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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