

[PB4-27] [ 2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function ]

**Inhibition of proliferation of human breast cancer cell (SK-BR3) and liver cancer cell (SK-Hep1) in tissue culture by the CCCA from Cordyceps militaris**

Lee Seungjeong, Han Shinha, Park Eunjung<sup>o</sup>, Lee Chong-Kil, You Byeongjin, Cho Kyunghae, Ha Nam-Joo, Kim Kyungjae

CM Biotec, Obongri 281-2, Kangnung, Kangwon, Korea, Department of Pharmacy, Sahmyook University, 26-21 Gongreung-Dong, Seoul, 139-742 South Korea, College of Pharmacy, Chungbuk National University, 48 Gaeshin-Dong, Chungju, 360-763 South Korea, Department of Food Science, Kangnung National University, Department of Biology, Seoul Women's University, 126 Gonglung-Dong, Seoul, 139-774 South Korea

Permanent cell culture lines derived from human cancer tissue are important experimental models in the study of human cancer cell proliferation. The in vitro effects of *C. militaris* and its extracted fractions on the human breast cancer (SK-BR3), liver cancer (SK-Hep1, HepG2), kidney cancer (p15), lymphoma (Jurkat) were studied. F1 (CCCA, crude cordycepin containing adenosine), F2 (ethanol precipitation), F3 (ethanol soluble supernatant) and F4 (fraction of through SK-1B) significantly stimulated in vitro cytotoxic activity in human cancer cell lines. Those compounds that are found to be potent in killing cancer cells or inhibiting cell growth are then further screened for their ability to suppress the growth of tumors in human cancer cell lines. In the present work, F1 and F4-treated human breast cancer (SK-BR3) and liver cancer (SK-Hep1) showed killing effects in a dose dependent manner between 15 and 60  $\mu\text{g/ml}$ . DNA fragmentation was also examined those cells exposed to F1 and F4. We conclude that CCCA and F4 may be useful in the control of human breast (SK-BR3) and liver cancer (SK-Hep1).

[PB4-28] [ 2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function ]

**Inhibition of IL-1 $\beta$  and IL-6 in osteoblast-like cell by Isoflavones extracted from Sophorae Fructus and its potential role in preventing from osteoporosis**

Joo SeongSoo, Won TaeJoon, Lee MinWon, Choi YoungWook, Lee Dolk<sup>o</sup>

Department of Immunology, College of Pharmacy, Chung-Ang University, Seoul 156-756, Korea

Isoflavone found in Leguminosae is one of natural phytoestrogens and its effect on bone remodeling is one of key investigational interests in terms of estrogen replacement therapy (ERT). As commonly known, osteoporosis is one of hormonal deficiency diseases, especially in menopausal women. When estrogen is blocked, local factors such as IL-1 $\beta$  and IL-6 that are related in bone resorption are increased and enhance osteoclastogenesis, which is responsible for bone resorption. In the present study, we investigated the effect of isoflavones (Isocal) extracted from Sophorae Fructus on bone resorption in vitro. From the study, we found that the active control (PIII) effectively enhanced the level of nitric oxide, attenuated local factors (IL-1 $\beta$  & IL-6), and inhibited osteoclastogenesis. The most efficient concentration was observed at 10<sup>-8</sup>% for three to five days, whereas comparative control (soybean isoflavone) was not effective in lower concentration. In conclusion, the product which contained enriched glucosidic isoflavone and nutrient supplements such as shark cartilage and calcium can be used for treatment of osteoporosis by its role of inhibiting local factors, IL-1 $\beta$  and IL-6, and nitric oxide produced through eNOS may play a role in inhibiting bone resorption.

[PB4-29] [ 2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function ]

**Isoflavones extracted from Sophorae Fructus upregulate the growth factors, IGF-I and TGF- $\beta$  in MG-63 cells**

Joo SeongSoo, Kang HeeChul, Lee MinWon, Choi YoungWook, Lee Dolk<sup>o</sup>

Department of Immunology, College of Pharmacy, Chung-Ang University, Seoul 156-756, Korea

Isoflavones have been a central subject in natural phytoestrogens found in Leguminosae. Their effects on bone

formation and remodeling are an important turning point in that they can act like estrogen by binding on estrogen receptors on target cell surface. We, therefore, believed that isoflavones may be applied in estrogen deficiency disease such as osteoporosis in terms of estrogen replacement therapy (ERT). As commonly known, osteoporosis is one of hormonal deficiency diseases, especially in menopausal women. When estrogen is no more produced in the body itself, a remarkable bone remodeling is occurred, and the events are regulated by growth factors in osteoblast lineage. In the present study, we investigated the effect of isoflavones (IsoCal) extracted from *Sophorae Fructus* on growth factors, IGF-I and TGF- $\beta$  related with bone formation in vitro. From the study, we found that the active control (PIII) effectively enhanced the level of nitric oxide, growth factors, and finally inhibited osteoclastogenesis. The most efficient concentration was observed at 10<sup>-8</sup>% for three to five days, whereas comparative control (soybean isoflavone) was not effective in lower concentration. In conclusion, the product which contained enriched glucosidic isoflavone and nutrient supplements such as shark cartilage and calcium can be used for treatment of osteoporosis by its role of enhancing the production of IGF-I and TGF- $\beta$ , and nitric oxide produced through eNOS may play a role in inhibiting bone resorption.

[PC1-1] [ 2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function ]

### **Cooper ions and hypochlorite are mainly responsible for oxidative inactivation of paraoxon-hydrolyzing activity in human high density lipoprotein**

Nguyen Duy Su<sup>o</sup>, Kim Ju Ryung, Sok Dai Eun

*College of Pharmacy, Chungnam National University*

Paraoxonase, an antioxidant enzyme, exclusively located on HDL is well known for both hydrolysis of organophosphate and prevention against LDL oxidation. It has been reported that PON1 decrease its activity under oxidative stress and that PON1 activity is lower in subject with higher vulnerability to organophosphate poisoning. The aim of our study is to examine the effect of oxidative system on paraoxon-hydrolyzing activity and to elucidate the plausible mechanisms responsible for the decline of HDL-associated PON1 activity in vivo system. Of various oxidative systems, Ascorbate/Cu<sup>2+</sup> was found to be the most potent in inactivating the paraoxon-hydrolyzing activity of purified PON1 as well as HDL-associated PON1. The inactivation of PON1 is protected by catalase but not other hydroxyl scavengers, supporting the important role of Cu<sup>2+</sup> in catalyzing oxidative inactivation. In addition, several lipids including oleic acid and phosphatidyl dioleoyl glycerol also expressed partial protection. Noteworthy, Cu<sup>2+</sup> cause HDL-associated PON1, but not purified PON, inactivation in a concentration-dependent manner, indicating that there may be a reducing component on HDL which facilitate the inactivation of Cu<sup>2+</sup>. Separately, PON1 both purified and HDL-associated form was also observed to be susceptible to HOCl. It is of interest that while susceptibility to hypochlorite (<1 mM) was similar between purified PON1 and HDL-associated PON1 the inactivation by hypochlorite at higher concentration seemed to be interfered by the membrane. Moreover, Ascorbate/Cu<sup>2+</sup> in concert with HOCl exhibited the cooperative effect in inactivating HDL-associated PON1 (maximum 73%). On the basis of these results, it is suggested that metal-catalysed oxidation and HOCl-generating system is likely to be responsible for the reduction of HDL-associated PON1 activity under oxidative stress.

[PC1-2] [ 2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function ]

### **ERGOPTHIONEINE RESCUES PC12 CELLS FROM BETA-AMYLOID-INDUCED APOPTOTIC DEATH**

Jang Jung-Hee<sup>o</sup>, Surh Young-Joon

*College of pharmacy, Seoul National University*

beta-Amyloid (A $\beta$ ) peptide is the major component of senile plaques and considered to have a causal role in the development and progression of Alzheimer's disease. There has been compelling evidence supporting that A $\beta$ -induced cytotoxicity is mediated through oxidative and/or nitrosative stress. Recently, considerable attention has been focused on dietary manipulation of oxidative and/or nitrosative damage. L-Ergothioneine (EGT) is a low-molecular weight naturally occurring thiol compound of dietary origin which exists in millimolar concentrations in