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A review on artificial blood

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REVIEW

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HISTORY

Blood substitutes have been required for as long as people have been bleeding to death due to a serious injury. In the years that followed, doctors experimented with a variety of substances as blood substitutes, including beer, urine, milk, plant resins, and sheep blood. One of the first of these materials was milk. To treat Asiatic cholera, patients were given milk injections in 1854. Milk injections were never popular among doctors due to their scepticism. It was tossed out after a short time. Salt or saline solutions could also be used as a replacement. It was discovered that frogs could survive for a brief period of time without blood circulation, which led to deception.

Saline was created as a plasma volume expander after a few years of research. A gum-saline solution containing galactoso-gluconic acid was utilised to prolong plasma during World War I. However, studies have revealed that chewing gum has certain harmful health impacts. During World War II, there was a renewed interest in the study of blood and blood substitutes. Human plasma was frequently utilised to replace blood and protect soldiers from haemorrhagic shock. Perfluorochemicals, a new type of blood replacement, were discovered in animal tests in 1966. (PFC). This sparked the notion of using PFC as a blood thinner.

Key Words

Artificial blood, blood substitutes, haemoglobin, perfluorocarbon

Introduction

Blood is a special type of connective tissue made composed of white cells, red cells, platelets, and plasma. It serves a number of purposes in the body. Blood is responsible for transporting oxygen throughout the body, releasing oxygen to tissues, and removing carbon dioxide from tissues. All of this is due to haemoglobin, a protein that transports oxygen and is found in red blood cells (erythrocytes). Hemoglobin, which makes up around 33 per cent of the mass of red blood cells, is the most critical component. There are around 280 haemoglobin molecules inside each RBC. It is made up of four pigments termed heme and a protein component called globin. Iron is used by the heme to form bonds with oxygen.

Artificial blood substitutes have been developed as a result of a number of factors. Artificial blood is a new biotechnology concept that mimics and performs some of the functions of blood. Oxygen therapeutic is another name for artificial blood. Although donor blood transfusion is a common and safe practise, blood replacements are being developed for a variety of reasons. Human RBC must be stored under strict conditions in order to maintain clinical effectiveness and decrease the danger of bacterial contamination[1].

The major goal is to provide a non-blood transfusion alternative. Artificial blood, which has fewer storage requirements, would be useful in these circumstances. The three major roles of red blood cells were accomplished by artificial red blood cells:

1. Oxygen transport
2. Carbon dioxide transport
3. Antioxidant functions

Artificial blood lacks plasma, red and white blood cells, yet it transports and delivers oxygen to bodily cells until the bone marrow regenerates the missing RBCs.

Synthetic manufacture, chemical isolation, and recombinant biochemical technology can all be used to create artificial blood. In two important groups of substitutes, haemoglobin solutions and perfluorocarbon (PFC) emulsions, significant progress has been made.

Composition of artificial blood

Perfluoro-octyl bromide	28 per cent
FO	12
Yolk lecithin	2.4
DSPE-50 H	0.12
Distilled water	57.48

Perfluorocarbons

A polymerization process occurs in PFC products. "Oxygen Therapeutics" were created by scientists and survived in animals. PFBOCs used organic compounds with high gas solubility to supply oxygen. They are biologically inert compounds capable of dissolving 50 times the amount of oxygen found in blood plasma. Fluorine-substituted hydrocarbons make up these chemically inert molecules. Because perfluorocarbons are not miscible with water, they must be processed into emulsions before being utilised as blood replacements. Oxygen is coupled to haemoglobin in cell free haemoglobin solutions in the same way it is bound to the native molecule[2]. Oxygen, on the other hand, rapidly dissolves in the chemically inert perfluorocarbon liquid and is readily absorbed by oxygen-depleted tissues. The same manner that oxygen binds to native haemoglobin, it binds to cell-free haemoglobin as well. In contrast, oxygen quickly dissolves in perfluorocarbon liquids but does not bind to them. Perfluorocarbons' oxygen loading capacity is proportional to the partial pressure of oxygen in equilibrium with the perfluorocarbon. Hemoglobin binds more oxygen than the perfluorocarbon can dissolve at a given partial pressure of oxygen. Fluosol DA was the first commercially marketed PFC. Pluronic F-68 was utilised as an emulsifying agent in this study, and it was able to achieve a balance between oxygen carrying capacity and tissue retention. Perfluorodecalin (PFD) and perfluorotrypropylamine (PFTA) are the two PFCs that make it up (FTPA). The half-lives of the two components differed, with PFD having a half-life of only 3 to 6 hours due to its fast clearance. PFCs that are linear, such as PFOB, dissolve oxygen better than cyclic PFCs, such as PFD. The quantity of fluorine atoms is directly related to the oxygen solubility, which is inversely proportional to the molecular weight.

Advantages and disadvantages of PFC

Advantages

1. Does not react with oxygen
2. Allows easy transport of oxygen in body
3. Increase solubility of oxygen in plasma
4. Minimise the effects of factors like pH and temperature in body

Disadvantages

1. Causes flu- like symptoms
2. Unable to remain mixed as aqueous solution
3. Takes approximately 18-24 months
4. A decrease in blood platelet count

Heamoglobine Based Oxygen Carriers (HBOCs)

HBOCs are an intriguing class of blood replacements that are currently undergoing clinical studies. These chemicals' therapeutic purpose is to avoid or decrease blood transfusion in various surgical and medical scenarios involving acute Hb insufficiency.

Curves of oxygen-hemoglobin dissociation. The amount of oxygen released or bound by native haemoglobin changes dramatically when the oxygen partial pressure changes. The oxygen-hemoglobin dissociation curve shifts to the right in situations of decreased pH, increased temperature, or an increase in the concentration of 2,3-DPG, allowing oxygen to be released to tissues at higher than typical oxygen partial pressures. The oxygen-hemoglobin dissociation curve shifts to the left with an increase in pH, temperature, or 2,3-DPG concentration, resulting in enhanced haemoglobin affinity for oxygen[3].

Hemoglobin Synthesis

The bacteria employed is E. coli, which has the potential to manufacture human haemoglobin. The protein is collected and the bacteria are killed over the course of three days. When pure bacteria are introduced in a test tube containing nutrients and growth regulators, the fermentation process begins. They are put into a huge seed tank containing nutrients, water, and an ammonia supply for large populations. It is put to a fermentation tank after a particular amount of growth. Growth media is also added to the fermentation tank. When bacteria create enough haemoglobin, it is separated using a centrifugal separator and then purified by frictional distillation. The artificial blood is made by mixing the haemoglobin with water and electrolytes.

Raw haemoglobin isn't safe to utilise since it breaks down into smaller, harmful substances in the body. The goal of hemoglobin-based artificial blood is to change the haemoglobin molecule to solve these issues[4].

1. **Recombinent Hb:** E.coli and human genes have been integrated. The two-chains of di-Hb are fused in a similar O2-dis. curve to RBC's Major Obstacles. Producing a high-yield product – Assembly – Purification cost currently generated without a NO receptor location.
2. **Polymerised Hb:** Polyheme-polymerizes Hb with Gluteraldehyde by connecting the amino groups on the surface of the molecule. Hemopure is similar to Polyheme, but it uses bovine haemoglobin.
3. **Intramolecular cross-linked Hb:** Diaspirin (3,5-dibromosalicyl fumarate; DBBF) was used to cross-link the -units and -units of Hb, resulting in diaspirin cross-linked Hb (DCL Hb).
4. **Conjugated Hb:** Hb conjugates and bigger molecules such as Dextran and Polyethylene Glycol (PEG). Conjugation increases molecule size, which results in a longer circulation time and a lower likelihood of

antibody formation. Bovine Hb is used to make PEG products.

Advantages and disadvantages of HBOCs

Advantages

1. Available in large quantities
2. Can be stored for large durations
3. It can be administered rapidly

Disadvantages

1. Reduce circulation half-life
2. Disruption in GI tract
3. Release free radicals in blood

Uses of Artificial Blood

1. The Use of Hemoglobin-Based Oxygen Carriers in Cancer Treatment
2. Because this substance can be preserved much more simply than blood, vast quantities could be transported by ambulances and the military with ease.
3. When natural human blood supplies run low, plastic blood cells could be utilised as a substitute.
4. Greater than a 25 per cent improvement in reperfusion recovery when compared to blood
5. Eliminates viral propagation completely
6. Transfusion-related mortality will be reduced by 76 per cent.

Future

A safe and effective artificial blood substitute is being developed by a number of firms. Transgenic pigs are being used to make transgenic Hb. RBCs of specific groups could be produced using stem cell culture techniques. New materials to carry oxygen in the body are expected to be discovered in the future. Longer-lasting goods, as well as products that perform blood's other tasks, should be created. As biotechnology advances, more blood substitutes will become available, with the potential to permanently replace natural blood. Artificial blood powder bears this kind of potential as a substitute.

Conclusion

Any transfusion service's ultimate goal is to develop a transfusion system that is free of side effects and provides more effective medical care. While the existing homologous blood system has a number of flaws, such as all sensitization and transfusion-transmittable diseases, it performs well in terms of cost, efficacy, and side effects. As a result, present artificial blood technologies will only be useful for short-term blood replacement. New materials to carry oxygen in the body are expected to be discovered in the future. Longer-lasting goods, as well as products that perform blood's other tasks, should be created.

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