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Can chlorine dioxide prevent the spreading of coronavirus or other viral infections? Medical hypotheses

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INTRODUCTION

Motivation

Viruses have caused many epidemics throughout human history. The novel coronavirus [10] is just the latest example. A new viral outbreak can be unpredictable, and development of specific defense tools and countermeasures against the new virus remains time-consuming even in today's era of modern medical science and technology. In the lack of effective and specific medication or vaccination, it would be desirable to have a nonspecific protocol or substance to render the virus inactive, a substance/protocol, which could be applied whenever a new viral outbreak occurs. This is especially important in cases when the emerging new virus is as infectious as SARS-CoV-2 [4].

Aim and structure of the present communication

In this editorial, we propose to consider the possibility of developing and implementing antiviral protocols by applying high purity aqueous chlorine dioxide (ClO_2) solutions. The aim of this proposal is to initiate research that could lead to the introduction of practical and effective antiviral protocols. To this end, we first discuss some important properties of the ClO_2 molecule, which make it an advantageous antiviral agent, then some earlier results of ClO_2 gas application

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against viruses will be reviewed. Finally, we hypothesize on methods to control the spread of viral infections using aqueous ClO_2 solutions.

PREVIOUS EXPERIENCE AND BACKGROUND OF USING ClO_2 AS AN ANTIVIRAL AGENT

Inactivating viruses with ClO_2 in aqueous phase

To our present knowledge, an aqueous solution of ClO_2 is able to inactivate all types of viruses. Disinfectants (in water phase) are compared by their CT values, which is the concentration (measured in mg/L) multiplied by the contact time (measured in minute). In CT tables, ClO_2 is indicated for viruses in general, without mentioning any exemptions. For example, according to [6], a CT value of 8.4 mg × min/L is needed to achieve a four-orders-of-magnitude ("4 log" or "99.99%") inactivation of viruses in an aqueous medium at 25 °C.

Chemical mechanism of virus inactivation: reaction of ClO_2 with amino acid residues

In 1986, Noss et al. [19] proved that the inactivation of bacterial virus f2 by ClO_2 was due to its reactions with the viral capsid proteins, and almost no inactivation of the infectious viral RNA occurred [8] when that was treated with ClO_2 separately. They found [19], however, that three discrete chemical moieties in the viral protein, namely the cysteine, tyrosine, and tryptophan amino acid residues were able to react with ClO_2 rapidly. In 1987, Tan et al. [28] tested the reactivity of ClO_2 on 21 free amino acids. ClO_2 reacted only with six amino acids dissolved in 0.1 M sodium phosphate buffer, pH 6.0. The reaction with cysteine, tryptophan, and tyrosine was too rapid to be followed by their technique. Three further amino acids (histidine, hydroxyproline, and proline) reacted with ClO_2 much more slowly, at a measurable rate.

The reactivity of the three fast-reacting amino acids (cysteine [12], tyrosine [17], and tryptophan [27]) was studied in Margerum's laboratory between 2005 and 2008. They found that cysteine had the highest reactivity among these amino acids. From their experimental data they calculated second order-rate constants (at pH 7.0, 25 °C and 1 M ionic strength) and obtained the following sequence: cysteine 6.9×10^6 M^{-1} s^{-1} >> tyrosine 1.3×10^5 M^{-1} s^{-1} > tryptophan 3.4×10^4 M^{-1} s^{-1} >> guanosine 5′-monophosphate 4.5×10^2 M^{-1} s^{-1}. (They studied guanosine 5′-monophosphate [18] as a model compound for guanine in nucleic acids. Data presented here are taken from Table 3 of ref. [18]).

In 2007, Ogata [22] found that the antimicrobial activity of ClO_2 is based on denaturation of certain proteins, which is primarily due to the oxidative modification of the tryptophan and tyrosine residues of the two model proteins (bovine serum albumin and glucose-6-phosphate dehydrogenase) used in his experiments. In 2012, it was again Ogata who showed [23] that the inactivation of influenza virus by ClO_2 was caused by oxidation of a tryptophan residue (W153) in hemagglutinin (a spike protein of the virus), thereby abolishing its receptor-binding ability.

In this context it is interesting to remark that the spike protein of the new coronavirus SARS_CoV-2 contains 54 tyrosine, 12 tryptophan, and 40 cysteine residues [29]. If we assume that in an aqueous solution all of these residues are able to react with ClO_2 just like the free amino acids, then the inactivation of the viruses can be extremely rapid even in a very dilute (e.g., in a 0.1 mg/L) ClO_2 solution.