CHAPTER I

INTRODUCTION

International Association for the Study of Pain (IAPA) definite the word "Pain" is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or describe in term of such damage.

The sensation of pain generally depends on the activation of a set of neural pathways (Kerr, 1975; Perl, 1971). These pathways include primary afferent fibers that terminate distally in nociceptors. The activity evoked in nociceptors is transmitted to the central nervous system where it activates neural circuits in the spinal cord or in the trigeminal nuclei. Ascending tract cells then transmit information concerning the noxious stimuli to the brain stem, thalamus, and cerebral cortex for sensory processing. Pain can be distinguished into acute pain and chronic pain due to their definitions as follows. Acute pain results from activation of nociceptors and the central pathway into which they feed and can usually are managed effectively by medical or surgical means (Willis WD Jr, 1985), while chronic pain results from injury to the nervous system. This type of pain and that produced by prolonged input from nociceptors differ from acute pain. Chronic pain may depend upon alterations in the way the central nervous system processes information (Willis WD Jr, 1985). Pathophysiological mechanism underlying the development of chronic pain is complex. Among several changes in somatosensory system, sensitisation of central neurons (known as central sensitisation) is regarded as the most important mechanism contributing to the development of chronic and persistent pain. The

molecular cascade underlying this event requires the interaction of several transmitters, their receptors and related intracellular messengers.

It is known that serotonin (5-hydroxytryptamine, 5-HT) play a critical role in central pain control circuit. In the central nervous system, the 5-HTergic neurons are concentrated in the midline brainstem nuclear complex known as raphe nuclei. This long brainstem nuclear complex extends from mesencephalon to medullary level. Rostral raphe nuclei, i.e. nucleus raphe dorsalis sends the up-ward projection to several cerebral cortical areas including somatosensory cortex as well as a number of subcortical structures while the caudal nuclear groups i.e. nucleus raphe magnus projects their descending axons to terminate in spinal cord. Both ascending and descending projection are important parts of the central pain control system

Until recently, it has been believed that 5-HT_2 receptor has minor role in nociceptive processing. This conclusion has been drawn from the findings that only small numbers of this receptor are expressed in the spinal dorsal horn. This view has been recently changed based on some pertinent. The demonstration of this receptor in nociceptive-modulating areas, i.e. periaquiductal grey (PAG), nucleus raphe, etc. reflects its involvement in the process. Experiments in animals showed that the expression of this receptor can be up-regulated in painful conditions, either by chemically induced peripheral tissue inflammation or injuries to the peripheral nerve. The area of receptor up-regulation involves spinal dorsal horn. Clinically, 5-HT_2 receptor up-regulation has been reported in some conditions, e.g. analgesic-induced transformed migraine (Srikiatkhachorn, 1998), etc. It is interesting that the state of receptor up-regulation usually coincides with low serotonin status. Since activation of this receptor usually causes excitatory effect on

post-synaptic cells, an increase in its expression in nociceptive pathway may contribute to the pro-nociceptive state.

Even thought, several studies about 5-HT_{2A} receptor had been done, the exact role of this receptor in modulation of pain (nociception) still disputed.

This study was performed to investigate (1) the role of 5-HT_{2A} receptor in chronic pain model as well as the development of chronic pain state (2) the effect of 5-HT depletion on the changes of pain sensation including role of 5-HT_{2A} receptor as well.