

## Blood Substitutes and the Need for Increased Attention Due to its Future Implications

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### Opinion

Blood is the connective tissue that runs throughout one's body, carrying chemical messages, oxygen, and defending the individual from disease; without it, not even the most basic bodily functions could be carried out. It carries many different hormones, secreted directly into the blood flow to the target cells, such as glucagon from the pancreas to the liver so that it will breakdown glucose.

Blood transfusions are necessary after traumatic accidents, and to treat certain chronic illnesses, when blood has been lost, or is insufficient. After incidents such as shootings, motor accidents, and deep wounds, a large amount of blood is lost. This impedes the ability of oxygen to be transported throughout the body and can lead to brain injury, tissue damage, or death.

In today's world blood is supplied by donors, and transported via an organized effort by blood centers and hospitals to insure the timely fulfillment of patients' hematological needs. Unfortunately the only way to obtain blood is through the goodwill of individuals, so the blood supply can be a fickle one. During the winter of 2010 – 2011, Scotland and surroundings areas had a brutal winter. The Scottish National Blood Transfusion Service admitted that it only barely was able to meet demand and deliver to areas that were extremely difficult to access (Morgan). The first blood bank was created during World War II in order to meet the huge demand for blood for injured troops (Werlin), yet even this very organized effort could not reach everyone in need. As a result of these numerous issues, many years of meticulous research have been conducted, but a reliable man-made substitute has yet to be developed. Such an invention would save millions of lives and have sales of over 7.6 billion dollars (Sarkar). Currently the use of artificial blood and blood substitutes can under some circumstances be justified, yet there is only one brand that is used even allowed to be used on humans, and research focusing on improving these products will lead to more common and wide-spread application in the future.

Blood substitutes are solutions that mimic blood in function and often times structure, but are not made from donated human blood components, which can address man issues with current transfusions and the medical system as a whole.

Physicians saw a need for such a substitute hundreds of years ago, yet one has not been approved by the FDA for human use. Among the materials tested early on were beer, urine, plant resins, sheep blood, and milk. Out of these, milk was the only one that was put into use. Patients were injected with milk in 1854 in order to treat Asiatic cholera; it was thought to stimulate the production of white blood cells. However, it was regarded with skepticism by many physicians and was soon thrown out as a viable substitute. A chemical met with

the greatest success during this time period was saline solution. Later it was put into use as a plasma expander, which improved blood flow and oxygenation of red blood cells. Arguably the most successful chemical found was Ringer's solution. Ringer's solution is a kind of saline solution that contains specific salts in the concentrations found in the body that are shown to keep the heart beating properly without the proper volume of blood, or even outside of the body (Thakkar). Since it does not replace the role of red blood cells carrying oxygen, it cannot be considered a true substitute for blood.

Antigens are the same protein that white blood cells use to find pathogens, bind to them, and destroy them. When blood is transfused into a patient with a different blood type, the immune system reacts harshly and swiftly due to the antigens on the transfused cells not matching those of the body's red blood cells. White blood cells produce antibodies that bind to the antigens and kill the cell, or cause them to bunch together, often forming a blood clot. The recipient becomes violently ill and can easily die. This discovery and fear of adverse reactions led to blood typing, which matched a recipient to a compatible donor, and made blood transfusions innumerable times safer. Interests in finding a substitute for blood still existed, and spiked during wars, and after HIV and hepatitis gained notoriety for being spread through blood transfusions (Sakar).

Although the blood bank system is well developed and serves many people, the properties of blood are what cause the greatest difficulties in treatment and management. Blood transfusions are well known for their use in emergency situations by hospitals. When patients are in critical condition and have lost a considerable amount of blood, one of the first actions taken is transfusing blood to the patient. However, in such situations, there is not time to test for the patient's blood type. The only choice is to transfuse O-negative blood, which can be transfused to anyone due to its lack of antigens (receptor proteins) on the cell membrane, which prevent the recipient's immune system from attacking and destroying the transfused blood. It is also the case that O-negative blood is the rarest blood type, so this type is constantly in desperate short supply. Without the proper amount of certain blood types on-hand, dangerous blood shortages could occur, and the lives of the chronically ill who need regular blood transfusions and those in emergency situations could have their lives put at significant risk. On the other hand, it is also bad for there to be an overabundance of blood. Red blood cells are kept refrigerated and only last about a month in this manner. Another issue with storage is that as time goes on, the oxygen-carrying ability of the red blood cells greatly diminishes. Experimental blood substitutes, however, have been shown to last up to two years at room temperature. Another issue with blood transfusions is that certain religious groups do not allow their adherents to receive transfusions, even when their lives are in danger. The most notable group is the Jehovah's Witnesses, who are notorious

for their outspoken opposition to blood transfusions. It is believed by many that the implementation of blood substitutes would appease these groups.

As simple and already well-implemented the technique described to mass-produce hemoglobin is, it is not actually what the main biotechnology companies use to manufacture their products. According to Bruce Leibensperger of HBO2 Therapeutics, the company that makes the two most used blood substitutes in the world, Oxyglobin and Hemopure, the corporation instead uses bovine blood to make their products. They slaughter the cow and drain it of its blood. They then isolate the hemoglobin, sterilize it, and package it in a sort of membrane so that it can be transferred around the body without it dissociating.

Hemoglobin is naturally located in red blood cells, which protect the molecule from disruptive forces. Outside of the cell, hemoglobin dissociates, or breaks apart, and becomes ineffective. It actually becomes harmful to the body. Dissociated hemoglobin can cause serious pulmonary and cardiac issues, and kidney failure. For this reason, hemoglobin must be encapsulated, similar to how it naturally is in the body. The search now is to find an encapsulation method that does not hinder the work of hemoglobin, and also does not get attacked by antibodies from the recipient, as happens in blood transfusions from incompatible types.

The use of blood substitutes is currently minimal, but due to ongoing research, a successful product will be developed and be put into use. Universities such as Rice University, University of Pittsburgh, and Texas Tech work independently, with grants, and with corporations in the continued search for the ideal blood substitute. As the need for a blood substitute grows, so will interest in developing one.

Hemopure is the most eminent and advanced blood substitute on the market right now. Its purpose is to create an “oxygen bridge.” This means that it does not act as a complete substitute for blood, rather it acts as a placeholder until the properly typed blood or any blood at all can be acquired to transfuse. This would drastically increase the efficiency of trauma settings, and would have positive impacts on the future.

Currently, Hemopure is being evaluated by the FDA. It has yet to get approval, but several studies including some being conducted presently provide evidence that Hemopure is indeed a safe alternative. In order for the FDA to see the full scale of the benefits Hemopure would create, physicians must vocalize support so that the FDA will be utterly convinced.