The amino acid histidine, apart from being the precursor of histamine, plays an important role in maintaining the tertiary structure of enzyme proteins. From the metabolic point of view histidine has a special significance in view of the fact that the pathways of biosynthesis of histidine and purine meet at a number of important junctions revealing one of the many molecular links between proteins and nucleic acid synthesis in the overall metabolism of the living cell. Nutritional studies have shown that histidine and purine can replace each other in sustaining the growth of some bacteria. The amino acid is, however, essential for the albino rat for its growth and reproduction. It is not surprising, therefore, that the metabolism of histidine and its biosynthesis have been the subject of intensive investigations in the last few years. The discovery of the pathway of biosynthesis of histidine in bacteria has indeed paved the way for understanding the mechanism of regulation of its metabolism by feed back control and repression of the relevant enzymes.

Although impairment of histidine metabolism has been implicated in a number of pathological manifestations, very little is known about the homeostatic regulation of circulating histidine or its biosynthesis in mammals. The elucidation of the mechanism of regulation of histidine metabolism in
bacteria has revealed the role of a number of enzymes in not only degrading histidine but also in maintaining a dynamic equilibrium between its synthesis and degradation within the cell.

Some aspects of the regulation of histidine metabolism in the rat form the subject of the present thesis. The results of this study broadly indicate that the liver enzymes of the urocanate pathway are assigned by nature a special function of regulating histidine metabolism. Histidine ammonia-lyase, the first enzyme of the degradative pathway shows greater adaptability under different conditions. Induction of this enzyme was, therefore, studied in detail. Inducible formation of the enzyme in the rat was suppressed by glucose reminiscent of catabolite repression in bacteria. Attempts were also made, but with little success, to demonstrate some of the enzymes of histidine biosynthesis (reported hitherto only in bacteria) in rat tissue. Induction in vitro of histidine ammonia-lyase and histidine pyruvate aminotransferase was also explored using liver slices. The two enzymes were observed to be released by the slices into the medium on incubation in isotonic physiological saline. The experimental findings of the present study can be used as a basis to evolve a working hypothesis for conducting a more detailed investigation of the molecular mechanism of the regulation of histidine metabolism in animals.