Home use of ozonated water for preventive-therapeutic oral care: General guidelines

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ABSTRACT - Background: *Ozone therapy in dentistry is gaining more attention and is the second most researched field after musculoskeletal in clinical studies. Dentists routinely prescribe oral antiseptics for home oral care and after in-office interventions. Ozonated water is well known for its antimicrobial, anti-inflammatory and accelerated wound healing properties, as well as for its extremely low cytotoxicity and side effects. To our knowledge, this is the first article to evaluate the performance, practicality and safety of a direct electrolytic ozone generator and to propose general guidelines for at-home use of ozonated water for preventive-therapeutic oral care regimen.*

Methods: *A direct electrolytic ozone generator was tested and the concentration of ozonated water, total oxidants, dissolved molecular hydrogen, and ambient ozone gas levels in air were measured.*

Results: *Ozonated water concentration reached a range of 2-5 mg/L, and ambient ozone gas levels in air were not detected.*

Conclusion - Practical implications: *At-home use of ozonated water is more convenient for both dentists and patients, especially when multiple applications are indicated. Water electrolysis is a safe and easy-to-use method to prepare ozonated water at efficient concentration.*

Introduction

Since its discovery by Christian Friedrich Schönbein in 1839 by water electrolysis (Rubin, 2001, Rubin, 2002), ozone is used in various fields of medicine (Madrid declaration on ozone therapy, 2020, Serra et al., 2023). Its application in dentistry is gaining more attention (Néri et al., 2017, Tiwari et al., 2017, Suh et al., 2019, Chaudhry et al., 2021, D'Amario et al., 2022), and is the second most researched field of application in ozone therapy (Zotero ISCO3 database), (Figure 1).

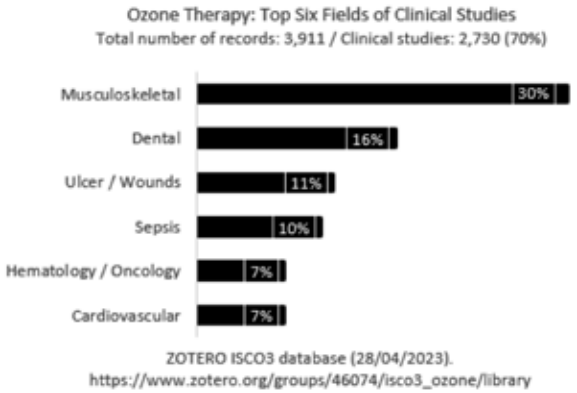

Figure 1 Top six fields of clinical research in ozone therapy.

Ozonated water is used in medicine (Martínez-Sánchez, 2019) and a literature analysis showed 89% of significant positive results in dentistry (Sabbah et al., 2018). Conventional preparation of ozonated water requires the use of an ozone gas generator, diffuser, contact vessel and oxygen gas cylinder (Sabbah and Domb, 2021). The complexity of this method might be a challenge for non-trained users and there is a need for a practical, efficient, and safe method for home use.

Electrolytic ozone generator (EOG), in its simplest form, both anode and cathode electrodes are immersed in water without a separating membrane. Advanced EOG employs a proton exchange membrane (PEM) which separates the electrodes, and the generated ozone gas concentration can be extremely high. The membrane-less EOG needs water with a minimum of 50 mg/L dissolved solids, and the evolved gases (O_2-O_3 and H_2) are dissolved

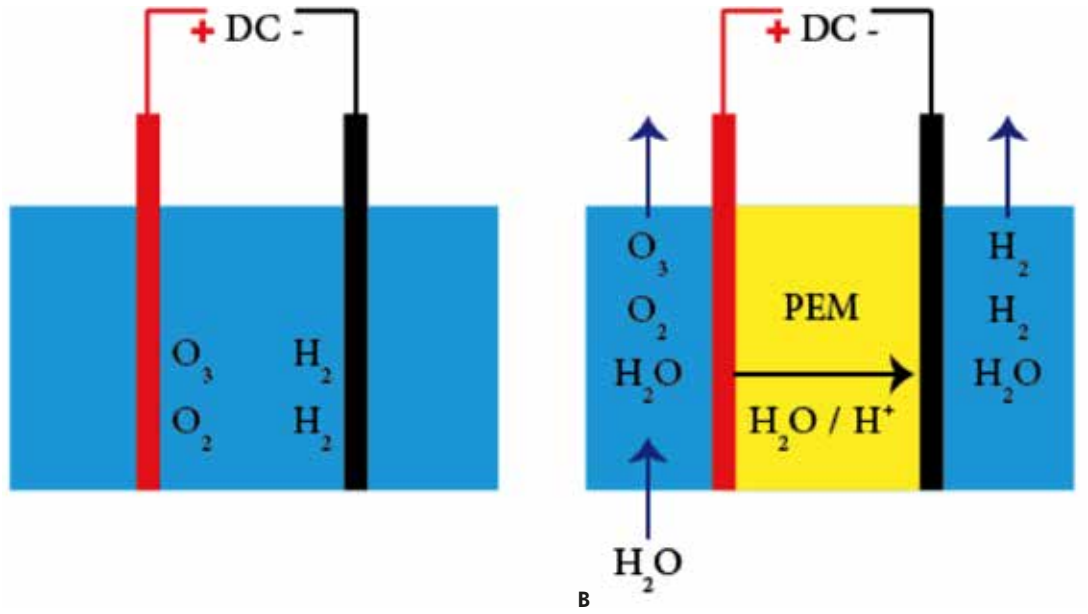

Figure 2 Membrane-less EOG (a); PEM EOG (b) - *Legend*. EOG: *Electrolytic ozone generator*. PEM: *Proton exchange membrane*. DC: *Direct current*.

in situ according to their respective solubility ratios. PEM EOG can work with ultra-pure water, O_2-O_3 gas mixture and H2 have separate outlets (Da Silva and Santana, 2003, Stucki et al., 2005, Okada and Naya, 2012, Christensen et al., 2013, Okada et al., 2019), (Figure 2).

The scope of this article is to evaluate the performance, practicality and safety of a direct electrolytic ozone generator and to propose general guidelines for at-home use of ozonated water for preventive-therapeutic oral care regimen.

Materials and Methods

A battery-operated direct EOG tumbler (Biotek Environmental Science, New Taipei, Taiwan) was evaluated with bottled drinking water (Table 1) at three different time settings. Ozonated water concentration was measured with an aqueous ozone monitor (2B Technologies, model UV-106-W, Boulder, USA) which uses a sparging technique to remove ozone gas from water, followed by UV (ʎ 254 nm) measurement of ozone in the gas phase. This mode of measurement is highly specific to ozone, without any interference from other oxidants which can be present in the tested water.

Total oxidants concentration (TOC) was measured with a photometer and potassium iodide (KI) / N,N-diethyl-p-phenylenediamine (DPD) Vacu-Vials kit (Chemetrics SAM K-7423, USA). KI/DPD test is not specific to ozone, and measures the concentration of other oxidants (i.e., hydrogen peroxide, hydroxyl radicals, hypochlorous acid, hypochlorite) which can oxidize iodide to iodine.

Table 1 Water characteristics

TDS	180 mg/L
Cl-	7 mg/L
Temp	20°C
Vol	140 mL
pH	6.7

Legend. TDS: *Total dissolved solids*; Cl- (*Chloride*)

Dissolved molecular hydrogen concentration was measured with a hydrogen sensor (Trustlex ENH-2000, Osaka, Japan).

Ambient ozone gas levels in air were monitored with a portable gas detector (PortaSens II, Analytical Technology Inc., USA) at 5 cm from the EOG during device activation.

The direct EOG tumbler has a preset working time of 2.5 min (One cycle). Tests were performed at 1, 2 and 3 consecutive cycles, 2.5 – 5 – 7.5 min operating time, respectively. Ozonated water tests were repeated five times, total oxidants and dissolved molecular hydrogen were analyzed by duplicate. Ambient ozone gas levels were monitored at 5- and 7.5-min operation time. Values are expressed as (X) ± SD.

Results

The EOG device operates at a constant current and the voltage is auto-adjusted according to water electrical conductivity. The lower the water conductivity or total dissolved solids (TDS), the

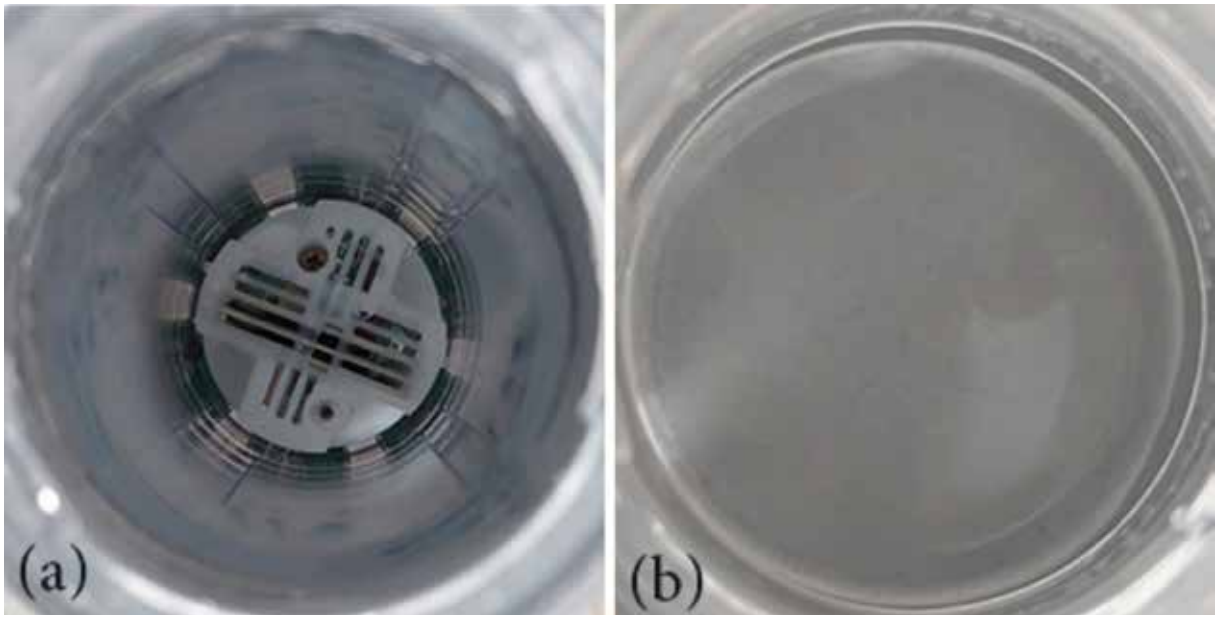

Figure 3 (a) Electrolysis cell visible; clear water; (b) Gas nanobubbles; opaque water.

higher is the operating voltage. This feature will ensure that the water electrolysis performance is stable within a large TDS range (50 – 400 mg/L). The concentration range of ozonated water, TOC, H2, and ambient ozone gas, are depicted in (Table 2).

Table 2 Ozonated water, TOC, H2 and ambient ozone gas concentrations

Time (min)	**Cw O_3** (mg/L)	**TOC** (ppm)	**Cw H_2** (ppm)	**Ca O_3** (ppm)
2.5	2.7±0.19	4.3±0.18	NT	NT
5	4.8±0.31	6.3±0.35	1±0.1	0
7.5	5.5±0.23	8.5±0.32.	NT	0

Legend. Cw O_3 (*Ozonated water concentration*), TOC (*Total oxidants concentration*), Cw H_2 (*Dissolved molecular hydrogen concentration*), CaO_3 (*Ambient air ozone gas concentration*), ppm (*parts per million*), NT (*Not Tested*).

It is noteworthy to mention that the evolved gas bubbles by water electrolysis have a sub-micron size, and the resulting increase of the gas/liquid contact area enhances gas dissolution into water. Another factor which can also contribute to dissolution rate and usage efficiency is the residency time of the nanobubbles inside water before total off-gassing, around 1 minute for the tested EOG device (Figure 3).

Discussion

Ozonated water concentration range in ozone therapy, especially in dentistry, can be classified as low (1-3 mg/L), medium (4-8 mg/L) and high (10-25+ mg/L) (Sabbah et al., 2018). In severely infected clinical cases, high range ozonated water concentration is first used and then reduced to medium/low according to the healing phase progression. In cases where there is a need for multiple applications of ozonated water, it would be more convenient for both dentists and patients to apply ozonated water at home, especially when low/medium concentrations are advisable.

The tested direct EOG device produces a low to medium ozonated water concentration range (2 - 5.5 mg/L), while the total oxidants concentration (TOC) range is 4 - 8.5 ppm (Table 2). Since the monitor used for dissolved ozone concentration measurement is highly specific to ozone, the higher TOC values correspond to reactive oxygen species generated by ozone decomposition in water and are measured by non-ozone specific methods. For safety reasons, maximum allowable ozone gas levels in ambient air is ≤ 0.070 ppm for an 8-hour period (EPA-United States Environmental Protection Agency). At 5- and 7.5-min continuous operation, ozone gas was not detected at 5 cm from the device.

Ozonated water is mostly known for its antimicrobial and disinfection property and has the lowest CT factor (Concentration x Time) among common oxidants used in various fields (Gomes et al., 2019, Azim et al., 2020, Romanovski et al., 2020, Epelle et al., 2023).

Dentists routinely prescribe oral antiseptics or over-the-counter mouthwash solutions (i.e., Chlorhexidine, triclosan, povidone-iodine, benzydamine-hydrochloride, essential oils, chlorine dioxide, hydrogen peroxide) for preventive/therapeutic oral care regimen, or after professional

in-office interventions. The most reported side effects of oral antiseptics and mouthwash solutions are teeth staining, burning sensation, taste alteration, mucosal desquamation and ulcers. Some formulations have food allergens which might trigger allergic reactions (Tartaglia et al., 2019, Coimbra et al., 2023).

Ozonated water at 1.2 – 20 mg/L showed no cytotoxic effects on human oral epithelial cells and gingival fibroblasts, while chlorhexidine, hydrogen peroxide 3% and sodium hypochlorite 0.2% showed cytotoxic effects. Mouthwash solutions cytotoxic effects on primary human gingival fibroblasts were highest with chlorhexidine, followed by benzydamine-HCl and essential oils (Huth et al., 2006, Mon et al., 2019, Alpaslan et al., 2021).

Several studies reported that ozonated water with a concentration range of 2-16 mg/L had no cytotoxic effects, induced increase of cellular metabolism, intracellular ATP, growth factors release, and contributed to cells proliferation and acceleration of wound healing (Ebensberger et al., 2002, Kuroda et al., 2015, Borges et al., 2017, Küçük et al., 2021, Leon et al., 2022). Ozonated water at 0.5 mg/L had the same local hemostatic effect as 4 mg/L and is as effective as liquid thrombin in decreasing bleeding time (Sakai et al., 2014).

All these beneficial properties as antimicrobial, anti-inflammatory, wound healing acceleration, absence of cytotoxicity and undesirable side effects, make ozonated water highly indicated for home oral care.

Home oral care – General guidelines

The treating dentist usually plans a customized preventive - therapeutic home oral care according to patient's risk factors. Long term daily use of mouthwash might decrease nitric oxide bioavailability by affecting the oral microflora and might cause blood pressure elevation (Joshipura et al., 2020).

Taking into consideration the potential long-term effect on normal oral microbiota, general preventive guidelines are here presented and should not be considered as specific protocols.

Caries and Periodontal diseases

Dental plaque biofilm is a key risk factor in caries and periodontal diseases which affect many people worldwide (Marsh, 2006, Frencken et al., 2017). Numerous studies showed ozonated water had good results in prevention and management of dental caries and periodontal diseases, as well as during orthodontics treatment, pregnancy, and halitosis management (Ramzy et al., 2005, Kshitish and Laxman, 2010, Bialoszewski et al., 2011, Dhingra and Vandana, 2011, Syed et al., 2012, Katti and Chava, 2013, Hayakumo et al., 2014, Sadatullah et al., 2014, Anumula et al., 2017, Jose et al., 2017, Hirai et al., 2019, Su et al., 2021, Tecco et al., 2022, Do Amaral et al., 2023). (Table 3).

Table 3 Caries and Periodontal diseases: General preventive guideline

Risk Factors	Dose	Three-month cycle*	Usage
Low		First week: every other day Week 2-4: twice per week	Swish/Gargle for 30-50 s. A waterjet can also be used for its beneficial effects on dental plaque breakdown and removal.
Medium	C_w 2.5 mg/L Volume 50 mL	First week: once daily Week 2-4: twice per week	
High		First week: once daily Second week: every other day Week 3-4: twice per week	

*: Re-assessment at dental office follow-up visits

Legend. C_w: *Ozonated water concentration.*

Soft tissue lesions

Ozonated water showed beneficial results for the management of chemotherapy-induced oral mucositis (Hayashia et al., 2019, Lazaro et al., 2020, Ghorbani et al., 2021), lichen planus (Mostafa and Zakaria, 2018, Veneri et al., 2020), ulcers (Miao et al., 2017), recurrent aphthae and herpetic lesions (Gawish and Bahammam, 2014, Al-Omiri et al., 2016), and methicillin-resistant staphylococcus aureus skin infections (Song et al., 2017). As a rule, especially in infected cases, start with a high ozonated water dose and reduce to medium/low dose according to the healing phase progression (Table 4).

Table 4 Soft tissue lesions. General guideline

	Dose	Frequency
High	C_w: 5 mg/L Vol. 50 mL	Four times per day Reduce to Medium/Low as healing progresses.
Medium	C_w: 5 mg/L Vol. 50 ml	Two times per day
Low	C_w: 2.5 mg/L Vol. 50 mL	2-3 times per day
Swish/Gargle for 30-60 s		

Legend. C_w: *Ozonated water concentration*

Post-surgery interventions

Ozonated water was shown to reduce post-surgery inflammation, pain, and to enhance healing

(Frascino et al., 2013, Ghosh et al., 2020, Glória et al., 2020, Kogila et al., 2022, Romary et al., 2023). Good home oral care is essential to avoid postoperative infections. Home use of ozonated water after surgical interventions is highly indicated to maintain the surgical wound clean and minimize potential post-surgery complications (Table 5).

Table 5 Post-surgery general guideline

Dose	Usage & Frequency
C_w: 5 mg/L Volume: 50 mL	Day 1-2: Fill a 50 mL disposable sterile syringe and gently rinse the surgical area. Dip a soft toothbrush in ozonated water and gently clean the wound. Repeat after each meal. 3-4 times per day. Day 3-10: Same as above or gentle swish.

Legend. C_w: *Ozonated water concentration.*

Removable Dentures – Oral appliances disinfection

Oral appliances and dentures can harbor bacteria and fungus (Glass et al., 2011) if not regularly cleaned and disinfected, and may cause stomatitis, staph or strep throat, as well as bad breath. Ozonated water is effective in eliminating the biofilm adhering to removable dentures and oral appliances (Arita et al., 2005). Clean and soak the appliance or dentures in ozonated water (5 mg/L) daily.

Conclusion

Ozonated water was shown to be highly effective and biocompatible in medical and dental applications. Its use as a mouthwash for preventive – therapeutic home oral care can be beneficial without causing undesirable side effects as seen with common mouthwash formulations. For home use, direct electrolytic ozone generation is practical, easy-to-use, and safe in comparison to the traditional ozonated water preparation and can reach an efficient concentration range suitable for home oral care. To our knowledge, this is the first article to propose general guidelines for at-home use of ozonated water. It is hopeful that future studies will be conducted, and to evaluate potential effects of long term at-home use of ozonated water on normal oral microflora.

Conflict of Interest

CD and MW declare no conflict of interest. FS is a scientific consultant to Biotek Environmental Science.

Biotek Environment Science donated the electrolytic ozone generator and had no role in the study design, in data collection and analysis, nor in writing the manuscript and submitting it for publishing.

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Authors' Contribution

FS contributed to the design of the study, to the data acquisition, analysis, and interpretation, and to the writing of the manuscript. CD and MW contributed to the data analysis and interpretation, to the revision of the manuscript and final approval of the version to be submitted for publication.

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