MODERN CLASSIFICATION AND CLINICAL APPLICATIONS OF ANTIDOTES

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Abstract: This scientific article provides a comprehensive analysis of antidotes and their role in toxicology and emergency medicine. The article examines the historical development stages of antidotes, their modern classification based on mechanisms of action (chemical, biochemical, and pharmacological), and detailed presentation of their pharmacodynamic and pharmacokinetic properties. Specific antidotes used in cases of poisoning with various toxic substances (heavy metals, pesticides, pharmaceuticals, industrial chemicals) are reviewed, along with their clinical efficacy and limitations in application. The article concludes with an examination of innovative approaches in antidote development and future research directions.

Keywords: antidote, counterpoisoning agent, toxicology, poisoning, pharmacology, detoxification, chemical antagonism, pharmacological antagonism, emergency medical care, toxin.

With the advancement of human civilization, the discovery and application of new substances in the chemical industry, pharmaceuticals, agriculture, and many other sectors has been expanding. While this progress facilitates human life, it has simultaneously increased the risk of exposure to toxic substances that may have adverse effects on the environment and the human organism. Toxicology is the science that studies the effects of toxic substances (toxins) on living organisms, and develops methods for prevention, diagnosis, and treatment of poisoning. In cases of poisoning, antidote therapy plays a central role in providing emergency medical care and preserving patient life.

Antidotes, or counterpoisoning agents (from Greek: antidoton — "given against poison"), are medicinal substances that neutralize toxic materials that have entered the organism through various routes, reduce their absorption, block their

mechanisms of action, or accelerate their elimination from the body. Since ancient times, physicians have sought remedies against poisons, and the earliest information about this is found in ancient manuscripts. However, the modern history of antidotes began in the nineteenth century with the rapid development of chemistry and medical research. Today, due to advances in pharmacology and toxicology, many specific and effective antidotes against various poisons have been developed and introduced into clinical practice.

This research is expected to have significant theoretical and practical importance for healthcare professionals managing cases of poisoning — physicians, pharmacologists, toxicologists, and students of medical higher educational institutions.

The history of seeking remedies against poisons traces back to ancient periods of humanity. In ancient medicine, many diseases were considered to result from external "poisons," and thus the search for effective remedies was often equivalent to searching for antidotes. In texts from pre-Christian periods, physicians including Hippocrates and Dioscorides documented information about antitoxic properties of substances derived from plants and animals. For example, texts about remedies used against snake and insect bites retained their significance for centuries.

In the Middle Ages, particularly in the works of Central Asian scholars, including Avicenna (Abu Ali ibn Sino), special attention was given to issues of pharmacology and toxicology. His work "The Canon of Medicine" (Kitab al-Qanun) contains valuable information about various poisons, their symptoms, treatment methods, and substances that could be used as antidotes. During this period, antidotes were often selected empirically (based on experience), and their mechanisms of action were not scientifically substantiated.

The modern history of antidotes began in the nineteenth century with the rapid development of chemistry and a new phase of medical research. During this period, the chemical composition of toxic substances and their biochemical effects on the organism began to be studied systematically. This, in turn, made it possible to create

rationally designed antidotes — substances that could specifically block or neutralize poison effects. For example, the development of chelators such as dimercaprol (BAL) against arsenical compounds represents a striking example of antidote therapy based on chemical antagonism.

Today, antidote therapy is an integral part of clinical toxicology. In emergency situations—such as industrial accidents, drug overdoses, or poisoning with agricultural pesticides—properly administered antidotes administered in time can be decisive in saving patient lives. Emergency medical departments must maintain supplies of essential antidotes needed to treat various types of poisoning.

The success of antidote therapy depends on several factors. First, rapid identification of the poison type and the amount that entered the organism is essential. Second, the optimal timing for antidote administration must be determined. Some antidotes are effective only when administered within a short time after poisoning (from several minutes to several hours). Third, antidote therapy is almost always conducted in combination with other treatment methods, including detoxification measures aimed at eliminating poison from the organism (stomach lavage, administration of activated charcoal) and supportive symptomatic treatment maintaining vital organ function.

Antidotes are divided into several major groups based on their mechanisms of action. This classification helps in selecting the most appropriate treatment strategy for each clinical situation. The scientific literature identifies three main groups of antidotes: chemical, biochemical, and pharmacological antidotes.

Chemical antidotes directly enter into a physicochemical reaction with a toxic substance, converting it into a non-toxic or less toxic compound. This process, called chemical antagonism, must occur before the toxin binds to vital receptors or enzymes. Chemical antagonism includes several types:

Neutralization Reaction: When poisoned by acids, alkaline substances (such as sodium bicarbonate, magnesium oxide) are used, or conversely, weak acids (citric

acid) are used for alkaline poisoning. As a result of this reaction, the poison transforms into a neutral, harmless substance.

Chelation: In cases of poisoning with heavy metals (lead, mercury, arsenic), substances called chelators are used, including unithiol, dimercaprol (BAL), calcium disodium EDTA, and D-penicillamine. They form stable, water-soluble complex compounds (chelates) with metal ions, facilitating their elimination from the organism through the kidneys. For example, unithiol forms a strong bond with arsenic, which prevents arsenic from binding to tissue proteins.

Adsorption: Adsorbents such as activated charcoal absorb many toxic substances in the gastrointestinal tract onto their surface and prevent their absorption into the blood. This is considered one of universal antidotes; however, it is not effective against all poisons (such as acids, alkalis, iron salts, and lithium).

Biochemical antidotes affect the metabolism (biotransformation) or distribution of poison in the organism. They alter the pharmacokinetics of the toxin, reducing its harmful effects. This group of antidotes can act through the following mechanisms:

Blocking Metabolic Activation: Some substances are relatively non-toxic when they enter the organism, but are converted into highly toxic metabolites under the influence of liver enzymes. Biochemical antidotes block these enzymes, preventing the formation of harmful metabolites. A striking example is poisoning with methanol or ethylene glycol. These alcohols are converted under the influence of the enzyme alcohol dehydrogenase into highly toxic formaldehyde and formic acid (from methanol) or glycolaldehyde and oxalic acid (from ethylene glycol). Ethanol or fomepizole (4-methylpyrazole) act as competitive inhibitors for this enzyme, slowing the conversion of methanol and ethylene glycol into toxic metabolites and allowing them to be excreted unchanged in urine.

In poisoning with organophosphorus compounds (OPC), such as pesticides (chlorophene, karbofos) or nerve agents (sarin, soman), complex use of pharmacological antidotes is of critical importance. These substances block the

enzyme acetylcholinesterase (ACE), resulting in a sharp increase in acetylcholine levels at synapses, leading to cholinergic crisis. Treatment requires simultaneous use of multiple antidotes:

Atropine: By blocking M-cholinergic receptors, it eliminates the muscarinic effects of acetylcholine (bronchospasm, bradycardia, salivation). However, atropine itself has no specific antidote, and overdose is dangerous.

Oximes (Pralidoxime, Diacetyl): They are called ACE reactivators. Oximes reactivate the enzyme bound to organophosphorus compounds, but this is only effective in the first hours after poisoning, before enzyme "aging" occurs.

Drug overdose is one of the most common causes of poisoning cases. In particular, poisoning with psychotropic, cardiovascular, and analgesic drugs is frequently encountered.

In summary, antidotes are a powerful tool of modern medicine, and their study, development, and rational application remain an urgent scientific and practical task. Healthcare workers, especially emergency medicine, intensive care, and general practice physicians, must possess deep knowledge of the basic principles of antidote therapy, the characteristics of existing antidotes, and guidelines for their application. This, in turn, serves to protect public health and reduce mortality and disability resulting from poisoning.

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