

# Ozone Therapy: The Boon for Periodontics

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**Abstract:** *The oral cavity is an open ecosystem, with a dynamic balance between the entrance of micro organisms, colonization modalities, and host defenses aimed at their removal. To avoid elimination, bacteria need to adhere to either hard dental surfaces or epithelial surfaces. The oral biofilm formation and development, and the selection of specific microorganisms have been correlated with the most common oral pathologies, such as dental caries, periodontal disease, and peri-implantitis. The mechanical removal of the biofilm and adjunctive use of disinfectants or various antibiotics have been the conventional methods for periodontal therapy. Ozone (O<sub>3</sub>) is a tri atomic molecule, consisting of three oxygen atoms, and its application in medicine and dentistry has been indicated for the treatment of 260 different pathologies. The ozone therapy has been more beneficial than present conventional therapeutic modalities that follow a minimally invasive and conservative application to dental treatment. The exposition of molecular mechanisms of ozone further benefits practical function in dentistry. [1] Ozone gas has a high oxidation potential and is 1.5 times greater than chloride when used as an antimicrobial agent against bacteria, viruses, fungi, and protozoa and also has the capacity to stimulate blood circulation and the immune response. Therefore it is the current interest in medicine and dentistry. It can be used for the treatment of alveolitis as a replacement for antibiotic therapy, as a mouthwash for reducing the oral microflora, as well as the adherence of microorganisms to tooth surfaces. [2]*

**Keywords:** ozone therapy, ozone, periodontitis

## 1. Introduction

Ozone is a chemical compound consisting of three oxygen atoms (O<sub>3</sub> – triatomic oxygen) and is a higher energetic form than normal atmospheric oxygen (O<sub>2</sub>). Thus, the molecules of these two forms are different in structure (Figure 1). It is one of the most important gases in the stratosphere due its ability to filter UV rays which is critical for the maintenance of biological balance in the biosphere. This protective layer can be seen as the blue-colored sky.

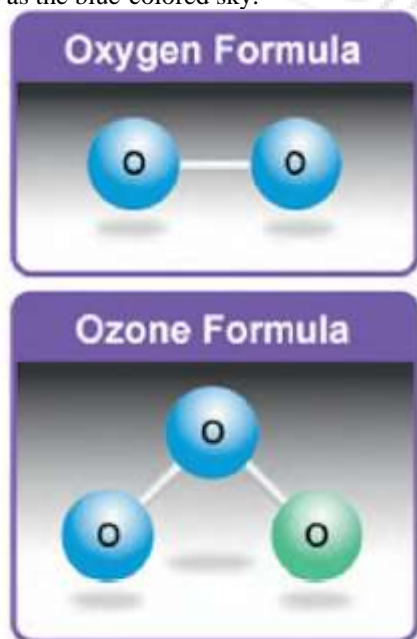


Figure 1: Oxygen and ozone formulas.

Ozone is produced naturally by the following natural

methods

- **From electrical discharges following thunderstorms.** Ozone is created when an oxygen molecule receives an electrical discharge breaking it into two oxygen atoms.

The individual atoms combine with another oxygen molecule to form an O<sub>3</sub> molecule (Figure 2).

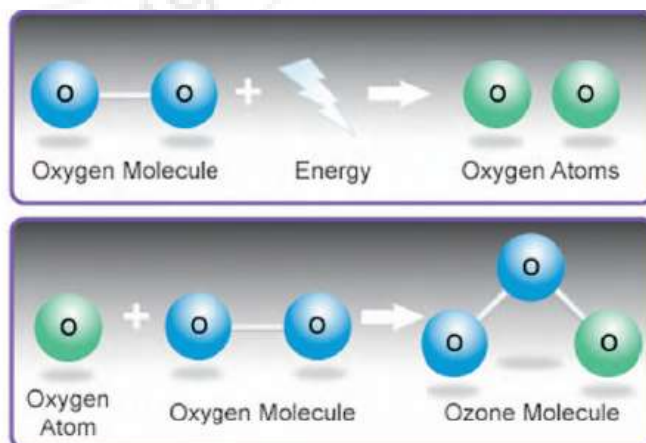


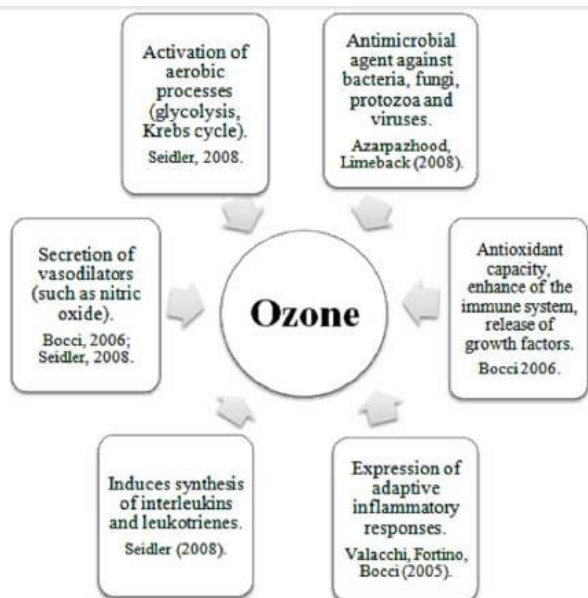
Figure 2: Production of ozone

- **From ultraviolet rays emitted from the sun** It plays the role of electrical discharge over oxygen present in the stratosphere, thus, creating the ozone layer which absorbs most of the ultraviolet radiation emitted by the sun.

Medical grade ozone is made from pure medical oxygen because oxygen concentration in the atmospheric air is variable. Atmospheric air is made up of nitrogen (71%),

oxygen (28%), and other gasses (1%) including ozone which is altered by processes related to altitude, temperature, and air pollution.

nature and actions of ozone. Mariniak and Delarive showed that it is an allotropic form of oxygen, and Mulliken and Dewar clarified its molecular structure.[5]



**Figure 3:** Biological effects of Ozone therapy [3]

#### Different systems for generating ozone gas:

##### Ultraviolet System:

It produces low concentrations of ozone. It is used in esthetics, saunas, and for air purification.

##### Corona Discharge System:

Produces high concentrations of ozone. It is the most common system used in the medical/ dental field. It is easy to handle and it has controlled ozone production rate.

##### Cold plasma system:

Used in air and water purification [4]

## 2. History

The German chemist, Christian Friedrich Schonbein regarded as the Father of ozone therapy (1840) first used the term OZONE (derived from the Greek word “ozein” which means odor) He subjected oxygen to electrical discharges and noted “the odor of electrical matter”. Joachim Hansler (1857), a German physicist and physician, along with German physician, Hans Wolff, developed the first ozone generator for medical use.

Dr. C. Lender (1870), for the first time applied O<sub>3</sub> into medical field. He purified blood in test tubes by using O<sub>3</sub>. In 1893, Ousbaden. Holland became the first city to utilize a water treatment plant using ozone. In World War I and II it was used to treat wounded soldiers in the trenches. In early 20th century Food and Drug Act, revised its use and effect in the field of medicine. Dr. E.A. Fisch (1950) a German dentist, was the first dentist to use ozone on regular basis in his dental practice in Zurich, Switzerland and published numerous papers on its application in dentistry. Numerous researchers since that time have worked to elucidate the

## 3. Mechanism of action

### Anti-microbial action

The anti-microbial effect of ozone is as a result of its action on cells by damaging its cytoplasmic membrane due to ozonolysis of dual bonds and also ozone-induced modification of intracellular contents because of secondary oxidants effects. This action is non-specific and selective to microbial cells; it does not damage human body cells because of their major antioxidative ability. Ozone is very efficient in antibiotics resistant strains. Its anti-microbial activity increases in liquid environment of the acidic pH. In viral infections the ozone action lies in the intolerance of infected cells to peroxides and change of activity of reverse transcriptase, which takes part in synthesis of viral proteins.

### Immuno-stimulating action

Ozone influences cellular and humoral immune system. It stimulates proliferation of immunocompetent cells and synthesis of immunoglobulins. It also activates function of macrophages and increases sensitivity of micro-organisms to phagocytosis. When administered at low concentrations, the organisms own resistance is mobilized, i.e. ozone (re) activates the immune system. As a response to this activation through ozone, the body's immune cells produce special messengers called cytokines. These molecules in turn activate other immune cells, setting off a cascade of positive change throughout the immune system, which is stimulated to resist diseases. This means that the application of medical ozone is extremely useful for immune activation in patients with a low immune status and/or immune deficit. Ozone causes the synthesis of biologically active substances such as interleukins, leukotrienes and prostaglandins which is beneficial in reducing inflammation and wound healing.<sup>8</sup>

### Antihypoxic action

Ozone brings about the rise of pO<sub>2</sub> in tissues and improves transportation of oxygen in blood, which results in change of cellular metabolism e activation of aerobic processes (glycolysis, Krebs cycle, b-oxidation of fatty acids) and use of energetic resources. It also prevents formation of erythrocytes aggregates and increases their contact surface for oxygen transportation. Its ability to stimulate the circulation is used in the treatment of circulatory disorders and makes it valuable in revitalizing organic functions.

### Analgesic & de toxicating action –

Ozone causes secretion of vasodilators such as NO which is responsible for dilatation of arterioles and venules.

### Bio energetic & biosynthetic action –

It activates mechanisms of protein synthesis, increases amount of ribosomes and mitochondria in cells. These changes on the cellular level explain elevation of functional activity and regeneration potential of tissues and organs.

Miscellaneous actions of ozone are circulatory enhancement,

disruption of tumor metabolism and stimulation of oxygen metabolism.

#### 4. Forms of Application

##### Systemic forms of application

- Major Auto Hemo Therapy (MAH) as extracorporeal blood treatment with O<sub>3</sub> and reinfusion of activated blood
- Rectal insufflations of O<sub>3</sub>:O<sub>2</sub> mixture
- Minor auto hemo therapy as intramuscular injection of activated blood.

##### Topical forms of application

- Transcutaneous ozone gas application in gas-tight and ozone-resistant plastic covers
- Ozonized water in the form of spray or compresses
- Rectal O<sub>3</sub>:O<sub>2</sub> insufflation
- Intraarticular injections
- Intramuscular injections
- Ozonated olive oil [5]

#### 5. Antibacterial Effect of Ozone on Plaque biofilm

Both caries and periodontal disease are caused primarily by plaque biofilm. Ozone might be useful to control oral infectious microorganisms in dental plaque. The antimicrobial property of ozone is not only effective in reducing the number of cariogenic bacteria, but also causes significant reduction in the micro organisms present in the root canal. However it was not successful in completely eliminating these bacteria embedded in the biofilm. Ozonated water is effective in killing grampositive, gram-negative bacteria and oral *Candida albicans* causing periodontal disease. Ozonated water had nearly the same antimicrobial activity as 2.5% sodium hypochlorite and also the metabolic activity of fibroblasts was high when the cells were treated with ozonated water. The aqueous form of ozone, as a potential antiseptic agent, showed less cytotoxicity than gaseous ozone or established antimicrobials like chlorhexidine digluconate, sodium hypochlorite or hydrogen peroxide under most conditions. Therefore, aqueous ozone fulfills optimal cell biological characteristics in terms of biocompatibility for oral application. Ozone may be considered as an adjunctive to conventional treatment strategy due to its powerful ability to inactivate microorganisms.

#### 6. Ozone for treatment of peri-implantitis

For the prevention of peri implantitis an adequate and steady plaque control regimen must be ensured. Ozone, a powerful antimicrobial kills the microorganisms causing peri implantitis. In addition ozone shows a positive wound healing effect due to the increase of tissue circulation. Gasiform ozone or ozonized water shows an increased healing compared to wound healing without ozone therapy

#### 7. Effect of ozone on wound healing

The impact of ozone on epithelial wound healing in the oral cavity was observed by Filippi. It was found that ozone-water can be used daily to speed up the healing rate in the oral mucosa. This effect can be seen in the first two postoperative days. The comparison with wounds without treatment showed that daily treatment with ozone water accelerates the physiological healing rate. Patients under ozone therapy healed more quickly and without the need for systemic medication, compared to the control group. Application of ozone after tooth extraction reduced the post-extraction complications. [6]

#### 8. Effect on bacteria, virus, fungus, protozoa

##### 1) Bacteria

Ozone acts on bacterial cell membranes, by oxidation of their lipid and lipoprotein components. There is evidence for interaction with proteins as well. Ozone seems to render the spores defective in germination, perhaps because of damage to the spore's inner membrane.

##### 2) Virus

All viruses are susceptible to ozone; yet differ widely in their susceptibility. Lipid-enveloped viruses are especially sensitive to ozone. Analysis of viral components showed damage to polypeptide chains and envelope proteins impairing viral attachment capability and breakage of viral RNA.

##### 3) Fungal and protozoa

Ozone inhibits cell growth at certain stages.

##### 4) Effect on blood cells

Ozone reduces or eliminates clumping of red blood cells and its flexibility is restored, along with oxygen carrying ability. There is a stimulation of the production of glutathione peroxidase, catalase, and superoxide dismutase which act as free radical scavengers.

##### 5) Effect on leukocytes

Ozone behaves as a weak cytokine such as tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), interleukin-2, interleukin-6, interleukin-8, transforming growth factor- $\beta$  [TGF- $\beta$ ] inducer. Ozone reacts with the unsaturated fatty acids of the lipid layer in cellular membranes, forming hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>), one of the most significant cytokine inducers.

##### 6) Platelets

H<sub>2</sub>O<sub>2</sub> generated by blood ozonation activate phospholipase C, phospholipase A<sub>2</sub>, cyclo-oxygenases and lipoxygenases, and thromboxane synthetase, allowing a step increase of intracellular Ca<sup>2+</sup>, release of prostaglandin E<sub>2</sub>, prostaglandin F<sub>2a</sub>, and thromboxane A<sub>2</sub> with irreversible platelet aggregation [7]

## 9. Advantages

- Disinfectant.
- Anti-inflammatory.
- Activation of intracellular metabolism of oral mucosa and dental wounds.
- Improvement of regional circulation.
- Stimulation of regenerative processes.
- Hemostasis in capillary bleedings.
- Painless procedures.

## 10. Disadvantages

- Ozone toxicity if the level increases at 0.0007% per application.
- Instability.
- Not readily available.

## 11. Indications

- Chronic or recurrent infections in the oral cavity.
- Prophylaxis and prevention of dental caries.
- Remineralization of pit and fissure caries, root and smooth surface caries.
- Bleaching of discolored root canal treated teeth.
- Sterilization of cavities, root canals, periodontal pockets, herpetic lesions.
- Desensitization of extremely sensitive tooth necks.
- Pre washing of surgical sites.
- Plaque control.
- Contamination control. [8]

**Table 1: Potential applications of ozone therapy**

Antimicrobial (bactericidal, viricidal, and fungicidal)
Damage to cytoplasmic membrane
Oxidation of intracellular contents
Specific to microbial cell
Effective in antibiotic resistive strain
Immuno-stimulating
Activates cellular and humoral immune system
Proliferation of immunocomplement cells
Synthesis of immunoglobulin's
Enhance phagocytosis activity
Activation of biological antioxidants
Analgesic
Anti-hypoxic and detoxicating
Activation of aerobic process (Krebs cycle, glycolysis, oxidation of fatty acids)
Bio-energetic and biosynthetic
Activates protein synthesis
Enhanced cell metabolism (Ribosome, mitochondria)
Biologically active substances
Synthesis of interleukins, leukotrienes and prostaglandins
Synthesis of immunoglobulin's

[9]

## 12. Contraindications and side effects

Contraindications <sup>[21]</sup>	Side effects <sup>[22]</sup>
Pregnancy	Epiphora
Hyperthyroidism	Rhinitis
Severe anemia	Cough
Severe	Headache
Active hemorrhage	Nausea and vomiting
Thrombocytopenia	
Cardiovascular instability	
Patients on ACE inhibitors	

[8]

## 13. Ozone safety and toxicity

There has been a reported case of death due to air embolism during the use of ozone in the treatment of psoriasis (Marchetti & Monaca, 2000). Apart from this, it has been reported that a 45-year-old woman complained of acute bilateral visual loss after intra-discal and peri-ganglionic injection of ozone-oxygen gas mixture for lumbar disk herniation (Lo Giudice, 2004). Corea (2004) also reported a case of vertebrobasilar stroke after treatment with ozone-oxygen for lumbar disc herniation. Ozone inhalation can be toxic to the pulmonary system and other organs.

Complications caused by ozone therapy are infrequent at 0.0007 per application. Known side-effects are epiphora, upper respiratory irritation, rhinitis, cough, headache, occasional nausea, vomiting, shortness of breath, blood vessel swelling, poor circulation, heart problems and at a times stroke. Because of ozone's high oxidative power, all materials that come in contact with the gas must be ozone resistant, such as glass, silicon, and Teflon. However, in the event of ozone intoxication the patient must be placed in the supine position, and treated with vitamin E and n acetyl cysteine. Hepatitis C and HIV infections have also been reported following ozone auto haemotherapy. [5]

## 14. Conclusions

In contrast with traditional medicine modalities such as antibiotics and disinfectants, ozone therapy is quite economical; it will markedly reduce both medical cost and invalidity. Dentistry is varying with induction of modern science to practice dentistry. The ozone therapy has been more beneficial than present conventional therapeutic modalities that follow a minimally invasive and conservative application to dental treatment. The exposition of molecular mechanisms of ozone further benefits practical function in dentistry. Treating patients with ozone therapy reduces the treatment time with an immense deal of variation and it eradicates the bacterial count more specifically. The treatment being painless, increases the patients' tolerability and fulfillment with minimal adverse effects.

Contraindications of this controversial method should not be forgotten. Further research is needed to regulate indications and treatment procedures of ozone therapy. [9]

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