

Previously, we found out that CW-2101, a isoquinoline alkaloid derivative selectively inhibited the hKv1.5 current expressing predominantly in human atrium without affecting the HERG current expressing mainly in ventricle. Additionally, CW-2101 inhibited the K<sup>+</sup> current in isolated human atrial myocytes. All our results suggest that CW-2101 would be one of the ideal antiarrhythmic drugs for atrial fibrillation. In this study, we compared the antiarrhythmic potential of CW-2101 with that of dofetilide developed as one of Class III antiarrhythmic drugs recently.

We examined the effects of CW-2101 and dofetilide on the action potentials in rabbit heart using conventional microelectrode technique. CW-2101 prolonged the action potential durations of atrial myocytes in a dose-dependent manner. Interestingly, CW-2101 prolonged APD in a frequency-dependent manner, whereas dofetilide did not affect the APD of atrial myocytes. In ventricular myocytes, CW-2101 at the concentrations of 0.1 and 0.3  $\mu$ M did not affect the APD. However, CW-2101 at the concentrations of 1 and 3  $\mu$ M shortened APD at the frequency of lower than 3 Hz, whereas prolonged APD at the frequency of higher than 3 Hz. In contrast, dofetilide (10 nM) prolonged APD in a reverse frequency-dependent manner. These results strongly suggest that CW-2101 could be superior to dofetilide in treating atrial fibrillation.

[PA1-25] [ 10/18/2001 (Thr) 14:00 - 17:00 / Hall D ]

### **The Pharmacological Profile of JOINS (SKI 306X) I : The cartilage-protective effects**

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Protective effects of JOINS (SKI 306X), a natural herbal product extracted from three herbs *Clematis mandshurica*, *Trichosanthes kirilowii*, and *Prunella vulgaris*, on articular cartilage were examined and compared with other osteoarthritis (OA) drugs using in vitro and in vivo models.

In vitro studies were performed using rabbit articular cartilage explants culture. The degradation of cartilage was induced by the recombinant human interleukin-1 $\alpha$  with or without plasminogen co-treatment and glycosaminoglycan and hydroxy-proline release were measured. For in vivo study, collagenase was intra-articularly injected twice into the right knee joint of rabbits and the degrees of OA-like changes were evaluated through a histological examination.

In vitro study revealed JOINS inhibited the degradation of PG and collagen in a concentration-dependent manner. *Trichosanthes kirilowii*, which is one of the components of JOINS, also significantly inhibited the cartilage degradation. JOINS reduced the OA-like histological changes in collagenase-injected rabbit knee joint.

These results strongly suggest that JOINS can be a good agent for ameliorating the OA symptoms by modifying the matrix destruction in OA patients..

[PA1-26] [ 10/18/2001 (Thr) 14:00 - 17:00 / Hall D ]

### **Sesquiterpene lactones from *Eupatorium chinense***

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Sesquiterpene lactones (1-3) have been isolated from *Eupatorium chinense* as active principles of the cytotoxic property toward human tumor cell lines such as A549, SK-ov-3, SK-mel-2, XF498 and HCT15 in vitro.

By means of spectral analysis, particularly by the aid of various two dimensional NMR experiments, all <sup>1</sup>H-NMR and <sup>13</sup>C-NMR signals of 1-3 were completely assigned.