Antidotes and their Mechanism of Action: A Systematic Review

ABSTRACT

An antidote is a therapeutic agent that counteracts the hazardous effects of a medicine or toxin, according to the International Programmed of Chemical Safety. Antidotes have been defined as agents that alter the poisonous substance's kinetics or interfere with its impact at receptor sites. This could be due to the poison being prevented from being absorbed, bound, and neutralized immediately, antagonizing its end-organ impact, or inhibiting conversion to more hazardous metabolites. The kind of toxin eaten, the anticipated amount taken by the individual, the route of exposure, clinical toxicity characteristics, half-life, and pharmacokinetics, as well as the risk versus benefit of administering the antidote, all influence the length of antidotal therapy. An infusion may be necessary if the antidote has a short half-life, especially if poisoning symptoms return. To treat the negative effects of toxins, it is required. Occasionally, that intervention is necessary. may entail the use of pharmacological antagonists, also referred to as an antidote The most common poisons, according to the American Association of Poison Control Centers, include Acetylcysteine, naloxone, atropine, and deferoxamine are some of the most widely used antidotes.

Key-Words: Antidote, Poison, Pesticides, Insecticides, Acetylcysteine

INTRODUCTION

Poisoning occurs when medications, chemicals, venoms, or gases are swallowed, inhaled, touched, or injected, resulting in harm or death. Many chemicals, such as pharmaceuticals and carbon monoxide, are only dangerous at large doses or concentrations. Others, like cleansers, are only harmful if consumed. Acute poisoning with diverse substances is not unusual to place everywhere [1]. The in advance the preliminary resuscitations, gastric decontamination and use of unique antidotes, the higher the outcome. Death because of poisoning has been acknowledged because of time immemorial. Poisoning is a prime hassle all around the world, although it's kind and the related morbidity and mortality range from the United States of America to the United States of America. According to the felony gadget (legal system) of our country, all poisoning dying instances are recorded as unnatural dying and a medico-felony post-mortem is routine [2].

Organophosphorus poisoning takes place very usually in southern India, in which farmers shape a widespread percentage of the populace who usually use organophosphorus compounds like parathion as insecticides. Thus, because of the clean accessibility of those compounds, a huge wide variety of suicidal instances are encountered in this region. In addition to that, snakebite is a not unusual place acute scientific emergency confronted through rural populations in tropical and subtropical nations with heavy rainfall and humid climate [1,3]. A general 1373 poisoning instances had been investigated. The prevalence and fatality fee changed into located to be better in men in comparison to females (M/F ratio 1.89:1). Insecticides had been located to be the agent of poisoning in 26.29 cases, and 11.07% of all of the instances had been agricultural workers. Pesticide self-poisoning is a not unusual place method of suicide in India. Banning quite dangerous insecticides from agricultural use has been a success in decreasing general suicide numbers in numerous South Asian nations without affecting agricultural output [2,4].

ANTIDOTES

Antidotes are substances that counteract the effects of poisons and toxins. Antidotes work by stopping the toxin from being absorbed, binding and neutralising the poison, antagonising the poison's end-organ impact, or inhibiting the toxin's conversion to more dangerous metabolites. Antidotes are pharmaceuticals that counteract the effects of a poison or toxin. Antidotes work by preventing the toxin from being absorbed, binding and neutralising the poison, antagonising the poison's end-organ effects, or inhibiting the toxin's conversion to additional toxic metabolites. Antidote management may result in not just a reduction in free or active toxin levels, but also a

reduction in the toxin's end-organ effects by mechanisms such as aggressive inhibition, receptor blockage, or direct antagonism of the toxin. The reduction of loose toxin levels can be achieved by using specific and non-specific retailers that bind to the toxin. Activated charcoal is the most often utilised non-specific binding agent. Chelating retailers, bio scavenger treatment, and immunotherapy are examples of specific binders. Stronger removal can be accomplished in some cases by using urinary alkalization or hem adsorption. Antidotes work by a variety of methods, including competitive inhibition of enzymes (e.g. ethanol for methanol poisoning), an increase of enzyme performance (e.g. oximes for organophosphorus poisoning), and aggressive receptor blocking (e.g. naloxone, flumazenil). In paracetamol and cyanide poisoning, drugs like N-acetyl cysteine and sodium thiocyanate reduce the development of toxic metabolites [3,4]. To prevent the end-organ effects of organophosphorus poisoning, drugs such as atropine and magnesium are utilised. Vitamins such as vitamin K, folic acid, and pyridoxine are used to counteract the effects of warfarin, methotrexate, and INH in the event of toxicity or overdose. This summary provides an overview of antidotes' role in the poisoning. An antidote is a therapeutic substance that counteracts the harmful effects of a medicine or toxin, according to the International Programme of Chemical Safety. Antidotes are defined as medications that "change the kinetics of the deadly chemical or interfere with its effect at receptor sites." four This might be due to the poison being prevented from being absorbed, bound, and neutralised directly, antagonising its end-organ impact, or inhibiting conversion to additional harmful metabolites. five The healing index or ratio (TD50/ED50), which is the ratio of the toxic dosage (TD) or death dose (LD) to the potent dose (ED), is used to characterise a chemical's protection (ED). According to this definition, an antidote is a substance that "increases the indicated lethal amount of poison [4,5].

Mechanism of antidotes against drugs acting on nervous system

There are various types of drugs which act on the CNS like anticonvulsants, narcotic analgesics, sedatives, antidepressants, CNS stimulants, NSAIDs etc. These drugs can speed up or slow down the transfer of electrochemical messages between neurons in the brain. Acetaminophen poisoning is very common among NSAIDs and acetylcystein used as the antidote for acetaminophen poisoning (Table 1). It acts by replenishing glutathione levels in the liver [1]. In anticholinergics poisoning, physostigmine is used as antidote. It is the only reversible acetylcholinesterase inhibitor capable of directly antagonising the CNS signs of anticholinergic toxicity [2]. Atropine is the mostly used antidote in anticholinesterases poisoning.

It prevents the effects of acetylcholine, including excess acetylcholine caused by cholinesterase inhibition [3]. Flumazenil is used as antidote in benzodiazepines poisoning which comes under sedatives class of drugs that act on CNS. It is a selective competitive antagonist of the gamma-aminobutyric acid receptor that is the sole specific antidote for benzodiazepine toxicity [4]. Opioid poisoning is the common in which naloxone is used as antidote. It potentially is a mu-opioid–receptor competitor that reverses all indications of opioid intoxication [5].

Levocarnitine is used as antidote in valproic acid poisoning. It reduces carnitine production by lowering alpha-ketoglutarate levels, which may contribute to carnitine insufficiency [6]. In barbiturates poisoning, bemigride is used as antidote which is a CNS stimulant [7]. Pilocarpine is commonly used as antidote in atropine poisoning. It acts by blocking acetylcholinesterase [8]. In amphetamine poisoning, Propanolol is used as antidote. It activates the sympathetic nervous system and inhibits the neuronal reuptake of catecholamines and induces the peripheral release of catecholamines [9]. In salicylates poisoning, sodium bicarbonate is used as antidote. Patients with salicylate intoxication are mediated by the formation of metabolic alkalosis, which reduces the quantity of lipid-soluble salicylate [10]. Caffeine is the CNS stimulant in which esmolol is used as antidote in caffeine poisoning. Hypotension and tachycardia are reversed when theophylline or caffeine overdose generates excessive beta-adrenergic activity [11]. Physostigmine is used as antidote in tricyclic antidepressants poisoning. It is capable of correcting both the central and peripheral aspects of the anticholinergic syndrome caused by tricyclic antidepressant overdosage [12]. In dopamine poisoning Phentolamine is used as antidote. It produces competitive inhibition of alpha-adrenergic receptors, which produces muscle relaxation and blood vessel enlargement. Blood pressure is lowered as a result of blood vessel widening [13].

Cyproheptadine is used as antidote in serotonin reuptake inhibitors poisoning. It produces 5-HT2A receptor-blocking action makes it a powerful 5-HT (serotonin) antagonist [14]. In bupivacaine poisoning, Intralipid is used as antidote. These are absorbed into the plasma's lipid emulsion and eliminated from toxicity-affected tissues and it elimination from cardiac tissues was improved by using a lipid emulsion [15]. Naloxone is the antidote used in clonidine poisoning. Endogenous opioid release is induced by clonidine, which should respond to naloxone administration [16]. In phenytoin poisoning which comes anticonvulsant class of drugs, Midazolam is the drug used as antidote. Midazolam's anticonvulsant properties are linked to the

brain's motor pathways becoming overloaded with GABA and it works by relaxing muscles by acting on glycine receptors [17]. Bromocriptine is used as antidote in haloperidol poisoning. Bromocriptine is an effective treatment for illnesses linked with prolactin hypersecretion because increased dopaminergic activity in the tuberoinfundibular pathway reduces prolactin secretion [18]. In salbutamol poisoning salbutamol is the drug used as antidote. It competes with sympathomimetic neurotransmitters for binding to receptors, which inhibits sympathetic stimulation of the heart [19]. Vasopressin is used as antidote in phenoxybenzamine poisoning. Vasopressin binds to V2 receptors on the cell surface of tubular cells, initiating an intracellular cascade that results in the generation of the water channel, aquaporin-2. In vercuronium poisoning, sugammadex is used as antidote. It selectively binds rocuronium or vecuronium, thereby reversing their neuromuscular blocking action [20]. Metoprolol is used as antidote in dobutamine poisoning. It works by blocking the action of certain natural chemicals in your body, such as epinephrine, on the heart and blood vessels [21]. Physostigmine is mostly used antidote in amitriptyline poisoning. It's a reversible inhibitor of acetylcholinesterase, the enzyme that breaks down acetylcholine in the neuromuscular junction's synaptic cleft [22].

In case of extrapyramidal symptoms diphenhydramine is used as antidote. It works as an inverse agonist at the H1 receptor, reversing histamine's actions on capillaries and so lowering allergic response symptoms [23]. Aspirin is the common poisoning in which N-acetylcysteine + NH_4Cl used as antidote. It provides cysteine for glutathione synthesis and possibly to form an adduct directly with the toxic metabolite of acetaminophen. Phentolamine is used as antidote in MAOI's poisoning. Vasodilation due to α1 blockade and the non-selective α-blockers can cause a much more pronounced reflex tachycardia than the selective α1 blockers [24]. In epinephrine poisoning Prazosin is used as antidote. It promotes vasodilation of blood vessels and so lowers blood flow resistance by inhibiting alpha-1 receptors on muscle cells that surround blood vessels [25]. Sodium bicarbonate used as antidote in noncyclic antidepressant poisoning. To battle clinical signs of acidosis, boosting plasma bicarbonate levels, which are known to buffer excess hydrogen ion concentration and so raise solution pH [10].

Mechanism of antidotes against metals, pesticides and chemicals:

In cyanide poisoing, Amyl nitrite it used as antidote. The cyanide antidote works by releasing the cyanide from the cytochrome by combining it with methemoglobin (ferric haemoglobin) [26]. Fomepizole is widely ethylene glycol antidote. It inhibits the harmful alcohol's binding via

interacting with the zinc element of ADH and the coenzyme nicotinamide-adenine dinucleotide [27]. Pralidoxime is used as antidote in organophosphates (OP). It functions by binding to the enzyme's anionic site (Table 2). The pralidoxime molecule is near the OP molecule at this location [3]. In iron poisoing, Deferoxamine is common used as antidote. Deferoxamine, a chelating medication that may remove iron from tissues and liberate iron from plasma, should be given to patients with systemic toxicity, metabolic acidosis, increasing symptoms, or a blood iron level indicative of moderate or severe toxicity [28]. Dimaval it has been used as antidote in the lead and mercury poisoning. Chelating agent that form complexes with various heavy metals. They are related to dimercaprol, which is another chelating agent [29]. Atropine it widely used as carbamates poisoning as antidote. Carbamates reversibly bind to acetylcholinesterase, resulting in acetylcholinesterase inhibition and a rise in acetylcholine levels, which atropine competitively antagonises at muscarinic receptors [3]. In arsenic poisoning, Dimercaprol is used as antidote. Dimercaprol is a dithiol that works by forming a stable five-membered ring between its sulfhydryl groups and certain heavy metals to neutralise toxicity and facilitate excretion [30]. Calcium gluconate it has been widely used as antidote in hydrofluoric acid poisoning. Calcium gluconate combines with hydrofluoric acid to generate calcium fluoride, which is insoluble and non-toxic [31].

In magnesium sulphate poisonin, Calcium gluconate is used as antidote. When taken orally, calcium gluconate is the gluconate salt of calcium, and calcium as the gluconate salt helps maintain calcium balance and prevent bone loss [32]. Dyeserkrepol, is mostly common used antidote in the treatment of antimony and stibine poisoning. It exerts its action by blocking toxin absorption, binding and neutralising the poison, or antagonising the poison's end-organ effect by chelation [33]. Dichlorvas it is the most poisoning substances in which, Pralidoxime is widely used as antidote. This aids in the reduction of cholesterol levels. Pralidoxime is used to reactivate cholinesterase that has been inactivated due to phosphorylation from an organophosphate pesticide or a similar substance. After that, the stored acetylcholine may be destroyed, and neuromuscular connections can resume normal function [34]. In Formaldehyde poisoning, folic acid is used as antidote. It transforms the formic acid that has been produced into water and carbon dioxide [35]. Hydrogen Sulphide Diethylenetriamine it common antidote that used in the treatment of hydrogen sulphide. Chelating agents bind to radioactive elements or poisons that enter the body and retain them there. The chelating agent is attached to a radioactive substance or toxin and subsequently excreted in the urine [36].

Dyeserkrepol, it is used commonly as antidote. In the treatment of antimony poisoning. It exerts its action by blocking toxin absorption, binding and neutralising the poison, or antagonising the poison end-organ effect by chelation [33]. In dichlorvas poisoning, Pralidoxime is used as antidote. Pralidoxime is used to reactivate cholinesterase that has been inactivated due to phosphorylation from an organophosphate pesticide or a similar substance. After that, the stored acetylcholine may be destroyed, and neuromuscular connections can resume normal function [34]. Diethylenetriamine is widely used as antidote in the uranium poisoning. Chelating agents bind to radioactive elements or poisons that enter the body and retain them there. The chelating agent is attached to a radioactive substance or toxin and subsequently excreted in the urine [36]. In Acetonitrile poisoning , Dicobalt is used as antideote. It's a cyanide antidote that relies on cobalt's capacity to produce stable cyanide complexes. Cobalt cyanides are formed when one mole of cobalt binds to six moles of cyanide, resulting in less hazardous Cobalt cyanides that can be eliminated in the urine. Penicillamine is mostly used as antiodote in the gold poisoning. Heavy metals such as lead, copper, and mercury are chelated and formed into a soluble complex that is eliminated in the urine by the kidneys [37].

In Thallium poisoning, Prussian Blue is used as antidote. It works through ion exchange, adsorption, and mechanical trapping inside the crystal structure, and it has a strong affinity for both radioactive and non-radioactive caesium and thallium [38]. Calcium is main antidote for fluoride poisoining. It to bind and inactivate the fluoride ion [39]. In Fluroacetate poisoning, Acetate is widely used as antidote. It binds to major histocompatibility complex molecules and inhibits the T cell response to several myelin antigens [40]. Calcium salt is used mostly as antidote in Strontium poisoning. It acts by neutralizing hydrochloric acid in gastric secretions. Haloalkylamine is used as antidote in cyclopropane poisoning. It by blocking the effect of nerves in the sympathetic nervous system [41]. Methylene blue is used as antidote in para-aminopropiophene poisoning. To boost the activity of NADH-methemoglobin reductase, an enzyme that assists in the transformation of ferric iron back to ferrous iron [42]. In Endosulfan poisoning, Cholestyramine is used commomly as antidote. It binds to bile acids in the intestine. This prevents their absorption, and the cholestyramine/bile acid complexes are eliminated in the stool. As a result, the body loses bile acids. Atropine sulphate is used mainly as antidote in malathion poisoning. It competitively inhibits the effects of acetylcholine at muscarinic cholinergic receptors, including excess acetylcholine caused to organophosphorus intoxication [3]. Copper sulphat is mostly used as antidote in phosphorus

poisoning. It bind to functional groups of protein molecules in fungi and algae and cause protein denaturation, producing cell damage and leakage [43].

Mechanism of antidotes against cardiovascular drugs

Glucagon by activating adenyl cyclase increases cardiac inotropy directly, circumventing beta blockage [44]. Phytonadione reduces the functional levels of vitamin K–dependent blood coagulation proteins [45]. Protamine sulfate forms a salt aggregation with a heparin, strongly anionic anticoagulant (Table 3). The resulting salt aggregate is inactive and lacks anticoagulant properties [46]. Oxygen, binds to haemoglobin, lowering oxygen-carrying capacity, and myoglobin, impairing cardiac output and resulting in cerebral ischemia and oxygen levels [47]. Methylene blue binds to heme group of methemoglobin is reduced from methemoglobin to haemoglobin [48]. Octreotide binds to somatostatin receptors, calcium channels shut, blocking calcium influx and consequent insulin release [49]. Digoxin Immune Fab attaches to digoxin molecules, preventing them from attaching to their action sites on cells in the body [50]. Sodium bicarbonate alkalinization raises the electrochemical gradient across cell membranes, which helps sodium channels unload [10]. Esmolol acts as a competitive antagonist of beta-1-adrenergic receptors [51]. Quinidine is a sodium channel blocker and using the sodium bicarbonate raises the serum pH and boosting extracellular sodium are both benefits of sodium bicarbonate [52]. Glucose raises blood glucose levels by blocking glycogen synthesis and boosting glucose production from proteins or fats [53]. Potassium Iodide prevents the thyroid from absorbing radioactive iodine in a radiation emergency, sparing it from harm and lowering the chance of thyroid cancer [54]. Aminocaproic Acid inhibits plasminogen activation, which reduces plasminogen conversion to plasmin [55].

The endogenous opioid release is induced by clonidine, which should respond to naloxone administration [16]. Heparin works primarily by speeding up the pace at which antithrombin neutralises certain active coagulation factors [56]. The oxytocin-mediated release of inositol trisphosphate from the myometrial cell membrane is inhibited by atosiban. Nitroprusside by attaching to oxyhaemoglobin, it produces cyanide, methaemoglobin, and nitric oxide. In vascular smooth muscle, NO stimulates guanylate cyclase, which increases intracellular cGMP synthesis [57]. Propranolol competes with sympathomimetic neurotransmitters for binding to receptors, which inhibits sympathetic stimulation of the heart [19]. Andexanet acts as a decoy and sequesters rivaroxaban or apixaban, inhibiting them from binding to natural factor

Xa [58]. Vasopressin binds to V2 receptors on the cell surface of tubular cells, initiating an intracellular cascade that results in the generation of the water channel, aquaporin-2. Aminocaproic acid destroys fibrin clots, fibrinogen, and other plasma proteins, including procoagulant factors V and VIII [59]. Metoprolol works by blocking the action of certain natural chemicals in your body, such as epinephrine, on the heart and blood vessels [21]. Sodium thiosulfate catalyses the conversion of cyanide to the harmless thiocyanate, which uses sodium thiosulfate as a sulphur donor [60]. Lipid emulsion infusion creates an expanded lipid phase, and the resulting equilibrium drives toxic drugs from tissue to the aqueous plasma phase than to the lipid phase [61]. Prazosin promotes vasodilatation (widening) of blood vessels and so lowers blood flow resistance [25].

Mechanism of antidotes against antibiotics and anticancer agents

Antibiotics are the drugs which destroy or slow down the growth of bacteria like penicillins and these fight certain infections and can save lives when properly used but overdose leads to antibiotics poisoning and where certain antidotes are used. Anticancer agents are the drugs like vincristine, fluorouracil, methotrexate etc. These are used to treat the cancer and certain antidotes are available for their overdose that leads to poisoning (Table 4). Pyridoxine is used as antidote in isoniazid poisoning. It inhibits pyridoxine phosphokinase, which causes pyridoxal-5'-phosphate to be depleted [62]. In methotrexate poisoning which belongs to antimetabolites class of anticancer drugs where leucovorin is used as antidote. It is a folate derivative that does not need to be reduced by the enzyme dihydrofolate reductase before it can be used in one-carbon transfer reactions like DNA synthesis in the body [3]. In cyclophosphamide poisoning mesna is used as antidote. It produces competitive inhibition of alpha-adrenergic receptors, which results in muscle relaxation and blood vessel dilation. Blood pressure is reduced as a result of the widening of blood vessels [63]. Leucovorin Calcium is used as antidote in fluorouracil poisoning. It is a folate derivative that does not need to be reduced by the enzyme dihydrofolate reductase before it can be used in one-carbon transfer reactions like DNA synthesis in the body [64]. In methotrexate poisoning folinic acid is used as antidote. Folic acid antagonists are neutralised by folic acid, whereas fluoropyrimidines are enhanced by folinic acid [65].

Hyaluronidase is used as antidote in vincristine poisoning. It cleaves hyaluronic acid, cleaves the glucosaminidic bond between C1 of glucosamine and C4 of glucuronic acid [66]. In dapsone poisoning methylene blue is used as antidote. It reduces MetHb levels by acting as a cofactor for

NADPH [67]. Uridine triacetate is used as antidote in capecitabine poisoning. Uridine reduces 5-FU-induced cell damage and death competitively [68]. In penicillin poisoning epinephrine is used as antidote. It produces increased vascular smooth muscle contraction, pupillary dilator muscle contraction, and intestinal sphincter muscle contraction [69].

Mechanism of antidotes used in animal bite and food poisonining

Polyvalent Immune fab is used as antidote in snakebite poisoning. It Works by binding and neutralizing venom toxins, facilitating their redistribution away from target tissues [70]. In mushroom poisoning, Acetylcysteine is used as antidote. It enhances glutathione stores. Phentolamine is the antidote in cheese reaction (Table 5). It causes muscle relaxation and blood vessel expansion by competitively blocking alpha-adrenergic receptors [24]. In curare poisoning, Tensilon is used as antidote. It works by reversible acetylcholinesterase inhibition [71]. In cholecalciferol (CCF) poisoning, Pamidronate Sodium used as antidote. It can attenuate CCF-induced toxicosis and other forms of hypercalcemia in dogs that are linked to accelerated bone resorption [72]. Antiserum which is also botulism antitoxin is used as antidote in botulism poisoning. It acts through antibody antigen-binding fragments that stop the bacterium species Clostridium botulinum from producing a neurotoxin [73]. Activated charcoal is used as the Universal antidote. It adsorbs ingested toxins within the gastrointestinal tract preventing the systemic absorption of that toxin [74]. In datura poisoning, Physostigmine is used as antidote. It acts by interfering with acetylcholine metabolism. It's a reversible inhibitor of acetylcholinesterase [75]. Antivenin is the antidote in black widow spider poisoning. It acts by binding to and neutralizing venoms [76]. Antirabies vaccine is used as antidote in dogbite poisoning. It works by causing your body to produce its protection (antibodies) against the rabies virus [77].

CONCLUSION

An antidote is a therapeutic agent that counteracts the hazardous effects of a medicine or toxin, according to the International Programmed of Chemical Safety. Antidotes have been defined as agents that alter the poisonous substance's kinetics or interfere with its impact at receptor sites. This could be due to the poison being prevented from being absorbed, bound, and neutralized immediately, antagonizing its end-organ impact, or inhibiting conversion to more hazardous metabolites. The majority of poisonings can be handled without requiring extensive medical attention. If treatment is needed, it is usually in the form of gastrointestinal

decontamination with activated charcoal to prevent the toxin from being absorbed and causing toxicity. To cure the harmful consequences of toxins, more severe life-support measures may be required in a small percentage of patients. The usage of pharmacological antagonists, sometimes may be used in some cases.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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Table 1. Mechanism of antidotes against drugs acting on nervous system

Drug/Poison	Antidote, Dose	Mechanism of Action	Reference
Acetaminophen	Acetylcysteine, 300 mg/kg total dose, infused as 150 mg/kg over 15 min, i.v.	It's a glutathione precursor that boosts the glutathione concentration available for NAPQI conjugation. Because of covalent binding to proteins and nucleic acids, NAPQI is particularly toxic to the liver. NAPQI, on the other hand, is rapidly detoxified by forming cysteine and mercapturic acid conjugates with glutathione. Acetylcysteine works to protect the liver by replenishing glutathione levels in the liver.	[1]
Anticholinergics	Physostigmine, Adults - Begin with 0.5 mg to 2 mg, with a minimum of 10 to 30 minutes between doses. Pediatrics-start at 0.02 mg/kg, with a maximum dose of 0.5 mg/dose, for a total of 2 mg; repeat every 5 to 10 minutes, i.v. or i.m.	Physostigmine, an uncharged tertiary amine that rapidly crosses the blood-brain barrier, is the only reversible acetylcholinesterase inhibitor capable of directly antagonising the CNS signs of anticholinergic toxicity.	[2]
Anticholinesterases	Atropine, 0.4 mg to 0.6 mg, i.v. or i. m. or s.c.	Atropine prevents the effects of acetylcholine, including excess acetylcholine caused by cholinesterase inhibition.	[3]
Benzodiazepines	Flumazenil, 0.1 mg/min infusion, i.v.	Flumazenil is a selective competitive antagonist of the gamma-aminobutyric acid receptor that is the sole specific antidote for benzodiazepine toxicity; it reverses the effects of Benzodiazepines.	[4]
Opioids	Naloxone, 0.5 to 15 mg, i.v.	It potentially is a mu-opioid–receptor competitor that reverses all indications of opioid intoxication.	[5]
Valproic acid	Levocarnitine, Based on the patient condition and other co-morbid conditions	Valproic acid reduces carnitine production by lowering alpha-ketoglutarate levels, which may contribute to carnitine insufficiency. Carnitine supplementation is thought to promote valproic acid	[6]

		beta-oxidation, hence decreasing cytosolic omega-oxidation and the formation of harmful metabolites linked to liver damage and ammonia buildup. A pre-existing carnitine shortage or a deficiency generated by valproic acid may aggravate valproic acid-associated hepatotoxicity and hyperammonemia encephalopathy.	
Barbiturates	Bemigride, Based on the patient condition and other co-morbid conditions	Bemegride is a CNS stimulant	[7]
Atropine	Pilocarpine, Adult-5 mg/7.5 mg, oral	By blocking acetylcholinesterase	[8]
Amphetamine	Propanolol, Adult-20 mg/5ml or 1 mg/ml Pediatric-4.28 mg/ml, oral/i.v.	Amphetamine activates the sympathetic nervous system and inhibits the neuronal reuptake of catecholamines and induces the peripheral release of catecholamines.	[9]
Salicylates	Sodium bicarbonate, 650 mg/75 mg/ml, oral/i.v.	The therapeutic benefits of sodium bicarbonate in patients with salicylate intoxication are mediated by the formation of metabolic alkalosis, which reduces the quantity of lipid-soluble salicylate.	[10]
Caffeine	Esmolol, 0.025-0.05 mg/kg/min, i.v. infusion	Hypotension and tachycardia are reversed when theophylline or caffeine overdose generates excessive beta-adrenergic activity.	[11]
Tricyclic antidepressants	Physostigmine, Depending on the patient condition	The only parasympathomimetic medicine capable of correcting both the central and peripheral aspects of the anticholinergic syndrome caused by tricyclic antidepressant overdosage is physostigmine salicylate.	[12]
Dopamine	Phentolamine, 2 to 5 mcg/kg, i.v. infusion	The therapeutic benefits of phentolamine are due to its competitive inhibition of alpha-adrenergic receptors, which produces muscle relaxation and blood vessel enlargement. Blood pressure is lowered as a result of blood vessel widening.	[13]

Serotonin Reuptake Inhibitors	Cyproheptadine, 4mg tablet 2 mg/5ml, oral/i.v.	Its 5-HT2A receptor-blocking action makes it a powerful 5-HT (serotonin) antagonist.	[14]
Bupivacaine	Intralipid, 1.5 ml/kg as initial bolus followed by infusion at 0.25 ml/kg/min for 30-60 mins, i.v.	Highly lipid-soluble medicines, such as local and non-local anaesthetics, are absorbed into the plasma's lipid emulsion and eliminated from toxicity-affected tissues. Bupivacaine elimination from cardiac tissues was improved by using a lipid emulsion.	[15]
Clonidine	Naloxone, Adults 0.4 mg – 2 mg Pediatrics -10 mg, i.v.	The endogenous opioid release is induced by clonidine, which should respond to naloxone administration.	[16]
Phenytoin	Midazolam, 2 mg/ml oral syrup or 1 mg/ml injectable solution, oral/i.v.	It had something to do with GABA and its affinity for benzodiazepine receptors. A shared chloride channel couples two distinct GABA and benzodiazepine receptors. It raises the frequency with which chloride channels open. Membrane hyperpolarization and neural inhibition occur when both receptors are occupied. Midazolam's anticonvulsant properties are linked to the brain's motor pathways becoming overloaded with GABA. Midazolam works by relaxing muscles by acting on glycine receptors.	[17]
Haloperidol	Bromocriptine, 0.5 mg -1 mg tablet, oral 1 mg/Mml injectable solution, i.v.	Lactotrophs in the anterior pituitary are prevented from secreting prolactin by dopamine. Bromocriptine is an effective treatment for illnesses linked with prolactin hypersecretion because increased dopaminergic activity in the tuberoinfundibular pathway reduces prolactin secretion.	[18]
Salbutamol	Propranolol, Oral/i.v. depending on the patient condition	It competes with sympathomimetic neurotransmitters for binding to receptors, which inhibits sympathetic stimulation of the heart.	[19]
Phenoxybenzamine	Vasopressin, 20 units/mL, i.v.	Vasopressin binds to V2 receptors on the cell surface of tubular cells, initiating an intracellular cascade that results in the generation of the water channel, aquaporin-2.	[19]

Vercuronium	Sugammadex, 100 mg/mL, i.v.	selectively binds rocuronium or vecuronium, thereby reversing their neuromuscular blocking action.	[20]
Dobutamine	Metoprolol, Initial dose: 100 mg orally per day in single or divided doses Maintenance dose: 100 to 450 mg orally per day,oral.	works by blocking the action of certain natural chemicals in your body, such as epinephrine, on the heart and blood vessels. This effect lowers the heart rate, blood pressure, and strain on the heart.	[21]
Amitriptyline	Physostigmine, 1 mg/mL, i.v.	Interfering with acetylcholine metabolism It's a reversible inhibitor of acetylcholinesterase, the enzyme that breaks down acetylcholine in the neuromuscular junction's synaptic cleft. It activates both nicotinic and muscarinic acetylcholine receptors indirectly.	[22]
Extrapyramidal Symptoms	Diphenhydramine, 3 to 4 times a day, 25 to 50 mg orally Parenteral: 10 to 50 mg deep i.m. or i.v. as needed, and may increase to 100 mg if required. Maximum dose: 400 mg/day, oral, Intravenous	Diphenhydramine works as an inverse agonist at the H1 receptor, reversing histamine's actions on capillaries and so lowering allergic response symptoms.	[23]
Aspirin	N-acetylcysteine + NH_4Cl, Injectable solution (200 mg/mL) or oral effervescent tablets for oral solution 500 mg	Provide cysteine for glutathione synthesis and possibly to form an adduct directly with the toxic metabolite of acetaminophen, N-acetyl-p-benzoquinone imine.	
Monoamine Oxidase Inhibitors	Phentolamine, powder for injection 5 mg injectable solution 0.4 mg/1.7 mL,oral	Its primary action is vasodilation due to α1 blockade. Non-selective α-blockers can cause a much more pronounced reflex tachycardia than the selective α1 blockers	[24]

Epinephrine	Prazosin, depending on the patient condition, oral	Prazosin promotes vasodilation (widening) of blood vessels and so lowers blood flow resistance by inhibiting alpha-1 receptors on muscle cells that surround blood vessels. Its usage has the general advantage of lowering blood pressure.	[25]
Noncyclic Antidepressants	Sodium bicarbonate, i.v. or oral (325or 650 mg)	To battle clinical signs of acidosis, boosting plasma bicarbonate levels, which are known to buffer excess hydrogen ion concentration and so raise solution pH.	[26]

Table 2. Mechanism of antidotes against metals, pesticides and chemicals

Drug/Poison	Antidote, Dose	Mechanism of Action	Reference
Cyanide	Amyl nitrite, Sodium nitrite, oxygen, 10 ml at the rate of 2.5 to 5 ml/min, i.v.	The cyanide antidote works by releasing the cyanide from the cytochrome by combining it with methemoglobin (ferric haemoglobin). When sodium thiosulfate is added, the cyanide is converted to thiocyanate, which is eliminated through the kidneys, while the iron in haemoglobin is returned to its ferrous state.	[26]
Ethylene glycol	Fomepizole, 15 mg/kg, i.v./p.o.	Fomepizole is a safe and effective competitive inhibitor of ADH (>8000 times higher affinity than ethanol). Fomepizole inhibits the harmful alcohol's binding via interacting with the zinc element of ADH and the coenzyme nicotinamide-adenine dinucleotide.	[27]
Organophosphates	Atropine, Pralidoxime, 20-40 mg/kg infusion, i.v.	Pralidoxime is an enzyme reactivator for the acetylcholinesterase enzyme. It functions by binding to the enzyme's anionic site. The pralidoxime molecule is near the OP molecule at this location. Because the pralidoxime molecule has a higher propensity for being phosphorylated by the OP chemical than the enzyme's serine site, the pralidoxime molecule is phosphorylated instead of the enzyme. It generates an organophosphate-pralidoxime complex, which rapidly hydrolyzes.	[3]
Iron	Deferoxamine, 10 to 15 mg/kg/hr, i.m.	Deferoxamine, a chelating medication that may remove iron from tissues and liberate iron from plasma, should be given to patients with systemic toxicity, metabolic acidosis, increasing symptoms, or a blood iron level indicative of moderate or severe toxicity.	[28]
Lead, Mercury	Dimaval, 250 mg with an interval of 3-4 hours, oral	Chelating agent that form complexes with various heavy metals. They are related to dimercaprol, which is another chelating agent.	[29]
Carbamates	Atropine, Adult and pediatric-0.25 mg/0.3 ml,	Carbamates reversibly bind to acetylcholinesterase, resulting in acetylcholinesterase inhibition and a rise in acetylcholine	[3]

	i.m.	levels, which atropine competitively antagonises at muscarinic receptors.	
Arsenic	Dimercaprol, 10-12 mg/kg/day, i.m.	Dimercaprol is a dithiol that works by forming a stable five-membered ring between its sulfhydryl groups and certain heavy metals to neutralise toxicity and facilitate excretion.	[30]
Hydrofluoric acid	Calcium gluconate, 100 mg/ml. i.v.	Calcium gluconate combines with hydrofluoric acid to generate calcium fluoride, which is insoluble and non-toxic.	[31]
Magnesium Sulphate	Calcium gluconate, 100 mg/ml, i.v.	When taken orally, calcium gluconate is the gluconate salt of calcium, and calcium as the gluconate salt helps maintain calcium balance and prevent bone loss.	[32]
Antimony and Stibine	Dyeserkrepol, 100 mg injectable solution, i.v.	It exerts its action by blocking toxin absorption, binding and neutralising the poison, or antagonising the poison's end-organ effect by chelation.	[33]
Dichlorvas	Pralidoxime, 10-20 mg/ml solution, i.v. infusion	This aids in the reduction of cholesterol levels. Pralidoxime is used to reactivate cholinesterase that has been inactivated due to phosphorylation from an organophosphate pesticide or a similar substance. After that, the stored acetylcholine may be destroyed, and neuromuscular connections can resume normal function.	[34]
Formaldehyde	Folic acid, 400 mcg to 1mg tablet, oral	It transforms the formic acid that has been produced into water and carbon dioxide.	[35]
Hydrogen Sulphide	Amyl nitrate, 0.3 ml liquid for inhalation	NO activates guanylate cyclase, which increases intracellular cGMP production in vascular smooth muscle. It decreases systemic and pulmonary arterial pressure (afterload) and cardiac output due to peripheral vasodilation rather than coronary artery dilation.	[78]
Uranium	Diethylenetriamine Penta acetic acid, Adults-1 gm Pediatrics-14 mg/kg, i.v.	Chelating agents bind to radioactive elements or poisons that enter the body and retain them there. The chelating agent is attached to a radioactive substance or toxin and subsequently excreted in the urine.	[36]
Acetonitrile	Dicobalt EDTA, depending on the patient condition	It's a cyanide antidote that relies on cobalt's capacity to produce stable cyanide complexes. Cobalt cyanides are formed when one mole of cobalt binds to six moles of	[36]

		cyanide, resulting in less hazardous Cobalt cyanides that can be eliminated in the urine.	
Gold	Penicillamine, 125 or 250 mg, oral	Heavy metals such as lead, copper, and mercury are chelated and formed into a soluble complex that is eliminated in the urine by the kidneys.	[37]
Thallium	Prussian Blue, 3 grams (6 capsules) orally 3 times a day; total daily dose of 9 grams, oral	Absorbent and chelating agent It works through ion exchange, adsorption, and mechanical trapping inside the crystal structure, and it has a strong affinity for both radioactive and non-radioactive caesium and thallium.	[38]
Fluoride	Calcium	Mechanism of these therapies is to bind and inactivate the fluoride ion.	[39]
Fluroacetate	Acetate, Monoacetin	Strong promiscuous binding to major histocompatibility complex molecules and inhibits the T cell response to several myelin antigens	[40]
Strontium	Calcium salt	Acts by neutralizing hydrochloric acid in gastric secretions.	[40]
Cyclopropane	Alpha-adrenergic blocking agents, Haloalkylamine	By blocking the effect of nerves in the sympathetic nervous system.	[41]
Para-aminopropiophene	Methylene blue, injectable solution 5 mg/mL (50 mg/10mL) single-dose ampule, i.v.	To boost the activity of NADH-methemoglobin reductase, an enzyme that assists in the transformation of ferric iron back to ferrous iron.	[42]
Endosulfan	Cholestyramine, 4g powder for oral suspension	Binds to bile acids in the intestine. This prevents their absorption, and the cholestyramine/bile acid complexes are eliminated in the stool. As a result, the body loses bile acids.	[42]
Malathion	Atropine sulphate, i.m. or i.v. depending on the patient condition	Competitively inhibits the effects of acetylcholine at muscarinic cholinergic receptors, including excess acetylcholine caused to organophosphorus intoxication.	[3]
Phosphorus	Copper sulphate, 5 mg, oral or i.v.	Copper ions appear to bind to functional groups of protein molecules in fungi and algae and cause protein denaturation, producing cell damage and leakage.	[43]

Gyrometrine	Pyridoxine, 100-500 mg, oral	Works via PLP as a chemical chaperone and a prosthetic group. Pyridoxine increases the expression, activity and peroxisomal targeting of AGT-170.	[79]
Carbon tetrachloride	Hyperbaric oxygen	Increases the generation of oxygen free radicals, which oxidize proteins and membrane lipids, damage DNA, and inhibit bacterial metabolic functions.	[80]
Mineral acids	Magnesium oxide, 140-400 mg, oral	neutralizes gastric acid by reacting with hydrochloric acid in the stomach to form magnesium chloride and water	[81]
Radioactive caesium	Prussian blue, 3 grams (6 capsules) orally 3 times a day; total daily dose of 9 grams, oral	Absorbent and chelating agent Within the crystal structure, it works by ion exchange, adsorption, and mechanical trapping.	[82]
Chlorine gas	Sodium bicarbonate	The major therapeutic action of sodium bicarbonate treatment is to raise plasma bicarbonate levels, which are known to buffer excess hydrogen ion concentration and, as a result, raise solution pH to counteract acidosis clinical symptoms.	[83]

Table 3. Mechanism of antidotes against cardiovascular drugs

Drug/Poison	Antidote, Dose	Mechanism of Action	Reference
Beta-Blocker	Glucagon, 1 mg, i.v.	By activating adenyl cyclase through a secondary mechanism distinct from that of catecholamines, glucagon increases cardiac inotropy directly, circumventing beta blockage.	[44]
Warfarin	Phytonadione, 5 mg / 2 mg/ml, oral/i.v.	Warfarin and other phenylamine antagonists block VKOR, disrupting the vitamin K cycle and reducing the functional levels of vitamin K–dependent blood coagulation proteins.	[45]
Heparin	Protamine Sulfate, Adult and pediatric - 10 mg/ml, i.v.	When exposed to the positive cationic arginine peptide of protamine, heparin, a strongly anionic anticoagulant, forms a salt aggregation. The resulting salt aggregate is inactive and lacks anticoagulant properties. Protamine has a fast start of the action, neutralises unfractionated heparin in less than 5 minutes, and has a half-life of around 10 minutes.	[46]
Carbon monoxide	Oxygen, Based on the patient condition and other co-morbid conditions	CO poisoning occurs when it binds to haemoglobin, lowering oxygen-carrying capacity, and myoglobin, impairing cardiac output and resulting in cerebral ischemia and oxygen levels in the blood and aiding in the removal of carbon monoxide from the circulation	[47]
Nitrates	Methylene blue, 1 mg/ml or 0.2 ml/kg, i.v. infusion	The heme group of methemoglobin is reduced from methemoglobin to haemoglobin once methylene blue is degraded to leucomethylene blue. Methemoglobin's half-life can be reduced from hours to minutes using methylene blue.	[48]
Sulfonylurea	Octreotide, Adult-20 mg/0.05 mg/ml Pediatric-0.05 mg/ml, oral/i.v.	When octreotide binds to somatostatin receptors, calcium channels shut, blocking calcium influx and consequent insulin release (Fig. 1). This mechanism contributes to octreotide's efficacy in the treatment of sulfonylurea-induced hypoglycemia because it binds "downstream" from where sulfonylureas act on the cells and blocks an event required for insulin production.	[49]
Digoxin	Digoxin Immune Fab, 40 mg/vial, i.v.	Digoxin immune fab attaches to digoxin molecules, preventing them from attaching to their action sites on cells in the body. The Fab fragment-digoxin complex builds up in the bloodstream before being eliminated by the kidney.	[50]

Sodium channel blockers	Sodium bicarbonate, 1 mEq/kg, i.v. bolus	Raising the serum pH and boosting extracellular sodium are both benefits of sodium bicarbonate. Alkalinization raises the electrochemical gradient across cell membranes, which helps sodium channels unload. It may also increase the offending agent's protein binding.	[10]
Metoproterenol	Esmolol, 10 mg/ml, i.v.	Esmolol is a cardio-selective, short-acting beta-blocker and that acts as a competitive antagonist of beta-1-adrenergic receptors in myocytes. It raises atrioventricular refractory time, lowers myocardial oxygen demand, and slows atrioventricular conduction.	[51]
Quinidine	Sodium bicarbonate, 1 mEq/kg, i.v. bolus	As quinidine is a sodium channel blocker and using the sodium bicarbonate raises the serum pH and boosting extracellular sodium are both benefits of sodium bicarbonate. Alkalinization raises the electrochemical gradient across cell membranes, which helps sodium channels unload. It may also increase the offending agent's protein binding.	[52]
Insulin	Glucose, Adult-1 mg/0.2ml Pediatric-0.5 mg/0.1ml, i.v.	The hormone glucagon is produced by the pancreas, and it raises blood glucose levels by blocking glycogen synthesis and boosting glucose production from proteins or fats. The breakdown of glycogen into glucose in the liver is likewise accelerated by glucagon.	[53]
Radioactive Iodine	Potassium Iodide, 5 mCi/ml solution, oral	It works by reducing the size of the thyroid gland and lowering thyroid hormone production. Potassium iodide prevents the thyroid from absorbing radioactive iodine in a radiation emergency, sparing it from harm and lowering the chance of thyroid cancer. It works by reducing the size of the thyroid gland and lowering thyroid hormone production. Potassium iodide prevents the thyroid from absorbing radioactive iodine in a radiation emergency, sparing it from harm and lowering the chance of thyroid cancer.	[54]
Tissue Plasminogen Activator	Aminocaproic Acid, 5 ml/hour oral solution, oral	Aminocaproic acid inhibits plasminogen activation, which reduces plasminogen conversion to plasmin, an enzyme that breaks down fibrin clots, fibrinogen, and other plasma proteins, including procoagulant factors V and VIII.	[55]
Clonidine	Naloxone, Adults 0.4	The endogenous opioid release is induced by clonidine, which	[16]

	mg – 2 mg Pediatrics -10 mg, i.v.	should respond to naloxone administration.	
Ergotamine	Heparin, 2 mg tablet, oral	It works primarily by speeding up the pace at which antithrombin neutralises certain active coagulation factors, but alternative processes are possible. Heparin's antithrombotic action is closely linked to factor Xa suppression.	[56]
Oxytocin	Atosiban, 0.9 ml IV bolus injection over 1 minute followed by 3 hours IV loading i.v. infusion	Atosiban is a competitive vasopressin/oxytocin receptor antagonist and a nonapeptide desamino-oxytocin analogue . The oxytocin-mediated release of inositol trisphosphate from the myometrial cell membrane is inhibited by atosiban.	[84]
Ergot alkaloids	Nitroprusside, 10 mcg/kg/min for 10 mins, i.v.	Nitric oxide is produced when sodium nitroprusside is broken down in the bloodstream. By attaching to oxyhaemoglobin, it produces cyanide, methaemoglobin, and nitric oxide. In vascular smooth muscle, NO stimulates guanylate cyclase, which increases intracellular cGMP synthesis.	[57]
Salbutamol	Propranolol, Oral/i.v. depending on the patient condition	It competes with sympathomimetic neurotransmitters for binding to receptors, which inhibits sympathetic stimulation of the heart.	[19]
Rivaroxaban	Andexanet, 100 mg/single-use, i.v.	Andexanet alfa acts as a decoy and sequesters rivaroxaban or apixaban, inhibiting them from binding to natural factor Xa.	[58]
Phenoxybenzamine	Vasopressin, 20 units/mL,i.v.	Vasopressin binds to V2 receptors on the cell surface of tubular cells, initiating an intracellular cascade that results in the generation of the water channel, aquaporin-2.	[58]
Fibrinolytics	Aminocaproic acid, 250-1000 mg, oral or i.v.	suppresses plasminogen activation, lowering plasminogen conversion to plasmin (fibrinolysin), an enzyme that destroys fibrin clots, fibrinogen, and other plasma proteins, including procoagulant factors V and VIII.	[59]
Dobutamine	Metoprolol, Initial dose: 100 mg orally per day in single or divided doses Maintenance dose: 100	works by blocking the action of certain natural chemicals in your body, such as epinephrine, on the heart and blood vessels. This effect lowers the heart rate, blood pressure, and strain on the heart.	[21]

	to 450 mg orally per day,oral.		
Mechlorethamine	Sodium thiosulfate, injection solution 100mg/mL (10%) 250mg/mL (25%)	Methemoglobinemia is caused by sodium nitrite, which eliminates cyanide from mitochondria. The enzyme rhodanese catalyses the conversion of cyanide to the harmless thiocyanate, which uses sodium thiosulfate as a sulphur donor.	[60]
Cardiotoxic drugs	Lipid Emulsion	Lipid emulsion infusion creates an expanded lipid phase, and the resulting equilibrium drives toxic drugs from tissue to the aqueous plasma phase than to the lipid phase	[61]
Epinephrine	Prazosin, 1-5 mg, oral	Prazosin promotes vasodilation (widening) of blood vessels and so lowers blood flow resistance by inhibiting alpha-1 receptors on muscle cells that surround blood vessels. Its usage has the general advantage of lowering blood pressure.	[25]

Table 4. Mechanism of antidotes against antibiotics and anticancer agents

Drug/Poison	Antidote, Dose	Mechanism of Action	Reference
Isoniazid	Pyridoxine, 5 gms over 5 to 10mins, i.v.	Isoniazid inhibits pyridoxine phosphokinase, which causes pyridoxal-5'-phosphate to be depleted. Reduced gamma-aminobutyric acid production and acute toxicity manifested as convulsions result from this inhibition.	[62]
Methotrexate	Leucovorin, 200 mg/ml, i.v.	Leucovorin is a folate derivative that does not need to be reduced by the enzyme dihydrofolate reductase before it can be used in one-carbon transfer reactions like DNA synthesis in the body.	[3]
Cyclophosphamide	Mesna, 400 mg/ 100 mg/ml, oral/i.v.	Phentolamine's therapeutic advantages are attributable to its competitive inhibition of alpha-adrenergic receptors, which results in muscle relaxation and blood vessel dilation. Blood pressure is reduced as a result of the widening of blood vessels.	[63]
Fluorouracil	Leucovorin Calcium, 200mg/m^2, i.v.	Leucovorin is a folate derivative that does not need to be reduced by the enzyme dihydrofolate reductase before it can be used in one-carbon transfer reactions like DNA synthesis in the body.	[64]
Methotrexate	Folinic acid, 5 mg tablet or 10 mg/ml injection, oral/i.v.	Folic acid antagonists are neutralised by folic acid, whereas fluoropyrimidines are enhanced by folinic acid. Despite the presence of methotrexate, folic acid can enter cells via the decreased folate carrier and be converted to tetrahydrofolate, saving these cells from methotrexate toxicity.	[65]
Vincristine	Hyaluronidase, 150 U/ml, i.v.	Hyaluronidase, which also cleaves hyaluronic acid, cleaves the glucosaminidic bond between C1 of glucosamine and C4 of glucuronic acid. The hydrolysis of hyaluronic acid improves connective tissue permeability.	[66]
Dapsone	Methylene blue, Adult and pediaatrics-5 mg/ml, i.v.	Methylene blue reduces MetHb levels by acting as a cofactor for NADPH, but at large dosages, it can also act as an oxidising agent, oxidising the ferrous iron of the reduced haemoglobin to ferric state, converting Hb to MetHb and causing methemoglobinemia.	[67]
Capecitabine	Uridine triacetate, 10 grams oral granules	Uridine reduces 5-FU-induced cell damage and death competitively.	[68]

		In both normal and malignant cells, 5-FU disrupts nucleic acid metabolism. FdUMP (5-fluoro-2'-deoxyuridine-5'-monophosphate) and FUTP (5-fluorouridine triphosphate) are cytotoxic intermediates formed when cells metabolize 5-FU. FdUMP inhibits the synthesis of thymidine, which is necessary for DNA replication and repair.	
Penicillin	Epinephrine, 0.1-1 mg/mL i.v. or i.m. or oral	Increased vascular smooth muscle contraction, pupillary dilator muscle contraction, and intestinal sphincter muscle contraction are all caused by epinephrine.	[69]

Table 5. Mechanism of antidotes used in animal bite and food poisonining

Drug/Poison	Antidote	Mechanism of Action	Reference
Snakebite	Polyvalent Immune fab, 20-50ml/hr, i.v.	Works by binding and neutralizing venom toxins, facilitating their redistribution away from target tissues and their elimination from the body.	[70]
Mushrooms	Acetylcysteine, Depending on the patient condition	It enhances glutathione stores	
Cheese Reaction	Phentolamine, 5 mg to 10mg, i.m./i.v.	Phentolamine causes muscle relaxation and blood vessel expansion by competitively blocking alpha-adrenergic receptors (which are predominantly excitatory responses of smooth muscle and exocrine glands).	[24]
Curare	Tensilon, Depending on the patient condition	By reversible acetylcholinesterase inhibition	[71]
Cholecalciferol	Pamidronate Sodium, 3 mg/ml, i.v.	Pamidronate disodium can attenuate CCF-induced toxicosis and other forms of hypercalcemia in dogs that are linked to accelerated bone resorption.	[72]
Botulism toxin	Antiserum, Depending on the patient condition	Botulinum antitoxin, commonly known as botulism antitoxin, is made up of antibodies or antibody antigen-binding fragments that stop the bacterium species Clostridium botulinum from producing a neurotoxin.	[73]
Universal antidote for many poisons	Activated charcoal, 1 g/kg or 25-100 g, oral	Activated charcoal adsorbs ingested toxins within the gastrointestinal tract preventing the systemic absorption of that toxin. Activated charcoal only adsorbs toxins that are in the dissolved liquid phase via direct contact.	[74]
Datura	Physostigmine, 1 mg/mL, oral, i.v.	interfering with acetylcholine metabolism. It's a reversible inhibitor of acetylcholinesterase, the enzyme that breaks down acetylcholine in the neuromuscular junction's synaptic cleft.	[75]
Black widow spider	Antivenin	Antivenoms act by binding to and neutralizing venoms	[76]
Dog bite	Antirabies vaccine, Oral, i.v.	the vaccine works by causing your body to produce its protection (antibodies) against the rabies virus	[77]