Oxygen Free Radical Stabilization

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Introduction

This project introduces novel methods of activating and stabilizing oxygen free radicals in an inert oxygenated Perfluorocarbon (PFC) solution through UV activation without substrate degradation. A lamp system has been designed for photo activation of oxygen free radicals in an inert PFC solution using light waves at a specific frequency, aimed to replace existing photodynamic and other free radical based therapies , where you irradiate the PFC substrate instead of tissues to induce radicals for a healing response.

Objectives

- Design an excimer lamp system specifically to induce free radicals within an inert PFC solution.
- Excite atoms to produce light waves with enough energy to break oxygen bonds in the PFC solution.
- Improved electrode design with conductive nano-tube film with transmittance of 95%
- Square waves with DC offset to hit natural frequency of system for efficient break down.
- Add Peaking capacitor to increase charge density for even distribution for dielectric breakdown of gas.
- Test different circuit designs to maximize efficiency at a wavelength of 194nm. (gas mixture is ArF)
- Have the technology ready for immediate licensing, its ready for commercializing in veterinary markets.

Existing Therapies

- **Photodynamic Therapy**:
  - A light sensitive agent is injected intravenously.
  - Light waves activate free radicals to cause apoptosis on damaged tissue.
- **Problems with existing method:**
  - Light waves do not penetrate tissue effectively.
  - Requires surgery to expose diseased tissue.
  - Oxygen is not water soluble causing too low concentration in saline.

Properties of Perfluorocarbons

The C-F bond is known as one of the strongest in chemistry. PFC liquids dissolve large volumes of oxygen. PFCs are linear, cyclic, or polycyclic hydrocarbons in which hydrogen atoms have been substituted with fluorine.

The two compounds most widely used in biological systems are Perfluorodecalin (C10F18), and Perfluorohexane (C6F14) . Perfluorohexane has had prior FDA approval for use as a contrast agent in imaging technology. This particular molecule has the highest known gas carrying capabilities and can carry 80% of its volume in gas.

Due to this molecule's geometry, C6F14 is one of the most resilient PFCs to oxidation and to photon degradation. Perflurohexane will be one of the main PFCs that will be utilized in this invention, due to availability, its reliance, and its prior FDA approved status for *in vivo* applications.

UV Band For Absorbance

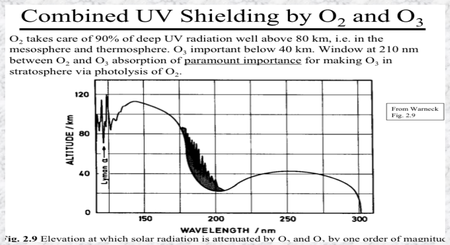
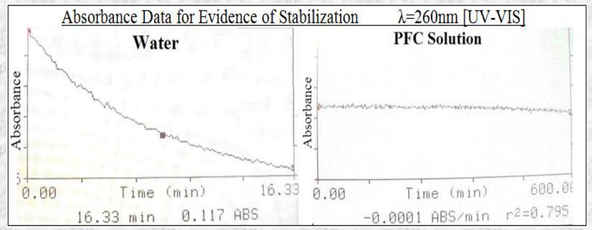


Fig. 2.9 Elevation at which solar radiation is attenuated by O_3 and O_2 by one order of magnitud

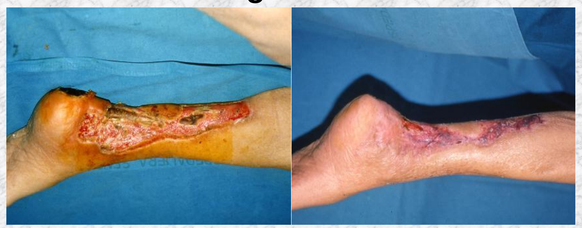
Oxygen absorbs 100 % of the UV radiation below 210 nm. Therefore, oxygen will shield the PFC substrate from radiation below 210 nm . This will be the major driving force for why there will be no PFC degradation at 194 nm. The gas we will be using is Argon Flouride, which has an wavelength of 194 nm which is within the "Schumann band region". Pic Courtesy of ; Prof. Jose-Luis Jimenez Atmospheric Chemistry CHEM-5151 / ATOC-5151 S

Experimental Evidence



Evidence shows free Oxygen radicals are stable within the PFC substrate for 10 hours at room temp or 30 days when frozen at full concentration. Where as 0_3 alone has an 8 min half life in saline at 1/100 of the concentration of dissolved oxygen within the saline solution after a few min. (PFC on right H_20 control on left), the decrease in concentration for PFC is less than .0001 per/min, more than ever expected. Truly a scientist medical break through; especially for solid tumors and for hard to heal wounds. The dose is appropriate for the therapeutic result desired. Modern medicine can now exploit the discovery of direct signaling synthetic stabilization technology for the first time .

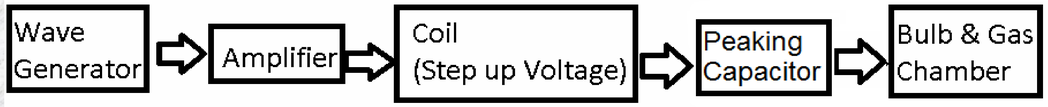
Cascading Immune response on festering diabetic wound



Before and after effects of Oxygen Gas free radical therapy on festering diabetic ulceration, this is really a profound result. But now for the first time, Oxygen free radicals are stabilized in a liquid PFC substrate and can be used to treat hard to heal wounds like this one.

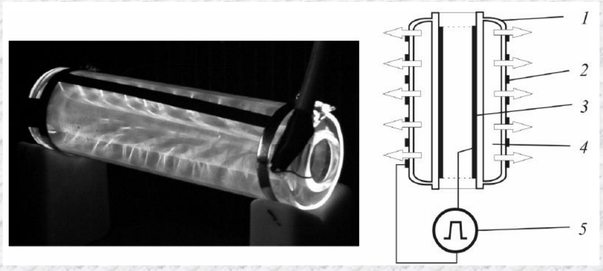
The reason why Oxygen Free radicals are so effective in treating wounds such as this one is because they stimulate the release of growth factors. Some of the growth factors induced that are part of the cascading immune response are , TNF, NFKappaB, PDGF, TGF, VEGF. We can induce a regeneration with out expensive stem cell harvesting, stem cells will migrate to the wound bed through a chemotaxis effect "Oxygen radicals are Cytokines". Direct signaling technology enables the molecule to bypass the pathways other drugs must pass through to act at the bio chemical level. Picture Retrieved from "www.Bio-Oxy.com"

Design Flow Chart



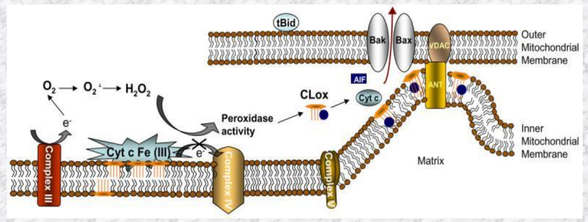
Block Diagram of Bulb system, which is used to stimulate radicals within the PFC substrate.

Bulb Design



Two competing bulb designs ,that would produce a peak wavelength of 194nm for radical activation. On the right are two GE type 214 quartz coaxial tube bulbs, to be filled with Argon Fluoride with a fixed ratio from manufacture. The working gas is Argon fluoride, and once excited releases photons at a single wave length, which is 194 nm. The theory of operation of the bulb system, is the working gas inside the bulb is the dielectric, and is catastrophically broken down using a potential of 65k volts between two electrodes; one on each end of the bulb. A peaking capacitor was added to the system (refer to block diagram), to make the system more efficient and intensify the final discharge. The voltage used during pre-ionization gets dissipated in the form of heat, but by using a peaking capacitor, the energy that other wise would be lost as heat is stored during the pre-ionization stage in the capacitor. Then during the discharge phase, this energy is dumped, which intensifies the discharge. A peaking capacitor in essence, increases the charge density and the intensity; with out extra work from the system. This feature is unique to our design. Picture on the left is a predicate experimental design, courtesy of ; E.A. Sosnin, S.M. Avdeev, V.F. Tarasenko, "Multi-wavelength dielectric barrier discharge excilamp with a mixture of krypton, chlorine, and bromine" *High Current Electronics Institute SB RAS, 2/3, Akademichesky Ave, Tomsk 634055, Russia.*

Mode of action for apoptosis in solid tumors



There are two common denominators that all cancer cells exhibit; they all derive there energy from fermentation (Glycolysis=Hypoxia) and they are not able to go through normal cell suicide (apoptosis). The lipid responsible for apoptosis induction is Cardiolipin (CL), in all cancers this lipid is not able to have a conformational change to release cytochrome C into the cytosol. This compound attacks the common denominator in all cancers. We stimulate Apoptosis by three main routes involving the mitochondria (the intrinsic pathway) and oxygen free radicals stimulate the activation of death receptors (the extrinsic pathway) on the outer membrane.

Both these pathways converge to induce the activation of caspases, the final executioner of cell death. Although, it should be noted that Free radicals also induce caspase-independent forms of apoptosis (Necrosis), Depending on the concentration of the highly reactive free radicals, if injected directly in a tumor this will oxidize organelles, endoplasmic reticulum , lysozymes, and CL in the mitochondria. This leads to an increase in calcium and the release of effector proteins that are frequently involved in caspase-independent cell death. With Necrosis no cancer cell can function and will die; and the effect is localized do to the powerful antioxidant system every mammal possesses. Reaction intermediates control the chemistry of the cell and oxygen signaling controls apoptosis.

Whereas modern drugs must pass through several signaling pathways and many independent chemical reactions to get an end result, oxygen radicals act directly at the biochemical level, by bypassing these pathways for an end result. With this invention, we show reaction intermediates can be stabilized in a biocompatible solution, thus giving us the ability to precisely control dosing and concentration for the first time in history. Pic retrieved from "www.Bio-Oxy.com"

Tests and Measurements

- Determined Stability of the oxygen radicals in a PFC substrate with out substrate degradation, results where more than ever expected, 10 hours stable 5 hours with no deviation, and up to 30 days frozen at -50^{O}C, can be 3 months or more at -80 C .
- Determined the best frequency and voltage potential for dielectric breakdown for bulb system
- Increase light intensity of system with a peaking capacitor to help achieve greater amperage for break down of gas.
- Determined the market size for discovery and other uses performing reactions that can not be performed in any other medium. Prostate cancer 4 billion dollar market, and wound management is a 2+ billion dollar market for diabetic ulcers a year .

Conclusion/Discussion

The key to this scientific breakthrough is that now, one can activate free radicals through UV means at a concentration that is therapeutically effective and appropriate for precise dosing control. This invention is based on the creation and stability of reactionary intermediates , which can now be exploited by medicine for the first time. The idea of stabilizing highly reactive free radicals in a solution that could be injected into a mammal was thought to be impossible due to the highly unstable reactive nature of the particles, but what this inventions shows is, that in using an inert PFC solution to stabilize and deliver electronically modified oxygen derivatives is the only way one can accomplish this feat. No other method previously awarded a patent solves the solubility, creation, and the stability of reaction intermediates. This method is superior to any method that came before and solves the problems that plagued free radical therapy from its inception.