

ABSTRACT

Haemoglobin is a fascinating substance with a number of orders of structure. At one time it was thought that the red cell was an inert bag full of haemoglobin. But we know now that the haemoglobin in red cells has an active metabolism in oxygen transport in the body. Crystallographers, Biochemists, Physical Chemists, Physicists, Biophysicists, Physiologists, Geneticists and Scientists from many disciplines of Medicine have been actively studying the structure and function of this protein and its role in oxygen transport for more than a hundred years. Many other chemical properties of the protein have also been investigated and an enormous literature is available on the subject. Some thirty to forty papers from all over the world are currently being published every month on various aspects of haemoglobin behaviour.

Since the discovery of Sickie Cell Anaemia and of the abnormal haemoglobin, Hb S, some 210 abnormal haemoglobins have been discovered and the properties of many of them have been investigated in detail.

In the last few years, a remarkable series of studies have been performed on the metabolism of the red cell as an organ of gas transport; for example, the presence of organic phosphates in the red cell and their effects on oxygen affinity have been discovered. The abnormal haemoglobin, Hb S, is particularly interesting. Deoxygenated haemoglobin S from the blood of patients with homozygous sickle cell anaemia aggregates into fibres and

crystallises in the erythrocytes and the cells become rigid and elongated. A number of differences between the behaviour of sickle haemoglobin and that of normal haemoglobin in the red cell have been demonstrated. Much data of apparent simplicity has been accumulated for haemoglobins in solution, but the situation is much more complex in the cell, where the haemoglobin concentration is 100- or 500- fold greater; intertetramer interactions must become more important within the erythrocyte.

A comparative study, presented in this Thesis, has been made of some of the equilibrium and kinetic behaviour of normal and sickle haemoglobin both in aqueous solution and in the intact erythrocyte.

SECTION I contains a review of the pertinent literature. The experimental methods and the materials employed, and the methods of calculation used, are described in SECTION II. SECTION III contains the results, and the discussion of these results, of a number of different but related experiments which are mostly concerned with the equilibrium and kinetic behaviour of normal and sickle haemoglobin in solution and in the red cell and of some of the simple derivatives of these haemoglobins.