

References

- Abdel-Halim MS, Sjoqvist B, Anggard E. Inhibition of prostaglandin synthesis in rat brain. *Acta Pharmacol Toxicol.*1978; 43: 266-272.
- Abramson SV and Weissman G. The mechanism of action of nonsteroidal anti-inflammatory drugs. *Arth Rheumat.*1989; 32: 1-9.
- Albert PR, Zhou QY, Van Tol HHM, Bunzow JR and Civelli O. Cloning, functional expression and messenger RNA tissue distribution of the rat 5-HT_{1A} receptor gene. *J Biol Chem.*1990; 265: 5825-5832.
- Alhaider AA. Antinociceptive effect of ketanserin in mice: involvement of supraspinal 5-HT₂ receptors in nociceptive transmission. *Brain Res.*1991; 543: 335-340.
- Alhaider AA, Kitto KF, Wilcox GL. Nociceptive modulation by intrathecally administered 5-HT_{1A} and 5-HT_{1B} agonists in mice. *Fed Amer Soc Exp Biol J.* 1990; 4: A988.
- Alhaider AA, Lei SZ, Wilcox GL. Spinal 5-HT₃ receptor-mediated antinociception: possible release of GABA. *J Neurosci.*1991; 11: 1881-1888.
- Alhaider AA and Wilcox GL. Differential roles of 5-HT_{1A} and 5-HT_{1B} receptor subtypes in modulating spinal nociceptive transmission in mice. *J Pharmacol Exp Ther.*1993; 265: 378-385.
- Ameer B and Greenblatt DJ. Acetaminophen. *Ann Int Med.*1977; 87: 202.
- Anderson S and Yakota T. Anatomical, pathophysiological and biochemical aspects of pain. In: Anderson S, Bond M, Mehta M, Swerdlow M, eds. *Chronic Non-Cancer Pain*. Lancaster: MTP Press, 1987: 17-30.

- Apud JA, Grayson DR, DeErasquin E and Costa F. Pharmacological characterization of regulation of phosphoinositide metabolism by recombinant 5-HT₂ receptors of the rat. *Neuropharmacol.*1992; 31: 1-8.
- Archer T, Jonsson G, Minor BG, Post C. Noradrenergic-serotonergic interactions and nociception in the rat. *Eur J Pharmacol.*1986; 120: 295-308.
- Archer T, Minor BG and Post C. Blockade and reversal of 5-methoxy-N,N-dimethyl-tryptamine-induced analgesia following noradrenaline depletion. *Brain Res.* 1985; 333: 55-61.
- Ashton, Golding JF, Marsh VR, Thompson JW. Effects of transcutaneous electrical nerve stimulation and aspirin on late somatosensory evoked potentials in normal subjects. *Pain* 1984; 18: 377-386.
- Attal N, Kayser V, Eschalièr A. Behavioural and electrophysiological evidence for an analgesic effect of a nonsteroidal anti-inflammatory agent, diclofenac. *Pain* 1988; 35: 341-348.
- Azamita EC. The serotonin-producing neurons of the mid brain median and dorsal raphe nuclei. In: Iversen S, Snyder S, eds. *Handbook of Psychopharmacology: Chemical Pathways in the brain.* New York: Plenum, 1978.
- Azamita EC and Gannon PJ. The primate serotonergic system. In: Fahn S, Morsden CD, van Woert M, eds. *Advances in Neurology: Myoclonus.* New York: Raven Press, 1986.
- Bannwarth B, demotes-Mainard F, Schaefferbeke T and Dehais J. Where are peripheral analgesics acting ?. *Ann Rhum Dis.* 1993; 52: 1-4.
- Bannwarth B, Memotes-Mainard F, Schaefferbeke T, Lebat L and Dehais J. Central analgesic effects of aspirin-like drugs. *Fundam Clin Pharmacol.* 1995; 9: 1-7.

- Bannwarth B, Netter P, Lopicque, F, Gillet P, Pere P, Boccard E, Royer, RJ and Gaucher A. Plasma and cerebrospinal fluid concentrations of paracetamol after a single intravenous dose of propacetamol. *Br J Clin Pharmacol.* 1992; 34: 79-81.
- Bannwarth B, Netter P, Pourel J, Royer RJ and Gaucher A. Clinical pharmacokinetics of nonsteroidal anti-inflammatory drugs in the cerebrospinal fluid. *Biomed Pharmacother.* 1989; 43: 121-126.
- Barbaccia ML, Brunello N, Chuang DM and Costa E. On the mode of action of imipramine: relationship between serotonergic axon terminal function and down-regulation of β -adrenergic receptors. *Neuropharmacol.* 1983; 22: 373-383.
- Basbaum AI. Descending control of pain transmission: possible serotonergic-enkephalinergic interactions. *Advances in Exp Med and Biol.* 1981; 133: 177-189.
- Basbaum AI, Clanton CH and Fields HL. Opiate and stimulus produced analgesia: Functional anatomy of a medullospinal pathway. *Proc Nat Acad Sci USA.* 1976; 73: 4685-4688.
- Basbaum AI and Fields HL. Endogenous pain control systems: brainstem spinal pathways and endorphin circuitry. *Ann Rev of Neurosci.* 1984; 7: 309-338.
- Basbaum AI, Marley NJE, O'Keefe J and Clanton CH. Reversal of morphine and stimulus-produced analgesia by subtotal spinal cord lesions. *Pain.* 1977; 3: 43-56.
- Baskin DS, Mehler WR, Hosobuchi Y. Autopsy analysis of the safety, efficacy, and cartography of electrical stimulation of the central gray in humans. *Brain Res.* 1986; 371: 231-236.

- Beall JE, Martin RF, Applebaum AE and Willis WD. Inhibition of primate spinothalamic tract neurons by stimulation in the region of the nucleus raphe magnus. *Brain Res.* 1976; 114: 328-333.
- Bennett GJ and Mayer DJ. Effects of microinjected narcotic analgesics into the periaqueductal gray (PAG) on the response of rat spinal cord dorsal horn interneurons. *Proc. Soc. Neurosci.* 1976; 2: 928.
- Bennet JP and Snyder SH. Serotonin and lysergic acid diethylamide binding in rat brain membranes: relationship to postsynaptic serotonin receptors. *Mol Pharmacol.* 1976; 12: 373-389.
- Bensemana D and Gascon AL. Relationship between analgesia and turnover of brain biogenic amines. *Can J Physiol Pharmacol.* 1978; 56: 721-730.
- Besson JM and Chaouch A. Peripheral and spinal mechanisms of nociception. *Physiol Rev.* 1987; 67: 67-186.
- Biella G and Gropetti A. Correlation between the antinociceptive effect of aspirin and central transmitters. In: *Progress in Pharmacology and Clinical Pharmacology: Central Mechanisms for Analgesia by Acetylsalicylate Acid and Functionally Related Compounds*. I Jurna and TL Yaksh (Eds.), Vol.10. Gustav Fischer, Stuttgart. 1993; 1-9.
- Bippi H and Frohlich JC. Effects of acetylsalicylic acid and paracetamol alone and in combination on prostanoid synthesis in man. *Br J Clin Pharmacol.* 1990; 29: 305-310.
- Bitz AJ. The sites of origin of brain stem neurotensin and serotonin projections to the rodent nucleus raphe magnus. *J Neurosci.* 1982; 2: 819-824.
- Bjorkman R. Central antinociceptive effects of nonsteroidal anti-inflammatory drugs and paracetamol. *Acta Anaesthesiol Scan.* 1995; 35:(suppl 103):1-44.

- Bjorkman RL, Hallman KM, Hedner J, Hedner T, Henning M. Localization of central antinociceptive effects of diclofenac in the rat. *Brain Res.* 1992; 590: 66-73.
- Bjorkman RL, Hallman KM, Hedner J, Hedner T, Henning M. Acetaminopen blocks spinal hyperalgesia induced by NMDA and substance P. *Pain.* 1994; 57: 259-264.
- Blundel JE. Serotonin and the biology of feeding. *Am J Clin Nutr.* 1992; 55: 155-159.
- Blundel JE, Lawton CL and Halford JCG. Serotonin, eating behaviour and fat intake. *Obes Res.* 1995; 3: 471-476.
- Boivie J, Meyerson AB. A correlative anatomical and clinical study of pain suppression by deep brain stimulation. *Pain.* 1982; 13: 113-126.
- Bonanno G and Raiteri M. Interaction between 5-HT uptake inhibition and activation of 5-HT autoreceptors by exogenous agonists in rat cerebral cortex slices and synaptosomes. *Naunyn Schmiedeberg's Arch Pharmacol.* 1987; 335: 219-225.
- Boreus LO, Sandberg F. The analgesic and antipyretic action of the combination of acetophenitidine and barbital. *Acta Physiol Scand.* 1953; 28: 6-13.
- Bovetto S and Richard D. Functional assessment of the 5-HT_{1A},_{1B},_{2A/2C}, and ₃-receptor subtypes on food intake and metabolic rate in rats. *Am J Physiol.* 1995; 268 (Regulatory Integrative Comparative Physiology 37): R14-R20.
- Bowker RM, Westlund KN and Coulter JD. Origins of serotonergic projections to the spinal cord in rat: An immunocytochemical retrograde transport study. *Brain Res.* 1981; 226: 187-199.
- Bowman WC and Rand MJ. *Textbook of Pharmacology.* 2nd ed. Blackwell Scientific Publications. Oxford 1980.

- Bradford, NM. A rapid and sensitive method for the quantification of microgram quantities of protein utilizing the principle of protein-dye binding. *Anal Biochem.* 1976; 72: 248-254.
- Bradley PB, Engel G, Feniuk W, Fozard JR, Humphrey PPA, Middlemiss DN, Mylecharane EJ, Ricardson BP and Saxena PR. Proposals for the classification and nomenclature of functional receptors for 5-hydroxytryptamine. *Neuropharmacol.* 1986; 25: 563-576.
- Branchek TA, Adham N, Macchi MJ, Kao H-T and Hartig PR. [³H]DOB (4-bromo-2,5-dimethoxyphenylpropylamine) and [³H]ketanserin label two affinity states of the cloned human 5-HT₂ receptor. *Mol Pharmacol.* 1990; 38: 604-609.
- Branchek TA, Zgombick J, Macchi M, Hartig P and Weinshank R. Cloning and expression of a human 5-HT_{1D} receptor. In: Fozard JR and Saxena PR. *Serotonin, Molecular Biology, Receptors and Functional Effects* (Edi). Birkhauser Verlag, Basel, Switzerland. 1991; 21-32.
- Briley M, Langer SZ, Raisman R, Sechter D and Zarifion E. [³H]imipramine binding sites are decreased in platelets of untreated depressed patients. *Science.* 1980; 209:303-305.
- Briley MS, Raisman R and Langer SZ. Human platelets possess high affinity binding sites for [³H]imipramine. *Eur J Pharmacol.* 1979; 58: 347-348.
- Brodie BB and Axelrod J. The fate of acetophenetidin (phenacetin) in man and methods for the estimation of acetophenetidin and its metabolites in biological material. *J Pharmacol Exp Ther.* 1949; 97: 58-67.
- Brooks PM and Day RO. Nonsteroidal anti-inflammatory drugs differences and similarities. *N Engl J Med.* 1991; 324: 1714-1722.

- Bromm B, Rundshagen I and Scharcin E. Central analgesic effects of acetylsalicylic acid in healthy men. *Arzneim Forsch Drugs*. 1991; 41: 1123-1129.
- Brucchausen FV and Baumann J. Inhibitory actions deacetylation products of phenacetin and paracetamol on prostaglandin synthase in neuronal and glial cell lines and rat renal medulla. *Life Sci*. 1982; 30: 1783-1791.
- Brune K. Spinal effects of antipyretics. *Drugs*. 1994; 47: 21-27.
- Brune K. The pharmacological basis for the rational use of non-opioid OTC analgesics: aspirin, paracetamol (acetaminophen), ibuprofen, and phenazones. In: Brune K and Santoso B (Eds.) *Antipyretic Analgesics : New Insights*, Yogyakarta, Birkhauser, Basel. 30 March 1990.
- Brune K and Alperman H. Non-acidic pyrazoles: inhibition of prostaglandin production, carrageenan oedema and yeast fever. *Agents Actions*. 1983; 13: 360-363.
- Brune K, Beck WS, Geisslinger G, Menzel-Saglowek S, Peskar BM and Peskar BA. Aspirin-like drugs may block pain independently of prostaglandin synthesis inhibition. *Experientia*. 1991; 47: 247-261.
- Brune K, Menzel-Saglowek S and Zeilhofer HU. New evidence for an additional (central) site of action of antipyretic analgesics. In: Jurna I and Yaksh TL (Eds.), *Progress in Pharmacology and Clinical Pharmacology: Central Mechanisms for Analgesia by Acetylsalicylate Acid and Functionally Related Compounds* Vol.10. Gustav Fischer, Stuttgart 1993; 1-9.
- Brune K, Menzel-Saglowek S and Zeilhofer HU. Differential analgesic effects of aspirin-like drugs. *Drugs*. 1992; 44 (suppl 5): 52-59.
- Carlsson KH, Monzel W and Jurna I. Depression by morphine and the non-opioid analgesic agents metamizol (Dipyrone), lysine acetylate and paracetamol of

- activity in rat thalamus neurons evoked by electrical stimulation of nociceptive afferents. *Pain*. 1988; 32: 313-326.
- Campbell IC, Marangos OJ, Murphy DL and Pearse AGE. Neurone specific enolase (NSE) in human blood platelets: implications for the neuronal model. *Recent Adv Neuropsychopharm*. 1981; 31: 203-211.
- Capetola RJ, Rosenthal ME, Dubinsky B, Me Guire JL. Peripheral analgesics: a review. *J Clin Pharmacol*. 1983; 23: 545-546.
- Carpenter D, Engberg I, Lundberg A. Differential supraspinal control of inhibitory and excitatory actions from the FRA to ascending spinal pathways. *Acta Physiol Scand*. 1965; 63: 103-110.
- Chambard J, van Obberghen-Schilling E, Haslam JR, Vouret V and Pouyssegur J. Chinese hamster serotonin (5-HT) type 2 receptor cDNA sequence. *Nucleic Acids Res*. 1990; 18:5282.
- Chaough A and Besson JM. Mecanismes peripheriques et medullaires de la nociception. *Rev Neurol (Paris)*. 1986; 142: 173-200.
- Chapman CR. Psychological aspects of postoperative pain control. *Acta Anaesthesiol Belg*. 1992; 43: 41-52.
- Chapman V and Dickenson AH. The spinal and peripheral roles of bradykinin and prostaglandins in nociceptive processing in the rat. *Eur J Pharmacol*. 1992; 219: 427-433.
- Charles RN, Strominger NL and Demarest RJ. *The Human Nervous System: Structure and Function*, 5th ed. The Williams & Wilkins Company, Baltimore, 1996.
- Chen ACN and Chapman CR. Aspirin analgesia evaluated by event-related potentials in man: possible central action in brain. *Exp Brain Res*. 1980; 39: 359-364.

- Cheng Zf, Fields HL and Heinricher MM. Morphine microinjected into the periaqueductal gray has differential effects on 3 classes of medullary neurons. *Brain Res.* 1986; 375: 57-65.
- Clark FM and Proudfit HK. Projections of neurons in the ventromedial medulla to pontine catecholamine cell groups involved in the modulation of nociception. *Brain Res.* 1991; 540: 105-115.
- Clineschmidt BV and Anderson EG. The blockade of bulbospinal inhibition by 5-HT antagonists. *Exp Brain Res.* 1970; 11: 175-186.
- Clissold SP. Paracetamol and Phenacetin. *Drugs.* 1986; 32 (suppl 4): 46-59.
- Coffield JA, Bowen Kk and Miletic V. Retrograde tracing of projections between the nucleus submedius, the ventrolateral orbital cortex, and the midbrain in the rat. *J Comp Neurol.* 1992; 321: 488-499.
- Cohen ML, Schenck KW, Colbert W. Role of 5-HT₂ receptors in serotonin-induced contractions of non-vascular smooth muscle. *J Pharmacol Exp Ther.* 1985; 232: 770-774.
- Conn PJ and Sanders-Bush E. Serotonin-stimulated phosphoinositide turnover: mediation by the S₂ binding site in rat cerebral cortex but not in subcortical regions. *J Pharmacol Exp Ther.* 1985; 234: 195-203.
- Connell LA and Wallis DI. 5-HT depolarizes neonatal rat motoneurons through a receptor unrelated to an identified binding site. *Neuropharmacol.* 1989; 28: 625-634.
- Cortes R, Soriano E, Pazos A, Probst A and Palacios JM. Autoradiography of antidepressant binding sites in the human brain: localization using [³H]-imipramine and [³H]paroxetine. *Neurosci.* 1988; 27: 473-496.

- Craig CR and Stitzel RE. *Modern Pharmacology with Clinical Applications*. USA. 1997.
- Creese I, Schneider R and Snyder SH. [^3H]-spiroperidol labels dopamine receptors in pituitary and brain. *Eur J Pharmacol*. 1977; 46: 377-381.
- Crisp T, Stafinsky JL, Spanos LS. Analgesic effects of serotonin and receptor-selective serotonin agonists in the rat spinal cord. *Gen Pharmacol*. 1991; 22: 247-251.
- D'Andrea G, Welch M, Riddle JM, Grunfeld S, Joseph S. Platelet serotonin metabolism and ultrastructure in migraine. *Arch Neurol*. 1989; 46: 1187-1189.
- D'Amato R, Largent BL, Snowman AM and Snyder SH. Selective labeling of serotonin uptake sites in rat brain by [^3H]citalopram contrasted to labeling of multiple sites by [^3H]imipramine. *J Pharmacol Exp Ther*. 1987; 242: 364-371.
- D'Amour FE, Smith DL. A method for determining loss of pain sensation. *J Pharmacol Exp Ther*. 1941; 72: 74-79.
- Da Prada M, Keller HH, Burkard WP, Schaffner R, Bonetti EP, Launay JM and Hoefely HT. In *Typical and Atypical Antidepressants: Molecular Mechanisms* (Costa, E. and Racagni, G., eds) Raven Press, New York. 1982; 235-248.
- Dahlstrom A and Fuxe K. A method for the demonstration of monoamine-containing fibers in the central nervous system. *Acta Physiol Scand*. 1964; 60: 293-295.
- Dahlstrom A and Fuxe K. Evidence for the existence of monoamine neurons in the central nervous system. II. Experimentally induced changes in the intraneuronal amine levels of bulbospinal neuron systems. *Acta Physiol Scand*. 1965; 247 (suppl): 1-36.
- Darmani NA, Martin BR, Glennon RA. Behavioural evidence for differential adaptation of the serotonergic system after acute and chronic treatment with

- (±)-1-(2,5-dimethoxy-4-iodophenyl-2-aminopropane (DOI) or ketanserin. *J Pharmacol Exp Ther.* 1992; 262: 692-698.
- De Souza EB and Kuyatt B. Autoradiographic localization of [³H]paroxetine-labeled serotonin uptake sites in rat brain. *Synapse.* 1987; 1: 488-496.
- Dembinska-Kiec A, Zmuda A and Krupinska J. Inhibition of prostaglandin synthetase by aspirin-like drugs in different microsomal preparations. In Samuelsen and Paoletti R.(eds). *Advance in Prostaglandin and Thromboxane Research*, Raven Press, New York, Vol.1, 1976: 99-103.
- Devoghel JC. Small intrathecal doses of lysine-acetylsalicylate relieve intractable pain in man. *J Int Med Res.* 1983; 11: 90-91.
- Domer F. Characterization of analgesic activity of ketorolac in mice. *Eur J Pharmacol.* 1990; 177: 127-135.
- Dordoni B, Willson RA, Thompson RPH, Williams R. Reduction of absorption of paracetamol by activated charcoal and cholestyramine: a possible therapeutic measure. *Br Med J.* 1973; 3: 86-87.
- Dubas TC and Parker JM. A central component in the analgesic action of sodium salicylate. *Arch Int Pharmacodyn.* 1971; 194: 117-122.
- Dupont X, Menigoux C, Lebrault C, Alfonsi P, Malassine P, Esteve M and Chauvin M. Comparative effect of ketorolac and ketoprofen on a nociceptive flexion reflex in humans. *Anaesthe.* 1993; 79 ASA Abstract A896.
- Dumius A, Bouhelal R, Sebbon M, Cory R and Bockaert J. A non-classical 5-HT receptor positively coupled with adenylate cyclase in the central nervous system. *Mol Pharmacol.* 1988; 34: 880-887.

- Eide PK and Hole K. Different role of 5-HT_{1A} and 5-HT₂ receptors in spinal cord in the control of nociceptive responsiveness. *Neuropharmacol.* 1991a; 30: 727-731.
- Eide PK and Hole K. Interactions between serotonin and substance P in the regulation of nociception. *Brain Res.* 1991b; 550: 225-230.
- Eide PK and Hole K. The role of 5-hydroxytryptamine (5-HT) receptor subtypes and plasticity in the 5-HT systems in the regulation of nociceptive sensitivity. *Cephalalgia.* 1993; 13: 75-85.
- Engberg I, Lundberg A and Ryall RW. Reticulospinal inhibition of transmission in reflex pathways. *J Physiol.* 1968; 194: 225-236.
- Erlander MG, Lovenberg TW, Baron BM, DeLecea L, Danielson PE, Rake M, Slone AL, Siegel BW, Foye PE, Cannon K, Burns JE and Sutcliffe JG. Two members of a distinct subfamily of 5-HT receptors differentially expressed in rat brain. *Proc Natn Acad Sci USA.* 1993; 90: 3452-3456.
- Fargin A, Raymond JR, Lohse MJ, Kobilka BK, Caron MG and Lefkowitz RJ. The genomic clone G-21 which resembles a β -adrenergic receptor sequence encodes the 5-HT_{1A} receptor. *Nature.* 1988; 335: 358-360.
- Feighner JB and Boyer WF. *Perspectives in Psychiatry: Selective Serotonin Re-Uptake Inhibitors*, vol 1. New York, NY: John Wiley & Sons. 1991; 11-13.
- Felder CC, Kanterman RY, MaAL and Axelrod J. Serotonin stimulates phospholipase A-2 and the release of arachidonic acid in hippocampal neurons by a type 2 serotonin receptor that is independent of inositol phospholipid hydrolysis. *Proc Natn Acad Sci USA.* 1990; 87: 2187-2191.

- Feniuk W, Hare J and Humphrey PPA. Analysis of the mechanism of 5-HT-induced vasopressor responses in ganglion-blocked anaesthetized dogs. *J Pharm Pharmacol*. 1981; 33: 155-160.
- Ferreira RA, Ward SJ, Zobre CM, van Liew DK, Perrone MH, Connell MJ and Haubrich DR. Estimation of the *in vivo* effect of cyclooxygenase inhibitors on prostaglandin E₂ levels in mouse brain. *Eur J Pharmacol*. 1990; 179: 25-34.
- Ferreira SH. Prostaglandins, aspirin-like drugs and analgesia. *Nature*. 1972; 240: 200.
- Ferreira SH, Lorenzetti BB and Correa FMA. Central and peripheral analgesic actions of aspirin-like drugs. *Eur J Pharmacol*. 1978; 53: 39-48.
- Fields HL. *Pain*. McGraw-Hill Book Company, New York. 1987.
- Fields HL and Basbaum AI. Central nervous system mechanism of pain modulation. In: Wall PD, Melzack E, editors. *Textbook of Pain*. New York: Churchill Livingstone, 1994: 243-260.
- Fields HL, Basbaum AI, Clanton CH and Anderson SD. Nucleus raphe magnus inhibition of spinal cord dorsal horn neurons. *Brain Res*. 1977; 126: 441-453.
- Flower RJ, Moncada S and Vane JR. Analgesic antipyretics and anti-inflammatory agents: drugs employed in the treatment of gout; In: Goodman and Gilman (eds.). *The Pharmacological Basis of Therapeutics*, 6th ed., Macmillan Publishing Company, New York. 1980; 682-782.
- Flower RJ and Vane JR. Inhibition of prostaglandin synthetase in brain explains the anti-pyretic activity of paracetamol (4-acetaminophenol). *Nature*. 1972; 240: 410-411.
- Flower RJ and Vane JR. Inhibition of prostaglandin biosynthesis. *Biochem Pharmacol*. 1974; 23: 1439-1450.

- Foguet M, Hoyer D, Pardo LA, Parekh A, Kluxen FW, Kalkman HO, Stuhmer W and Lubbert H. Cloning and functional expression of the rat stomach fundus seroto-nin receptor. *EMBO J*. 1992; 11: 3481-3487.
- Forrest JAM, Clements JA and Prescott LF. Clinical pharmacokinetic of paracetamol. *Clin Pharmacokinet*. 1982; 7: 93-107.
- Fozard JR. 5-HT₃ receptors and cytotoxic drug-induced vomiting. *Trends Pharmacol Sci*. 1987; 8: 44-45.
- Frazer A, Maayani S and Wolfe BB. Subtypes of receptors for serotonin A. *Rev Pharmac Toxic*. 1990; 30: 307-348.
- Galzin AM, Moret C, Verzier B and Langer SZ. *J Pharmacol Exp Ther*. 1985; 235: 200-211.
- Gazzard SP, Ford-Hutchinson AW, Smith MJH and Williams R. The binding of paracetamol plasma proteins of man and pig. *J Pharm Pharmacol*. 1973; 25: 964-967.
- Glaum SR, Proudfit HK and Anderson EG. Reversal of the antinociceptive effects of intrathecally administered serotonin in the rat by a selective 5-HT₃ receptor antagonist. *Neurosci Lett*. 1988; 95: 313-317.
- Glaum SR, Proudfit HK and Anderson EG. 5-HT₃ receptors modulate spinal nociceptive reflexes. *Brain Res*. 1990; 510: 12-16.
- Glowinsky J and Iversen LL. Regional studies of catecholamines in the rat brain. I. The disposition of [³H]norepinephrine, [³H]dopamine and [³H]dopa in various regions of the brain. *J Neurochem* 1966; 13: 655-669.
- Graham D and Langer SZ. In: Osborne NN and Hamon M (eds). *Neuronal Serotonin*. J. Wiley & Sons 1988; 367-391.

- Graham D and Solomon ZL. Advance in sodium-ion coupled biogenic amine transporter. *Life Sci.* 1992; 51: 631-645.
- Granados-Soto V, FJ Lopez-Munoz G, Castanedo-Hernandez LA, Salazar, JE, Villareal and Flores-Murrieta FL. Characterization of the analgesic effects of paracetamol and caffeine combinations in the pain-induced functional impairment model in the rat. *J Pharm Pharmacol.* 1993; 45: 627-633.
- Gray TS, Magnuson DJ. Peptide immunoreactive neurons in the amygdala and the bed nucleus of stria terminalis project to the midbrain central gray in the rat. *Peptides.* 1992; 13: 451-460.
- Gropetti A, Braga PC, Biella G, Parenti M, Rusconi and Martegazza P. Effects of aspirin on serotonin and met-enkephalin in brain. *Neuropharmacol.* 1988; 27: 499-505.
- Guiou R, Blin O, Pouget J and Serratrice G. Analgesic effect of indomethacin shown using the nociceptive flexion reflex in humans. *Ann Rheum Dis.* 1992; 51: 391-393.
- Guilbaud G, Besson JM, Oliveras JL. Suppression by LSD of the inhibitory effect exerted by dorsal raphe stimulation on certain spinal cord interneurons in the cat. *Brain Res.* 1973; 61: 417-422.
- Guzman F and Lim RKS. Central and peripheral mechanism of analgesia and pain. *Arch Biolog Med Experimentalis.* 1967; 4: 180-186.
- Habert E, Graham D, Tahraoui L, Claustre Y and Langer SZ. Characterization of [³H]paroxetine binding to rat cortical membranes. *Eur J Pharmacol.* 1985; 118: 107-114.
- Hagbarth KE, Kerr DIB. Central influences on spinal afferent conduction. *J Neurophysiol.* 1954; 17: 295-307.

- Hamblin M and Metcalf MA. Primary structure and functional characterisation of a human 5-HT_{1D} type serotonin receptor. *Mol Pharmacol*. 1991; 40:143-148.
- Hanks GW. Nonprescription analgesics. II. Paracetamol. *Clin Ther*. 1983; 5 (suppl 5b): 23-36.
- Hardisty RM and Stacey RS. 5-Hydroxytryptamine in normal human platelets. *J Physiol*. 1955; 130: 711-720.
- Hardy SGP, Leichnetz GR. Cortical projects to the periaqueductal gray in the monkey: a retrograde and orthograde horseradish peroxidase study. *Neurosci Lett*. 1981; 22: 97-101.
- Hartig P, Kao H-T, Macchi M, Adham N, Zgombick J, Weinshank R and Branchek TA. The molecular biology of serotonin receptors: An overview. *Neuropsychopharmacol*. 1990; 3: 335-347.
- Hartig PR. Molecular biology of 5-HT receptors. *Trends Pharmacol Sci*. 1989; 10: 64-69.
- Headley PM, Duggan AW, Griersmith BT. Selective reduction by noradrenaline and 5-hydroxytryptamine of nociceptive responses of cat dorsal horn neurons. *Brain Res*. 1978; 145:185-189.
- Heller WA and Baraban JM. Potent agonist activity of DOB at 5-HT₂ receptors in the guinea pig trachea. *Eur J Pharmacol*. 1987; 138: 115-117.
- Herbert H, Saper CR. Organization of medullary adrenergic and noradrenergic projections to the periaqueductal gray matter in the rat. *J Comp Neurol*. 1992; 314:34-52.
- Hoyer D, Clarke DE, Fozard JR, Hartig PR, Martin GR, Mylecharane EJ, Saxena PR and Humphrey PPA. International Union of Pharmacology Classification of receptors for 5-HT. *Pharmac Rev*. 1994; 46: 157-203.

- Hoyer D, Engel G and Kalkan HO. Characterization of the 5-HT_{1B} recognition site in rat brain: binding studies with [¹²⁵I]iodocyanopindolol. *Eur J Pharmacol.* 1985; 118: 1-12.
- Hoyer D, Pazos A, Probst and Palacios JM. Serotonin receptors in the human brain II. Characterization and autoradiographic localization of 5-HT_{1C} and 5-HT₂ recognition sites. *Brain Res.* 1986; 376:97-107.
- Hoyer D and Schoeffter P. 5-HT receptors: subtypes and second messengers. *J Recept Res.* 1991; 11: 197-214.
- Humphrey PPA, Hartig P and Hoyer D. A proposed new nomenclature for 5-HT receptors. *Trends Pharmacol Sci.* 1993; 14: 233-236.
- Hunskaar S. Similar effects of acetylsalicylic acid morphine on immediate responses to acute noxious stimulation. *Pharmacol Toxicol.* 1987; 60: 167-170.
- Hunskaar S, Berge OG, Hole K. Dissociation between antinociceptive and anti-inflammatory effects of acetylsalicylic acid and indomethacin in the formalin test. *Pain.* 1986; 25: 125-132.
- Hunskaar S, Fasmer OB and Hole K. Acetylsalicylic acid, paracetamol and morphine inhibit behavioural responses to intrathecally administered substance P or capsaicin. *Life Sci.* 1985; 37: 1835-1841.
- Hunskaar S and Hole K. The formalin test in mice: dissociation between inflammatory and non-inflammatory pain. *Pain.* 1987; 30: 103-114.
- Hyttel J. Citalopram-pharmacological profile of a specific serotoninuptake inhibitor with antidepressant activity. *Prog Neuro-Psychopharmacol & Biol Psychiat.* 1982; 6: 277-295.

- leni JR, Tobach E, Zukin SR, Barr, GA and Van Pragg HM. Multiple [3 H]imipramine binding sites in brains of male and female Fawn-Hooded and Long-Evans rats. *Eur J Pharmacol.* 1985; 112: 261-264.
- Iversen LL. Neuronal and extraneuronal catecholamine uptake mechanisms. In: *Frontiers in Catecholamine Research*, edited by Usdin E and Snyder SH. Pergamon Press, New York, 1973; 403-407.
- Jackson CH, MacDonald NC and Cornett JWD. Acetaminophen. *Can Med Assoc J.* 1984; 131-134.
- Julius D, Huang KN and Livelli TJ. The 5-HT₂ receptor defines a family of structurally distinct but functionally conserved serotonin receptors. *Proc Natl Acad Sci USA.* 1990; 87: 928-932.
- Julius D, MacDermott AB, Axel R and Jessel TM. Molecular characterisation of a functional cDNA encoding the 5-HT_{1C} receptor. *Science.* 1988; 214: 558-564.
- Jurna I and Brune K. Central effect of nonsteroidal anti-inflammatory agents, indomethacin, ibuprofen, determined in C fiber-evoked activity in single neurons of the rat thalamus. *Pain.* 1990; 41: 71-80.
- Kandel ER and Schwartz JH. *Principles of Neural Science.* Prentice Hall International Limited, London. 1991.
- Kao H-T, Adham , Olsen MA, Weinshank RL, Branchek TA and Hartig PR. Site-directed mutagenesis of a single residue changes the binding properties of the 5-HT₂ receptor from a human to a rat pharmacology. *FEBS Lett.* 1992; 307: 324-328.
- Kaumann AJ. Piglet sinoatrial 5-HT receptors resemble human atrial 5-HT₄-like receptors. *Naunyn Schmiedebergs Arch Pharmacol.* 1990; 342: 619-622.

- Kendall DA, Nahorski SR. 5-HT-stimulated inositol phospholipid hydrolysis in rat cerebral cortex slices: pharmacological characterization of the effects of antidepressants. *J Pharmacol Exp Ther.* 1985; 233: 473-479.
- Kenigsberg RL and Trifaro JM. Presence of a high affinity uptake system for catecholamines in cultured bovine adrenal chromaffin cells. *Neurosci.* 1980; 5: 1547-1556.
- Kjøfsvik A, Størkson, Tjølsen A, Hole K. Activation of spinal 5-HT₂ receptors increases nociception in rats. *Society for Neurosci Abst.* 1994; 20: 553P.
- Kobal G, Hummel C, Neurnberg B, Brune K. Effects of pentazocine and acetylsalicylic acid on pain-related evoked potentials and vigilance in relationship to pharmacokinetic parameters. *Agents Actions.* 1990; 29: 342-259.
- Kobilka BK, Frielle T, Collins S, Yang-Feng T, Kobilka TS, Francke U, Lefkowitz RJ and Caron MG. An intronless gene encoding a potential member of the family of receptors coupled to guanine nucleotide regulatory proteins. *Nature.* 1987; 329: 75-77.
- Kovachich GB, Aronson CE, Brunswick J and Frazer A. Quantitative autoradiography of serotonin uptake sites in rat brain using [³H]cyanoimipramine. *Brain Res.* 1988; 454: 78-88.
- Kudraw L. Paradoxical effects of frequent analgesic use. *Adv Neurol.* 1982; 33: 335-341.
- Kuhn DM, Wolf WA and Youdim MB. Does brain 5-HIAA indicate serotonin release or monoamine oxidase activity? *Eur J Pharmacol.* 1985; 109: 381-387.
- Kursar JD, Nelson DL, Wainscott DB, Cohen ML and Baez M. Molecular cloning, functional expression and pharmacological characterization of a novel

- serotonin receptor (5-HT_{2F}) from rat stomach fundus. *Mol Pharmacol.* 1992; 42: 549-557.
- Laburn H, Mitchell D, Stephen J. Effects of intracerebroventricular floctafenine and indomethacin on body temperature in febrile rabbits. *Br J Pharmacol.* 1980; 71: 525-528.
- Langer SZ, Javoy-Agid F, Raisman R, Briley H and Agid Y. Distribution of specific high affinity binding sites for [³H]imipramine in human brain. *J Neurochem.* 1981; 37: 267-271.
- Langer SZ, Moret C, Raisman R, Dubocovich ML and Briley M. High affinity [³H]imipramine binding in rat hypothalamus: association with uptake of serotonin but not of norepinephrine. *Science.* 1980; 210: 1133-1135.
- Langer SZ, Zarifian E, Briley M, Raisman R and Sechter D. High affinity binding of [³H]imipramine in brain and platelets and its relevance to the biochemistry of affective disorders. *Life Sci.* 1981; 29: 211-220.
- Lanz R, Polster P, Brune K. Antipyretic analgesics inhibit prostaglandin release from astrocytes and macrophages similarly. *Eur J Pharmacol.* 1986; 130: 105-109.
- Le Bars D. Serotonin and Pain. In: Osborne N and Hamon M (eds). *Neuronal Serotonin*. Wiley and Sons, London 1988; 171-230.
- Leonhardt S, Herrick-Davis K and Teitler M. Detection of a novel serotonin receptor subtype (5-HT_{1E}) in human brain: interaction with a GTP-binding protein. *J Neurochem.* 1989; 53: 465-471.
- Leysen JE. The use of 5-HT receptor agonists and antagonists for the characterization of their respective receptor sites. In: Boulton AA, Baker GB, Juorio AV (eds). *Neuromethods, Neuropharmacology II: 'Drugs as tools in neurotransmitter research'*. Humana Press, Clifton, New Jersey, 1989.

- Leysen JE, Niemegeers CJE, Van Neuten JM and Laduron PM. [³H]ketanserin (R41468), a selective [³H]-ligand for serotonin receptor binding sites. *Mol Pharmacol*. 1981; 21: 301-304.
- Leysen EJ and Powels PJ. 5-HT₂ receptors, roles and regulations. *Ann NY Acad Sci*. 1990; 600: 183-193.
- Lidof HGW, Grzanna R and Molliver ME. The serotonin innervation of the cerebral cortex in the rat, an immunocytochemical analysis. *Neurosci*. 1980; 207-227.
- Lin MT, Chandra A, Chi ML, Kau CL. Effects of increasing serotonergic receptor activity in brain on analgesic activity in rats. *Exp Neurol*. 1980; 68: 548-554.
- Lin MT, Chi ML, Chandra A and Tsay BL. Serotonergic mechanisms of beta-endorphin- and clonidine-induced analgesia in rats. *Pharmacol*. 1980; 20: 323-328.
- Longhue M, Roccasalva P, Parenti M and Groppetti A. Effect of pertussis toxin on aspirin-mediated analgesia. *Pharmacol Res Commun*. 1988; 20S:133-138.
- Lovenberg TW, Baron BM, de Lecea L, Miller JD, Prosser RA, Rea MA, Foye PE, Racke M, Slone AL, Siegel BW, Danielson PE, Sytcliffe JG and Erlander MG. A novel adenylyl cyclase-activating serotonin receptor (5-HT₇) implicated in the regulation of mammalian circadian rhythms. *Neuron*. 1993; 11: 449-458.
- Malgouris C, Flamand F and Doble A. Autoradiographic studies of RP62203, a potent 5-HT₂ receptor antagonist. *In vitro* and *ex vivo* selectivity profile. *Eur J Pharmacol*. 1993; 233: 29-35.
- Malmberg AB and Yaksh TL. Antinociceptive actions of spinal nonsteroidal anti-inflammatory agents on the formalin test in the rat. *J Pharmacol Exp Ther*. 1992; 263: 135-146.

- Malmberg AB and Yaksh TL. Hyperalgesia mediated by spinal glutamate or substance P receptor blocked by spinal cyclooxygenase inhibition. *Science*. 1992; 257: 1276-1279.
- Malmberg AB and Yaksh TL. Antinociceptive produced by the spinal delivery of the S and R enantiomers of flurbiprofen in the formalin test. *Eur J Pharmacol*. 1994; 256: 205-209.
- Malmgren R. Platelets and biogenic amines. 2. Indications for a discrete low affinity uptake mechanism shared by norepinephrine and 5-HT in human platelets. *Psychopharmacol*. 1986; 90: 384-389.
- Malmgren R and Hasselmark L. The platelet and the neuron: Two cells in focus in migraine. *Cephalalgia*. 1988; 8: 7-24.
- Martin GR. Vascular receptors for 5-hydroxytryptamine: distribution, function and classification. *J Pharmac Exp Ther*. 1994; 254: 253-257.
- Martin RF, Jordan JM and Willis WD. Differential projections of cat medullary raphe neurons demonstrated by retrograde labeling following spinal cord lesions. *J Comp Neurol*. 1978; 182: 77-88.
- Mastini A, Bondiolotti GP, Sacerdote P. Diclofenac increases beta-endorphin plasma concentrations. *J Int Med Res*. 1984; 12: 92-95.
- Matthes H, Boschert U, Amlaiky N, Grailhe R, Plassat JL, Muscatelli F, Mattei M-G and Hen R. Mouse 5-HT_{5A} and 5-HT_{5B} receptors define a new family of serotonin receptors: cloning, functional expression and chromosomal localization. *Mol Pharmacol*. 1993; 43: 313-319.
- Maura G, Roccatagliata E, Ulivi M and Raiteri. Serotonin-glutamate interaction in rat cerebellum: involvement of 5-HT₁ and 5-HT₂ receptors. *Eur J Pharmacol*. 1988; 145: 31-38.

- Mayer DJ and Liebeskind JC. Pain reduction by focal electrical stimulation of the brain: an anatomical and behavioral analysis. *Brain Res.* 1974; 68: 73-93.
- Mayer DJ and Price DD. Central nervous system mechanisms of analgesia. *Pain.* 1976; 2: 379-404.
- Mayer DJ, Wolfle TL, Akil H. Analgesia from electrical stimulation in the brainstem of the rat. *Science.* 1971; 174: 1351-1354.
- Mc Cormack K. Nonsteroidal anti-inflammatory drugs and spinal nociceptive processing. *Pain.* 1994; 59: 9-43.
- Mc Cormack K. The spinal actions of nonsteroidal anti-inflammatory drugs and the dissociation between their anti-inflammatory and analgesic effects. *Drugs.* 1994; 47 (suppl 5): 28-45.
- Mc Cormack K and Brune K. Dissociation between the anti-nociceptive and anti-inflammatory effects of the nonsteroidal anti-inflammatory drugs: a survey of their analgesic efficacy. *Drugs.* 1991; 41: 533-547.
- Meller T, Lewiss SJ, Brody MJ and Gebhart GF. The peripheral nociceptive actions of intravenously administered 5-HT in the rat requires dual activation of both 5-HT₂ and 5-HT₃ receptor subtypes. *Brain Res.* 1991; 561: 61-68.
- Melzack R and Wall PD. Pain mechanisms: a new theory. *Science.* 1965; 150: 971-979.
- Meredith TJ and Goulding R. Paracetamol. *Postgrad Med J.* 1980; 56: 459-473.
- Messing RB and Lytle LD. Serotonin-containing neurons: their possible role in pain and analgesia. *Pain.* 1977; 4: 1-21.
- Meyerhof W, Obermuller F, Fehr S and Richter D. A novel rat serotonin receptor: primary structure, pharmacology and expression pattern in distinct brain regions. *DNA Cell Biol.* 1993; 12: 401-409.

- Millan MK. Serotonin and pain: evidence that activation of 5-HT_{1A} receptors does not elicit antinociception against noxious thermal, mechanical and chemical stimuli in mice. *Pain*. 1994; 58: 45-61.
- Miller RR. Analgesics in *Drug Effects in Hospitalized Patients: Experiences of the Boston Collaborative Drug Surveillance Program*, John Wiley and Sons 1976: 134-135.
- Minor BG, Post C and Archer T. Blockade of intrathecal 5-HT induced antinociception in rats by noradrenaline depletion. *Neurosci Lett*. 1985; 54: 39-44.
- Mjelle N, Lund A, Eide PK, Storkson R and Tjølsen a. The role of 5-HT_{1A} and 5-HT_{1B} receptors in spinal nociceptive transmission and in the modulation of NMDA-induced behaviour. *Neuroreport*. 1992; 3: 1061-1064.
- Monsma FJ Jr, Shen Y, Ward RP, Hamblin MW and Sibley DR. Cloning and expression of a novel serotonin receptor with high affinity for tricyclic psychotropic drugs. *Mol Pharmacol*. 1993; 43: 320-327.
- Moore UJ, Marsh VR, Ashton CH. Effects of peripherally and centrally acting analgesics on somatosensory evoked potentials. *Br J Clin Pharmacol*. 1995; 40: 111-117.
- Mulder AH, Van den Berg WB and Stoof JC. Calcium-dependent release of radio-labeled catecholamines and serotonin from rat brain synaptosomes in a superfusion system. *Brain Res*. 1975; 99: 419-424.
- Munson PJ and Rodbard D. LIGAND: A versatile computerized approach for characterization of ligand-binding systems. *Ann Biochem*. 1980; 107: 220-239.

- Muramatsu M, Tomaki-Ohashi J, Usuki C, Araki H and Aihara H. 5-HT₂ receptor-mediated regulation of release of acetylcholine by minaprine in cholinergic nerve terminals of hippocampus of rat. *Neuropharmacol.* 1988a; 27: 603-609.
- Muramatsu M, Tomaki-Ohashi J, Usuki C, Araki H and Aihara H. 5-HT₂ antagonists and minaprine block the 5-HT induced inhibition of dopamine release from rat brain striatal slices. *Eur J Pharmacol.* 1988b; 153: 89-95.
- Mylecharane EJ. Agonists and antagonists of 5-HT₂ receptors. In: Saxena PR, Wallis DI, Wouters W and Bevan P (eds) : *Cardiovascular Pharmacology of 5-Hydroxytryptamine. Prospective Therapeutic Applications.* Kluwer Academic Publisher, Dordrecht Netherlands. 1990; 81-100.
- Nanra RS. Clinical and Pathological aspects of analgesic nephropathy. *Brit J Clin Pharmacol* 1980; 10: 359S-368S.
- Neuman RG, Wilson BD, Bradley M, Kimball ES, Weichman BM, Wood DD. Inhibition of prostaglandin biosynthesis by etodolac. I. Selective activities in arthritis. *Agents Actions.* 1987; 21: 160-166.
- North RA and Uchimura N. 5-HT acts 5-HT₂ receptors to decrease potassium conductance in rat nucleus accumbens neurons. *J Physiol.* 1989; 417: 1-12.
- Ochs HR, Greenblatt DJ, Abernethy DR, Erenat RM, Gerloff J, Eichelkraut W and Hahn N. Cerebrospinal fluid uptake and peripheral distribution of centrally acting drugs: Relation to lipid solubility. *J Pharma Pharmacol.* 1985; 37: 428-431.
- Oksenberg D, Marster SA, O'Dowd BF, Jin H, Havlik S, Peroutka SJ and Ashkeazi A. A single amino acid difference confers major pharmacological variation between human and rodent 5-HT_{1B} receptors. *Nature.* 1992; 360: 161-163.

- Okuyama S and Aihara H. Hyperalgesic action in mice of intracerebroventricularly administered arachidonic acid, PGE₂, PGF₂ alpha and PGD₂: effects of analgesic drugs on hypergesia. *J Pharmacobiodyn.* 1986; 9: 902-908.
- Okuyama S and Aihara H. The mode of action of analgesic drugs in adjuvant arthritic rats as an experimental model of chronic inflammatory pain: possible central action of acidic nonsteroidal anti-inflammatory drugs. *Jpn J Pharmacol.* 1984; 35: 95-103.
- Oliveras JL, Redjemi G, Guilbaud G and Besson JM. Analgesia induced by electrical stimulation of the inferior centralis nucleus of the raphe in the cat. *Pain.* 1975; 1: 139-145.
- Palkovits MR, Raisman R, Briley M and Langer SZ. Regional distribution of [³H]imipramine in rat brain. *Brain Res.* 1981; 210: 493-498.
- Pansky B. *Review of Neuroscience.* 2nd ed. McGraw-Hill Book Company New York, 1992.
- Pascaul J. Serotonin, serotonin receptors, serotonin receptor subtype agonists and pain. *Pain.* 1990; 40: 115-116.
- Paul S, Rehavi MM, Skolnick P and Goodwin FK. Demonstration of specific high affinity binding sites [³H]imipramine of human platelets. *Life Sci.* 1980; 26: 953-958.
- Pazos A, Cortes R and Palacios JM. Quantitative autoradiography mapping of serotonin receptors in the rat brain. II Serotonin-2 receptors. *Brain Res.* 1985; 346: 231-249.
- Pazos A, Probst A and Palacios JM. Serotonin receptors in the human brain, IV Autoradiographic mapping of 5-HT₂ receptors. *Neurosci.* 1987; 21: 123-139.

- Pelissier T, Alloui A, Paleile C and Eschalier A. Evidence of a central antinociceptive effect of paracetamol involving spinal 5-HT₃ receptors. *Neuroreport*. 1995; 6: 1546-1548.
- Pelissier T, Alloui A, Caussade F, Cloarec A, Lavarenne J, Eschalier A. Evidence of a spinal tropisetron-inhibited antinociceptive effect of paracetamol. *Fundam Clin Pharmacol*. 1994; 8: 263.
- Peroutka SJ. 5-hydroxytryptamine receptor subtypes. *Annu Rev Neurosci*. 1988; 11: 45-60.
- Peroutka SJ. 5-hydroxytryptamine receptor subtypes. *Pharmacol Toxicol*. 1990; 67: 373-383.
- Peroutka SJ. 5-hydroxytryptamine receptors. *J Neurochem*. 1993; 60: 408-416.
- Peroutka SJ and Snyder SH. Multiple serotonin receptors: differential binding of [³H]5-HT, [³H]lysergic acid diethylamide and [³H]spiroperidol. *Mol Pharmacol*. 1979; 16: 687-699.
- Perry EK, Marshall EF, Blessed G, Tomlinson BE and Perry RH. Decreased imipramine binding in the brains of patients with depressive illness. *Br J Psychiatry*. 1983; 142: 188-192.
- Peters JR and Graham-Smith DG. Human platelets 5-HT receptors: characterization and functional association. *Eur J Pharmacol*. 1980; 68: 243-256.
- Pickel VM, Joh TH and Reis DJ. Monoamine-synthesizing enzymes in central dopami-nergic, noradrenergic and serotonergic neurons: Immunocytochemical localization by light and electron microscopy. *J Histochem Cytochem*. 1976; 24: 792-806.

- Pini LA, Sandrini M and Vitale G. Involvement of brain serotonergic system in the antinociceptive action of acetyl-salicylic acid in the rat. *Inflamm Res.* 1995; 44: 30-36.
- Pini LA, Sandrini M and Vitale G. The antinociceptive action of paracetamol is associated with changes in the serotonergic system in the rat brain. *Eur J Pharmacol.* 1996; 308: 31-40.
- Pini LA, Trenti T, Vitale G and Sandrini M. Action of analgesic drugs on brain 5-HT receptors as a model to study chronic drug-sustained headaches. In: Clifford RR (eds). *New Advances in Headache Research 4*. London: Smith-Gordon, 1994: 159-166.
- Pini LA, Vitale G and Sandrini M. Nonsteroidal anti-inflammatory drugs' influence on pain threshold and serotonin receptors in the rat brain. *Br J Pharmacol.* 1994; 111: 161P.
- Pini LA, Vitale G, Ottani A and Sandrini M. Naloxone-reversible antinociception by paracetamol in the rat. *J Pharmacol Exp Ther.* 1997; 280: 934-940.
- Pini LA, Vitale G and Sandrini M. The role of serotonin brain receptors in the analgesic effect of phenazone. *Drug Exp Clin Res.* 1993; 19: 13-17.
- Piletta P, Porchet HC and Dayer P. Central analgesic effect of acetaminophen but not of aspirin. *Clin Pharmacol Ther.* 1991; 49: 350-354.
- Plassat JL, Boschert U, Amlaiky N and Hen R. The mouse 5-HT₂ receptor reveals a remarkable heterogeneity within the 5-HT_{1D} receptor family. *EMBO J.* 1992; 11: 4779-4786.
- Pletcher A. Metabolism, transfer and storage of 5-HT in blood platelets. *Br J Pharmacol.* 1968; 32: 1-16.

- Pletcher A and Laubscher A. Blood platelets as a model for neurons uses and limitations. *J Neural Transm.* 1980; 7 (suppl 16):7-16.
- Post C, Minor BG, Davies M, Archer T. Analgesia induced by 5-HT receptor agonist is blocked or reversed by noradrenaline depletion in rats. *Brain Res.* 1986; 363: 18-27.
- Pritchett DB, Bach AWJ, Wozny M, Taleb O, Dal Toso R, Shih JC and Seeburg PH. Structure and functional expression of cloned rat 5-HT₂ receptor. *EMBO J.* 1988; 7: 4135-4140.
- Proudfit HK and Anderson EG. New long latency bulbospinal evoked potentials blocked by serotonin antagonists. *Brain Res.* 1974; 65: 542-546.
- Proudfit HK and Anderson EG. Morphine analgesia: Blockade by raphe magnus lesions. *Brain Res.* 1975; 98: 612-619.
- Puig S, Rivot JP and Besson JM. Effect of subcutaneous administration of the chemical algogen formalin on 5-HT metabolism in the nucleus raphe magnus and the medullary dorsal horn: A voltammetric study in freely moving rats. *Brain Res.* 1992; 590: 250-254.
- Puig S, Rivot JP and Besson JM. Effect of RU 24969 on 5-HT metabolism in the medullary dorsal horn as studied by in vivo voltammetry. *Brain Res.* 1993; 618: 171-174.
- Raffa RB and Codd EE. Lack of binding of acetaminophen to 5-HT receptor or uptake sites (or even other binding/uptake assays). *Life Sci.* 1996; 59: PL37-40.
- Raisman R, Briley M and Langer SZ. High affinity [³H]imipramine binding in rat cerebral cortex. *Eur J Pharmacol.* 1979; 54: 307-308.
- Raisman R, Briley M and Langer SZ. Specific tricyclic antidepressant binding sites in rat brain. *Nature.* 1979; 281: 148-150.

- Raisman R, Briley M and Langer SZ. Specific tricyclic antidepressant binding sites in rat brain characterized by high affinity [³H]imipramine binding. *Eur J Pharmacol.* 1980; 61: 373-380.
- Ramwell PW. Biologic importance of arachidonic acid. *Archives of Int Med.* 1981; 141: 275-278.
- Randic M and Yu HH. Effects of 5-HT and bradykinin in cat dorsal horn neurons activated by noxious stimuli. *Brain Res.* 1976; 111: 197-203.
- Rehavi M, Paul SM, Skolnick P and Goodwin FK. Demonstration of specific high affinity binding sites for [³H]imipramine in human brain. *Life Sci.* 1980; 26: 2273-2279.
- Reichling DB, Basbaum AI. Contribution of brainstem GABAergic circuitry to descending antinociceptive controls. I. GABA-immunoreactive projection neurons in the periaqueductal gray matter and nucleus raphe magnus. *J Comp Neurol.* 1990; 302: 370-377.
- Reimherr FW, Byerley WF, Ward MF, Lebeque BJ and Wender PH. Sertraline, a selective inhibitor of serotonin uptake, for the treatment of outpatients with major depressive disorder. *Psychopharmacol Bull.* 1988; 24: 200-203.
- Reynolds DV. Surgery in the rat during electrical analgesia induced by focal brain stimulation. *Science.* 1969; 164: 444-445.
- Rivot JP, Chiang CY, Besson JM. Increase of serotonin metabolism within the dorsal horn of the spinal cord during nucleus magnus stimulation, as revealed by in vivo electrochemical detection. *Brain Res.* 1982; 238: 117-126.
- Rittenhouse PA, Bakkum EA, Herbert G, Betha CL and Van de Kar LD. Serotonin receptor subtypes mediating neuroendocrine responses to DOI. *Pharmacologist.* 1990; 32: 185.

- Roberts MHT, Sizer AR and Rees H. 5-HT and neuronal activity in the dorsal horn of the spinal cord. In: Besson JM (eds) *Serotonin and Pain*. Elsevier Press, Amsterdam, 1990.
- Roth BL. Multiple serotonin receptors: clinical and experimental aspects. *Ann Clin Psych*. 1994; 6: 67-78.
- Ruangpattanatawee U. Role of serotonin receptors type I and II in pain modulation in rat. *Master's Thesis*, Inter-department of Physiology, Graduate School, Chulalongkorn University, 1998.
- Ruat M, Traiffort E, Arrang J-M, Tardivel-Lacombe J, Diaz J, Leurs R and Schwartz J-C. A novel rat serotonin (5-HT₆) receptor: molecular cloning, localization and stimulation of cAMP accumulation. *Biochem Biophys Res Comm*. 1993a; 193: 268-276.
- Ruat M, Traiffort E, Leurs R, Tardivel-Lacombe J, Diaz J, Arrang J-M and Schwartz J-C. Molecular cloning, characterization and localization of a high affinity serotonin receptor (5-HT₇) activating cAMP formation. *Proc Natn Acad Sci USA*. 1993b; 90: 8547-8551.
- Ruda MA, Hayes RL, Price DD, Hu JW and Dubner R. Inhibition of nociceptive reflexes in the primate by electrical stimulation or narcotic microinjections at medial mesencephalic and diencephalic sites: Behavioural and electrophysiological analgesia. *Proc Soc Neurosci*. 1976; 2: 952.
- Rudnick G. In: Holmsen H. (eds). *Platelet Function and Metabolism*. Press, New York, Vol 2, 1986; 1-27.
- Sacerdote P, Monza G, Mantegazza P, Pancrai AE. Diclofenac and piroprofen modify pituitary and hypothalamic beta-endorphin concentrations. *Pharmacol Res Commun*. 1985; 17: 679-684.

- Sandrini G, Alfonsi E, DeRisky C, Marini S, Facchinetti F and Nappi G. Evidence for 5-HT₂ receptor involvement in analgesia in humans. *Eur J Pharmacol.* 1986; 130: 311-314.
- Sandrini G, Ruiz L, Capararo M, Garafoli F, Beretta A and Noppi G. Central analgesic activity of ibuprofen, a neurophysiological study in humans. *Int J Clin Pharm Res.* 1992; 12: 197-204.
- Sandrini M, Vitale G, Pini LA, Sternieri E and Bertolini A. Effects of chronic treatment with phenazone on the hot plate test and [³H]serotonin binding sites in pons and cortex membranes of the rat. *Pharmacol.* 1993; 47: 84-90.
- Salzman AG, Morse B, Whitman MW, Ivanshchenko Y, Jaye M and Felder S. Cloning of the human 5-HT₂ and 5-HT_{1C} receptor subtypes. *Biochem Biophys Res Commun.* 1991; 181: 1469-1478.
- Sawynock J. The role of ascending and descending noradrenergic and serotonergic pathways in opioid and non-opioid antinociception as revealed by lesion studies. *Can J Physiol Pharmacol.* 1989; 67: 975-988.
- Sawynock J and Reid A. Noradrenergic mediation of spinal antinociception by 5-HT: characterization of receptor subtypes. *Eur J Pharmacol.* 1992, 223: 49-56.
- Scheffel U and Hartig PR. In vivo labeling of serotonin uptake sites with [³H]paroxetine. *J Neurochem.* 1989; 52: 1605-1612.
- Schmidt AW and Peroutka SJ. Three dimensional steric molecular modeling of the 5-HT₃ receptor pharmacophore. *Mol Pharmacol.* 1989; 36:505-511.
- Segonzac A, Raisman R, Tateishi T, Schoenmaker H, Hicks PE and Langer SZ. Tryptamine, a substrate for the serotonin transporter in human platelets, modifies the dissociation kinetics of [³H]imipramine. *J Neurochem.* 1985; 44: 349-356.

- Segonzac A, Schoenmaker H and Langer SZ. Temperature dependence of drug interaction with the platelet 5-HT transporter. A clue to the imipramine selectivity paradox. *J Neurochem.* 1987; 48: 331-339.
- Sette M, Briley MS and Langer SZ. Complex inhibition of [³H]imipramine binding by serotonin and non-tricyclic serotonin uptake blockers. *J Neurochem.* 1983; 40: 622-625.
- Sette M, Raisman R, Briley MS and Langer SZ. Localization of tricyclic antidepressant binding sites on serotonin nerve terminals. *J Neurochem.* 1981; 37: 40-42.
- Sharpley AL, Solomon RA, Fernando AI, da Roza Davis JM and Cowen PJ. Dose-related effects of selective 5-HT₂ receptor antagonists on slow wave sleep in humans. *Psychopharmacol.* 1990; 101: 568-569.
- Shen Y, Monsma FJ Jr, Metcalf MA, Jose PA, Hamblin MW and Sibley DR. Molecular cloning and expression of a 5-HT₇ receptor subtype. *J Biol Chem.* 1993; 268: 18200-18204.
- Shopsin B, Cassano GB and Contin L. In: Enna SJ, Malik JB and Richelson E (eds). *Antidepressants: Neurochemical and Clinical Perspectives* by, Raven Press, New York. 1981; 219-251.
- Shyu KW and Lin MT. Hypothalamic monoaminergic mechanisms of aspirin-induced analgesia in monkeys. *J Neural Transm.* 1985; 62: 285-288.
- Siegel GJ, Bernard W, Agranoff RW and Molnoff PB. *Basic Neurochemistry: Molecular, Cellular and Medical aspects.* 5th ed. Raven Press New York. 1994.

- Smullin DH, Skilling SR, Larson AA. Interactions between substance P, calcitonin gene-related peptide, taurine and excitatory amino acids in the spinal cord. *Pain*. 1990; 42: 93-101.
- Sneddon JM. Blood platelet as a model for monoamine containing neurons. *Prog Neurobiol*. 1973; 1: 153-198.
- Snyder SH. Putative neurotransmitter in the brain: selective neuronal uptake, subcellular localization and interactions with centrally acting drugs. *Biol Psychiatry*. 1970; 2: 367-389.
- Solomon RE and Gebhart CF. Intrathecal morphine and clonidine: Antinociceptive tolerance and cross-tolerance and effects on blood pressure. *J Pharmacol Exp Ther*. 1988; 245: 905-912.
- Srikiatkachorn A and Anthony M. Platelet serotonin in patients with analgesics induced headache. *Cephalalgia*. 1996; 16: 423-426.
- Srikiatkachorn A, Govitrapong P, Limthavon C. Up-regulation of 5-HT₂ receptor: a possible mechanism of transformed migraine. *Headache*. 1994; 34: 8-11.
- Stark P, Fuller RW and Wong DT. The pharmacologic profile of fluoxetine. *J Clin Psychiat*. 1985; 46: 7-13.
- Steinbusch HWM. Distribution of serotonin-immunoreactivity in the central nervous system of the rat cell bodies and terminals. *Neurosci*. 1981; 6: 557-618.
- Steinbusch HWM. Serotonin-immunoreactive neurons and their projections in the CNS. In: Bjorklund A, Hokfelt T and Kuhar MJ. (eds). *Handbook of Chemical Neuroanatomy, Vol.3, Classical Transmitters and Transmitter Receptors in the CNS, Part II*. Elsevier, Amsterdam. 1984; 68-125.

- Taber RI and Latranyi MB. Antagonism of the analgesic effect of opioid and non-opioid agents by p-chlorophenylalanine (PCPA). *Eur J Pharmacol.* 1981; 75: 215-222.
- Taiwa YO and Levine JD. Prostaglandins inhibit endogenous pain control mechanisms by blocking transmission at spinal noradrenergic synapses. *J Neurosci.* 1988; 8: 1346-1349.
- Talvenheimo J, Fishkes H, Nebon PJ and Rudnick G. The serotonin transporter-imipramine "receptor". *J Biol Chem.* 1983; 258: 6115-6119.
- Talvenheimo J, Nelson PJ and Rudnick G. Mechanism of imipramine inhibition of platelet 5-hydroxytryptamine transport. *J Biol Chem.* 1979; 254: 6431-6435.
- Teitler M, Leonhardt S, Weisberg EI and Hoffman BJ. 4-[¹²⁵I]Iodo-(2,5-dimethoxy) phenylisopropylamine and [³H]ketanserin labeling of 5-HT₂ receptors in mammalian cell transfected with a rat 5-HT₂ cDNA: evidence for multiple states and not multiple 5-HT₂ receptor. *Mol Pharmacol.* 1990; 38: 594-598.
- Thomas DR, Nelson DR and Johnson AM. Biochemical effects of the antidepressant paroxetine, a specific 5-HT uptake inhibitor. *Psychopharmacol.* 1987; 93: 193-200.
- Tjølsen A, Lund A and Hole K. Antinociceptive effect of paracetamol in rats is partly dependent on spinal serotonergic systems. *Eur J Pharmacol.* 1991; 193: 193-201.
- Todd AJ and Millar J. Receptive fields and responses to iontophoretically applied noradrenaline and 5-HT of units recorded in lamina I-III of cat dorsal horn. *Brain Res.* 1982; 288: 159-167.
- Todd AJ and Millar J. Antagonism of 5-HT-evoked excitation in the superficial dorsal horn by methysergide. *Neurosci Lett.* 1984; 48: 167-170.

- Tolman EL, Fuller BL and Marinan BA. Tissue selectivity and variability of effect of acetaminophen on arachidonic acid metabolism. *Prostaglandins Leukotrienes Med.* 1983; 12: 347-356.
- Tsou A-P, Kosaka A, Bach C, Zuppan P, Yee C, Tom L, Alvarez R, Ramsey S, Bonhaus DW, Stefanich E, Jakeman L, Eglen RM and Chan HW. Cloning and expression of a 5-hydroxytryptamine₇ receptor positively coupled to adenylyl cyclase. *J Neurochem.* 1994; 63: 456-464.
- Uphouse LA, Welch SP, Ward CR, Ellis EF and Embrey JP. Antinociceptive activity of intrathecal ketorolac is blocked by the κ -opioid receptor antagonist, norbinaltorphimine. *Eur J Pharmacol.* 1993; 242: 53-58.
- Vane J. The evolution of nonsteroidal anti-inflammatory drugs and their mechanisms of action. *Drugs.* 1987; 33 (suppl 1) : 18-27.
- Vane JR. Inhibition of prostaglandin synthesis as a mechanism of action for aspirin-like drugs. *Nature.* 1971; 231: 232-235.
- Vescovi P, Passeri M, Cerra G and Grossi E. Naloxone inhibits the early phase of diclofenac analgesia in man. *Pain Clinic.* 1987; 19: 151-155.
- Vitale G, Pini LA and Sandrini M. The effect of chronic treatment with phenazone on [³H]serotonin binding sites in pons and cortex membranes of the rat. *Pharmacol Res.* 1992; 25 (suppl 1) : 53-57.
- Von Meyring J. Beitrage zur Kenntniss der Antipyretica. *Therap Mschr.* 1893; 7: 577-587.
- Wainscott DB, Cohen ML, Schenck KW, Audia JE, Nissen JS, Baez M, Kursar JD, Lucaites VL and Nelson DL. Pharmacological characteristics of the newly cloned rat 5-HT_{2F} receptor. *Mol Pharmacol.* 1993; 43: 419-426.

- Walker MJK, Poulos CX, Le AD. Effects of acute selective 5-HT₁, 5-HT₂, 5-HT₃ receptor and α 2 adrenoceptor blockade on naloxone-induced antinociception. *Psychopharmacol.* 1994; 113: 527-533.
- Wall PD. The laminar organization of dorsal horn and effects of descending impulses. *J Physiol.* 1967; 188: 403-423.
- Wallis DI, Wu J, Wang XC. Is 5-HT mediating descending inhibition in the neonatal spinal cord through different receptor subtypes ? *Eur J Pharmacol.* 1993; 250: 371-377.
- Wang BC, Li D and Hiller J. The antinociceptive effect of S-(+)-ibuprofen in rabbits: epidural versus intravenous administration. *Anesth Analg.* 1995; 80: 92-96.
- Wang HY and Friedman E. Central 5-HT receptor-linked protein kinase C translocation: a functional postsynaptic signal transduction system. *Mol Pharmacol.* 1989; 37: 75-79.
- Wang JK. Antinociceptive effect of intrathecally administered serotonin. *Anaesthesiology.* 1977; 47: 269-271.
- Wang JP and Teng CM. Effects of anti-inflammatory drugs on rat hind-paw swelling caused by phospholipase A2 from *Naja naja* atra venom. *Naunyn Schmiedeburg's Arch Pharmac.* 1991; 344: 377-381.
- Warner RL, Hudson-Howard C and Skolnik M. Serotonin involvement in analgesia induced by transcranial electrostimulation. *Life Sci.* 1990; 48: 1131-1136.
- Weiss CF. Acetaminophen: potential pediatric hazard. *Pediatrics.* 1973: 52:883.
- Weissman G. Prostaglandins as modulators of inflammation, New Standards. *Arthr Care.* 1992; 3: 3-5.

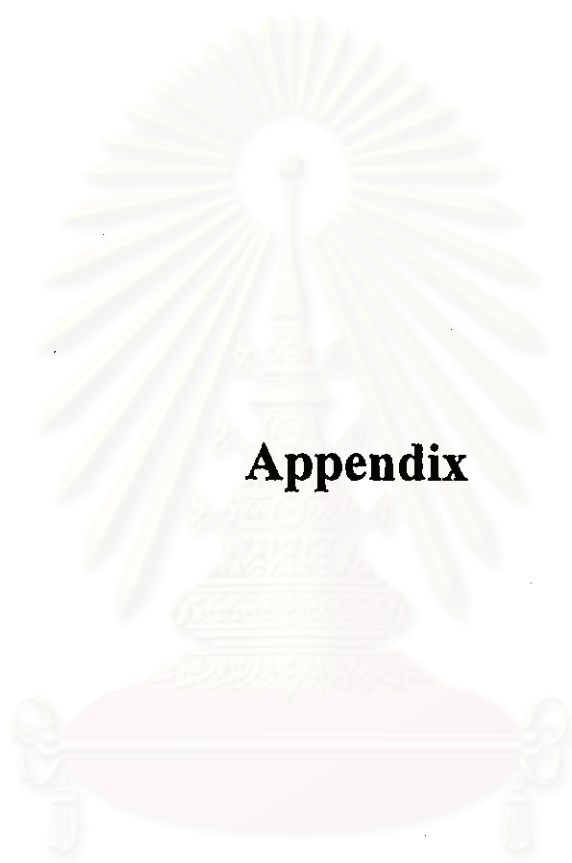
- Wilckens T, Schweiger U and Pirke KM. Activation of alpha2-adrenoceptors suppresses excessive wheel running in the semistarvation-induced hyperactive rat. *Pharmacol, Biochem and Behav.* 1992; 43: 733-738.
- Wilson MA, Molliver ME. The organization of serotonergic projections to cerebral cortex in primates: regional distribution of axon terminals. *Neurosci.* 1991a; 44: 537-553.
- Wilson MA, Molliver ME. The organization of serotonergic projections to cerebral cortex in primates. Retrograde transport studies. *Neurosci.* 1991b; 44: 555-570.
- Weksler BB, Pett SB, Alonso D. Differential inhibition by aspirin of vascular and platelet prostaglandin synthesis in atherosclerotic patients. *N Engl J Med.* 1983; 308: 800-805.
- Xu W, Qiu XC and Han JS. Serotonin receptor subtypes in spinal antinociception in the rat. *J Pharmacol Exp Ther.* 1994; 269: 1182-1189.
- Yaksh TL. Direct evidence that spinal serotoni and noradrenaline terminals mediate the spinal antinociceptive effects of morphine in the periaqueductal gray. *Brain Res.* 1979; 160: 180-185.
- Yaksh TL and Hammond DL. Peripheral and central substrates involved in the rostral transmission of nociceptive information. *Pain.* 1982; 13: 1-85.
- Yaksh TL and Rudy TA. Narcotic analgetics: CNS sites and mechanisms of action as revealed by intracerebral injection techniques. *Pain.* 1978; 4: 299-359.
- Yaksh TL and Wilson PR. Spinal serotoni terminal system mediates antinociception. *J Pharmacol Exp Ther.* 1979; 208: 446-453.
- Yang W, Chen K, Grimsby J and Shih JC. Human 5-HT₂ receptor encoded by a multiple intron-exon containing gene. *Soc Neurosci Abstr.* 1991; 17: 405.

Zemlan FP, Kow L-M and Plaff DW. Spinal serotonin receptor subtypes and nociception. *J Pharmacol Exp Ther.* 1983; 226: 477-485.

Zemlan FP, Murphy AZ and Behbehani MM. 5-HT_{1A} receptors mediate the effect of the bulbospinal serotonin system on spinal dorsal horn nociceptive neurons. *Pharmacol.* 1994; 48: k1-10.



สถาบันวิทยบริการ
จุฬาลงกรณ์มหาวิทยาลัย



Appendix

สถาบันวิทยบริการ
จุฬาลงกรณ์มหาวิทยาลัย

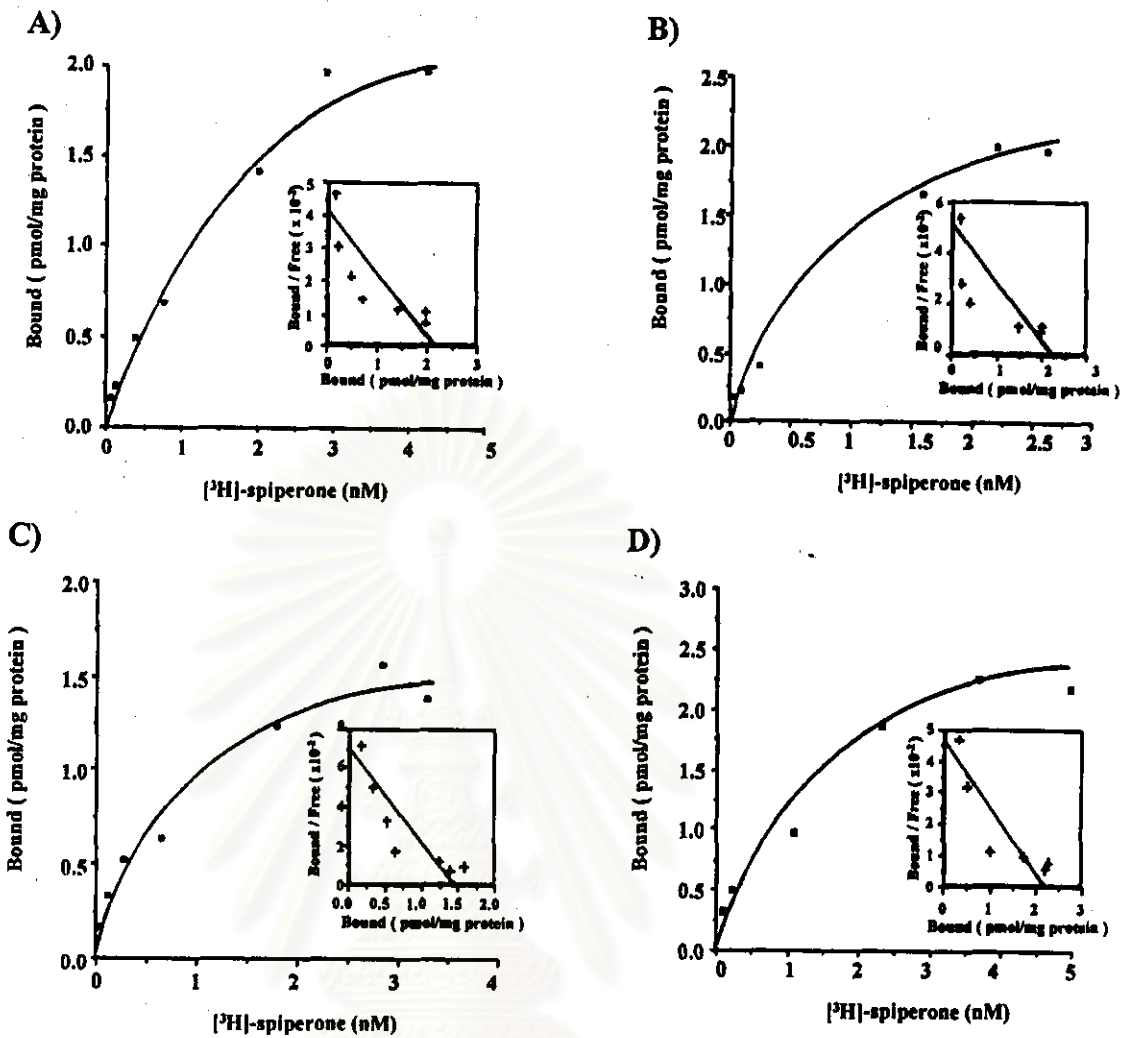


Figure 87A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -spiperone binding on frontal cortex membrane of control rat number 1 - 4, treated with vehicle i.p. once daily for 15 days. The binding was carried out in the concentrations of $[^3\text{H}]$ -spiperone ranging from 0.02 - 5 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -spiperone. The line of best fit was analysed by the LIGAND computer program. The result of this experiment was shown and provided a K_d value of 1.9 (A), 1.3 (B), 0.8 (C), 1.3 (D) nM and B_{max} value of 2.24 (A), 2.26 (B), 1.49 (C), 2.28 (D) pmol/mg protein.

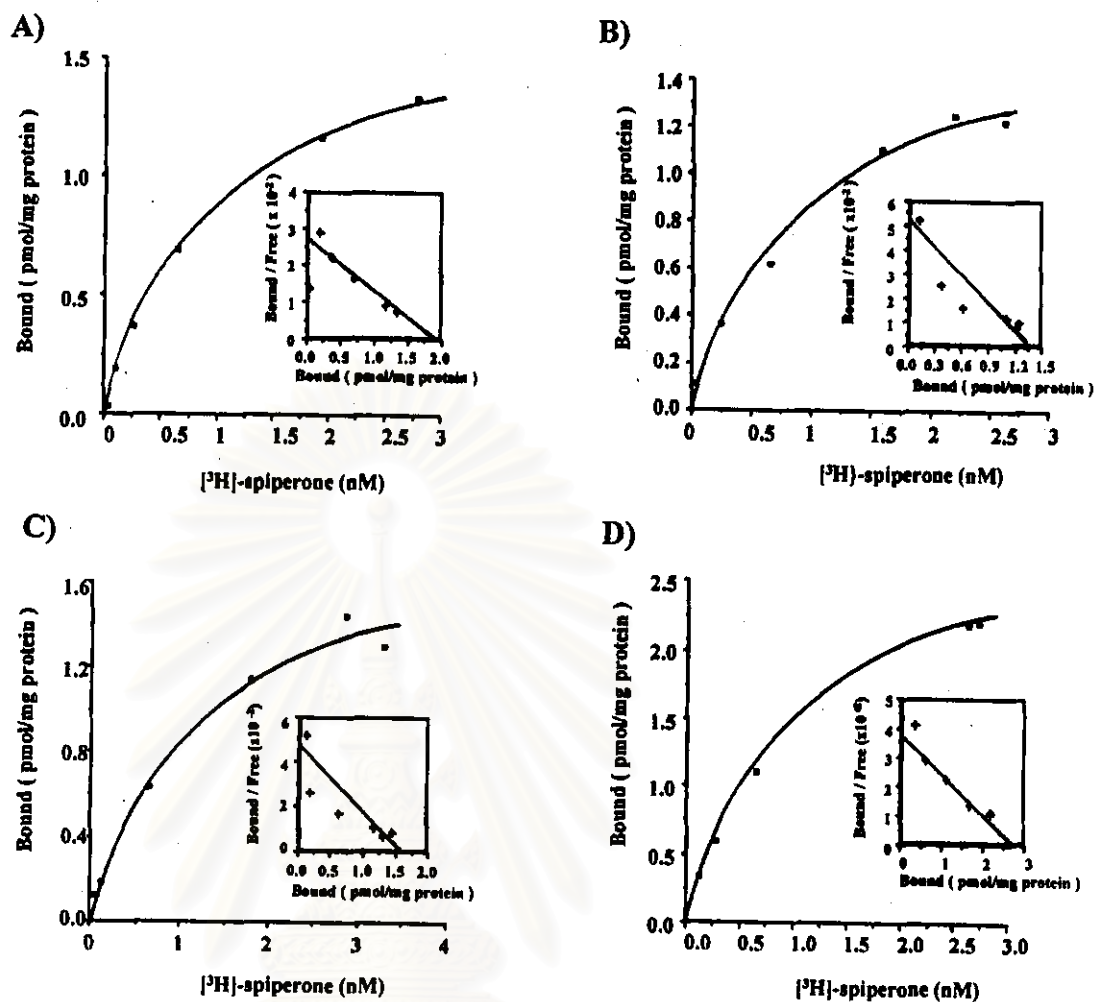


Figure 88A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -spiperone binding on frontal cortex membrane of rat number 7 - 10, treated with paracetamol 200 mg/kg/day i.p. for 15 days. The binding was carried out in the concentrations of $[^3\text{H}]$ -spiperone ranging from 0.01 - 4 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -spiperone. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 2.5 (A), 0.9 (B), 1.2 (C), 1.7 (D) nM and B_{max} value of 2.01 (A), 1.38 (B), 1.55 (C), 2.76 (D) pmol/mg protein.

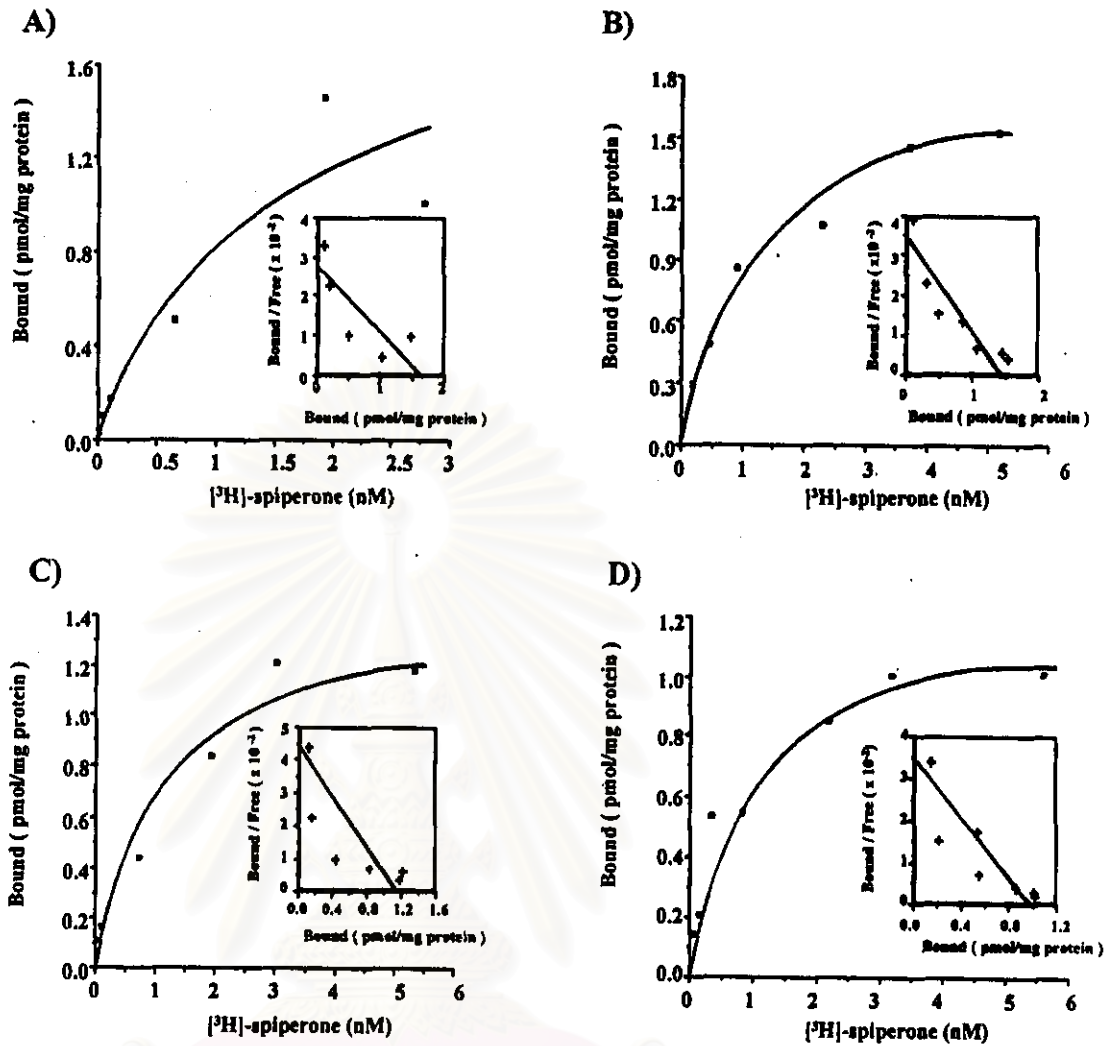


Figure 89A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -spiperone binding on frontal cortex membrane of rat number 11 - 14, treated with paracetamol 300 mg/kg/day i.p. for 15 days. The binding was carried out in the concentrations of $[^3\text{H}]$ -spiperone ranging from 0.03 - 6 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -spiperone. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 1.2 (A and B), 1.1 (C), 0.7 (D) nM and B_{max} value of 1.54 (A), 1.42 (B), 1.17 (C), 0.99 (D) pmol/mg protein.

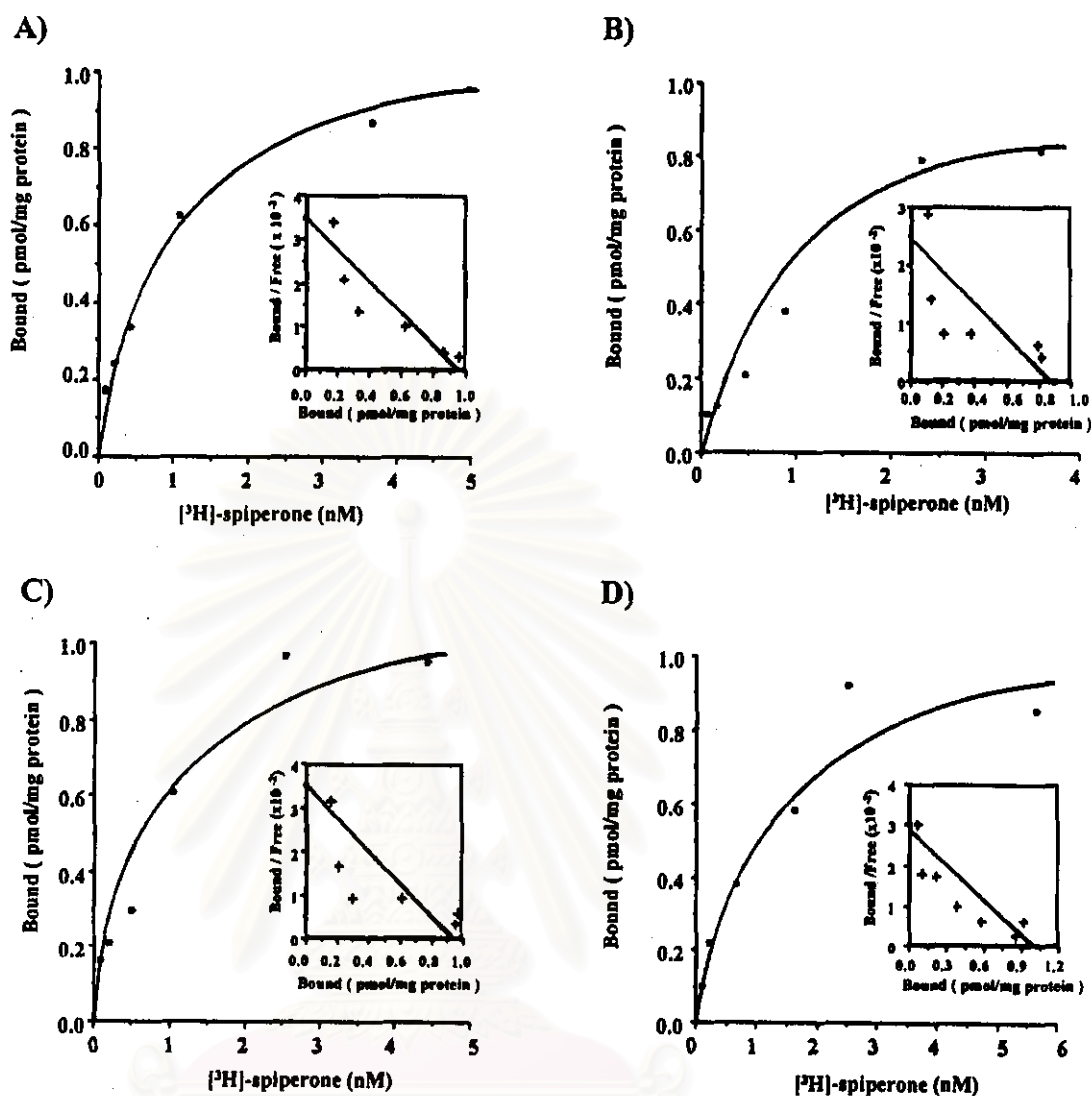


Figure 90A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -spiperone binding on frontal cortex membrane of rat number 16-19, treated with paracetamol 400 mg/kg/day i.p. for 15 days. The binding was carried out in the concentrations of $[^3\text{H}]$ -spiperone ranging from 0.01 -6 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -spiperone. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 1.0 (A), 1.5 (B), 1.4 (C), 1.3 (D) nM and B_{max} value of 0.96 (A), 0.88 (B), 0.95 (C), 0.94 (D) pmol/mg protein.

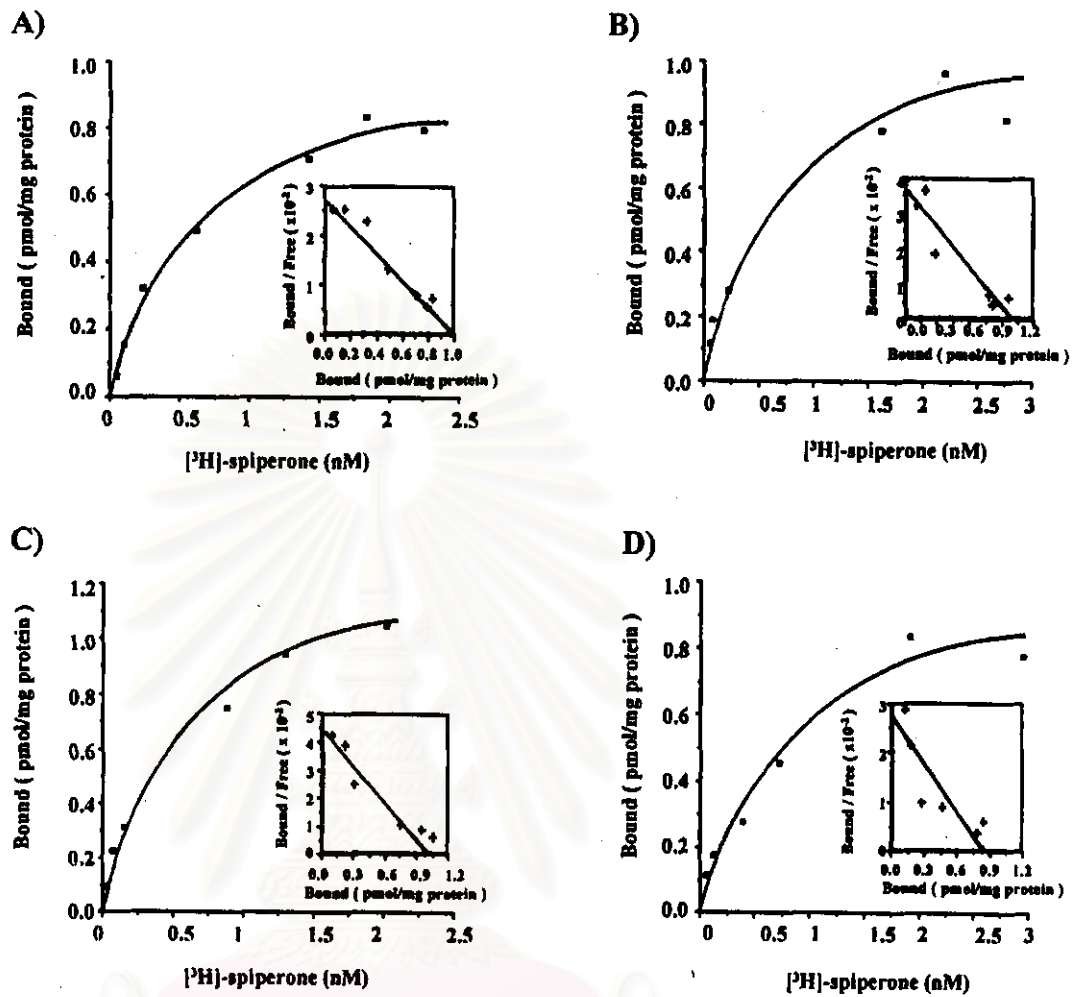


Figure 91A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -spiperone binding on brain stem membrane of control rat number 1 - 4, treated with vehicle i.p. once daily for 15 days. The binding was carried out in the concentrations of $[^3\text{H}]$ -spiperone, ranging from 0.02 - 3 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -spiperone. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 1.2 (A), 0.8 (B), 0.6 (C), 0.9 (D) nM and B_{max} value of 1.03 (A), 0.99 (B), 1.12 (C), 0.86 (D) pmol/mg protein.

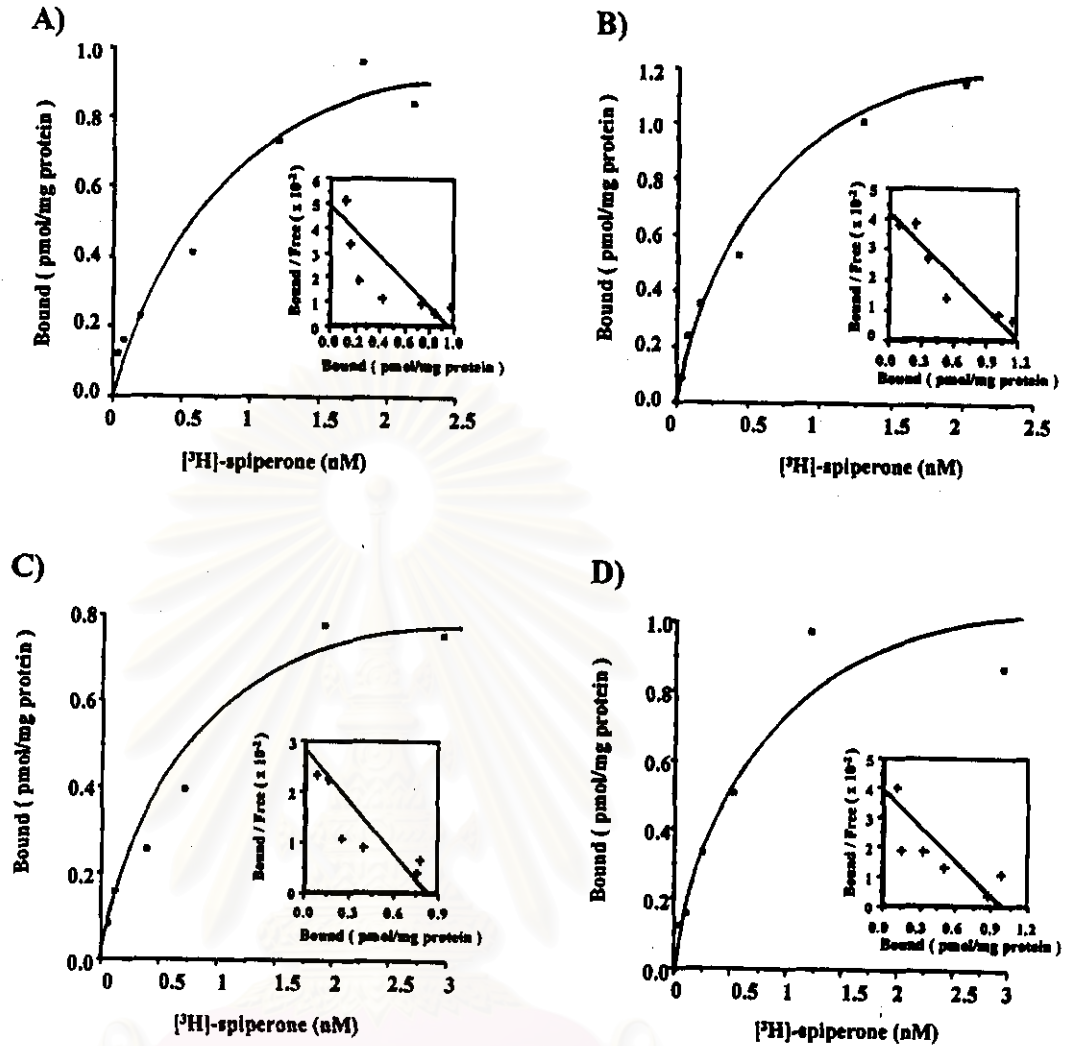


Figure 92A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -spiperone binding on brain stem membrane of rat number 7-10, treated with paracetamol 200 mg/kg/day i.p. for 15 days. The binding was carried out in the concentrations of $[^3\text{H}]$ -spiperone ranging from 0.01 - 3 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -spiperone. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 0.6 (A), 0.7 (B), 1.2 (C), 0.8 (D) nM and B_{max} value of 0.91 (A), 1.23 (B), 0.88 (C), 1.05 (D) pmol/mg protein.

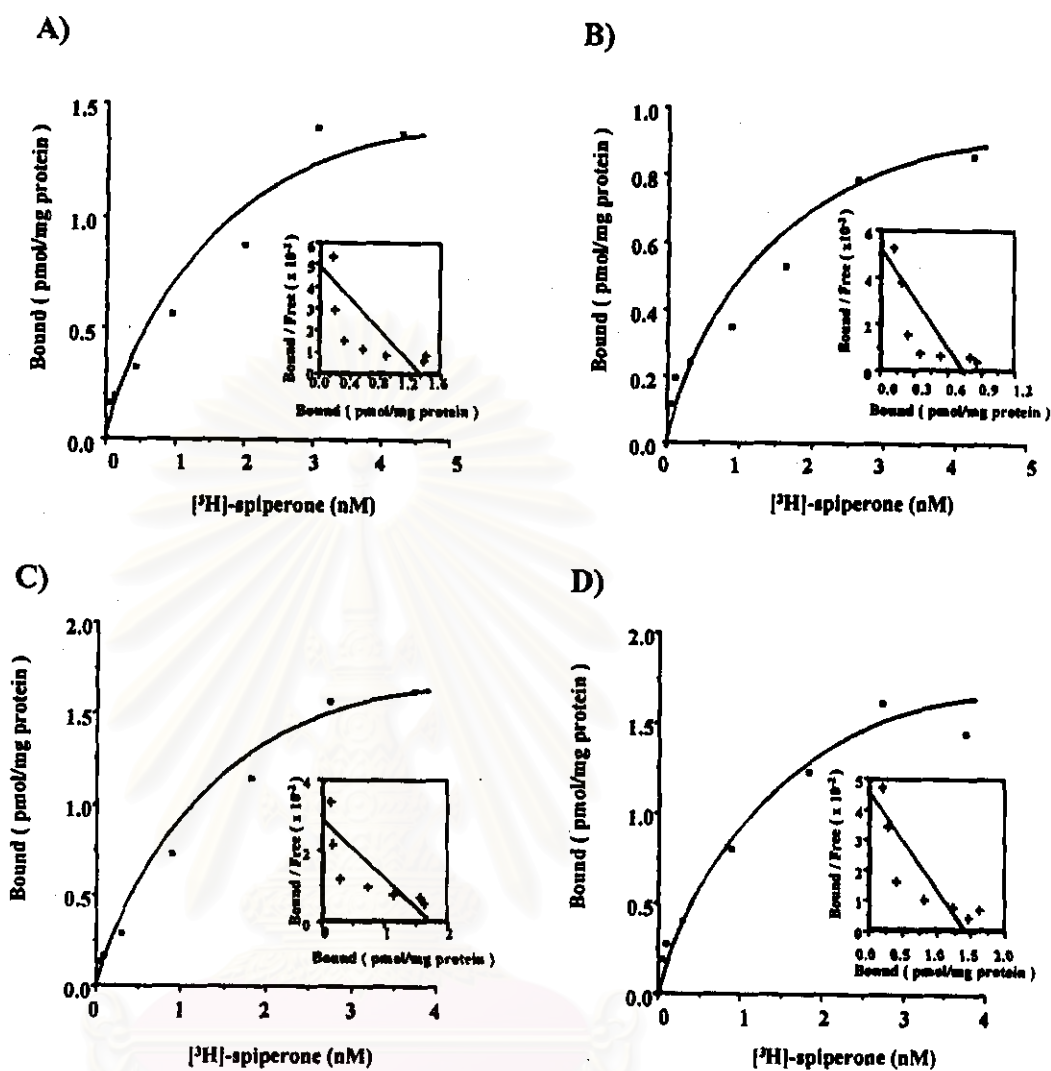


Figure 93A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -spiperone binding on brain stem membrane of rat number 11 - 14, treated with paracetamol 300 mg/kg/day i.p. for 15 days. The binding was carried out in the concentrations of $[^3\text{H}]$ -spiperone ranging from 0.01 - 5 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -spiperone. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 1.0 (A), 0.5 (B), 1.6 (C), 0.8 (D) nM and B_{max} value of 1.28 (A), 0.71 (B), 1.79 (C), 1.49 (D) pmol/mg protein.

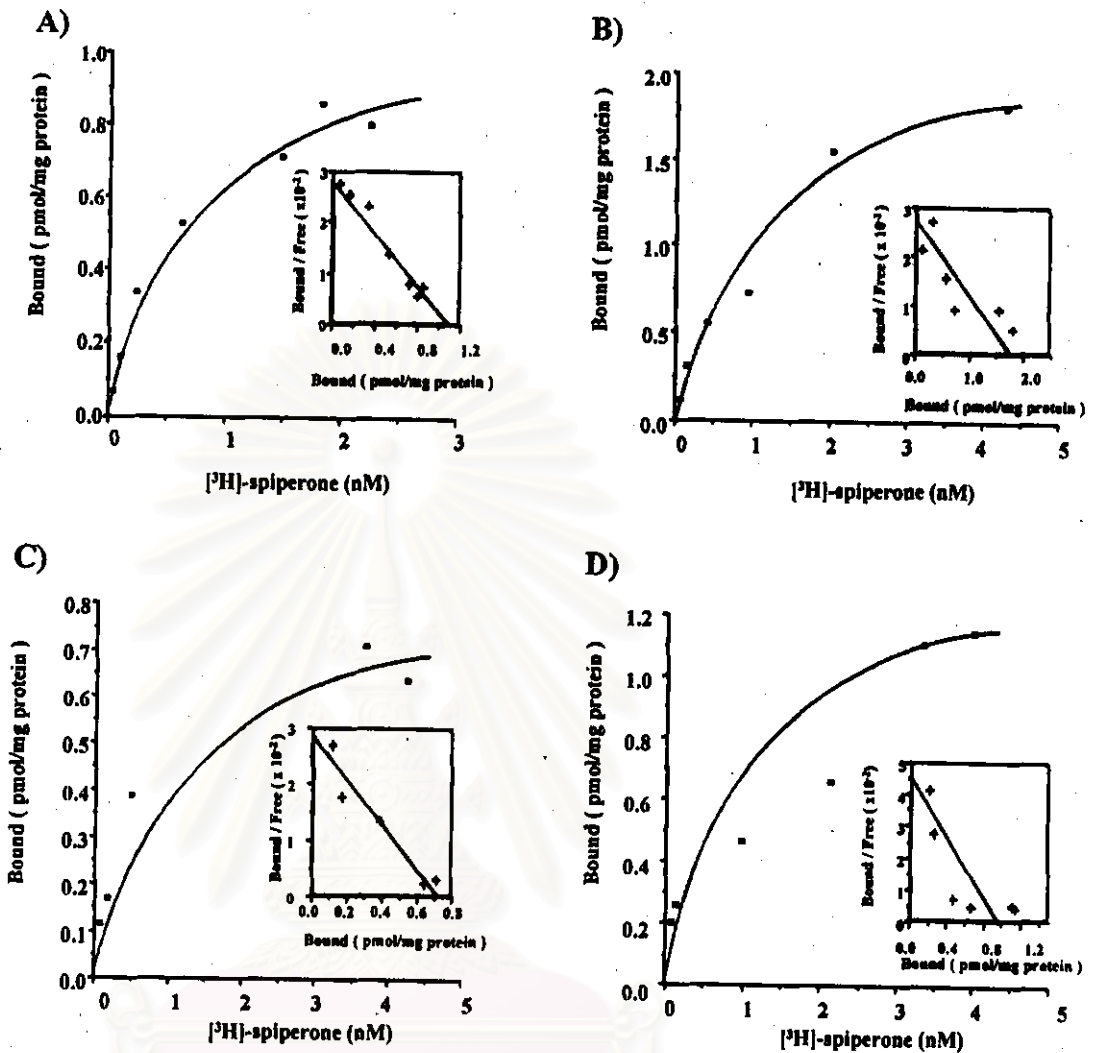


Figure 94A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -spiperone binding on brain stem membrane of rat number 15 - 18, treated with paracetamol 400 mg/kg/day i.p. for 15 days. The binding was carried out in the concentrations of $[^3\text{H}]$ -spiperone ranging from 0.01 - 5 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -spiperone. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 1.0 (A), 1.0 (B), 0.9 (C), 0.7 (D) nM and B_{max} value of 1.02 (A), 1.57 (B), 0.74 (C), 0.99 (D) pmol/mg protein.

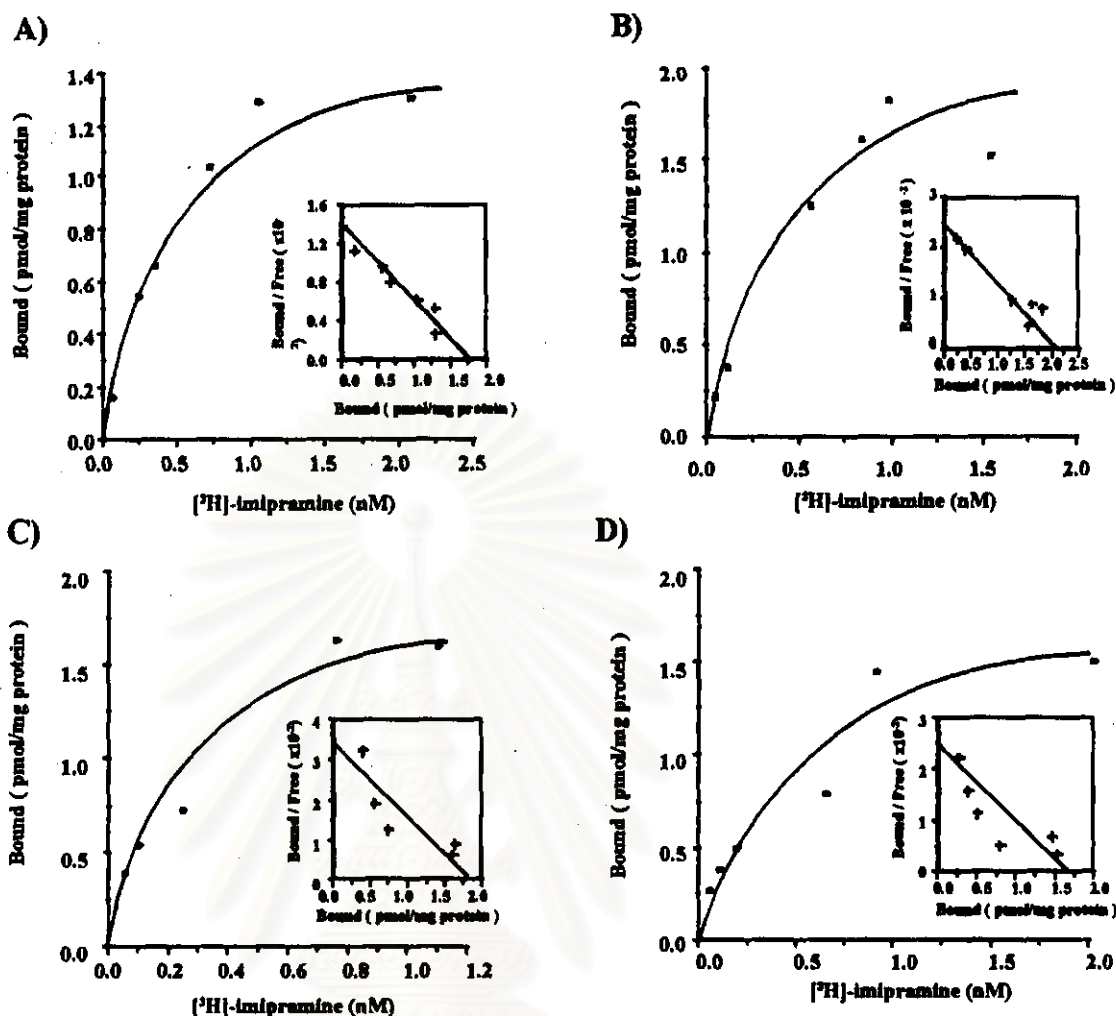


Figure 95A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -imipramine binding on frontal cortex membrane of control rat number 1-4, treated with vehicle for 15 days. The binding was carried out in the concentrations of $[^3\text{H}]$ -imipramine ranging from 0.02 - 2.5 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -imipramine. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 2.41 (A), 1.86 (B), 1.00 (C), 1.29 nM and B_{max} value of 1.85 (A), 2.28 (B), 1.91 (C), 1.63 (D) pmol/mg protein.

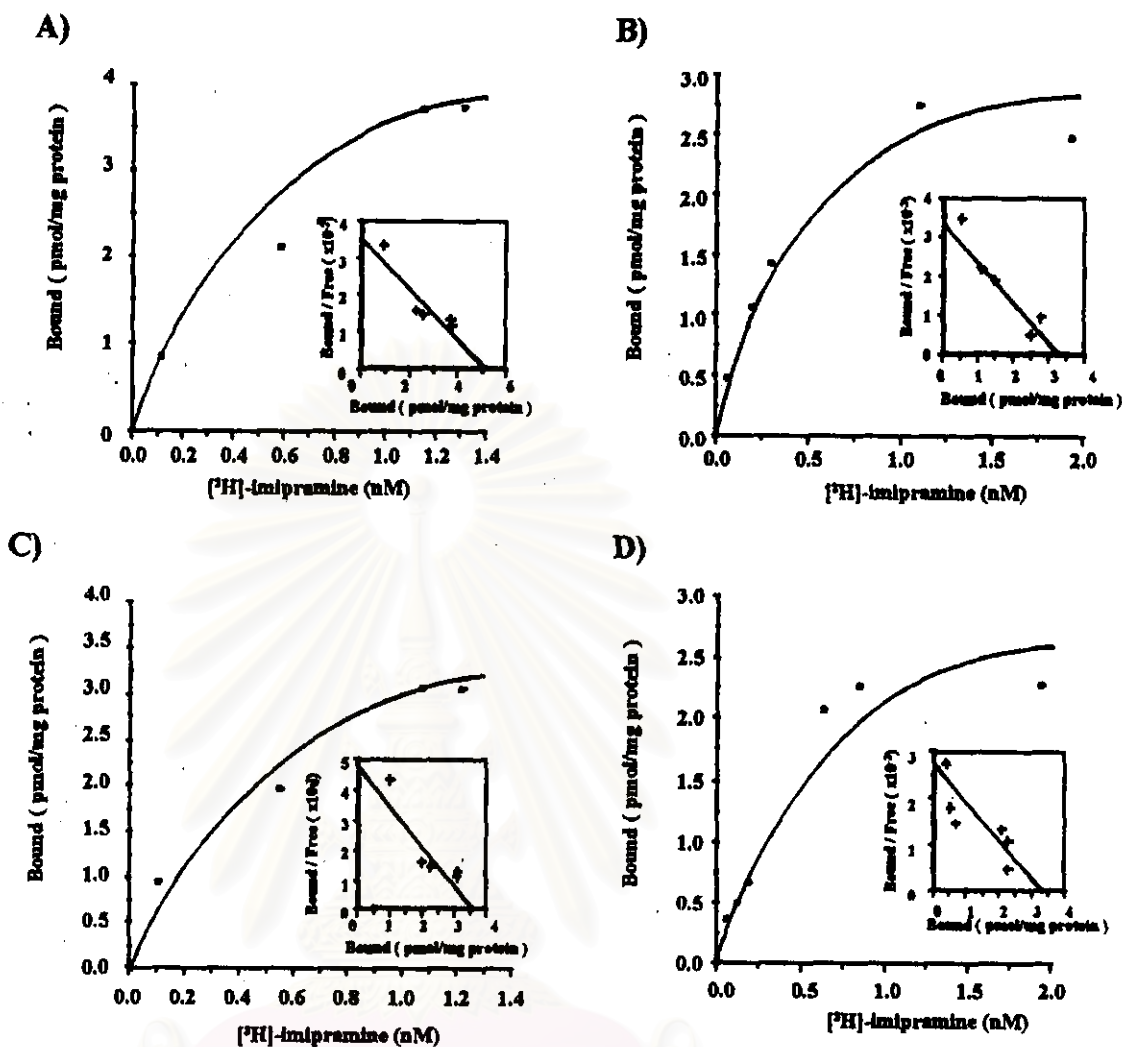


Figure 96A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -imipramine binding on frontal cortex membrane of rat number 6-9, treated with paracetamol 300 mg/kg/day i.p. for 15 days. The binding was carried out in the concentrations of $[^3\text{H}]$ -imipramine ranging from 0.1- 2 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -imipramine. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 2.23 (A), 1.24 (B), 1.22 (C), 2.11 (D) nM and B_{max} value of 5.03 (A), 3.11 (B), 3.51 (C), 3.30 (D) pmol/mg protein.

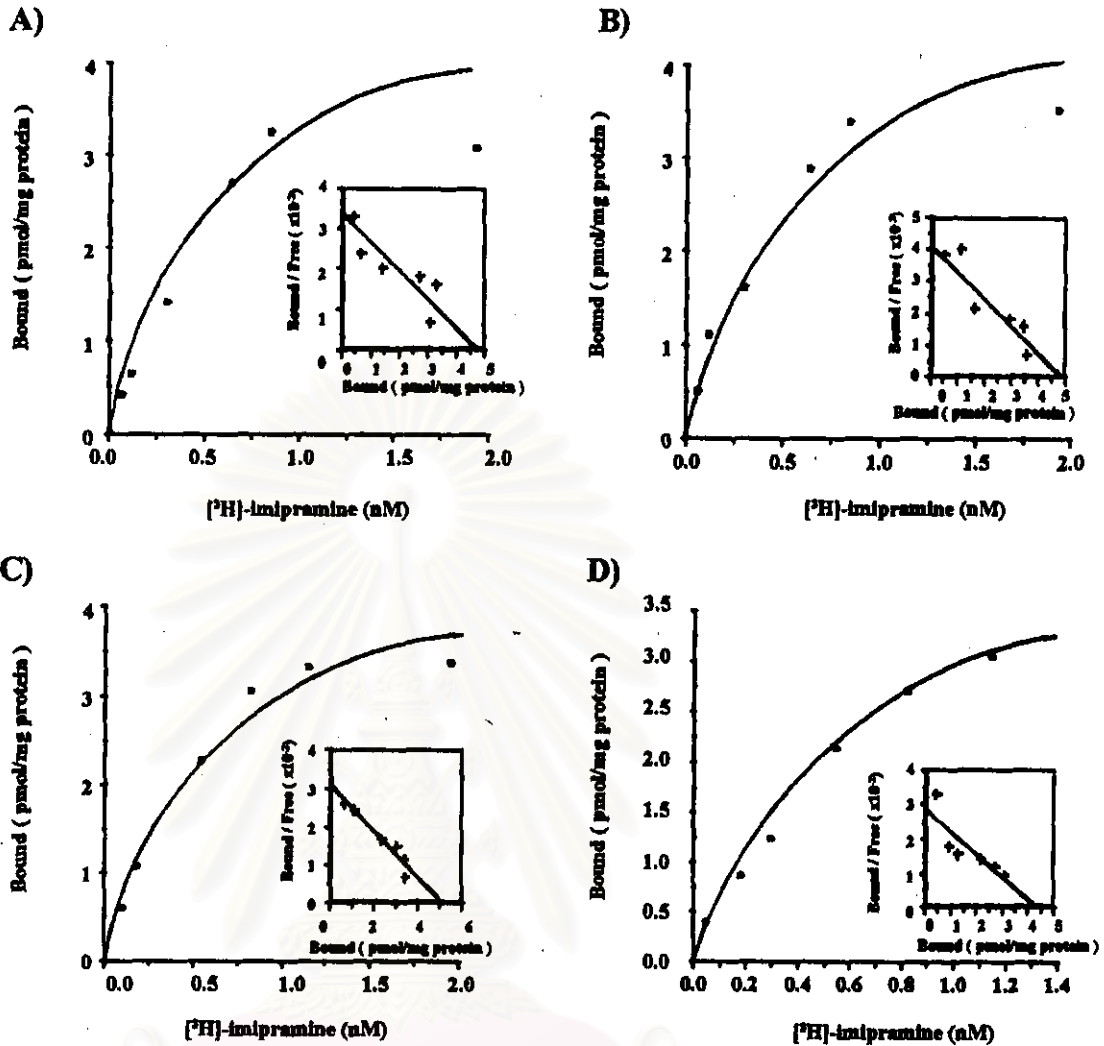


Figure 97A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -imipramine binding on frontal cortex membrane of rat number 10-13, treated with paracetamol 400 mg/kg/day i.p. for 15 days. The binding was carried out in the concentrations of $[^3\text{H}]$ -imipramine ranging from 0.02 - 2 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -imipramine. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 2.37 (A), 1.53 (B), 2.52 (C), 2.01 (D) nM and B_{max} value of 4.75 (A), 4.49 (B), 5.02 (C), 4.12 (D) pmol/mg protein.

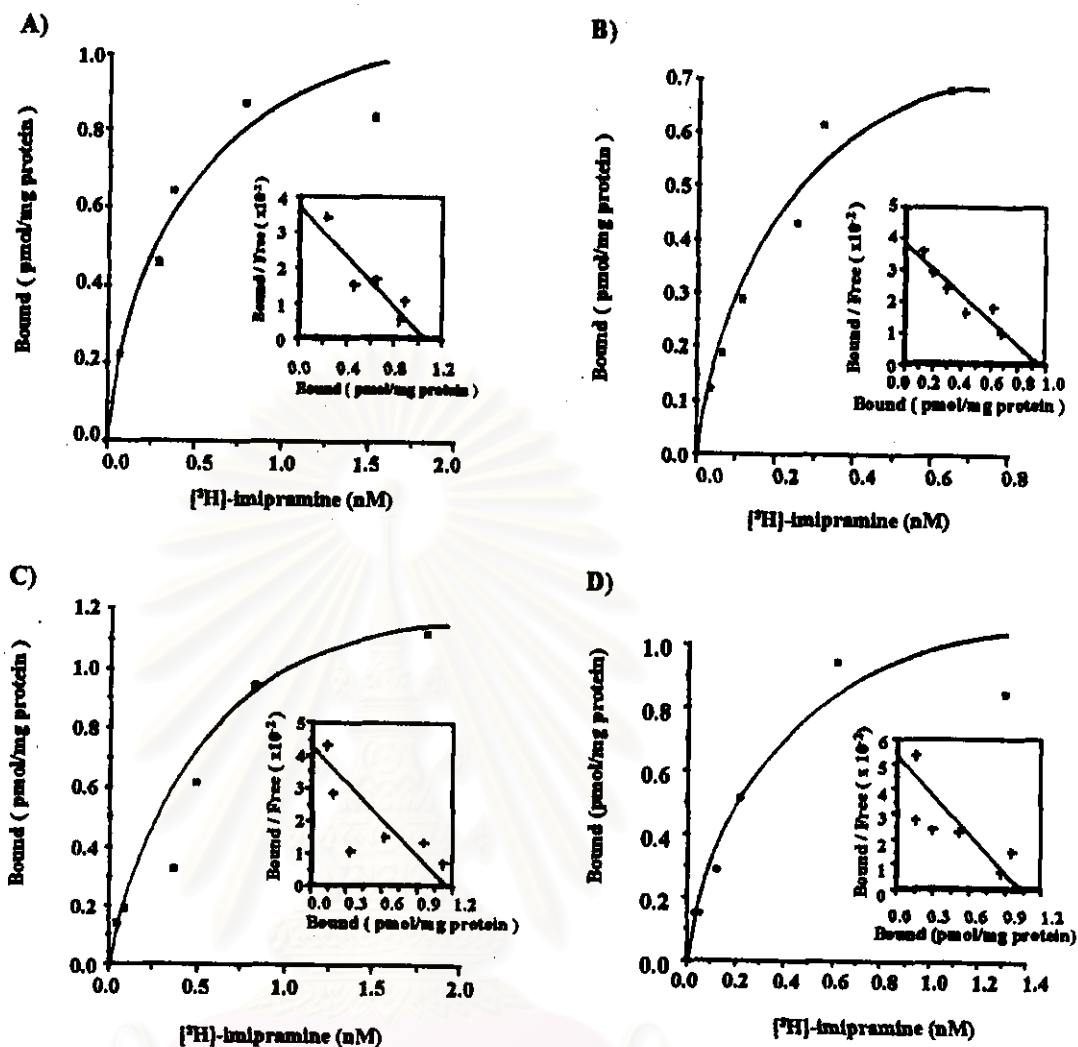


Figure 98A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -imipramine binding on brain stem membrane of control rat number 1- 4, treated with vehicle i.p. for 15 days. The binding was carried out in the concentrations of $[^3\text{H}]$ - imipramine ranging from 0.02 - 2 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -imipramine. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 0.91 (A), 0.89 (B), 1.47 (C) and 0.95 (D) nM, B_{max} value of 1.01 (A), 0.95 (B), 1.17 (C) and 1.10 (D) pmol/mg protein.

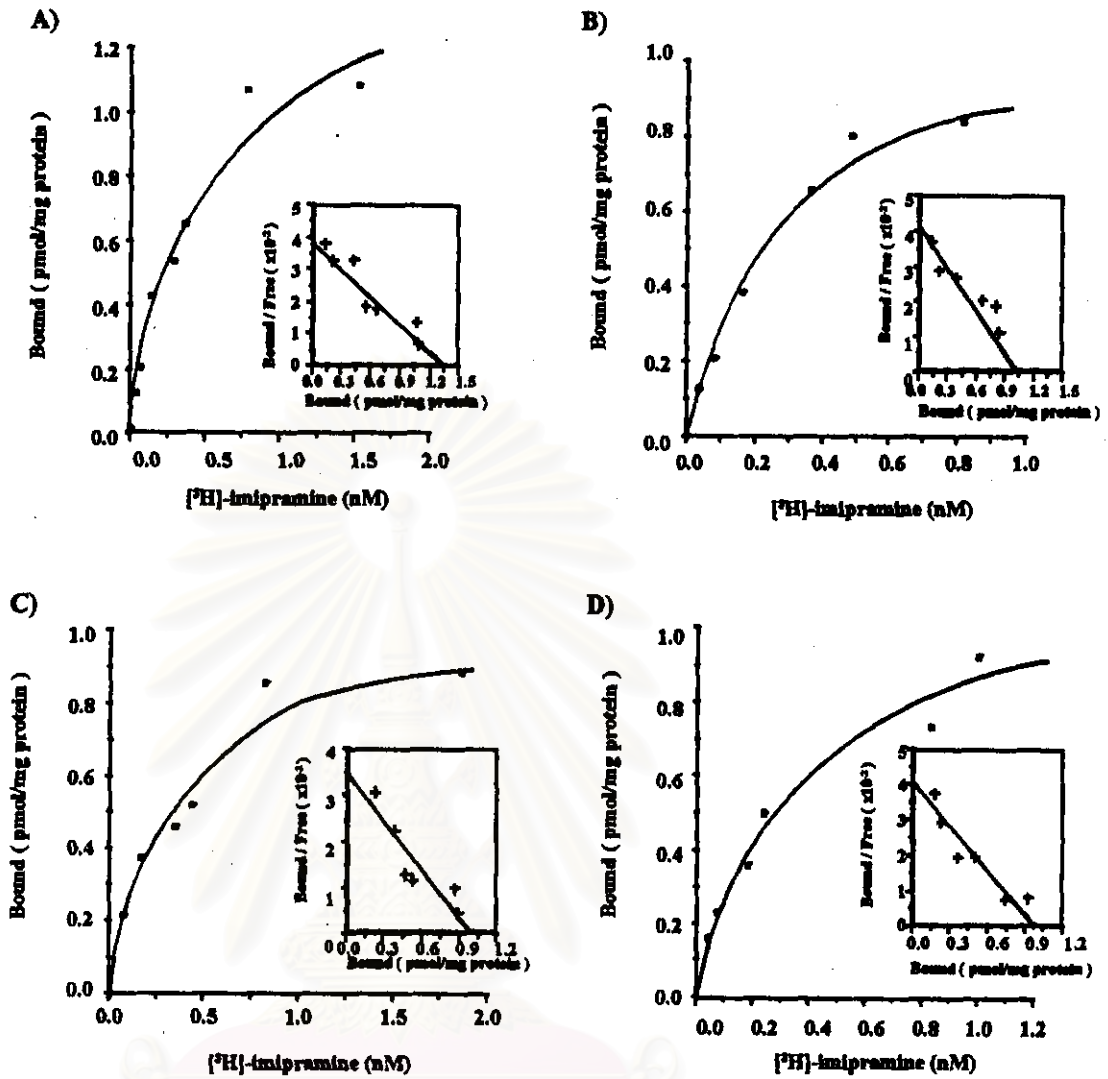


Figure 99A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -imipramine binding on brain stem membrane of control rat number 5- 8, treated with paracetamol 300 mg/kg/day i.p. for 15 days. The binding was carried out in the concentrations of $[^3\text{H}]$ - imipramine ranging from 0.01 - 3 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ - imipramine. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 1.29 (A), 1.50 (B), 1.04 (C) and 0.91 (D) nM and B_{max} value of 1.34 (A), 0.98 (B and C), 1.01 (D) pmol/mg protein.

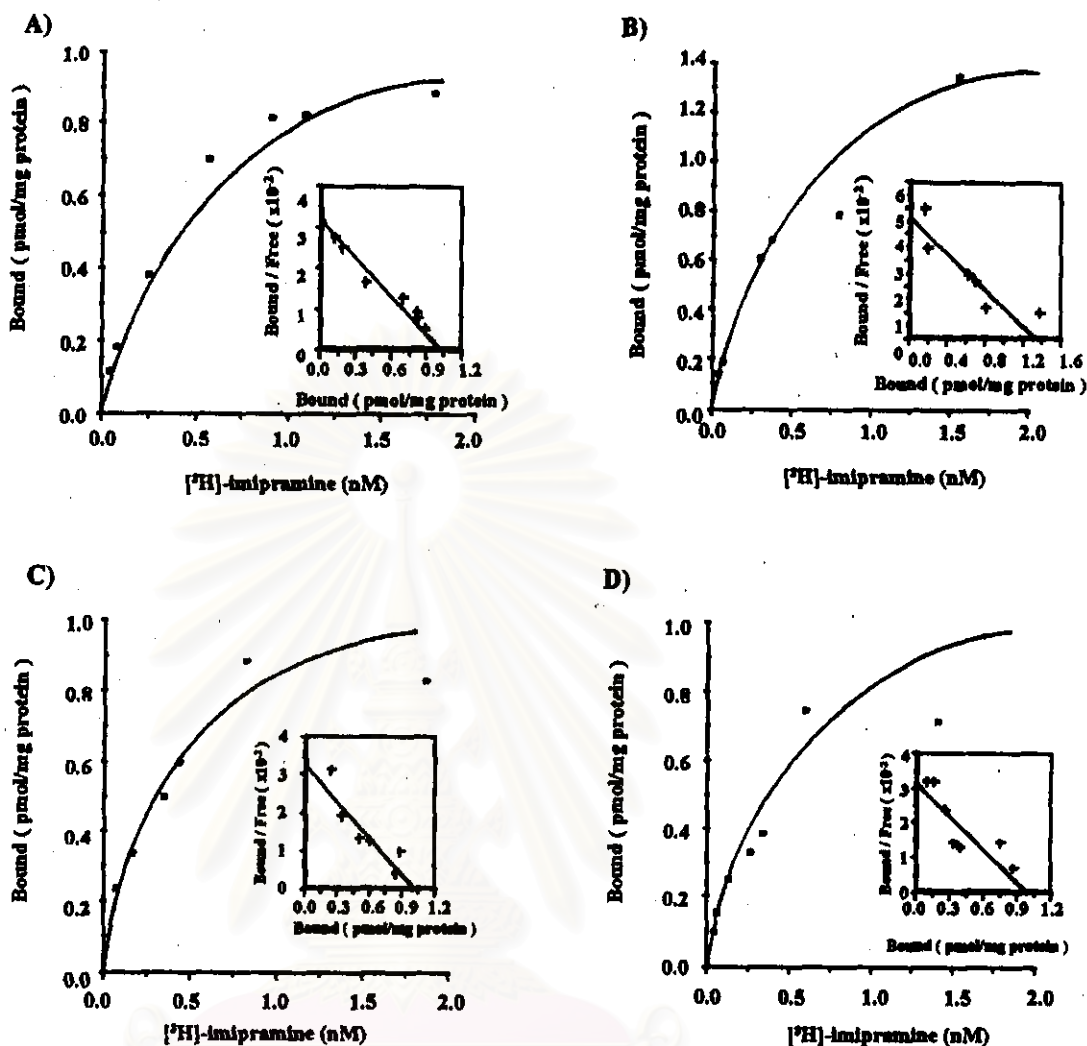


Figure 100A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -imipramine binding on brain stem membrane of control rat number 9- 12, treated with paracetamol 400 mg/kg/day i.p. for 15 days. The binding was carried out in the concentrations of $[^3\text{H}]$ - imipramine ranging from 0.01 - 3 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ - imipramine. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 1.54 (A), 1.32 (B), 1.00 (C) and 1.36 (D) nM and B_{max} value of 1.12 (A), 1.37 (B) 0.98 (C), 1.00 (D) pmol/mg protein.

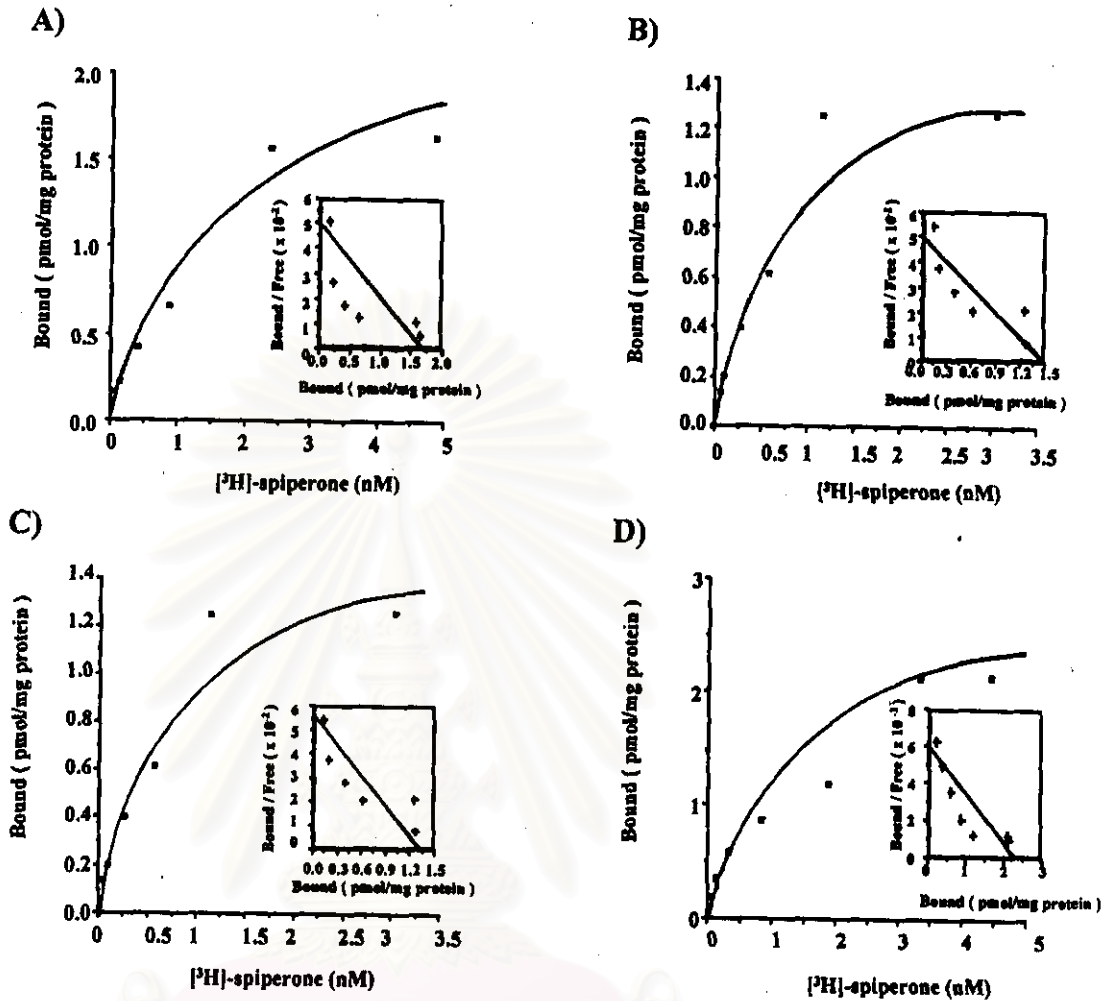


Figure 101A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -spiperone binding on frontal cortex membrane of control rat number 1-4 , treated with vehicle i.p. once daily for 30 days. The binding was carried out in the concentrations of $[^3\text{H}]$ -spiperone, ranging from 0.05 - 5 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -spiperone. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 1.4 (A), 1.2 (B and C), 1.5 (D) nM and B_{max} value of 1.67 (A), 1.55 (B), 2.83 (C), 2.14 (D) pmol/mg protein.

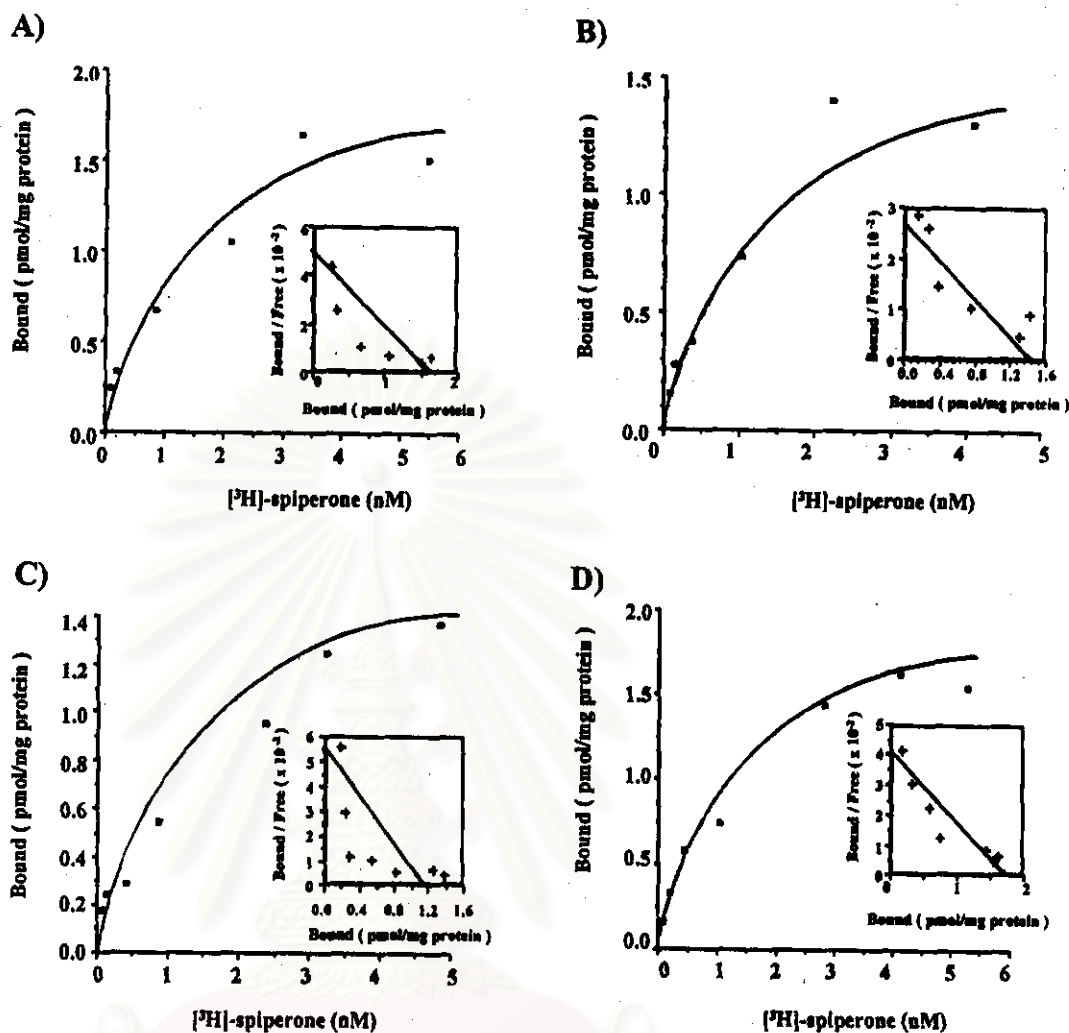


Figure 102A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -spiperone binding on frontal cortex membrane of rat number 7-10, treated with paracetamol 300 mg/kg/day i.p. for 30 days. The binding was carried out in the concentrations of $[^3\text{H}]$ -spiperone ranging from 0.3-6 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -spiperone. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 1.0 (A), 1.5 (B), 0.9 (C), 1.5 (D) nM and B_{max} value of 1.51(A), 1.57 (B), 1.14 (C), 1.71 (D) pmol/mg protein.

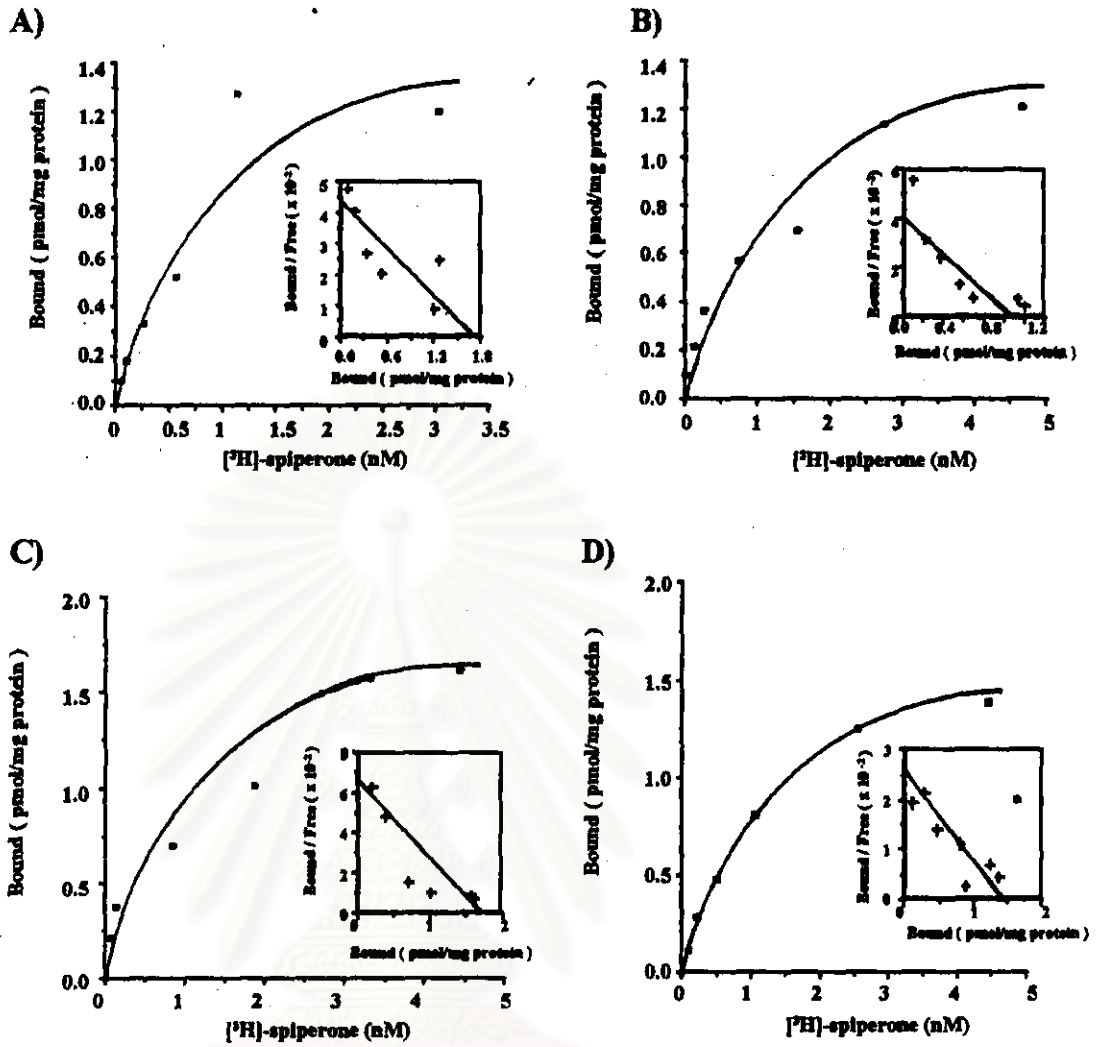


Figure 103A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -spiperone binding on frontal cortex membrane of rat number 12 - 15, treated with paracetamol 400 mg/kg/day i.p. for 30 days. The binding was carried out in the concentrations of $[^3\text{H}]$ -spiperone ranging from 0.01 - 5 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -spiperone. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 1.5 (A), 0.8 (B), 0.9 (C), 1.7 (D) nM and B_{max} value of 1.65 (A), 1.09 (B), 1.52 (C), 1.48 pmol/mg protein.

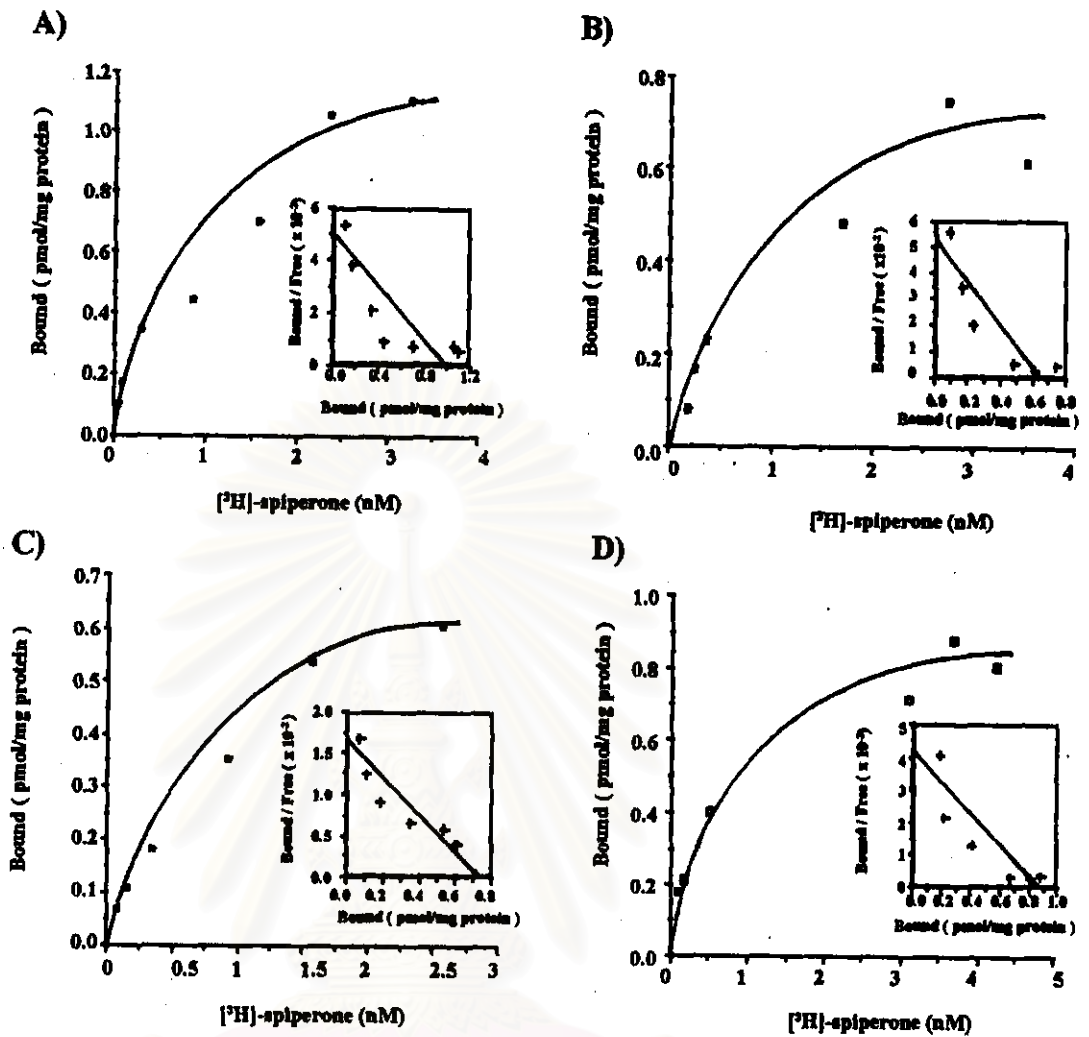


Figure 104A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -spiperone binding on brain stem membrane of control rat number 1 - 4 , treated with vehicle i.p. for 30 days. The binding was carried out in the concentrations of $[^3\text{H}]$ -spiperone ranging from 0.01 - 5 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -spiperone. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 0.7 (A), 0.5 (B), 1.6 (C), 0.6 (D) nM and B_{max} value of 0.97 (A), 0.66 (B), 0.76 (C), 0.82 (D) pmol/mg protein.

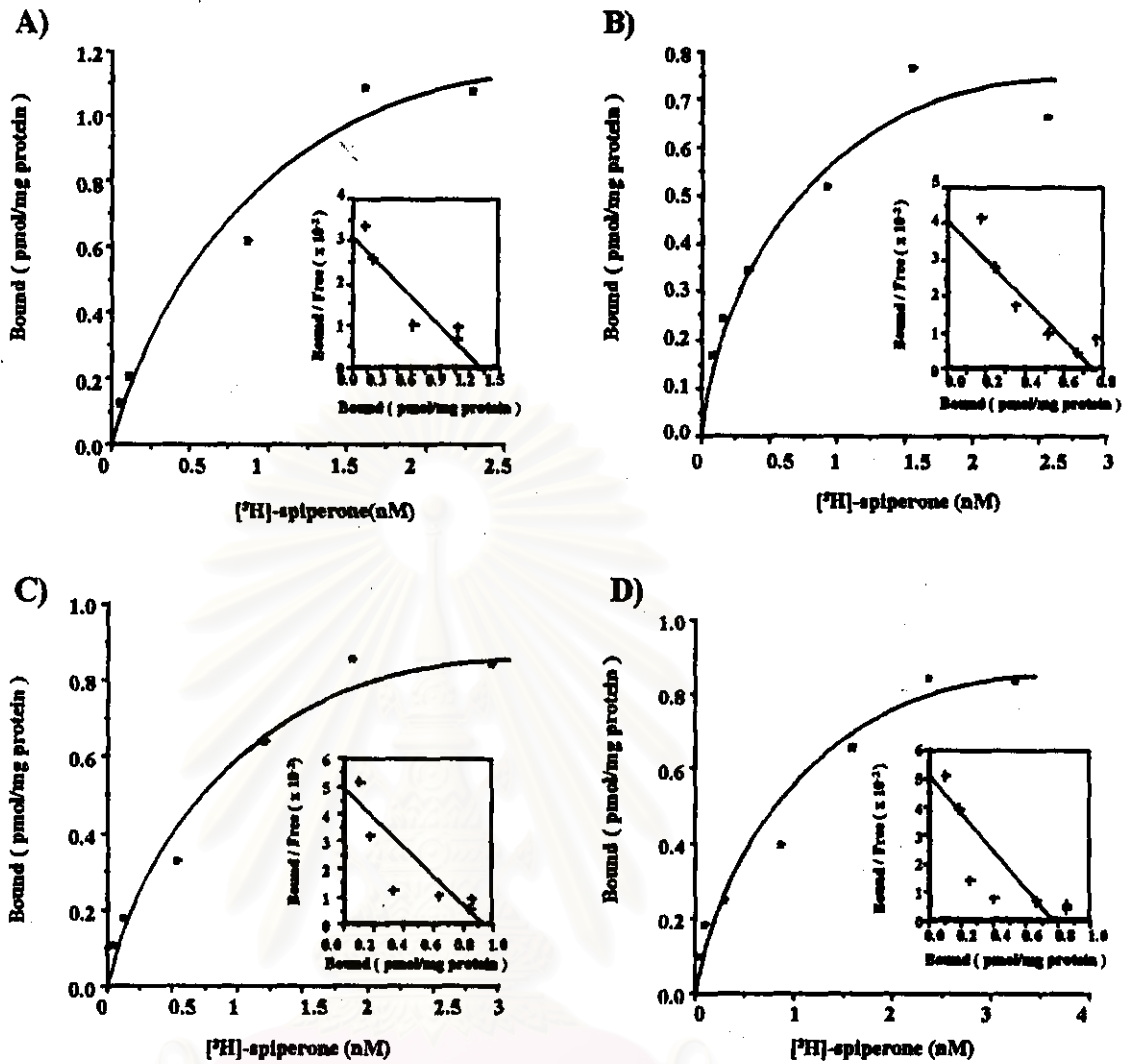


Figure 105A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -siperone binding on brain stem membrane of rat number 7-10, treated with paracetamol 300 mg/kg/day i.p. for 30 days. The binding was carried out in the concentrations of $[^3\text{H}]$ -siperone ranging from 0.01-4 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -siperone. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 1.0 (A), 0.6 (B), 0.7 (C), 0.5 (D) nM and B_{max} value of 1.28 (A), 0.75 (B), 0.87 (C), 0.76 (D) pmol/mg protein.

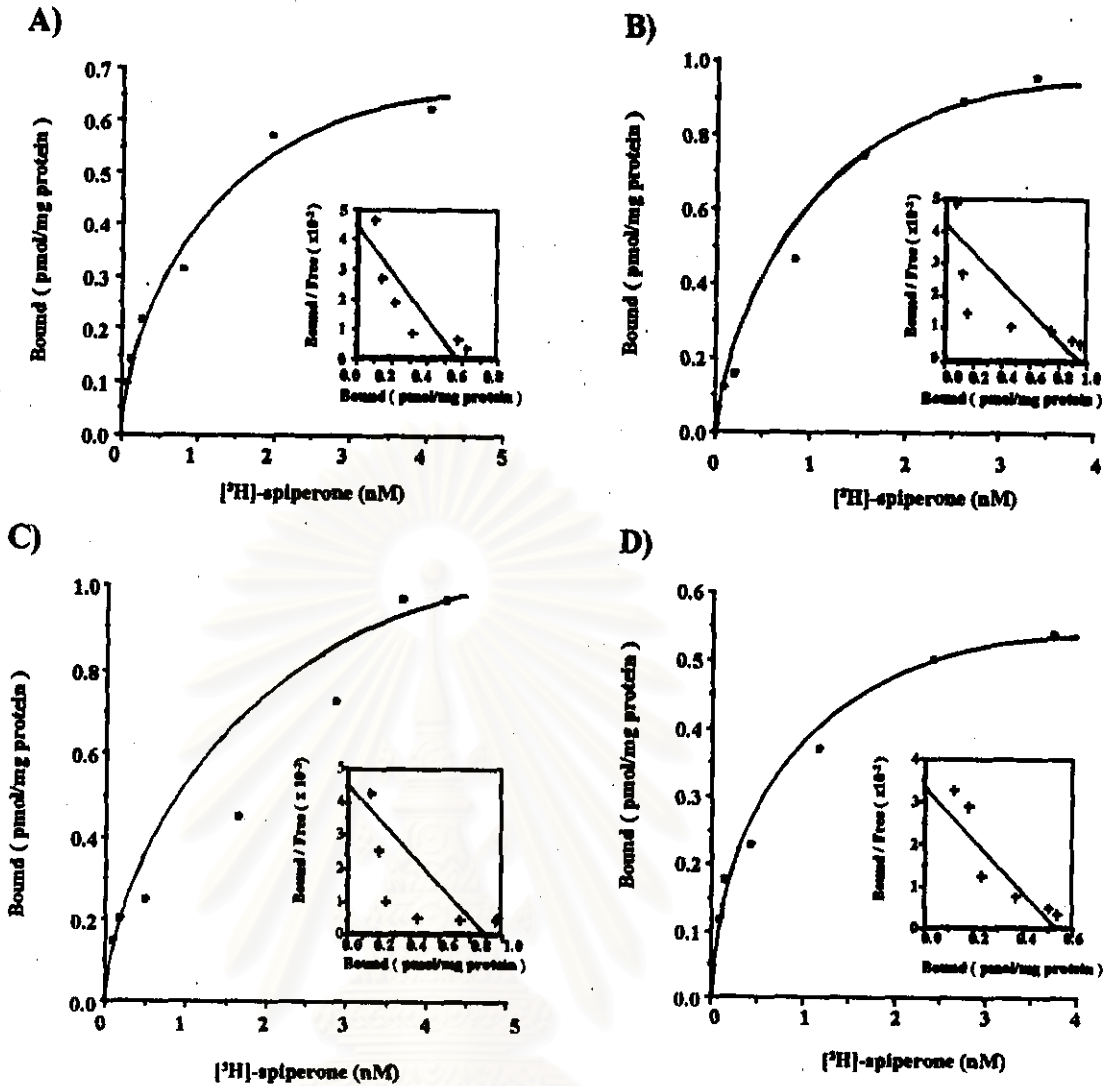


Figure 106A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -spiperone binding on brain stem membrane of rat number 11-14, treated with paracetamol 400 mg/kg/day i.p. for 30 days. The binding was carried out in the concentrations of $[^3\text{H}]$ -spiperone ranging from 0.01-5 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -spiperone. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 0.6 (A), 1.0 (B), 0.9 (C), 0.6 (D) nM and B_{max} value of 0.58 (A), 0.98 (B), 0.86 (C), 0.52 (D) pmol/mg protein.

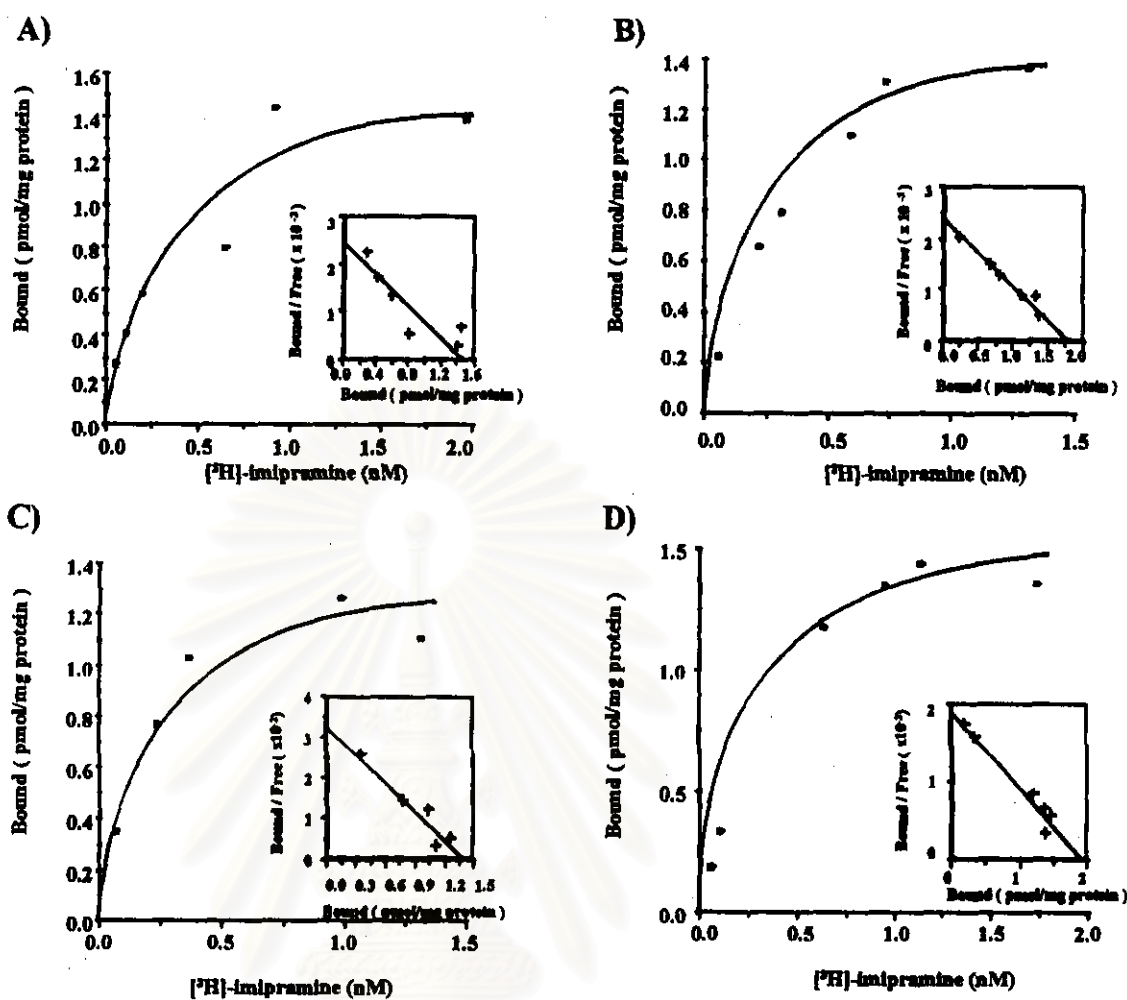


Figure 107A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -imipramine

binding on frontal cortex membrane of control rat number 1-4, treated with vehicle i.p. for 30 days. The binding was carried out in the concentrations of $[^3\text{H}]$ -imipramine ranging from 0.02 - 2 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -imipramine. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 1.08 (A), 1.58 (B), 0.68 (C), 1.76 (D) nM and B_{max} value of 1.53 (A), 1.88 (B), 1.40 (C), 1.91 (D) pmol/mg protein.

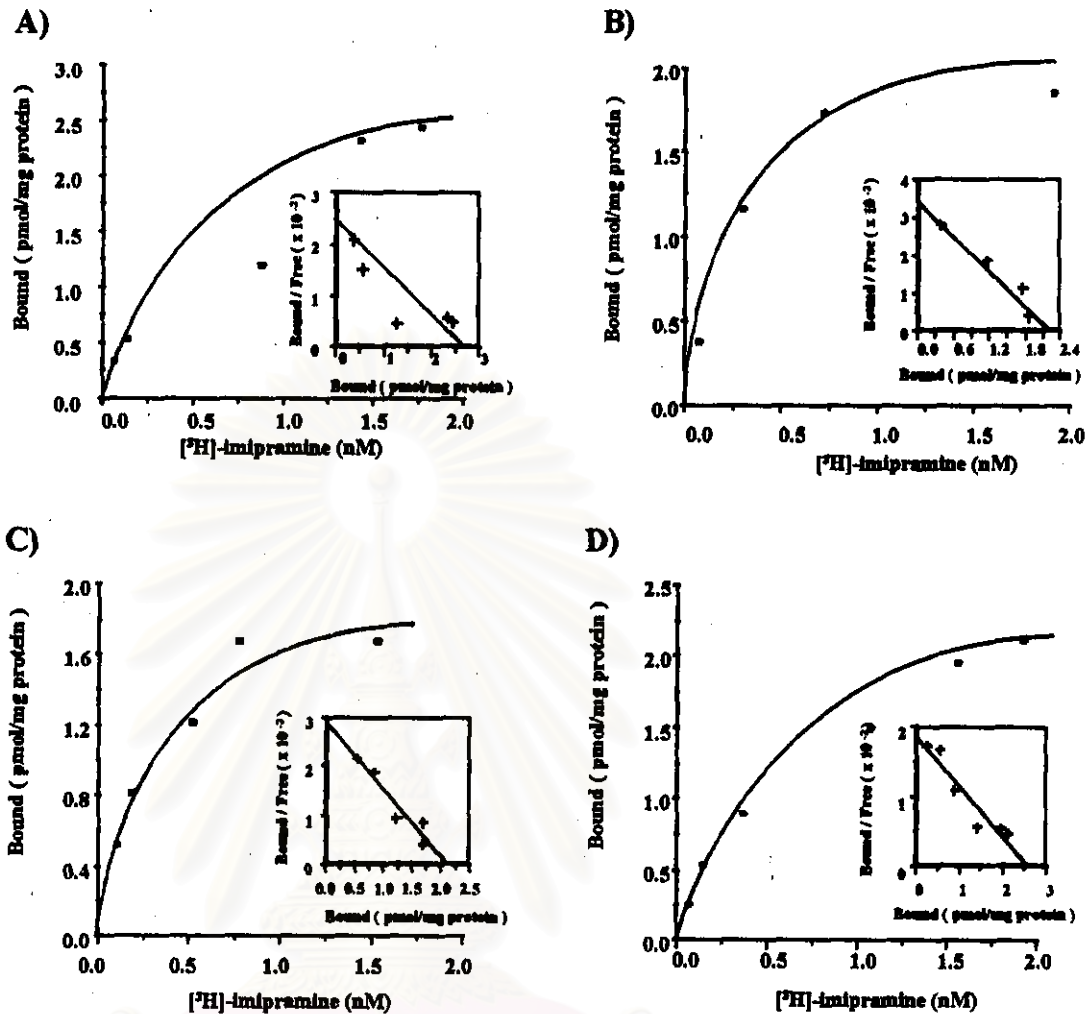


Figure 108A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -imipramine binding on frontal cortex membrane of rat number 6-9, treated with paracetamol 300 mg/kg/day i.p. for 30 days. The binding was carried out in the concentrations of $[^3\text{H}]$ -imipramine ranging from 0.02 - 2 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -imipramine. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 1.99 (A), 1.19 (B), 1.07 (C), 2.23 (D) nM and B_{max} value of 2.67 (A), 2.30 (B), 2.03 (C), 2.51 (D) pmol/mg protein.

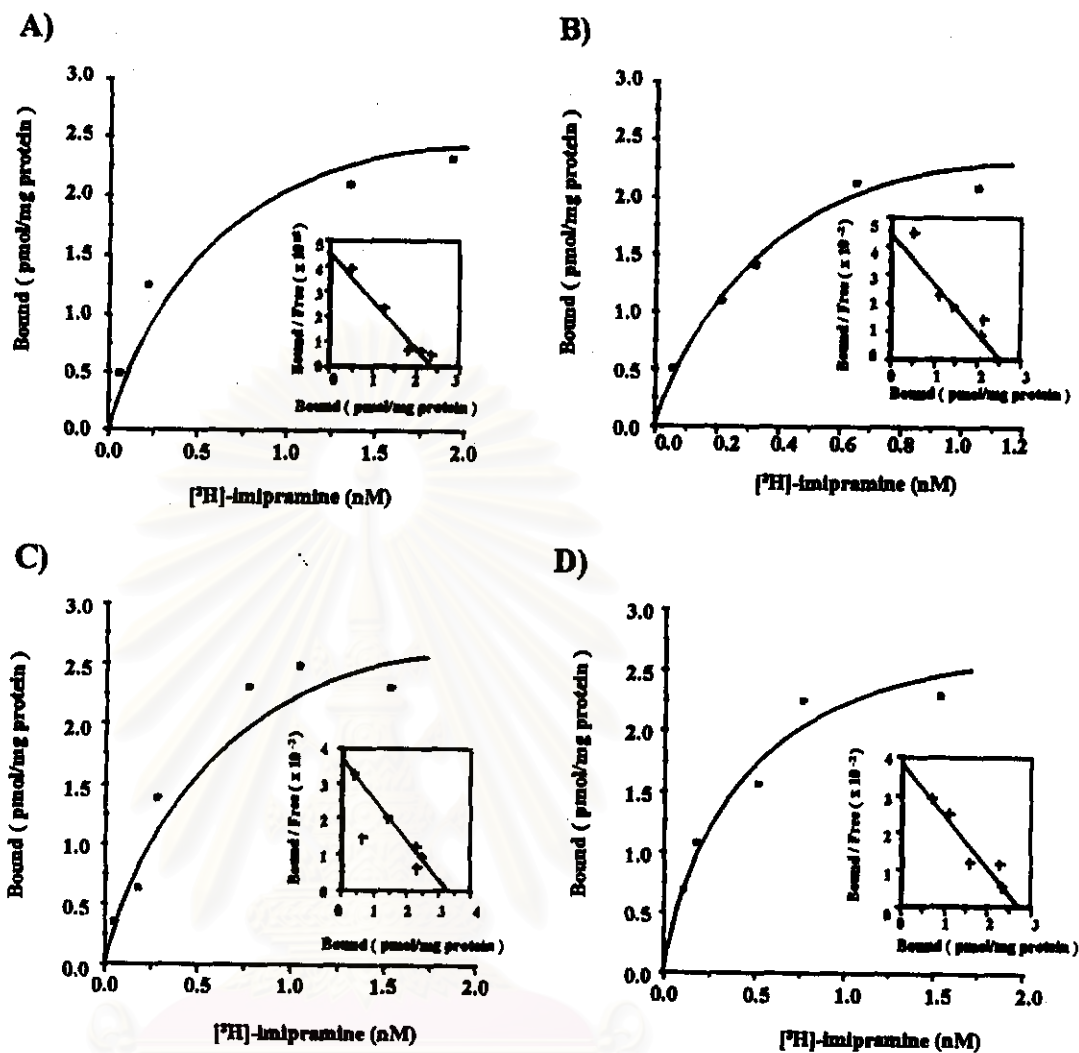


Figure 109A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -imipramine binding on frontal cortex membrane of rat number 10 - 13, treated with paracetamol 400 mg/kg/day i.p. for 30 days. The binding was carried out in the concentrations of $[^3\text{H}]$ -imipramine ranging from 0.02 - 2 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -imipramine. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 0.76 (A), 0.85 (B), 1.58 (C), 1.12 (D) nM and B_{max} value of 2.37 (A), 2.52 (B), 3.19 (C), 2.76 (D) pmol/mg protein.

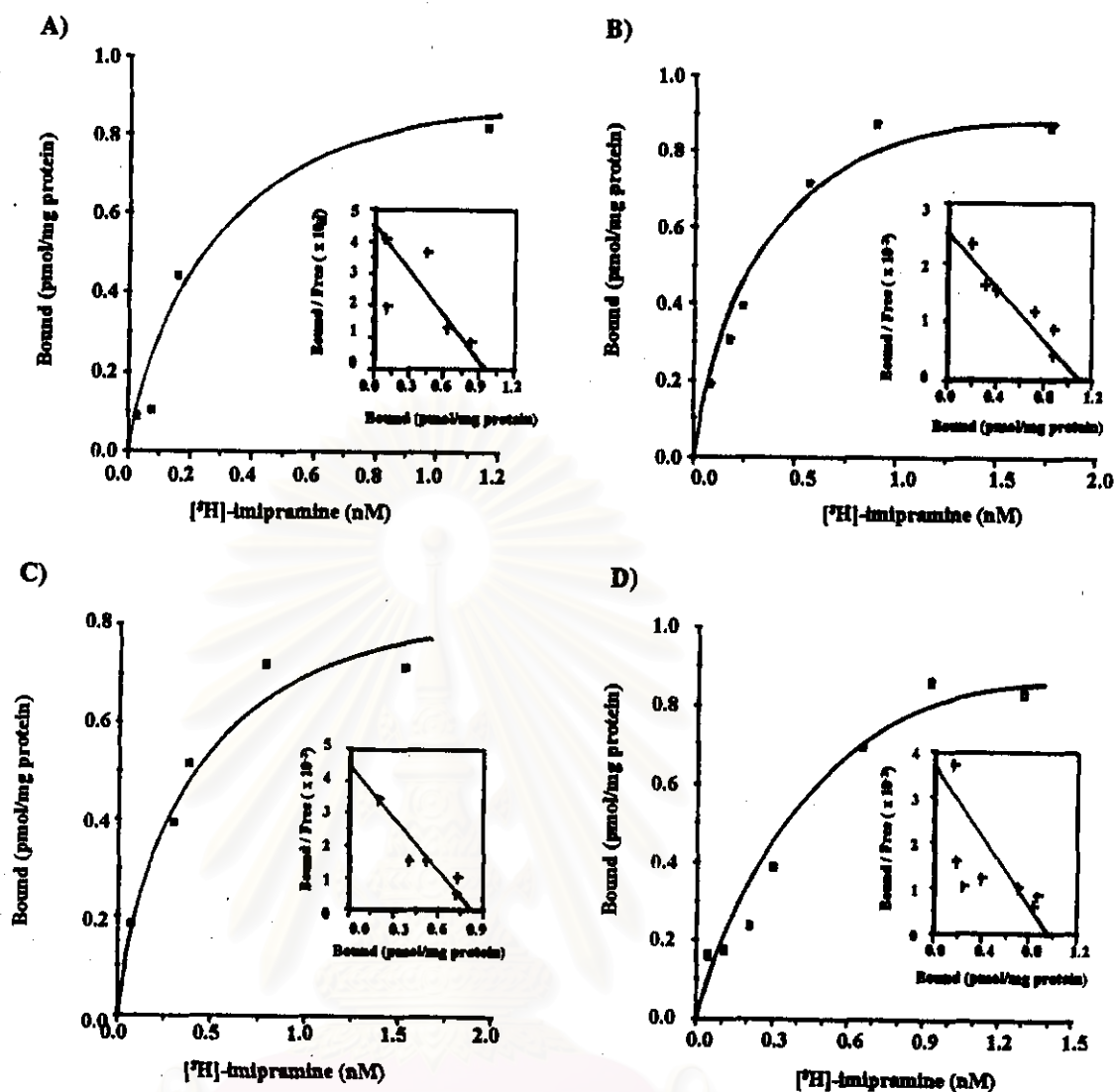


Figure 110A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -imipramine binding on brain stem membrane of control rat number 1-4, treated with vehicle i.p. once daily for 30 days. The binding was carried out in the concentrations of $[^3\text{H}]$ -imipramine ranging from 0.01 - 2.0 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -imipramine. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 1.3 (A), 1.6 (B), 0.88 (C), 1.23 (D) nM and B_{max} value of 1.05 (A), 1.16 (B), 0.84 (C), 0.98 (D) pmol/mg protein.

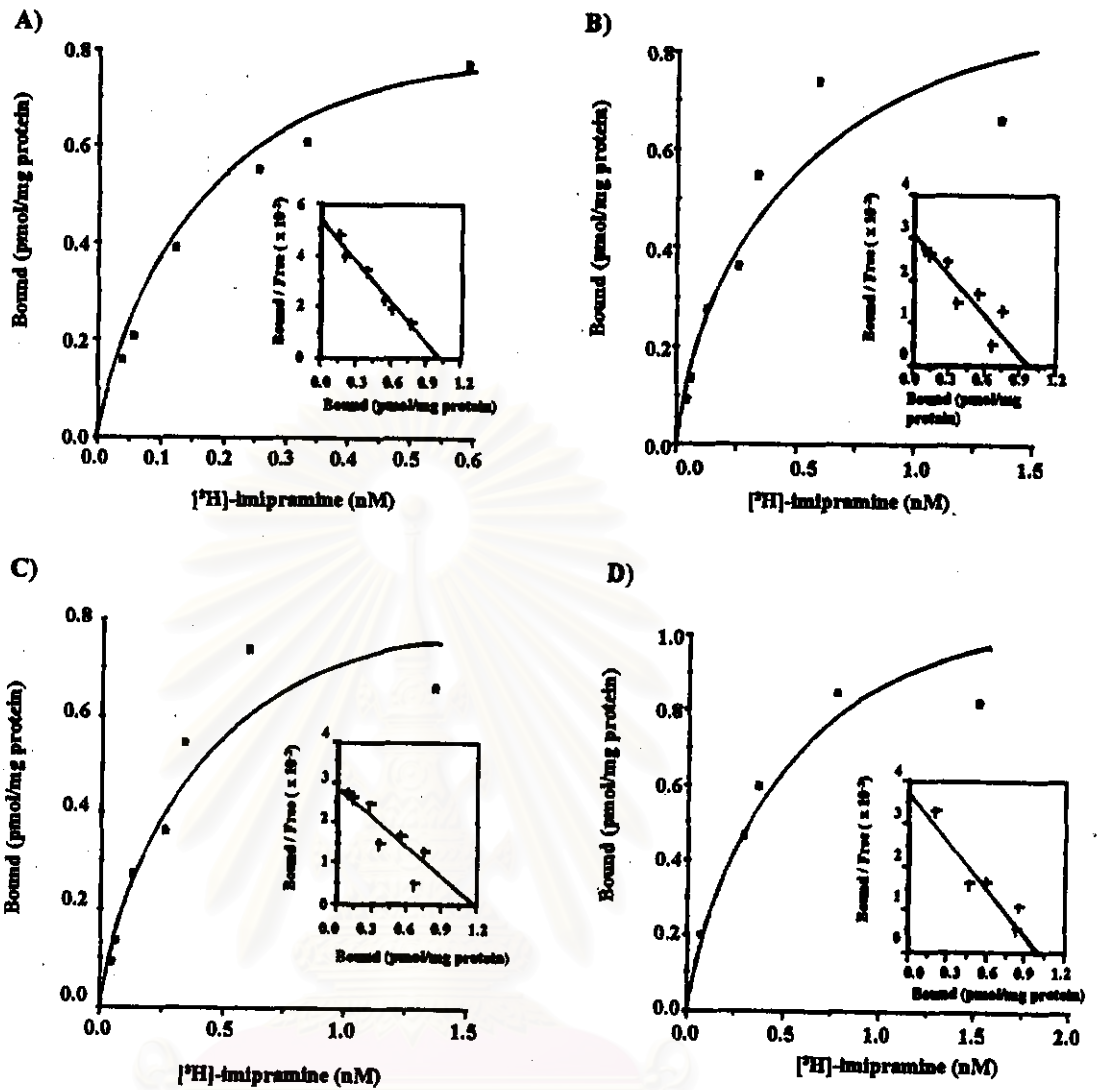


Figure 111A-D. Saturation curve and Scatchard analysis (in the inset) of [³H]-imipramine binding on brain stem membrane of rat number 5-8, treated with paracetamol 300 mg/kg/day i.p. for 30 days. The binding was carried out in the concentrations of [³H]-imipramine ranging from 0.05 - 0.6 nM. The plots were obtained from duplicate determinations and represented the specific binding of [³H]-imipramine. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 0.73 (A), 1.25 (B), 1.59 (C), 0.98 (D) nM and B_{max} value of 0.98 (A), 0.96 (B), 1.21 (C), 1.01 (D) pmol/mg protein.

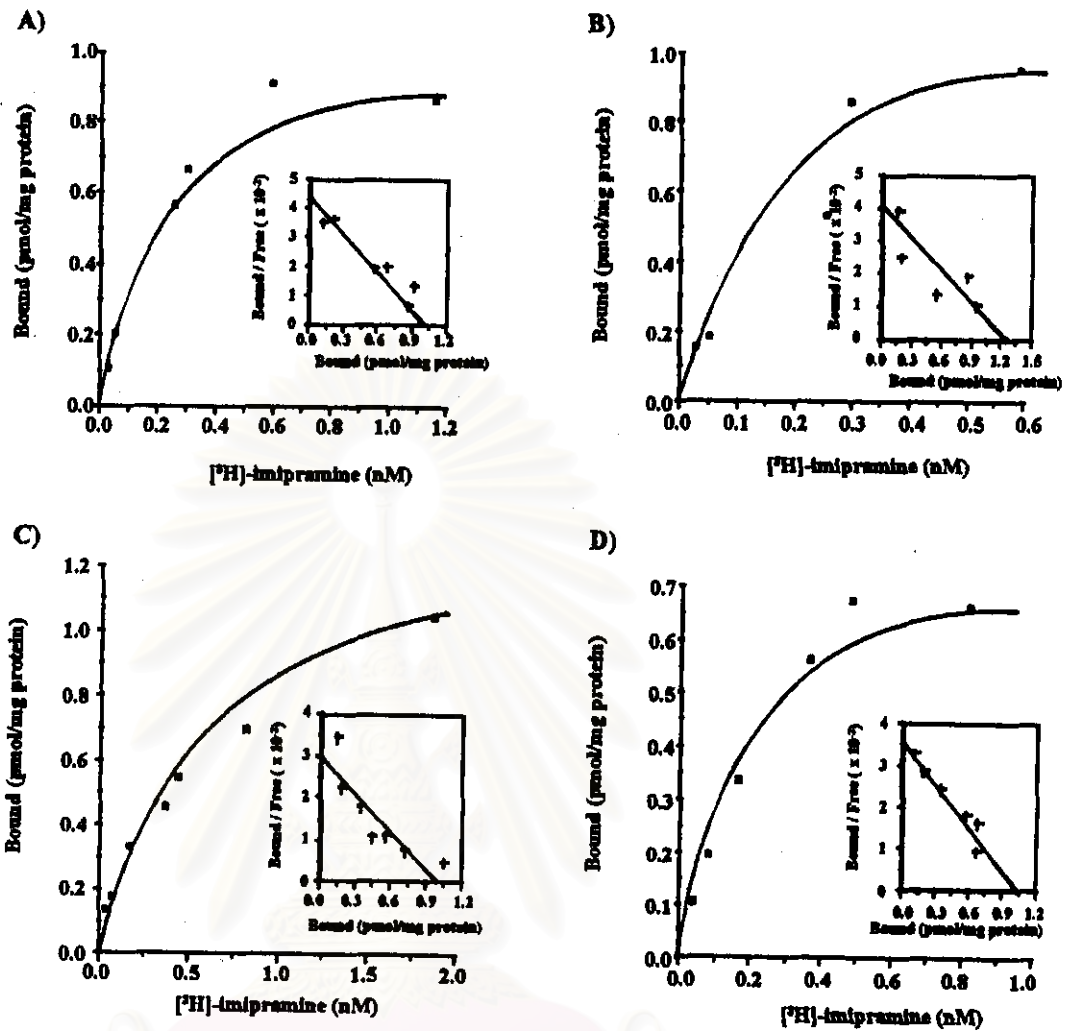


Figure 112A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -imipramine binding on brain stem membrane of rat number 9-12, treated with paracetamol 400 mg/kg/day i.p. for 30 days. The binding was carried out in the concentrations of $[^3\text{H}]$ -imipramine ranging from 0.01 - 1.2 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -imipramine. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 0.93 (A), 0.89 (B), 1.06 (C), 1.28 (D) nM and B_{max} value of 1.15 (A), 1.29 (B), 0.98 (C), 1.04 (D) pmol/mg protein.

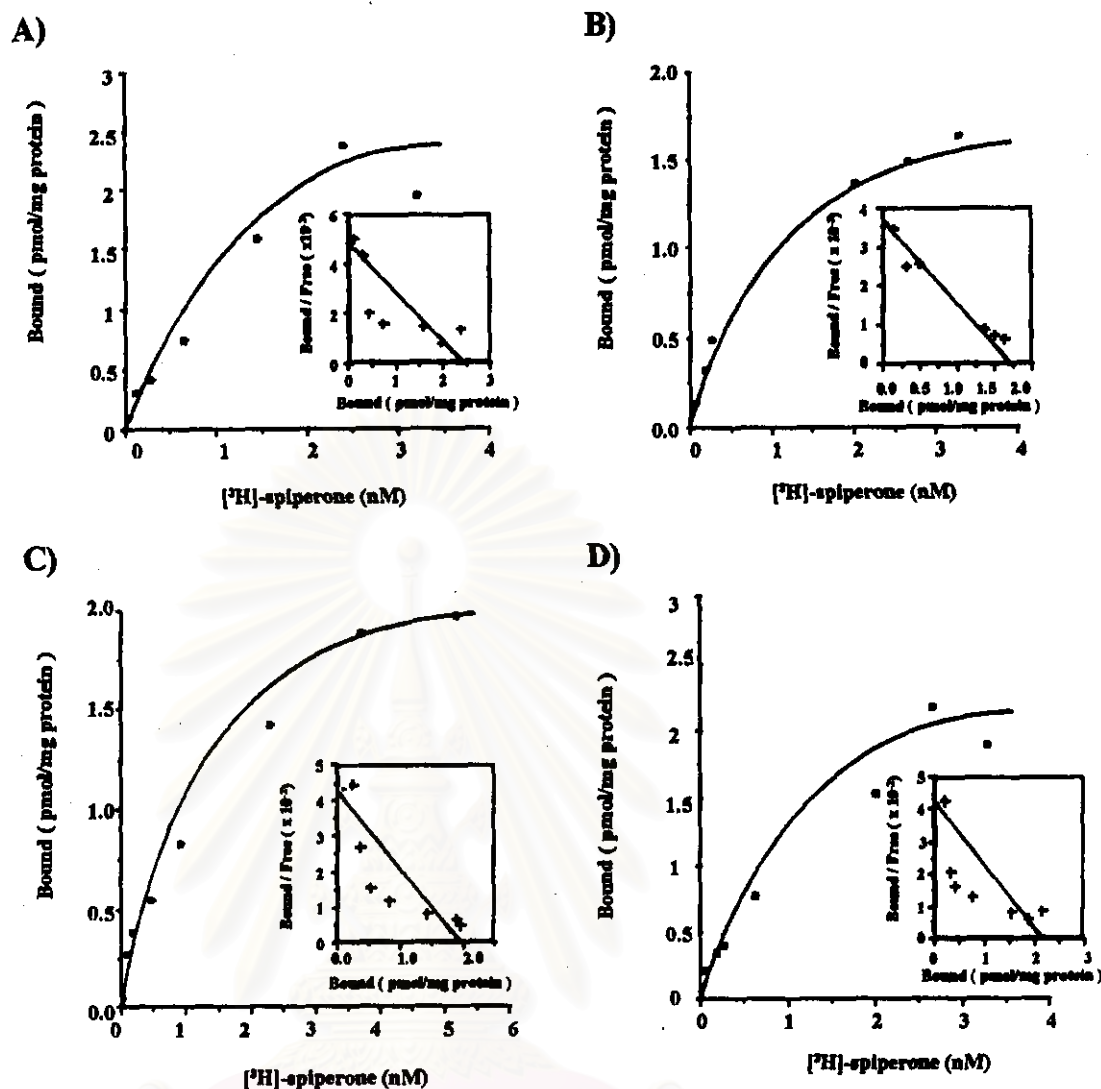


Figure 113A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -spiperone binding on frontal cortex membrane of control rat number 1-4, treated with vehicle i.p. for 90 min. The binding was carried out in the concentrations of $[^3\text{H}]$ -spiperone ranging from 0.04 - 4 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -spiperone. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 1.5 (A), 1.4 (B) 1.3 (C), 1.5 (D) nM and B_{max} value of 2.44 (A), 1.92 (B), 1.93 (C), 2.26 (D) pmol/mg protein.

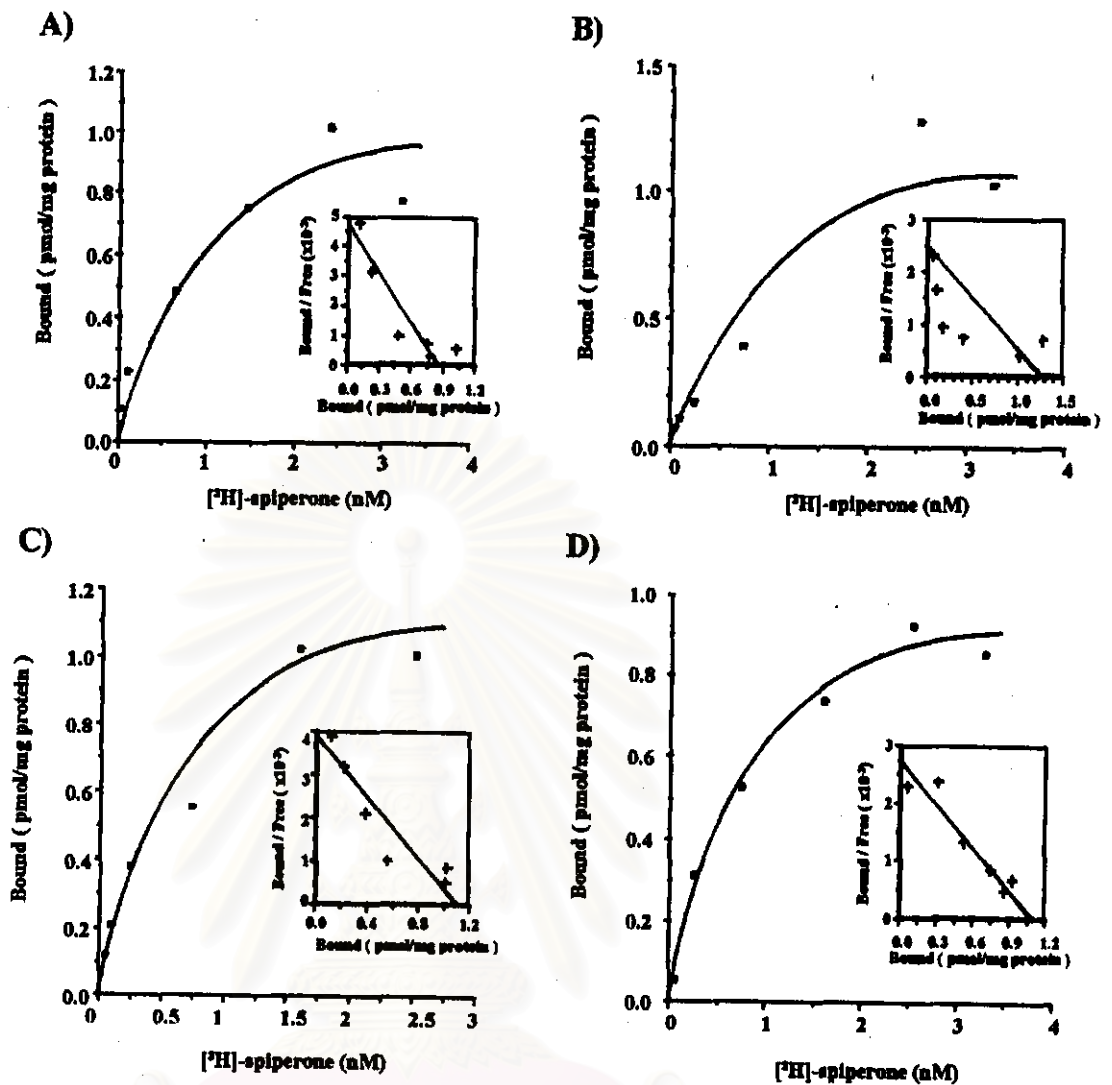


Figure 114A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -spiperone binding on frontal cortex membrane of rat number 7-10, treated with paracetamol 300 mg/kg i.p. for 90 min. The binding was carried out in the concentrations of $[^3\text{H}]$ -spiperone ranging from 0.01-4 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -spiperone. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 0.5 (A), 2.3 (B), 0.7 (C), 1.5 (D) nM and B_{max} value of 0.89 (A), 1.43 (B), 1.09 (C), 1.12 (D) pmol/mg protein.

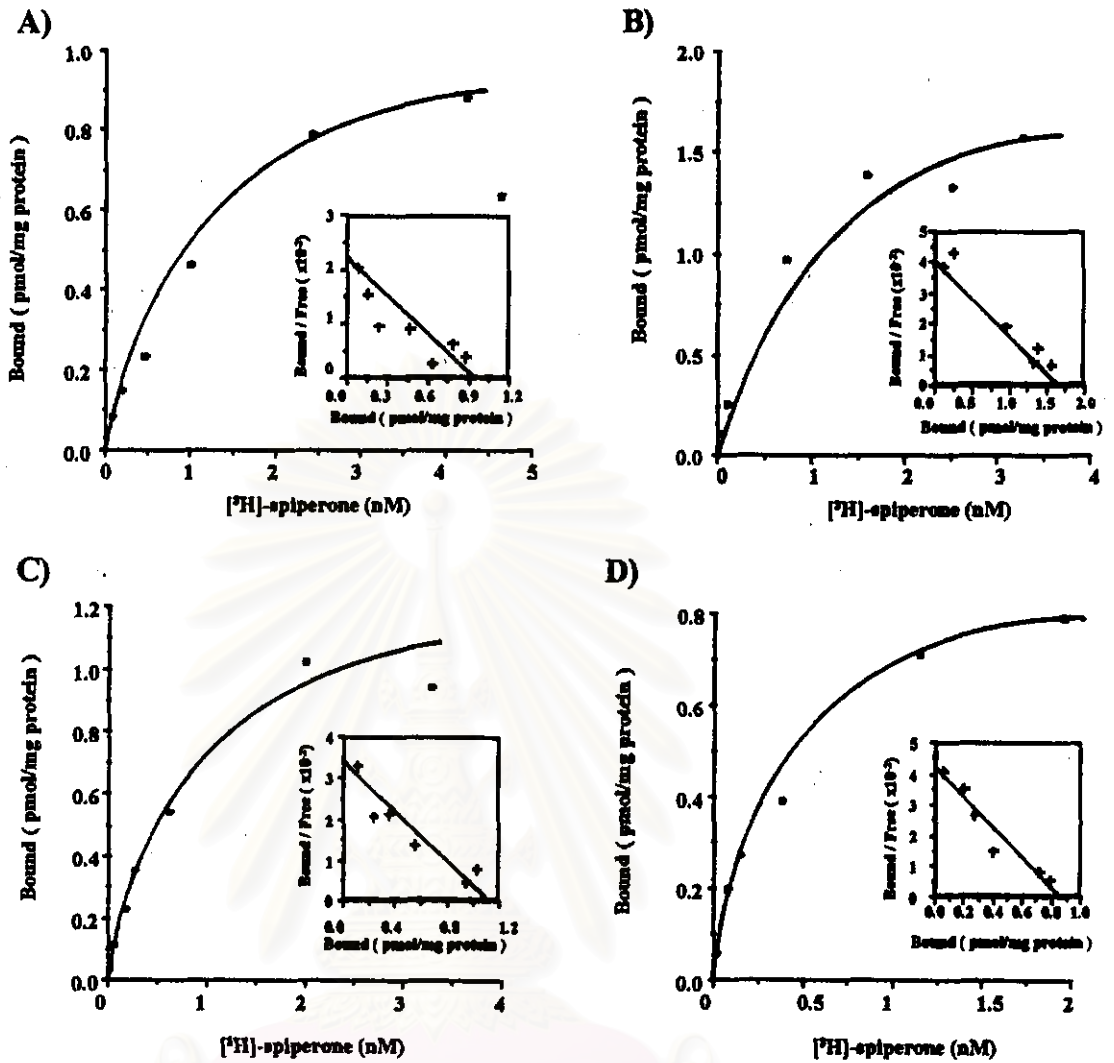


Figure 115A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -spiperone binding on frontal cortex membrane of rat number 12 - 15, treated with paracetamol 400 mg/kg i.p. for 90 min. The binding was carried out in the concentrations of $[^3\text{H}]$ -spiperone ranging from 0.01-4 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -spiperone. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 1.9 (A), 1.1 (B and C), 0.6 (D) nM and B_{max} value of 0.94 (A), 1.73 (B), 1.15 (C), 0.85 (D) pmol/mg protein.

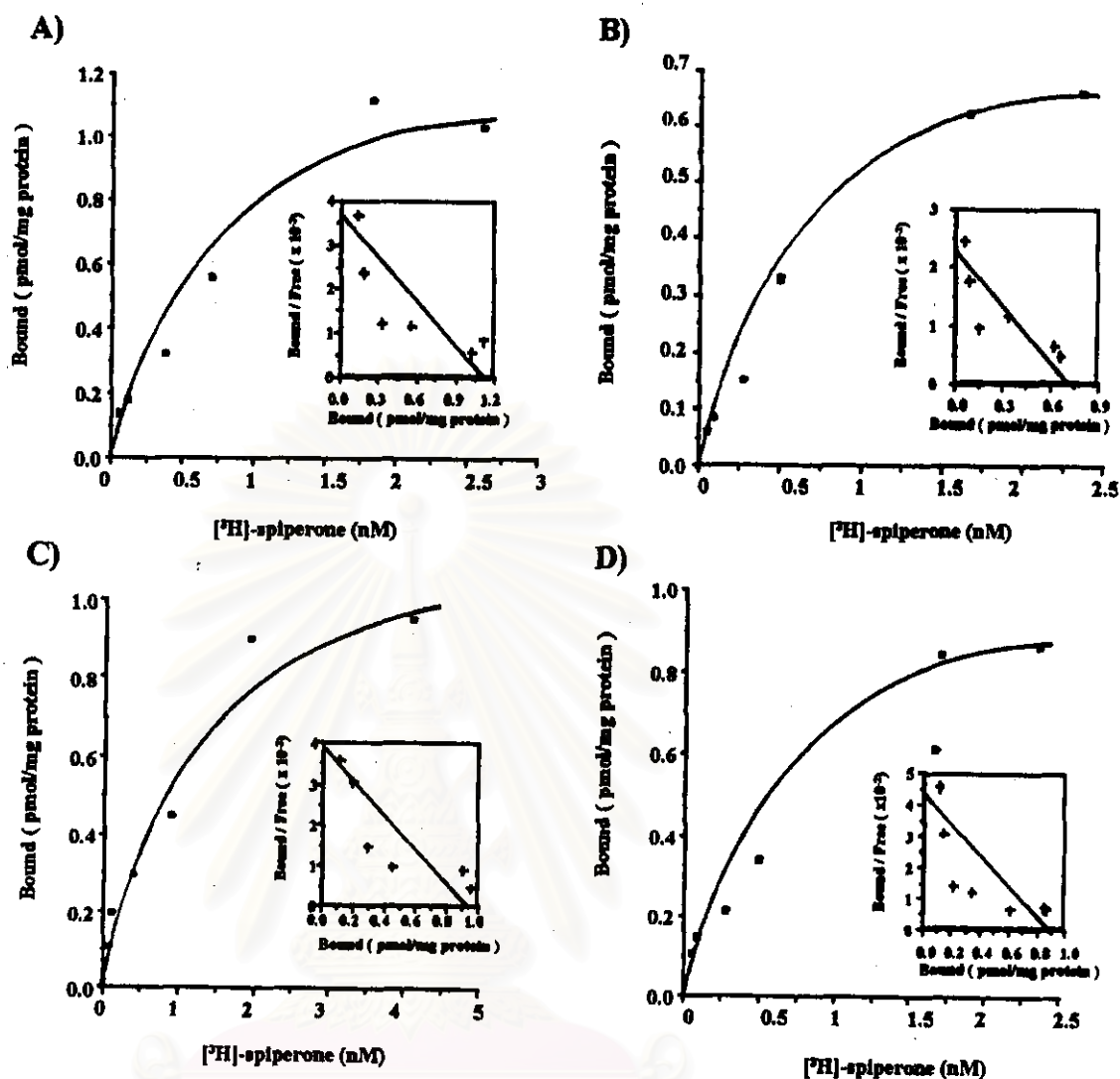


Figure 116A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -spiperone binding on brain stem membrane of control rat number 1 - 4, treated with vehicle i.p. for 90 min. The binding was carried out in the concentrations of $[^3\text{H}]$ -spiperone ranging from 0.01 - 5 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -spiperone. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 1.0 (A), 1.3 (B), 1.0 (C), 0.8 (D) nM and B_{max} value of 1.19 (A), 0.82 (B), 0.98 (C), 0.84 (D) pmol/mg protein.

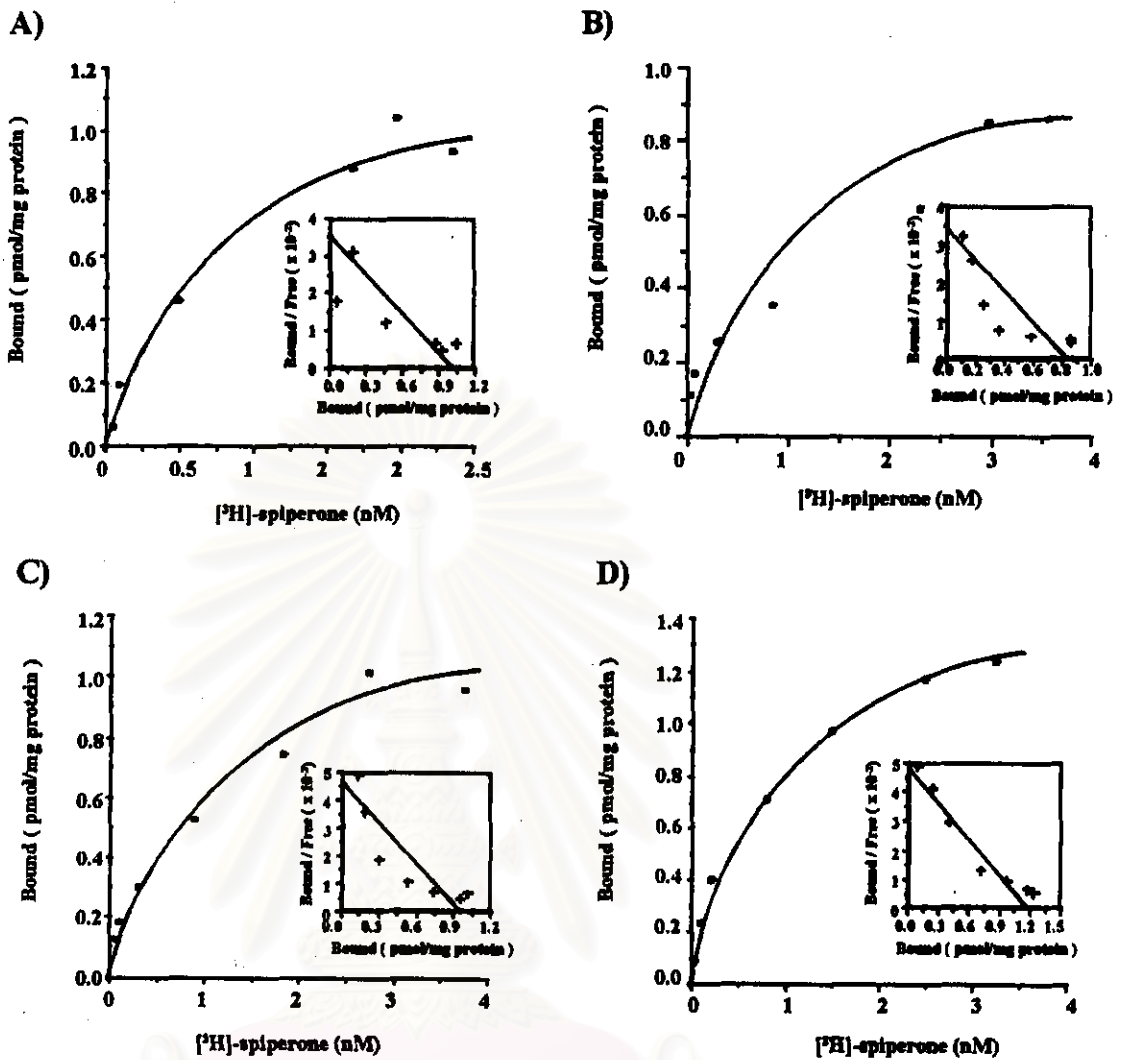


Figure 117A-D. Saturation curve and Scatchard analysis (in the inset) of [³H]-spiperone binding on brain stem membrane of rat number 7 - 10, treated with paracetamol 300 mg/kg/day i.p. for 90 min. The binding was carried out in the concentrations of [³H]-spiperone, ranging from 0.01 - 4 nM. The plots were obtained from duplicate determinations and represented the specific binding of [³H]-spiperone. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 1.0 (A), 1.1 (B), 0.7 (C and D) nM and B_{max} value of 1.13 (A), 0.83 (B), 0.95 (C), 1.25 (D) pmol/mg protein.

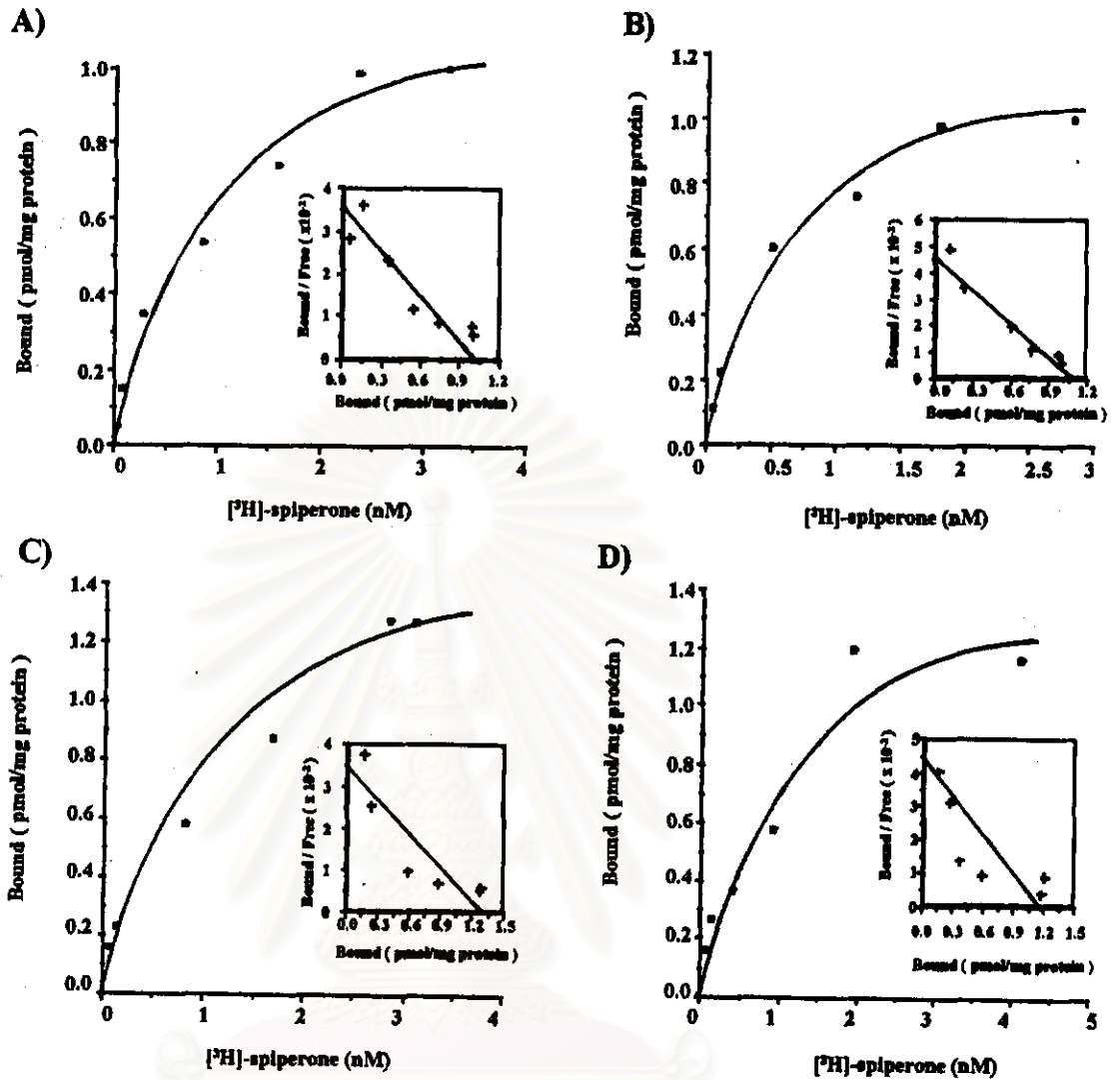


Figure 118A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -spiperone binding on brain stem membrane of rat number 12 - 15, treated with paracetamol 400 mg/kg/day i.p. for 90 min. The binding was carried out in the concentrations of $[^3\text{H}]$ -spiperone, ranging from 0.01 - 5 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -spiperone. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 1.2 (A), 0.7 (B), 0.9 (C), 1.0 (D) nM and B_{\max} value of 1.12 (A), 1.08 (B), 1.29 (C), 1.18 (D) pmol/mg protein.

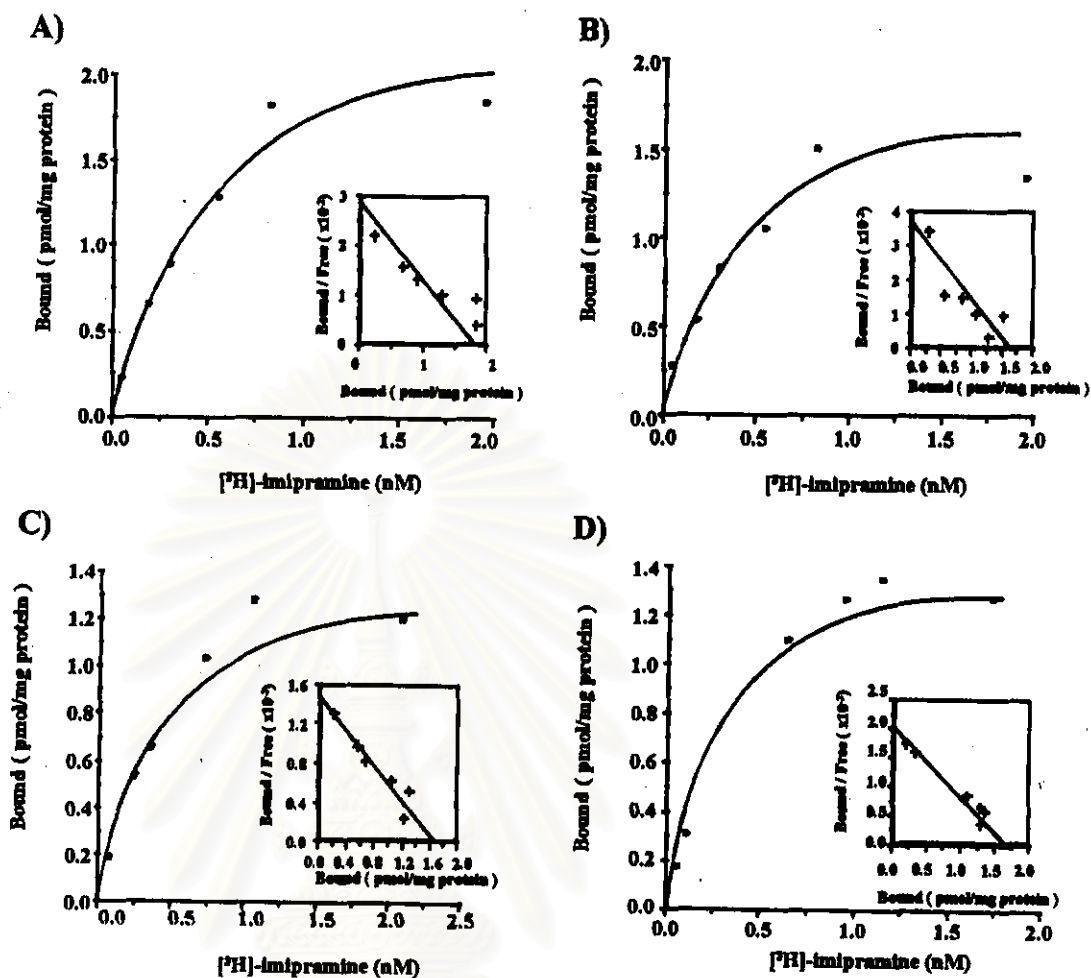


Figure 119A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -imipramine binding on frontal cortex membrane of control rat number 1-4 treated with vehicle i.p. for 90 min. The binding was carried out in the concentrations of $[^3\text{H}]$ -imipramine ranging from 0.02 - 3 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -imipramine. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 1.77 (A), 0.86 (B), 1.90 (C), 1.76 (D) nM and B_{max} value of 1.96 (A), 1.52 (B), 1.66 (C), 1.79 (D) pmol/mg protein.

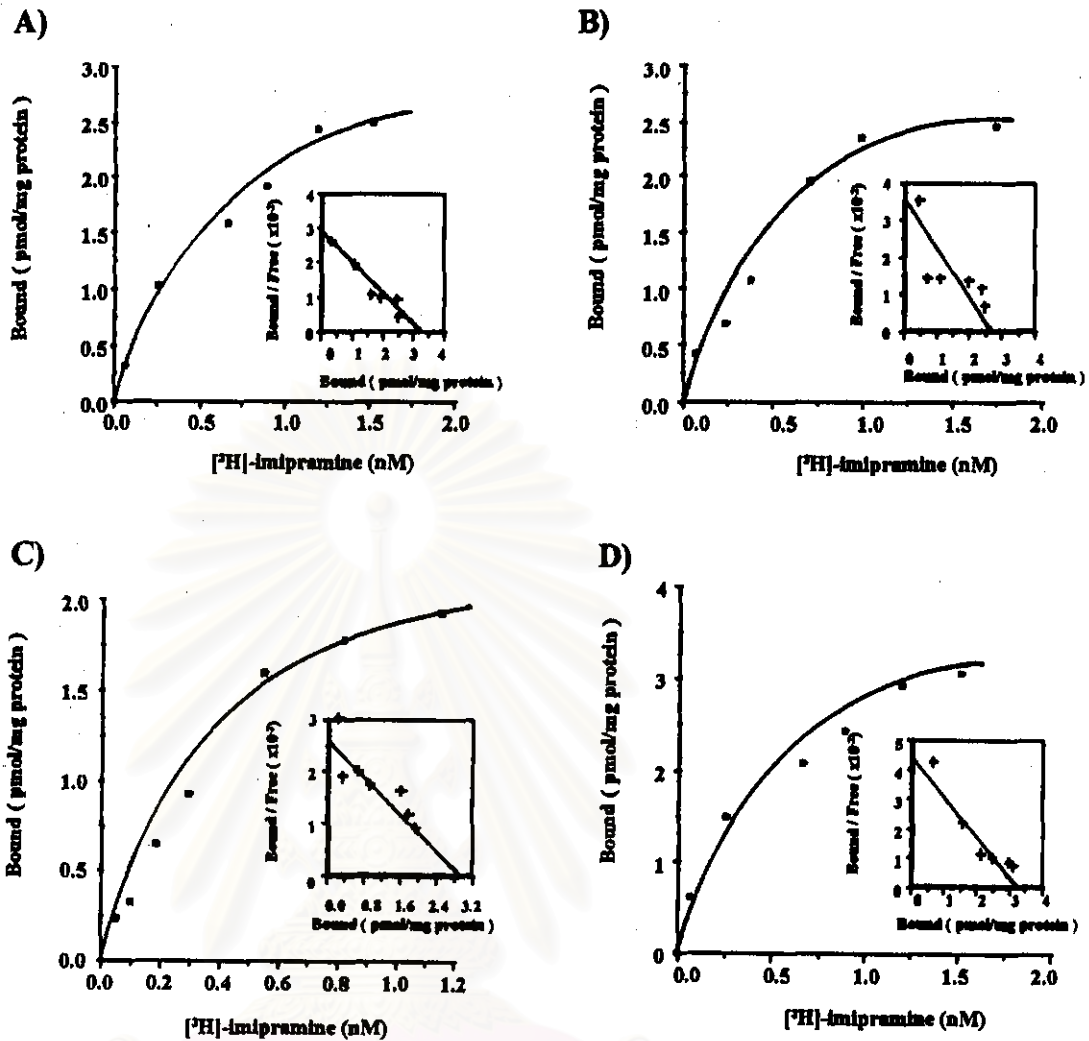


Figure 120A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -imipramine binding on frontal cortex membrane of rat number 6-9, treated with paracetamol 300 mg/kg i.p. for 90 min. The binding was carried out in the concentrations of $[^3\text{H}]$ -imipramine ranging from 0.02 -2 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -imipramine. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 2.05 (A), 1.81 (B), 2.46 (C), 0.98 (D) nM and B_{max} value of 3.21 (A), 2.99 (B), 3.09 (C), 3.27 (D) pmol/mg protein.

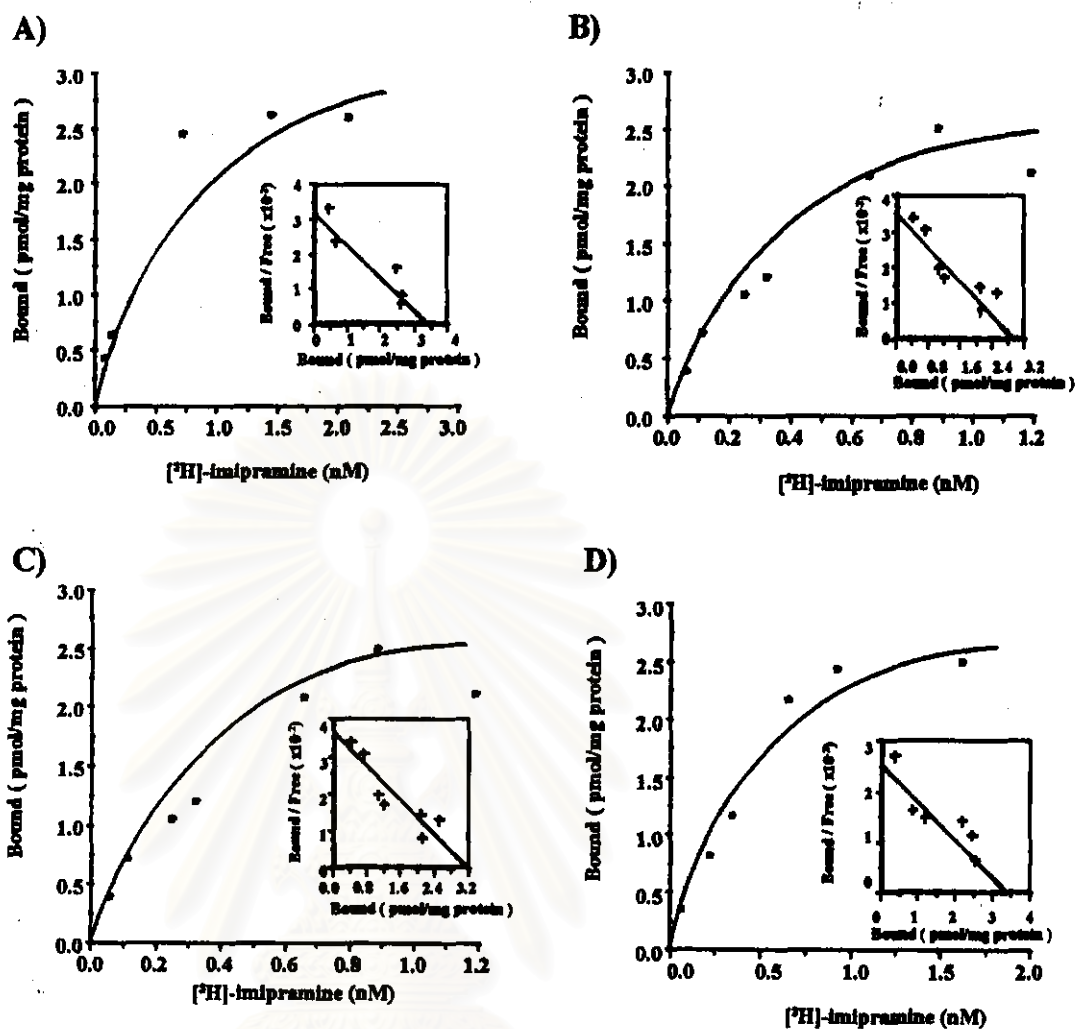


Figure 121A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -imipramine binding on frontal cortex membrane of rat number 10 - 13, treated with paracetamol 400 mg/kg i.p. for 90 min. The binding was carried out in the concentrations of $[^3\text{H}]$ -imipramine, ranging from 0.02 -3 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -imipramine. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 1.79 (A), 1.51 (B), 2.51 (C), 1.48 (D) nM and B_{max} value of 3.45 (A), 3.07 (B), 3.68 (C), 3.45 (D) pmol/mg protein.

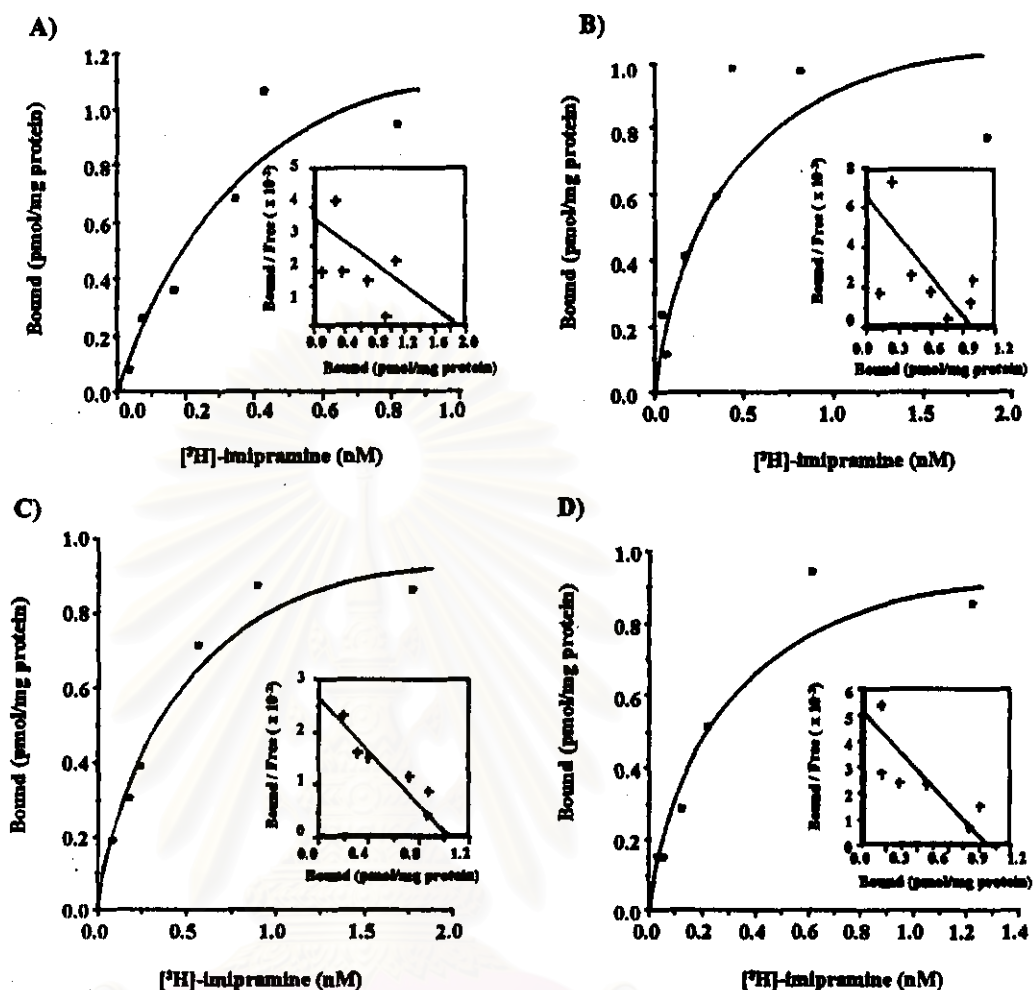


Figure 122A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -imipramine binding on brain stem membrane of control rat number 1-4 , treated with vehicle i.p. for 90 min. The binding was carried out in the concentrations of $[^3\text{H}]$ -imipramine ranging from 0.02 - 2 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -imipramine. The line of best fit was analysed by the LIGAND computer program. The result of this experiment was shown and provided a K_d value of 2.3 (A), 0.7 (B), 1.6 (C), 0.95 (D) nM and B_{max} value of 1.98 (A), 1.03 (B), 1.16 (C), 1.10 (D) pmol/mg protein.

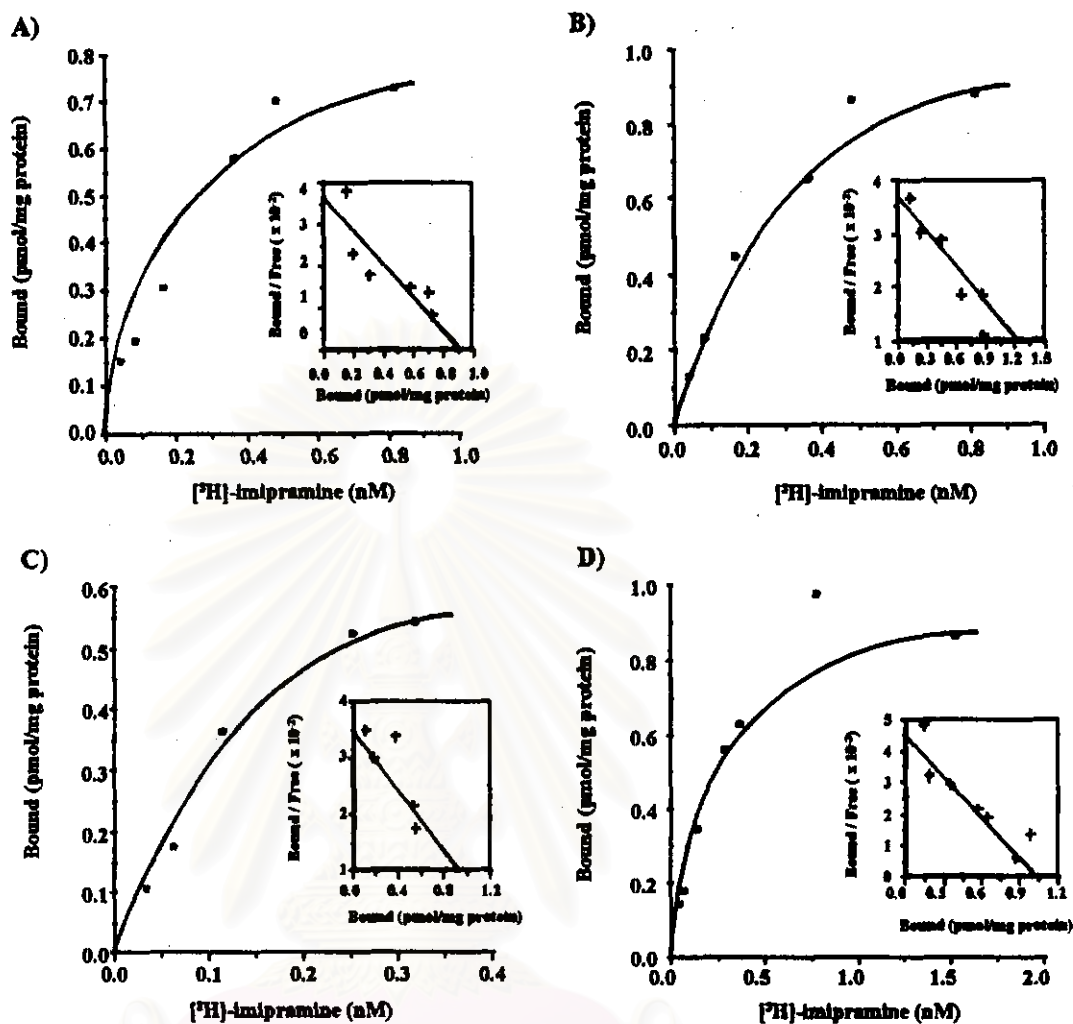


Figure 123A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -imipramine binding on brain stem membrane of rat number 6-9, treated with paracetamol 300 mg/kg i.p. for 90 min. The binding was carried out in the concentrations of $[^3\text{H}]$ -imipramine, ranging from 0.02 - 2 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -imipramine. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 0.98 (A), 1.37 (B), 1.10 (C), 1.03 (D) nM and B_{max} value of 0.96 (A), 1.34 (B), 1.09 (C), 1.11 (D) pmol/mg protein.

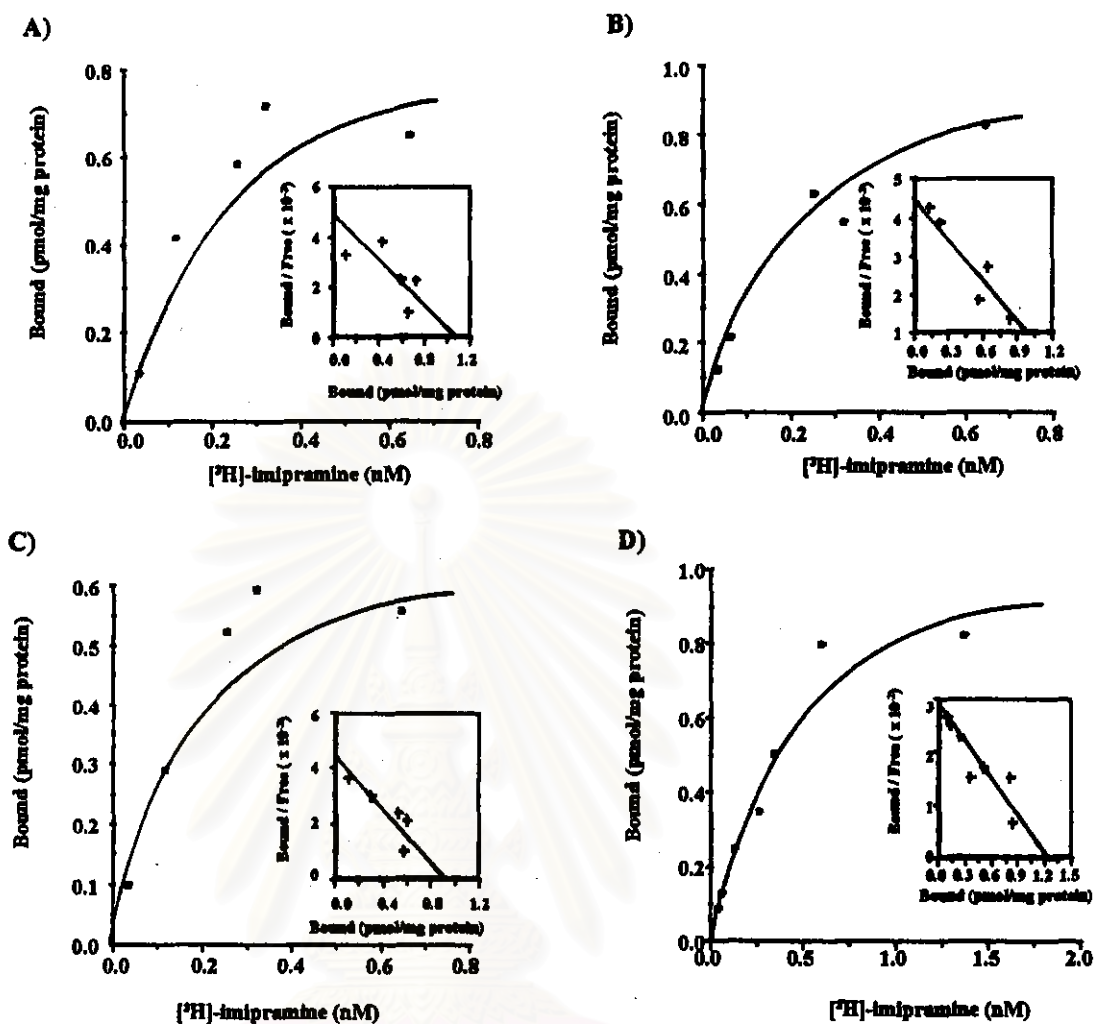


Figure 124A-D. Saturation curve and Scatchard analysis (in the inset) of $[^3\text{H}]$ -imipramine binding on brain stem membrane of rat number 10 - 13, treated with paracetamol 400 mg/kg i.p. for 90 min. The binding was carried out in the concentrations of $[^3\text{H}]$ -imipramine ranging from 0.02 - 2 nM. The plots were obtained from duplicate determinations and represented the specific binding of $[^3\text{H}]$ -imipramine. The line of best fit was analysed by the LIGAND computer program. The result provided a K_d value of 0.93 (A), 0.98 (B), 0.94 (C), 1.92 (D) nM and B_{max} value of 1.11 (A), 1.13 (B), 0.92 (C), 1.21 (D) pmol/mg protein.

BIOGRAPHY

Mrs. Naovarat Tarasub was born on November, 5th 1959, in Bangkok Thailand. She graduated with Bachelor of Science (Nursing and Midwifery) from Mahidol University in 1982 and graduated with Master of Science (Anatomy) from Mahidol University in 1987. Then, she was studied further with the Doctor of Philosophy of Science at Inter-department of Physiology in Chulalongkorn University in 1992. She started to work as a teacher at Department of Anatomy, Faculty of Science, Rangsit University from 1989 up to present.



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