Ryu JeiMan°, Seong SeungKyoo, Bae EunJung, Song YoungJun, Jung YongHo, Kwak Chul, Park MunSoo, Lee SangEun, Shigematsu Akiyo, Shin ByungChul, Park KyongBae

Dong Wha Pharm. Ind. Co. Ltd.;Seoul National University College of Medicine;Institute of Whole Body Metabolism;Korea Atomic Energy Research Institue

166Ho-chitosan complex (HC) is a new radiopharmaceutical approved in Korea for liver cancer. In these studies, therapeutic effect against prostate cancer and biodistribution of HC were evaluated in animal models using the technique of intraprostatic administration. For evaluation of the therapeutic effect, noble rats with AIT orthotopic or subcutaneous prostate cancer were used. In orthotopic model of prostate cancer, group 1 was a sham control, group 2 received 1 mCi of chitosan-free 166Ho, group 3 received 0.5 mCi of HC and group 4 received 1.0 mCi of HC. In the meantime, the injection doses of HC were 10, 20 and 30 mCi in subcutaneous model. After 4 weeks post injection in subcutaneous model, inhibition rates of tumor growth in each group were 90.7, 96.9 and 82.9%, respectively. To determine the fate of HC, SD rats were used by studying its absorption, distribution and excretion after administration into the prostate gland. About 100 μCi of HC [0.1875 mg of Ho(NO3)3·5H2O and 0.25 mg chitosan/head] was administered intraprostatically to male rats. Radioactive concentrations in blood, urinary and fecal excretion and radioactive distribution in tissues were examined. The radioactive concentrations in blood were not observed, and cumulative urinary and fecal excretions for 72hr were negligible. The radioactive concentrations in tissues and the whole body autoradiography images showed that most of the administered radioactivity was localized at the administration site (>98% at 144 hr post administration), and only slight radioactivity was distributed in the bone, liver, spleen and kidney. These studies reveal that HC could be a safe and efficacious radiopharmaceutical candidate against prostate cancer.

Poster Presentations - Field A3. Hygienics

[PA3-1] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

CKD-501 INDUCED GLUCOSE TRANSPORT WAS MAINLY CAUSED BY THE STIMULATION OF GLUCOSE TRANSPOTER-TRANSLOCATION IN L6-MYOTUBES

Moon CK, Kim MH, Jung AY°, Lee YH, Chae SH, Kim KS, Jo YY, Kim MH, [1]Moon KS, [1]Kim JK, [1]Ahn SK, [1]Hong CI

Lab of hygienic chemistry, college of pharmacy, Seoul National University, Seoul, Korea
[1]CKD, Research Institute, Chonan, Korea

A newly synthesized thiazolodinedione derivative, CKD-501, was confirmed to have antihyperglycemic effect in in vivo study.
The present study was undertaken to investigate the effect of CKD-501 on glucose transport and its stimulating mechanism in L6-myotubes.
L6 myoblasts were cultured and differentiated to myotubes by reducing serum concentration in media from 10% to 2%. CKD-501 was added to culture media of myotubes to determine its effects on glucose uptake and insulin signaling pathway.
CKD-501 was found to increase the 2-deoxyglucose uptake in a dose-dependent manner with maximal stimulation at 10mM. Total protein levels of GLUT-1 and GLUT-4 were not changed by the treatment of CKD-501. But the translocation of GLUT-4 from the light microsome to the plasma membrane was markedly increased by CKD-501. Simultaneous treatment of insulin and CKD-501 did not result in any synergistic effect on 2-deoxyglucose uptake. Inhibitors of PI3-kinase and MAPK which are the major transducers of insulin signaling pathway, did not block CKD-501 induced glucose uptake. Some effects of CKD-501 on insulin independent signaling

pathway were also investigated. Nitric oxide production was not increased by CKD-501 treatment and CKD-501 induced glucose uptake was not inhibited by L-NAME, a nitric oxide synthase (NOS) inhibitor. Intracellular Ca2+ depletion abolished the increase in glucose transport induced by either insulin or CKD-501.
In conclusion, CKD-501 might improve the hyperglycemia by increasing GLUT-4 translocation, leading to the stimulation of glucose transport and this stimulation might be at least partially caused by the increase in intracellular calcium.

[PA3-2] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Induction of Apoptosis by N-nitrosocarbofuran, via Cytochrome c-Mediated Activation of Caspase-3 protease

Lee BangWool°, Oh SeonHee, Lee ByungHoon

Collage of Pharmacy and Medicinal Resources Research Center WonKwang University

Carbofuran(CF) is one of the most widely used carbamate pesticides in the world applied for insect and nematode control. Due to its widespread use in agriculture and households, contamination of food, water, and air has become serious, and consequently adverse health effects are inevitable in humans, animals, wildlife and fish, it has reported that CF alone or in combination with other carbamate insecticides influences the level of reproductive and metabolic hormones such as thyroxine and corticosterone, and results in impairment of endocrine, immun behavioral functions. we investigated the effects of NOCF on the Chinese hamster lung fibroblast (CHL) induction of apoptosis. The treatment of CHL cells with NOCF caused activation of caspase-3 , 8 protease. NOCF did not affect the expression of proapoptotic protein Bid but did cause a release of mitochondrial cytochrome c into cytosol. In conclusion, our results demonstrate that NOCF induced apoptotic cell death of CHL cells via cytochrome c dependent pathway.

[PA3-3] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

EFFECTS OF CADMIUM CHLORIDE ON GLUCOSE TRANSPORT IN 3T3-L1 ADIPOCYTES

Kim MH, Kim KS°, Lee HB, Chae SH, Jung AY, Jo YY, Kim MH, Moon CK

Lab of hygienic chemistry, college of pharmacy, Seoul National University, Seoul, Korea

Cadmium is well known as a toxic metal and has insulin mimicking effects in rat adipose tissue. To investigate the effect of CdCl2 on glucose transport and its mechanism, this study was performed in 3T3-L1 adipocytes.
10 and 25mM of CdCl2 exposed to cells for 12 hours increased 2-deoxyglucose uptake to 2.2 and 2.8 fold, respectively. Nifedipine, a calcium channel blocker, inhibited the 2-deoxyglucose uptake stimulated by CdCl2. This indicates that CdCl2 enters into the cell through the Ca2+ channel to affect glucose transport. Wortmannin, PI3 kinase inhibitor, and PD98059, MEK inhibitor, did not affect 2-deoxyglucose uptake. From these results, it is thought that CdCl2 may act on glucose uptake via insulin independent pathway.
ROS were also considered to increase glucose transport. To examine the relationship between Cd-induced glucose uptake and Cd-induced ROS production, [ROS]i and GSH level were measured. The fluorescence signal of reduced form of DHDCF-DA by cellular ROS,was measured with confocal microscope and was found to be dramatically increased by CdCl2