ILLUSTRATED TOXICOLOGY

WITH STUDY QUESTIONS

PK GUPTA

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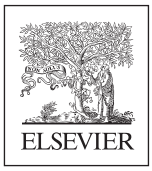

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Preface

The book *Illustrative Toxicology, With Study Questions* is aimed to make the study of toxicology simple and understandable through illustrations, images, custom-made drawings, self-explanatory tables, and questions and answers collated from standard and authoritative textbooks which are widely scanned. Author's own experience in different branches of toxicology including environmental and veterinary toxicology is also abstracted in this book. The book is written in a manner to stimulate interest on various facets of the subject and make it more exciting. It is a general experience that theoretical descriptions do not attract as much attention and interest as illustrations and images do. At the same time the information learnt through questions and their satisfactory answers makes the topics easier to grasp.

This book serves as a comprehensive and quick reference for various examinations. However, it should be noted that this book serves only as a supplement and not as a replacement for any textbook and classroom learning.

The book has 17 chapters that cover several topics such as general toxicology, principles of toxicology, risk assessment, disposition, mechanism of toxicity, toxic effects of various xenobiotics, poisonings of poisonous and venomous organisms, plant toxins, poisonous and food poisonings, radiation hazards, and abuse of drugs. It also deals with the adverse effects on environment and ecosystem exposed to various toxicants and poisonings as relevant to domestic and other animals. One chapter is exclusively devoted to clinical toxicology, principles of diagnosis, followed by general management of poisoning of the patients including methods of removal of poisons from the body and treatment of poisoning. Finally, a chapter deals with brainstorming questions that will be helpful as a review for students so that they understand the concepts delivered.

Each chapter is in the format of questions and answers, data interpretation, multiple choice questions, true/false or correct/incorrect statements, fill in the blanks, and matching the statements. It is a unique book in toxicology having more than 31 self-explanatory tables, 237 custom-made illustrations and images, and about 3400 questions and answers. It is equally useful for students and teachers practicing in medical sciences, toxicology, pharmacology, medicine, pharmacy, environmental toxicology, and veterinary sciences. Therefore, I believe that this book would serve the students, academic institutions and industry as follows:

- It is a good alternative to be used for various courses and an excellent contribution for the students who need a study aid for toxicology but want more than a textbook as they need a self-testing regime.
- It will be a useful tool for the teachers of toxicology who need inspiration when composing questions for their students.

- It will also help the established toxicologists to test their own knowledge of understanding the subject matter.
- It will be useful at universities and colleges and in industry for in-house training courses in toxicology, which I know exist in some pharmaceutical and chemical companies.
- It is required for those studying for the toxicology boards and other examinations.

Thus, the main strength of this book is that it reflects the breadth and multi-disciplinary nature of toxicology with illustrative approach to the subject needed to improve the engagement with and understanding of the subject having a very wide audience.

Toxicology is a rapidly evolving field. Suggestions and comments are welcome to help the author improve the contents of the book. Please also suggest the deficiencies need to be covered at drpkg_brly@yahoo.co.in or drpkg1943@gmail.com if you have any topics you feel should be better covered in any future editions.

PK Gupta

CHAPTER

General toxicology

1

CHAPTER OUTLINE

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1.1 DEFINITIONS AND SUBDISCIPLINES OF TOXICOLOGY

Q. Definition

The traditional definition of toxicology is "the science of poisons." As our understanding of how various agents can cause harm to humans and other organisms, a more descriptive definition of toxicology is "the study of the adverse effects of chemicals or physical agents on living organisms."

Explanation: The word "toxicology" is derived from the Greek word "toxicon" which means "poison" and logos means to study. It also includes study of special effects of toxicants developmental toxicity, teratogenicity, carcinogenicity, mutagenesis, immune-toxicity, neurotoxicity, endocrine disruption, etc. Adverse effects may occur in many forms, ranging from immediate death to subtle changes not realized until months or years later. They may occur at various levels within the body, such as an organ, a type of cell, or a specific biochemical. Knowledge of how toxic agents damage the body has progressed along with medical knowledge. It is now known that various observable changes in anatomy or body functions actually result from previously unrecognized changes in specific biochemicals in the body.

Q. Define xenobiotics.

Xenobiotic: Xenobiotics (xeno is a Greek word which means "strange or alien") are the substances which are foreign to the body and are biologically active. These cannot be broken down to generate energy or be assimilated into a biosynthetic pathway. It is a very wide class and structurally adverse agents, both natural and synthetic chemicals such as drugs, industrial chemicals, pesticides, alkaloids, secondary plant metabolites and toxins of molds, plants and animals, and environmental pollutants.

Q. What are the subdisciplines of toxicology?

Biochemical toxicology
Reproductive toxicology
Development toxicology
Teratology
Genetic toxicology
Clinical toxicology
Forensic toxicology
Analytical toxicology
Nutritional toxicology
Veterinary toxicology
Environmental toxicology
Occupational (industrial) toxicology
Regulatory toxicology
Mechanistic toxicology
Aquatic toxicology
Ecotoxicology
Food toxicology

Formal toxicology

Descriptive toxicology.

Q. Define occupational (industrial) toxicology.

Occupational (industrial) toxicology is concerned with health effects from exposure to chemicals in the workplace. It deals with the clinical study of workers of industries and environment around them.

Q. Define regulatory toxicology.

It deals with administrative functions concerned with the development and interpretation of mandatory toxicology testing programs and controlling the use, distribution, and availability of chemicals used commercially and therapeutically. For example, Food and Drug Administration (FDA) regulates drugs, cosmetics, and food additives. Regulatory toxicology gathers and evaluates existing toxicological information to establish concentration-based standards of "safe" exposure. The standard is the level of a chemical that a person can be exposed to without any harmful health effects.

Q. Define regulation.

Regulation is the control, by statute, of the manufacture, transportation, sale, or disposal of chemicals deemed to be toxic after testing procedures or according to criteria laid down in applicable laws.

Q. Describe in brief requirements of the following regulations.

Brief requirements of selected regulations (question and answer format) in United States are summarized in Table 1.1.

Table 1.1 Requirements of Selected Regulations in the United States

Regulation Questions	Answers (Brief Requirements)
Under Clean Air Act, EPA requires	the registration of fuels and fuel additives. Part of the registration process includes in vivo fertility assessment/teratology testing (a rat is the preferred species for testing).
Under FIFRA, teratogenicity and reproduction studies require	two generation testing in two mammalian species (e.g., rat, mouse, rabbit, hamster).
Under TSCA (Toxic Substances Control Act), testing requirements for reproduction and fertility effects call for	the use of rats, although other mammalian species are acceptable with justification.
Specific guidelines for evaluation of developmental toxicity under the Federal Food, Drug, and Cosmetic Act (FFDCA) may vary depending on the Center but typically require	testing of rats and/or rabbits.
The Center for Food Safety and Applied Nutrition identifies testing for	reproductive and developmental toxicity under "Toxicological Principles for the Safety Assessment of Direct Food Additives and Color Additives Used in Food."

Q. Define food toxicology.

It deals with natural contaminants, food and feed additives, and toxic and chemoprotective effects of compounds in food.

Explanation: Food toxicology is involved in delivering a safe and edible supply of food to the consumer. During processing, a number of substances may be added to food to make it look, taste, or smell better. Fats, oils, sugars, starches, and other substances may be added to change the texture and taste of food.

All of these additives are studied to determine if and at what amount they may produce adverse effects. A second area of interest includes food allergies. Almost 30% of the American people have some food allergy. For example, many people have trouble digesting milk and are lactose intolerant. In addition, toxic substances such as pesticides may be applied to a food crop in the field, while lead, arsenic, and cadmium are naturally present in soil and water, and may be absorbed by plants. Toxicologists must determine the acceptable daily intake (ADI) level for those substances.

Q. Define formal toxicology.

It deals with the formal toxicological studies which are prerequisite for release of a new drugs/chemical, e.g., calculation of lethal dose-50 (LD_{50}) and minimum toxic dose.

Q. Define descriptive toxicology.

Descriptive toxicology is concerned with gathering toxicological information from animal experimentation. These types of experiments are used to establish how much of a chemical would cause illness or death. The US Environmental Protection Agency (EPA), the Occupational Safety and Health Administration (OSHA), and the Food and Drug Administration (FDA) use information from these studies to set regulatory exposure limits.

Q. Define mechanistic toxicology.

Mechanistic toxicology makes observations on how toxic substances cause their effects. The effects of exposure can depend on a number of factors, including the size of the molecule, the specific tissue type, or cellular components affected, whether the substance is easily dissolved in water or fatty tissues, all of which are important when trying to determine the way a toxic substance causes harm, and whether effects seen in animals can be expected in humans.

Q. Define nutritional toxicology.

Nutritional toxicology is the study of toxicological aspects of food/feed stuffs and nutritional products/habits.

Q. Define toxicodynamics.

It deals with the study of biochemical and physiological effects of toxicants and their mechanism of action.

Q. Define toxicokinetics.

It deals with the study of absorption, distribution, metabolism, and excretion of toxicants in the body.

Q. Define toxicovigilance.

It deals with the process of identification, investigation, and evaluation of various toxic effects in the community with a view of taking measures to reduce or control exposures involving the substances that produce these effects.

Q. Define toxinology.

It deals with assessing the toxicity of substances of plant and animal origin and those produced by pathogenic bacteria/organism.

Q. Define toxicoepidemiology.

It refers to the study of quantitative analysis of the toxicity incidences in organisms, factors affecting toxicity, species involved, and the use of such knowledge in planning of prevention and control strategies.

1.2 TYPES OF TOXICANTS

Q. Define poison.

Poison is derived from Latin "potus," a drink that could harm or kill. It is any substance which when taken inwardly in a very small dose or applied in any kind of manner to a living body depraves the health or entirely destroys life. Although the word toxicant has essentially the same medical meaning, there are psychological and legal implications involved in the use of the word poison that makes manufacturer reluctant to apply it to chemicals, particularly those intended for widespread use in large quantities, unless they are required to do so by law. The term toxicant is more acceptable to both manufacturer and legislators.

Q. Define toxicant.

Toxicant is synonym of poison, produced by living organism in small quantities and is generally classified as biotoxin. These may be phytotoxins (produced by plants), mycotoxins (produced by fungi), zootoxins (produced by lower animals), and bacteriotoxins (produced by bacteria).

Q. Define different types of toxins.

1. Endotoxins are found within bacterial cells.
2. Exotoxins: elaborated from bacterial cells.

Q. Define venom.

Venom is a toxicant synthesized in a specialized gland and ejected by the process of biting or stinging. Venom is also a zootoxin but is transmitted by the process of biting or stinging.

Q. Define pollutant.

It is any undesirable substance to solid, liquid, or gaseous matter resulting from the discharge or admixture of noxious materials that contaminate the environment and contributes to pollution.

Q. Define systemic toxicant.

It is a toxicant that affects the entire body or many organs rather than a specific site. For example, potassium cyanide is a systemic toxicant that affects virtually every cell and organ in the body by interfering with the cell's ability to utilize oxygen.

Q. Define organ toxicant.

It is toxicant that affects only specific organs or tissues (may be called tissue toxicant) while not producing damage to the body as a whole. For example, benzene is a specific organ toxicant in that it is primarily toxic to the blood-forming tissues.

1.3 TOXICITY AND TOXIC EFFECTS

Toxic and toxicity are relative terms commonly used in comparing one chemical with another.

Q. Define toxicity.

It is a state of being poisonous or capacity to cause injury to living organisms.

Q. Define toxicosis.

It is the condition or disease state that results from exposure to a toxicant. The term toxicosis is often used interchangeably with the term poisoning or intoxication.

Q. Define toxic effects.

These are undesirable effects produced by a toxicant/drug which are detrimental to either survival or normal functioning of the individual.

Q. Define side effects.

These are undesirable effects which result from the normal pharmacological actions of drugs. These results may not be detrimental or harmful to the individual.

Q. Define selective toxicity.

It is the toxicity produced by a chemical to one kind of living matter without harming another form of life even though the two exist in intimate contact.

Q. Define plant toxins.

Different portions of a plant may contain different concentrations of chemicals. Some chemicals made by plants can be lethal. For example, taxon, used in chemotherapy to kill cancer cells, is produced by a species of the yew plant.

Q. Define animal toxins.

Animal toxins can result from venomous or poisonous animal releases. Venomous animals are usually defined as those that are capable of producing a poison in a highly developed gland or group of cells, and can deliver that

toxin through biting or stinging. Poisonous animals are generally regarded as those whose tissues, either in part or in their whole, are toxic. For example, venomous animals, such as snakes and spiders, and poisonous animals, such as puffer fish, or oysters may be toxic to some individuals when contaminated with *Vibrio vulnificus*.

1.3.1 TOXICITY IN RELATION TO FREQUENCY AND DURATION OF EXPOSURE

The exposure of experimental animals to chemicals can be divided into four categories: acute toxicity and repeated exposure (subacute, subchronic, and chronic).

Q. Define acute toxicity.

Acute toxicity is defined as an exposure to a chemical for less than 24 hours. The exposure usually refers to a single administration; repeated exposures may be given within a 24-hour period for some slightly toxic or practically nontoxic chemicals. Acute exposure by inhalation refers to continuous exposure for less than 24 hours, most frequently for 4 hours.

Q. Define repeated exposure.

Repeated exposure is divided into three categories:
(1) subacute, (2) subchronic, and (3) chronic.

subacute exposure to a chemical is for 1 month or less, subchronic for 1−3 months, and chronic for more than 3 months (usually this refers to studies with at least 1 year of repeated dosing).

Explanation: Acute or repeated exposure can be by any route, but most often they occur by the oral route, with the chemical added directly to the diet. In human exposure situations, the frequency and duration of exposure are usually not as clearly defined as in controlled animal studies. However, almost same terms are used to describe general exposure situations. Thus, workplace or environmental exposures may be described as acute (occurring from a single incident or episode), subchronic (occurring repeatedly over several weeks or months), or chronic (occurring repeatedly for many months or years).

1.3.2 TOXICITY IN RELATION TO TIME OF DEVELOPMENT AND DURATION OF INDUCED EFFECTS

Q. Define transient or reversible or temporary toxicity.

It is the toxicity or harmful effect that remains for short duration of time, e.g., narcosis produced organic solvents.

Q. Define persistent or permanent or irreversible toxicity.

It is the toxicity or harmful effect that persists throughout the life span of the individual and is of permanent nature, e.g., scarring of skin produced by corrosives.

Q. Define immediate toxicity.

It is the toxicity that develops shortly after a single exposure to a toxicant, e.g., cyanide poisoning.

Q. Define delayed toxicity.

It is the toxicity or harmful effect which has delayed onset of action, e.g., peripheral neuropathy produced by some organophosphorus (OP) insecticides and radiation sickness.

Q. Define cumulative toxicity.

It is a progressive toxicity or harmful effect produced by summation of incremental injury resulting from successive exposures, e.g., liver fibrosis produced by ethanol.

Q. Accumulative effects occur in two ways:

1. Accumulation of toxin: exposure to heavy metals (lead, mercury) that have long half-lives result in disease due to metal accumulation.
2. Accumulation of effect: low-level exposure to organophosphate pesticides depresses acetylcholine esterase to a point where symptoms occur.

1.4 OTHER TERMS USED IN TOXICOLOGY

Q. Define cheminformatics.

Cheminformatics (also known as chemoinformatics, chemioinformatics, and chemical informatics) is the use of computer and informational techniques applied to a range of problems in the field of chemistry. These in silico techniques are used in, for example, pharmaceutical companies in the process of drug discovery.

Q. Define end point study record.

End point study record or IUCLID (International Uniform Chemical Information Database) format of the technical dossier is used to report study summaries and robust study summaries of the information derived for the specific end point according to the REACH regulation.

Q. Define end point of study design.

End point: an observable or measurable inherent property/data point of a chemical substance. For example, a physical–chemical property like vapor pressure or degradability or a biological effect that a given substance has on human health or the environment, e.g., carcinogenicity, irritation, and aquatic toxicity.

Q. Define in vitro test.

In vitro test: literally stands for “in glass” or “in tube,” refers to the test taking place outside of the body of an organism, usually involving isolated organs, tissues, cells, or biochemical systems.

Q. Define in vivo test.

In vivo test: a test conducted within a living organism.

Q. Define in silico test.

In silico: in silico (a phrase coined as an analogy to the familiar phrases in vivo and in vitro) is an expression used to denote "performed on computer or via computer simulation." It means scientific experiments or research conducted or produced by means of computer modeling or computer simulation.

Q. Define IUCLID flag.

IUCLID flag: an option used in the IUCLID software to indicate submitted data type (e.g., experimental data) or its use for regulatory purposes (e.g., confidentiality).

Q. Define prediction model.

Prediction model is a theoretical formula, algorithm, or program used to convert the experimental results obtained by using a test method into a prediction of the toxic property/effect of the chemical substance.

Q. Define Quantitative structure−activity relationship (QSARs) and Structure−activity relationship (SARs).

QSARs and SARs: theoretical models that can be used to predict in a quantitative or qualitative manner the physical, chemical, biological (e.g., (eco)toxicological), and environmental fate properties of compounds from knowledge of their chemical structure. A SAR is a qualitative relationship that relates a (sub)structure to the presence or absence of a property or activity of interest. A QSAR is a mathematical model relating one or more quantitative parameters, which are derived from the chemical structure, to a quantitative measure of a property or activity.

Q. Define test or assay, validation test, and validation.

Test (or assay): an experimental system set up to obtain information on the intrinsic properties or adverse effects of a chemical substance.

Validation test: a test for which its performance characteristics, advantages, and limitations have been adequately determined for a specific purpose.

Validation: the process by which the reliability and relevance of a test method are evaluated for the purpose of supporting a specific use.

Q. Define vertebrate animal.

Animals that belong to subphylum Vertebrata; chordate with backbones and spinal columns is known as a vertebrate animal.

Q. Define accidental poisoning.

Accidental poisoning may occur when human beings or animals take toxicant accidentally or is added unintentionally in food or through in its feed, fodder, or drinking water. Such toxicants come from either natural or man-made sources. The natural sources include ingestion of toxic plants, biting or stinging by poisonous reptiles, ingestion of food contaminated with toxins, and contaminated water with minerals. Man-made sources include therapeutic agents, household products, and agrochemicals.

Q. Define malicious poisoning.

It is the unlawful or criminal killing of human beings or animals by administering certain toxic/poisonous agents. Incidence of such poisonings is more prevalent in human beings and less in animals.

Q. What is REACH regulation?

REACH regulation is concerned with registration, evaluation, authorization, and restriction of chemicals in European Union (EU). It entered into force on June 1, 2007. It streamlines and improves the former legislative framework on chemicals of the EU.

1.5 CLASSIFICATION OF TOXIC AGENTS

Toxic agents are classified in number of ways depending on the interests and needs of the classifier. There is no single classification applicable for the entire spectrum of toxic agents and hence combinations of classification systems based on several factors may provide the best rating system. Classification of poisons may take into account both the chemical and biological properties of the agent; however, exposure characteristics are also useful in toxicology.

Q. Classify toxic agents.

In toxicology, compounds are classified in various ways, by one or more of the following classes:

1. Use, e.g., pesticides (atrazine), solvents (benzene), food additives (NutraSweet), metals, and war gases
2. Effects, e.g., carcinogen (benzo[a]pyrene), mutagen (methylnitrosamine), and hepatotoxicant ($CHCl_3$).
3. Physical state such as oxidant (ozone), gas (CO_2), dust (Fe_2O_3), and liquid (H_2O).
4. Chemistry such as aromatic amine (aniline) and halogenated hydrocarbon (methylene chloride).
5. Sources of toxicants, e.g., plant or animal or natural.
6. Mechanism of action: cholinesterase inhibitor (malathion), methemoglobin producer (nitrite), etc.

Q. Classification based on sources of toxicants

1. Plant toxins
2. Animal toxicants
3. Mineral toxicants
4. Synthetic toxicants
5. Physical or mechanical agents.

Q. Classification based on physical state of toxicants

1. Gaseous toxicants
2. Liquid toxicants
3. Solid toxicants
4. Dust toxicants.

Q. Classification based on target organ or system
1. Neurotoxicants
2. Hepatotoxicants
3. Nephrotoxicants
4. Pulmotoxicants
5. Hematotoxicants
6. Dermatotoxicants
7. Development and reproductive toxicants.

Q. Classification based on chemical nature/structure of toxicants
1. Metals
2. Nonmetals
3. Acids and alkalis
4. Organic toxicants (carbon compounds other than oxides of carbon, the carbonates, and metallic carbides and cyanides).

Q. Classification based on analytical behavior of toxicants
1. Volatile toxicants
2. Extractive toxicants
3. Metals and metalloids.

Q. Classification based on type of toxicity
1. Acute
2. Subacute
3. Chronic.

Q. Classification based on toxic effects
1. Carcinogens
2. Mutagens
3. Teratogens
4. Clastogens.

Q. Classification based on their uses
1. Insecticides
2. Fungicides
3. Herbicides
4. Rodenticides
5. Food additives, etc.

Q. Classification based on symptoms produced
1. Corrosive poisons
2. Irritant poisons
3. Systemic poisons
4. Miscellaneous poisons.

In addition, there are other types of classifications that are based on the environmental and public health considerations and so on.

Q. Summarize examples of some poisons (caustics) based on symptoms produced.

Examples: corrosive poisons (Table 1.2), irritant poisons (Table 1.3), systemic poisons (Table 1.4), and miscellaneous poisons (Table 1.5).

Table 1.2 Corrosive Poisons

Strong Acids		Strong Alkalis	
Inorganic or mineral acids	**Organic acids**	**Hydrates of**	**Carbonates of**
Sulfuric acid Nitric acid	Carbolic acid Oxalic acid Hydrochloric acid	Sodium Sodium	Potassium Potassium

Table 1.3 Irritant Poisons

Inorganic	Organic	Mechanical
Nonmetallic: phosphorus, halogens Metallic: arsenic, mercury, lead, copper, etc.	Vegetable: *Abrus*, castor, croton, calatropia, ergot, etc. Animal: snake or insect bites and stings	Diamond dust, glass powder, hair, nails, pins, etc.

Table 1.4 Systemic Poisons

CNS (Neurotoxins)	Cardiovascular	Lungs (Asphyxiants)
Central somniferous – Opium – Pethidine Inebriants – Alcohols, anesthetics – Sedative hypnotics – Insecticides (hydrocarbons) – Benzodiazepines, etc. Delirients – Datura – Cannabis – Cocaine, etc. Spinal Strychnine, gelsemium, etc. Peripheral Curare, conium, etc.	Oleanders, aconite, nicotine	Carbon monoxide, carbon dioxide, irrespirable gas, cyanogens gas, cyanides

Table 1.5 Miscellaneous Poisons

Domestic poisons	Insecticides (aluminum phosphide, rat kill), kerosene, diesel, petrol, cleaning agents, soaps, detergents, disinfectants, cosmetics, etc.
Therapeutic substance	Salicylates, paracetamol, antidepressants, sedatives, antipsychotics, insulin, etc.
Food poisons	Bacterial, viral, mushrooms, chemicals, etc.
Drugs of dependence	Alcohol, tobacco, hypnotics, hallucinogens, stimulants, organic solvents, etc.

1.6 TOXICITY RATING

Q. Describe briefly the term "toxicity rating."

A system of "toxicity rating" has been evolved for common poisons. The higher the toxicity rating for a particular substance (over a range of 1–6), the greater is the potency. The toxicity rating based on toxic potential of substances (super toxic, extremely toxic, very toxic, moderately toxic, slightly toxic, and practically nontoxic) is summarized in Table 1.6.

Table 1.6 Toxicity Rating

Toxicity Rating or Class	Probable LD (Human)	
	mg/kg	For 70 kg man
6 (Super toxic)	Less than 5 mg/kg	A few drops
5 (Extremely toxic)	5–50 mg/kg	"A pinch" to one teaspoonful
4 (Very toxic)	51–500 mg/kg	One tea spoonful to two table spoonful
3 (Moderately toxic)	501 mg/kg to 5 g/kg	One once to 1 pint (1 pound)
2 (Slightly toxic)	5.1 g/kg to 15 g/kg	1 pint to 1 quart (2 pounds)
1 (Practically nontoxic)	More than 15 g/kg	More than 2 pounds

1.7 HISTORICAL STALWARTS

Q. Who is regarded as father of rational medicine?

Hippocrates (460–375 BC) is regarded as the "father of rational medicine" (Fig. 1.1). He created the Hippocratic Oath. He believed that disease came naturally and not from superstitions and god. He advocated hot oil as an antidote in poisoning and induced vomiting to prevent absorption of the poisons.

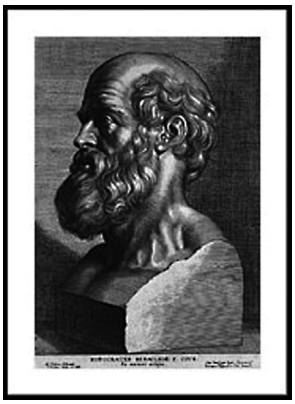

FIGURE 1.1

Hippocrates (460–375 BC).

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Q. Who was Paracelsus?

Theophrastus Paracelsus Bombastus Von Hohenheim (1493–1541), a 1st century Roman physician (Fig. 1.2), promoted a focus on the toxicon, the toxic agent, as a chemical entity. He recognized the dose–response concept and in one of his writings stated, "All substances are poisons, there is none which is not a poison. The right dose differentiates a poison and a remedy."

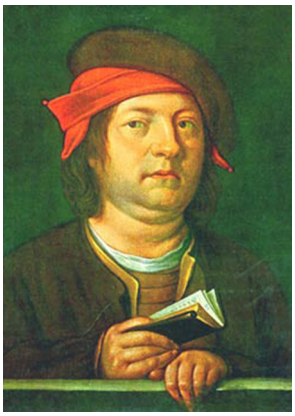

FIGURE 1.2

Theophrastus Paracelsus Bombastus Von Hohenheim (1493–1541).

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Q. What is the contribution of Friedrich Serturner?

Friedrich Serturner (1783–1841) was a German pharmacist who isolated the specific narcotic substance from opium and named as morphine after Morpheus (Fig. 1.3), the Roman God of sleep.

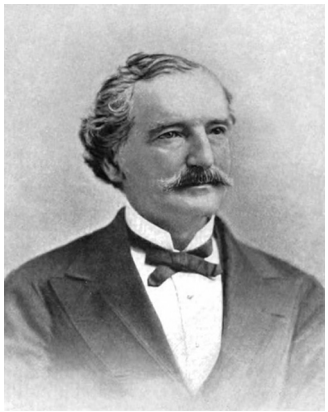

FIGURE 1.3

Friedrich Serturner (1783–1841).

https://upload.wikimedia.org/wikipedia/commons/c/ca/Colton_Gardner_Q.jpg

Q. Who is the father of toxicology?

M.J.B. (Mathieu Joseph Bonaventure) Orfila (1787–1853), a Spanish physician, is considered as a "father of toxicology" (Fig. 1.4).

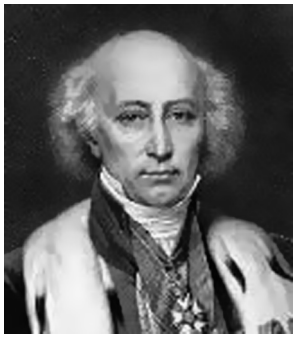

FIGURE 1.4

Father of toxicology—Mathieu Joseph Bonaventure Orfila (1787–1853).

https://encrypted-tbn0.gstatic.com/images?q = tbn: ANd9GcSsrNZMTcRLMNs2nlvZnnHE19szBbR6Fpd_bHfArlhroJEqTKSIkA

Q. Describe in brief the contributions of M.J.B. Orfila (1787–1853).

He established toxicology as a discipline distinct from others and defined toxicology as the study of poisons. He advocated the practice of autopsy followed by chemical analysis of viscera to prove that poisoning has taken place. His "treatise" Traite des Poisons published in 1814 laid the foundations of forensic toxicology.

Q. Who is the father of experimental pharmacology? Describe in brief his contributions.

Francois Magendie (1783–1855) is known as the "father of experimental pharmacology," a pioneer French physiologist and toxicologist studied the mechanism of action of emetine, morphine, quinine, strychnine, and other alkaloids (Fig. 1.5).

FIGURE 1.5

Francois Magendie.

http://www.culture.gouv.fr/culture/actualites/celebrations2005/images/099.jpg

Q. Who was Claude Bernard?

Claude Bernard (1813–78) was a French physiologist who is considered the "father of modern experimental physiology" (Fig. 1.6). Claude Bernard's first important works were carried out on the physiology of digestion, particularly the role of the pancreas exocrine gland, the gastric juices, and of the intestines. In addition to this, Bernard also made other important contributions to the neurosciences.

FIGURE 1.6

Claude Bernard (1813–78).

https://encryptedtbn1.gstatic.com/images?q = tbn: ANd9GcRngOYbgCoQt0OrIvsnzzZ9UCvw3WvdrVp9KG_DZ2qOnBWsy4n0

Q. Who was Louis Lewin (1854–1929)?

Louis Lewin (1854–1929) was a German scientist who took up the task of classifying drugs and plants in accordance with their psychological effects (Fig. 1.7). He also published many articles and books dealing with toxicology of methyl alcohol, ethyl alcohol, chloroform, opium, and some other chemicals. His important publications are *Toxicologist's View of World History* and *A Textbook of Toxicology*.

FIGURE 1.7

Louis Lewin (1854–1929).

https://upload.wikimedia.org/wikipedia/de/thumb/3/30/Louis_Lewin.jpg/220px-Louis_Lewin.jpg

Q. Who discovered the insecticidal properties of dichlorodiphenyltrichloroethane (DDT)?

Paul Hermann Muller in 1939 (Fig. 1.8) discovered the insecticidal properties of DDT. He was awarded Nobel Prize in 1948 "for his discovery of the high efficiency of DDT as a contact poison against several arthropods." (Fig. 1.9).

FIGURE 1.8

Paul Hermann Muller (1899–1969)—synthesized DDT.

http://www.nobelprize.org/nobel_prizes/medicine/laureates/1948/muller_postcard.jpg

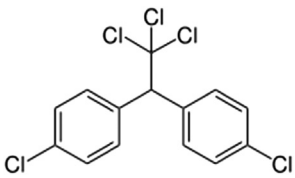

FIGURE 1.9

Dichlorodiphenyltrichloroethane.

https://upload.wikimedia.org/wikipedia/commons/thumb/0/0b/P%2Cp%27-dichlorodiphenyltrichloroethane.svg/300px-P%2Cp%27-dichlorodiphenyltrichloroethane.svg.png

Q. Who is the "father of nerve agents"?

Gerhard Schrader (1903–90) was a German chemist who accidentally developed the toxic nerve agents serin, tabun, soman, and cyclosarin while attempting to develop new insecticides (Fig. 1.10). Schrader and his team, thus, introduced a new class of synthetic insecticides, the OP insecticides, and defined the structural requirements for insecticidal activity of anticholinesterase compounds. He is known as the "father of nerve agents."