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RANEE SACHDEV : THE ROLE OF CLONIDINE-DISPLACING SUBSTANCE (CDS) EXTRACT FROM PORCINE CEREBRAL CORTEX ON ALPHA2-ADRENOCEPTOR. THESIS ADVISORS: DARAWAN PINTHONG, Ph.D., YUPIN SANVARINDA, Ph.D., SURIN PLASEN, M.D., Ph.D., LADDAWAL PHIVTHONGNGAM, Ph.D. 107P. ISBN 974-664-482-3

The purpose of this study was to examine the properties and functions of "clonidine-displacing substance" (CDS) and to determine whether it could be an endogenous substance that acts at alpha2-adrenoceptor apart from at non-adrenoceptor, imidazoline binding sites. Agmatine, a candidate for CDS was also studied in comparison with CDS extract.

In this study CDS was prepared from porcine cerebral cortex using methanolic extract and CDS activity is determined by the amount of the extract that displaces 50% of [^{3}H]clonidine binding to porcine cerebral cortex membranes. The activity of CDS in porcine brain extract was 7.71±1.96 unit/g wet weight tissue (n=5). From the saturation binding assay, the maximum number of alpha2-adrenoceptor on porcine cerebral cortex membranes labeled by [^{3}H]clonidine was 41.91±2.38 fmol/mg protein with Kd value of 3.009±0.371 nM (n=15). The maximum number of imidazoline receptor binding sites on porcine renal cortex membranes labeled by [^{3}H] idazoxan was 368.89±60.55 fmol/mg protein with Kd 9.423±2.791 nM (n=7). Based on radioligand binding assays, porcine CDS extracts in this study recognized both alpha2-adrenoceptor and non-adrenoceptor, imidazoline binding sites with 2.7 fold more potent at imidazoline receptor on porcine renal cortex membranes labeled by [^{3}H]idazoxan (IC_{50}=7.424±1.635 µl/ml) than at alpha2-adrenoceptors on porcine cerebral cortex membranes labeled by [^{3}H]clonidine (IC_{50}=20.6±2.958 µl/ml).

The effect of porcine brain CDS extract on ADP-induced human platelet aggregation was investigated and compared to the effect of clonidine. Clonidine potentiated ADP-induced human platelet aggregation in a concentration dependent manner and the effect was inhibited by an alpha2-adrenoceptor antagonist, yohimbine. On the contrary, CDS inhibited ADP-induced human platelet aggregation in a concentration dependent manner and the effect was not reversed by yohimbine. The inhibitory effect of CDS on ADP-induced platelet aggregation is not due to alpha2-adrenoceptor activation but may be via a non-adrenoceptor site. Agmatine, a putative substance for CDS, showed only small potentiated effect on ADP-induced platelet aggregation at even the concentration as high as 10^{-4} M. This study supports previous observations that agmatine possesses distinct biological activity from that of CDS, therefore, it cannot account for CDS activity in the extract.

In conclusion, CDS is able to recognize alpha2-adrenoceptors but the functional activity in modulating human platelet aggregation does not involve with alpha2-adrenoceptor activation. The possibility that CDS is an endogenous ligand at alpha2-adrenoceptors and non-adrenoceptor imidazoline binding sites is still to be clarified.