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Review Article

A Review on Artificial Blood

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ABSTRACT

Artificial blood is a productive concept of transfusion medicine where explicitly defined compounds play the role of transport and delivery of oxygen in the body to supplement this function of allogenic human blood transfusion. Several molecules are formed over a long period of time to accomplish this goal and continuous refinements are consistently made in the mission of the ideal blood substitute. Currently, accessible innovation makes counterfeit blood from hemoglobin acquired from outdated human/bovine blood (Hemoglobin Based Oxygen Carriers; HBOC) or using Perfluorocarbons (PFC). These manufactured/synthetic blood substitutes are beneficial that they don't need similar testing, are free from blood borne diseases, have prolonged span of shelf life and do not need refrigeration. Artificial blood is projected to altogether affect the improvement of clinical consideration in the future times. It can supplement the current blood products for transfusion and make a steady inventory of protected and powerful substitutes. It is probably going to decrease the prerequisites of blood transfusions particularly during injury and medical procedure, also reducing the dependence on banked donated blood.

Keywords: Artificial blood; Hemoglobin; Oxygen carrier; Transfusion; PFC; HBOC

INTRODUCTION

The perpetual increase in knowledge and the expanding scope over newer generation's products, substitutes and materials ace the fields of research; whilst many components hand in areas, one of them is artificial blood. One amongst the human creations is saline solutions that help to expand volume of blood, which could help maintain blood pressure and aid RBC to continue regenerating. A life-sustaining measure (artificial blood) is playing a crucial role in severe blood loss. With the exceptional expansion in the number of surgeries (both elective and emergency) and injury/trauma, the demand for human blood for transfusion has seen a mind-boggling rise. The quantity of units gathered from blood donors is lacking to adapt with the expanding necessities of human blood which current medication and surgeries demands. Moreover, donated human blood is loaded with concerns identified with short storage life, probability of transmission of blood borne contamination, unfavorably susceptible responses and expanding expenses of collection, preparing and cross-matching. To moderate this steadily extending dissimilarity between the interest and supply of blood and the challenges related with human blood, artificial blood has risen as a promising choice. Artificial blood serves to give a substitute of ordinary blood transfusion where blood or blood substitutes got from one individual is implanted into another. The term artificial blood is regularly utilized conversely with blood substitutes or surrogates and all of them are really misnomers as artificial blood does not have various fundamental credits of human blood like hemostatic cycles, grouping and immunologic defence of the body, in any case it serves to do the significant function of delivering oxygen and carbon dioxide all through the body. In this manner, the appropriate terms for these substances can be Red Blood Cell (RBC) substitutes or Artificial Oxygen Carriers (AOC) [1].

Blood is an important, life-supporting fluid that gets oxygen in the lungs and carries it to the heart and rest of the body. Blood performs many activities like transferring supplements from digestive system, eliminating poisons and waste, and battling germs. Blood is made out of a watery substance considered plasma just as three distinct sorts of cells or portions of cells that float in the plasma. The formed elements are platelets, White Blood Cells (WBCs) and Red Blood Cells (RBCs). White blood cells are important for the body's immune system that

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annihilates infections and microorganisms, the microbes that cause diseases. Platelets form clots/clumps to keep draining from cuts and injuries. RBCs represent over 90% of the formed elements in the blood. These bountiful cells transport oxygen and carbon dioxide through arteries and veins. RBCs are disc shaped formed with a huge surface region for absorption and delivering oxygen. These cells don't have a core in the middle, however rather contain a molecule i.e. Hemoglobin (Hb) that collects and deliveries oxygen. Artificial blood has universal blood group O negative, they can be given to patients of any blood group. Patients directed artificial blood won't encounter immunologic responses, yet they would confront genuine medical issues on the off chance that they get donated blood. At the point when blood substitutes are produced they can be disinfected to obliterate microscopic organisms and infections. This wipes out the danger for irresistible infections in a blood transfusion – a significant issue in many places of sub-Saharan Africa. With a more drawn out time span of usability than human blood, some blood substitutes can be put away for one to three years without refrigeration. Artificial blood can be securely retired external medical clinics and afterward quickly managed to patients in crisis circumstances. Additionally, patients whose strict convictions keep them from tolerating blood from donors would profit from blood substitutes, for example, PFCs that are not obtained from blood items.

Origin of blood substitutes

Focused innovative work in this field got a stimulus during the 1980's after the apprehensions brought about by the chance of HIV infected blood. Relationship of other irresistible sicknesses like Hepatitis B, Hepatitis C, West Nile infection encephalitis, COVID, human T cell leukemia infection and bacterial contaminations with blood transfusions turned out to be progressively perceived. Allogenic blood transfusions likewise brought about specific non-infectious complications like haemolytic transfusion response, transfusion related intense lung injury, host rejection versus graft, hypersensitivity and post transfusion purpura. The measure of donated blood was progressively being not able to adapt up with the expanding request and subsequently an insufficiency is projected in the years to come. The increasing use of collecting, storing and preparing blood and items is additionally rising progressively [2]. Total impacts of these elements gave a significant lift to the improvement of artificial blood in the couple of years. The principle reason for these substances is to offer transient help to the circulatory system till the bone marrow has recovered adequate RBC's. They focus on one of the significant capacity of blood which is oxygen transportation to the cells and tissues. Artificial blood is a hypothetical substitute blood that can do the most indispensable activities of blood, which is the vehicle of oxygen and carbon dioxide. Artificial blood could be a day to day existence supporting measure, particularly in the midst of serious blood loss during disasters; in any case, the products being developed currently can't complete auxiliary elements of blood like battling infections. The main indications where artificial blood is used clinically; cardiovascular surgery, elective surgery, trauma, perfusion of ischemic tissue, preservation of organs, drug carriers, oxygenation of solid tumors.

Desirable qualities of artificial blood,

- Absence of adverse effects and pathogens
- In addition to transportation, it can effectively deliver oxygen to tissues.
- At room temperature has long shelf life.
- No pre-requisite of cross matching, blood grouping and compatibility tests.
- Survival in circulation for considerable time.

COMPOSITION OF ARTIFICIAL BLOOD

Perfluorocarbons (PFCs)

These are synthetic artificial blood products which are derived from fluorine-and carbon-containing synthetic compounds. They are artificially inactive, however more viable than water or blood plasma in dissolving and retaining oxygen in the lungs and transporting oxygen throughout the body. PFCs remain in the circulatory system for around 48 hours. In light of their oxygen-dissolving capacity, PFCs were the principal artificial blood products considered by researchers. They are the original blood substitutes. Unlike, red colored HBOCs, PFCs are typically white. In any case, since they don't blend in with blood they should be emulsified before giving to patients. PFCs are such acceptable oxygen transporters that scientists are currently attempting to discover it they can lessen enlarged cerebrum tissue in serious brain injury. PFC particles may cause influenza like side effects in certain patients when they breathe out these mixtures. These particles are equipped for dissolving many gases including oxygen. PFCs can convey more oxygen than red platelets do. PFCs are hydrophobic (water-repellent), so they are first emulsified in other substance before intravenous infusion. The emulsified drops segregate inside the vein, and the PFC circulates in blood by releasing oxygen. The PFC ultimately delivered through the lungs as the individual exhales, similar to carbon dioxide is processed out of the lungs, and the liver and kidney eliminate the emulsifiers. Examples of PFC blood substitutes include: oxygent, perftoran, fluosol-DA-20, PHER-O2, oxycyte.

Limitations of PFC: Original PFCs were liable for supplement activation. Particularly those which were lecithin based demonstrated cytotoxicity of phagocytic cells like granulocytes and monocytes. PFC is known to make influenza like manifestations which happens due opsonisation and phagocytosis of PFC emulsion by the individual's immune system capacity. Openings to high oxygen focus during PFC implantation can lead to oxygen toxicity. PFC is additionally involved in transient decrease in platelet counts which starts 3-4 days after administration and standardizes by 7 to 10 days [3]. Additionally, PFC products can't be utilized by the human body and should be eliminated; this cycle requires nearly 18-24 months. They can over-burden the reticulo-endothelial system and reduce its capacity.

Hemoglobin-based oxygen carriers (HBOCs)

HBOCs are made from sterilized hemoglobin and look fairly like real blood. These dim red or burgundy shaded blood substitutes are regularly produced using RBCs of expired human blood, cow blood, hemoglobin-delivering genetically adjusted microbes, or human placentas. The components of artificial hemoglobin are adjusted to make a strong framework to work without the protective cover of RBCs. Through a compound interaction called polymerization, at least two three atoms bonded together to shape a large HBOC particle. HBOCs are more modest than regular RBCs. While normal RBCs remain active in the circulatory system for around 100 days, HBOCs circulate in human blood for just a day. Results of HBOCs might incorporate raised circulatory strain, abdominal distress, and a transient reddish tinge of the eyes or skin. Hemoglobin, which is found in the blood, is the regular oxygen transporter, and substitute blood products made with hemoglobin are a significant space of exploration. Hemoglobin without the cell membrane (stroma-free hemoglobin), breaks down rapidly and can cause coagulating issues, hypertension and kidney damage. Analysts developing this type of experimental blood substitute should purify and change the hemoglobin to make it steadier [4]. Examples include hemopure, engineered hemoglobin, polyheme, MPO4X, hemotech. Techniques used to stabilize hemoglobin include; recombinant hemoglobin, polymerized hemoglobin, hemoglobin wrapped in fatty capsule, hemoglobin cross-link with enzymes, conjugated hemoglobin, etc.

HBOCs are prepared to fulfil following activities: 1) In order to increase tissue unloading, inherent decrease in oxygen capacity, 2) Decrease in colloidal osmotic activity, 3) prolong intravascular retention, 4) source in absence of renal toxicity.

Limitations of HBOC: HBOC's circulation half-life is limited than normal RBCs. Larger part of HBOC stay available for use for around 20-30 hours while entire blood transfusion lasts 34 days. They discharge free revolutionaries inside the body from free hemoglobin and the breakdown product like haem and iron. Methemoglobin concentrations likewise increase because of the oxidative properties of HBOC's. The best option for getting hemoglobin is obsolete human blood which has a restricted stock. Subsequently bovine blood must be used for acquisition of hemoglobin [5,6].

Figure 1: Artificial red blood cells.

Manufacturing process for synthetic hemoglobin based product

To derive hemoglobin, a strain of E. coli microscopic organisms that can deliver human hemoglobin is utilized. In the period of three days, the protein is collected and the microorganisms are destroyed. To initiate fermentation system, sample of pure microorganisms (bacteria) culture is moved to a test tube that contains required nutrient supplement. This underlying immunization makes the microscopic organisms duplicate. After gaining necessary amount of bacteria, they are moved to a seed tank. A seed tank is a huge tempered steel kettle that gives an optimal climate to developing microscopic organisms. It is loaded up with warm water, food, and ammonia source which are completely needed for the developing hemoglobin. Other development factors like nutrients, amino acids, and minor supplements are likewise added. The bacterial arrangement inside the seed tank is continually washed with compressed air and blended to keep it moving. At the point when enough time has elapsed, the substance of the seed tank is transferred to fermentation tank. The fermentation tank is a larger version of seed tank. It is additionally loaded up with a growth media required for the microorganisms to develop and deliver hemoglobin. Since pH control is fundamental for ideal development, ammonia water is added to the tank as vital. At the point when enough hemoglobin has been delivered, the tank is exhausted so that isolation can start with a diffusive separator that segregates a significant part of the hemoglobin. It tends to be additionally isolated and filtered utilizing fractional distillation. This standard column separation met hod depends on the guideline of boiling liquid to isolate at least required components and utilize vertical constructions called fractionating columns. From this column, the hemoglobin is moved to a final processing tank. Later it is mixed with water and other electrolytes in order to produce the artificial blood, followed by pasteurization and put into an appropriate packaging. The quality of compounds is checked at each step of the process (importantly, checking bacterial culture). Various physical and chemical properties of the final product are checked such as melting point, pH, moisture content, etc. This method of production has a capacity to produce batches as large as 2,640 gal (10,000 L) [7].

CONCLUSION

Artificial blood is inevitable and referred in many serious incidences of trauma. The approved form of life saving product has many uses and applications. The main components of artificial blood are PFC and HBOC which also take-part in adverse effects in human body such as lung damage, increased incidence of stroke, abdominal pain, oliguria, jaundice, skin rash, hemoglobinuria respectively. The components in artificial blood are extracted from universal blood group (O negative), which is explicit, plausible and exemplary. Many researches are in process for developments and further details of the artificial blood. The flushing sequence in serious trauma and lack or unavailability of blood which may lead to death and hazardous state of humans which lead them to risk, wherein artificial blood takes a tremendous role as a lifesaving agent. The mere

applications of artificial blood, its components and their drawbacks are well addressed to the range of use and further reliance.

REFERENCE

1. Haldar R, Gupta D, Chitranshi S, Singh MK, Sachan S. Artificial Blood: A Futuristic Dimension of Modern Day Transfusion Sciences. Cardiovasc Hematol Agents Med Chem. 2019;17(1):11-16.
2. Henkel-Honke T, Oleck M. Artificial oxygen carriers: A current review. AANA J. 2007;75(3):205–211.
3. Scott M.G, Kucik DF, Goodnough LT, Monk TG. Blood substitutes: Evolution and future applications.Clin Chem. 1997;43(9):1724–1731.
4. Pape A, Habler O. Alternatives to allogeneic blood transfusions. Best Pract Res Clin Anaesthesiol. 2007;21(2):221-239
5. Jahr JS, Nesargi SB, Lewis K, Johnson C. Blood substitutes and oxygen therapeutics: an overview and current status. Am J Ther. 2002;9(5): 437-443.
6. Shander A, Alalawi R, Seeber P, Lui J. Use of a hemoglobin-based oxygen carrier in the treatment of severe anemia. Obstet Gynecol. 2004;103(5 Pt 2):1096-1099.
7. Sarkar S. Artificial blood. Indian J Crit Care Med. 2008;12(3): 140-144.