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A Comprehensive Study on Properties that Makes Some Molecules Toxic

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ABSTRACT

Poisons are substances causing disease and sometimes death in living organisms. Some believe that nothing is worthless in the world. Poisons might be no exception to this pattern. In particular interest in this realm is the reason why some molecules are poisonous. Does it have to do with the nature or chemical properties of the molecule or is it the inappropriate application or accumulation of these molecules in the wrong location within the organism which causes the so-called poisonousness phenomenon? But can poisons be employed to neutralize other life-threatening problems? The present short essay aims to address this question through a review of the current literature on the topic.

KEY WORDS: Molecules, molecular properties, poisons, toxic.

1. INTRODUCTION

Undoubtedly, our world has survived due to the existence of an order to which all its members belong. Every substance in this world has its own unique position and hierarchy, and any change on its path can alter the existing balance, giving rise to numerous problems. One of the most significant materials in this worldly order of existence is the poison. Poisons are substances capable of causing catastrophic changes in an organism's molecular activities inhibiting certain chemical reactions in the organism's cells upon exposure to sufficient quantities (Trestrail, 2007).

One big misconception about poisons is to assume that, they are "special" molecules which are toxic. However, a poison can be any liquid, solid, gas and even a highly energetic source finding their way into the organisms' body where they are not normally found. Moreover, the dosage in which poisons accumulate in the body is also a crucial factor in disruption of balances in the organism's biological functions, which might prove fatal (McGraw-Hil, 1989). A simple example of such lethal poison is a cup of distilled water in your lungs or a vial of pure oxygen in your veins. Nearly all poisons, whether exogenous or endogenous, are not of instant exposure-kill scenario types. Rather, these poisons operate within a narrow range where they are not harmful (and even beneficial), a narrow range which is surrounded by the massive deadliness region. This border is mainly determined with specific reference to the dosage at which various poisons are taken, the pathway from which they enter (Ingestion, Inhalation, Tropical and Injection) and where they accumulate in the body. The degree of toxicity varies substantially from one species to another. For instance, antibiotics are greatly poisonous to bacteria and yet we can ingest them without any harm. Moreover, the poisoning effect even varies within a species (i.e., age, sex, genetics), subject to the organisms' bodily response to the toxin introduced (Budavari, 1989).

Literature: To address the stated objectives, the following methodology is adopted to present poisons in categories of where they originate and by which mechanisms is their effect fatal.

Neurotoxin: Neurotoxins generally refer to the spectrum of toxins affecting the nervous system of organisms. These toxins usually cease impulse transfer, cause paralysis and render body organs such as heart and lungs dysfunctional, eventually leading to death of the organism (Heaton, 2000; Bajgar, 2004; Nishiwaki, 2001).

For instance, Hemlock as a highly toxic flowering plant (Lopez, 1999) is so poisonous that only about 6 leaves (100 mg) is fatal to an adult human. This is due to the neurotoxins present in the leaves, which attack human neurons upon absorption, causing paralysis. However, unlike snake neurotoxins which attack the brain, Hemlock's victims stay totally alert with a healthy brain but the victim's motor neurons do not respond to the commands sent from the brain resulting in respiratory system failure and death in a matter of minutes (Schep, 2009). Hemlock is notorious for poisoning the great Greek philosopher Socrates who was sentenced to death in 399 BC for the sake of disbelief in the gods of the state (Wiki, 2018).

Atropa belladonna, meaning beautiful woman, is a plant which was used as a beauty and makeup product for women in the Middle Ages, so that a few drops of the diluted extract of this plant caused the pupil to dilate, and the person seemed prettier (Berdai, 2012). Even though the berries of the plant are extremely poisonous and fatal, low dosage causes delirium and hallucinations, which explains why it was used in this manner. The plant was also used by ancient doctors as an anaesthetic.

Tetrodotoxin is a toxic substance found in marine creatures (such as Blue Octopus and Balloon fish). The octopus is known to be dangerous. The quantity of poison injected each time is so high that it can kill 26 adult people, and surprisingly the bite of this aquatic organism is painless. Like most poisons, Tetrodotoxin is an inhibitor, in this case, a sodium channel blocker binding to the voltage-gated sodium channels in nerve cells causing the cessation of firing action potentials in the cells, blocking nervous impulse transfer, and flexing muscles in response to nervous stimulation (Lago, 2015; Bane, 2014; Chau, 2011).

If you have been watching Sherlock Holmes so far, you are certainly familiar with Botulinum which is produced by the bacterium Clostridium botulimun and unarguably the strongest neurotoxin ever discovered (Arnon, 2001). There are various forms of Botulinum toxin (A-H), of which, different types are lethal to different species. For instance, an injection of only 2-billionths of a gram (2 ng) from type H can cause death to an adult. Clostridium botulimun prevents the release of the neurotransmitter acetylcholine from axon endings at the neuromuscular junction thus causing flaccid paralysis, which consequently leads to the breakdown of the respiratory system and ultimate death of the victim (Montecucco and Molgo, 2005).

Bioaccumulation: Bioaccumulation of certain molecules can be greatly poisonous. Meanwhile, bioaccumulation is a slow process in which symptoms may take months or years to fully develop and cause death, by which time treatment is no longer a solution. A good example of this is the accumulation of mercury in organisms' body. Absorption of only about 0.1 ml either by inhaling mercury compound vapour (from broken fluorescent lamps) or indirect ingestion through food products such as polluted fish are proven to be fatal. Mercury is notorious for both its lethal property and its brain neuron degeneration. A study done by University of Calgary provided direct visualized evidence on how mercury effects the brain (Hahn, 1989). This heavy metal binds to the Tubulin (proteins which surround the nerve tissues and responsible for the formation of neural cell membrane), making them unstable to bind to one another thus deforming neuro fibrils ceasing neuron growth whose fact is responsible for decreases in intelligence, Alzheimer's Disease and kidney problems (Bose-O'Reilly, 2010; Mercury, 2018; Bernhoft, 2012).

Given the increasing use of technology in everyday life and the maintenance of heavy waste around us, toxic substance content should be carefully considered. For example, lead is one of the most toxic elements in technology-rich societies. Lead contamination is caused by the combustion in various types of machinery and in industries that cause many complications in people especially children. Although lead is a highly beneficial metal, used in many industries, it is also a toxic substance. But what makes substances such as lead so poisonous? Well, it is all about lead's heavy property and its ability to replace other metals such as calcium, iron, and sodium in numerous chemical reactions taking place in the body. The worst interference occurs when certain genes turn on and off, when metals in the molecule are displaced. This changes the shape of the protein molecule (denatures it) in such a way that it can no longer perform its function. This explains why over 200 enzymes can be affected by lead poisoning. Furthermore, lead can also be classed as a neurological toxin. This is because displacing calcium in neuron transmitting impulses to the brain, diminishes one's ability to think or recall information. Nevertheless, lead poisoning adversely affects both respiratory, circulatory and excretory systems as well. This cycle begins by inhaling lead compounds which directly affects lungs and iron metabolism leading to anaemia (Waldron, 1966). Subsequently, lead concentration of blood increases and so breaking of this toxin in liver will override, causing sever blood abnormalities by disrupting blood concentration balance. Finally, even if lead does end up being excreted, it will damage the kidneys on the way out (Needleman, 2004). This is why lead is a great example of why toxic molecules do not have to always be chemically reactive to be poisonous, rather just being a very heavy element could easily disrupt biological balances leading to severe symptoms.

Another form of bioaccumulation is that of carbon monoxide. Being completely colourless, odourless, and tasteless gas, it is also known as the "Silent Killer". Meanwhile, what makes CO molecules particularly poisonous is the fact that they directly bind to haemoglobin of red blood cells in blood. Binding to the haemoglobin reduces the space for oxygen absorption which in turn results in oxygen starvation and suffocation of the victim (Chatterjee, 2004).

Cytotoxin and Hemotoxin: Cytotoxins are generally classes of toxin which directly cause normal body cell death through puncturing cell membranes rendering them fully permeable such that they will not be able to maintain their integrity. A typical example is found in lymphocyte T cells. Once the body is infected by virus, they host inside the body cells and are undetectable to be destroyed. However, once a T cell discovers an unhealthy cell, it produces cytotoxic proteins which will damage the cells surface membrane to destroy the infected cell (Hivroz, 2012).

Meanwhile, hemotoxins are cytotoxins which specifically target red blood cells. Hemotoxins use the same mechanism as cytotoxins to bring about red blood cell lysis. The detrimental effects of Hemotoxins can range from red blood cell lysis to organ degeneration, provided the intake dosage is sufficient. Hemotoxins are mostly produced be venomous snakes alongside neurotoxins.

Radioactive Poisoning: Most radiations are indeed not dangerous at all. It is only highly energetic radiations known as ionizing radiation which do pose threats to living organisms. These radiations are mostly found in nuclear substances going through particle decay. Ionizing radiation emitted by radioactive elements (e.g. Uranium and Plutonium) damage atoms due to their high energy. Since all matter is composed of atoms, damage to them would mean whole molecules would be altered, leading to cell death and consequently the body would also be affected. On the other hand, radiation poisoning purely depends on dosage to which organisms are exposed. The humankind is constantly exposed to background radiation present all around us. Nevertheless, we are not affected by radiation poisoning and we do not present any symptoms either (Ryan, 2012). Consider the example of sugar cubes.

Consumption of one sugar cube a day is totally alright, but ingestion of 10000 sugar cubes at once would certainly kill you. The same analogy holds true for radioactive substances. When a single dental X-Ray is taken, 8 millisieverts of radiation enters your body leaving no side effects. However, if about 125 X-Rays are taken at once, you will hit the lowest level of radioactive poisoning. Under these circumstances, radiation from the radioactive substances would kill bone marrow cells and bone marrow destruction means no white blood cells and no platelet production. This, in turn, would mean having the most severe AIDs without an actual HIV invasion. Thus, the victim is likely to die from infection or blood loss if left untreated. Meanwhile, if dosage of radiation taken in exceeds 10 Sieverts, as in nuclear explosion or direct consumption of nuclear materials (similar to having 2500 X-Rays at the same time), catastrophic things can occur. These include, breakdown of cardiovascular system leading to fluid leakage, death of gastrointestinal cells which cease absorption, electrolyte imbalances and finally total destruction of the nervous system, which causes the whole body to fail and certain death (Ryan, 2012; Mettler and Voelz, 2002).

Polonium is a slow-killer radioactive poison with no known cure. Only one gram of steamed polonium can destroy more than 1.5 million people over a few months of scorching particle decays.

Energy Starvers: Arsenic is also known as the "King of Poisons" for its devastating power and impact. This poisonous substance leaves no trace of its own, so it has always been used as a hidden weapon to kill popular figures such as Napoleon Bonaparte and King George III. The mechanism by which arsenic strikes is rather quite tactical. This is due to the fact that Arsenic is able to substitute phosphate in numerous reactions. Since phosphate ions play a fundamental role in ATP formation, substituting phosphate ceases mitochondrial process which in turn diminishes ATP formation. Failure to produce ATP causes the catastrophic effect of subsequent organ failures, just like having multiple heart attacks in various organs at the same time (Sherwood, 2011; Chavanet, 2011). On the other hand, at very low dosages, this toxic substance forms a harmless solution capable of whitening and smoothening skin, a perfect cosmetic ingredient like Belladonna during the Queen Victorian era.

Another example of deadly plants is Aconite (Wolf's bane). This killer contains the alkaloid pseudaconitine toxin, which interferes with the heart's pacemaker, resulting in irregular heartbeat (Flanagan, 2012). This in turn causes hallucination at low dosage and chocking when overdosing. The most amazing fact about this plant is that its poison is absorbed through skin whose fact was used by Romans who applied very diluted solutions of it over their bodies in parties.

Cyanide, as one of the strongest, fastest and most fatal, definitely merits special attention in this essay. This was the most widely used poison in World War II. Cyanotic acid is a liquid with a smell of bitter and lightly eddy almonds that easily fumes. Cyanide metal compounds form the basis of cyanide the most dangerous of which are cyanide sodium and cyanide potassium, which in the presence of air or in the stomach produce cyanide acid. The mechanisms of action of cyanide, just like arsenic, is to cease the production of ATP leading to energy starvation (Banay-Schwartz, 1974). A bitter almond has 1 mg of cinnabar acid. The toxic dose of Cyanuric acid is 0.01 g and its lethal dose is 0.05 g. Meaning, eating 50 bitter almonds at the same time has the potential of killing you (Shragg, 1982).

Corrosive Chemical: Corrosive chemicals are either strong acids or strong bases. Many sources suggest that corrosive substances act slightly differently from poisons in that poisons function by causing a systemic toxic effect and take some time for symptoms to develop while corrosives have a simpler hydrolysis mechanism of action and are immediately harm-causing substances. The author of the present essay has decided to categorize them as a form of poison for the following reasons. Firstly, the two terms are loosely defined with a large common grey area in between. Since poisons are defined as any substance which can alter biochemical reaction at a certain dosage when ingested, corrosive chemicals can easily fit into the wide spectrum of poisonous molecules. Secondly, most substances which are corrosive, do cause a toxic effect when absorbed, even if they are diluted to reduce their corrosive effect. Finally, there is no strong reason and evidence to preclude a corrosive from being a poison.

The mechanism of action of corrosive chemicals on living tissues is based upon acid-base reaction causing hydrolysis of amides and ester bonds. Hydrolysis of amides leads to breakdown of amino acid chain and hence the denaturation of protein molecules including enzymes. While, hydrolysis of ester bonds, decomposes lipids, any other inorganic substance (calcium ions, sodium ions and Irons) present in the body will react with these acids or bases being phased out of normal body functional use. Thus, no biological being is safe from the harmful, detrimental, and devastative effects of corrosives (Beatle, 2012).

Use of Poisons in Targeted Drugs: An old adage says, "if worms did not come to existence, life would have lacked something important". People tend to underestimate the importance of worms in the cycle of ecosystem. It is evident that every single creature is serves a particular purpose, be it energy (arguably the cause of life) or deadly molecules such as poison. This is why humans have learned to extract poisons from nature or synthesise them artificially in order to evolve them for beneficial uses within industries such as agriculture, food preservation and medicine.

Poisons have long formed strong bonds with human civilisation for centuries. They have been used for far more purposes than just anonymous assassinations and biological weapons of warfare, bringing about mass murders

of people and fall of cities. A prominent aspect of how beneficial poisons can be, is their uses in tackling and treating various forms of acute diseases such as cancer. Targeted drug delivery has formed cutting edge research in this realm. Targeted drugs used in the treatment of malignant cancer cells interfere with the action of molecules impeding the growth and development of tumours (Brannon-Peppas and Blanchette, 2012; Schrama, 2006; Morgillo, 2007). This is done through the destructive formation of complex protein, which in turn restricts the proliferation and spread of cancerous cells limiting or even stopping the mitosis stage of cell cycle (Sverdlov, 2011; De Ruysscher, 2009). Examples include Imatinib mesylate, for the treatment of gastrointestinal stromal tumours (Jager, 2004), Lapatinib, for some advanced or metastatic breast cancers (Cameron, 2008) and Gefitinib, for advanced lung cancer (Fukuoka, 2003).

Other targeted drugs use poisonous molecules in different ways. One of these methods is direct cell death through apoptosis (cell suicide) by transferring toxic substances into malignant cells, stimulating the immune system to recognize and destroy cancerous cells. Targeted therapies are astonishingly well-suited to the recognition of cancer cells because targets play a key role in the growth or survival of the cancer cells (Chourasia and Jain, 2003).

Another method by which targeted drugs can be used to treat cancer is anti-angiogenesis. In this process, poisons from drugs target development and spread of blood vessels enriching tumour with blood, oxygen, and food to grow and increase in size. As a result, ceasing angiogenesis can prevent tumour growth.

Most targeted drugs use monoclonal antibodies. Typically, conjugated monoclonal antibodies also known as chemo labeled, carry chemotherapy or other form of poisons to cancer cell and directly toxify the goals within the cells. Poisoning cancer cells will eventually lead to their death with minimum damage to the rest of the body. On the other hand, other approaches for monoclonal antibodies use binding to the outer membrane of the specific cell stimulating an immune response and destroying the cell by framing it as an infected cell; a perfect example of how a molecule can act as a poison in a beneficial way. For example, breast tumours require the estrogen-derived female sex hormone receptor to grow; therefore, they were set to be the target for these antibodies to attack.

Last but not the least, one can refer to a type of targeted poisonous drugs called inhibitors. You might be thinking how an inhibitor can ever be a beneficial drug for treatment? To illustrate, consider the following example. Aromatase inhibitor is a competitive inhibitor of the enzyme estrogen. Estrogen is responsible for the growth of ER (Estrogen Receptor) plus breast tumours and aromatase is an essential enzyme in the production of estrogen in the body. Therefore, reducing the aromatase activity would reduce estrogen levels and prevent the growth of a tumour (Simpson, 1994; Bagheri, 2014).

2. CONCLUSION

Poisons are not distinct molecules that are far too different from what we encounter in our daily life. Poisons can be found in various places, ranging from the air we breathe to almonds and fried fish on our dinner tables. Poisons can literally be any foreign molecules that are perfectly harmless to where they are found, but capable of altering biochemical reactions required to sustain life, when they are introduced into another organism's body. Meanwhile, the degree to which such fatal changes occur is prominently determined by the level of how poisonous a molecule is, what dosage and concentration of the poison is taken in, which chemical reactions they alter, which system(s) of the organisms' body they shoot down all of which makes them particularly dangerous. This explains why one can classify any foreign molecule introduced into an organism as being poisonous, provided they can disrupt a biological balance to bring about either negative or positive side effects.

In sum, as poisons are molecules capable of affecting specific regions in an organism and cause death, they have a great potential to be evolved in such way to become the wonders of tomorrow and steps taken towards this goal today can prove to be the key to defeating a wide range of diseases in future. It is hoped that, further research into the use of poisons would pave the path to treat acute and terminal diseases.

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