Hemoglobin Based Oxygen Carriers As Red Cell Subs

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Hemoglobin Based Oxygen Carriers As Red Cell Subs ***2021-12-27***

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Outstanding Marine Molecules John Wiley & Sons
Human blood performs many important functions including

defence against disease and transport of biomolecules, but perhaps the most important is to carry oxygen – the fundamental biochemical fuel - and other blood gases around the cardiovascular system. Traditional therapies for the impairment of this function, or the rapid replacement of lost blood, have centred around blood transfusions. However scientists are developing chemicals (oxygen therapeutics, or “blood substitutes”) which have the same oxygen-carrying capability as blood and can be used as replacements for blood transfusion or to treat diseases where oxygen transport is impaired. Chemistry and Biochemistry of Oxygen Therapeutics: From Transfusion to Artificial Blood links the underlying biochemical principles of the field with chemical and biotechnological innovations and pre-clinical development. The first part of the book deals with the chemistry, biochemistry, physiology and toxicity of oxygen, including chapters on hemoglobin reactivity and regulation; the major cellular and physiological control mechanisms of blood flow and oxygen delivery; hemoglobin and myoglobin; nitric oxide and oxygen; and the role of reactive oxygen and nitrogen species in ischemia/reperfusion Injury. The book then discusses medical needs for oxygen

supply, including acute traumatic hemorrhage and anemia; diagnosis and treatment of haemorrhages in "non-surgical" patients; management of perioperative bleeding; oxygenation in the preterm neonate; ischemia normobaric and hyperbaric oxygen therapy for ischemic stroke and other neurological conditions; and transfusion therapy in β thalassemia and sickle cell disease Finally “old”and new strategies for oxygen supply are described. These include the political, administrative and logistic issues surrounding transfusion; conscientious objection in patient blood management; causes and consequences of red cell incompatibility; biochemistry of red blood cell storage; proteomic investigations on stored red blood cells; red blood cells from stem cells; the universal red blood cell; allosteric effectors of hemoglobin; hemoglobin-based oxygen carriers; oxygen delivery by natural and artificial oxygen carriers; cross-linked and polymerized hemoglobins as potential blood substitutes; design of novel pegylated hemoglobins as oxygen carrying plasma expanders; hb octamers by introduction of surface cysteines; hemoglobin-vesicles as a cellular type hemoglobin-based oxygen carrier; animal models and oxidative biomarkers to evaluate pre-clinical safety of

extracellular hemoglobins; and academia – industry collaboration in blood substitute development.
Chemistry and Biochemistry of Oxygen Therapeutics: From Transfusion to Artificial Blood is an essential reference for clinicians, haematologists, medicinal chemists, biochemists, molecular biologists, biotechnologists and blood substitute researchers.
The Effects of Hemoglobin-based Oxygen Carriers on Mean Arterial Pressure, Arteriolar Diameter, and Nitric Oxide in the Microcirculation
Elsevier
Each chapter of this volume is a contribution from an expert in the field, chosen by the editors to contribute to the 1997 "Current Issues in Blood Substitute Research and Development" course given in San Diego, March 17-19. The contributors were selected because of their expertise in areas which the editors believe to be critical to the advancement of the field, and which reflect activity in "hot" areas of relevant research. While there is a continuity in style for the annual course, each year brings changes in emphasis and content. In previous years, we were often not able to provide time for participants to present their views and opinions. Consequently, this year we encouraged discussion after each

presentation. These sessions were recorded, transcribed, and are printed with the chapters herein. We believe that the product is very close to the capturing this year's course in print, and trust readers will enjoy reading the always candid and often provocative remarks from the audience. The price paid for inclusion of the discussion transcriptions was a delay in publication. Each author was allowed to edit his/her discussion section as well as the final version of the chapters prior to publication. The changes are mainly for grammar, and we tried, when possible, not to alter the conversational style of these interchanges.

Blood Substitutes and Oxygen Biotherapeutics John Wiley & Sons

Using a number of outstanding examples, this text introduces readers to the immense variety of marine natural compounds, the methodologies to characterize them and the approaches to explore their industrial potential. Care is also taken to discuss the function and ecological context of the compounds. Carefully produced and easy to read, this book serves students and professionals wishing to familiarize themselves with the field, and is ideally suited as a course book for both industry to academia.

Hemoglobin-based Artificial Oxygen Carriers Evaluated in

Critically Ischemic Skin Flaps Am Cncl on Science, Health Hemoglobin-based oxygen carriers (HBOCs) offer a safe, more plentiful and long term alternate to blood banks. However, they have been found to increase blood pressure which can be attributed to an increase in total peripheral resistance (TPR). Lumenal nitric oxide (NO) scavenging by these HBOCs seems to be responsible for this hypertensive effect. In addition, it is believed that hemoglobin (Hb) tetramers and dimers may extravasate and consume additional nitric oxide in the perivascular and interstitial space. The purpose of the present study was to elucidate the role of NO scavenging and to confirm extravasation as a contributor to HBOC vasopressor effects in the spinotrapezius muscle. The present study investigated the vessel reactivity and mean arterial pressure response to three HBOCs: HBOC 201, HBOC 205 MW 400, and HBOC 205 MW 600. These varied in molecular weight (MW) and percentage of tetramers and dimers. It was found that larger polymers of HBOC showed no significant decrease in vasoactivity. Although larger polymers are less likely to extravasate, the remaining tetramers and dimers seem sufficient to contribute to the observed vasoactivity. Using NaNO2, a NO donor, in

conjunction with the HBOCs almost completely abolished this hypertensive effect at higher concentrations. Further examination utilizing a nitric oxide synthase (NOS) inhibitor to mimic the HBOC vasopressor effects demonstrated that lower concentrations of $NaNO_2$ were able to abolish the hypertensive effect. In vitro studies only further supported these results by demonstrating that NO consumption increases with HBOC dose. HBOC labeled with TRITC showed conclusive evidence that extravasation also plays a role in NO scavenging, even when minimal amounts of tetramers and dimers are present. In conclusion, the present study offers strong evidence that NO scavenging is responsible for the observed vasopressor effects. It also offers evidence supporting the theory that HBOC extravasation may be contributing to these vasopressor effects as well.

Encyclopedia of Pharmaceutical Technology Clinics: Nursing

This book contains the selected papers presented at the seventh International Symposium on Blood Substitutes (7th ISBS) held at the International Conference Center of Waseda University in Tokyo on 7-10 September 1997. In keeping with the scientific design of the 7th ISBS Symposium, chapters have been

carefully selected and organized to showcase the advancements in recent research. This book includes up-to-date clinical results of leading companies which are manufacturing hemoglobin-based or fluorocarbon-based blood substitutes, and covers issues of hemoglobin toxicity and side effects such as vasoconstriction in more detail using carefully designed in vivo and ex vivo techniques. This book is also a collection of various new types of red cell substitutes such as recombinant Hbs, recombinant albumine-lipidheme complex, modified red blood cells, and perfluorochemicals using material science and molecular engineering.

Advances in Blood Substitutes Biota Publishing

The Encyclopedia of Pharmaceutical Technology presents authoritative and contemporary articles on all aspects of drug development, dosage forms, manufacturing, and regulation-enabling the specialist and novice alike to keep abreast of developments in this rapidly evolving and highly competitive field. A dependable reference tool and a solid investment for years to come--maintaining currency through its supplements [Volume 18/Supplement 1: Published November, 1998] The Encyclopedia contains interdisciplinary contributions in a wide array of subjects,

including Drugs decomposition metabolism pharmaceutical incompatibilities pharmacokinetics physicochemical properties preformulation stability Drug Delivery Systems and Devices-Development and Manufacture analysis and controls bioavailability use of computerization formulation and processing alternatives national and international registration packaging patents process validation scale-up safety and efficacy stability standards Post-Production and Practical Considerations governmental/industrial/professional organizations legal aspects national and international agencies patent life of drugs patient compliance ...and much, much more!

Engineering Cellular Hemoglobin-based Oxygen Carriers for Use in Transfusion Medicine World Scientific

Hemoglobin-based Oxygen Carriers is an exciting and evolving alternative to blood transfusion. This issue explores its potential with topics on: "HBOCs from Human or Bovine Hemoglobin", "Comparison of HBOCs to Stored Human Red Blood Cells," "HBOCs and Tissue Oxygenation," "HBOCs: Role in surgery, resuscitation or hemorrhagic shock?" and more!

Hemoglobin Based Oxygen Carriers Springer Science &

Business Media
Red blood cell (RBC) transfusions have been a life-saving procedure following trauma for decades. Ex vivo storage of RBCs is limited to 42 days, as the RBCs degrade during storage. Recent evidence suggests that transfusions of stored RBCs are associated with adverse events and increased mortality. Blood shortages are frequent and are expected to increase as the population ages. My research explored new methods to prolong ex vivo RBC storage, and alternatives to RBCs. A novel improvement to RBC storage is storage under anaerobic conditions to minimize oxidative stress. Anaerobically stored RBCs improved RBC recovery and resuscitation from hemorrhagic shock compared to conventionally stored RBCs. However, anaerobic storage only slowed the degradation of RBCs, without further extending the RBC storage period. Therefore, we explored hemoglobin (Hb)-based O2 carriers (HBOCs) as an alternative to RBCs. HBOCs are advantageous relative to blood, as they are shelf-stable, not limited by donors for supply, and do not require blood-type matching before infusion. Clinical trials of previous generations of HBOCs failed due to unforeseen side-effects. The next generation of HBOCs involves high molecular weight Polymerized Hb (PolyHb), which is the

most promising and scalable HBOC formulation that alleviates the side effects of previous HBOCs. We compared fresh and stored PolyHb to RBCs in a hemorrhagic shock resuscitation model. The results confirm that PolyHb was as effective as fresh RBCs to recover from shock and significantly superior to stored RBCs, and that PolyHb's properties or efficacy did not change during long term storage. Finally, we assessed the safety of PolyHb in guinea pigs, as they are more human-relevant than other preclinical models. This study demonstrated that increasing the molecular size of PolyHb alleviates side-effects of previous HBOC formulations, and that PolyHb toxicity is transient. Future work will focus on the safety of PolyHb, particularly in vulnerable patient populations.

Effective Implementation of a Hemoglobin-based Oxygen Carrier (HBOC-201) in Resuscitation of Severe, Uncontrolled Hemorrhagic Shock

Springer Science & Business Media

This document is the final report for the research project "Evaluation of Hemopure (HBOC-201) during cardiopulmonary bypass in domesticated swine (sus scrufa)" funded by AF Surgeon General. This final report will be published in the Journal of Thoracic and

Cardiovascular Surgery, details TBD.
Hemoglobin-based Oxygen Carriers (HBOCs) Springer Nature
Op hemoglobine gebaseerde zuurstofdragers (HBOC's) kunnen een alternatief zijn voor het toedienen van bloed bij ernstige bloedingen. Ze leveren niet alleen volume en zuurstof, maar zijn ook direct of indirect van invloed op de spanning in bloedvaten. Mat van Iterson onderzocht bij varkens de effecten van verschillende HBOC's op de zuurstofvoorziening naar het hart en de darmen na een gecontroleerde bloeding. HBOC's zijn effectief in het transporteren van zuurstof naar de microcirculatie (de kleinste vaten), maar door het samenknijpen van bloedvaten wordt een tekort aan bloedvolume gemaskeerd. Om de effectiviteit van HBOC's vast te stellen, is het beoordelen van de microcirculatie daarom een voorwaarde.
Hemoglobin--molecular, Genetic, and Clinical Aspects CRC Press
This volume of the Keio University International Symposia for Life Sciences and Medicine contains the proceedings of the 13th symposium held under the sponsorship of the Keio University Medical Science Fund. The fund was est-lished by the generous donation of the late Dr. Mitsunada Sakaguchi. The Keio University International Symposia for Life Sciences and

Medicine constitute one of the core activities sponsored by the fund,of which the objective is to contribute to the international community by developing human resources, promoting scienti?c knowledge, and encouraging mutual exchange. Each year, the Committee of the International Symposia for Life Sciences and Medicine selects the most signi?cant symposium topics from applications received from the Keio medical community. The publication of the proce- ings is intended to publicize and distribute the information arising from the lively discussions of the most exciting and current issues presented during the symposium. On behalf of the Committee, I am most grateful to the late Dr. Sakaguchi, who made the series of symposia possible. We are also grateful to the prominent speakers for their contribution to this volume. In addition, we would like to acknowledge the ef?cient organizational work performed by the members of the program committee and the staff of the fund. Naoki Aikawa, M. D. , D. M. Sc. , F. A. C. S.

Regulation of Tissue Oxygenation, Second Edition Saunders

Currently, hemoglobin (Hb)-based oxygen carriers (HBOCs) are leading candidates as red blood cell substitutes. In addition, HBOCs are also potential oxygen

therapeutics for treatment of patients with critical ischemic conditions due to atherosclerosis, diabetes and other conditions. This book will provide readers a comprehensive review of topics involved in the HBOC development. It focusses on current products and clinical applications as well as on emerging technologies and future prospects.

International Review of Cytology [116]. Elsevier

This presentation describes various aspects of the regulation of tissue oxygenation, including the roles of the circulatory system, respiratory system, and blood, the carrier of oxygen within these components of the cardiorespiratory system. The respiratory system takes oxygen from the atmosphere and transports it by diffusion from the air in the alveoli to the blood flowing through the pulmonary capillaries. The cardiovascular system then moves the oxygenated blood from the heart to the microcirculation of the various organs by convection, where oxygen is released from hemoglobin in the red blood cells and moves to the parenchymal cells of each tissue by diffusion. Oxygen that has diffused into cells is then utilized in the mitochondria to produce adenosine triphosphate (ATP), the energy currency of all cells. The mitochondria are able to produce

ATP until the oxygen tension or PO2 on the cell surface falls to a critical level of about 4–5 mm Hg. Thus, in order to meet the energetic needs of cells, it is important to maintain a continuous supply of oxygen to the mitochondria at or above the critical PO2 . In order to accomplish this desired outcome, the cardiorespiratory system, including the blood, must be capable of regulation to ensure survival of all tissues under a wide range of circumstances. The purpose of this presentation is to provide basic information about the operation and regulation of the cardiovascular and respiratory systems, as well as the properties of the blood and parenchymal cells, so that a fundamental understanding of the regulation of tissue oxygenation is achieved.

Hemoglobin-based Oxygen Carriers: in Vitro Hemocompatibility and Functionality

Springer Science & Business Media

This study compared the effects on oxygen (O2) transport of four fluids: 5.9% human serum albumin (HSA) a non-O2 carrying iso-oncotic solution (volume control);HBOC-201 (Hemopure, Biopure Corp., Cambridge, MA); MP50, HBOC-201 with a P50 of 18 mmHg; and lastly LP50, an HBOC-201 with P50 of 17 mmHg and higher viscosity (4 cP). It has been proposed that HBOC with a higher O2 affinity and a viscosity

closer to that of whole blood will cause less vasoconstriction and thus a lower MAP than Hemopure (P50 = 40 mmHg and 2.2 cP). Intravital microscopic measurements were made on the spinotrapezius muscle of anesthetized, male Sprague-Dawley rats. Interstitial PO2 was measured using phosphorescence quenching microscopy at baseline and following four top-loading infusions, in which increasing concentrations of HBOC-201 were infused to reach target plasma concentrations of 1, 10, 100 and 300 [micro]M. Both HBOC-201 and MP50 increased PO2 by about 10%, but PO2 was unchanged with LP50. LP50 was more hypertensive (160 [plus or minus] 5mmHg) than HBOC-201 (144 [plus or minus] 5) and MP50 (14 [plus or minus] 6). Arteriolar diameters were not significantly different among the three HBOCs. The lower P50 HBOCs did not lead to higher PO2 compared with HBOC-201 and the higher viscosity HBOC led to higher MAP. Hemorrhage and Resuscitation This study compared the efficacy of three resuscitation fluids in a model of hemorrhage and resuscitation: HBOC-201, a hemoglobin-based oxygen carrier ([Hb] = 13 [plus or minus] 1 g/dl; Biopure Corp.), HBOC-201 with 92 [micro]g/ml nitroglycerin (NTG), and 5.9% human serum albumin, a non-

oxygen carrying colloid solution. Intravital microscopic measurements were made on the spinotrapezius muscle of anesthetized, male Sprague-Dawley rats. Interstitial fluid (ISF) oxygen tension (PO2) was measured using phosphorescence quenching microscopy at baseline, post-hemorrhage and three post-resuscitation time points. Following 40% blood volume withdrawal, animals were maintained in this condition for 30 minutes before resuscitation was begun. Baseline ISF PO2 (65 [plus or minus] 2 mmHg) decreased during hemorrhage (3.6 [plus or minus] 0.4 mmHg) and all resuscitation fluids increased ISF PO2 towards baseline. HBOC-201 with nitroglycerin produced the highest PO2 throughout the experimental time course, and the findings are consistent with the NO scavenging theory because adding NO alleviated known side effects such as increased vascular resistance and hypertension that are associated with HBOC-201 infusions.

Hemoglobin-based Oxygen Carrier Treatment Induces Pulmonary Vascular Leak in a Rat Model

Purpose: To compare the effects of resuscitation with hemoglobin- based oxygen-carriers and conventional crystalloid and colloid resuscitation fluids on hemodynamics, oxygen transport, and

oxygen consumption in an animal model of the field medical use of these fluids in the treatment of hemorrhagic shock. Protocol: Twenty-eight immature swine were surgically prepared, allowed to recover five days, water deprived for 48 hours, hemorrhaged of 25 m1/kg over one hour, resuscitated promptly with 1) Ringer's lactate, 75 m1/kg, 2) 7% albumin in Ringer's acetate, 25 m1/kg, 3) 9% unmodified hemoglobin in Ringer's acetate, 25 ml/kg, or 4) 9% alpha alpha-crosslinked hemoglobin in Ringer's acetate, 25 ml/kg, observed with three hours of hemodynamic and oxygen transport measurements, and, finally, blood which had been removed previously was returned.

Hemoglobin Based Oxygen Carriers

This book functions as a comprehensive and authoritative reference book in blood transfusion and blood substitutes. It is a collection of the latest developments and the newest investigations, and individual chapters are written by world experts in the arena. The book begins with a historical review on the practice of transfusions as well as the components and physiology of blood. The following chapters cover various topics, including platelet substitutes, hemoglobin-based oxygen carriers, perfluorocarbon based oxygen carriers, and safety issues related to artificial hemoglobin.

All chapters provide a bulleted highlights list to facilitate readers in mastering the main points of each individual chapter. Blood Substitutes and Oxygen Biotherapeutics is an invaluable reference book for perioperative care providers, hematologists, anesthesiologists, surgeons, obstetricians and gynecologists.

Microvascular and Tissue Oxygenation in Rat Muscle During Hemodilution with Hemoglobin-based Oxygen Carriers

Blood substitutes are solutions designed for use in patients who need blood transfusions, but for whom whole blood is not available, or is not safe. This interest has intensified in the wake of the AIDS and hepatitis C epidemics. Blood Substitutes describes the rationale, current approaches, clinical efficacy, and design issues for all blood substitutes now in clinical trials. The many summary diagrams and tables help make the book accessible to readers such as surgeons and blood bankers, who have less technical expertise than the biochemists and hematologists who are designing and testing blood substitutes. * Includes chapters necessary to the understanding of blood substitutes, including history, toxicity, physiology, and clinical applications * Presents detailed descriptions of the various products that have been developed and have advanced to clinical

trials, and some that are in earlier states of development

Blood Substitutes: Hemoglobin-Based Oxygen Carriers

Abstract: The main goal of the research discussed in this dissertation is to create effective and safe cellular hemoglobin (Hb)-based oxygen (O2) carriers (HBOCs) for use in transfusion medicine. This dissertation focuses on the development and scale up production of cellular HBOCs composed of novel lipid formulations and polymers. The research concentrates on the development of cellular HBOCs over acellular HBOCs and abiotic O2 carriers, owing to their various advantages, such as, longer shelf-life, high Hb content, increased circulation half-life, biocompatibility, and absence of vasoactivity and hypertension in vivo. This dissertation presents various novel large scale methods for the production of cellular HBOCs. The methods discussed are very efficient as HBOCs are produced with very reproducible biophysical properties. All the methods are designed with cost effectiveness in mind. The methods presented are simple and easily scalable to an industrial scale. In addition, they eliminate the use of energy consuming equipment/methods used in the production of other cellular HBOCs. Moreover, all the scale up methods are designed to satisfy important design criteria required to

develop an effective O2 carrier, such as, high Hb content, suitable biophysical properties to ensure proper O2 delivery to tissues and organs and absence of any free Hb in the dispersions. This dissertation also outlines detailed insights on the role of the intracellular diffusion barrier, as a result of Hb encapsulation, on binding/release of gaseous molecules to Hb. It emphasizes the importance of the cellular membrane and Hb encapsulation, as well as the pivotal role it plays in regulating O2 delivery or consumption of nitric oxide (NO) by Hb in cellular HBOCs. In addition, the ex vivo experiments in rat arterial segments discussed in this dissertation provide for the correlation between O2 delivery and NO consumption to Hb-induced vasoconstriction by using exogenous and endogenous sources of NO. Overall, this dissertation presents novel cellular HBOCs with a potential of being safe and effective O2 carriers for use in transfusion medicine.

Blood Conservation in Cardiac Surgery

This definitive volume will provide the reader with up to date information and the most recent science of the fast-evolving area of nanobiotherapeutic-based blood substitutes. Long studied, there are recent updates that make their use in patients more promising, and with

one product approved for human use, many more in the pipeline. These include 2nd generations and even third generation ones, the later with enhancement of red blood cell functions. In addition, there are carefully written and referenced updates on the recent history and products in the field, complete with pathophysiologic and pharmacologic studies to validate and verify the efficacy and safety of many of these new products.

Analysis of a Novel Polymerized Hemoglobin Based Oxygen Carrier