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MLS 512

A Poison is defined as any substance ( solid, liquid or gaseous) which when administered in living body through any route (Inhalation, Ingestion, surface absorption etc) will produce ill‐health or death by its action which is due to its physical, chemical or physiological properties.

Classification of poisons can be done according to

A) Mode of action

B) Chemical nature

**A. mode of action:** A mode of action defines a functional or anatomical modification, at the cellular level, stemming from the exposure of a living organism to a material or a substance. In comparison, a mechanism of action describes such changes at the molecular level.

1. Corrosive Poisons A corrosive poison is simply a highly active irritant and not only produces inflammation but also actual ulceration of the tissues. Basically a corrosive poison fixes, destroy and erodes the surface with which it comes in contact i.e. they produces local action. They act by extracting water from the tissues and coagulate cellular proteins and convert hemoglobin into haematin. This group consists of strong acids and strong alkalis. These include mineral acids, such as sulphuric acid, nitric acid, hydrochloric acid; organic acids, such as oxalic acid, carbolic acid, acetic acid, salicylic acid; concentrated alkalis such as, caustic soda, carbonates, ammonium, sodium and potassium.

2. Irritant Poisons Irritant poisons causes pain in abdomen, vomiting and purging. In post-mortem appearance they are usually evident to the naked eye and shows redness or ulceration of the gastrointestinal tract. This group is further divided into; inorganic, organic, and mechanical substances. Corrosives in dilute solutions act as irritants.

* Inorganic irritant poisons The inorganic subgroup consists of non-metallic and metallic poisons. Examples of nonmetallic poisons are phosphorous, chlorine, bromine and iodine etc. The metallic poisons include arsenic, antimony, mercury, lead, copper, thallium, zinc, manganese, barium and radioactive substances.
* Organic irritant poisons This group of poisons comprises of animal and plant poisons. Examples of plant poison are abrus precatorius, castor, marking nut, ergot, calotropis etc. The animal poisons include snakes, insects, cantharides, spider etc.
* Mechanical substances This group includes coarsely powdered glass, chopped hairs, dried sponge and diamond dust.

3. Systematic poisons This class of poisons directly affects the main organs of the body system and therefore they are referred to as systematic poisons. It includes nervous system (neurotics), cardiovascular system (cardiac), Respiratory system (asphyxiate).

* Neurotics Poisons Neurotic poisons act chiefly on the nervous system though some neurotics have a local irritant action. All alkaloids poisons fall into this group. This group consists of poisons that have specific action on the cerebrum, spinal cord and peripheral nerves, the poisons being known as cerebral, spinal and peripheral respectively.
* Cerebral Poisons The poisons acting on the cerebrum may have a somniferous, inebriant or deliriant effect. The somniferous poisons include opioids; the inebriant ones include alcohols, anaesthetics, sedatives and hypnotics, fuels and agrochemical compounds. The deliriant are dhatura , belladonna, cannabis indica.
* Spinal Poisons The poisons acting on the spinal cord include nux vomica and its alkaloids and gelsemium.
* Peripheral Poisons The poisons acting on the peripheral nerves include curare and conium.
* Cardiac Poisons These are poisons acting on the heart and it includes digitalis, oleander, aconite and nicotine.
* Asphyxiant Poisons: These poison acts on the respiratory system and it include irrespirable gases such as carbon monoxide, carbon dioxide, sewer gases and some war gases.
* Miscellaneous Poisons: The poisons having different pharmacological action are put together in this group. It includes analgesics. Antipyretics, antihistaminic, tranquilizers, antidepressants, street drugs and designer drugs.

B) Nature of Poison

1. Gaseous Poisons: These types of poison are in gaseous state and if inhaled, hamper the competence of the blood as a carrier of oxygen and may damage the tissues of the air passages and lungs. Some the examples of gaseous poisons are carbon monoxide, carbon dioxide, hydrogen sulphide, sulphur oxide, chlorine, nitrous oxide, tear gas etc.
2. Volatile Inorganic Poisons: Acute poisoning with volatile substances usually follows the slow inhalation of vapors in order to become intoxicated. Cyanide, phosphine, arsine, phosgene, chloride, etc. are few Volatile Inorganic Poisons.
3. Volatile Organic Poisons: These are organic chemicals that have a high vapor pressure at ordinary room temperature. The high vapor pressure which results from a low boiling point, causes large numbers of molecules to sublimate from the liquid or solid form of the compound and enter the surrounding air. Examples of Volatile Organic Poisons are ethanol, ethanol, formaldehyde, and acetaldehyde.
4. Non-Volatile Inorganic (anions) Poisons: Examples are halides, dichromate, chlorates, azides , nitrites ,sulphate, phosphide , cyanide etc.
5. Non-Volatile Inorganic (cations) Poisons: Examples are mercury, arsenic, barium, thallium, lead, antimony, bismuth etc.
6. Non-Volatile Organic Neutral Poisons (pesticides): Examples of Non-Volatile Organic Neutral Poisons are organophosphates, organochlorates, carbmates, pyrethroides.
7. Non-Volatile Organic Acidic Compound (acidic drugs). Drugs/ Poisons, which are acidic in nature, are called Acidic Drugs. These drugs readily reacts with bases to form salts. Few of the examples are barbiturates, sulpha, phenolic compounds (Phenol, Cresols etc.), salicylates.
8. Non-Volatile Organic Alkaline Compounds (basic drugs): If the drugs contain a nitrogen atom with a lone pair of electrons available for reaction with protons they will behave as bases only Examples alkaloids, benzodizepine.
9. Plant Poisons: The active constituents of plants that exert toxic effects are organic compounds and non-volatile in nature. Examples: - Dhatura, aconite, oleander, nux vomica etc.
10. Miscellaneous Poisons: These poisons may be organic or norganic, volatile or non-volatile and or animal, plant origin or toxins produced thereof.

I. Mechanical poisons: Examples: - diamond dust, glass powder, chopped hair.

II. Food poisoning: (mycotoxins)

III. Animal /insect poisons: Examples: - snake venom, scorpion, poisons bees.

2a.Pharmacokinetics refers to the study of the time course of a drug within the body (extent and duration of systemic exposure to the drug) and also incorporates the process about the drug’s absorption, distribution, metabolism, and excretion (ADME) pattern. In general, pharmacokinetic parameters are derived from the measurement of drug concentrations in blood or plasma

* ABSORPTION

Absorption takes place across the biological membrane. Lipid drugs are absorbed by transcellular mechanism where the drug distributes into the lipid core of the membrane which diffuses into the other side of the membrane. The solute may also diffuse across the cell membrane and enter into the circulation. The transport of drugs across membranes involves one or more of the following processes: 1) passive diffusion, 2) filtration, 3) bulk flow, 4) active transport, 5) facilitated transport, 6) ion-pair transport, 7) endocytosis, and 8) exocytosis. Drug absorption also depends on a number of physicochemical factors, the two most important of which are lipophilicity and solubility. The membrane of the gastrointestinal epithelial cells is composed of tightly packed phospholipids interspersed with proteins. Thus, the transcellular passage of drugs depends on their permeability characteristics to penetrate the lipid bilayer of the epithelial cell membrane, which is in turn dependent on the lipophilicity of the drugs. Although correlations have been established between lipophilicity and increased permeability, lipophilicity is not always predictive of permeability.

* Distribution

Distribution provides information on the extent and time course of tissue accumulation and the elimination of drug and/or its metabolites. The disposition of drug into the organs and tissues via circulation depends upon the nature of the drug. The more lipophilic the drug is, the better will be the distribution into the organs and tissues. Lipid solubility is a major factor affecting the extent of drug distribution, particularly to the brain, where the blood–brain barrier restricts the penetration of polar and ionized molecules. Highly lipid-soluble drug can enter the tissues. Lipid-insoluble drugs are mainly confined to the plasma and interstitial fluid; most do not enter the brain following acute dosing. Lipid soluble drugs reach all compartments and may accumulate in fat. For drugs that accumulate outside the plasma compartment, volume of distribution may exceed the total body volume.

* Transport across cell membranes

Passive diffusion

The concentration gradient provides energy for the transportation of the drug across the membrane, and also partitioning of the drug in favor of the lipid membrane decides the quantity of the drug absorbed. The unionized drug is absorbed markedly higher than the ionized form. Passive diffusion could be explained with Fick’s first law which relates the diffusive flux to the concentration under the assumption of steady state. It postulates that the flux goes from regions of high concentration to regions of low concentration, with a magnitude that is proportional to the concentration gradient, or in simplistic terms, the concept that a solute will move from a region of high concentration to a region of low concentration across a concentration gradient.

* Biotransformation/Metabolism

Biotransformation or drug metabolism is the enzyme-catalyzed conversion of drugs to their metabolites. A lipophilic drug can pass easily into the surrounding tissues. The stronger the blood supply to an organ or tiisue the greater the amount drug taken into the organ. At the same time lipophilic drugs are excreted somewhere poorly from the body because they can be largely reabsorbed in the kidney. Accordingly such substances are metabolized in the liver subsequently excreted into the bile and eliminated from the body. The liver is the major site for drug metabolism, but biotransformation can also occur by the kidney and intestine. Conversion of lipophilic drugs to more polar metabolites by the liver may increase excretion in the bile and kidney, and thus may decrease half-life.

Phase 1 = Convert lipophilic molecules into more polar molecules (hydrolysis, oxidation, reduction). Phase 2 = Further convert lipophilic molecules into more polar molecules through conjugation with glucuronic acid, sulfuric acid, acetic acid, or amino acid.

* Clearance (Elimination)

Drug clearance (CL) is defined as the volume of plasma in the vascular compartment cleared of drug (only free, i.e., not protein bound) per unit time by the processes of metabolism and excretion. Clearance is related to the concentrations of the drug present in blood after administration. Clearance of drug occurs by the perfusion of blood to the organs of extraction. Reduction in lipophilicity is observed when compared to the parent molecule during administration. renal clearance decreases with lipophilicity. Metabolic clearance increases with increasing log D, and this becomes the major clearance route of lipophilic compounds. The degree of reabsorption (all along the nephron) depends on the physicochemical properties (degree of ionization and intrinsic lipophilicity) of the drug. After absorption, the equilibrium is reestablished in the kidney where the unbound drug in the urine and unbound drug in plasma are present on both sides of the membrane.

2B. Absorption for hydrophilic substances is by facilitated diffusion which is the passive movement of molecules across the cell membrane via the aid of a membrane protein. Excretion process is through the kidney.

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| Poisonous substances | Antidote |
| Benzodiazepine overdose | Flumazenil |
| opioid overdose | Naloxone |
| acetaminophen poisoning | Acetylcysteine |
| Neuromuscular blocking agents (eg, curare) | Neostigmine, edrophonium |
| β-Blockers | Glucagon |
| Ethylene glycol | Ethanol |
| Iron salts | Desferrioxamine |
| Organophosphates | Atropine |
| Thallium | Berlin (Prussian) blue |
| Isoniazide | Pyridoxine (vitamin B6) |
| Selenocystthionine | Cystine |
| Bromide | Chloride |
| Thallium | Potassium salts |
| Histamine | Antihistamines |
| Cyanide | Methehemoglobin |
| Carbamates | Atropine and protopam |
| Carbon monoxide | Oxygen |
| Amino acid analogs | Amino acids |
| Fluoroacetate | Acetate, monoacetin |
| Methanol | Ethanol |

3B. The following test are carried out

1. Complete blood count (CBC), which includes a red blood cell (RBC) count, white blood cell (WBC) count, platelet count, hemoglobin, and basophilic stippling;
2. Blood sugar, including insulin, fasting blood sugar (FBS), and 2-hour postprandial (2-h PP) blood sugar
3. Liver enzymes, including aspartate aminotransferase (AST), alanine aminotransferase (ALT), and gamma glutamyl transferase
4. Inflammatory markers, including C-reactive protein (CRP), low-density lipoprotein (LDL), oxLDL, and triglycerides;
5. Metabolites (bilirubin and uric acid)

CBC: These can be early indicators of toxin exposure. Another useful indication from the standard CBC is basophilic stippling of the RBCs, which occurs in both arsenic and lead poisoning.

Liver Enzymes: Liver enzymes are typically measured to detect hepatitis. Many liver enzymes play important roles in detoxification and are induced as needed. Gamma glutamyl transeferase levels increases with alcohol poisoning

The harmful effect of these substances can also be studied by:

1. Behavioural study: to know if the individual is agitated or at peace

2. Immunological effects

3. Teratogenic effects

4. Mutanogenic effect: to check if the substance drug will induce mutation

5. Carcinogenic effect: to check if it can induce carcinogenicity. This can be done by checking the cellular architecture

6. Molecular effect