Recently, we developed a new anti-osteoporotic agent, DW-1350, which not only inhibited osteoclast formation but also induced osteoblast differentiation through the in vitro randomized screening studies.
We identified inhibitory activities of DW-1350 for each step of osteoclast differentiation, fusion and pit formation process in co-culture system with mouse bone marrow and primary osteoblasts. As a result of these studies, we found that DW-1350 suppressed the formation of TRAP-positive osteoclasts induced by 1a,25(OH)2D3 and dexamethasone. This study also showed that DW-1350 exhibited significant decrease of the fusion process to mature osteoclasts and the bone-resorbing activity measured by pit number formed on dentine slice in a dose-dependent manner. In osteoblastic MC3T3-E1 cell, DW-1350 affected cell proliferation and up-regulated differentiation markers such as alkaline phosphatase (ALP) activity. And we identified the positive effects of DW-1350 on bone nodule formation determined by amount of minerals deposited on the formed bone matrix.
These results suggest that DW-1350 might be a promising agent for treatment of osteoporosis not only by inhibiting osteoclast formation and bone-resorbing action, but also by stimulating osteoblast differentiation.

[PA2-3] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

DW1350, a Newly Synthetic Anti-osteoporotic Agent : 2. Effect on Ovariectomized Osteoporosis Rat Model,a Histomorphometrical Aspect.

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In the present study, the effect of DW-1350, a newly synthesized anti-osteoporotic agent, was evaluated in ovariectomized Rat. Female SD Rat mice underwent bilateral ovariectomy for prevention study that test article was administered from 2 days after ovariectomy for 6 weeks, for therapeutic study it was conducted from 6 weeks after ovariectomy for three months. Body weight, bone weight and histological profiles of epiphyseal regions of tibia and femur such as cortical bone thickness, trabecular bone number, thickness and length with trabecular bone volume percentage (TBV), were observed respectively. Results were compared to that of alendronate, well-documented anti-osteoporotic agents. Histomorphometrical changes were observed or calculated using image analyzer system, AnalySIS-auto (SIS Co., Germany). In prevention and therapeutic studies, DW-1350 showed favorable inhibitory effect to histomorphometrical changes induced by ovariectomy. We can also find that DW-1350 dose-dependently (10 or 50mg/kg, {i}p.o{/i}) increased the TBV, trabecular bone length and width, and cortical bone width or decreased the osteoclast cell numbers. Especially more favorable effects were observed in DW-1350 compared to that of alendronate on cortical bone thickness. Base on these results, DW-1350 may act as both a suppressor of bone resorption and an enhancer of bone formation {i}in vivo{/i}. In conclusion, it should be suggested that DW-1350 has enough and favorable effect to prevention and therapy of estrogen-deficient osteoporosis.

[PA2-4] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

The protective and antioxidant effect of Solanum lycopersicum extract in liver fibrosis induced rats

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The adducts of lipid peroxidation and related aldehydic end are mediators of chronic poisoning and affect the development of chronic liver damage leading to fibrosis and cirrhosis. Substances delayed or suppresed lipid peroxidation could have an antioxidant and protective effect in liver disease. In this study, it was attempted to find out above mentioned effect of Solanum lycopersicum investigated in CCl4 induce liver fibrosis model.
The female Sprague-Dawley rats were divided into 3 groups(Normal, AC: CCl4 treated group AC-SL: CCl4 and Solanum lycopersicum treated group) and liver fibrosis was developed by CCl4 administration. The rats were observed for 4 weeks and sacrificed. The liver and blood were prepared and used for quantitative measurement of enzyme activity, MDA and SOD.
As a result, the level of clinical parameters in sera of AC, AC-SL group ($p<0.005 \sim 0.001$), when compared to AC group, AC-SL group showed significantly lower value of AST, ALT, ALP, BUN and total-bilirubin ($p<0.05 \sim 0.001$). The metabolite of lipid peroxidation (MDA) in liver tissue increased significantly in both of CCl4 group ($p<0.0001$). And the concentration of MDA in liver of AC-SL group decreased significantly 24.8% compared with AC group ($p<0.0001$). The value of SOD appeared 4.35 ± 0.12 in normal group, 4.07 ± 0.03 in AC and 4.32 ± 0.14 U/0.1g liver in AC-SL group, which the value of AC-SL group was significantly increased compared to AC group ($p<0.01$).
In conclusion, Solanum lycopersicum extract may have the improvement of hepatic function and the antioxidative effect in experimental liver fibrosis.

[PA2-5] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Convenient Therapy with Specially Designed Radionuclide, 166Ho Skin Patch for Skin Cancer

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166Ho, a β-emitting radionuclide, was incorporated within polyurethane film for possible application for the therapy of skin cancers. The aim of this study was to investigate skin irritant after radiation with 166Ho patch in rabbits and to estimate the efficacy of this therapy for skin cancer patients. Six NZW rabbits were used for skin irritant in this study. The dorsal hair of rabbits was removed with an electric clipper and blade. Three different radiation doses (control, 35Gy and 70Gy) were applied on skin of the shaved rabbit. Two weeks after radiation, desquamation, erythema or erosion developed in applied sites but these acute radiation reactions healed gradually. For the evaluation of the efficacy of this therapy, 26 sites of Bowen's disease in 12 patients, 8 lesions of basal cell carcinoma in 8 patients, 3 lesions of squamous carcinoma in 3 patients and 18 lesions of Kaposi sarcoma in 4 patients were treated with 166Ho patches (45-95 year old; 0.5-8 cm in size). The patches were applied to the surface of skin cancers for 30-60 min for a total radiation dose of 35 or 80 Gy according to the type of cancer. All of 26 lesions of Bowen's disease, 6 of 8 lesions of basal cell carcinoma, all of 3 lesions of squamous carcinoma and 17 of 18 lesions of Kaposi sarcoma showed complete response with single treatment. It was concluded from these studies that the 166Ho patch is a safe, convenient, cosmetic and effective therapeutic modality without adverse effects on the surrounding normal tissue and bone.

[PA2-6] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Development of a Radiopharmaceutical using 166Ho-chitosan Complexes against Prostate Cancer