INTERNATIONAL RESEARCH JOURNAL OF ENGINEERING & APPLIED SCIENCES
ISSN: 2322-0821(O) VOLUME 11 ISSUE 3
ISSN: 2394-9910(P) July 2023 - Sep 2023
www.irjeas.org

Original Article

A Detailed Perspective on Artificial Blood

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DOI – 10.55083/irjeas.2023.v11i03008

Abstract: Hospitals routinely perform blood transfusions, a critical medical procedure. However, natural blood products have limitations such as limited availability and the potential for adverse reactions. To address these challenges, scientists have dedicated nearly four decades to researching artificial blood components. The primary objective is to create effective and selective alternatives capable of performing the same vital functions as natural blood products. These substitutes consist of precisely defined compounds designed for the transportation and distribution of oxygen within the human body, ultimately enhancing the efficacy of allergenic human blood transfusions. Over time, a multitude of molecules have been developed and continuously refined in pursuit of the perfect blood substitute. Recent advancements have led to the production of artificial blood using materials like PFC or hemoglobin derived from outdated human or bovine blood sources. This represents a significant step forward in the quest to provide a comprehensive range of blood alternatives.

Keywords: Artificial blood, Haemoglobin-based oxygen carriers, oxygen carrier, Red blood cells, Per fluorocarbons
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1. INTRODUCTION:

Blood is an indispensable fluid in the human body, serving a multitude of life-sustaining functions. It represents a specialized form of connective tissue, comprising various cells suspended within a liquid component known as plasma. These cellular components include white blood cells (leukocytes), red blood cells (erythrocytes), and platelets, each carrying out specific roles. Erythrocytes, commonly known as red blood cells, serve the essential function of transporting oxygen from the lungs to various tissues in the body, simultaneously removing carbon dioxide from these tissues and transporting it back to the lungs for exhalation. Leukocytes, or white blood cells, function as the body's primary defense mechanism against infections and foreign invaders, safeguarding our health. Platelets play a crucial role in the blood clotting process, preventing excessive bleeding in the event of an injury. Furthermore, blood plays a vital role in the transportation of nutrients, hormones, and waste products throughout the body, ensuring the proper functioning of various bodily systems.It contributes to the regulation of body temperature, pH levels, and electrolyte balance. Additionally, blood is integral to medical treatments, including blood transfusions, which are used to replace blood lost due to injury or illness.

The study of blood and its related disorders falls under the field of hematology, with specialists known as hematologists. A profound comprehension of blood's composition and functions is vital for diagnosing and treating a wide range of diseases and conditions.

Crucial to the body's ability to transport oxygen and carbon dioxide are red blood cells, which contain hemoglobin, a protein binding and releasing oxygen to and from tissues. Additionally, blood type, a significant factor in transfusion medicine, is determined by specific proteins on red blood cell surfaces. It's important to note that current artificial blood products mainly focus on replicating the oxygen-carrying function of red blood cells rather than mimicking the intricate composition and functions of natural blood. Therefore, these products are often referred to as "oxygen carriers" rather than complete blood substitutes.

Historically, the quest for a suitable alternative to human blood dates back centuries, with proposals ranging from using ale, wine, and morphine by Sir Christopher Wren in the seventeenth century to various substances like urine, plant resin, and sheep plasma in later years. Notable advancements in blood transfusion safety came with Karl Landsteiner's discovery of different blood groups, laying the foundation for safer and more established transfusion procedures.

The early 1900s witnessed progress as researchers recognized the need for type-specific allogeneic transfusions and explored the use of cell-free hemoglobin for resuscitation. However, initial attempts were hindered by side effects, such as renal failure, gastrointestinal bleeding, and immunogenicity.

Current research into artificial blood primarily involves two approaches: perfluorocarbon (PFC) emulsions and hemoglobin-based oxygen carriers (HBOCs). PFCs are clear, inert liquids with the potential to carry oxygen, while HBOCs involve modified hemoglobin. Hemoglobin vesicles (HbV), enclosing high-concentration hemoglobin in a phospholipid bilayer, show promise as safe and practical options for artificial blood.

The need for artificial blood is underscored by blood supply shortages, which often fall far short of demand, posing risks of disease transmission and transfusion errors. Artificial blood offers the advantage of mitigating these risks while also reducing the cost and complexity associated with traditional blood collection, screening, and storage.

Ideal artificial blood products should be safe, function effectively in the human body, transport and release oxygen as needed, be free from pathogens that trigger immune responses, and serve as oxygen carriers without replicating the broader functions of natural blood cells.

2. STRUCTURE AND TYPES:

Artificial blood products have evolved over time, with various compositions explored. One example includes perfluorocarbons (PFCs), composed of 28% perfluoro-octyl bromide, 12% Fo-9982, 4% egg lecithin, 0.12% DSPE-50H, and 57.48% distilled water. PFCs, originally introduced as the first generation of artificial blood, possess advantages such as a high oxygen-carrying capacity, long shelf life, and resistance to temperature and pH changes. However, challenges include the need for emulsification for water solubility and linear breathing to maintain tissue oxygenation.

While PFCs have potential, they are not without disadvantages, including potential reductions in platelet counts and impacts on immune system function when administered in large doses.

Artificial blood research remains a dynamic field, aiming to develop safe and effective blood substitutes to address challenges in traditional transfusion methods. Further research is needed to refine and optimize these alternatives for clinical use.

In conclusion, artificial blood represents a critical area of research with the potential to revolutionize medical treatments. While challenges remain, ongoing efforts hold promise for developing safe and effective blood substitutes that can address the limitations of natural blood products.

Table 1 PFC product summary.

PFC Product	**Generation**	**Approval**	**Clinical Trials**
Fluosol-DA-20	1st	Endorsed by the FDA	the year 1994

Oxygent	2nd	Due to its adverse effects, it is not approved.	clinical study phase III due of its stability
Oxycyte	3rd	No recognition in nations	clinical trials in phase III
Perftoran	3rd	Russia's approval came in 1996	Russia for human consumption
PHER-O	3rd	No approval	Pre-clinical trials

3. HEMOGLOBIN-BASED OXYGEN CARRIERS (HBOC'S):

HBOCs constitute a category of blood substitutes designed to replicate the essential function of natural blood, which is to transport oxygen to various tissues and organs throughout the body. The process involves isolating hemoglobin from either human or animal blood and then modifying it to enhance its stability and capacity to carry oxygen. HBOCs have the potential to be employed in critical situations where traditional blood transfusions are unavailable or impractical, such as military operations or remote locations. Nevertheless, the utilization of HBOCs is still under investigation due to potential adverse effects, including elevated blood pressure, vasoconstriction, and tissue damage. Intensive research aims to refine the production process and ensure the safety and efficacy of HBOCs for medical use.

The concept of artificial blood or blood substitutes has been in existence for over a century. The initial endeavor to develop a blood substitute dates back to the early 1900s when human hemoglobin was first isolated (24). However, it wasn't until the 1980s that the first generation of HBOCs was created and assessed for medical applications. These initial attempts encountered challenges related to adverse effects and limited oxygen-carrying capacity. Substantial advancements have since been made in refining the manufacturing process and enhancing the safety and effectiveness of HBOCs. Ongoing research and development in this field continue to push the boundaries of medical science and technology.

Various techniques are employed to augment the stability of hemoglobin-based oxygen carriers (HBOCs), leading to different categories of solutions. Some of these categories include:

(i) Cross-linked hemoglobin (XLHb): This method involves chemically cross-linking hemoglobin molecules to prevent their degradation and extend their circulation time in the bloodstream.

(ii) Polymerized hemoglobin (PolyHb): In this approach, polymers are added to hemoglobin molecules to enhance their stability and oxygen-carrying capacity.

(iii)Encapsulated hemoglobin (EHb): This technique entails encapsulating hemoglobin molecules within a membrane to safeguard them against degradation and prevent adverse immune responses.

(iv) Recombinant hemoglobin (rHb): This method utilizes genetically engineered hemoglobin molecules produced through recombinant DNA technology.

(v) Hemoglobin vesicles (HbV): In this approach, hemoglobin is enclosed within a phospholipid bilayer to create a stable and functional hemoglobin vesicle (25, 26).

These diverse techniques represent ongoing efforts to develop HBOCs that can safely and effectively mimic the oxygen-carrying function of natural blood, thus addressing critical medical needs and advancing the field of blood substitutes.

Table 2: Overview of based product (27,28)

Type of HBOC	**Product Name**	**Source of Hemoglobin**
Cellular Hb-based oxygen carriers	Neo Red Cell	Human Hemoglobin

Cellular Hb-based oxygen carriers	liposome-encapsulated hemoglobin (LEH)	Outdated Human RBC
Cellular Hb-based oxygen carriers	Hemoglobin vesicle (Hb V)	Carbonyl Human Hemoglobin
Cellular Hb-based oxygen carriers	Hemopure	Glutaraldehyde Bovine Hemoglobin
Acellular Hb-based oxygen carriers	polymer-encapsulated hemoglobin (PEH)	Human and Bovine Hemoglobin
Acellular Hb-based oxygen carriers	Oxyglobin	Bovine Hemoglobin
Acellular Hb-based oxygen carriers	Diaspirin cross-linked Hb (DCLHb) or HemAssist	Human Hemoglobin
Acellular Hb-based oxygen carriers	PolyHeme	Glutaraldehyde, pyridoxal Human Hemoglobin

4. CONCLUSION

In critical situations, such as during surgeries involving significant blood loss, synthetic blood can serve as a dependable alternative to traditional blood transfusions. Although it cannot completely replace natural blood, it can play a vital role in filling the vascular space and transporting essential gases. Synthetic blood, also known as blood surrogates or blood substitutes, can supply oxygen to tissues, sustaining life until the patient's own red blood cells regenerate or until they receive a transfusion of stored blood. Additionally, it can mitigate the risk of false-negative results that may occur with real blood.

Hemoglobin-based oxygen carriers (HBOCs) hold great promise for a wide range of applications beyond the core physiological function of blood, including aiding in the treatment of various diseases and combating pathogens. The development of lab-grown artificial blood has the potential to revolutionize healthcare by offering a reliable source of blood that is independent of blood type or donor availability. Nevertheless, rigorous testing in both laboratory and living organism environments is essential to ensure consistent composition, reproducible manufacturing, safety, and therapeutic efficacy. Achieving the desired outcome will require a collaborative effort involving biomedical and materials engineers, hematologists, immunologists, and regulatory agencies.

Although human trials for synthetic blood are on the horizon, it will take some time before it can be widely utilized. Nonetheless, these advancements hold the potential to reshape the future of healthcare.

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__Conflict of Interest Statement:__ The author declares that there is no conflict of interest regarding the publication of this paper.