©Copyright 1984 by The Humana Press Inc.
All rights of any nature whatsoever reserved.
0273–2289/84/9000–0143$02.00

Preparation and Biophysical Properties of Hemolysate-Loaded Liposomes

MASAYUKI ARAKAWA, ATSUSHI KATO, AND TAMOTSU KONDO*

Faculty of Pharmaceutical Sciences and Institute of Colloid and Interface Science, Science University of Tokyo, Shinjuku, Tokyo 162, Japan

Received November, 1983; Accepted December, 1983

Index Entries: Preparation, of hemolysate-loaded liposomes; biophysical properties, of hemolysate-loaded liposomes; properties, of hemolysate-loaded liposomes, hemolysate-loaded liposomes; liposomes, hemolysate-loaded.

Recently, many reports have been published on the red cell substitutes (*1,2*). Still more recently, several attempts have been made to prepare highly biocompatible liposomes containing hemoglobin solution as a red cell substitute (*3*).

In the present work, sheep hemolysate-loaded liposomes are prepared by using a modified interfacial deposition technique with which the liposomes are strengthened by a tightly combined polysaccharide, carboxymethylchitin. The hemolysate-loaded liposomes are called artificial red blood cells (ARBC).

When the ARBC are prepared by using our technique, the percentage of hemoglobin solution encapsulated into liposomes appears to be dependent on the pH and ionic strength of the medium, the concentration of carboxymethylchitin, the volume ratio of aqueous phase to oil phase, and temperature. The percentage of encapsulation is found to decrease with increasing pH and ionic strength of the medium if the carboxymethylchitin concentration (0.2%, w/v) and the volume ratio (1:1) are constant. For example, the percentage of encapsulated hemoglobin solution into liposomes is about 45% at pH 7.5.

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

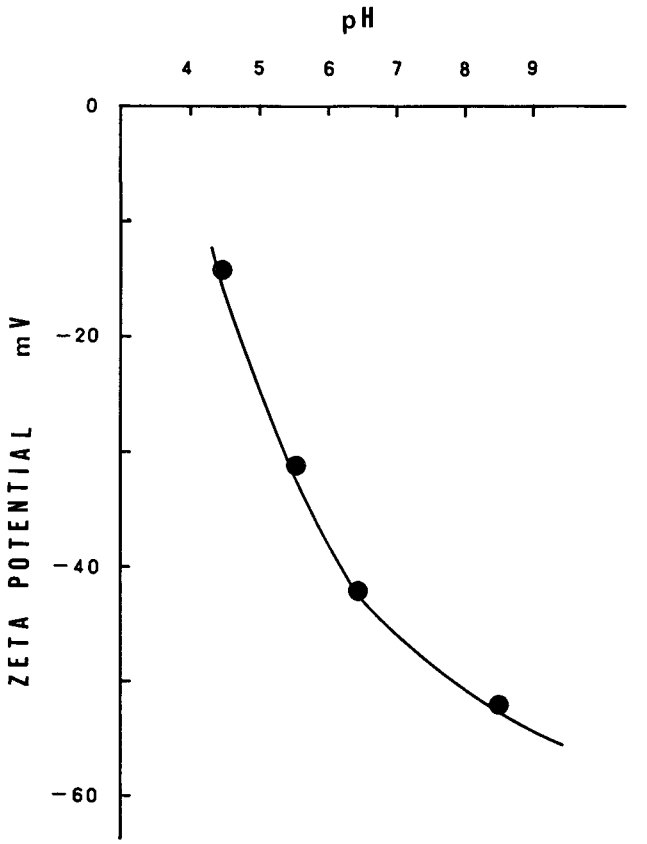

Fig. 1. Zeta-potential of the ARBC as a function of pH of the buffer solution (ionic strength, 0.01) at 25°C.

Figure 1 shows the zeta-potential of the ARBC as a function of pH of the medium (ionic strength, 10^{-2}). The zeta-potential of the ARBC is gradually increased with increasing pH of the medium. This is because of the dissociation of carboxymethyl groups from carboxymethylchitin on the ARBC surface.

Figure 2 illustrates the relationship between relative viscosity and mixing ratio for mixed suspensions in human plasma of the ARBC and human red blood cells (HRBC).

The total particle concentration in the mixed suspensions is kept at 40%. It is recognized that the effect of the ARBC on the flow properties of the mixed suspension becomes remarkable when the mixing ratio of the ARBC to HRBC exceeds 50%. This decrease of relative viscosity in the mixed suspension could be caused by a reduction in the particle–particle interaction in shear flow caused by the strong hydration forces of carboxymethylchitin.

Hence, the hemolysate-loaded liposomes can be said to come close to one of the red cell substitutes clinically usable in that they are modified with respect to their biophysical properties by carboxymethylchitin.

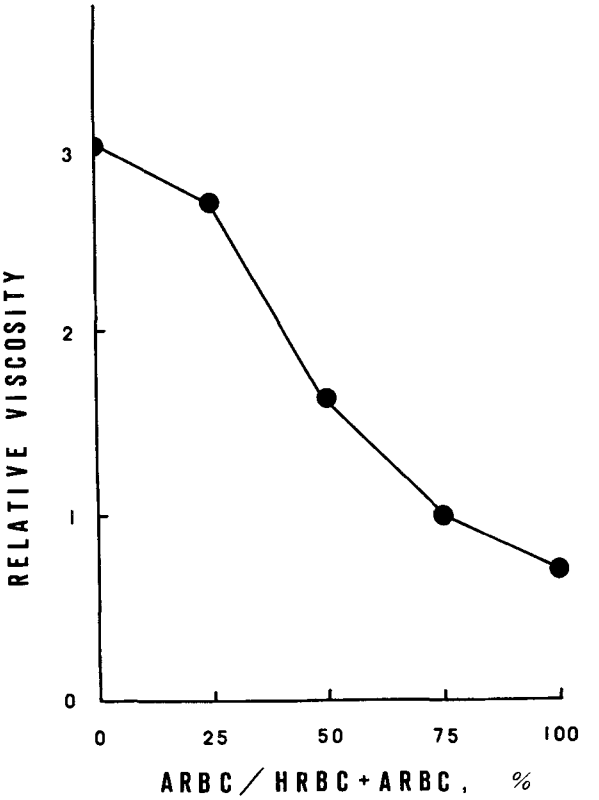

Fig. 2. The relationship between relative viscosity and mixing ratio for mixed suspensions in human plasma of the ARBC and HRBC at 37°C.

REFERENCES

1. Yokoyama, K., Yamanouchi, K., and Murashima, r. (1975), *Chem. Pharm. Bull.* **23,** 1368.
2. Arakawa, M., and Kondo, T. (1981), *J. Pharm. Sci.* **70,** 354.
3. Kato, A., Arakawa, M., and Kondo, T. (1983), *Biorheology* **20,** 593.