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3H-ZK 91587: A new synthetic, highly specific ligand for mineralocorticoid receptor (MinR) determination  
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Determination of MinR was hampered by using 3H-aldosterone which is not stable under conditions of receptor assay and binds significantly to GlucR. We want to present first results with the new 3H-ZK 91587 (7 $\alpha$ -(3H-methoxy)-carbonyl-15 $\beta$ ,16 $\beta$ -methylene-3-oxo-17 $\alpha$ -pregn-4-ene-21,17-carbolactone, spec. activity 77.2 Ci/mmol) which is stable under conditions of receptor assay. The relative binding affinity (RBA) for rat kidney MinR is 4.0 (aldosterone 1.0), but only 0.008 for rat liver GlucR (dexamethasone 1.0, aldosterone 0.10). Half live of dissociation was 6.25 hrs (aldosterone 1.12hrs).  $K_D$  determined by Scatchard plot analysis was  $2.21 \pm 0.6 \times 10^{-9}$  mol/l (3H-aldosterone  $6.19 \pm 3.56 \times 10^{-9}$  mol/l, n=10). Mean MinR levels (n=10) were  $19.8 \pm 8.6$  fmoles/mg protein for 3HZK 91587,  $55.5 \pm 8.7$  fmoles/mg protein for 3H-aldosterone alone but  $16.3 \pm 4.5$  fmoles/mg protein for 3H-aldosterone plus a 50-fold excess of RU 28362, which blocks selectively GlucR binding. 3H-ZK 91587 proofed to be a highly specific ligand for MinR determinations.

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#### STEROID HORMONES MODULATE THE HYPOTHALAMIC OPIOID IN OVARECTOMIZED RATS

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 The site of action in the modulation of central neuroendocrine pathways regulating the gonadotropin secretion is still debated. Several reports have evidenced the role of different neuropeptides and neurotransmitters in the release of LHRH in the pituitary portal vessels. The endogenous opioid peptides exert tonic inhibitory effect on the LHRH neurons, which seems to be modulated by gonadal changes. The aim of this study was to evaluate the changes in the hypothalamic concentrations of two of the most diffuse opioid peptides, i.e. (IR) beta-endorphin (B-EP) and IR met-enkephalin (MET-ENK) after chronic treatments with estrogens, gestagens and androgens in castrated female rats. The changes of hypothalamic LHRH concentrations were also measured. Female rats were ovariectomized under anesthesia. 3 weeks after surgery they started a daily treatment with estradiol benzoate (2ug), progesterone (2.5mg), desogestrel (10ug), medroxyprogesterone acetate (0.5mg), noretisterone enantate (0.5mg) dehydroepiandrosterone sulphate (0.1 mg) or cyproterone acetate (2.5mg). Medial basal hypothalamus (MBH) was dissected from the rats' brain and IR B-EP (AE, Panerai M.D.), IR MET-ENK (UCB) and IR LHRH (Eurodiagnostic, NL) were measured by radioimmunoassay. In ovariectomized rats LHRH contents were higher than in sham operated rats, while no difference were found in their B-EP and MET-ENK. The estradiol benzoate treated rats conversely showed LHRH contents when compared to ovariectomized non-treated rats, thus showing the highest concentrations of B-EP and MET-ENK. Among gestagens progesterone only induced a significant increase in LHRH contents. Like androgens all gestagens active in blocking the B-EP and MET-ENK changes induces by estrogens. These results indicate an important role of estrogens in increasing the opioid peptide concentrations. This effect is modulated by gestagens and support the participation of these peptides to the regulations of hypothalamus-pituitary-ovaries.