

Thesis Title            The Study of Opioid Receptors in  
                                 Bovine Pineal Gland

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#### ABSTRACT

Evidence exists that endogenous and exogenous opioids on the one hand and the pineal gland and/or its hormone melatonin on the other hand may interact in some as yet not clear ways in determining their various physiological and pharmacological effects. This study is an attempt to investigate the existence of opioid receptors in bovine pineal gland and their function, related to the activity of serotonin N-acetyltransferase (SNAT). By using the radioligand binding technique, the opioid receptor sites have been identified and characterized in bovine pineal gland. The radioligand used was [<sup>3</sup>H]-diprenorphine and the drug to define the non-specific binding was naloxone. The saturation experiment of opioid receptor sites in bovine pineal gland revealed a single binding site with a

dissociation equilibrium constant ( $K_D$ ) of  $1.36 \pm 0.31$  nM and a receptor density ( $B_{max}$ ) of  $17.93 \pm 5.22$  fmol/mg protein. In the inhibition experiment, the concentration of the drugs required to inhibit 50% of the binding ( $IC_{50}$ ) was determined in descending order of potency in competition with ligand binding to be naltrexone > fentanyl > naloxone > nalbuphine > morphine > nalorphine > DAGO > dynorphin > met-enkephalin. In order to indicate the function of the opioid system on the pineal gland, the effect of both the opioid agonist and antagonist on the basal activity of SNAT was examined in the bovine pineal explants in culture. The exogenous opioid agonist morphine significantly potentiated the SNAT activity in dose-dependent fashion. In addition, the stimulating effect of opioid agonist was inhibited by the opioid antagonist naloxone. In conclusion, the results of these studies indicate that the opioid receptor obviously exists and moreover, that it plays the pivotal role to potentiate SNAT activity in bovine pineal gland. However, the precise mechanism(s) whereby the endogenous opioid peptides exert their effects in the pineal gland still requires further elucidation.