

Introduction to toxicology

Toxicology

- The name from the Greek toxon (arrow) or toxicon (a poisonous substance into which Hecate dipped arrowheads) and logos (science, debate).
- It uses the knowledge of biological sciences (molecular biology, genetics, botany, zoology, microbiology, medical sciences) and chemical sciences (analytical, inorganic, organic chemistry, biochemistry).
- It is not just the sum of knowledge about poisons and their effects.
- It deals with the interaction of chemicals and living organism.
- Most substances undergo transformations after they enter the organism - biotransformations.
- Toxicology has a descriptive, experimental and theoretical side.
- Toxicology is related to pharmacology, which studies the beneficial and adverse effects of drugs.

Definition of poison

- Paracelsus (1492-1541): All compounds are poisons. There's no compound that isn't poison. The difference between the drug and the poison is the dose.
- Riedel, Vondracek (1954): By poison, we understand a substance that enters the body in small amounts (several micrograms to tens of grams), produces morbid changes that can also lead to the demise of the organism.
- Merhold (1962): Poison is a substance that damages the body in small doses. The line between a small and a large dose is not precisely determined.
- **Dose** - the amount of substance that reaches the body is absorbed.
- So we consider poisons only those substances that are capable of producing an adverse effect - poisoning already in small doses.
- **Antidote** - a substance that reverses the effect of the poison on the body.

Basic terms

Toxicity - the ability of a substance to harm a living organism. It depends on the physico-chemical properties of the substance, the way the substance enters the body, the metabolism of the substance, the frequency of administration, the dose, etc.

Xenobiotics - an extraneous substance alien to the organism or environment is not a product or intermediate in physiological metabolism.

Poison - toxic substance. Whether the substance is poison depends on the dose and conditions of action. The poison results in a toxic effect on the living organism.

Ecotoxicity - a property of a substance that has an immediate or delayed adverse effect on the environment by being bioaccumulated or acting toxically on biotic systems. Bioaccumulation represents an increase in the concentration of foreign substances in tissues of organisms due to exposure from the environment or food intake.

Polutant - a substance contaminating, polluting environments, especially as a product of human activity.

Contaminant - a substance whose presence causes deviation from the natural composition of the surrounding environment. A contaminant is not classified as a pollutant unless it damages its surroundings.

Hazardous to the environment - a substance that is capable of producing a toxic effect in the environment. It can be dangerous already in small concentrations, resistant to various forms of decay. It accumulates in both abiotic and biotic components of the environment.

Environmentally persistent substance - is characterised by the duration of the substance in the environment. It is expressed using half-life ($T_{1/2}$), the time at which the concentration of the substance falls to half its original value.

Bioindicator - organism (microorganism, protozoa, fungus, plant, lower or higher animal) used to assess the toxicity of substances or the action of external conditions.

Biotest - a process in which the test system (organism, population) is exposed to different concentrations of the test substance under well-defined conditions.

PEC (Predicted Environmental Concentration) - predicted concentration of the substance in the environment.

PNEC (Predicted No Effect Concentration) - the highest predicted concentration of a substance with no harmful effects.

PEC/PNEC < 1.0 - the risk from the presence of the substance in the environment is low.

Risk - the likelihood of its toxicity occurring with a defined exposure to a substance. The size of the risk takes values from 0 to 1.0.

Zero risk means there will never be any damage to the organism.

Risk = 1.0 means that damage to the organism will occur in all cases.

The risk assessment shall include:

- an evaluation of the hazards of the substance;
- an evaluation of the relationship between the dose of the substance and the biological response;
- evaluated exposures;
- risk characterization.

Risk management - risks can not only be estimated but also managed, thus limiting their impact on the environment (e.g. avoiding or limiting contact with a toxic substance - use of protective equipment for humans, decontamination of the environment, rapid dissemination of accurate risk reports).

WHO - World Health Organisation
EPA - U. S. Environmental Protection Agency

Dose-based toxicity scale for humans and rats

Dose characteristics	Rat	Human	Examples of substances
Supertoxic substance	< 5 mg/kg	trace - 7 drops	Nicotine, As ³⁺ , botulinum toxin
Extremely toxic substance	5-50 mg/kg	7 drops - teaspoon	BaCO ₃ , KClO ₃
Highly toxic substance	50-500 mg/kg	teaspoon - 50 ml	Cd ²⁺ , Pb ²⁺ , methanol
Slightly toxic substance	0,5-5 g/kg	50 - 500 ml	NaCl, FeSO ₄
Low toxic substance	5-15 g/kg	0,5-1,0 l	ethanol
Practically non-toxic substance	> 15 g/kg	více než 1,0 l	BaSO ₄

Exposure - the process by which an organism comes into contact with a substance and by which the substance can be expected to enter the body.

Effect - is the body's response to substance exposure. The toxic effects depend on the concentration and dose of the substance, the mode of contact with the organism, the metabolites of the substance, the location of action.

Breakdown of toxic substances by WHO and EPA criteria

Toxicity\Characterisation of substance	WHO criteria	Rat LD ₅₀ mg/kg	EPA criteria	Rat LD ₅₀ mg/kg
Extremely toxic	1a	< 5	I	< 50
Highly toxic	1b	5-50	II	50-500
Toxic	II	50-500	III	500-5000
Low toxic	III	> 501	IV	> 5000

Acute effect - immediate after single dose of toxic substance

Chronic effect - after prolonged exposure to the substance

LD₅₀ - a lethal dose at which 50% of the subjects studied die. The more toxic the substance, the lower its numerical value. Depends on the type of tested animal (mouse, rat, dog) and the method of administration (digestive, respiratory, skin, etc.).

LD₅₀ of selected substances

Substance	Ethanol	NaCl	Morphine	Phenobarbital	Nicotine	Dioxin	Botulinum toxin
LD ₅₀ mg/kg	10 000	4 000	900	150	1	0,001	0,000 01

ED - effective dose - indicates what percentage of subjects in the test set react after exposure to the test substance.

ED₅₀ - effective dose at which 50% of subjects in the population respond

ED0 - effective dose at which no individual in the test set responds

Toxic substances according to the mechanism of action

- **Direct toxicity** - the xenobiotic acts directly harmfully on the organ (liver, kidneys, lungs), tissue or cells. For example, oxalic acid crystallizes in the form of calcium oxalate in the tubules of the kidneys. Strong acids and bases damage the parts of organisms they have come into contact with. Lipophilic substances (alkanes, ethers) can reversibly disrupt the cell membrane of e.g. nerve cells.
- **Organ toxicity** - A xenobiotic acts on an organ. The cells of an organ are damaged until they die:
 - liver - hepatotoxic damage;
 - kidneys - nephrotoxic damage;
 - lung - pneumotoxic damage;
 - nervous system - neurotoxic damage.

- **Mutagenic effect** - the action of a xenobiotic to alter the structure of a nucleic acid base (DNA and RNA). DNA stores the genetic information of the organism, it is made up of double helices. Bases, adenine - thymine and guanine - cytosine are bound together by hydrogen bridges. The violation of the chemical composition and thus the structure of the DNA are caused by oxidative substances or alkylating agents. When the individual bases of DNA are alkylated - formation of a methyl derivative of the same base - there is a change in the coded or transmitted genetic information. The mutation is a change in the base sequence of DNA, it is a change in the order of nucleosides in nucleic acids. Mutation is a change in genetic information that results in a change in the characteristics of the next generation.
- **Carcinogenic effects** - changes in the cell that lead to malignant tissue growth, tumor is formed. Changes are triggered by:
 - **damaging of repair mechanisms** capable of repairing or replacing damaged DNA;
 - **by other mechanisms** of action of the chemical, which may be highly likely to cause malignant tumours.
- **Teratogenic effects** - damage to the foetus (embryos) that leads to the formation of a defective individual that is viable.
- **Immunotoxic effects** - the response of the immune system to the entry of a substance into the body. If the substance is recognised as foreign, it triggers the production of an antibody in the immune system. Immune responses range from skin irritation, urticaria, breathing problems to anaphylactic shock. Xenobiotics either suppress the immune process (immunosuppression is caused by e.g. benzene, polycyclical aromates, PCBs, ozone) or increase (allergic reaction). An allergic reaction is triggered when the organism is re-exposed to a foreign substance. Antibodies that are already formed react with an foreign substance.

Links

Related articles

- Metal contamination
- Industrial chemicals
- Ecotoxicology

Source

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