SOLUMIUM DENTAL: the hyper-pure chlorine dioxide solution and its applications in dentistry I.

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Abstract

This series of papers consisting of three communications describes the properties and applications of chlorine dioxide (ClO_2) with a special emphasis on its hyper-pure aqueous solution available commercially in Hungary under the trade name SOLUMIUM DENTAL since the end of 2008. This first part of the series discusses the history of chlorine dioxide as a disinfectant, its properties and its fields of applications. It is also explained why chlorine dioxide is regarded as an ideal biocide and why its medical applications were delayed until now in spite of its advantageous properties as a biocide.

The history of chlorine dioxide ClO_2 and its fields of application

Chlorine dioxide is a greenish yellow gas, easily soluble in water and aqueous solutions. It had been known for long. It was discovered by Sir Humphry Davy in 1811, however it became well known in the XX century only. The largest quantities are used in the paper industry for whitening cellulose. In this application it replaced chlorine because the latter produces dioxin which is carcinogenic.

Its second most important field of application is the disinfection of municipal water. For this purpose it was first used in the small town of Niagara Falls next to the Niagara Water Falls in 1944 substituting chlorine. Chlorine dioxide has many favourable properties compared to chlorine. Its disinfectant effect exceeds that of chlorine, moreover it does not chlorinate organic compounds.
In Niagara Falls the water was contaminated with phenol, which caused the problems, because chlorine transformed phenol into chlorophenol, which gave the water a really bad taste. What is more, during the chlorination of water so-called trihalo methanes (THM) are formed, which are carcinogenic. It is therefore advisable to change over from the cheaper chlorine to the more expensive but healthier chlorine dioxide where the water contains a higher amount of organic materials. This had been done first in 1956 in Bruxelles among the big cities.

Application of ClO_2 in the food industry, oral hygiene and dentistry

Recently chlorine dioxide solutions were introduced for other purposes, like in the United States for washing fruits and meats. Besides disinfection chlorine dioxide can be used also for deodorizing, for mouthwash, and for other purposes. Chlorine dioxide not only kills all the bacteria responsible for bad breath but directly reacts with the sulphur containing compounds (like sulphur-hydrogen, methyl-mercaptan and dimethyl-sulphide) causing the bad breath, and this way successfully stops halitosis as demonstrated by a very thorough Japanese study [1]. The same paper emphasizes two important advantages of mouthwashes made with chlorine dioxide compared to those containing chlorohexidine: the former does not discolour the teeth and tongue and even its continuous use does not produce unwanted side effects. The wide spread of these mouthwashes has been hindered as besides chlorine dioxide they also contained other chemicals which unfavourably affect on one side the quality and on the other side the long term stability of these mouthwashes. To avoid problems caused by the instability chlorine dioxide can be prepared on the spot by mixing the necessary chemicals. This procedure is used e.g. by the DioxiCare [2] system of the Frontier Pharmaceutical firm in New York, which is recommended also for stopping toothache. The local production of chlorine dioxide solves only the problem of durability, however, the chemicals needed for the ClO_2 production still stay in the mixture.

Routine methods of ClO_2 production on the spot

ClO_2 can be produced on the spot in several ways. Here we only describe a method which is suitable for human purposes. The simplest way is adding some acid to sodium chlorite ($NaClO_2$) because $NaClO_2$ disproportionates into ClO_2 and Cl^- ion in acidic medium. Optimum yield and shortest reaction time would be achieved with hydrochloric acid but that can be used in industrial applications only. For human purposes hydrochloric acid is replaced with some organic acid, mostly citric acid. However, ClO_2 production with citric acid is slow and incomplete, which is problematic not only because of the low yield but mainly because of the unreacted chlorite staying in the solution. Moreover ClO_3^- is also formed which also a toxic contaminating component. The biggest problem, however, is the citric acid itself which is rather harmful for tooth enamel. In addition, as we have already mentioned above, the chlorine dioxide solution produced this way is unstable because of its contaminants: it decomposes easily, and this is why it must be produced on the spot.

A Hungarian invention: the SOLUMIUM

To solve the above problems we started a research aiming to produce pure chlorine dioxide solution free of any contaminants. As a result we managed to develop a membrane technology capable to produce "hyper-pure" ClO_2 solution. A patent application for this method was filed in 2006 by Zoltan Noszticzius and co-workers in Hungary [3], and now the patent is pending in several countries all over the world. A further advantage of the hyper-pure aqueous chlorine dioxide solution is that –despite the long lasting scientific misbelief - it decomposes only very slowly and therefore it has a long shelf life. SOLUMIUM DENTAL [4] is such a hyper-pure chlorine dioxide solution in which the concentration of ClO_2 is 1200 ppm and which is applied successfully already in the dental practice. Before listing the possible applications, however, first we show why ClO_2 is one of the most effective disinfectants –maybe the most effective one–, that is "the ideal biocide", and – despite its excellent properties – why it has not been used in human medicine.

Why ClO_2 is an ideal biocide?

Below we list 6 advantageous properties of chlorine dioxide which make it an ideal disinfectant:

1) First of all, ClO_2 can be successfully applied against all types of microbes – thus against bacteria, fungi, viruses and protozoa and usually it is more effective than other disinfectants.

Table I [5] shows for several disinfectants those minimal disinfectant concentrations in ppm (mass/mass) units which is necessary to achieve sufficient disinfectant effect within 2.5 minutes. The Table compares the effectiveness of various disinfectants for 5 different microorganisms.

The Table demonstrates that while in the case of chlorine dioxide often 1 ppm is sufficient, higher concentrations are needed using other disinfectants to obtain the same effect. Which means that among all the typical disinfectants displayed in the Table chlorine dioxide is the most effective one.

Table 1.

Disinfectant	Microorganism				
	E. coli	S. aureus	MRSA	B. subtilis (spore)	A. niger
Glutar-dialdehyde	100.000	100.000	100.000	100.000	100.000
Phenol	10.000	>10.000	>10.000	>10.000	>10.000
Abs. ethanol	500.000	500.000	500.000	500.000	500.000
Chlorine hexidine digluconate	100	10	1.000	1.000	>10.000
Benzalconium chloride	100	10	100	1.000	10.000
Polivynil pirrolidon (Povidon)-iodine complex	10	100	100	>1.000	1.000
Sodium hypochlorite	10	10	10	>1.000	1.000
Chlorine dioxide	1	1	1	100	10

2) The second very advantageous property of ClO_2 is that for humans it is not dangerous at all, at least not in a small quantity. As previously mentioned chlorine dioxide is used mainly for disinfecting water, therefore first it was demonstrated with animal experiments – applying mostly rats– that it is practically harmless for mammals. For example, in one experiment [6] rats were drinking water containing chlorine dioxide over a period of 90 days and it did not make any harm in the animals even if the ClO_2 concentration was 200 ppm in their drinking water. The only symptom observed was the inflammation of the respiratory tract but that was not due to the water consumed but to the ClO_2 evaporated from water and inhaled subsequently. Nevertheless, when in the United States more and more cities switched to ClO_2 to disinfect municipal water then human experiments were also started in the beginning of the 1980's at the Ohio State University with 60 volunteer young men at the ages of 21 to 35 years [7]. They drunk 1 litre of water containing ClO_2, and after that they were subjected to very extensive clinical tests over 4 days. When no clinical change was found at anybody, they were asked to drink again 1 litre of water but with a higher concentration of ClO_2. This way increasing gradually the quantity of the ClO_2 it was concluded that consumption of 24 mg of ClO_2 per day does not cause any measurable change in a healthy human being. The only reason why higher doses were not tested is that larger quantities cannot be consumed with drinking water, and the aim of these experiments was to prove that it is safe to use ClO_2 for the disinfection of municipal water.

Furthermore, it is important to mention that the report of the Agency for Toxic Substances & Disease Registry [8] states that ClO_2 is not carcinogenic and it is not an allergen either.

3) The third advantageous property of ClO_2 is that while it dissolves very well in water which is one of the most polar solvents, at the same time it also dissolves very well in apolar organic solvents like hexane, cyclohexane, benzene [9] or silicon rubber [3]. Consequently it also dissolves well in the apolar lipid phase of the cell membrane which means that cell membranes cannot prevent the penetration of ClO_2 to the tissues. This is the reason why ClO_2 disinfects not only on the surface of the skin or mucous membranes, but it can disinfect in depth. It can penetrate – depending on the concentration and the time applied – to several tenths of a mm or even deeper into the skin. This is a most important property in the case of biofilms. For example, although ozone is accepted as the strongest disinfectant ever in free aqueous solutions, in case of biofilms it is almost ineffective, because the solubility of ozone is too small therefore it cannot penetrate into the biofilms. Chlorine dioxide on the other hand, is very effective against biofilms.

4) The fourth advantageous property of ClO_2 is that it reacts with very few materials. It oxidizes Fe(II) to Fe(III) and Mn(II) to Mn(IV) but it does not react (or reacts only very slowly) with alcohols, aldehydes, monounsaturated hydrocarbons, with the DNS and we could go on listing some more. Among the 20 amino acids, which occur in living beings, it only reacts with 4 but with those very swiftly. These 4 are the 2 amino acids which contain sulphur: the cysteine and the methionine (the attraction of ClO_2 to sulphur has been mentioned earlier), and also the aromatic tyrozine and tryptophan. Its disinfecting effect can be attributed to these reactions, although the exact mechanism of the effect is not yet known.

If a disinfecting is carried out in a medium which contains materials that can be oxidized and chlorinated then ozone and chlorine will be consumed rapidly in the oxidizing and chlorinating reactions so a lot of them is needed. ClO_2 on the other hand reacts with few materials only, so its consumption is low even under such conditions.

5) The fifth very advantageous property of chlorine dioxide which should be emphasized is that microbes are not able to develop resistance against chlorine dioxide. This was established in the toxicological report [8] on the basis of experiments but this can be expected theoretically as well. Namely, all living creatures, including microbes are composed of the same 20 amino acids, so that none of them can live without cysteine, methionine, tyrozine and tryptophan. As chlorine dioxide

reacts with these materials bacteria are not able to develop resistance against it. This can have special significance in our days, when new strains appear continuously, which are resistant to various antibiotics, like the well-known MRSA (methycillin resistant Staphylococcus Aureus).

6) Finally, a practical advantage of chlorine dioxide is its volatility. Namely, the disinfectant is needed only as long as the pathogen microbes are killed. When they are already dead the presence of the disinfectant is not only unnecessary but can be even harmful because it can impede the healing process. When a hyper-pure chlorine dioxide solution is applied, nothing remains after the evaporation of the water and chlorine dioxide, thus it can be regarded as an ideal biocide in this respect as well.

Why ClO_2 was not applied until now in human medicine?

After all that a logical question emerges, why has not chlorine dioxide been introduced as a disinfectant for humans and animals long ago? We can list 4 reasons:

1) There was no method, whereby a pure enough aqueous chlorine dioxide solution could be easily and swiftly produced. The introduction of SOLUMIUM solution solves the problem.

2) It was believed that the aqueous solution of chlorine dioxide decomposes fast and therefore the aqueous solution cannot be stored. As it was mentioned fortunately this is not the case; the pure solution can be stored at room temperature even for years. As a matter of fact, when storing chlorine dioxide solution the problem is not its decomposition but rather its volatility. The vapour pressure of the solution and this way the loss can be significantly diminished if the SOLUMIUM DENTAL solution is being stored in a refrigerator – especially after the start of its use.

3) Those advantageous properties of chlorine dioxide, which we set forth in the previous paragraph were generally not known as a whole. Furthermore the level of danger which ClO_2 might cause could easily lead to misunderstandings. Namely, in high concentration it can explode – although it is rather called “puff” as it is weak –, and as a result of persistent inhaling it can cause lung oedema. According to international standards, however, ClO_2 solutions under 3000 ppm are not to be considered dangerous as the above mentioned dangers can only appear if the concentration is several times over this limit.

4) Finally we remark that the big pharmaceutical companies are not interested in dealing with known molecules (and ClO_2 has been known for two centuries) as these molecules cannot be patented and therefore the prospective profit is smaller.

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