Characterization, Mode of Action and Clinical Outcome of Dioxychlor®

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Introduction

The following is a description of the characterization and mechanism of action of Dioxychlor®, researched and developed by American Biologics®, as relates to its antiviral, antibacterial, antimycoplasmal and antifungal activities. Dioxychlor® has been in clinical use for over fifteen years with tens of thousands of infusions at the American Biologics® Integrative Hospital and Medical Center as well as other clinics and hospitals throughout the world.

To understand fully the action of Dioxychlor® on target organisms, it is necessary to describe in detail the chemical structure of this oxidant as well as the biochemical structures of substances found in these target organisms with which Dioxychlor® interacts. These targets include viruses (the nucleic acids, RNA, DNA), bacteria and fungi.

Chemical Definition

Dioxchlor® is an inorganic (containing no carbon) sodium salt of only electronegative elements bound together by electrostatic, covalent and coordinate covalent bonds. See Chart 1, The Atomic Structure of Dioxychlor®. The chemical structure of Dioxychlor® is pH-dependent, that is, the stability or instability of this substance is determined in large measure by the concentration of hydrogen ions (H^+ or protons) in the surrounding medium.

Under acidic conditions, Dioxychlor® becomes unstable and decomposes into a variety of products including but not limited to chloride ions, hyperchlorous ions and nascent (atomic) oxygen. It is for this reason that Dioxychlor®, when bottled and stored for long periods of time, is buffered. Under acidic conditions, Dioxychlor® results in a neutral molecule consisting of three electronegative atoms held together by covalent and coordinate covalent bonds. From this cluster, a single atom of highly reactive nascent oxygen is liberated onto the target organisms. As we shall see below, nascent oxygen is the active agent of Dioxychlor® and, unless it is liberated, the antiviral, antibacterial and antifungal activity will not occur. See Chart 1, The Atomic Structure of Dioxychlor®.

Virus Inactivation

A virus typically consists of an outer shell or coating of protein encapsulating a nucleic acid which may be either DNA or RNA (a retrovirus). The skeletal backbone of nucleic acids

includes derivatives of phosphoric acid (H_3PO_4, a very strong acid) in which two of the original three hydroxy groups (-OH) are substituted, leaving only one active hydroxy group per phosphate. See Chart 3, Segment of Extended DNA Chain Showing Alternating Deoxyribose-Phosphate Linkage.

Some viruses may have glycoproteins incorporated into their protein coat, that is, proteins to which polysaccharides (sugar chains) have been attached. The bound polysaccharides may attach to specific sites on the protein coat, effectively converting a protein surface into a poly-sugar surface.(1) This new surface has specificity for certain polysaccharides found on the surfaces of specific cell types, thereby conveying specificity to virus binding as well as a degree of immunological protection.

Once bound to the appropriate cell type, the nucleic acid component of the virus is injected into the cell and in many ways, takes over the protein synthesis processes of the cell. Certain segments of the viral nucleic acid consist of genes that are reponsible for the replication of the coat. The nucleic acid component replicates by a process known as "base-pairing", in which each base of the original strand attracts and binds the corresponding base, forming a pair (A-T and C-G, described more fully below) through hydrogen bonding. The result is the replication of the complete virus until the cell bursts, releasing many additional viral particles into the surrounding medium. In the presence of these acidic nucleic acids, the Dioxychlor® molecule becomes unstable and releases nascent oxygen into the medium.

Nucleic acids, both RNA and DNA, have many characteristics in common, in fact, they are almost chemically identical. Each consists of a chain of alternating sugar (a modification of ribose, deoxyribose) and phosphate groups, known as the "phosphate-sugar backbone". Attached to a specific carbon of each deoxyribose group is an organic ring compound known as a "base". Altogether, there are only four types of bases found in DNA, namely, guanine (G), cytosine (C), adenine (A) and thymine (T). It is the sequence of these four units along the chain that makes one segment of DNA differ from another. RNA differs chemically from DNA in that the base thymine is replaced by the base uracil (U), representing a very subtle biochemical difference. There is also a subtle difference in the sugar deoxyribose. See Chart 2, The Release of Nascent Oxygen from Chlorine Dioxide in an Acidic Environment.

The base guanine, found in both RNA and DNA, is very sensitive to oxidation, forming 8-oxoguanine as the oxidation product.(2) The release of Dioxychlor® results in the oxidation of the guanine residue with the formation of 8-oxoguanine, thereby disallowing the replication of the viral nucleic acid by base pairing. Although the replication of the protein coat may continue, the formation of a complete functional virus has been blocked by Dioxychlor® oxidation.

Aerobic and Anaerobic Bacteria

When life began on earth but before the presence of oxygen in the earth's atmosphere, bacteria consisted of what are known today as the anaerobes. These bacteria survive only in the absence of oxygen and include many pathogenic organisms. With the appearance of algae, carbon dioxide, present in large proportion in the primordial atmosphere, was converted by algae to carbohydrates, generating oxygen as a byproduct. At first, oxygen reacted with iron salts in the primitive oceans to generate extensive deposits of iron oxide (iron ore). When soluble iron in the

oceans became exhausted, oxygen concentration in the atmosphere began to rise. At the present time, oxygen comprises approximately 20% of the earth's atmosphere while carbon dioxide levels have dropped to about 2%.

Some bacteria were able to survive the increased levels of oxygen in the atmosphere by any of three paths. The presence of oxygen in the atmosphere resulting from algae and other plants containing the green pigment chlorophyll, allowed the development of the wide range of life forms both in the ocean and on land known today as animals. Some anaerobic bacteria took up residence in oxygen-free environments within the bodies of animals, notably, the intestines. Other anaerobes solved the problem of oxygen toxicity by evolving metabolic ways to cope with its universal presence. These include the development of the enzyme superoxide dismutase (SOD), which in its most primitive form, contained iron.[3] Later refinements included the incorporation of manganese (in mitochondria) and finally, a combination of copper and zinc.

It is widely believed that still another solution to oxygen toxicity lay in the development of organisms that have the ability to utilize oxygen in their metabolism. These organisms are known today as the aerobes or aerobic bacteria. One form of these organisms may have been the precursor of an inclusion organism found in many animal and human cells known as the mitochondria, having its own circular DNA.

It is well known that cultures of many bacteria become acidic, typically generating lactic, acetic and other simple carboxylic (organic) acids. The acidic medium surrounding many bacteria triggers the decomposition of Dioxchlor and the subsequent liberation of nascent oxygen. Nascent oxygen is a particularly potent oxidizing agent for anaerobic organisms because it is essentially a free radical seeking not one, but two electrons. Anaerobic organisms have not developed adequate defenses against the onslaught of oxygen, particularly nascent oxygen, and quickly succumb to its lethal action.

One possible mechanism for the liberation of nascent oxygen from the chlorite ion (ClO_2^-) in an acidic environment involves the association or binding of H^+ (proton, normally bound to the oxygen of water as H_3O^+) to any of the three pairs of unused electrons in the outer shell of chlorine. This association is equivalent to the formation of a hydrogen – chlorine (H – Cl) covalent bond. Because of the single electron deficiency of the chlorine atom, only one covalent bond is permitted at any one time. Since the H – Cl bond is stronger (the H – O bond of water is almost the strongest bond known) than the existing O – Cl covalent bond, the O – Cl bond is disrupted by the ejection of nascent oxygen. This leads to the dissociation of the acidic proton from chlorine and the formation of the hypochlorous ion (ClO^-) and sodium hypochlorite (NaOCl). See Chart 2, The Release of Nascent Oxygen from Chlorine Dioxide in an Acidic Environment and Chart 4, The Decomposition of Dioxychlor® to Nascent Oxygen and Sodium Hypochlorite in an Acidic Environment.

$$\mathbf{Na^+ ClO_2^-} \xrightarrow{\mathbf{H^+}} \mathbf{Na^+ + ClO_2} \longrightarrow \mathbf{Na^+ + ClO^- + [O]}$$

Dioxchlor®	Sodium Ion	Chlorine Dioxide	Sodium Ion	Hypochlorous Ion	Nascent Oxygen
			Sodium Hypochlorite		

During World War I, this instability of chlorite ion was exploited by Alexis Carrel (1873–1944, Nobel laureate 1912), best known for his prolonged culture of chicken heart cells at Rockefeller University, New York. Carrel sucessfully administered a crude solution topically (similar to Dioxychlor®) to war casualties having embedded shell fragments.(4) The anaerobic organisms responsible for gas gangrene in these wounds were quickly quenched, saving many soldiers that would have otherwise perished.(5)

Absence of Dioxychlor® Activation

There are only a small number of basic biological substances found in living organisms. These include proteins, lipids, carbohydrates and nucleic acids. The ability of nucleic acids (in the form of viruses) to activate Dioxychlor® has been discussed previously. Lipids and carbohydrates are both neutral substances, carrying neither an electric charge nor acidic groups. The possibility of proteins activating Dioxychlor® is discussed below.

Many proteins, particularly those that are soluble and found free in both the blood and in the medium surrounding tissues, contain on their surfaces organic groups, both acidic and basic (alkaline) in nature. In most soluble (globular) proteins either one or the other of these two types of groups predominate. Proteins in which the acidic groups outweigh the basic groups are acidic proteins and those in which the basic groups predominate are known as basic proteins.

A technique has been developed to determine, for a given protein, in which category it may lie. Either acidic or basic proteins migrate under the influence of an applied electric field. This laboratory technique, known as electrophoresis, has been used to determine the acidity or basicity of proteins. As the pH of the surrounding medium into which a protein has been solubilized is changed, the protein will migrate either in one direction or the other. When a pH is found that will result in no migration, the protein is said to be at its isoelectric point. The pH value at which this occurs for a given protein is known as the isoelectric point of that protein. The isoelectric points of most proteins are not far from 7 or neutrality. Such proteins are not capable of activating Dioxychlor® to decomposition, partly accounting for low toxicity.

Dioxychlor® as an Antifungal Agent

Fungi are considered as plants without chlorophyll and lack the ability to generate carbohydrates from sunlight and carbon dioxide. They were probably derived in an oxygen-free atmosphere but some have developed the ability to tolerate low levels of oxygen. Most fungi prefer an oxygen-poor environment and live best under these conditions. They obtain their energy requirements from the decomposition (through enzyme activity) of existing organic matter and, in this light, may be considered as parasitic.

Because of their low tolerance for nascent oxygen and the acidic medium in which they thrive (from the liberation of organic acids), fungi in the mycelial form are sensitive to the destructive action of Dioxychlor®. One example of a human pathogenic fungus is *Candida albicans*, invading finger and toenails. A second example is the fungus responsible for “atheletes foot”, thriving between toes in a moist environment while still another example is “ringworm”, propagating on the dead cells found on skin (as well as generating many mycotoxins affecting homeostasis).

From all of the above considerations, it is apparent that Dioxychlor® is essentially activated only by viruses, acidic bacteria and fungi.

Clinical Outcome Studies of Dioxychlor®

Extensive clinical applications of Dioxychlor® to Epstein-Barr virus (EBV)[6], cytomegalovirus (CMV), hepatitis virus A, B, HIV (AIDS virus) and others are being used continually. The DNA of EBV within the virus itself is in a linear form. Sometime after infection, the ends are linked together, forming the circular form (episome). Once this form of DNA is firmly established, the cell is said to be in a latent state. The virus remains in this state in certain B-cells for the remainder of the patient's life. About 10% of the B-cells are in the actively proliferating state.[7] An Epstein-Barr clinical study was conducted in the American Biologics Medical Center over a four year period from 1992 to 1996.

Case Load

There were 1207 patients treated with the Dioxychlor® protocol.
784 patients were female - 65%.
423 patients were male - 35%.

Ages ranged from 16 to 52 years

Initial Status

High IgG serum titers ranged from 400 to 5800

Intensive treatment for 14 days

Medication

All medications supplied by American Biologics

Therapy (Baseline)

- Dioxychlor® - intravenous drip, 10 cc in 100 cc saline, daily

  Intravenous studies at the American Biologics Medical Center have established that 10 ml of 25,000 ppm Dioxychlor® in 100 ml of physiologic saline administered over 30 minutes is a safe dosage level.

- Dioxychlor® - sublingual, 10 drops under tongue, twice daily

- Thymus extract (im) – weekly

- Vitamin C – 15 g parenteral (drip)

Results (Averages)

Minimun time clinical improvement: 3 days

Significant clinical improvement: 10 – 20 days

Antibody (IgG), 90% reduction, < 35 days

Microbiological Laboratory Studies

In 1986 the Microbiology Laboratory at Stanford University performed a series of tests showing the efficacy of Dioxychlor® in neutralizing a variety of viruses. The concentration of Dioxychlor® used was 0.75 ppm in all the studies.

The viruses included Herpes II, HTLV III and Cytomelagalovirus. The study also included the bacterium Pseudomonas. Electron micrographs show the complete eradication of the viruses and Pseudomonas following treatment.[8]

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