Dr. Katz's TheraBreath™ with New Active Ingredient–Pharmagene®

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Chlorine dioxide (ClO_2) is a powerful molecule that is used in the treatment of halitosis and various periodontal diseases. There is enormous scientific evidence, that ClO_2 kills the harmful bacteria and destroys the odor causing molecules by reacting with them. As a result, in the past few years, several ClO_2 based mouthwash products have been introduced in the market for the treatment of halitosis. Although the proclaimed basis for the action of these product is ClO_2, there is usually no ClO_2 in these formulations. The primary ingredient in most ClO_2 based mouthwash products is chlorite ion (ClO_2^-), a precursor of ClO_2. Odor causing bacteria and compounds in the mouth generally create a low pH condition in the oral cavities where they are concentrated. Under acidic conditions, ClO_2^- converts to ClO_2. The mechanism that relates to the sensitivity of this conversion is referred as "trigger mechanism". The primary difference between the different ClO_2 based mouthwash products is in their trigger mechanisms. The more sensitive the trigger mechanism, the more efficacious the mouthwash is in controlling bad breath. Although, the chlorite ion can also react with the odor causing compounds, these reactions are quite sluggish in nature.

Generally, the chlorite solutions that are used for manufacturing commonly available ClO_2 based mouthwash formulations, are obtained from technical grade concentrates of chlorite. Some companies claim that they have free ClO_2 present in their product. These products require the addition of household bleach in the mouthwash formulation. Regarding these products, three points must not be forgotten: i) formulations containing bleach not only have unpleasant odor and taste, but are known to form carcinogenic compounds known as trihalomethanes (THM)[1-4]; ii) the concentration of free ClO_2 in these products is too small to make any difference and depletes almost instantaneously by the organic load in the mouth; and iii) it is extremely difficult to stabilize free ClO_2 in a solution for more than a few days. We performed iodometric analysis on a product that was claimed to contain free ClO_2. 5 ppm of free ClO_2 was detected. However, the concentration rapidly dropped to negligible within two weeks.

Based on his extensive research, now, Dr. Katz introduces a new active ingredient in his TheraBreath™ mouthwash formulation. This powerful ingredient is called Pharmagene®. Pharmagene® is not simply a solution of tech-grade sodium chlorite. Pharmagene® is a concoction of stabilized oxychloro complexes which are in dynamic equilibrium with free chlorine dioxide. The quantity of ClO_2 present in this solution at any given time is extremely small. However, the dynamic state of the oxychloro complex enables it to produce copious amounts of ClO_2 on demand. The chemical equilibrium may be summarized as shown below, where K_{eq} is the equilibrium constant:

$$\text{Latent precursors} \overset{K_{eq}}{\rightleftharpoons} ClO_2$$

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The consumption of free ClO_2 in this solution would lead to the replenishment of this component by a simple Le Chatelier shift of the equilibrium to the right. The demand for ClO_2 is caused by the odor causing bacteria and the volatile sulfur compounds (VSC) that are produced in the mouth. The solutions of tech grade sodium chlorite would react much slower with the bacteria and VSCs. However, due to its very sensitive trigger mechanism, Pharmagene® kills the bacteria and reacts with the VSCs at a much faster rate. Moreover, Pharmagene® is manufactured using a propriety manufacturing technique that does not require the addition of any extraneous stabilizing elements or buffers which are generally needed for the production of sodium chlorite. Thus, owing to its high purity, Pharmagene® provides a much longer residual effect in controlling bad breath.

The behavior of Pharmagene® that leads to production of ClO_2 on demand can be demonstrated using the Palin titration procedure.[5] This procedure involves the reduced form of diethyl-p-phenylenediamine (H_2DPD)

$$2\ ClO_2 + H_2DPD \rightleftharpoons 2ClO_2^{\cdot} + DPD + 2\ H^+$$

The end point is obtained by titrating with a standard solution of ferrous ammonium sulfate until the red color of DPD disappears:

$$DPD + 2H^+ + 2\ Fe^{2+} \rightleftharpoons H_2DPD + 2\ Fe^{3+}$$

When Pharmagene® solutions are subject to this analysis, they exhibit reappearance of the red color after the end point has been established. This is true even if the titrations are conducted under nitrogen atmosphere. Additions of titrant to reestablish the end point are repeatedly followed by the reappearance of the color. This phenomenon, i.e., reestablishment of the red color, repeated on one sample over 20 times within the time period of a few minutes. Similar behavior is not observed for solutions of tech-grade sodium chlorite, or even for the pure solution of ClO_2.

It is speculated that Pharmagene® contains a combination of oxychloro species with oxidation states ranging from -1 to +7. Conventional analytical procedures for the investigation of chlorine-containing species are, in general, inadequate to quantify the individual components and the extent of dynamic nature of Pharmagene®. Conventional techniques are typically designed to measure one of the chlorine-containing components by itself. Such methods also frequently ignore the dynamic equilibrium processes which control individual concentrations. As an example, the most readily applicable instrumental technique for the determination of both ClO_2 and $ClO_2^{\cdot}$ is UV-Vis spectroscopy. However, this technique is insufficient to unravel the true nature of Pharmagene® for two reasons. First, the nature of Pharmagene® is such that it does not contain large concentration of free ClO_2—it only provides ClO_2 on demand. Secondly, the various other oxychloro species present in Pharmagene absorb light at the λ_{max} for both ClO_2 (360 nm) and

ClO_2^- (262 nm).

Procedures such as ion chromatography are also unable to detect species that exist as radicals. ClO_2 in this technique is detected as ClO_2^-.

A unique method which allows characterization of the dynamic equilibrium of Pharmagene® is Electron Spin Resonance Spectroscopy also known as ESR. This technique is responsive to unpaired electrons. Using the ESR technique, it was demonstrated that Pharmagene® is quite unique in its nature as compared to the other sodium chlorite solutions. Quick-frozen solution of Pharmagene® in liquid nitrogen displayed peaks at 3.2 kG demonstrating its paramagnetic character. No peaks were observed when similar technique was adopted for generic sodium chlorite solution.

It can be concluded that unlike the tech-grade sodium chlorite, Pharmagene® is in dynamic equilibrium that readily triggers the formation of ClO_2 on demand. Electron spin resonance spectroscopy demonstrates the existence of dynamic equilibrium. Technical grade sodium chlorite solutions do not have such properties and therefore, they require the addition of acid and bleach to generate free ClO_2. Since TheraBreath contains Pharmagene®, it does not require the addition of any undesired chemicals to accelerate its activity. TheraBreath™ is a perfect solution for halitosis that instantaneously destroy the odor causing bacteria and compounds in the mouth. Additionally, it provides long residual effect in preventing bad-breath and biofilm formation.

References:

1) Richardson, S.D.; Thruston, A. D., Jr.; Caughran, T.V.; Collette, T.W.; Patterson, K.S.; Lykins, B.W., Jr. *Food Tech.*, **1998**, 52, 58-61.

2) Narkis, N.; Kott, Y. *Wat. Sci. Tech.*, **1992**, 26, 1483-1492.

3) Li, Jun Wen; Yu, Zuobin; Cai, Xinpei; Gao, Ming; Chao, Fuhuan C. *Wat. Res.* **1996**, 30, 2371-2376.

4) Myers, A. G. *Journal AWWA*, **1990**, 78-84.

5) Palin, A. J. Inst. Water Eng., **1974**, 28, 139.

The following report was compiled by Dr. Neeraj Khanna, Director of Research and Development at Bio-Cide International. He has completed diverse research evaluation of mouthwash products. An analytical chemist with ten years of research in the field, Dr. Khanna is highly regarded as an expert in the field of chlorine dioxide.

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