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A Blood Substitute from Hydroxyethyl Starch and Hemoglobin

L. C. CERNY,* E. L. CERNY, J. ROBACH, M. REATH, AND L. PONTERO

The Masonic Medical Research Laboratory and Utica College of Syracuse University, Utica, NY

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ABSTRACT

One method to increase the retention time of hemoglobin (Hgb) is to react it with a hydroxyethyl starch (HES) molecule. To examine this hypothesis, polymer-bound hemoglobin compounds were synthesized by the dialdehyde route. The electrophoretic mobility patterns indicate complete binding of the Hgb. Preliminary exchange-transfusion experiments in rates showed that they could survive for at least 10 h at Hct < 10% when transfused with 6% HES-Hgb solutions. The retention time of the Hgb in the urine was increased to 12 h with these new polymers.

Index Entries: Starch, and hemoglobin as a blood substitute; blood substitute, starch and hemoglobin as a; hemoglobin, and starch as a blood substitute.

INTRODUCTION

It is possible to synthesize a suitable blood substitute from hydroxyethyl starch (HES) and hemoglobin (Hgb). The HES provides the needed oncotic and rheological properties, whereas the Hgb can transport the needed oxygen. In this paper, characterized HES-Hgb polymers are presented along with their biophysical properties in exchange-transfusion experiments. It appears that the HES-Hgb compounds could serve as useful blood substitutes.

*Author to whom all correspondence and reprint requests should be addressed.

METHODS

The HES-Hgb polymer was synthesized by the dialdehyde method. Essentially this involves reacting an HES polymer with $NaIO_4$ to give the corresponding dialdehyde starch. Subsequent reaction with Hgb yields an HES-Hgb polymer. The number-average molecular weights of the starting HES polymers were 199,000, 141,000, and 6600. The electrophoretic mobility patterns showed complete Hgb binding. The optical density–distance graphs from the densitometer indicate a separate and sharp peak with no residual intramolecular interactions. The oxidation step is efficient and quantitative; however, there may be some chain degradation, as shown by the decrease in intrinsic viscosities. The new polymers appear to be small and tightly bound molecules, almost globular in nature. Also the Hgb content in a 6% polymer solution is significantly higher than by other methods (*1*).

RESULTS

Exchange-transfusion experiments were performed in rats. In this series, the concentration of the polymers was adjusted to have a hemoglobin content of 6%. The preliminary data indicate that in replacements between 50 to 75%, the retention times of the dialdehyde polymers were increased. In most cases, Hgb did not appear in the urine before 18 h. In a typical experiment where the Hct was reduced to 11%, the total Hgb level was 9 g/100 mL. The oxygen saturation curves were determined by biotonometry and showed a continuous shift to the left at lower Hct. However, these curves do show some cooperativity, as indicated by the sigmoidal shape, the values of Hill's n, and the affinity constant, K.

DISCUSSION

It is possible to synthesize a potential blood substitute from HES and Hgb by means of a dialdehyde intermediate. This polymer is similar in size and shape to a globular molecule. Using polymers containing 6% Hgb, it is possible to maintain rats at a 10% Hct level. From polymer considerations, this material has the correct oncotic and viscometric properties.

SUMMARY

A polymer formed with HES and Hgb has been shown to be a potential blood substitute. It can maintain life at low Hct levels and has an increased retention time when compared to Hgb solutions.

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REFERENCES

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