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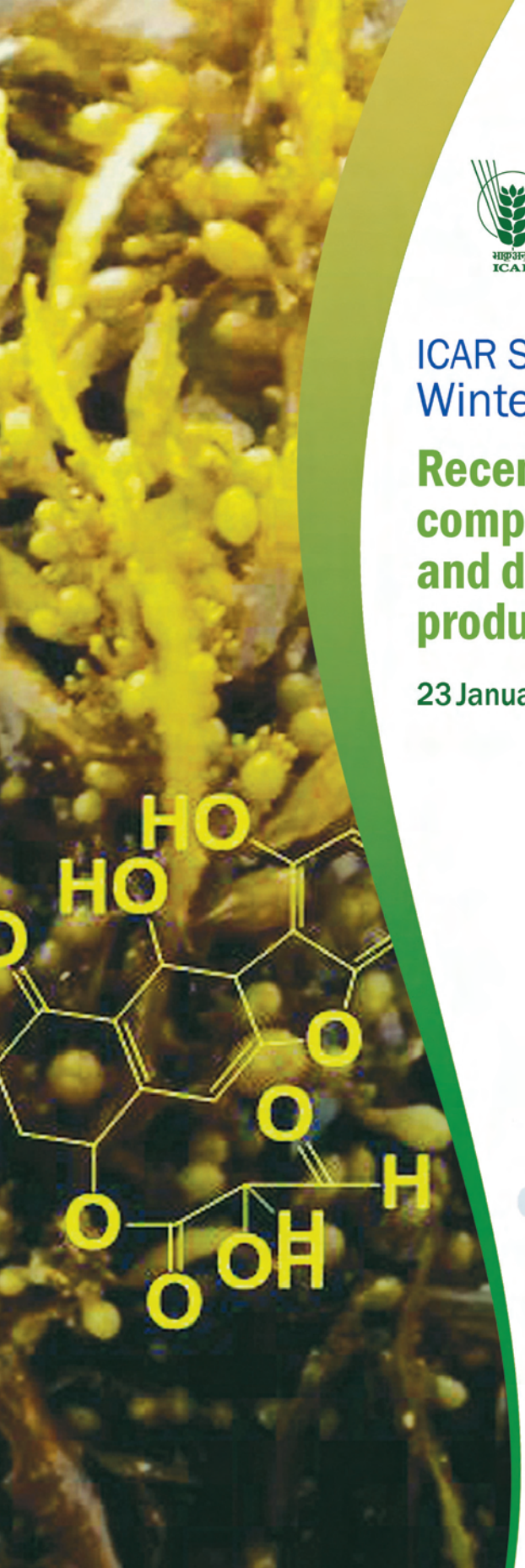
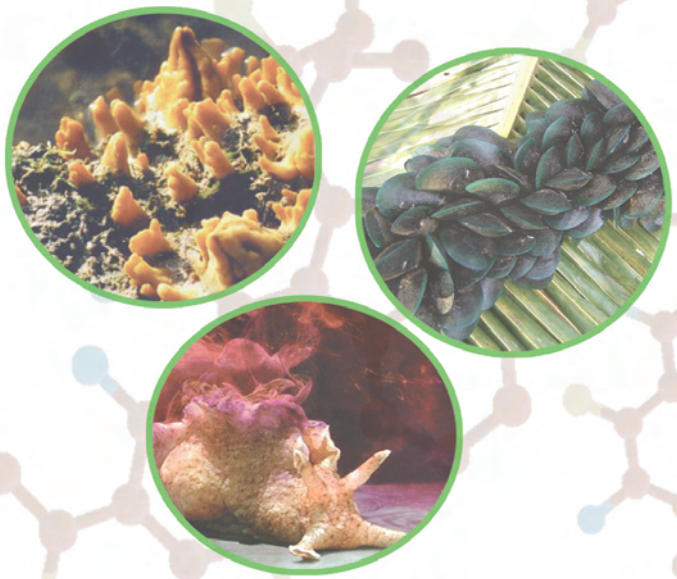


ICAR Sponsored Winter School on

Recent advances in bioactive compounds from marine organisms and development of high value products for health management

23 January to 12 February 2018



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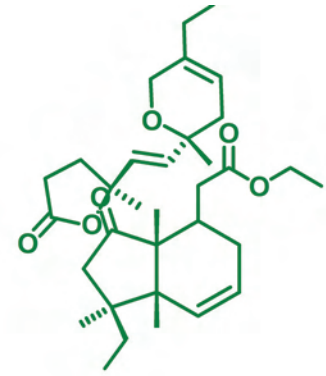

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Course Manual

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ICAR-Central Marine Fisheries Research Institute,
23 January - 12 February, 2018

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FOREWORD

There has been a growing interest in the marine derived bioactive compounds in the recent years, and the functional foods, enriched with natural ingredients have been proved to provide beneficial action for human health. Marine derived bioactive components and the functional food ingredients demonstrated to possess potential health benefits. High value secondary bioactive metabolites from the marine organisms are attracting attention because of the growing demand for new compounds of 'marine natural' origin, having potential applications in pharmaceutical fields, and concerns about the adverse effects by synthetic drugs and their derivatives. The pioneering R & D works at ICAR-Central Marine Fisheries Research Institute on marine bioprospecting envisaged a systematic approach involving chemical profiling of major species of marine organisms for bioactive pharmacophore leads for activity against various diseases, and a library of molecules with bioactive potential. The research work in this institute developed protocols to prepare various pharmaceutical leads, nutraceuticals/ functional food supplements enriched with lead molecules with different properties against various drug targets for use against various life-threatening diseases.

ICAR-Central Marine Fisheries Research Institute is the pioneering marine research institute in India to work in the frontier area of bioactive molecule discovery from marine organisms as promising therapeutic agents against various diseases, aquatic food product technology, and development of high value products for health management. This prestigious research institute of Indian Council of Agricultural Research is working in the broad national interest of producing high value bioactive leads from the marine organisms, which would provide promising therapeutic agents against various diseases. This institute has developed and commercialized the nutraceutical products Cadalmin™ Green Algal extract (Cadalmin™ GAe) and Antidiabetic extract (Cadalmin™ ADe) as green alternatives to synthetic drugs to combat rheumatic arthritic pains and type-2 diabetes, respectively to a leading biopharmaceutical company in India. The anti-inflammatory nutraceutical Cadalmin™ Green Mussel extract (Cadalmin™ GMe) from Asian green mussel Perna viridis has been commercialized with Amalgam Group of Companies. Cadalmin™ Antihypercholesterolemic extract (Cadalmin™ ACe) has been developed from seaweeds to combat dyslipidemia leading to obesity, and the product was out-licensed to a leading Indian MNC in wellness and obesity management. Antimicrobial therapeutic product from marine bacteria as oral applicant has been developed and the product is in pipeline for commercialization. Seaweed-derived natural template inspired synthetic derivatives as potential pharmacophores were designed and developed. Several nutraceutical and cosmeceutical products from marine organisms are in pipeline, and are being commercialized.

The objective of the National level ICAR Winter School on "Recent advances in bioactive compounds from marine organisms and development of high-value products for health management" is to provide up-to-date information and acquaint the participants with the latest technologies on isolation and characterization of marine natural products of pharmaceutical importance from marine organisms, general and advanced methods of isolation procedures by chromatography, classification of organic compounds and their characterization by advanced spectroscopic experiments. This program further aims to give exposure to the chemical perspectives of marine organisms, primary and secondary bioactive metabolites from fish and marine organisms to develop bioactive compounds and high-value functional food products. Theory and practical classes will be conducted in these areas to provide the participants a hands-on experience.

This ICAR Winter School is organized with the full funding support from ICAR, New Delhi, and the twenty-five participants from various parts of India who are attending this programme were selected after scrutiny of their applications based on their bio-data. They are serving as academicians, such as Professors/Scientists, and in similar posts. The faculties include the knowledgeable scientists and professors from various parts of India and abroad. This training will enable the participants to efficiently carry out their academic programmes, and to plan research on bioactive molecule discovery in their respective laboratories and institutes so that they can formulate the strategies for research.

The Winter School on "Recent advances in bioactive compounds from marine organisms and development of high value products for health management" is very ideal for the current scenario of increasing lifestyle diseases and human health. Understanding the importance of natural products in the health care system of India, ICAR-Central Marine Fisheries Research Institute has reasonably contributed in the various aspects. The Manual released on this occasion covers all aspects of marine natural products prepared by the experts in their respective fields. I congratulate the Course Director of this programme, Dr. Kajal Chakraborty and Head of the Marine Biotechnology Division, Dr. P. Vijayagopal, along with other staff members of Marine Biotechnology Division and Central Marine Fisheries Research Institute for their sincere efforts in bringing out the manual in time, and to arrange the programme in a befitting manner.

A. Gopalakrishnan
Director, ICAR-Central Marine Fisheries Research Institute
Kochi, Kerala

PREFACE

Marine-derived bioactive components and the functional food ingredients with potential health benefits are an emerging area of research. The rich diversity of flora and fauna in the marine and coastal habitats of the Indian subcontinent represent an untapped reservoir of bioactive compounds with valuable pharmaceutical and biomedical use. Considering the underutilization of these groups of marine organisms, exploring bioactive compounds and development of any biologically useful products have benefits as health products. Comprehensive analyses demonstrated that during the last decade the average proportion of bioactive compounds among the new compounds is declining, though there are a large number of marine natural products yet to be explored. This may indicate that the research level of bioactivity is not keeping up with the discovery of new compounds. Thus, the research tools and methods for finding bioactivity need to be improved. The first improvement is about methods of spectral and bioactivity-guided separation and purification of marine-derived secondary metabolites, which combine the discovery of new compounds. These improvements in technology are dependent upon the automation in spectroscopy, which also allows the study of the functions of new compounds extracted from the target marine organisms. Second, for the discovery of new lead compounds and artificial intelligence for drug development evolved to a more mechanistic approach that targets specific molecular lesions. Combined with high-throughput screening through a large number of drug targets, bioactivity research against various life-threatening diseases will be effective in revealing the potentially useful biological properties of marine natural products. Furthermore, the discovery of new bioactive compounds from marine metabolites will form the basis for new drug leads. Thus, the new compounds will absolutely compose an abundant resource for future bioactivity research and drug development. Various medicinal and biomedical products from marine flora and fauna provide a myriad of benefits for human health and multiple life-threatening diseases, and therefore, are the attractive options for the food and pharmaceutical industry. The increasing interest in marine-based functional food ingredients and nutraceutical formulations in the last decade along with increased number of patents filed/granted have appropriately demonstrated the possibilities of bioactive from marine organisms to maintain and improve human health and well-being.

The present ICAR Winter School on "Recent advances in bioactive compounds from marine organisms and development of high-value products for health management" is designed to acquaint the participants with the advances in marine bioactive compounds with emphasis on the latest technologies on isolation and characterization of marine natural products of pharmaceutical importance. The course is planned in such a way that it covers both theoretical and practical aspect of recent advances in bioactive compounds from marine organisms. This programme will strengthen the knowledge of participants with regard to

the general and advanced methods of isolation procedures by chromatography, and their characterization by advanced spectroscopic experiments aspects.

I wish to thank the Education Division of Indian Council of Agricultural Research for giving us an opportunity to organize this ICAR Winter School. We are grateful to Dr. A. Gopalakrishnan, Director, ICAR-Central Marine Fisheries Research Institute, for his guidance, continuous interest in the course and providing all necessary facilities. I am highly obliged to Dr. P. Vijayagopal, Head, Marine Biotechnology Division for his guidance and support for the programme. All the scientists of Marine Biotechnology Division, technical staff, supporting staff and research scholars supported us in organizing the ICAR Winter School. I recall with gratitude the marvellous effort and help in preparing this manual by Minju Joy, Research Scholar of Marine Biotechnology Division. I take this opportunity to thank all the faculty members who have devoted their valuable time and contributed material for the preparation of the manual. I am confident that the Course Manual would aid the participants to enhance their knowledge and competence in the area of marine bioactive compounds and their applications for the development of high-value products for health management.

Kajal Chakraborty
Course Director

January, 2018

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CHAPTER

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SAFETY AND HAZARDS IN A CHEMICAL LABORATORY

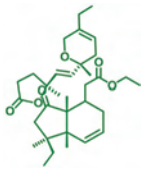
Kajal Chakraborty, Minju Joy, Vinaya K. K., Aswathy Elizabeth Mani

Bioprospecting Section of Marine Biotechnology Division,
ICAR-Central Marine Fisheries Research Institute, Kochi

A key element of planning an experiment is assessing the hazards and potential risks associated with the chemicals and laboratory operations to be used. The primary responsibility for proper hazard evaluations and risk assessments lies with the person performing the experiment. The actual evaluations and assessments may be performed by trained laboratory personnel, but these should be checked and authorized by the supervisor. The supervisor is also responsible for ensuring that everyone involved in an experiment and those nearby understand the evaluations and assessments. Some organizations have environmental health and safety offices, with industrial hygiene specialists to advise trained laboratory personnel and their supervisors in risk assessment. As part of a culture of safety, the supervisor and scholars in the laboratory must work cooperatively to create a safe environment and to ensure that hazards are appropriately identified and assessed prior to beginning work. All laboratory personnel should be familiar with and have ready access to their institution's chemical hygiene plan. In some laboratories, chemical hygiene plans include standard operating procedures for work with specific chemical substances, and the chemical hygiene plan may be sufficient as the primary source of information used for risk assessment and experiment planning. However, most chemical hygiene plans provide only general procedures for handling chemicals, and prudent experiment planning requires that laboratory personnel consult additional sources for information on the properties of the substances that will be encountered in the proposed experiment. Many laboratories require documentation of specific hazards and controls for a proposed experiment.

MATERIAL SAFETY DATA SHEETS (MSDSS)

Federal regulations (OSHA Hazard Communication Standard 1910.1200) require that manufacturers and distributors of hazardous chemicals provide users with material safety data sheets (MSDSs), which are designed to provide the information needed to protect users from any hazards that may be associated with the product (Globally Harmonized System for Hazard Communication). MSDSs have become the primary vehicle through which the potential hazards of materials obtained from commercial sources are communicated to trained laboratory personnel. Institutions are required by law (OSHA Hazard Communication Standard) to retain and make readily available the MSDSs provided by chemical suppliers. OSHA recommends the general 16-part format created by the American National Standards Institute (ANSI Z400.1). The information typically found in an MSDS follows:



1. Supplier (with address and phone number) and date MSDS was prepared or revised.
2. Chemical.
3. Physical and chemical properties.
4. Physical hazards related to flammability, reactivity, and explosion hazards.
5. Toxicity data.
6. Health hazards-Acute and chronic health hazards together with the signs and symptoms of exposure.
7. Storage and handling procedures.
8. Emergency and first-aid procedures.
9. Disposal considerations.
10. Transportation information.

MSDSs remain the best single source of information for the purpose of evaluating the hazards and assessing the risks of chemical substances. However, laboratory personnel should recognize the limitations of MSDSs as applied to laboratory-scale operations. If MSDSs are not adequate, specific laboratory operating procedures should be available for the specific laboratory manipulations to be employed:

1. The quality of MSDSs produced by different chemical suppliers varies widely.
2. Unique morphology of solid hazardous chemicals may not be addressed in MSDSs; for example, an MSDS for nano-size titanium dioxide may not present the unique toxicity considerations for these ultra-fine particulates.
3. MSDSs must describe control measures and precautions for work on a variety of scales.
4. Many MSDSs comprehensively list all conceivable health hazards associated with a substance without differentiating which are most significant and which are most likely to actually be encountered. As a result, trained laboratory personnel may not distinguish highly hazardous materials from moderately hazardous and relatively harmless ones.

GLOBALLY HARMONIZED SYSTEM (GHS) FOR HAZARD COMMUNICATION

The GHS of Classification and Labeling of Chemicals is an internationally recognized system for hazard classification and communication (available at http://www.unece.org.). It was developed with support from the International Labour Organization (ILO), the

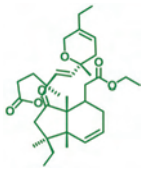
Organisation for Economic Co-operation and Development, and the United Nations Sub-Committee of Experts on the Transport of Dangerous Goods with the goal of standardizing hazard communication to improve the safety of international trade and commerce. GHS recognizes 16 types of physical hazards, 10 types of health hazard, and an environmental hazard.

Physical hazards include

- explosives;
- flammable gases;
- flammable aerosols;
- oxidizing gases;
- gases under pressure;
- flammable liquids;
- flammable solids;
- self-reactive substances;
- pyrophoric liquids;
- pyrophoric solids;
- self-heating substances;
- substances which, in contact with water, emit flammable gases;
- oxidizing liquids;
- oxidizing solids;
- organic peroxides; and
- corrosive to metals.

Health hazards include

- acute toxicity,
- skin corrosion or irritation,
- serious eye damage or eye irritation,
- respiratory or skin sensitization,
- germ cell mutagenicity,



- carcinogenicity,
- reproductive toxicology,
- target organ systemic toxicity—single exposure,
- target organ systemic toxicity—repeated exposure, and
- aspiration hazard.

Environmental hazard includes

- Hazardous to the aquatic environment: acute aquatic toxicity or chronic aquatic toxicity with bioaccumulation potential rapid degradability.

LABORATORY CHEMICAL SAFETY SUMMARIES (LCSSS)

Although MSDSs are invaluable resources, they suffer some limitations as applied to risk assessment in the specific context of the laboratory. LCSSs provide information on chemicals in the context of laboratory use. These documents are summaries and are not intended to be comprehensive or to fulfill the needs of all conceivable users of a chemical. LCSS gives essential information required to assess the risks associated with the use of a particular chemical in the laboratory. LCSSs also contain a concise critical discussion, presented in a style readily understandable to trained laboratory personnel, of the toxicity, flammability, reactivity, and explosivity of the chemical; recommendations for the handling, storage, and disposal of the title substance; and first-aid and emergency response procedures.

LABELS

Commercial suppliers are required by law (OSHA Hazard Communication Standard) to provide their chemicals in containers with precautionary labels. Labels usually present concise and non-technical summaries of the principal hazards associated with their contents. It is of note that precautionary labels do not replace MSDSs and LCSSs as the primary sources of information for risk assessment in the laboratory. However, labels serve as valuable reminders of the key hazards associated with the substance.

ADDITIONAL SOURCES OF INFORMATION

The resources described above provide the foundation for risk assessment of chemicals in the laboratory. Although MSDSs and LCSSs include information on toxic effects, in some situations laboratory personnel should seek additional more detailed information. This step is particularly important when laboratory personnel are planning to use chemicals that have a high degree of acute or chronic toxicity or when it is anticipated that work will be conducted with a particular toxic substance frequently or over an extended period of time. The following annotated list provides references on the hazardous properties of chemicals

and which are useful for assessing risks in the laboratory.

1. *International Chemical Safety Cards* from the International Programme on Chemical Safety (IPCS, 2009). The IPCS is a joint activity of the ILO, the United Nations Environment Programme, and the World Health Organization. The cards contain hazard and exposure information from recognized sources and undergo international peer review. They are available in 18 languages and can be found online through the NIOSH Web site, www.cdc.gov/niosh, or through the ILO Web site, www.ilo.org.

2. *NIOSH Pocket Guide to Chemical Hazards* (HHS/ CDC/NIOSH, 2007). This volume is updated regularly and is found on the NIOSH Web site (http://www.cdc.gov/niosh). These charts are quick guides to chemical properties, reactivities, exposure routes and limits, and first-aid measures.

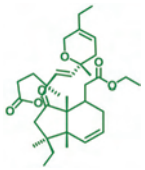
3. *A Comprehensive Guide to the Hazardous Properties of Chemical Substances*, 3rd edition (Patnaik, 2007). This particularly valuable guide is written at a level appropriate for typical laboratory personnel. It covers more than 1,500 substances; sections in each entry include uses and exposure risk, physical properties, health hazards, exposure limits, fire and explosion hazards, and disposal or destruction. Entries are organized into chapters according to functional group classes, and each chapter begins with a general discussion of the properties and hazards of the class.

4. *2009 TLVs and BEIs: Based on the Documentation of the Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices*. A booklet listing ACGIH threshold limit values (TLVs) and short-term exposure limits (STELs). These values are under continuous review, and this booklet is updated annually. The multivolume publication *Documentation of the Threshold Limit Values and Biological Exposure Indices* reviews the data that were used to establish the TLVs.

5. *Fire Protection for Laboratories Using Chemicals* (NFPA, 2004). This is the national fire safety code pertaining to laboratory use of chemicals. It describes the basic requirements for fire protection of life and property in the laboratory

6. *Fire Protection Guide to Hazardous Materials*, 13th edition (NFPA, 2001). This resource contains hazard data on hundreds of chemicals and guidance on handling and storage of, and emergency procedures for those chemicals.

7. *Hazardous Chemicals Handbook*, 2nd edition (Carson and Mumford, 2002). This book is geared toward an industrial audience. It provides basic information about chemical hazards and synthesizes technical guidance from a number of authorities



in chemical safety. The chapters are organized by hazard (e.g., "Toxic Chemicals," "Reactive Chemicals," and "Cryogens").

A number of Web-based resources also exist. Some of these are NIOSH Databases and Information Resources (www.cdc.gov/niosh) and TOXNET through the National Library of Medicine (NLM; www.nlm.nih.gov).

THE NATIONAL LIBRARY OF MEDICINE DATABASES

The databases supplied by NLM are easy to use and free to access via the Web. TOXNET is an online collection of toxicological and environmental health databases. TOXLINE, for example, is an online database that accesses journals and other resources for current toxicological information on drugs and chemicals. It covers data published from 1900 to the present. Databases accessible through TOXNET include the Hazardous Substance Data Base (HSDB) Carcinogenic Potency Database (CPDB), the Developmental and Reproductive Toxicology Database (DART), the Genetic Toxicology Data Bank (GENE-TOX), the Integrated Risk Information System (IRIS), the Chemical Carcinogenesis Research Information System (CCRIS), and the International Toxicity Estimates for Risk (ITER). Other databases supplied by NLM that provide access to toxicological information are PubMed, which includes access to MEDLINE, PubChem, and ChemIDPlus. Free text searching is available on most of the databases. Another source of toxicity data is Chemical Abstracts Service (CAS). In addition to the NLM, several services provide CAS, including DIALOG, ORBIT, STN, and SciFinder. Searching procedures for CAS depend on the various services supplying the database. Additional information can be found on the CAS Web site, www.cas.org. Searching any database listed above is best done using the CAS registry number for the particular chemical.

TRAINING

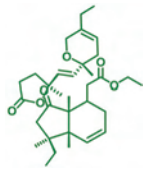
One important source of information for laboratory personnel is training sessions, and the critical place it holds in creating a safe environment should not be underestimated. Facts are only as useful as one's ability to interpret and apply them to a given problem, and training provides context for their use. Hands-on, scenario-based training is ideal because it provides the participants with the chance to practice activities and behaviors in a safe way. Such training is especially useful for learning emergency response procedures. Another effective tool, particularly when trying to build awareness of a given safety concern, is case studies. Prior to beginning any laboratory activity, it is important to ensure that personnel have enough training to safely perform required tasks. If new equipment, materials, or techniques are to be used, a risk assessment should be performed, and any knowledge gaps should be filled before beginning work.

TOXIC EFFECTS OF LABORATORY CHEMICALS

The chemicals encountered in the laboratory have a broad spectrum of physical, chemical, and toxicological properties and physiological effects. The risks associated with chemicals must be well understood prior to their use in an experiment. The risk of toxic effects is related to both the extent of exposure and the inherent toxicity of a chemical. As discussed in detail below, extent of exposure is determined by the dose, the duration and frequency of exposure, and the route of exposure. Exposure to even large doses of chemicals with little inherent toxicity, such as phosphate buffer, presents low risk. In contrast, even small quantities of chemicals with high inherent toxicity or corrosivity may cause significant adverse effects. The duration and frequency of exposure are also critical factors in determining whether a chemical will produce harmful effects. A single exposure to some chemicals is sufficient to produce an adverse health effect; for other chemicals repeated exposure is required to produce toxic effects. For most substances, the route of exposure (through the skin, the eyes, the gastrointestinal tract, or the respiratory tract) is also an important consideration in risk assessment. For chemicals that are systemic toxicants, the internal dose to the target organ is a critical factor. Exposure to acute toxicants can be guided by well-defined toxicity parameters based on animal studies and often human exposure from accidental poisoning. The analogous quantitative data needed to make decisions about the neurotoxicity and immunogenicity of various chemicals is often unavailable.

When considering possible toxicity hazards while planning an experiment, recognizing that *the combination of the toxic effects of two substances may be significantly greater than the toxic effect of either substance alone* is important. Because most chemical reactions produce mixtures of substances with combined toxicities that have never been evaluated, it is prudent to assume that mixtures of different substances (i.e., chemical reaction mixtures) will be more toxic than their most toxic ingredient. Furthermore, chemical reactions involving two or more substances may form reaction products that are significantly more toxic than the starting reactants. This possibility of generating toxic reaction products may not be anticipated by trained laboratory personnel in cases where the reactants are mixed unintentionally. For example, inadvertent mixing of formaldehyde (a common tissue fixative) and hydrogen chloride results in the generation of bis(chloromethyl)ether, a potent human carcinogen.

All laboratory personnel must understand certain basic principles of toxicology and recognize the major classes of toxic and corrosive chemicals. The next sections of this chapter summarize the key concepts involved in assessing the risks associated with the use of toxic chemicals in the laboratory.



DOSE-RESPONSE RELATIONSHIPS

Toxicology is the study of the adverse effects of chemicals on living systems. The basic tenets of toxicology are that no substance is entirely safe and that all chemicals result in some toxic effects if a high enough amount (dose) of the substance comes in contact with a living system. For example, water, a vital substance for life, results in death if a sufficiently large amount (i.e., gallons) is ingested at one time. On the other hand, sodium cyanide, a highly lethal chemical, produces no permanent (acute) effects if a living system is exposed to a sufficiently low dose. The single most important factor that determines whether a substance is harmful (or, conversely, safe) to an individual is the relationship between the amount (and concentration) of the chemical reaching the target organ, and the toxic effect it produces. For all chemicals, there is a range of concentrations that result in a graded effect between the extremes of no effect and death. In toxicology, this range is referred to as the dose-response relationship for the chemical. The dose is the amount of the chemical and the response is the effect of the chemical. This relationship is unique for each chemical, although for similar types of chemicals, the dose-response relationships are often similar. Among the thousands of laboratory chemicals, a wide spectrum of doses exists that are required to produce toxic effects and even death. For most chemicals, a threshold dose has been established (by rule or by consensus) below which a chemical is not considered to be harmful to most individuals.

Some chemicals (e.g., dioxin) produce death in laboratory animals exposed to microgram doses and therefore are extremely toxic. Other substances, however, have no harmful effects following doses in excess of several grams. One way to evaluate the acute toxicity (i.e., the toxicity occurring after a single exposure) of laboratory chemicals involves their lethal dose 50 (LD_{50}) or lethal concentration 50 (LC_{50}) value. The LD_{50} is defined as the amount of a chemical that when ingested, injected, or applied to the skin of a test animal under controlled laboratory conditions kills one-half (50%) of the animals. The LD_{50} is usually expressed in milligrams or grams per kilogram of body weight. For volatile chemicals (i.e., chemicals with sufficient vapor pressure that inhalation is an important route of chemical entry into the body), the LC_{50} is often reported instead of the LD_{50}. The LC_{50} is the concentration of the chemical in air that will kill 50% of the test animals exposed to it. The LC_{50} is given in parts per million, milligrams per liter, or milligrams per cubic meter. Also reported are LC_{LO} and LD_{LO} values, which are defined as the lowest concentration or dose that causes the death of test animals. In general, the larger the LD_{50} or LC_{50}, the more chemical it takes to kill the test animals and, therefore, the lower the toxicity of the chemical. Although lethal dose values may vary among animal species and between animals and humans, chemicals that are highly toxic to animals are generally highly toxic to humans.

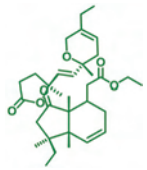
ASSESSING RISKS OF EXPOSURE TO TOXIC LABORATORY CHEMICALS

Exposure to a harmful chemical results in local toxic effects, systemic toxic effects, or both. Local effects involve injury at the site of first contact; the eyes, the skin, the nose and lungs, and the digestive tract are typical sites of local reactions. Examples of local effects include (1) inhalation of hazardous materials causing toxic effects in the nose and lungs; (2) contact with harmful materials on the skin or eyes leading to effects ranging from mild irritation to severe tissue damage; and (3) ingestion of caustic substances causing burns and ulcers in the mouth, esophagus, stomach, and intestines. Systemic effects, by contrast, occur after the toxicant has been absorbed from the site of contact into the bloodstream and distributed throughout the body. Some chemicals produce adverse effects on all tissues of the body, but others tend to selectively injure a particular tissue or organ without affecting others. The affected organ (e.g., liver, lungs, kidney, and central nervous system) is referred to as the target organ of toxicity, although it is not necessarily the organ where the highest concentration of the chemical is found. Hundreds of systemic toxic effects of chemicals are known; they result from single (acute) exposures or from repeated or long-duration (chronic) exposures that become evident only after a long latency period.

Laboratory chemicals are grouped into several classes of toxic substances, and many chemicals display more than one type of toxicity. The first step in assessing the risks associated with a planned laboratory experiment involves identifying which chemicals in the proposed experiment are potentially hazardous substances. The term "health hazard" includes chemicals that are carcinogens, toxic or highly toxic agents, reproductive toxins, irritants, corrosives, sensitizers, hepatotoxins, neurotoxins, agents that act on the hematopoietic systems, and agents that damage the lungs, skin, eyes, or mucous membranes. The OSHA Laboratory Standard further requires that certain chemicals be identified as particularly hazardous substances (PHSs) and handled using special additional procedures. PHSs include chemicals that are select carcinogens (those strongly implicated as a potential cause of cancer in humans), reproductive toxins, and compounds with a high degree of acute toxicity. This will provide a second set of trained eyes to review the safety protocols in place and will help ensure that any special emergency response requirements can be met in the event of exposure of personnel to the material or accidental release. The following are the most common classes of toxic substances encountered in laboratories.

ACUTE TOXICANTS

Acute toxicity is the ability of a chemical to cause a harmful effect after a single exposure. Acutely toxic agents cause local toxic effects, systemic toxic effects, or both, and this class of toxicants includes corrosive chemicals, irritants, and allergens (sensitizers). In assessing the risks associated with acute toxicants, it is useful to classify a substance according to acute toxicity hazard level as shown in table.



ACUTE TOXICITY HAZARD LEVEL

Hazard Level	Toxicity Rating	Oral LD_{50} (rats, per kg)	Skin Contact LD_{50} (rabbits, per kg)	Inhalation LC_{50} (rats, ppm for 1 h)	Inhalation LC_{50} (rats, mg/m^3 for 1 h)
High	Highly toxic	<50 mg	<200 mg	<200	<2,000
Medium	Moderately toxic	50 to 500 mg	200 mg to 1 g	200 to 2,000	2,000 to 20,000
Low	Slightly toxic	500 mg to 5 g	1 to 5 g	2,000 to 20,000	20,000 to 200,000

Special attention is given to any substance classified according to the above criteria as having a high level of acute toxicity hazard. Chemicals with a high level of acute toxicity make up one of the categories of PHSs defined by the OSHA Laboratory Standard. The following table lists some of the most common chemicals with a high level of acute toxicity that are encountered in the laboratory.

Examples of Compounds with a High Level of Acute Toxicity

	Acrolein	Methyl fluorosulfonate
	Arsine	Nickel carbonyl
	Chlorine	Nitrogen dioxide
	Diazomethane	Osmium tetroxide
	Diborane (gas)	Ozone
	Dimethyl mercury	Phosgene
	Hydrogen cyanide	Sodium azide
	Hydrogen fluoride	Sodium cyanide (and other cyanide salts)

TYPES OF TOXINS

Irritants, Corrosive Substances, Allergens, and Sensitizers

Lethal dose and other quantitative toxicological parameters generally provide little guidance in assessing the risks associated with corrosives, irritants, allergens, and sensitizers because these toxic substances exert their harmful effects locally. It would be very useful for the chemical research community if a quantitative measure for such effects were developed. When planning an experiment that involves corrosive substances, basic prudent handling practices should be reviewed to ensure that the skin, face, and eyes are protected adequately by the proper choice of corrosion-resistant gloves and protective clothing and eyewear, including, in some cases, face shields. Similarly, LD_{50} and LC_{50} data are not indicators of the irritant effects of chemicals, and therefore special attention should be paid to the identification of irritant chemicals by consulting LCSSs, MSDSs, and other sources of information. Allergens

and sensitizers are another class of acute toxicants with effects that are not included in LD_{50} or LC_{50} data.

ASPHYXIANTS

Asphyxiants are substances that interfere with the transport of an adequate supply of oxygen to vital organs of the body. The brain is the organ most easily affected by oxygen starvation, and exposure to asphyxiants leads to rapid collapse and death. Simple asphyxiants are substances that displace oxygen from the air being breathed to such an extent that adverse effects result. Acetylene, carbon dioxide, argon, helium, ethane, nitrogen, and methane are common asphyxiants. Certain other chemicals have the ability to combine with hemoglobin, thus reducing the capacity of the blood to transport oxygen. Carbon monoxide, hydrogen cyanide, and certain organic and inorganic cyanides are examples of such substances.

NEUROTOXINS

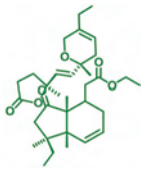
Neurotoxic chemicals induce an adverse effect on the structure or function of the central or peripheral nervous system, which can be permanent or reversible. The detection of neurotoxic effects may require specialized laboratory techniques, but often they are inferred from behavior such as slurred speech and staggered gait. Neurotoxins are chronically toxic substances with adverse effects that are not immediately apparent. Chemical neurotoxins tmay be found in laboratory are mercury (inorganic/organic), organophosphate pesticides, carbon disulfide, xylene, tricholoroethylene, and *n*-hexane.

REPRODUCTIVE AND DEVELOPMENTAL TOXINS

Reproductive toxins are defined by the OSHA Laboratory Standard as substances that cause chromosomal damage (mutagens) and substances with lethal or teratogenic (malformation) effects on fetuses. These substances have adverse effects on various aspects of reproduction, including fertility, gestation, lactation, and general reproductive performance, and can affect both men and women. Various reproductive hazards have been noted following exposure to halogenated hydrocarbons, nitro aromatics, arylamines, ethylene glycol derivatives, mercury, bromine, carbon disulfide, and other chemical reagents.

CARCINOGENS

A carcinogen is a substance capable of causing cancer. Cancer, in the simplest sense, is the uncontrolled growth of cells and can occur in any organ. The mechanism by which cancer develops is not well understood, but the current thinking is that some chemicals interact directly with DNA, the genetic material in all cells, to result in permanent alterations. Other chemical carcinogens modify DNA indirectly by changing the way cells grow. Carcinogens are chronically toxic substances; that is, they cause damage after repeated or



long-duration exposure, and their effects may become evident only after a long latency period. Carcinogens are particularly insidious toxins because they may have no immediate apparent harmful effects.

FLAMMABLE, REACTIVE, AND EXPLOSIVE HAZARDS

In addition to the hazards due to the toxic effects of chemicals, hazards due to flammability, explosivity, and reactivity need to be considered in risk assessment. Reactive hazards arise when the release of energy from a chemical reaction occurs in quantities or at rates too great for the energy to be absorbed by the immediate environment of the reacting system, and material damage results. The following outline provides a summary of the steps that laboratory personnel should use to assess the risks of managing physical hazards in the laboratory.

1. Identify chemicals to be used and circumstances of use.
2. Consult sources of information. Consult an up-to-date laboratory chemical safety summary, material safety data sheet, or NIOSH *Pocket Guide to Chemical Hazards* (HHS/CDC/NIOSH, 2007).
3. Evaluate type of physical, flammable, explosive, or reactive hazard(s) posed by the chemicals.
4. Evaluate the hazards posed by chemical changes over the course of the experiment.
5. Evaluate type of physical hazard(s) posed by the equipment required.
6. Select appropriate procedures to minimize risk.
7. Prepare for contingencies. Be aware of institutional procedures in the event of emergencies and accidents.

FLAMMABLE HAZARDS

Flammable substances, those that readily catch fire and burn in air may be solid, liquid, or gaseous. The most common fire hazard in the laboratory is a flammable liquid or the vapor produced from such a liquid. An additional hazard is that compounds can enflame so rapidly that it produces an explosion. Proper use of substances that cause fire requires knowledge of their tendencies to vaporize, ignite, or burn under the variety of conditions in the laboratory.

FLAMMABILITY CHARACTERISTICS

FLASH POINT

The flash point is the lowest temperature at which a liquid has a sufficient vapor pressure to form an ignitable mixture with air near the surface of the liquid. Note that many common

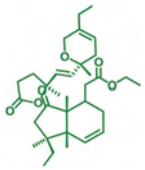
organic liquids have a flash point below room temperature: for example, acetone (-18°C), benzene (-11.1°C), diethyl ether (-45°C), and methyl alcohol (11.1°C). The degree of hazard associated with a flammable liquid also depends on other properties, such as its ignition point and boiling point. At ambient pressure and temperature, an acetone spill produces a concentration as high as 23.7% acetone in air. Although it is not particularly toxic, with a flash point of -18°C and upper and lower flammable limits of 2.6% and 12.8% acetone in air, respectively clearly an acetone spill produces an extreme fire hazard.

NFPA Fire Hazard Ratings, Flash Points (FP), Boiling Points (bp), Ignition Temperatures, and Flammable Limits of Some Common Laboratory Chemicals

	NFPA Flammability Ratinga	Flash Point (°C)	Boiling Point (°C)	Ignition Temperature (°C)	Flammable Limits (% by volume)	
					Lower	Upper
Acetaldehyde	4	-39	21	175	4	60
Acetic acid (glacial)	2	39	118	463	4	19.9
Acetone	3	-20	56	465	2.5	12.8
Acetonitrile	3	6	82	524	3	16
Carbon disulfide	4	-30	46	90	1.3	50
Cyclohexane	3	-20	82	245	1.3	8
Diethylamine	3	-23	57	312	1.8	10.1
Diethyl ether	4	-45	35	180	1.9	36
Dimethyl sulfoxide	2	95	189	215	2.6	42
Ethyl alcohol	3	13	78	363	3.3	19
Heptane	3	-4	98	204	1.05	6.7
Hexane	3	-22	69	225	1.1	7.5
Hydrogen	4		-252	500	4	75
Isopropyl alcohol	3	12	83	399	2	12.7 @ 200 (93)
Methyl alcohol	3	11	64	464	6	36
Methyl ethyl ketone	3	-9	80	404	1.4 @ 200 (93)	11.4 @ 200 (93)
Pentane	4	<-40	36	260	1.5	7.8
Styrene	3	31	146	490	0.9	6.8
Tetrahydrofuran	3	-14	66	321	2	11.8
Toluene	3	4	111	480	1.1	7.1
p-Xylene	3	25	138	528	1.1	7

[a] 0, will not burn under typical fire conditions; 1, must be preheated to burn, liquids with FP e" 93.4°C (200°F); 2, ignitable when moderately heated, liquids with FP between 37.8°C (100°F) and 93.4°C (200 °F); 3, ignitable at ambient temperature, liquids with FP < 22.8°C (73 °F), bp e" 37.8 °C (100°F) or FP between 22.8°C and 37.8°C (100°F); 4, extremely flammable, readily dispersed in air, and burns readily, liquids with FP < 22.8°C (73°F), bp < 37.8°C (100°F).

SOURCE: Adapted with permission from Fire Guide to Hazardous Materials (13th Edition), Copyright © 2001, National Fire Protection Association.



IGNITION TEMPERATURE

The ignition temperature (autoignition temperature) of a substance, whether solid, liquid, or gaseous, is the minimum temperature required to initiate or cause self-sustained combustion independent of the heat source. The lower the ignition temperature, the greater the potential for a fire started by typical laboratory equipment. For instance, carbon disulfide has an ignition temperature of 90°C, and it can be set off by a steam line or a glowing light bulb. Diethyl ether has an ignition temperature of 160°C and can be ignited by a hot plate.

REACTIVE HAZARDS

WATER REACTIVES

Water-reactive materials are those that react violently with water. Alkali metals (e.g., lithium, sodium, and potassium), many organometallic compounds, and some hydrides react with water to produce heat and flammable hydrogen gas, which ignites or combines explosively with atmospheric oxygen. Some anhydrous metal halides (e.g., aluminum bromide), oxides (e.g., calcium oxide), and nonmetal oxides (e.g., sulfur trioxide), and halides (e.g., phosphorus pentachloride) react exothermically with water, resulting in a violent reaction if there is insufficient coolant water to dissipate the heat produced.

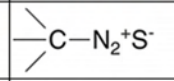
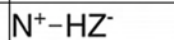
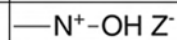
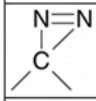
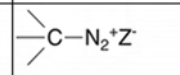
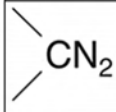
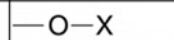
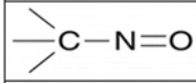
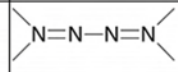
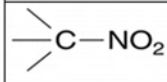
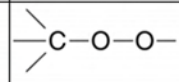
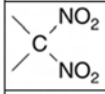
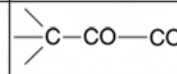
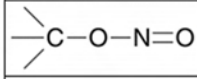
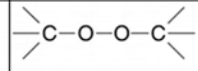
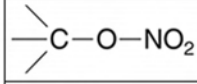
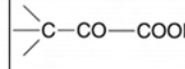
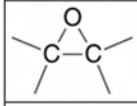
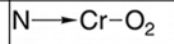
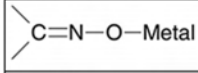
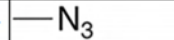
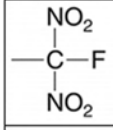
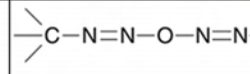
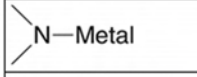
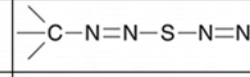
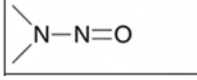
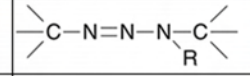
PYROPHORICS

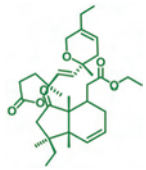
For pyrophoric materials, oxidation of the compound by oxygen or moisture in air proceeds so rapidly that ignition occurs. Many finely divided metals are pyrophoric, and their degree of reactivity depends on particle size, as well as factors such as the presence of moisture and the thermodynamics of metal oxide or metal nitride formation. Other reducing agents, such as metal hydrides, alloys of reactive metals, low-valent metal salts, and iron sulfides, are also pyrophoric.

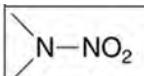
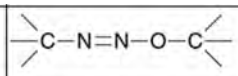
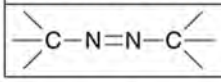
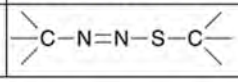
EXPLOSIVE HAZARDS

An explosive is any chemical compound or mechanical mixture that, when subjected to heat, impact, friction, detonation, or other suitable initiation, undergoes rapid chemical change, evolving large volumes of gases that exert pressure on the surrounding medium. Hydrogen and chlorine react explosively in the presence of light. Acids, bases, and other substances catalyze the explosive polymerization of acrolein, and many metal ions can catalyze the violent decomposition of hydrogen peroxide. Shock-sensitive materials include acetylides, azides, nitrogen triiodide, organic nitrates, nitro compounds, perchlorate salts (especially those of heavy metals such as ruthenium and osmium), many organic peroxides, and compounds containing diazo, halamine, nitroso, and ozonide functional groups. The following table lists a number of explosive compounds. Some are set off by the action of a metal spatula on the solid; some are so sensitive that they are set off by the action of their own crystal formation. Diazomethane (CH_2N_2) and organic azides, for example, may decompose explosively when exposed to a ground glass joint or other sharp surfaces.

FUNCTIONAL GROUPS IN SOME EXPLOSIVE COMPOUNDS

Structural Feature	Compound	Structural Feature	Compound
	Acetylenic compounds		Diazoniumsulfides and derivatives, "xanthates"
	Metal acetylides		Hydrazinium salts, oxosalts of nitrogenous bases
	Haloacetylene derivatives		Hydroxylammonium salts
	Diazirines		Diazonium carboxylates or salts
	Diazo compounds		Alkyl perchlorates, chlorite salts, halogen oxides, hypohalites, perchloric acid, perchloryl compounds
	Nitroso compounds		High-nitrogen compounds, tetrazoles
	Nitroalkanes, *C*-nitro and polynitroaryl compounds		Alkylhydroperoxides
	Polynitroalkyl compounds		Peroxyacids
	Acyl or alkyl nitrites		Peroxides (cyclic, diacyl, dialkyl)
	Acyl or alkyl nitrates		Peroxyesters
	1,2-Epoxides		Aminechromium peroxocomplexes
	Metal fulminates or aci-nitro salts		Azides (acyl, halogen, nonmetal, organic)
	Fluorodinitromethyl compounds		Bis-arenediazo oxides
	N-Metal derivatives		Bis-arenediazo sulfides
	N-Nitroso compounds		Trizazenes (R = H, —CN, -OH, —NO)



	N-Nitro compounds		Arenediazoates
Structural Feature	**Compound**	**Structural Feature**	**Compound**
	Azo compounds		Arenediazo aryl sulfides

SOURCE: Carson and Mumford (2002). Reprinted from *Hazardous Chemicals Handbook* (Second Edition), Carson, P. and Mumford, C. "Reactive Chemicals", p. 228, Copyright 2002, with permission from Elsevier.

AZOS, PEROXIDES, AND PEROXIDIZABLES

Organic azo compounds and peroxides are among the most hazardous substances handled in the chemical laboratory but are also common reagents that often are used as free radical sources and oxidants. They are generally low-power explosives that are sensitive to shock, sparks, or other accidental ignition. They are far more shock sensitive than most primary explosives such as TNT. Inventories of these chemicals should be limited and subject to routine inspection. Liquids or solutions of these compounds should not be cooled to the point at which the material freezes or crystallizes from solution, however, because this significantly increases the risk of explosion. Refrigerators and freezers storing such compounds should have a backup power supply in the event of electricity loss. Users should be familiar with the hazards of these materials and trained in their proper handling. Certain common laboratory chemicals form peroxides on exposure to oxygen in air (see the following table). Over time, some chemicals continue to build peroxides to potentially dangerous levels, whereas others accumulate a relatively low equilibrium concentration of peroxide, which becomes dangerous only after being concentrated by evaporation or distillation.

CLASSES OF CHEMICALS THAT CAN FORM PEROXIDES

Class A: Chemicals that form explosive levels of peroxides without concentration	
Isopropyl ether	Sodium amide (sodamide)
Butadiene	Tetrafluoroethylene
Chlorobutadiene (chloroprene)	Divinyl acetylene
Potassium amide	Vinylidene chloride
Potassium metal	

Class B: These chemicals are a peroxide hazard on concentration (distillation/evaporation). A test for peroxide should be performed if concentration is intended or suspected.	
Acetal	Dioxane (*p*-dioxane)
Cumene	Ethylene glycol dimethyl
Cyclohexene	ether (glyme)
Cyclooctene	Furan
Cyclopentene	Methyl acetylene

Diaacetylene	Methyl cyclopentane
Dicyclopentadiene	Methyl-isobutyl ketone
Diethylene glycol dimethyl	Tetrahydrofuran
ether (diglyme)	Tetrahydronaphthalene
Diethyl ether	Vinyl ethers

Class C: Unsaturated monomers that may autopolymerize as a result of peroxide accumulation if inhibitors have been removed or are depleted

Acrylic acid	Styrene
Butadiene	Vinyl acetate
Chlorotrifluoroethylene	Vinyl chloride
Ethyl acrylate	Vinyl pyridine
Methyl methacrylate	

* These lists are illustrative, not comprehensive. SOURCES: Jackson et al., (1970) and Kelly (1996).

Essentially all compounds containing C—H bonds pose the risk of peroxide formation if contaminated with various radical initiators, photosensitizers, or catalysts. For instance, secondary alcohols such as isopropanol form peroxides when exposed to normal fluorescent lighting and contaminated with photosensitizers, such as benzophenone. Acetaldehyde, under normal conditions, autoxidizes to form acetic acid.

PHYSICAL HAZARDS

COMPRESSED GASES

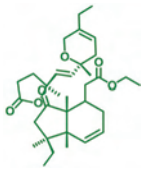
Compressed gases can expose the trained laboratory personnel to both mechanical and chemical hazards, depending on the gas. Hazards can result from the flammability, reactivity, or toxicity of the gas; from the possibility of asphyxiation; and from the gas compression itself, which could lead to a rupture of the tank or valve.

NONFLAMMABLE CRYOGENS

Nonflammable cryogens (chiefly liquid nitrogen) can cause tissue damage from extreme cold because of contact with either liquid or boil-off gases. In poorly ventilated areas, inhalation of gas due to boil off or spills can result in asphyxiation. Another hazard is explosion from liquid oxygen condensation in vacuum traps or from ice plug formation or lack of functioning vent valves in storage Dewars. Because 1 volume of liquid nitrogen at atmospheric pressure vaporizes to 694 volumes of nitrogen gas at 20 °C, the warming of such a cryogenic liquid in a sealed container produces enormous pressure, which can rupture the vessel.

HIGH-PRESSURE REACTIONS

Experiments that generate high pressures or are carried out at pressures above 1 atm can lead to explosion from equipment failure. For example, hydrogenation reactions are



frequently carried out at elevated pressures, potential hazard is formation of explosive O_2/H_2 mixtures and reactivity/pyrophoricity of catalyst. High pressures can also be associated with the use of supercritical fluids.

VACUUM WORK

Precautions to be taken when working with vacuum lines and other glassware used at sub-ambient pressure are mainly concerned with the substantial danger of injury in the event of glass breakage. The degree of hazard does not depend significantly on the magnitude of the vacuum because the external pressure leading to implosion is always 1 atmosphere. Thus, evacuated systems using aspirators merit as much respect as high-vacuum systems. Injury due to flying glass is not the only hazard in vacuum work. Additional dangers can result from possible toxicity of chemicals contained in vacuum system, and from fire following breakage of a flask (solvent stored over sodium or potassium).

ULTRAVIOLET, VISIBLE, AND NEAR-INFRARED RADIATION

Ultraviolet, visible, and infrared radiation from lamps and lasers in the laboratory can produce a number of hazards. Medium-pressure Hanovia 450 Hg lamps are commonly used for ultraviolet irradiation in photochemical experiments. Ultraviolet lights used in biosafety cabinets, as decontamination devices, or in light boxes to visualize DNA can cause serious skin and corneal burns. Powerful arc lamps can cause eye damage and blindness within seconds. When incorrectly used, the light from lasers poses a hazard to the eyes of the operators and other people present in the room and is also a potential fire hazard. Depending on the type of laser, the associated hazards can include mutagenic, carcinogenic, or otherwise toxic laser dyes and solvents; flammable solvents; ultraviolet or visible radiation from the pump lamps; and electric shock from lamp power supplies.

ELECTRICAL HAZARDS

The electrocution hazards of electrically powered instruments, tools, and other equipment are almost eliminated by taking reasonable precautions, and the presence of electrically powered equipment in the laboratory need not pose a significant risk. But, in the laboratory these safety features should not be defeated by thoughtless or ill-informed modification. Equipment malfunctions can lead to electrical fires. Some special concerns arise in laboratory settings. The insulation on wires can be eroded by corrosive chemicals, organic solvent vapors, or ozone (from ultraviolet lights, copying machines, and so forth). Eroded insulation on electrical equipment in wet locations such as cold rooms or cooling baths must be repaired immediately.

MAGNETIC FIELDS

Increasingly, instruments that generate large static magnetic fields (NMR spectrometers)

are present in research labs. Such magnets typically have fields of 14,000 to 235,000 G (1.4 to 23.5 T), far above that of Earth's magnetic field, which is approximately 0.5 G. The magnitude of these large static magnetic fields falls off rapidly with distance. Many instruments now have internal shielding, which reduces the strength of the magnetic field outside of the instrument. Strong attraction occurs when the magnetic field is greater than 50 to 100 G and increases by seventh power as the separation is reduced.

ERGONOMIC HAZARDS IN THE LABORATORY

General workplace hazards also apply in the laboratory. For example, laboratory personnel are often involved in actions such as pipetting and computer work that can result in repetitive-motion injuries. Working at a bench or at a microscope without considering posture can result in back strain, and some instruments require additional in-room ventilation that may raise the background noise level to uncomfortable or hazardous levels. With these and other issues such as high or low room temperatures and exposure to vibrations, it is important to be aware of and to control such issues to reduce occupational injuries. For example, microscope users may find that using a camera to view images on a screen, rather than direct viewing through the eyepiece, reduces back and eye strain. The Centers for Disease Control and Prevention (CDC) and the National Institutes of Health have information on their Web sites (www.cdc.gov and www.nih.gov, respectively) describing specific ergonomic concerns for laboratories and proposed solutions. The CDC provides a downloadable self-assessment form to aid in evaluating these hazards. NIOSH (www.cdc.gov/niosh) and OSHA (www.osha.gov) provide information about vibration, noise levels, and other workplace hazards.

BIOHAZARDS

Biohazards are a concern in laboratories in which microorganisms, or material contaminated with them, are handled. Anyone who is likely to come in contact with blood or potentially infectious materials at work is covered under OSHA's Bloodborne Pathogen Standard. These hazards are usually present in clinical and infectious disease research laboratories but may also be present in any laboratory in which bodily fluids, tissues, or primary or immortalized cell lines of human or animal origin are handled. Biohazards are also present in any laboratory that uses microorganisms, including replication-deficient viral vectors, for protein expression or other *in vitro* applications. Risk assessment for biological toxins is similar to that for chemical agents and is based primarily on the potency of the toxin, the amount used, and the procedures in which the toxin is used.

SUGGESTED READINGS

OSHA Hazard Communication Standard 1910.1200
Dedicated website: http://www.unece.org
IPCS. 2009. International Chemical Safety Cards from the International Programme on Chemical Safety.
Dedicated website: www.cdc.gov/niosh
Dedicated website: www.ilo.org
NIOSH Pocket Guide to Chemical Hazards (HHS/ CDC/NIOSH, 2007
Dedicated website: http://www.cdc.gov/niosh
Patnaik. 2007. A Comprehensive Guide to the Hazardous Properties of Chemical Substances, 3rd ed.
Hazardous Chemicals Handbook, 2nd edition (Carson and Mumford, 2002
NIOSH Databases and Information Resources (www.cdc.gov/niosh
TOXNET through the National Library of Medicine (NLM; Dedicated website: www.nlm.nih.gov
Dedicated website: www.cas.org
NIOSH Pocket Guide to Chemical Hazards (HHS/CDC/NIOSH, 2007
Dedicated website: www.cdc.gov
Dedicated website: www.nih.gov
Dedicated website: www.cdc.gov/niosh
Dedicated website: www.osha.gov

Inauguration of winter school 2018 by Padma Bhushan Dr. Manju Sharma

Photo with Dr. K. Gopakumar, Formerly DDG ICAR (Fy)

Field visit to India Sea Foods

Field visit to BOS Naturals

Field visit to Accelerated Freeze Drying Co. Ltd

Photo with Dr. Meledath Govindan

Lectures and Interactive Sessions

Practical Sessions


ICAR-CENTRAL MARINE FISHERIES RESEARCH INSTITUTE
Ernakulam North P.O., Kochi-682018, Kerala
ICAR Sponsored Winter School on Recent Advances in Bioactive Compounds from Marine Organisms and Development of High Value Products for Health Management
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Central Marine Fisheries Research Institute
കേന്ദ്ര സമുദ്ര മത്സ്യ ഗവേഷണ സ്ഥാപനം
WELCOME
Sitting (L to R) Minimol K.C., Grace Thomas, Kajal Chakraborty (Course Director), P. Vijayagopal (Head, Marine Biotechnology Division), A. Gopalakrishnan (Director), Paulson Mathew, Sathu T., Radhakrishnan E.K.
Standing (L to R) Aswathy Elizabeth Mani, Sreemol C.K., Prima Francis, Soumya Krishnan, Minju Joy, V. Rani, Seeja Thomachan Panjikkaran, Sheneya Festus, Drishya K., Anie Y., Suja Rani S., Sindhu Issac, Teena P. Varghese, Magna Thomas, Santwana Palai, Norma Xavier Chelat, Naheef K., Satya Narayan Sahoo, Jaimin Hareshbhai Bhatt, Ajoy Saha, Senthil Kuppusamy, Kedar Shashikant Damle, Shubhajit Dhara, Midhun Dominic C.D., Manukuttan K.S., Suji Chandru, Tima Antony, Soumya Salas

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