Preface

High blood glucose level in diabetes mellitus causes nonenzymatic glycation of several proteins of which hemoglobin is utmost important. Recently, estimation of glycated hemoglobin is being routinely used as an objective index of long-term glycemia in diabetes mellitus. However, not much is known about glycated hemoglobin with respect to its structural and functional aspects and its possible involvement in observed pathophysiological complications commonly found in diabetes mellitus. In this thesis, we have reported some of the differential structural and functional activities of glycated (HbA1c) and nonglycated (HbA0) human adult hemoglobin.

The investigation was carried out in the Department of Biophysics, Molecular Biology & Genetics, University of Calcutta, under the supervision of Dr. Abhay Sankar Chakraborti.

The thesis consists of four chapters. The first chapter covers a brief review of hemoglobin, glycated hemoglobin, oxidative stress in diabetes mellitus and trifluoperazine, phenothiazine drug, which has been used as a probe to understand the differential functional properties of HbA0 and HbA1c. The second chapter presents Aims and scope of the work. The third chapter contains Materials and Methods. Different materials used and techniques utilized for our studies have been discussed. The fourth chapter (Results and Discussion) consists of three sections. In Section-1, we have made a comparative study on 'free reactive iron' level of purified hemoglobins isolated from blood samples of different diabetic and normoglycemic individuals. This section also deals with studies on H2O2-
mediated lipid peroxidation, deoxyribose degradation with HbA₀ and HbA₁c isolated by cation exchange chromatography. This section also reports on some functional and structural aspects of HbA₁c in comparison to HbA₀. These include peroxidase activity thermal denaturation, stability of heme-globin linkage study, determination of surface accessibility of tryptophan, circular dichroic study etc. In section-2, we have studies drug-protein interaction using trifluoperazine as a probe. Significance of such interaction with regards to conformational change and oxygen affinities of HbA₀ and HbA₁c have been discussed. In Section-3, drug induced (trifluoperazine) morphological change, membrane damage and hemolysis of erythrocytes, isolate from normoglycemic and diabetic individuals have been studies. The level of plasma haptoglobin, a heme binding protein in these individuals have also been compared. Finally, summary and conclusion of this dissertation have been presented.

Part of the work in the thesis has been published and the reprints are enclosed at the end of the thesis.