INTRODUCTION
Life is a continuous adjustment of internal relations to external affairs.

- H. Spencer

The problem of ageing and death started when life came into existence. Ageing is a slow and gradual process from birth till natural death. The secret of health and happiness lies in successful adjustment to the ever-changing conditions on this earth. Due to modernization of life, many challenging problems are being faced by man and rhythmic life which human beings used to enjoy in the past has received a rude shock. Stress and strain of every day life pose a big threat to the peace and tranquility hitherto enjoyed by man. There is no doubt that one of the hallmarks of the twentieth century is the increase in human life span, in both industrialized and developing countries. This increase is due to several factors: for example, better clinical and pharmacological control of infectious diseases, better sanitation and improved nutrition. However, due to such a large demographic change in last 80 years, the life expectancy in industrialized countries has increased by 50%, resulting in a 20-40% increase in the number of individuals over 65 years of age. This has created substantial social stresses. Now-a-days stress, long considered alien to the Indian life style, is a major health hazard. It is fast becoming the leading contributor, directly or indirectly, to the five big adult killers in the country: heart attacks, cancer, lung ailments, accidents and suicides. Studies indicate that it is responsible for aggravating or hastening peptic ulcers, arthritis, allergies, constipation and even impotency. According to Vihang Vahia
"Stress is India's newest scourge". More than 80% of people suffer from stress-related symptoms. The "stress-epidemic" has triggered a wave of measures across the country to cope with the menace. Part of the rise in stress arises from desperate efforts to cope with the constraints of daily living. Therefore, every move is now a challenge (Fig. 1.1).

Ageing and stress are universal and inevitable scientific and social challenges confronting humanity. If ageing in man is at all different from ageing of other species, it may be because of the higher degree of organismal organization, quite probably not more evident in any tissues than in those of the central nervous system (CNS). While it is clear, that the more highly integrated an organ system becomes, the more vulnerable it will be to perturbations of any sort. Increasing attention has been directed toward the role of the brain and endocrine organs as "pacemakers" of ageing. It has been widely accepted that stress-induced activation of the limbic system, hypothalamic-pituitary-adrenal axis in mammals invariably involves biochemical and ultrastructural changes in these regions.

Central nervous system plays an important role in adaptation to environment, because all the vital activities of the body are controlled by brain. Various researchers conclude that there is a relationship between the species and life span, the perfection of CNS structure and function, and the level of 'cephalization and neocorticalization' (Hansche, 1975;
Fig. 11. CORRELATION BETWEEN SCIENTIFIC DEVELOPMENTS STRESS AND ITS EFFECT ON AGEING.
Sacher, 1975). In this view, especially interesting is a qualitative leap in the life span, which occurred in the evolution of the animal world, particularly at the stage of man's appearance with his perfect forms of environmental adaptation associated with developing functions of the CNS, higher nervous activity and metabolism. CNS is the most stable and long lived system of all organisms' systems. Neurons are postmitotic, highly specialized cells of the CNS, and incapable of division but recent research has revealed a limited regeneration potential (Gispen and Trabor, 1983; Scheff, 1984). Their life span is equal to that of the entire organism. Changes in the metabolism, structure and function of the CNS lead to significant shifts in the activity of many organs and systems with ageing.

The tremendous complexity of the ageing process becomes apparent, that is, ageing appears to, and probably every cell does affect every tissue, organ and physiological function of an organism (Ordy and Brizzee, 1975; Finch and Hayflick, 1977; Frolkis and Bezrukov, 1979; Bondareff, 1980). It is well documented that different organs of the body age at different rates. The "biological clock" of ageing is thus organ specific. The hypothalamus plays a commanding role in the regulation of homeostasis. Glees (1971) has drawn attention to the probability that the "biological clock" for ageing of the body may be located in the hypothalamus. Furthermore, the environmental factors which influence ageing process appear to act through the hypothalamus and anterior pituitary (Everitt, 1973).
Ageing is characterized by a failure to maintain homeostasis under the conditions of stress, thus leading to the decreased viability and increased vulnerability of the individual to death (Davies, 1984; Hazzard, 1987). According to Rattan (1989), ageing is a post-reproductive process and includes degenerative changes in the structure and functions of an organism, accompanied by many biochemical changes at cellular and molecular level. An evolutionary perspective is that essentially all metabolic processes result from a trade off between beneficial versus harmful side effects. Metabolic pathways in human and other organisms are far from being the most efficient possible. There always appears room for improvement. An example is the utilization of oxygen for the production of ATP which is essential for high energy efficiency. The toxic effects of oxygen are well known, and its metabolism produces not only beneficial products like ATP, but also a large number of active oxygen species, such as the superoxide radical $O_2^-$, the hydroxyl radical $'OH$, hydrogen peroxide, $H_2O_2$, hydroperoxides, ROOH, and aldehydes (Pryor, 1978; Chance et al., 1979; Leibovitz and Siegal, 1980). On the other hand, all mammalian species have a common set of repair, protective, or defence processes against the toxic effects of these active oxygen species. Such processes include the DNA repair systems and antioxidants. Antioxidants enhance the life span and increase the potentiality of trapping pernicious free radicals, hence stabilize the differentiated state of cells (Cutler, 1984; Omaye et al., 1986; Weber and Miquel, 1986). According to Rosenfeld (1985) the goal of a gerontologist is not to find the "Fountain of youth" but to permit the individual "to die young as late as possible".
1.1 Aims and Objectives of the Present Study:

Keeping the above aspects in mind, the present study was undertaken to investigate the effects of ageing, stress and the protective effect of N-acetylcystein thiolactone (citiolone) on the various regions of CNS. The brain is made up of heterogeneous cell populations (neurons, glia), which are independent. The CNS also exhibits functional and morphological heterogeneity and is divisible into different geographical regions. These discrete regions generally have different types of neuronal populations, probably related to the metabolic needs and the chemical messengers they employ for communication. This study on the male albino rats, Charles Foster Strain, of different age groups was undertaken with the following main objectives:

1. To evaluate the quantitative effect of ageing following restraint stress on the various neurochemical parameters in different regions of CNS. The following parameters were studied:

   (i) Total lipid, phospholipid, cholesterol, triglyceride, gangliosides.

   (ii) Lipid peroxides, lipid hydroperoxides, conjugated dienes, lipofuscin.

   (iii) Total -SH, Free -SH or reduced glutathione (GSH), protein -SH, oxidized glutathione (GSSG) and GSSG/GSH ratio.

   (iv) Antioxidant enzymes: Superoxide dismutase (SOD), catalase (CAT), glutathione reductase (GR), glutathione peroxidase (GSHPx) and glutathione-S-transferase (GST).
(v) Monoamine oxidase (MAO)

(vi) Nucleic acids (DNA and RNA), DNA/RNA ratio and nucleases (DNase and RNase) and protein.

(vii) Serum cortisol.

2. To observe the possible protective effect of N-acetylhomocysteine-thiolactone (citiolone) on various neurochemical parameters viz.:

(i) Lipid peroxides, lipid hydroperoxides, lipofuscin.

(ii) Reduced glutathione, oxidized glutathione.

(iii) Antioxidant enzymes: SOD, CAT, GR, GSHPx and GST.

3. To evaluate qualitative effect of ageing following restraint stress (histochemically) on various neurochemical parameters, such as total lipids, phospholipids, DNA, RNA and lipofuscin.

4. To observe light microscopic changes in the brain after restraint stress.

5. To observe ultrastructural changes in the brain of different ages following restraint stress.