An Overview on Synthetic Blood

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Abstract—**Artificial blood is a product made to act as a substitute for red blood cells, blood substitutes areused to fill fluid volume and/or carry oxygen and other blood gases in the cardiovascular system.More accurate terms are volume expanders for inert products, and oxygen therapeutics for oxygencarryingproducts. Ideal blood substitute should have Universal compatibility: elimination of cross matching, Pathogen free, Minimal side effects, Survivability over a wider range of storage temperatures, Long shelf life, Cost efficient etc. Their main function is replacing lost blood volume and oxygen carrying capacity. Haemoglobin-based oxygen carriers vaguely resemble blood. They are very dark red or burgundy and are made from real, sterilized haemoglobin, which can come from a variety of sources. Their main function is replacing lost blood volume and oxygen carrying capacity. Haemoglobin-based oxygen carriers vaguely resemble blood. Unlike haemoglobin -based oxygen carriers, perfluoro chemicals are entirely synthetic. It's concluded that large-scale production of blood substitutes would also help to meet the anticipated increase in demand for blood.**

KEYWORDS: Artificial blood, Haemoglobin-based oxygen carriers, Perfluoro chemicals.

I. INTRODUCTION

We humans and other animals are constantlyleft exposed to the ferocity of certain viruses,and blood services are substantially affectedby those viral entities.Regarding research on artificial blood, the "Field of Artificial BloodDevelopment" was inaugurated in 1997, supported by the Ministry of Health andWelfare Grant-in-Aid for Health Science Research, for intensive research activitiesin the three sub-fields, i.e., artificial red blood cells, artificial platelets, and artificialantibodies. Developed by molecular assembling technology, artificial red bloodcells, in the form of haemoglobin vesicles comprising haemoglobin encapsulated witha phospholipid bilayer as a highly efficient oxygen carrier, are now under investigationin laboratory animals to verify their function and safety. These vesicles arecharacterized by a particle size about 1/30 that of erythrocytes, preserve ability in aliquid state for 2 years at room temperature, and a sufficient retention time incirculating blood without evoking activation of platelet or complements. The haemoglobinvesicles have proven both to possess a high oxygen-carrying capacity inmassive exchange transfusion studies in rodents, and to be remarkably safe,based on blood biochemical tests and pathologic findings in load-dosing andrepeated-dose studies. Their noticeable safety against active oxygen has alsobeen demonstrated. A joint industry, government, and university research projecton artificial red blood cells is in progress with the present objective of developinga complement to transfusion therapy for emergency lifesaving.

TYPES OF ARTIFICIAL BLOOD

There are two main types of artificial blood: HBOC and PFC as shown in figure 1:

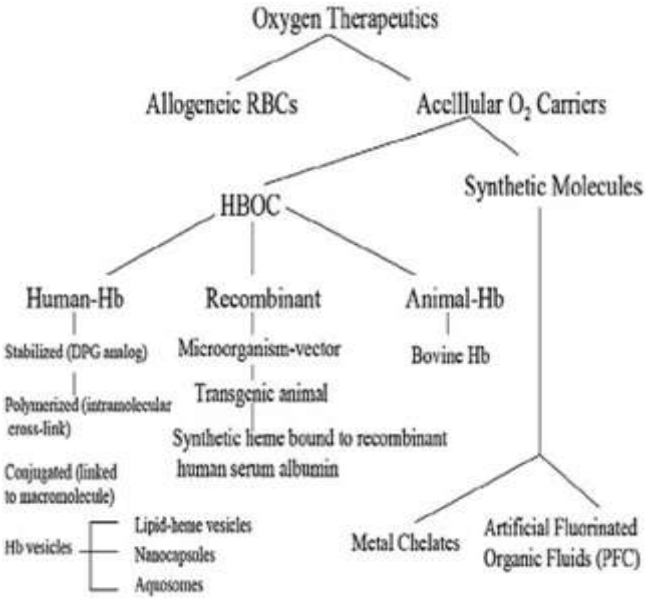

Fig 1: Blood substitutes classification

PROBLEMS WITH HUMAN BLOOD

1. Human blood has to be kept cool, and it has a shelf life of 42 days.
2. Doctors must make sure the blood is the right type: A, B, AB or O before giving it to
a patient. If a patient receives the wrong type of blood, a deadly reaction can result.
3. Viruses like HIV and hepatitis can contaminate the blood.

IDEAL CHARACTERISTICS OF BLOOD SUBSTITUTES

1. Safe to use.
2. Compatible in the human body.
3. Able to transport and release oxygen where needed.

4. Storable and durable for longer time periods.
5. Is free of pathogens and toxins which would produce an immune system response inthe human body.

II. MATERIALS USED FOR MANUFACTURING OF ARTIFICIAL BLOOD

Depending on the type of artificial blood that is made, various raw materials are used.Hemoglobin-based products can use either isolated hemoglobin or synthetically produced hemoglobin. To produce hemoglobin synthetically, manufacturers use compounds knownas amino acids. All the amino acid molecules share certain chemical characteristics. They aremade up of an amino group, a carboxyl group, and a side chain. hemoglobin synthesis also
requires a specific type of bacteria and all of the materials needed to incubate it. This includeswarm water, molasses, glucose, acetic acid, alcohols, urea, and liquid ammonia

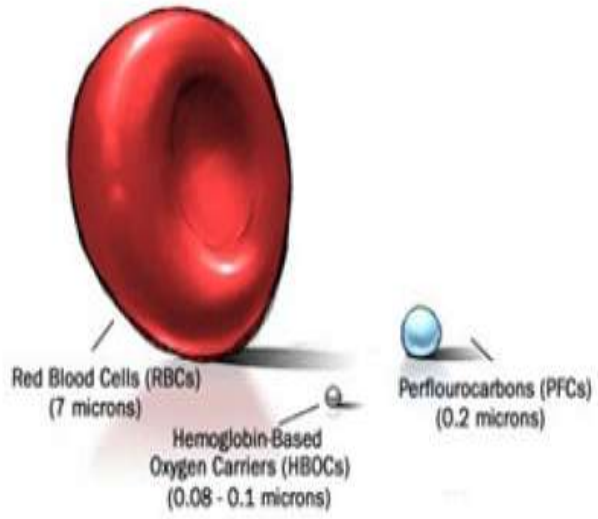

Fig 2: Comparison of normal red blood cell with HBOC and PFC cells.

Artificial blood is a product made to act as a substitute for red blood cells Blood substitutes (also called artificial blood or blood surrogates) are used to fill fluid volume and/or carry oxygen and other blood gases in the cardiovascular system. Although commonly used, the term is not accurate since human blood performs many important functions which blood substitutes may not. Red blood cells transport oxygen, white blood cells defend against disease, platelets promote clotting, and plasma proteins perform various functions. The preferred and more accurate terms are volume expanders for inert products, and oxygen therapeutics for oxygen-carrying products .

Examples of these two "blood substitute" categories:

Volume expanders

They are inert and merely increase blood volume. These may be crystalloid-based (Ringer's lactate, normal saline, D5W dextrose 5% in water) or colloid-based (Voluven, Haemaccel, Gelofusin).

Oxygen therapeutics

They mimic human blood's oxygen transport ability. Examples: Hemopure, Oxycyte, Oxygent, PolyHeme and Perftoran. Oxygen therapeutics is in turn broken into two categories based on transport mechanism: Perfluorocarbon based and Hemoglobin based.

When severe trauma occurs, a serious danger is that blood volume will be reduced to a point where the remaining red blood cells can no longer oxygenate body tissue, which can result in tissue damage or death. In such an emergency situation, doctors will often give patients volume expanders, like saline, to make up for lost blood volume. This helps to restore normal blood pressure and lets the remaining red blood cells continue to carry oxygen. Sometimes, this is enough to keep the body going until it can produce new blood cells and other blood elements. If not, doctors can give patients blood transfusions to replace some of the lost blood. Blood transfusions are also fairly common during some surgical procedures.

This process works pretty well, but there are several challenges that can make it difficult or impossible to get patients the blood they need:

- Human blood has to be kept cool, and it has a shelf life of 42 days. This makes it impractical for emergency crews to carry it in ambulances or for medical staff to carry it onto the battlefield. Volume expanders alone may not be enough to keep a badly bleeding patient alive until he reaches the hospital.
- Doctors must make sure the blood is the right type -- A, B, AB or O -- before giving it to a patient. If a person receives the wrong type of blood, a deadly reaction can result.
- The number of people who need blood is growing faster than the number of people who donate blood.
- Viruses like HIV and hepatitis can contaminate the blood supply, although improved testing methods have made contamination less likely in most developed countries.

This is where artificial blood comes in. Artificial blood doesn't do all the work of real blood. Sometimes it can't even replace lost blood volume. Instead, it carries oxygen in situations where a person's red blood cells can't do it on their own. For this reason, artificial blood is often called as oxygen therapeutics

III. DESIGN

Ideal blood substitute

Blood substitutes or synthetic blood are currently labelled as "oxygen carriers". This is because they are unable to mimic many of the other functions of blood. They do not contain

cells, antibodies, or coagulation factors. Their main function is replacing lost blood volume and oxygen carrying capacity. The ideal blood substitute could be defined by the following terms:

- Increased availability that would rival that of donated blood, even surpass it
- Oxygen carrying capacity, equaling or surpassing that of biological blood
- Volume expansion
- Universal compatibility: elimination of cross matching
- Pathogen free: elimination of blood contained infections
- Minimal side effects
- Survivability over a wider range of storage temperatures
- Long shelflife
- Cost efficient

IV. MANUFACTURING PROCESS

The production of artificial blood can be done in a variety of ways. For hemoglobin-based products, this involves isolation or synthesization of hemoglobin, molecular modification then reconstitution in an artificial blood formula. PFC products involve a polymerization reaction. A method for the production of a synthetic hemoglobin-based product is outlined below.

Hemoglobin synthesis

- To obtain hemoglobin, a strain of *E. coli* bacteria that has the ability to produce human hemoglobin is used. Over the course of about three days, the protein is harvested and the bacteria are destroyed. To start the fermentation process, a sample of the pure bacteria culture is transferred to a test tube that contains all the nutrients necessary for growth. This initial inoculation causes the bacteria to multiply. When the population is great enough, they are transferred to a seed tank.
- A seed tank is a large stainless steel kettle that provides an ideal environment for growing bacteria. It is filled with warm water, food, and an ammonia source which are all required for the production of hemoglobin. Other growth factors such as vitamins, amino acids, and minor nutrients are also added. The bacterial solution inside the seed tank is constantly bathed with compressed air and mixed to keep it moving. When enough time has passed, the contents of the seed tank is pumped to the fermentation tank.
- The fermentation tank is a larger version of the seed tank. It is also filled with a growth media needed for the bacteria to grow and produce hemoglobin. Since pH control is vital for optimal growth, ammonia water is added to the tank as necessary. When enough hemoglobin has been produced, the tank is emptied so isolation can begin.
- Isolation begins with a centrifugal separator that isolates much of the hemoglobin. It can be further segregated and purified using fractional distillation. This standard column separation met hod is based on the principle of boiling a liquid to separate one or more components and utilizes vertical structures called fractionating columns. From this column, the hemoglobin is transferred to a final processing tank.

Final processing

- Here, it is mixed with water and other electrolyte to produce the artificial blood. The artificial blood can then be pasteurized and put into an appropriate packaging. The quality of compounds is checked regularly during the entire process. Particularly important are frequent checks made on the bacterial culture. Also, various physical and chemical properties of the finished product are checked such as pH, melting point, moisture content, etc. This method of production has been shown to be able to produce batches as large as 2,640 gal (10,000 L).

V. ADVANTAGES

Oxygen therapeutics, even if widely available, would not eliminate the use of human blood, which performs various functions besides oxygen transport. However oxygen therapeutics has major advantages over human blood in various situations, especially trauma.

Blood substitutes are useful for the following reasons:

1. Donations are increasing by about 2-3% annually in the United States, but demand is climbing by between 6-8% as an aging population requires more operations that often involve blood transfusion.
2. Although the blood supply in the US is very safe, this is not the case for all regions of the world. Blood transfusion is the second largest source of new HIV infections in Nigeria. In certain regions of southern Africa, it is believed that as much as 40% of the population has HIV/AIDS, although testing is not financially feasible. A disease-free source of blood substitutes would be incredibly beneficial in these regions.
3. In battlefield scenarios, it is often impossible to administer rapid blood transfusions. Medical care in the armed services would benefit from a safe, easy way to manage blood supply.
4. Great benefit could be derived from the rapid treatment of patients in trauma situations. Because these blood substitutes do not contain any of the antigens that determine blood type, they can be used across all types without immunologic reactions.

5. While it is true that receiving a unit of transfused blood in the US does not carry many risks, with only 10 to 20 deaths per million units, blood substitutes could eventually improve on this. There is no practical way to test for prior-transmitted diseases in donated blood, such as Mad Cow and Creutzfeld-Jacob disease, and other disease could emerge as problems for the blood supply, including smallpox and SARS.
6. Transfused blood is currently more cost effective, but there are reasons to believe this may change. For example, the cost of blood substitutes may fall as manufacturing becomes refined.
7. Blood substitutes can be stored for much longer than transfusable blood, and can be kept at room temperature. Most haemoglobin-based oxygen carriers in trials today carry a shelf life of between 1 and 3 years, compared to 42 days

REFERENCES

1. Takagi, H., Goto, S., Matsui, M., Manabe, H. and Umemoto, T., A contemporary meta-analysis of Dacron versus polytetrafluoroethylene grafts for femoropopliteal bypass grafting. *J. Vasc. Surg.*, 2010, **52**(1), 232–236.
2. Jeanmonod, P. *et al.*, Silver acetate coating promotes early vascularizationof Dacron vascular grafts without inducing host tissueinflammation. *J. Vasc. Surg.*, 2013, **58**(6), 1637–1643.
3. Nerem, R. M. and Seliktar, D., Vascular tissue engineering. *Annu.Rev. Biomed. Eng.*, 2001, **3**, 225–243.
4. Uttayarat, P. *et al.*, Micropatterning of three-dimensional electrospunpolyurethane vascular grafts. *ActaBiomater.,*2010, **6**(11),4229–4237.
5. Bergmeister, H. *et al.*, Electrospun small-diameter polyurethanevascular grafts: ingrowth and differentiation of vascular-specifichost cells. *Artif. Organs*, 2012, **36**(1), 54–61.