

ISSN: 2394-2371 Review Article

## Ozone Therapy: An Appreciable cure in the Treatment of Back Pain

Shruti Joshi<sup>1</sup>, Shiv Kumar Garg\*<sup>2</sup>, Piush Sharma<sup>3</sup>

<sup>1</sup>Research Scholar, Maharishi Arvind College of Pharmacy, Ambabari, Jaipur-302023, Rajasthan, India <sup>2</sup>Associate Professor, Maharishi Arvind College of Pharmacy, Ambabari, Jaipur-302023, Rajasthan, India <sup>3</sup>Principal, Maharishi Arvind College of Pharmacy, Ambabari, Jaipur-302023, Rajasthan, India

## **ABSTRACT**

Back pain is the most common health problem affecting the population worldwide and is still remains unsolved due to the lack of a precise treatment and a proper cure. Some of the main causes of back pain include spinal stenosis, sciatica, muscle strain, bulging or herniated discs and degenerative disc disease. Ozone therapy has emerged as an appreciable and effective treatment method; which involves introduction of ozone gas administered with various gases and liquids into the body via-intramuscularly, subcutaneously, or intravenously, including rectum and vagina. Ozone is a pure form of oxygen formed from three atoms of oxygen (O3) which splits into (O) and (O2) molecules in the presence of UV rays. Ozone comprises of strong analgesic, anti-bacterial, anti-viral, anti-fungal and anti- inflammatory properties which imparts an extra-ordinary potential to ozone from which ozone can oxygenate the swollen tissues of the disc and is capable to promote the healing of damaged tissues, and can effectively cure the spinal injury and back-pain.

**Key Words-** Ozone therapy, Back Pain, Oxygen, UV.

## **INTRODUCTION**

Back pain is a leading cause of disability affecting most of the population worldwide but it is most frequently seen in elders, including impairment and difficulties in activities of daily

\*Corresponding Author:

**Dr. Shiv Kumar Garg** 

**Associate Professor** 

Maharishi Arvind College of Pharmacy, Ambabari,

Jaipur-302023, Rajasthan, India E.Mail: <u>gargshiv81@yahoo.co.in</u> **Article** Received on: 17-11-2014

Revised on: 25-12-2014

Accepted/Published on: 30-12-2014

life and causes functional limitations. In addition to conventional pharmacological and surgical treatments, an effective non-surgical interventional procedure known as ozone therapy is used as an appreciable alternative for the treatment of low back pain.[11]

Some of the main causes of back pain include spinal stenosis, muscle strain, sciatica, bulging or herniated discs and degenerative disc disease. Herniated intervertebral discs (HID) are the most common cause of low back pain associated with a defined structural abnormality. The most common treatments for HID include surgical discectomy, epidural steroid injection and the use of non-steroidal anti- inflammatory drugs (NSAIDs). Other therapies have included chemonucleolysis, prolotherapy, contraction and conservative therapy.[2]

Ozone is a naturally-occurring modified form of oxygen, highly reactive molecule consisting of three atoms of oxygen. Thus, it is triatomic oxygen. [15]

Ozone or trioxygen, is an inorganic molecule with the chemical formula O3. It is a pale blue gas with a distinctively pungent smell. It is an allotrope of oxygen that is much less stable than the diatomic allotrope O2, breaking down in the lower atmosphere to normal dioxygen. Ozone is found naturally in the Earth's atmosphere where it shields us from the harmful ultraviolet rays of sun.(8.) Ozone is formed from dioxygen by the action also of ultraviolet light and atmospheric electrical discharges, and is present in low concentrations throughout the Earth's atmosphere. In total, ozone makes only 0.6 ppm of the atmosphere. Ozone's odor is sharp, reminiscent of chlorine, and detectable by many people at concentrations of as little as 10 ppb in air. The molecule was later proven to have a bent structure and to be diamagnetic.

In standard conditions, ozone is a pale blue gas that condenses at progressively cryogenic temperatures to a dark blue liquid and finally a violet-black solid. Ozone is a powerful oxidant and has many industrial and consumer applications related to oxidation.[9]

### STRUCTURE OF OZONE

evidence According experimental to from microwave spectroscopy, ozone is a bent molecule, with  $C_{2v}$  symmetry (similar the water molecule). The O - O distances are 127.2 pm(1.272 Å). The O – O – O angle is 116.78°.[11] The central atom is sp<sup>2</sup> hybridized with one lone pair. Ozone is a polar molecule a dipole moment of 0.53 D.[12] The with bonding can be expressed as a resonance hybrid with a single bond on one side and double bond on the other producing an



### PROPERTIES OF OZONE

It is blue or deep blue in colour and is found in all three states of matter i.e. solid, liquid and gas. The blue colour of sky is due to the presence of ozone gas in the atmosphere. While both liquid ozone (-112 c) and solid ozone(-193 c) are of deep blue colour.[14]

## **Physical properties**

Ozone is colourless or slightly bluish gas, slightly soluble in water and much more soluble in inert non-polar solvents such as carbon tetrachloride or fluorocarbons, where it forms a blue solution. At 161 K (-112 °C; -170 °F), it condenses to form a dark blue liquid. It is dangerous to allow this liquid to warm to its boiling point, because both concentrated gaseous ozone and liquid ozone can detonate. At temperatures below 80 K (-193.2 °C; -315.7 °F), it forms a violet-black solid.[9]

Most people can detect about 0.01 µmol/mol of ozone in air where it has a very specific sharp odor somewhat resembling chlorine bleach. Exposure of 0.1 to 1 µmol/mol produces headaches, burning eyes and irritation to the respiratory passages. Even low concentrations of ozone in air are very destructive to organic materials such as latex, plastics and animal lung tissue.

### **Production of ozone**

Ozone often forms in nature under conditions where  $O_2$  will not react. Ozone used in industry is measured in  $\mu$ mol/mol (ppm, parts per million), nmol/mol (ppb, parts per billion),  $\mu$ g/m<sup>3</sup>, mg/h (milligrams per hour) or weight percent. The regime of applied concentrations ranges from 1 to 5% in air and from 6 to 14% in oxygen for older generation methods. New

electrolytic methods can achieve up 20 to 30% dissolved ozone concentrations in output water. Temperature and humidity plays a large role in how much ozone is being produced using traditional generation methods such as corona discharge and ultraviolet light. Old generation methods will produce less than 50% its nominal capacity if operated with humid ambient air than when it operates in very dry air. New generators using electrolytic methods can achieve higher purity and dissolution through using water molecules as the source of ozone production.

## Corona discharge method

This is the most common type of ozone generator for most industrial and personal uses. While variations of the "hot spark" coronal discharge method of ozone production exist, including medical grade and industrial grade ozone generators, these units usually work by means of a corona discharge tube. They are typically cost-effective and do not require an oxygen source other than the ambient air to produce ozone concentrations of 3-6%. Fluctuations in ambient air, due to weather or other environmental conditions. variability in ozone production, and they also produce nitrogen oxides as a by-product.

### Ultraviolet light method

UV ozone generators, or vacuum-ultraviolet (VUV) ozone generators, employ a light source

that generates a narrow-band ultraviolet light, a subset of that produced by the Sun. The Sun's UV sustains the ozone layer in the stratosphere of Earth.

While standard UV ozone generators tend to be less expensive, they usually produce ozone with a concentration of about 0.5% or lower. Another disadvantage of this method is that it requires the air (oxygen) to be exposed to the UV source for a longer amount of time, and any gas that is not exposed to the UV source will not be treated. This makes UV generators impractical for use.

### **Electrolytic method**

Electrolytic ozone generation (EOG) splits water molecules into H<sub>2</sub>, O<sub>2</sub>, and O<sub>3</sub>. In most EOG methods, the hydrogen gas will be removed to leave oxygen and ozone as the only reaction products. Therefore, EOG can achieve higher dissolution in water without other competing gases found in corona discharge method, such as nitrogen gases present in ambient air. This method of generation can achieve concentrations of 20–30% and is independent of air quality because water is used as the source material. Production of ozone electrolytically is typically unfavorable because of the high overpotential required to produce ozone as compared to oxygen.

Thus, Ozone (O3) is produced from oxygen (O2) in an electronic generator and it having

multiple medical uses, both intravenously and locally. Medical ozone treatment as a non-surgical pain relief alternative has not only been proved to be a successful and effective treatment, but is almost completely free of complications, side effects and contraindications.

That's why, Ozone therapy has been considered as an extremely safe medical treatment, free from side effects and is described as a safest known medical therapy.

## **Ozone Therapy**

Ozone therapy is a non-surgical, radiologically guided injection of oxygen and ozone into bulging or herniated discs results in pain relief and restoration of function as back surgery with fewer complications and shorter recovery time. This groundbreaking therapy involves injecting a gaseous mixture of oxygen and ozone into a damaged spinal disc, using an imaging machine to guide the needle. The ozone causes a slight shrinkage of the disc, which relieves internal disc pressure and lessens back pain.

These data may supports the role of ozone therapy for the treatment of back pain (and other painful musculoskeletal disorders), this clarification is essential

Table 1: Medium-term follow-up in patients with and without disk disease as a function of treatment type

	Outcome				
Treatment Group	Excellent	Good	Poor	Total	
Patients with disk disease					
0 <sub>2</sub> -0 <sub>3</sub>	67	9	10	86	
Steroid	54	14	12	80	
Total	121	23	22	$166 \chi^2 = 2.42$	
Patients without disk disease					
$0_2$ - $0_3$	55	9	6	70	
Steroid	49	10	11	70	
Total	104	19	17	$140 \chi^2 = 1.86$	

Table 2: Long-term follow-up in patients with and without disk disease as a function of treatment type

	Outcome				
Treatment Group	Excellent	Good	Poor	Total	
Patients with disk disease					
$0_2$ - $0_3$	64	9	13	86	
Steroid	46	16	18	80	
Total	110	25	31	$166 \chi^2 = 5.51$	
Patients without disk disease					
$0_2$ - $0_3$	53	11	6	70	
Steroid	44	11	15	70	
Total	97	22	21	$140 \chi^2 = 4.68$	

O<sub>2</sub>O<sub>3</sub> therapy is used in medicine to treat various conditions and is based on the exploitation of the chemical properties of ozone (O<sub>3</sub>), an unstable allotropic form of oxygen. In the treatment of LDH, O<sub>2</sub>O<sub>3</sub> therapy has been proposed above all because it has: (i) a direct effect on the proteoglycans composing the disc's nucleus pulposus, which results in the release of water molecules and the subsequent cell degeneration of the matrix; this matrix is in turn replaced by fibrous tissue, which leads to a reduced disc volume (ii) analgesic and anti-

inflammatory effects, which may counteract disc-induced pain.

Intraforaminal and intradiscal injections of a combination of O<sub>2</sub>O<sub>3</sub>, steroids, and an anesthetic are more effective at 6 months than injections of a steroid and an anesthetic alone in the same sites in the management of radicular pain related to acute LDH. According to Andreula et al, a combined intradiscal and periganglionic injection of medical O<sub>3</sub> and a periganglionic injection of steroids has a cumulative effect that enhances the overall outcome of treatment for pain caused by disc herniation.

An array of ill-effects are observed owing to the reactivity of O<sub>3</sub> viz oxidation, peroxidation or generation of free radicals and giving rise to cascade of reactions like peroxidation of lipids leading to changes in membrane permeability, lipid ozonation products (LOP) act as signal transducer molecules. The main reason for this being presence of unsaturated fatty acids in both lung lining fluid and pulmonary cell bilayers, O<sub>3</sub> reacts with unsaturated fatty acids to give their specific products i.e., LOP, which activates the lipases triggering the release of endogenous mediators of inflammation. The loss of functional groups in enzymes leading to enzyme inactivation. These reactions further results in cell injury or eventual cell death. Combinations of  $O_3$  and NO<sub>2</sub> occur

photochemical smog, have hazardous effects on lung alveoli and act additively or synergistically. Dietary antioxidants or free radical scavengers like vitamin E, C, etc., can prevent aforementioned effects of O<sub>3</sub>.

- Diabetic complications are attributed to the oxidative stress in the body, O<sub>3</sub> was found to activate the antioxidant system affecting the level of glycemia.
- Ozone prevented oxidative stress by normalizing the organic peroxide levels by activating superoxide dismutase.
- Ozone was found to completely inactivate
  the HIV in vitro, this action of O<sub>3</sub> was dosedependent. Concentration used for
  inactivation was found to be non-cytotoxic.
  The inactivation was owing to the reduction
  of the HIV p24 core protein.
- Ozone was also found to increase the host immunity by increasing the production of cytokine.
- In an in vitro study, it was observed that
   O<sub>3</sub> is very effective in reducing the
   concentrations of Acinetobacter baumannii,
   Clostridium difficile and methicillin resistant Staphylococcus aureus in dry as
   well as wet samples, hence it can be used as
   a disinfectant.
- Oxygen/ O<sub>3</sub> mixture was also found to prolong the appearance of arrhythmia

induced by potassium chloride, aconitine, etc., in laboratory animals like rats.

## Advantage of ozone therapy

- Promotes metabolism
- Detox the body
- Reduce chances of development and spreading of cancer
- Stimulates the immune system
- Purifies the blood and lymph system
- Reduce chances of shock and stroke
- Prevents/reverses degenerative diseases
- Eliminates auto-immune diseases.
- Kills bacteria, fungi and viruses at lower concentrations than chlorine and also been shown to kill parasites.
- Oxidizes toxins including phenolic, pesticides, detergents, chemical manufacturing wastes and aromatic compounds more rapidly and effectively than chlorine.
- Immune system activation while reducing inflammation.
- Improves cellular oxygen utilization through increasing oxygen delivery and reducing oxidative stress.
- It causes the release of growth factors that stimulate regeneration of damaged joints and degenerative discs and Increases fibroblastic activity to help expedite repair.

- Reduce or eliminate chronic pain in many cases through its action on pain receptors.
- Healing effects have been demonstrated and published for interstitial cystitis, chronic hepatitis, inflammatory colitis, herpes, HPV, dental infections, diabetes, kidney glomerulonephritis, retinitis pigmentosa, macular degeneration, gangrene, toenail fungus, Parkinson's, Alzheimer's disease, and many more diseases.

### **Utilization of Ozone in various Diseases**

Ozone has been used for a wide variety of treatment modalities ranging from peripheral vascular disease, macular degeneration, cutaneous and mucosal infections and even ulcerative colitis, including disc herniation and low back pain; and many more like -:

- Arthritis, knee joint pain, back pain
- Athletic injuries
- Fractures
- chronic fatigue syndrome
- Neurological condition like
   Paralysis/Stroke, Parkinson's disease,
   Progressive supranuclear palsy,
   Myopathy
- Skin ulcers, burns, Pimples, Warts
- infected wounds, Gangrene

- Respiratory diseases like asthma, bronchitis, COPD diseases, and ARDS diseases.
- GI disturbance like acidity, peptic ulcer ,colitis
- Diabetes and its complications
- Circulatory diseases
- Cardiovascular disease, angina
- Cancer
- Viral diseases (Hepatitis B, Herpes, etc)
- Cough, cold, viral fever, sore throat
- AIDS
- Fungal infections
- Herpes, Venereal diseases
- Hepatitis
- Periodontal disease
- Sickle cell anemia
- Psoriasis disorders.

### **Action of Ozone**

The treatment of all diseases is maximally enhanced in the presence of optimal oxygen utilization. Ozone is a potent regulator of the immune system, it stimulates increased intake and utilization of oxygen, it improves circulation and is anti-inflammatory.

With anti-aging effects, ozonotherapy has been found useful in various diseases because it: Activates and boosts the immune system in infectious diseases. Improves the cellular utilization of oxygen that reduces ischemia in

cardiovascular diseases. Increases energy production in our cells Causes the release of growth factors that stimulate damaged joints and degenerative discs to regenerate. Can dramatically reduce or even eliminate many cases of chronic pain through its action on pain receptors. Chelates all metals from the body, such as lead, mercury, aluminum, arsenic, and so forth, by extracting them from blood, cells and nerve tissue. Makes red blood cells flow with less viscosity and become more flexible to flow through narrowed or clogged arteries.

Reduces the level of acidity of your body Increases the activity of your "anti-oxidant enzyme systems".

The ozone treatment works by reducing levels of prostaglandins compounds in the body that trigger inflammation and pain. This helps to shrink the disc tissue so that it no longer presses on surrounding nerves and relieves pain. Ozone is so reactive, that it is able to stimulate fiberoblastic and chondroblastic activity that is needed to rebuild ligaments, tendons, and cartilage.

### **OZONE ACTIONS**

- Ozone activates the enzymes involved in peroxide or oxygen "free radical" destruction i.e. glutathione, catalase, s.o.d.
- Accelerates glycolysis (breakdown of glycogen) in RGSs, thus it:Increases the

- release of 02 from the hemoglobin in the blood to the tissues.
- Enhances formation of acetyl coenzyme-a, which is vital in metabolic detoxification.
- Influences the mitochondrial transport system which enhances the metabolism of all cells and safeguards against mutagenic changes.
- Increases red blood cell pliability, blood fluidity and arterial P02 (oxygen content) and a decrease in rouleaux formation (clumping) which interferes with the normal functioning of red blood cell metabolism.
- Increases leukocytosis (production of the white blood cells) and phagocytosis (the manner in which certain white blood cells destroy foreign matter). Both processes are part of the immune defense system.
- Stimulates the reticulo-endothelial system, the rebuilding of tissue.
- Strong germicide inactivates enteroviruses, coliform bacteria, saphylococcus aureus and aeromona hydrophilia.
- Disrupts the cell envelope of many pathogenic organisms which are composed of phospholipids, peptidoglycans and polysaccharides.

- Opens the circular plasmid DNA which lessens bacterial proliferation.
- Fungicidal, inhibits candida cell growth.
- Low doses stimulate the immune system.
- High doses inhibit the immune system.
- Limit dose to 3,000 ug.

## MECHANISM OF ACTION OF OZONE THERAPY

The ozone gas is first mixed with steroid medicine, which helps to dampen down inflammation, and injected directly into the damaged disc under a local anaesthetic.

The action of ozone therapy is due to the active oxygen atom liberated from breaking down of ozone molecule. When ozone is injected into the disc, the active oxygen atom called the singlet oxygen or the free radical attaches with the proteo-glycan bridges in the jelly-like material or nucleus pulposus. They are broken down and they no longer capable of holding water. As a result, disc shrinks and mummified resulting decreased inflammation of nerve roots, decompression of nerve roots and increased oxygenation to the diseased tissue for repair work.

## How is ozone used medically?

Ozone treatments can be used in a variety of ways depending on the individual clinical situation. Dosages, methods of administration, and treatment intervals are important

considerations in order to obtain the greatest benefit. Some of the common ways that ozone can be administered are:

- Major or minor autohemotherapy (mixing ozone with blood and re-infusing)
- Dissolved in IV fluid solutions ( saline or distilled water)
- Intestinal insufflations (rectal & vaginal)
- Auricular insufflations
- Limb bagging
- Topical exposure (ozonated olive oil)

### Methods of administration of ozone

### **Invasive method**

- Inta–articular
- Peri-articular
- Intradiscal
- Subcutaneous
- Intradermal
- Micro-injections at biologically active points
- Intravenous infusion of Ozonated saline
- Major Auto-haemotherapy
- Minor Auto-haemotherapy.

### Non-invasive method

- Ear Insufflation
- Rectal Insufflation
- Vaginal Insufflation

### Miscellaneous

- Ozonated Water
- Ozonated Oil

- Bagging, Cupping, Ozone Bath
- Internal Applications.

## **Uses of ozone therapy**

- Preventing dental cavities from getting worse. An analysis of studies of ozone therapy for dental caries shows no reliable evidence to support ozone therapy for this use.
- Diabetes. There is some evidence that ozone gas administered locally or rectally improves blood sugar and other measures of diabetes.
- "Slipped disks" in the spine.
- Heart disease.
- Parkinson's disease.
- Abscesses.
- Ulcers
- Macular degeneration.
- Cancer.
- Other conditions.

## **Applications of Ozone Therapy**

- Disinfect laundry in hospitals, food factories, care homes etc.
- Disinfect water in place of chlorine
- Deodorize air and objects, such as after a fire. This process is extensively used in fabric restoration
- Kill bacteria on food or on contact surfaces
- Sanitize swimming pools and spas
- Kill insects in stored grain

- Scrub yeast and mold spores from the air in food processing plants;
- Wash fresh fruits and vegetables to kill yeast, mold and bacteria;
- Chemically attack contaminants in water (iron, arsenic, hydrogen sulfide, nitrites, and complex organics lumped together as "colour");
- Provide an aid to flocculation (agglomeration of molecules, which aids in filtration, where the iron and arsenic are removed);
- Manufacture chemical compounds via chemical synthesis

## **IN Aquaculture**

Ozonation - a process of infusing water with ozone - can be used in aquaculture to facilitate organic breakdown. Ozone is also added to recirculating systems to reduce nitritelevels through conversion into nitrate. If nitrite levels in the water are high, nitrites will also accumulate in the blood and tissues of fish, where it interferes with oxygen transport (it causes oxidation of the heme-group of hemoglobin from ferrous (Fe2+) to ferric (Fe3+), making haemoglobin unable to bind O2). Despite these apparent positive effects, ozone use in recirculation systems has been linked to reducing the level of bioavailable iodine in salt water systems,

resulting in iodine deficiency symptoms such as goitre and decreased growth in Senegalese sole (Solea senegalensis) larvae.

## **IN Agriculture**

Ozone application on freshly cut pineapple and banana shows increase in flavonoids and total phenol contents when exposure is up to 20 minutes. Decrease in ascorbic acid (one form of vitamin C) content is observed but the positive effect on total phenol content and flavonoids overcome can the negative effect. Tomatoes upon treatment with ozone shows an increase in β-carotene, lutein and lycopene. However, ozone application strawberries in pre-harvest period shows decrease in ascorbic acid content.

Ozone facilitates the extraction of some heavy metals from soil using EDTA. EDTA forms strong, water-soluble coordination compounds with some heavy metals (Pb, Zn) thereby making it possible to dissolve them out from contaminated soil.

# Merits of ozone therapy over conventional surgical treatment

- Success rate is about 88% which is comparable to surgical discectomy (50% to 90%).
- Complications are remarkably low and much less than surgery.

- Cost of Ozone therapy for slip disc is also much less compared to surgery.
- Ozone therapy is gradually gaining popularity in various medical fields especially in pain management. Newer modification in techniques and administration of ozone, more and more publication of scientific materials in the medical journals and animal studies has made it more acceptable to the medical community and thus, gradually it is becoming more popular than the conventional surgical treatment method.

### **CONCLUSION**

Treatment of acute LBP with or without radiating pain is a major concern. Although the natural history of acute LBP is often selflimiting, conservative therapies are not always effective; in such cases, O<sub>2</sub>O<sub>3</sub> intramuscular lumbar paravertebral injections, which are minimally invasive, seem to safely and effectively relieve pain, as well as reduce both disability and the intake of analgesic drugs. Ozone therapy is the use of ozone gas to treat certain medical conditions It is most commonly practiced in Europe. Ozone therapy is used for "slipped disks" in the spine, diabetes, disease, cancer, an eye disease called macular degeneration, and Parkinson's disease. It is also used for treating abscesses

and other signs of infections. Ozone is sometimes used to stop dental cavities from progressing.

### REFERENCES

- 1. Streng, A. G. "Tables of Ozone Properties". Journal of Chemical Engineering Data.1961; 6 (3): 431–436.
- 2. Hoffmann, Roald. "The Story of Ozone". American Scientist.2004; 92 (1): 23.
- 3. Rubin, Mordecai B. "The History of Ozone. The Schönbein Period,2001; 1839–1868" (PDF). Bull. Hist. Chem. 26 (1).
- 4. Ibanez, Jorge Rodrigo G.; Mayen-Mondragon and M. T. Moran-Moran ."Laboratory **Experiments** on the Electrochemical Remediation ofthe Environment. Part 7: Microscale Production of Ozone". Journal of Chemical Education. 2005;82 (10): 1546.
- 5. Matsumi, Yutaka; Kawasaki, Masahiro. "Photolysis of Atmospheric Ozone in the Ultraviolet Region". Chemical Reviews. 2003;103 (12): 4767–82.
- 6. Half-life time of ozone as a function of air conditions and movement McClurkin, J.D.\*#1, Maier, D.E.2. DOI: 10.5073/jka.2010.425.167.326
- 7. Koike, K; Nifuku, M; Izumi, K; Nakamura, S; Fujiwara, S; Horiguchi, S."Explosion properties of highly concentrated ozone gas". Journal of Loss Prevention in the Process Industries.2005; 18 (4–6): 465.
- 8. "Measured Ozone Depletion". Ozone-Information.com. Archived from the original on 2013-09-14. Retrieved 2014-01-22.

- 9. Mutters, Randall (March 1999). "Statewide Potential Crop Yield Losses From Ozone Exposure". California Air Resources Board. Archived from the original on 2004-02-17. Retrieved 2006-05-10.
- 10. Smith, LL. "Oxygen, oxysterols, ouabain, and ozone: a cautionary tale". Free radical biology & medicine. 2004; 37 (3): 318–24.
- 11. "Chemical Synthesis with Ozone". Ozone-Information.com. Archived from the original on 2008-04-10. Retrieved 2008-05-17.
- 12. Lestan, D.; Hanc, A.; Finzgar, N. "Influence of ozonation on extractability of Pb and Zn from contaminated soils". Chemosphere.2005; 61 (7):1012-1019.
- 13. Bonetti M, Fontana A, Coticelli B, et al. Intraforaminal <sub>O2</sub>–<sub>O3</sub> versus periradicular steroidal infiltrations in lower back pain: randomized controlled study. AJNR Am J Neuroradiol 2005;26:996–1000
- 14. Andreula CF, Simonetti L, De Santis F, Agati R, Ricci R, Leonardi M: Minimallyinvasive oxygen-ozone therapy for lumbar disk herniation. AJNR Am J Neuroradiol. 2003 May;24(5):996-1000.
- 15. Bocci V, Pogni R, Corradeschi F, Busu E, Cervelli C, Bocchi L, Basosi R: Oxygenozone in orthopaedics: EPR detection of hydroxyl free radicals in ozone-treated "nucleus pulposus" material. RIVISTA DI NEURORADIOLOGIA, 2001; 14: 55-59.