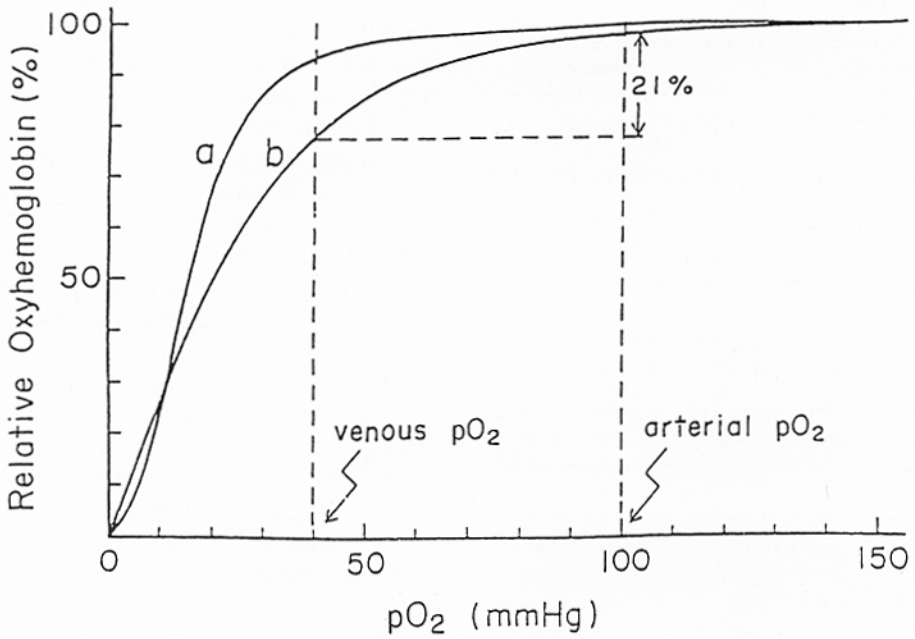

Fig. 6 Oxygen equilibrium curve of human erythrocyte (a) and stabilized hemoglobin (b).

Table 3 Characteristics of Stabilized Hemoglobin Solution

Hb concentration	6.3%
Methemoglobin (MetHb)	3.5%
P_{50} (37 °C)	24.2 mmHg
Colloidal osmotic pressure	38.0 mmHg
Viscosity (37 °C)	2.7 cp
Pyrogenicity	Pass test
Sterility	Pass test

the experimental animals. Follow-up studies for one year after injection did not reveal any abnormal physiology. Recently, this product is in Phase III clinical studies and it was demonstrated that less than 100 ml infusion of this solution was clinically effective.

Proper Hemoglobin Concentration in SHb

As indicated in Table 3, the highest concentration of SHb in the solution was in the range of 6% in order to maintain its colloid osmotic pressure within the physiological ranges. Unfortunately, a well-accepted guideline for the indication of blood transfusion is a hemoglobin level of patients below 7 g/dl. Thus, in the past, many well respected hematologists warned this author's group that the SHb containing only 6 g/dl hemoglobin would not demonstrate any clinical benefits as a blood substitute. This author has been stressing the differences between the oxygen carrier in plasma and the oxygen carrier in red cells, and has justified the different requirements of the amount of oxygen carrying hemoglobin. Unfortunately, it was very difficult to convince others of the clinical benefits of such a product having a low hemoglobin level. Actually, a well-qualified FDA consultant strongly recommended increasing the hemoglobin concentration in SHb from 6% to 8%. At least 5 years were wasted on FDA application processing due to this misconception. As described above, it was recently proven that there is no essential hemoglobin level for the oxygen-carrying macromolecule solution. However, it is essential that this solution should be composed physiologically as close as possible to the patient's plasma.

Conclusion

The oxygen-carrying macromolecules are clinically more effective and safer with a small infusion volume that those of the unprocessed red cells. It is expected that the oxygen-carrying macromolecules are not a substitute for blood transfusion, but are a therapeutic agent for any hypoxic conditions of the patient, organs and tissues.

References

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