MODIFIED SURFACE HEMOGLOBIN (PEG HB, PHP, HAEMOSPAN):

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Modified surface hemoglobin is produced by attaching large molecules, such as polyethylene glycol, to the surface groups of lysine. This modification increases the viscosity and oncotic pressure of the solution [4]. These solutions can moderately constrict blood vessels. Due to the small size of the hemoglobin molecules, they can pass through small vessels and saturate areas with oxygen that are inaccessible to erythrocytes [2,5]. This makes it useful for treating patients with strokes, as well as increasing the sensitivity of tumor cells to radiation or chemotherapy. Additionally, the vasopressor effects can be used to treat hypotension after septic shock. This type of hemoglobin also has a low frequency of antibody production.

Intramolecular Cross-linked Hemoglobin: intramolecular cross-linked hemoglobin (Hema-ssist, r-Hb1-1, r-Hb 2-0) is stabilized by cross-linking two α- and two β-subunits, preventing the filtration of hemoglobin through the kidneys. This cross-linking also reduces hemoglobin's affinity for oxygen. Cross-linking agents such as 3,5-dibromosalicylic fumarate (DBBF) and nor-2-formylpyridoxal-5-phosphate (NFPLP) are commonly used.

Polymerized Hemoglobin: polymerized hemoglobin (Polyheme, Hemopure, Hemolink) is produced by linking the amino acid groups of hemoglobin using reagents like glutaraldehyde. These compounds may cause mild side effects. This product has been used several times for transfusions for compassionate use. The administration of polymerized hemoglobin to patients who underwent infrarenal aorta reconstruction showed that 27% of patients were able to avoid the transfusion of allogeneic blood [6].

Hemoglobin Encapsulated in Liposomes: purified hemoglobin is encapsulated in a stable lipid membrane. The liposomes consist of a phospholipid bilayer with added cholesterol molecules to improve rigidity and mechanical stability. Inside the liposomes is a hemoglobin solution without stroma, along with 2,3-diphosphoglycerate or inositol hexaphosphate. For additional stabilization, ultraviolet radiation or redox potential inhibitors are used, which induces the polymerization of unsaturated phospholipids. Stabilization can also be achieved by coating the liposomes with polymers. Encapsulated hemoglobin (or hemosomes) allows for changes in their physicochemical properties and circulation time. With these modifications, the affinity for oxygen can be regulated, improving oxygen unloading. Encapsulation prevents hemoglobin denaturation and enhances its biodistribution. Further modification with polyethylene glycol increases the half-life, makes the hemoglobin water-soluble, reduces antigenicity, and improves targeted delivery. Liposomes, consisting of purified hemoglobin or lipids, are compatible with the immune system. Nanocapsules of hemoglobin made from biodegradable polymers like polylactide, which is converted into water and carbon dioxide in the body and does not accumulate in the reticuloendothelial system, have also been developed.

Types of Hemoglobin Modifications and Their Features: hemoglobin modification improves its properties and makes it more effective in various medical applications. The most common types of modifications include:

Polyethylene Glycol (PEG) Hemoglobin: adding polyethylene glycol to the surface of hemoglobin helps increase its stability, circulation time in the body, and reduce the immune response. This is particularly important for blood substitute therapy, as PEG-hemoglobin can remain in the body longer, reducing the need for frequent transfusions.

Polymerized Hemoglobin: the polymerization process creates larger hemoglobin molecules, preventing them from being rapidly filtered by the kidneys. This modification helps reduce the chance of hemoglobin accumulation in the reticuloendothelial system and also reduces its aggregation, which can prevent possible complications during its use.

Liposome Encapsulation: this method involves encapsulating hemoglobin in lipid membranes, which protects hemoglobin molecules from oxidation and denaturation, improves their bioavailability, and reduces the immune response. Liposomes can be used to deliver hemoglobin to specific areas of the body, which is particularly useful in treating diseases related to circulatory disorders and oxygen deprivation in tissues.

Advantages and Potential Risks of Using Modified Hemoglobin: modified hemoglobin offers several advantages:

Improved Oxygen Delivery: due to enhanced oxygen-binding properties, modified hemoglobin can deliver and release oxygen more effectively in tissues with deficiencies. This is especially beneficial in acute conditions like shock, stroke, and heart failure.

Longevity in the Blood: Thanks to changes in its physicochemical properties, modified hemoglobin has a longer half-life in the bloodstream, reducing the need for multiple transfusions and improving treatment efficiency.

Reduced Immune Reactions: Many types of modifications, such as PEG-hemoglobin, significantly reduce the likelihood of immune reactions, such as antibody formation, which is important for repeated use.

However, despite these advantages, there are potential risks:

Toxicity and Side Effects: although modifying hemoglobin improves its properties, it may also lead to unpredictable side effects, such as increased blood viscosity, which may lead to clot formation or worsened microcirculation.

Need for Further Research: Despite promising results, the effectiveness and safety of various types of modified hemoglobin have not been fully explored, and further clinical trials are necessary to confirm their long-term safety and efficacy.

Applications of Modified Hemoglobin in Medicine: modified hemoglobin has many applications in medicine, particularly in cases where traditional blood transfusions are not possible or desirable:

Blood Substitute Therapy: Modified forms of hemoglobin can be used as blood substitutes in situations of blood shortage, especially in emergencies such as trauma or surgeries that require large blood volumes.

Treatment of Anemia and Hypoxia: Modified hemoglobin can be used to treat conditions related to oxygen deficiency in the body, such as anemia, chronic obstructive pulmonary disease (COPD), or hypoxia due to heart and vascular diseases.

Patients seeking medical help initially have symptoms of anemia, thrombocytopenia, and other changes in blood composition. Moderate cytopenia develops at the stage of decompensation of liver cirrhosis of viral etiology. The proportion of viral etiology of liver cirrhosis (in the outcome of chronic hepatitis B, C, and B+D) ranges from 10 to 23.5% of all cirrhosis [2]. Diagnosis of the disease is difficult, it is recommended to exclude other causes of the disease [3]. This became especially difficult after the COVID-19 pandemic, as chronic diseases began to progress and the death rate increased dramatically [1].

Burns and Sepsis: Modified hemoglobin use may help improve tissue perfusion and oxygen supply in cases of severe burns or sepsis, where traditional treatment methods may be less effective.

Thus, hemoglobin modification is a powerful tool in medicine, opening new possibilities for treating diseases related to oxygen deprivation and potentially serving as a foundation for developing new therapeutic agents in the future.

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