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Review Article

A REVIEW ON VARIOUS TYPES OF TOXINS

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ABSTRACT

Toxins are poisonous substances which are produced naturally by organisms like plants, bacteria, algae, fungi, etc. They are also synthesized by man in the form of chemical pesticides, fungicides, etc. They are liberated into the atmosphere in the form of smoke from industries and into water bodies in the form of industrial effluents. Toxins cause harmful effects in humans in the form of ailments like food poisoning, caused by ingestion of food contaminated by microorganisms; cancer by inhalation of toxic fumes from industries etc. To prevent such ailments which may be fatal, one must take care to minimize exposure to sources of toxins and find alternative options which could help minimize pollution of the environment and make it safer for all organisms living in it.

Keywords: Toxins Contaminated, Pesticides, Pollution, Fungicides.

INTRODUCTION

Toxins are poisonous substances which, when ingested, inhaled or injected into an organism causes deleterious effects on the functioning of its organ systems. These could be either natural or artificial toxins. Natural toxins are synthesized in certain organisms as products of certain metabolic pathways and are generally used by them as a means of defense against predators. Artificial toxins are synthesized by human beings to eliminate harmful pathogens and pests which reduce the quality of life and the food we eat. Artificial toxins like smoke and harmful metals like mercury and lead are released into the atmosphere as industrial effluents. The effect of a toxin on living organisms is called toxicity and the branch of science which deals with various types of toxins and their effect on the metabolic activity of living organisms is called toxicology. Toxicity can be classified into four main categories namely, acute, sub acute, sub chronic and chronic toxicity, depending on the time taken for the appearance of symptoms and the severity of these symptoms.

Acute toxicity occurs due to exposure to a particular toxin for short intervals of time. Acute toxicity to titanium dioxide is seen in experimental animals in the form of pulmonary inflammation and increase in heart rate.[1,2] Tetrodotoxin, which occurs naturally in puffer fish causes symptoms of poisoning in patients within 24 hours.[3] Consumption of 100 g of the fish could be fatal.[3] Ingestion of agricultural pesticides results in appearance of symptoms within few hours, which could be fatal if treatment is not provided to the patient.[4] Acute toxicity to Cu, Cr and Zn causes death, loss of equilibrium and bloating of abdomen in White Sturgeon.[5] Acute toxicity to TiO_2 is manifested as necrosis of hepatocytes, swelling of the glomerulus, lesions in the brain, and a number of other symptoms.[1] In sub acute toxicity, the organism's

health is affected after few days of exposure. Sub acute exposure to a group of nine chemicals (dichloromethane, cadmium chloride, DEHP, aspirin, paraformaldehyde, loperamide, BHA, stannous chloride, spermine hydrochloride) showed signs of toxicity in rats after 28 days of exposure.[6] Sub chronic toxicity occurs when a substance causes toxic effect for more than one year but, less than the lifespan of the organism. Sub chronic diesel exhaust exposure for a period of six months caused neuroinflammation and worsened early signs of neurodegenerative disease in rats.[7] Sub chronic exposure to nanosilver causes signs of toxicity like inflammation, hepatocyte degradation, hepatic cord destruction, etc in guinea pigs.[8] Sub chronic exposure to a large dosage the juice of *Physalis peruviana* L. causes myocardial damage in experimental animals.[9] Chronic toxicity occurs when a substance causes toxic effects in an organism in a long period which may be as long as the lifespan of the organism. Chronic exposure to arsenic contaminates drinking water and causes cancers, especially of the lung and the skin.[10] Chronic exposure to lead causes damage to the basal ganglion, frontal and occipital lobes of the brain in adults working in lead paint factories.[11] Chronic exposure to ammonium nitrate fertilizers causes deformities of the head and the digestive system in tadpoles.[12] Toxins are classified on the basis of a number of criteria. On the basis of the source from which the toxin was produced or obtained, they can be of various types such as:

Metals as Toxins

Mercury

Mercury is released into the environment from sources like volcanic eruptions, combustion of fossil fuels and biomass and also from industries producing paints, batteries, etc.[13,14] Mercury is not only an environmental pollutant, but it also causes toxicity in human beings and other organisms. When mercury is released into water bodies, it is consumed by smaller organisms like crustaceans like shellfish. This later accumulates in the form methyl mercury in higher organisms like tuna and swordfish, as they feed on these crustaceans. The toxin enters human beings after consuming the crustaceans, tuna or sword fish.[15] The Minamata disease is a result of mercury toxicity.[16] This disease got its name from the fact that about two thousand people of Minamata in Japan who had consumed seafood developed neurological problems due to the destruction of nervous tissue.[16] The main symptoms of Minamata disease include convulsions, speech and eye sight problems, muscle weakness, swelling of neurons, etc.[16] It even caused salivation in cats. Patients with dental diseases who use dental amalgam and the doctors who apply the amalgam fillings have the risk of mercury exposure due to the vapour produced from them.[17] Exposure to mercury increases the risk of cardiovascular disease and myocardial infarction.[13]

Toxicity of Lead

Lead is released into the atmosphere during the combustion of fuel like gasoline containing lead and also by smoking tobacco.[18] Lead contaminates water by the use of lead pipes for water supply.[18] Lead can occur in the household dust of those houses where paints containing lead are used.[18,19] Lead is found in seaweeds, in large concentrations.[20] Lead effects the bone by increasing bone resorption, which can be indicated by the presence of crosslinked N-telopeptides of type I collagen in the urine. These telopeptides are obtained by the degradation of bone collagen.[21] Lead, being a neurotoxin has an adverse effect on the nervous system.[19] Children affected by lead poisoning suffer from convulsions, hyperactivity disorder and have lower IQ level.[19] Bone lesions can also be observed in infants suffering from lead poisoning.[19] There is a risk of lead poisoning among people who consume animals shot using lead bullets during hunting.[22] According to Bjerregaard and colleagues, the natives of Greenland who

consume the meat of waterfowls hunted using lead bullets had higher levels of lead, depending on the amount of flesh consumed.[22]

Microbial Toxins

Microbial toxins can be of different types like bacterial, fungal and algal toxins. Bacterial toxins are neurotoxins.[23] *Clostridium botulinum* produces botulinum neurotoxin, which enters into the body through consumption of contaminated food, gets diffused through the intestinal mucosa and enters into the blood stream through the intestinal villi.[23] After circulation through the blood, it affects the motor neuron endings.[23] The toxin blocks various neurotransmitters like acetylcholine, dopamine, aspartate, etc.[23] Tetanus toxin, which is produced by *Clostridium tetani* enters the body through wounds infected by the bacterium and eventually reaches the adrenergic, sensory and motor neurons.[23] It binds to receptors on the nerve endings, where it blocks a number of neurotoxins like serotonin, GABA (Gamma amino butyric acid), etc.[23] Algae like *Gonyaulax catenella,* when present in large concentration in sea water cause red tides which are highly toxic.[24] The toxin enters humans due to the consumption of fish affected by the toxin.[24] The algae *Pyrodinium phoneus,* which causes paralytic shellfish poisoning and *Mytillus californicus,* which causes mussel poisoning cause toxicity when consumed by humans.[24] Symptoms of algal poisoning include blockage of muscle and axonal conduction.[24] Toxins such as hepatotoxins, carcinogens and immunosuppressants can be produced by different species of *Alternaria, Fusarium, Aspergillus*, etc.[25] Fungal toxins like aflotoxin, which is produced by *Aspergillus flavus* and *Aspergillus parasiticus* causes mutations in DNA due to the formation of DNA adducts. This results in diseases like cancer. Fusaric acid methylamide is commonly found on contaminated fruits and vegetables.[26] On the basis of the substances contaminated, toxins are of various types, such as:

Food Contaminants

Selenium is a food contaminant which enters into the food chain when inorganic forms of selenium are converted into organic forms by plants and microorganisms.[15] Selenium toxicity, which is also called selenosis causes symptoms like hair fall, diarrhea, fatigue, loss of nails, deformity, etc.[15] Heterocyclic aromatic amines are present in excess, in pan fried and grilled meat and polycyclic aromatic hydrocarbons occur in food due to cooking methods like roasting and smoking or by the combustion of fossil fuels and firewood in the process of cooking.[15] Both categories of compounds are carcinogenic.[15] Saxitoxin, which is found in certain genera of shellfish like *Alexandrium* and *Gymnodium* causes paralytic shellfish poisoning.[15] Brevitoxin, which is found in *Karenia brevis* causes neurotoxic shellfish poisoning.[15] Dairy products like cheese are generally contaminated by *Escherichia coli, Staphylococcus aureus, Penicillium roqueforti.*[27] Contamination by *penicillium roqueforti* provides Roquefort cheese its flavour.

Honey can be contaminated by pesticides such as aldrin, amitraz, flumethrin, etc. are used to control pests and microorganisms which cause bee diseases.[28] The consumption of contaminated honey causes cancer, infertility, disorders of the endocrine system.[28] The consumption of fruits and vegetables, grown in soil contaminated by lead, causes neurotoxicity and hematological toxicity and the consumption of fish contaminated by mercury, causes inflammation of the digestive tract, damage to the kidneys and the nervous system.[29] Drinking water is contaminated by microorganisms like coliforms, which are found in the feces of organisms and by viruses like viruses like hepatitis virus, adenoviruses, etc. Consumption of the contaminated water causes diseases like gastroenteritis, hepatitis, etc.

Agricultural Contaminants

Agricultural contaminants include chemical insecticides, pesticides, fungicides, fertilizers

which not only pollute the environment, but also cause death and other harmful effects in human beings and other organisms. Exposure to insecticides like anticholinesterase, herbicides like paraquat, propanil and pesticides like endosulphan caused majority of deaths due to self poisoning in Srilanka.[30] Due to this, the use of chemicals like paraquat and endosulphan was banned.[30] *Bacillus thuringiensis* is used as a natural insecticide against insects of orders *Lepidoptera, Coleoptera* and *Diptera* due to the production of endotoxins like Cry proteins by the bacterium.[31] Cry proteins do not harm humans but the various virulence factors produced by the bacillus may harm humans.[31] *Bacillus cereus* produces endotoxins like Cyt K which causes food poisoning when consumed in the form of contaminated fruits and vegetables.[31] Exposure to household dust and soil containing organochlorine and organophosphate pesticides caused chronic and acute toxicity respectively, in the children of agricultural families.[32] Water contaminated by pesticides like DDT, HCB, which are drained from agricultural lands enters into the food chain through phytoplankton and later accumulates in higher levels of the food chain like fish, seabirds and eventually humans through biomagnifications.[33] The pesticide aldicarb which is generally used on banana effects humans by causing signs of toxicity like diarrhea, vomiting and improper functioning of the nervous system.[34]

Biosolids, which are obtained from sludge during the treatment of waste water contain many organic compounds such as polychlorinated biphenyls, polycyclic aromatic hydrocarbons, chlorinated naphthalene, synthetic musk, etc.[35] These compounds pollute the soil and cause symptoms of toxicity in humans by the consumption of contaminated farm products.[35]

Absorption and Binding of Toxin

Toxins can enter into the body through various routes such as oral consumption in the case of Botulinum toxin[36]; Dermal absorption of tetanus toxin through infected wounds[23] and ethidium bromide[37], and by respiration in the case of industrial chemicals. Toxins can also be absorbed through the mucosal membrane of the gastrointestinal tract. In case of the respiratory tract, some of the toxins are trapped by the mucus of the trachea and are pushed upwards by the action of cilia of the membrane to the pharynx where they are either coughed or swallowed.[38] Absorption of toxins can occur by passive diffusion, which is direct transport through the lipid membrane; active transport, which uses energy rich compounds like ATP; facilitated diffusion, which makes use of carrier molecules and endocytosis.[39] The absorbed toxins are transported to the target sites through blood circulation or extracellular fluid. Toxins can bind to various proteins, at various binding sites present on them through various types of interactions such as covalent, non covalent, van der Waals forces, hydrogen bond and hydrophobic interactions. After binding to the target sites they produce various effects like blockage of neurotransmitters, as in the case of neurotoxins.[23]

Mechanism of Toxin Elimination

Certain tissues and organs as well as mechanisms help in the removal of some of the toxins from the body. The skin helps in removal of water soluble toxic chemicals through sweat which is produced by the sweat glands.[40] The nephrons of the kidney also help in toxin removal.[40] The blood entering the glomerulus of the nephron contains various toxins which diffuse through Bowman's capsule.[40] After selective reabsorption in the proximal convoluted tubule, loop of Henle and the distal convoluted tubule, urine enters the collecting ducts, followed by larger ducts and ureters.[40] After storage in the urinary bladder, it is excreted through the urethra.[40] The lungs are also a site for toxin removal. Toxins diffuse into the alveoli from blood capillaries depending on their partial pressure and are

exhaled from the alveoli through the nostrils.[40] The hepatocytes of the liver also help to filter out various toxins through bile.[41]

Analysis of Toxins

HPLC (High Performance Liquid Chromatography)[42-44] is generally used to separate the desired substance from a mixture of liquid chemical substances. In this method, the mobile phase containing the toxin is generally stored in a reservoir. It is transported from a reservoir to a mixer using a pump which generally operates at high pressure levels. The mobile phase then passes into a column which is normally made of materials like steel or glass. A detector is then used to analyze the product coming out of the column for the presence of the desired compound (toxin). A fraction collector can also be used to separate the product from the column into various fractions. A recorder provides the data in a form which can be read by the user. Using, LC- MS (Liquid Chromatography- Mass Spectroscopy)[42-44], the desired substance can be separated from a mixture of various substances depending on their ability to travel through a stationary phase, by using liquid chromatography and can be analyzed on the basis of the mass/ charge ratio using mass spectroscopy. The substance to be analyzed first undergoes chromatography in which various components get separated on a stationary phase. The desired component is then inserted into the sample holder of the spectroscope after which it is ionized in an ionization chamber. The ions produced then pass through the mass analyzer which separates the ions on the basis of their mass or charge. The ions are then analyzed by the detector which gives the user an output in the form of a graph.

In Thin Layer Chromatography (TLC)[43], the substances are analyzed by separation on a chromatographic plate containing an adsorbent like silica gel which acts as the stationary phase. A solvent which acts as a mobile phase moves up the stationary phase, thus separating the sample into various components. Thus the desired component can be obtained. Enzyme linked immunosorbent assay (ELISA)[45-46] is based on an antigen antibody reaction which uses an antigen, which is the toxin sample; primary antibody; enzyme linked secondary antibody and a substrate. It could be of various types such as Dot ELISA, Indirect ELISA, Competitive ELISA, Sandwich ELISA and RELISA (Receptor- specified ELISA). Biosensor[47] are also used for the determination of toxins. Tissue biosensors[47] are used for the detection of tetrodotoxin and saxitoxin. Enzyme sensors[47] are used for the detection of insecticides. Electrochemical sensors[47] are used for the detection of seafood toxins.

CONCLUSION

Toxins are thus obtained in various forms and from various sources which can on one hand be useful to humans but on the other hand can deteriorate various ecosystems and can harm the organisms living within them. Hence, instead of using inorganic and harmful products, we should switch on to organic, biodegradable and less toxic alternatives which can help minimize pollution and the incidents of various disorders and mortalities among various organisms.

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