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1 Classification of poisonous substances

Poisons are substances which when administered on an organism whether accidentally or by design will produce harmful effects. **Poisons** are substances that cause death, injury or harm to organs, usually by chemical reactions or other activity on the molecular scales, when an organism absorbs a sufficient quantity. In regard to poisoning, chemicals can be divided into four broad groups: agricultural and industrial chemicals, drugs and health care products, biological poisons—i.e., plant and animal sources and radiation.

## Agricultural chemicals: The majority of agricultural chemicals are pesticides, which include insecticides, herbicides, fungicides, fumigants, and rodenticides. The four main classes of insecticides are organophosphates, carbamates, chlorinated hydrocarbons, and insecticides derived from plants (botanical). Organophosphate and carbamate insecticides act by [inhibiting](https://www.merriam-webster.com/dictionary/inhibiting) acetylcholinesterase, the enzyme that degrades acetylcholine (the messenger of the parasympathetic nervous system). As a result, acetylcholine levels remain high, exaggerating the normal functions of the parasympathetic system. Herbicides are chemicals used to kill plants. Their potential to produce toxicity in humans is rather low. Rodenticides e.g Warfarin was originally developed as a drug to treat thromboembolism, a disease caused by blood clots, since it [inhibits](https://www.merriam-webster.com/dictionary/inhibits) the synthesis of a factor essential for the clotting of blood. The inhibition of blood clotting by warfarin can lead to internal bleeding, however. Because of its ability to induce internal bleeding, warfarin is also used as a rodenticide. Examples are organophosphates malathion, parathion, carbamates (e.g., carbaryl, carbofuran) etc.

## Industrial Chemicals: The term industrial chemicals is used to refer to chemicals used neither in agriculture nor as drugs. Therefore, it includes chemicals used in industry, as well as chemicals found in or near households. Poisoning with industrial chemicals occurs most often by either percutaneous or inhalation routes. They are divided into organic and inorganic compounds. The organic compounds can cause the depression of the central nervous system is a common effect of most hydrocarbons. Examples of common hydrocarbons include gasoline, toluene, and heptanes; n-hexane; and benzene, alcohols like methanol and ethanol, aldehydes, ketones, esters etc. The inorganic compounds are metals compounds toxic to humans include manganese, lead, cadmium, nickel, and arsenic compounds, beryllium oxide, and the elemental vapours, inorganic salts, and mercury. Exposure to some of these metals can damage the brain, resulting in a condition with symptoms similar to Parkinson’s disease, such as slurred speech, masklike face, and rigidity. General air pollutants like sulfur dioxide is an acidic pollutant, that irritates the respiratory tract, causes violent coughing when it irritates the throat, and may result in shortness of breath, lung edema, and pneumonia when it reaches the lungs.

## Drugs and health care products: Painkillers (analgesics) are the most commonly used drugs and account for many poisoning cases. Examples include aspirin and acetaminophen. Aspirin interferes with the oxidative burning of fuel by cells. Examples are acetaminophen, morphine, aspirin etc. Other types of drugs are Tranquilizers and sleeping pills, Antipsychotic drugs, Antiseptics, Vitamins and iron pills, Antiasthmatics, Antiasthmatics etc. These drugs are primarily toxic to the central nervous system; amphetamine and cocaine cause stimulation of the system (hallucinations and delirium), and heroin causes the depression of the system (depressed respiration and coma). In contrast, phencyclidine and methaqualone are biphasic, producing first depression (drowsiness) and then stimulation of the central nervous system (delirium and seizures). Amphetamines also affect the gastrointestinal tract (anorexia, nausea, vomiting, diarrhea) and stimulate the cardiovascular system (increased blood pressure and heart rate, palpitations, and abnormal heart rhythm).

## Biologic poisons: Biotoxins can be conveniently grouped into three major categories: Microbial toxins, poisons produced by bacteria, blue-green algae, dinoflagellates, golden-brown algae, etc., Phytotoxins, poisons produced by plants, Most of the poisonous higher plants are angiosperms, or flowering plants, but only a small percentage are recognized as poisonous. Several systems have been devised for the classification of poisonous plants, none of which is completely satisfactory. Poisonous plants may be classified according to the chemical nature of their toxic [constituents](https://www.merriam-webster.com/dictionary/constituents), their phylogenetic relationship, or their botanical characteristics. The following classification, which is based on their toxic effects, has been found to be useful: (1) plants that are poisonous to eat, (2) plants that are poisonous upon contact, (3) plants that produce photosensitization, and (4) plants that produce airborne allergies. Zootoxins, poisons produced by animals Zootoxins can be divided into several categories: (1) oral poisons—those that are poisonous when eaten; (2) parenteral poisons, or venoms—those that are produced by a specialized poison gland and administered by means of a venom apparatus; and (3) crinotoxins—those that are produced by a specialized poison gland but are merely released into the [environment](https://www.merriam-webster.com/dictionary/environment), usually by means of a pore.

## Radiation: Radiation is a flow of energy through space or matter. It takes the form of particles (e.g., alpha and beta particles) or electromagnetic waves (e.g., X rays, gamma rays, and visible and ultraviolet [UV] light). Radiation can be classified as either ionizing or nonionizing depending on its ability to produce ions in the matter it interacts with. Ionizing radiation is more toxic than nonionizing radiation. Ionizing radiation is radiation that produces ions in matter during interaction with atoms in the matter. The toxic effect of ionizing radiation is related to the ionization. It is believed that ionization of tissues, composed mainly of water, generates H2O+ and H2O− ions, which in turn form H and OH radicals. Because radicals are very reactive chemically, biological damage, such as attacks on DNA and proteins, results. Radiation leads to the decreased production of blood cells, nausea, vomiting, diarrhea, malabsorption by the intestine, skin burns, and hair loss.

2a Hydrophobic drug roughly describes a heterogeneous group of molecules that exhibit poor solubility in water but that are typically, but certainly not always, soluble in various organic solvents. Other types of hydrophobic drugs show even a lower aqueous solubility of only a few ng/ml. Pharmacokinetics is a branch of pharmacology that examines how drug concentrations change with respect to time as a function of absorption, distribution, metabolism and excretion. These are disparate but interrelated processes that occur between drug administration and its irreversible elimination from the body. Another way to consider pharmacokinetic processes is to group them into two components:

1. intake, which describes the time course of drug movement from the site of administration, e.g. mouth, to the site of measurement, e.g. blood.

2. disposition, which describes the time course of drug distribution and elimination from the site of measurement e.g. blood.

Once absorbed into the body, drug compounds are distributed reversibly to various tissues of the body including the eliminating organs, such as liver and kidney, which results in a decrease in blood or plasma drug concentration. The decrease in the blood concentration could be due to reversible loss of drug from the blood to the tissues, defined as distribution, or the irreversible loss of drug from blood, defined as elimination. Disposition is therefore a combination distribution and elimination.

Distribution

Once in the systemic circulation, the blood or plasma concentrations of a drug will depend on how extensively it is distributed to extravascular sites. Drug concentration in whole blood represents the total concentrations of drug in the circulatory system. Plasma concentration do not account for drug molecules that are sequestered into red or white blood cells. In general, the blood and the plasma concentrations are assumed to be equal unless the drug is preferentially sequestered by red blood cells. Drug distribution will be influenced by tissue/organ blood flow, whether the drug is able to passively diffuse across cell membranes or is a substrate for active uptake or efflux transporters, and its extent of binding to plasma protein and tissue sites.

**Tissue/organ blood flow**

The transfer of many drug compounds from the systemic circulation to various tissues/organs follows the perfusion-rate diffusion process. This typically applies to drug compounds that are lipid soluble. Under perfusion-rate diffusion, the rate of delivery from the systemic circulation to a specific tissue/organ is primarily dependent on the blood flow within an organ or tissue. Organs like the liver and the heart are highly perfused with blood. By contrast, the bone and the adipose tissues experience less blood perfusion.

**Passive diffusion across cell membranes**

A major factor affecting drug distribution is the physicochemical properties of the drug since these would influence the permeability of the drug to various tissues. A drug that is highly lipophilic, such as chloroquine, may readily cross the lipidic bilayer of endothelial cells and most cell membranes to reach into the intracellular space via passive transcellular diffusion. Lipid-soluble drugs, because of their high partition coefficient, can also accumulate in organs or sites with fat deposits.

**Influx or efflux transporters**

Influx and efflux transporter are found in many tissues/organs and play a role in the distribution of drugs in the body. The efflux transporter, P-glycoprotein (P-gp), which is expressed in the liver and the kidney, functions to keep drugs out of tissues. By contrast, the influx transporter OATP1B1, an organic anion transporter expressed in the liver and the brain, acts on drug substrates to move them from the extracellular matrix into the tissue spaces. Since these transporters are subject to genetic polymorphisms, their underexpression or overexpression will result in differences in the extent of drug distribution between patients.

**Plasma protein and tissue binding**

Another factor influencing drug distribution is the preferential binding to plasma proteins and tissues. It is the unbound or free portion of the drug that diffuses out of the plasma into the tissues/organs. Albumin and α1-acid glycoprotein are the two major proteins in plasma that are responsible for the binding of most drug compounds in the systemic circulation. The extent of plasma protein binding of a drug can be drug- or protein-concentration dependent, based on the affinity and capacity of the plasma protein. A drug’s protein-binding characteristics also depend on its physicochemical properties, with lipophilic drugs more likely to bind to plasma proteins and consequently, less available to the intracellular spaces. Binding to tissues also affects drug concentrations in the blood/plasma and the tissues/organs. However, compared to plasma protein binding, much less is known about tissue binding or the sequestration of drugs, since reliable methods for estimating binding to tissue components in vivo are experimentally more challenging.

Elimination

Effective drug therapy involves achieving optimal efficacy without causing toxicity. To this end, drug intake into and distribution within the body must be balanced with elimination so that appropriate concentrations at the receptor sites can be achieved. Elimination refers to the irreversible removal of a drug or its metabolite(s) from the body. For the majority of drugs, metabolism is the major pathway of elimination. The primary organ involved is the liver, although the gastrointestinal (GI) tract, kidney, lung and skin may also contain drug metabolising enzymes and may contribute to regional concentrations of the drug and the metabolites. Excretion of drugs and their metabolites mainly occur in the kidneys, but may also involve the GI tract and lung.

Liver metabolism

In the liver, a wide array of enzymes exists to biotransform drugs, producing less active (or in some cases more active) metabolites. Drug metabolism is defined as the biotransformation of lipid-soluble chemicals into water-soluble forms, so that these can be excreted in the urine. Metabolism is divided into two phases. Drugs may undergo one phase only, or be metabolised through both phases sequentially.

Phase I metabolism

Phase I reactions involve the introduction into or unveiling of a polar functional group (e.g. –OH, –SH) on the drug molecule, rendering it a suitable substrate for conjugation with another molecule during phase II metabolism. Such reactions typically involve oxidation, reduction or hydrolysis processes. Often, the by-product of phase I metabolism, called a derivative, is pharmacologically inactive but more chemically reactive than the parent drug, and may be toxic or even carcinogenic.

The major liver enzyme system involved in phase I metabolism (oxidation) is the cytochrome P450 (CYP) enzyme system. Thus far, 18 CYP families have been identified in mammals, although only CYP1, CYP2, CYP3 and CYP4 are involved in drug metabolism, with CYP1A2, CYP2C9, CYP2C19, CYP2D6, CYP2E1 and CYP3A4 being responsible for the biotransformation of greater than 90% of drugs undergoing phase I metabolism

In addition to genetic polymorphism, liver CYP enzymes are subject to induction and inhibition by certain drugs. As a consequence, elimination of such CYP enzyme–substrate drugs administered concomitantly may increase or decrease. Additionally, where metabolic pathways involve the production of pharmacologically active or toxic metabolites, induction or inhibition of CYP enzymes could result in unanticipated changes in plasma drug concentrations, with potential clinical relevance to its therapeutic or toxicity profile.

Phase II metabolism

The derivative undergoes a phase II reaction that brings about the conjugation of its functional group(s) to various hydrophilic endogenous compounds. Examples of phase II reactions include sulfation, glucuronidation and glutathione conjugation. Sufficient water solubility is normally achieved in conjugates, which facilitate renal excretion. In addition, the insertion of a large polar substrate to the parent drug or derivative would make it more amenable for active secretion into the bile for subsequent excretion into the GI tract.

**Prodrugs**

After a phase I metabolism reaction, a drug may become “activated” or pharmacologically active. This biotransformation process is the basis for the development and usage of prodrugs.

The prodrug is typically a structural derivative of the active drug and synthesised by adding or changing a functional group(s) on the active drug structure. The ester is a common prodrug form of drug with hydroxyl or carboxylic groups. Esters can be synthesised with desired degrees of lipophilicity or hydrophilicity, and with controlled rates of the activating hydrolytic reaction. Once the prodrug gets inside the body, enzymes work to metabolically cleave the prodrug in order to form the active drug. Examples of prodrugs include levodopa, which is an amino acid derivative form of dopamine, and codeine, which is metabolised in the body to form morphine for analgesic effect.

There are many reasons to administer a prodrug in lieu of the active drug. The active drug may be for transfer across into the lipidic cell membranes to reach receptor sites, such as in neurons. Under such conditions, a functional group, such as carboxylic or hydroxyl group, may be attached to the active drug in order to enhance membrane transport. After absorption and distribution to the site of action, the functional group is cleaved via metabolism to release the active drug. In this regard, esterases found in almost all tissues make conversion of prodrugs into active drugs relatively straightforward. Other reasons for synthesising prodrugs are poor stability or poor patient acceptability (odour, pain on injection, gastric irritation) of the active drug, or a need to prolong the stay of the drug in the body.

Drug excretion

Excretion is the principal mode of termination of drug and metabolite effects. Drugs and their metabolite(s) are most commonly removed from the body via two main routes: renal and biliary excretion.

Renal excretion

About 25% of cardiac output goes to the kidney at which a significant portion of foreign compounds are filtered out. Renal excretion incorporates the processes of glomerular filtration, reabsorption from the renal tubular lumen, and tubular secretion as the drug passes through the nephron, the functional excretory unit of the kidney.

As blood passes through the glomerulus, entities within it are filtered to form the renal filtrate in the tubular lumen. The process of filtration is passive in nature and is driven by a combination of the large hydrostatic and concentration gradients present across the glomerulus-Bowman’s capsule junction. Nevertheless, large-sized components cannot be filtered through the glomerular membrane, which implies that large drugs (e.g. heparin), plasma proteins and plasma protein-bound drugs (e.g. warfarin) cannot cross into the tubular filtrate.

Water is reabsorbed along the nephron tubule so that only 1% of the original filtrate is passed out of the body as urine. Approximately 99% of substances filtered at the glomerulus are reabsorbed along the renal tubules. The majority of filtered, unmetabolised drug molecules are also reabsorbed, especially if these are lipophilic. This is because such drugs are more likely to cross the membranes of the cells lining the tubules. By contrast, polar drugs e.g. gentamicin and digoxin, are unable to do this. Such drugs will therefore be excreted unchanged in the urine because they do not need to undergo biotransformation to increase their water solubility.

Active secretion into the renal tubules occurs for some drugs that are not readily filtered in the glomerulus. This pathway occurs via a carrier mechanism and is sufficiently efficient as to not depend on binding between plasma proteins and drugs, ensuring almost complete clearance of drugs such as penicillin. Other drugs excreted by this process include anti-inflammatory drugs and methotrexate.

Biliary excretion

While in the liver, drugs or metabolites can also be secreted into the bile in much the same manner as the kidney secretes drugs into the nephron tubular filtrate. Biliary excretion is facilitated by active transport systems located in the canalicular membrane of the hepatocyte, and can be an important hepatic elimination pathway for many compounds. Since bile is an aqueous solution, it is suitable for dissolving hydrophilic drugs. In addition, bile acids allow solubilisation of lipid-soluble drugs. Thus, all types of species (anionic, cationic and un-ionised drugs), polar and lipophilic, can be secreted into the bile. These include drug metabolites that have undergone conjugation with glucuronate during phase II metabolism. The main criterion for significant biliary excretion seems to be molecular weight > 500.

Once bile and its constituents enter into the intestines, many organic biliary constituents, including bile salts and cholesterol, are reabsorbed from intestines back into the blood with high efficiency. These components then return to the liver via the hepatic portal vein. Drugs or metabolites excreted in the bile may recirculate in the same manner. If the drug has favourable physicochemical properties, it can be partially reabsorbed from the intestines back into the blood stream just like an orally ingested drug. Metabolites with glucuronate or sulfate groups may be removed by enzymes produced by the resident bacteria of the lower small intestine and colon, and the now-active drug is able to be reabsorbed. One example is mycophenolic acid. This immunosuppressant drug undergoes conjugation to glucuronate in the liver. The glucuronide metabolite of mycophenolic acid is secreted into the bile, cleaved in the small intestines, and reabsorbed back into the systemic circulation as the parent drug compound. Thus, a reservoir of the drug is established in the enterohepatic circulation, with an ongoing cycle of absorption, metabolism, secretion into the bile and reabsorption. Enterohepatic circulation hence increases the persistence of drugs in the body, and reduces overall clearance in the bile.

2b. hydrophilic substance Q

Absorption

Once absorbed into the body, drug compounds are distributed reversibly to various tissues of the body including the eliminating organs, such as liver and kidney, which results in a decrease in blood or plasma drug concentration.

Distribution

The transfer of many drug compounds from the systemic circulation to various tissues/organs follows the perfusion-rate diffusion process. Here, we assume that cell membranes do not present any barrier to drug transfer. Drugs are likely to distribute more rapidly to tissues/organs that are more richly perfused with blood. Drugs that are more water soluble and polar, such as aminoglycosides, do not distribute well into most tissues/organs. For such drug molecules, entry into the tissue spaces may rely on either paracellular diffusion via gaps in-between cells or carrier-mediated uptake transport processes

Elimination

Hydrophilic substances undergo just one phase of metabolism, and then directly excreted as urine. The derivative undergo just phase I metabolism which is excreted via the urine immediately if high aqueous solubility is achieved.

There are many reasons to administer a prodrug in lieu of the active drug. The active drug may be too polar or hydrophilic for sufficient absorption and oral bioavailability to be attained.

Excretion

Excretion process is through the kidney, and the process has been earlier explained under renal excretion of hydrophobic substances.

3a Poisonous substances and their respective antidotes

Poisons Antedotes

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| 1 Methanol | Ethyl alcohol, Fomepizole |
| 2 Methemoglobinemia | Methylene blue, vitamin C (ascorbic acid) |
| 3 Organophosphate | Atropine, pralidoxime |
| 4 Opiates | Naloxone |
| 5 Lead | Dimercaprol, BAL |
| 6 Valproate | Carnitine |
| 7 Iron | Desferrioxamine |
| 8 Heparin | Protamine |
| 9 Warfarin | Vitamin K |
| 10 Calcium channel blockers | Calcium, glucagon, high dose insulin |
| 11 Clonidine | Naloxone |
| 12 Magnesium | Calcium |
| 13 Methotrexate | Folinic acid |
| 14 Antimuscarinic agents | Physostigmine |
| 15 Tricyclic antidepressants | Sodium bicarbonate |
| 16 Class 1 antiarrhythmics | Sodium bicarbonate |
| 17 Paraquat | Fuller's Earth, bentonite clay |
| 18 Dystonic crisis due to classical antipsychotics | Benztropine |
| 19 Serotonin syndrome | Cyproheptadine |
| 20 Carbon monoxide | Oxygen, |

3b. Ways by which the clinical effects of poisons can be studied

1. **Observational study**: Observational studies have been recognised to be essential for investigating the safety profile and effects of medications. Numerous observational studies has to be conducted on the platform of large population databases, which provide adequate sample size and follow-up length to detect infrequent and/or delayed clinical outcomes. Cohort and case–control are well-accepted traditional methodologies for hypothesis testing, while within-individual study designs are developing and evolving, addressing previous known methodological limitations to reduce confounding and bias. Respective examples of observational studies of different study designs using medical databases are shown. Methodology characteristics, study assumptions, strengths and weaknesses of each method are discussed in this review.
2. **Environmental study**: Environmental study is the multidisciplinary study of the effects of manmade and natural chemicals on health and the environment. This includes the study of the effects of chemicals on organisms in their natural environments and in the ecosystems to which they belong. It is the scientific study of the health effects associated with exposure to toxic chemicals occurring in the natural, work, and living environments. The term also describes the management of environmental toxins and toxicity, and the development of protections for humans and the environment.
3. **Veterinary study**: Veterinary toxicology involves the evaluation of toxicosis and deficiencies, identification and characterization of toxins and determination of their fate in the body of animals, and treatment of toxicosis. Toxicology has been receiving even more attention in the general public with the widespread interest in crime scene investigator (CSI) television shows. The recent worldwide melamine contamination in pet and swine feed, pet jerky treats causing illness and death, and concerns with use of β-agonists in food animals demonstrates the relevancy of veterinary toxicology to current animal health and food safety. Veterinary toxicology can be challenging because of the low frequency of cases observed in a practice setting. When a toxicosis occurs, it often involves a large number of animals and may also involve litigation.
4. **Forensic study**: Thisis the use of toxicology and disciplines such as analytical chemistry, pharmacology and clinical chemistry to aid medical or legal investigation of death, poisoning, and drug use. The primary concern for forensic toxicology is not the legal outcome of the toxicological investigation or the technology utilized, but rather the obtainment and interpretation of results. A toxicological analysis can be done to various kinds of samples. A forensic toxicologist must consider the context of an investigation, in particular any physical symptoms recorded, and any evidence collected at a crime scene that may narrow the search, such as pill bottles, powders, trace residue, and any available chemicals. Provided with this information and samples with which to work, the forensic toxicologist must determine which toxic substances are present, in what concentrations, and the probable effect of those chemicals on the person. It is basically the establishment of fact that an individual was poisoned whether accidentally or by design.
5. **Clinical study**: This is a discipline within toxicology which is concerned with the impact of drugs and other chemicals on humans. From their sources to their effects on the health and body