical, and health and safety matters, which are also considered. In addition, the programme contains a case study of the use of DDT, its successes and failures; this is a good example of an application to environmental chemistry.

A definition of toxicology

Toxicology is the science of the assessment of how substances, whether natural or synthetic, can harm life by physico-chemical 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.

Learning programme

This programme consists of seven main sections as indicated in **Table I**. They 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.

Although one of these sections refers specifically to the environment, there is an environmental aspect to each section. In addition to these main sections, there are other parts to the programme, which are listed in **Table II**.

Table I — Summary of main sections

Section	Summary of section
1	General considerations
2	Factors affecting risk of poisoning
3	Environmental toxicology
4	Hazard and risk
5	Management of potentially toxic substances
6	Risk assessment and risk management
7	Common types of chemical that cause health risks

Of these sections, health and safety and ethical considerations are of general interest to all chemists and of significant importance. The case study of dichlorodiphenyltrichloroethane (DDT) is an important study of the use of a particular insecticide and is of particular relevance to green chemists.

The assessment exercises accompany each of the main seven sections.

General considerations

This section 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 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 section, and which it is important that the student understands as these 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.

Table II — Other parts to the programme

Description
Health and safety
DDT Case study
Ethical considerations
Assessment exercises

Factors affecting risk of poisoning

This section 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 in living organisms. The inter-relationship 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 metals, *e.g.*, cadmium, mercury and lead and some drugs, *e.g.*, gentamycin, cyclosporin and lithium, 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 behaviour of the substance, and what controls its absorption, distribution, metabolism and excretion. These concepts are introduced in this section.

The situation is further complicated by the fact that there may be interactions between difference 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.

Global impacts

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 is the consequences of the nuclear power station disaster at Chernobyl in the Ukraine in 1982. The effects of this are still being noted in lambs in some parts of Britain even now.

Air pollution

The greatest source of air pollution is 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 *p*H of waterways to below 6.0, aluminium ions become soluble and bioavailable and toxic to marine life. (At a *p*H above 6.0, aluminium is mostly in the insoluble hydroxide form which is not biologically available).

Ozone depletion

The depletion of ozone in the upper stratosphere has been one of the consequences 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 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 cancers most particularly skin cancers.

The Montreal protocol

The Montreal protocol was an international agreement signed by many countries in 1987 reducing the release of CFCs into the environment.

Global warming

The release of carbon dioxide and water vapour into the atmosphere from the burning of fossil fuels does not impair solar radiation from reaching the earth, but it does impair 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 this. Ecological changes result in increased microbiological activity converting more chemicals, more quickly, into volatile organic compounds, which are released into the atmosphere.

Global risk assessment

This section introduces the concept of risk assessment. 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 defined as 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 section 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 the grave'. It is illustrated in this section by reviewing the chloralkali process from 'cradle to grave'. This 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 may 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 III**.

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, *e.g.* prior informed consent (PIC), a United Nation's 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

Table III — Hazards of the chloroalkali process

Process	Hazard
Mining of NaCl	Hazardous for miner 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^{o}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

consumption on a daily basis; the publication of international chemical safety cards prepared by the International Programme on Chemical Safety in collaboration with the Commission of the European Communities[5].

Risk assessment and management

Risk assessment has been mentioned in the section on environmental toxicology, but is dealt with herein 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 lead tetraacetate was regarded as an essential ingredient of motor fuel but now is regarded as socially unacceptable because of its toxic properties.

In manufacturing, risk management must include the siting of factories, giving cognisance to chemical containment and waste disposal. At the domestic level the labelling 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, *e.g.*, 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 inter-relationship 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 inter-relationship 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 chemical that cause health risks

In this section, chemicals are sub divided into six common groups and some examples in each group are considered for their toxicity and health risk. These are summarised in **Table IV**.

Health and safety

This section looks specifically and 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

Table IV — 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 haemoglobin
	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

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 organised laboratories, but in many countries it is now a legal requirement.

DDT case study

This is an interesting case study for both toxicologists and environmentalists. DDT was first synthesized in 1874 but was not recognised 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 organisations 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.

Ethical considerations

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. In this section, a definition of ethics is considered; a code of conduct and a consequent code of ethics is presented; and a teaching programme is reviewed.

Self-assessment

Each of the seven main sections finishes with a self-assessment. This 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

The distance learning programme freely available through the IUPAC website and in CD form 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 programme should be limited to the sections presented here; in the longer term it will be expanded to cover other aspects of toxicology, especially those now incorporated in the second edition of the associated textbook. The textbook, now simply entitled ‘Fundamental toxicology’[2], will have additional chapters on toxicogenomics, the behaviour of chemicals in the environment, pharmaceutical toxicology and toxicology in the clinical laboratory. The ‘Curriculum of fundamental toxicology for chemists’, which is included in the book, has been modified to incorporate this new material and corresponding new distance learning modules may be expected. This is all part of wider IUPAC activity in toxicology that already includes a number of publications[6-10], 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 towards the end of 2006.

Acknowledgement

This paper has also been submitted to the IUPAC journal Pure and Applied Chemistry as part of the proceedings of the 2nd International Symposium on Green/Sustainable Chemistry, 10-13 January 2006, Delhi, India.

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