both physiological and stimulated mucin release from airway epithelial cells without significant cytotoxicity and PLL lost its activity under the range of 14mer. This finding suggests that polymer of basic amino acid like PLL might function as a regulator for hypersecretion of mucus manifested in various respiratory diseases.

[PA1-14] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

A newly antiarrhythmic drug CW-2202 is ideal in treating atrial fibrillation

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A number of patients suffering from atrial fibrillation are increasing and many cardiologists are trying to develop the ideal antiarrhythmic drugs for atrial fibrillation. Previously, we found out that CW-2202, a furanocoumarin derivative inhibited the hKv1.5 current expressing predominantly in human atrium without affecting the HERG current expressing mainly in ventricle. From those results, we proposed that CW-2202 would be one of the leading compound in developing the ideal antiarrhythmic drugs for atrial fibrillation. In this study, we examined the effects of CW-2202 on cardiac action potentials as well as K+ currents expressed in Ltk-cells using conventional microelectrode technique and patch clamp method. CW-2202 reduced the tail current amplitude recorded at -50 mV after 250 ms depolarizing pulses to +60 mV, and slowed the deactivation time course resulting in a 'crossover' phenomenon when the tail currents recorded under control conditions and in the presence of CW-2202 were superimposed. These results indicate that CW-2202 primarily block activated hKv1.5 channels in a time-, voltage-, frequency- and concentration-dependent manner. Additionally, CW-2202 prolonged the action potential durations of atrial myocytes and Purkinje fibers in a dose-dependent manner. These results strongly suggest that CW-2202 could be an ideal antiarrhythmic drug specific for atrial fibrillation.

[PA1-15] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

Induction of apoptosis by benz[f]indole-4.9-dione analog in human lung cancer cells through p53-dependent mechanism

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A synthetic naphthoquinone alkaloid, 2-amino-3-ethoxycarbonyl-1-methyl pyrolo (3,2-b) naphtho-4,9-dione (compound 1), showed a potent cytotoxicity in a panel of cancer cell lines with an IC50 ranged from 0.1 to 0.3 microgram/mL. Prompted by a potent cytotoxic activity, the mechanism action study was performed with cultured A549 of human lung cancer cells. Flow cytometric analysis showed G2/M cell cycle arrest and microscopic investigation was also characterized with apoptotic morphological features. The apoptotic cell death was induced in a concentration- and time-dependent manners. In addition, Compound 1 increased p53 expression level in A549 cells. But the bcl-2 protein level was not much affected. Our results demonstrate that compound 1 may be a good candidate for additional evaluation as a potential therapeutic agent for human lung cancer and possibly other types of cancer.(This work was supported in part by Korea research Foundation Grant, KRF-2001-005-F00023).

[PA1-16] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]