Introduction
INTRODUCTION

The central nervous system (CNS) neurotransmitters play an important role in the regulation of glucose homeostasis. The hypothalamic adrenergic and serotonergic neurons are the major components which play an important role in the release of releasing factors from the neurohormonal cells (Brownstein, 1977). The neurotransmitters are shown to help in restoring the glucose induced insulin and glycogen secretion in experimental diabetic animals (Ho, et al., 1995). In turn, it is shown from in vitro experiments that glucose modulates the release of endogenous catecholamines (Jung et al., 1993). The recent demonstration of CNS cell groups projecting into the pancreatic vagal motor neurons showed that they receive inputs from adrenergic, noradrenergic and serotonergic neurons of the lower brain stem and a dopaminergic input from paraventricular nucleus of hypothalamus (Lowey, et al., 1994). This evidently showed the importance of CNS neurotransmitters in the pancreatic hormone secretion and their importance in the glucose homeostasis.

The metabolic disorder -diabetes mellitus- is associated with peripheral as well as central nervous system neuropathy (Satoshi et al., 1993, Yagihashi, et al., 1985). In contrast to many diabetes associated complications, the chronic diabetic complications of the CNS are subtle and remain unrecognized (Mooradian, et al., 1988). The diabetic rats are reported to have altered hypothalamic growth hormone (GH) and leuitinising hormone (LH) function (Martin, et al. 1992). The counter regulatory responses from the brain neuroregulatory centres through the hormone stimulus is also defective in diabetic state (Powell, et al, 1993). These studies reveal that diabetic CNS complications are themselves impaired and are not counter regulated effects of an altered hormonal status. Many pathogenic mechanisms have been suggested for the CNS dysfunction (Nowak, et al., 1995; Karasu, et al., 1995). Studies on the treatment of diabetic neuropathy with several
compounds not only helped in the treatment but also helped in understanding the pathologic mechanism of the neuropathy (Ido, et al., 1994; Schmidt, et al., 1989). Though considerable work has been done on diabetes related peripheral neuropathy as could be seen from the valuable contributions of Schmidt et al., (1989, 1993), Nowak et al., (1995), Maeda et al., (1993), Stevens et al., (1994), Sima et al., (1993) and Schneider et al., (1993), the available information on the diabetic central nervous system in relation to neurotransmitters is limited (Mooradian and Scarpace, 1988; 1988a, ; Bitar, et al., 1987, 1992; Moratinos, et al., 1975, 1988; Mans et al., 1987; Garris, 1990, 1995; Xiang and McNeill, 1987, 1990; Satoshi, et al., 1993 ). The strong evidences for a possible role for brain neurotransmitters and their receptors in glucose homeostasis have come from related studies. These findings emphasized more on the role of brain monoamines in glucose regulating function under normal conditions. All these findings show a requirement of carrying out such studies in diabetic state (Chaouloff et al., 1987, Furman et al., (1974, 1980), Gagliardino et al., (1971), Smith , (1977), Smythi et al., (1984, 1992), Iverson (1973), Hiyoshi et al., (1995), Oda (1994), Sugimoto et al., (1994), Yamada et al., (1994), Hirose et al, (1993a,1993b). Another feature emerged from such studies is a close association of both adrenergic and serotonergic system in gluco-regulatory function. This close association was studied using the drug 8-hydroxy-2-(di-n-propylamino)tetralin (8-OH-DPAT) (Chen and Reith 1995). The monoamine interactions measured after i.c.v.administration showed 8-OH-DPAT, though a 5H1A agonist, produced releasing effects on noradrenergic and dopaminergic neurons. Also, activation of 5-HT receptors is reported to release [3H]NE in rat limbic structure ( Guillot et al., 1995). A close association between adrenergic and serotonergic nerves of hypothalamic region suspected to be involved in gluco-regulatory functions. The pharmacological studies have contributed greatly to the understanding of the receptor subtypes involved in this gluco-regulatory function in CNS (James and Hodgson 1995, Hirose et al., 1993; Jannicky et al., 1993;
Xiang et al., 1990, Hirose, et al., 1993a, Alvarez, et al., 1993). The stress induced hypothalamic variations in neurotransmitters and their receptors have given more insight into a possible involvement of hypothalamic-adrenal axis in the glucose homeostasis (Takao, et al., 1995; Yehuda et al., 1984; Smythe et al., 1983). The hypophagia and obesity research also pointed to a possible role of the hypothalamo-pituitary-adrenal (HPA) axis and its involvement in the diabetic state (Grignaschi, et al., 1993; Levin, et al., 1993). The research on the involvement of brain neurons in glucoregulatory function prompted us to take this problem. In the present study the neurotransmitters, its metabolites and receptors in streptozotocin (STZ) induced diabetes with special emphasis on α-2 adrenergic and serotonin pathways were carried out.