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Review Article

NANOTECHNOLOGY REVOLUTION: RESPIROCYTES AND ITS APPLICATION IN LIFE SCIENCES

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ABSTRACT

"Necessity is the mother of invention". This necessity has made human now to stand at the verge of science. Nano technology is termed as application of science and technology at the nano level. From the many conditions which can do harm to the human body, one of the most fundamental and fast acting is a lack of perfusion of oxygen to the tissue. Insufficient oxygenation can be accoutred by problems with oxygen uptake in the lungs, problems with blood flow in the arteries due to obstruction or problems with oxygen transportation, as with anaemia. Heart attack is the death of part of the heart muscle due to its sudden loss of blood supply. Typically, the loss of blood supply is caused by a complete blockage of a coronary artery by a blood clot .To overcome this, respirocytes are proposed. An artificial nano-medical erythrocyte, or "respirocytes" --intended to duplicate all of the important functions of the red blood cell - provides treatment for anaemia, heart attack, choking, lung diseases, asphyxia, and other respiratory problems. These nano-robots, will be able to keep a patient's tissues safely oxygenated for up to about 4 hours (at maximum dosage) if their heart has stopped beating in case of a heart attack. The simplest possible design for an artificial respirocyte is a microscopic pressure vessel, spherical in shape for maximum compactness made from flawless diamond or sapphire constructed atom by atom.

Keywords: nano technology, oxygen uptake, artificial red blood cells- respirocytes, pressure.

INTRODUCTION:[1-4]

Nanotechnology by definition is the study of manipulating matter on an atomic and molecular scale [1] This results in manmade molecules, typically 1-100 billionths of a metre [2], which can be manipulated in various ways to suit differing medical applications. The extremely small size of nanoparticles allows them to penetrate cells and interact with them [2] some techniques are currently in use today whilst others exist only in the imagination

An artificial nanomedical erythrocyte, or "respirocyte" — intended to duplicate all of the important functions of the red blood cell — could serve as a universal blood substitute, preserve living tissue and provide treatment for anaemia, choking, lung diseases, asphyxia, and other respiratory problems.[3]

The first artificially prepared red blood cells were fulfilling the following 3 major functions of red blood cells: (1) oxygen transport (2) carbon dioxide transport and (3) antioxidant functions. This method was in routine clinical use in South Africa and Russia. But, serious interest in this area did not start until the HIV contaminated donor blood crisis. Till then, there was no time to carry out the much required basic research. Firstly prepared Respirocytes are nano machines, very small mechanical devices designed to operate on the molecular level. Each respirocyte is between 0.2 and 2 microns in diameter.[4] Respirocytes function as artificial prepared red blood cells, which carries oxygen and carbon dioxide molecules throughout the body.

Function of red blood cells in body

Red cells comprise at least 80% of all native cells in the human body. The biochemistry of respiratory gas transport in the blood is well understood. In brief, oxygen and carbon dioxide gas exchange are carried between the lungs and the other tissues, mostly within the red blood cells. Haemoglobin, the principal protein in the red blood cell, combines reversibly with oxygen, forming oxyhemoglobin. About 95% of the O_2 is carried in this form, the rest being dissolved in the blood. At human body temperature, the haemoglobin in 1 litre of blood holds 200 cm^3 of oxygen, 87 times more than plasma alone (2.3 cm^3) can carry.

Carbon dioxide also combines reversibly with haemoglobin; about 25% of the CO_2produced during cellular metabolism is carried in this form, with another 65% transported inside the red cells as bicarbonate ion and the remaining 10% dissolved in blood plasma.

Respiratory gases are taken up or released by haemoglobin according to their local partial pressure. There is a reciprocal relation between haemoglobin's affinity for oxygen and carbon dioxide. The relatively high level of O_2 in the lungs aids the release of CO_2, which is to be expired. The high CO_2 level in other tissues aids the release of O_2 for use by those tissues.

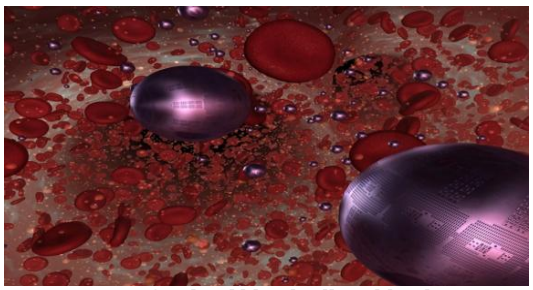

Fig 1: Artificial red blood cells in blood stream

Respirocytes :A boon to life sciences [5-9]

In the simplest case, continuous oxygen release throughout the body could be obtained. If slightly more sophisticated would be a system that releases gas in response to local O_2 partial pressure. But these simple proposals fall short due to two reasons.

First, if the device is discharged it will become useless. And the discharge time is too short. If there were no natural red cells around to help it out, it may create life threatening condition. The O_2 contained in a 1 cm^3 injection of 1000 atm microtanks would be exhausted in only 2 minutes. Second, throughout a capillary bed along with the existing red cell population, placement of a lot of sources of O_2 emission were placed which would cause a serious problem. These extra emitters are functionally equivalent to RBCs whose CO_2 transport and acid-buffering capabilities have been selectively disabled. Their addition to the blood causes higher CO_2 tension and hydrogen ion concentration. These higher concentrations would rapidly lead to carbon dioxide toxicity and acidosis (hypercapnia), especially in anaemic, nonrespiratory, ischemic patients, as well as hyperoxic haemolysis and other complicated situations.

The solution for the first problem of short duration is to continuously recharge the micro vessels with O_2 gas at the lungs. Carbon dioxide toxicity can be prevented by providing extra tankage for CO_2 transport and by designing a mechanism that actively loads the gas in the tissues and then unloads it at the lungs.

The size of the respirocytes must be designed in a manner so they have ready access to all tissues via blood vessels. They can't be larger than human capillaries of average 8 microns in diameter but may be as small as 3.7 microns[5] – so narrow that natural red blood cells (7.8 micron x 2.6 micron biconcave disks) must fold in half so that it can be easily pass.[6]

According to the study design, as radius decreases, surface area per unit volume increases rapidly. Thus smaller cells require more hollow tankage for a given amount of volume capacity. A careful study of operational requirements and minimum required sizes suggests that the optimum respirocyte diameter is about 1 micron.

In the simplest case, oxygen release could be continuous throughout the body [**7**]. Slightly more sophisticated is a system responsive to local O_2 partial pressure, with gas released either through a needle valve [**8**] controlled by a heme protein that changes conformation in response to hypoxia [**9**], or by diffusion via low pressure chamber into a densely packed aggregation of heme-like molecules trapped in an external fullerene cage porous to environmental gas and water molecules, or by molecular sorting rotors

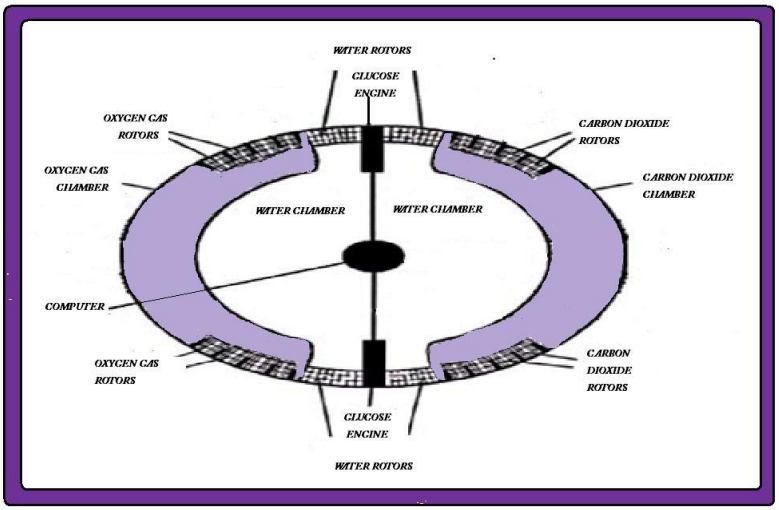

Fig 2: schematic representation of respirocytes

PRESSURE VESSEL

The main goal is transport of oxygen from the lungs to other body tissues, the simplest possible design contains microscopic pressure vessel, spherical in shape for higher compactness.

Mostly proposals for durable respirocytes contains the strongest materials, like flawless diamond or sapphire, constructed atom by atom. A conservative applied stress in such structures would be as high about 100,000 atmospheres (atm) of pressure. But due to such high pressure, risk of rupture and explosive energy rises, so a standard 1000 atm of operating pressure appears optimum. This relatively low pressure will offer very high packing density of the gas molecules, while providing an extremely conservative 100-fold structural safety margin.

Tank storage capacity can be calculated by van der waals equation that takes account of inter molecular forces due to finite sized tightly packed molecules= $[nRT/(V-nB)] - [An^2/V^2]$, where P in atm, n in moles of gas, R = 8.206 x 10^{-5} m^3-atm/mole-°K, T = 310 °K (human body temperature), V in m^3, and constants A and B determined experimentally for each gas . If comparison is done with natural red blood cells regarding storage of oxygen at an equivalent 0.51 atm pressure, of which only 0.13 atm is deliverable to tissues.

MOLECULAR SORTING ROTORS [10-11]

Transport of the gas molecules into, and out of, pressurized microvessels is the main requirement for the successful respirocyte. Molecular sorting rotors have been proposed that would be ideal for this task .Each rotor is having binding sites called "pockets" along with the rim that are exposed alternately to the blood plasma and inner chamber by the rotation of the disk. Each pocket selectively binds with a specific molecule when exposed to the plasma. Once the binding site exposed to the interior chamber, the bound molecules are forcefully ejected by rods. These devices can sort small molecules of 20 or fewer atoms at a rate of 10^6 molecules/sec and pump against head pressures up to 30,000 atm at an additional energy cost up to 10^{-19} joule/molecule. Rotors are fully reversible, so they can be used to load or unload gas storage tanks, depending upon the direction of rotor rotation. (It should be possible to recover most of the sorting energy by adding a generator subsystem, or by compressing one gas using energy derived largely from the decompression of the other [**10**] using differential gearing. Neither

alternative, which might reduce power consumption by a factor of ~10-100, was pursued in the present design because the energy resource -- serum glucose -- appears plentiful.)Typical molecular concentrations in the blood for target molecules of interest (O_2, CO_2, N_2 and glucose) are ~10^{-4}, which should be sufficient to ensure at least 90% occupancy of rotor binding sites at the stated rotor speed [**11**]

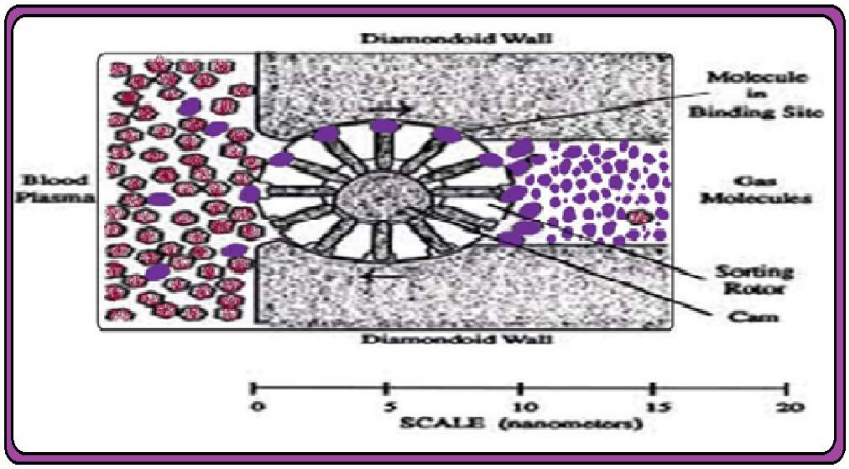

Fig 3: Molecular sorting rotors

MINIMUM THERAPEUTIC DOSE [11]

The average male human body has 28.5 trillion red blood cells, each containing 270 million haemoglobin molecules. Each of them binds with four O2 molecules. However, since haemoglobin normally operates between 95% arterial blood flow and 70% venous blood flow, only 25% of stored oxygen is accessible to the tissues.

In comparison with red blood cells, each respirocyte stores up to 1.51 billion oxygen molecules, 100% of them are accessible to the tissues. To fulfil the complete requirement of human body, we have to supply 5.36 trillion devices. If respirocytes are administered via hypodermal injection or transfusion in a 50% aqueous colloidal suspension, this requires a standard ~5.61 cm^3 therapeutic dose of activated suspension. One therapeutic dose can duplicate natural red cell function indefinitely if the patient is breathing. For the patients who have stopped breathing, it can supply all respiratory gas requirements from onboard storage alone for nearly 2 minutes.

In normal case, the alveolar membrane of human lungs can transmit a maximum of 3.2x 10^{21} O_2 molecules/sec across its surface, enough to fully load 42% of all therapeutic respirocytes during one transit time (5-10 sec [**11**]) of lung capillaries. Body blood circuit time is approx 60 sec in resting conditions, so only 17% of injected respirocytes are present in the lungs at any one time. And since respirocytes can establish higher osmotic gradients than natural red blood cells, the rate of alveolar oxygen diffusion should not limit reoxygenation of an exhausted therapeutic dose.

POTENTIALITY OF RESPIROCYTES

one of the potential benefits of nonmedical devices is their ability to extend natural human capabilities. Suppose you wanted to permanently maximize the oxygen-carrying capacity of your blood by infusing the largest possible number of respirocytes. The maximum safe augmentation dosage is probably about 1 litre of 50% respirocyte suspension, which puts 954 trillion devices into your bloodstream. You could then hold your breath for 3.8 hours, at the normal resting metabolic rate. At the maximum human metabolic rate, something like a continuous Olympic-class 50-meter dash exertion level, you could go for a full 12 minutes without taking a breath. Afterwards, your entire capacity is recharged by hyperventilating for just 8 minutes – then you're ready to go again.

SAFETY REGARDING USE OF RESPIROCYTES [12-13]

Assumptions regarding malfunctions will detect simple failure modes like jammed rotor banks, plugged exhaust ports, and gas leaks, either switching to backup systems or using those backups to safely place the device into a fail-safe dormant mode pending removal by filtration. Respirocytes are extremely reliable as a simple analysis of likely radiation damage suggests that the average respirocyte should last about 20 years before failing.

If other malfunctions like all the glucose powerplant get jammed or refuse o turn off while the respirocyte is in the bloodstream, its temperature will not rise at all. That's because the 7.3 picowatts of continuous thermal energy which is generated by device is easily absorbed by the huge aqueous heat sink, which has a bountiful heat capacity.

In the worst case, it leads to complete structural failure of a respirocyte in vivo. Patients will suffer a high-speed head-on automobile collision experience instantaneous accelerations of 100-10,000 g's (gravity is 1 g), [12] but due to the presence of spherical diamonded shell will resist accelerations up to 10^8-10^{10} g's. Crushing respirocyte-impregnated human tissue in a hydraulic press is unlikely to destroy any devices, as they will simply slide out of the way. The same logic applies to gunshot wounds, knife accidents that cut deep to hard bone, and blunt object blows to the skull. [13]

Indeed, the other respirocyte explosion scenario is dental grinding. As the tooth enamel is the hardest natural substance in the human body, and a patient with an oral lesion could spread respirocyte-impregnated blood over the teeth. Single respirocyte explosions may not be detectable; several thousand going off at once might produce"fizziness" in the mouth. Simultaneously crushing 20 million respirocytes (the count in a 0.5-mm droplet of augmentation-dose blood) could produce a maximum jaw-speed (0.1 m/sec) explosive impulse.

Collisions with respirocytes or their spinning sorting rotors are unlikely to cause serious physical damage to other cells in the bloodstream such as platelets, white cells, or natural red cells, nor will collisions injure blood vessel walls. While definitive experimental data is not yet available, preliminary tests show diamondoid surfaces to be very biocompatible, unlikely to draw a major response from leukocytes, the immune system, or other natural body defences.

APPLICATIONS:

The artificial respirocyte is a nanotechnological device whose primary applications include transfusable blood substitution; treatment for anaemia, perinatal and neonatal disorders, and a variety of lung diseases and conditions; contribution to the success of certain aggressive cardiovascular and neurovascular procedures, tumour therapies and diagnostics; prevention of asphyxia;

maintenance of artificial breathing in adverse environments; and a variety of sports, veterinary, battlefield and other applications.

Transfusion of blood and perfusion of organs [14]

Respirocytes can be used as the active oxygen-carrying component of a universally transfusable blood substitute which is free of disease vectors such as hepatitis, venereal disease, malarial parasites or AIDS, storable indefinitely and readily available and doesn't require any cross-matching.[**14**]. In current scenario, organs must be transplanted soon after harvest; respirocytes could be used as a long-duration perfusant to preserve living tissue, especially at low temperature, for grafts (kidney, marrow, liver and skin) and organ transplantation**.**

Treatment of Anaemic conditions [15]

Oxygenating respirocytes offer complete or partial symptomatic treatment for virtually all forms of anaemia, including acute anaemia which is caused by a sudden loss of blood after any injury or surgical intervention; secondary anaemia caused by bleeding typhoid, duodenal or gastric ulcers; chronic, gradual, or post-hemorrhagic anaemia from bleeding gastric ulcers (including ulcers caused by hookworm),excessive menstrual bleeding, or battle injurie, haemorrhoids in war zones; hereditary anaemia including haemophilia, leptocytosis and sicklemia, thalassemia, haemolytic jaundice and congenital methemoglobinemia; chlorosis and hypochromic anemia, endocrine deficiency anaemia, pernicious and other nutritional anemias; anaemia resulting from infectious diseases including rheumatism, scarlet fever, tuberculosis, syphilis, chronic renal failure and cancer, or from haemoglobin poisoning such as by carbon monoxide inhalation; haemolytic anemias including chemical haemolysis (including malarial, snake bite, etc.), paroxysmal hemoglobinuria, and chronic haemolytic anaemia from hypersplenism due to cirrhosis of the liver; leukaemia and other idiopathic or toxic aplastic anemias caused by chemicals, radiation, or various antimetabolic agents; and diseases involving excessive red cell production such as polycythemia.[15]

Fetal abnormalities and Child-Related Disorders

Respirocytes may be useful in prenatal medicine, as for example infusions of device suspension to treat erythroblastosis fetalis, neonatal haemolytic disease, or in utero asphyxia from partial detachment of the placenta or maternal hypoxia, to restore the oxygen-carrying ability of fetal blood. Asphyxia neonatorum, as from umbilical cord compression during childbirth, may fatally deprive the infant of oxygen; prenatal respirocyte treatment could be preventative. Many cases of Sudden Infant Death Syndrome (SIDS) or crib death, the leading cause of neonatal death between 1 week and 1 year of age, and also for respiratory distress syndrome involve recurrent oxygen deprivation or abnormalities in the automatic control of breathing, both of which could be delethalized using a therapeutic dose of red cell devices. Respirocytes could also aid in the treatment of childhood afflictions such as whooping cough, cystic fibrosis, rheumatic heart disease and rheumatic fever, congenital heart disorders and laryngotracheobronchitis (croup).

Respiratory tract and breathing Disorders [16-17]

Current treatments for a variety of respiratory tract diseases, including pneumonia, bronchopneumonia and pleuropneumonia; pneumoconiosis including asbestosis, silicosis and berylliosis; emphysema, emphysema, abscess, pulmonary enema and pleurisy; epidemic pleurodynia; diaphragm diseases such as diaphragmatic hernia, tetanus, and hiccups; blood flooding in lungs (hemoptysis, tuberculosis, chronic histoplasmosis, and bronchial tube rupture); bronchitis and bronchiectasis; atelectasis and pneumothorax; chronic obstructive lung disease; arterial chest aneurysm; influenza, dyspneas, and even laryngitis, snoring, pharyngitis, hay fever and colds could be improved using respirocytes to reduce the need for strong, regular breathing.

The devices can be used as an effective long-term drug-free symptomatic treatment for asthma, and can also assist in the treatment of hemotoxic and neurotoxic , snake bites; hypoxia, stress polycythemia and lung disorders resulting from cigarette smoking and alcoholism; neck goiter and cancer of the lungs, pharynx, or thyroid; pericarditis, coronary thrombosis, hypertension, and even cardiac neurosis; obesity, quinsy, botulism, diphtheria, tertiary syphilis, amyotrophic lateral sclerosis, uremia, coccidioidomycosis (valley fever), and anaphylactic shock; and Alzheimer's disease where hypoxia is speeding the development of the condition.

Respirocytes could also be used to treat conditions of low oxygen availability in nerve tissue, as occurs in advanced atherosclerotic narrowing of arteries, strokes, diseased or injured reticular formation in the medulla oblongata (controlling autonomic respiration), birth traumas leading to cerebral palsy, and low blood-flow conditions seen in most organs of people as they age. Even poliomyelitis, which still occurs in unvaccinated Third World populations, could be treated with respirocytes and a diaphragmatic pacemaker.

Cardiovascular and Neurovascular diseases [17-21]

Respirocytes perfusion could be useful in maintaining tissue oxygenation during anaesthesia, coronary angioplasty, organ transplantation, Siamese-twin separation, other aggressive heart and brain surgical procedures [**17-18**], in postsurgical cardiac function recovery, and in cardiopulmonary bypass solutions [**19**]. The device could help prevent gangrene and cyanosis, for example, during treatment of Reynaud's Disease, a condition in which spasms in the superficial blood vessels of the extremities cause fingers and toes to become cyanotic, then white and numb. Therapeutic respirocytes dosages can delay brain ischemia under conditions of heart or lung failure, and might be useful in treating senility, which has apparently been temporarily reversed in patients treated with hyperbaric oxygen [**20-21]**

Treatment of tumour and Diagnostics [22-24]

Cancer patients are usually anaemic. X-rays and many chemotherapeutic agents require oxygen to be maximally cytoxic, so boosting systemic oxygenation levels into the normal range using respirocytes might improve prognosis and treatment outcome [22-23]. Fluorocarbon emulsions have been used to probe tissue oxygen tension ;similarly, respirocytes could be used as reporter devices to map a patient's whole-body blood pressure or oxygenation profile, storing direct sensor data in each computer along with positional information recorded from a network of precisely positioned acoustic transponders, to be later retrieved by device filtration and data reconstruction . A similar network of acoustic transmitters, making possible respirocytes auto triangulation hence precise internal positional knowledge, could allow preferential super oxygenation of specific tissues, enhancing treatment effectiveness. [24]

Asphyxia conditions [25-26]

Respirocytes make breathing possible in oxygen-poor environments or in cases where normal breathing is physically impossible. Prompt injection with a therapeutic dose, or advance infusion with an augmentation dose, could greatly reduce the number of choking deaths and the use of emergency tracheotomise, artificial respiration in first aid, and mechanical ventilators. The device provides an excellent prophylactic treatment for most forms of asphyxia, including drowning, strangling, electric shock (respirocytes are purely mechanical), nerve-blocking paralytic agents, carbon monoxide poisoning, underwater rescue operations, smoke inhalation or fire fighting activities, anaesthetic/barbiturate overdose, confinement in airtight spaces like closets, bank vaults, mines, submarines), and obstruction of breathing by a chunk of meat or a plug of chewing tobacco lodged in the larynx, by inhalation of vomitus, or by a plastic bag pulled over the head of a child. Respirocytes augment the normal physiological responses to hypoxia, which may be mediated by pulmonary neuroepithelial oxygen sensors in the airway mucosa of human and animal lungs [25]

A design alternative to augmentation infusions is a therapeutic population of respirocytes that loads and unloads at an artificial nano lung, implanted in the chest, which exchanges gases directly with the natural lungs or with exogenous gas supplies. (An

intravascular oxygenator using a bundle of hollow fibre membranes inserted into the vena caval bloodstream (which functions as an "artificial lung") is in clinical trials [26]

Underwater Breathing

Respirocytes could serve as an in vivo SCUBA (Self-Contained Underwater Breathing Apparatus) device. With an augmentation dose or nano lung, the diver holds his breath for 0.2-4 hours, goes about his business underwater, then surfaces, hyperventilates for 6-12 minutes to recharge, and returns to work below. (Similar considerations apply in space exploration scenarios.)

The same device can be used for temporary relief from nitrogen narcosis while diving, since N_2 has an aesthetics effect beyond 100 feet of depth.

Direct water-breathing, even with the help of respirocytes, is problematic for several reasons: (1) Seawater contains at most one-thirtieth of the oxygen per lungful as air, so a person must breathe at least 30 times more lungful of water than air to absorb the same volume of respiratory oxygen; lungs full of water weigh nearly three times more than lungs full of air, so a person could hyperventilate water only about one-third as fast as the same volume of air. As a result, a water-breathing human can absorb at most 1%-10% of the oxygen needed to sustain life and physical activity. (2) Deep bodies of water may have low oxygen concentrations because oxygen is only slowly distributed by diffusion; in swamps or below the thermocline of lakes, circulation is poor and oxygen concentrations are low, a situation aggravated by the presence of any oxygen-consuming bottom dwellers or by oxidative processes involving bottom detritus, pollution, or algal growth. (3) Both the diving reflex and the presence of fluids in the larynx inhibit respiration and cause closure of the glottis, and inhaled waterborne micro flora and micro fauna such as protozoa, diatoms, dinoflagellates, zooplankton and larvae could establish (harmful) residence in lung tissue.

Other Application area[27-36]

Respirocytes also permit major new sports records to be achieved, because the devices can deliver oxygen to muscle tissues faster than the lungs can provide, for the duration of the sporting event. This would be especially useful in running, swimming, and other endurance-oriented events, and in competitive sports such as basketball, football and soccer where extended periods of sustained maximum exertion are required. Blood doping [27] and erythropoietin injection [28-30], though illegal, are common among athletes to increase tissue oxygenation, hence performance.) Aerobic capacity in men declines with age, from ~6.9 kg O_2/day at age 25 to ~3.7 kg O_2/day at age 75 [31], so respirocytes could improve geriatric sports participation.

Hyperbaric oxygenation by respirocytes could helps in treatment of various anaerobic and aerobic [32] infections such as clostridia myonecrosis, chronic refractory osteomyelitis, and necrotizing soft tissue infections including cutaneous ulcers, and could assist in burn recovery by reducing fluid requirements, improving microcirculation, and reducing the need for grafting [33].

Artificial blood substitutes may also use in veterinary medicine [34-35], especially in cases of vehicular trauma and renal failure where transfusions are required, and in battlefield applications demanding blood replacement or personnel performance enhancement. Swallowed in pill form, respirocytes could be an effective, though temporary, cure for flatulence, which gas is largely swallowed air and CO_2 generated by fermentation in the stomach. With suitable modifications, respirocyte technology could provide a precisely metered ingestible or injectable drug delivery system, or could assist in the management of serum glycerides, fatty acids or lipoproteins, diabetic ketosis and gestational diabetes, and other dietary conditions. [36]

CONCLUSION:

The present paper represents a simple artificial erythrocyte nano device. Such artificial blood cells carry function similar to natural red blood cells. It includes transport of oxygen and elimination of carbon dioxide. The artificial respirocyte can deliver 236 times more oxygen to the tissues per unit volume than natural red blood cells, and facilitates a similar advantage in carbon dioxide transport.

The respirocyte is constructed of tough diamond like material, having a variety of chemical, thermal and pressure sensors, also having nano computer which enables the device to display many complex responses, that can be remotely programmed by external signals to modify existing or to install new protocols, and draws power from natural serum glucose supplies, thus is capable of operating intelligently and virtually indefinitely, unlike red blood cells which have a natural lifespan of 4 months.

Such respirocytes found application in various field like artificial breathing, under water breathing and in asphyxia condition. It is also helpful in various disorders associated with respiration, cardiovascular, neurological, etc.It also serves a diagnostic purpose. Such device can't be executed today. However today it's a world of advancement and invention, future technologies in molecular machines permits formation of such artificial respirocytes which can be applied in advanced medical system.

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