Basic, Biological and Therapeutic Processes of Ozone Therapy in

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Ozone In Medicine. The Low-Dose Ozone Concept and Its Basic Biochemical Mechanisms of Action In Chronic Inflammatory Diseases
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Int. J. Mol. Sci. 2021, 22, 7890. **https://doi.org/10.3390/ijms22157890**

Abstract
Low-dose ozone acts as bioregulator in chronic inflammatory diseases, biochemically characterized by high oxidative stress and a blocked regulation. During systemic applications "Ozone peroxides" are able to replace H_2O_2 in its specific function of regulation, restore redox signaling and improve the antioxidant capacity.
Two different mechanisms have to be understood; in systemic treatments the indirect, ionic mechanism is to be discussed: "ozone peroxide" will be directly reduced by the glutathione system, informing the nuclear factors to start the regulation. The GSH/GSSG balance outlines the ozone dose and concentration limiting factor. Antioxidants are regulated, in case of inflammatory diseases up-regulated; cytokines are modulated, here downregulated.
Rheumatoid arthritis RA as a model for chronic inflammation: RA -in preclinical and clinical trials- reflects the pharmacology of ozone in a typical manner: SOD (superoxide dismutase), CAT (catalase)… and finally GSH (reduced glutathione) increase, followed by a significant reduction of oxidative stress. Inflammatory cytokines are downregulated. Accordingly the clinical status improves.
The pharmacological background investigated in a remarkable number of cell experiments, preclinical and clinical trials, well documented and published in international peer reviewed journals, should encourage clinicians to set up clinical trials with chronic inflammatory diseases integrating medical ozone as a complement.

Intra Articular Ozone Modulates Inflammation and Has Anabolic Effect on Knee Osteoarthritis: IL-6 and IGF-1 as Pro-Inflammatory and Anabolic Biomarkers
Processes **2022**, *10*(1), 138; **https://doi.org/10.3390/pr10010138**

Male vs. Female Differences in Responding to Oxygen–Ozone Autohemotherapy (O_2-O_3-AHT) in Patients with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS)***J. Clin. Med.*** 2022**, *11*(1), 173;** https://doi.org/10.3390/jcm11010173
Fatigue Symptoms When Treated with Oxygen-Ozone Autohemotherapy***J. Clin. Med.*** 2022**, *11*(1), 29;** https://doi.org/10.3390/jcm11010029

The Relationship between Ozone and Human Blood in the Course of a Well-Controlled, Mild, and Transitory Oxidative Eustress ***Antioxidants*** 2021**, *10*(12), 1946;** https://doi.org/10.3390/antiox10121946

The Biological Effects of Ozone Gas on Soft and Hard Dental Tissues and the Impact on Human Gingival Fibroblasts and Gingival Keratinocytes ***Processes*** 2021**, *9*(11), 1978;** https://doi.org/10.3390/pr9111978

Systemic Review: Ozone: A Potential New Chemotherapy *Int. J. Mol. Sci.* 2021, *22*(21), 11796; https://doi.org/10.3390/ijms222111796

Comparison of the Efficacy of Dextrose Prolotherapy and Ozone in Patients with Knee Osteoarthritis: A Randomized Cross-Sectional Study ***Appl. Sci.*** 2021**, *11*(21), 9991;** https://doi.org/10.3390/app11219991

Low Ozone Concentrations Differentially Affect the Structural and Functional Features of Non-Activated and Activated Fibroblasts In Vitro ***Int. J. Mol. Sci.*** 2021**, *22*(18), 10133;** https://doi.org/10.3390/ijms221810133

Ozone as Modulator of Resorption and Inflammatory Response in Extruded Nucleus Pulposus Herniation. Revising Concepts ***Int. J. Mol. Sci.*** 2021**, *22*(18), 9946;** https://doi.org/10.3390/ijms22189946

Ozonized Water Administration in Peri-Implant Mucositis Sites: A Randomized Clinical Trial ***Appl. Sci.*** 2021**, *11*(17), 7812;** https://doi.org/10.3390/app11177812

Potential Short-Term Air Pollution Effects on Rheumatoid Arthritis Activity in Metropolitan Areas in the North of Italy: A Cross-Sectional Study ***Int. J. Environ. Res. Public Health*** 2021**, *18*(16), 8490;** https://doi.org/10.3390/ijerph18168490

Ozone Gel in Chronic Periodontal Disease: A Randomized Clinical Trial on the Anti-Inflammatory Effects of Ozone Application ***Biology*** 2021**, *10*(7), 625;** https://doi.org/10.3390/biology10070625

Application of Ozone Therapy in the Conservative Surgical Treatment of Osteonecrosis of the Jaw: Preliminary Results https://doi.org/10.3390/proceedings2019035022

Modulation of Oxidative Stress by Ozone Therapy in the Prevention and Treatment of Chemotherapy-Induced Toxicity: Review and Prospects ***Antioxidants*** 2019**, *8*(12), 588;** https://doi.org/10.3390/antiox8120588

The Role of Nrf2 in the Antioxidant Cellular Response to Medical Ozone Exposure ***Int. J. Mol. Sci.*** 2019**, *20*(16), 4009;** https://doi.org/10.3390/ijms20164009

A Systematic Review of Oxygen Therapy for the Management of Medication-Related Osteonecrosis of the Jaw (MRONJ) *Appl. Sci.* **2019**, *9*(5), 026; **https://doi.org/10.3390/app9051026**

Intraperitoneal Administration of Oxygen/Ozone to Rats Reduces the Pancreatic Damage Induced by Streptozotocin
Biology **2018**, *7*(1),10; **https://doi.org/10.3390/biology7010010**