Thai J. Pharmacol.
Vol.7 No.3,4 Jul.-Dec. 1985

ROLES OF ARACHIDONIC ACID METABOLISM ON TESTOSTERONE PRODUCTION IN MOUSE LEYDIG CELLS

Wacharee Limpanasithikul, Darawan Dechachart and Udom Chantharaksri

Department of Pharmacology, Faculty of Science, Mahidol University, Rama 6 Road, Bangkok 10400, Thailand

Like many other endocrine glands, the suspected functional significance of the arachidonic acid metabolism in the leydig cells has been searched. It has been shown that prostaglandin F2-alpha, a cyclooxygenase metabolite of arachidonic acid suppresses plasma testosterone in the male rats and its inhibitory action on leydig cell response to gonadotropin stimulation is dimonstrated *in vitro*. The modulating role of the endogeneous prostaglandin on leydig cell reponse to gonadotropic stimulation has been repeatedly supported by experiments using cyclooxygenase inhibitors which are shown to potentiate the steroidogenic response to gonadotropic stimulation both *in vivo* and *in vitro*. The existence and involvement of lipoxygenase metabolite (s), product(s) of the other known metabolic pathway of cellular arachidonic acid metabolism is demonstrated in this study.

Mouse leydig cells were isolated and purified by Ficolldensity gradient centrifugation. The calibrated leydig cell suspensions, in a balanced salt solution were incubated in a constant shaking water bath under the atmosphere of $95\%O_2/5\%CO_2$ with gonadotropin, in the presence or absence of arachidonic acid (AA)and/or a known lipoxygenase inhibitor,nordihydroguaiaretic acid (NDGA). Mice treated with indomethacin (IND) were also used in this study. Arachidonic acid (doses upto 20 μM) caused a minimum but significant elevation of basal testosterone production in the midium. Addition of NDGA (12.5 to 50 μM) into the medium caused more increase in testosterone production over the stimulatory effect of AA and IND, this effect of NDGA is not dose dependent. The additive effect of NDGA on the basal steroidogenic action of AA and indomethacin is attributable to the non-specific cyclooxygenase inhibitory activity of the NDGA.

In the hCG-stimulated response, AA dose dependently increased the steroidogenic response to hCG (10 mIU) stimulation and the production of testosterone was further increased in mouse treated with IND. NDGA in the contrary dose dependently suppressed testosterone production in mouse leydig cells from both the controls and mice treated with indomethacin. The maximum suppressive dose of NDGA could be dose dependently overcome by AA. Suggesting that the lipoxygenase in the leydig cells may be the site of action of NDGA. We therefore conclude that the metabolites of arachidonic acid, both from cyclooxygenase and lipoxygenase pathways may be functioning as intracellular regulators of gonadotropic hormone in the leydig cells.