Various biopolymers to prepare the drug carrier have been used by many investigator due to their biocompatibility and biodegradability. Among these polymers, PLGA, the copolymer of lactide and glycolide, is suitable material as drug carrier in this point. They were approved by the Food and Drug Administration (FDA) for several therapeutic products and can formulate to release macromolecules over a long period. In this study, we prepared the nanoparticle utilizing PLGA by dialysis method without surfactant and physicochemical properties such as particle size and drug contents were investigated against various solvents. And the nanoparticles of PLGA showed good spherical shapes from scanning electron microscopy (SEM) and transmission electron microscopy (TEM) observations. Biodegradation rate of PLGA nanoparticles prepared from DMF was faster than that of acetone, indicating that the biodegradation of PLGA nanoparticles was size-dependent. Resultantly, the higher drug contents and the larger particle size resulted in slower the drug release.

[PA1-3] [04/20/2001 (Fri) 10:30 - 11:30 / Hall 4]

The mechanism of C2-ceramide-induced contraction of smooth muscle cells in cat esophagus

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We previously have shown that C_2-ceramide (C_2) plays a role in mediating contraction of cat esophagus. We have isolated smooth muscle cells by enzymatic digestion with collagenase F.C_2 induced contraction of smooth muscle cells in cat esophagus, which is blocked by PKC inhibitors, H-7 or chelerythrine. To confirm that PKC-mediated contraction may be isozyme specific, we examined the effect of different PKC antibodies on the contraction. PKC-ϵ antibody inhibited the contraction by C_2, which suggest that PKC-ϵ may mediate the contraction induced by C_2. To characterize the specific PKC isozymes that mediate contraction of the smooth muscle cells, we used N-myristoylated peptides (Myr-PKC) derived from the pseudosubstrate sequences of PKC-$\alpha\beta\gamma$, -α, -δ, and -ϵ. Myr-PKC-ϵ only inhibited the contraction, which was concentration-dependent, suggesting that PKC-ϵ isozyme is involved in the contraction. To examine which MAP kinase is involved in C_2-induced contraction, p44/p42 MAP kinase inhibitor, PD98059, or p38 MAP kinase inhibitor, SB202190 was used. Preincubation of PD98059 only blocked the contraction induced by C_2 in a concentration dependent manner. C_2 increased the intensity of the bands identified by phosphospecific p44/p42 MAP kinase antibody and preincubation of PD98059 decreased the intensity of bands as compared with C_2 stimulated cells.

In conclusion, C_2 produced the contraction of smooth muscle cells. The contraction is mediated by PKC-ϵ-protein, resulting in the activation of p44/p42 MAP kinase

[PA1-4] [04/20/2001 (Fri) 10:30 - 11:30 / Hall 4]

Reversal of multidrug-resistance by benzodiazepin and benzotriazepin analogues in cancer cells

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A major mechanism by which tumor cells can develop resistance to anticancer drugs is by decreasing the intracellular bioavailability of the anticancer drug. Such a multidrug-resistance (MDR) phenotype of tumor cells is usually mediated by the overexpression of a membrane protein, P-glycoprotein (Pgp),