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The purpose of this study was to investigate the prevalence of antibiotics resistance macrolide, lincosamide, and streptogramin B antibiotics (MLS) in Gram-positive bacteria. The 1037 clinical isolates were provided by hospital laboratories in Seoul between May 1999 and January 2000. The determination of MICs(㎍/ml) was made by the agar dilution method recommended by the National Commit for Clinical Laboratory Standards(NCCLS) and the French Society for Microbiology (FMS).
S. aureus had erythromycin MICs between 0.125㎍/ml and 64㎍/ml and the resistant strains was 71% (MIC, 8 ㎍/ml) to this antibiotic.
The strains were also highly resistant (MIC 50/MIC90, 64㎍/ml) to clarithromycin, josamycin, azithromycin, and clindamycin, 70%, 64%, 72%, and 63% of the isolates were resistant to this antibiotics, respectively. But the strains were susceptible to pristinamycin (13% resistance). By NCCLS interpretive criteria, 59%, 61%, 43% 66%, 41% and 4% of Coagulase-negative staphylococci (CNS) clinical isolates were resistant to erythromycin, clarithromycin, josamycin, azithromycin, clindamycin and pristinamycin, respectively. Enterococci had 59%, 61%, 43%, 66%, 41%, and 4% resistance ratio to erythromycin, clarithromycin, josamycin, azithromycin, clindamycin and pristinamycin, respectively.
In this study Gram-positive bacteria in Seoul were resistant to Macrolide(erythromycin, clarithromycin, josamycin, azithromycin) and Lincosamide(clindamycin), but these bacteria were susceptible to Streptogramin B(pristinamycin).

[PA1-4] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

In vitro Antibacterial Effect of YJA20379-8 on Helicobacter pylori

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We compared the susceptibility of Helicobacter pylori to two antiulcer agents, expressed as MICs and as bactericidal effectiveness in short (24 hours) time and long time (7 days) killing studies. MIC values of YJA20379-8 and omeprazole were about 6 mg/L and 31 mg/L respectively, for 10 strains of Helicobacter pylori. Long time-killing kinetic study demonstrated that YJA20379-8 produced decrease of viability within 1 day but omeprazole did not show bactericidal effect in the same drug concentration. Short time-killing kinetic study showed YJA20379-8 produced 2.9 log decrease in viability, but omeprazole slightly increased. As a results of MIC and time-kill data, a growth inhibitory effect of YJA20379-8 on Helicobacter pylori was observed and more potent than that of omeprazole.

[PA1-5] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

5-FU inhibits the production of nitric oxide in stomach cancer cells

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Nitric oxide (NO) is synthesized in mammalian cells from the amino acid L-arginine by a family of enzymes, the nitric oxide synthases (NOS). This molecule plays a key role in many physiological as well as pathological processes, including inflammation and neoplasia. 5-fluorouracil (5-FUra), an antimetabolite effective against colon and gastric tumors, has been shown to suppress nitric oxide biosynthesis in colon carcinoma cell line, DLD-1. (Jin, Y., Heck, D.E., DeGeorge, G., Tian, Y., and Laskin, J.D. (1996) Cancer Res. 56, 1978). However, the exact mechanism how 5-Fura reduces NO production has not been known. In the present study, we characterized the effect of 5-Fura on NO

production by gastric (NCI-N87) adenocarcinoma cells. The NO production by gastric adenocarcinoma cell lines was increased by IFN-γtreatment, which was inhibited by pretreatment of 5-FUra. Pretreatment of 5-FUra showed much higher reduction of NO production than by L-NAME, L-NMMA, well known NOS inhibitors. 5-FUra reduced the mRNA production of inducible NOS in carcinoma cells. Gel retardation result showed that 5-FUra decreased the NF-kB binding into iNOS promoter. Taken together, these data suggest that 5-FUra inhibits NO production in colon and stomach adenocarcinoma cells by inactivating NF-kB.

[PA1-6] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

YH3096 causes G2/M enrichment and induces Anoikis in human tumor cells harboring K-ras mutation

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The ability of Ras oncoproteins to cause malignant transformation requires their post-translational modification by prenyl group. Prenylation allows the ras oncoprotein to localize to the plasma membrane where it plays a pivotal role in growth factor signalling and malignancy. For this reason, inhibition of Ras prenylation is being pursued as a way of developing anticancer drug. YH3096 inhibits anchorage dependent and independent growth of human tumor cells which express mutated K-ras. Furthermore, the prenylation of oncogenic ras in A549 human lung cancer cell lines was disrupted by YH3096. This leads to cell cycle arrest in G2/M phase as well as anokis, induction of detachment-mediated apoptosis. This accounts for the ability of YH3096 to inhibit tumor cell growth and to abolish the malignancy of cancer cells. Therefore, it is concluded that YH3096 is a potent inhibitor of Ras processing leading to mitotic arrest and loss of ras-driven malignancy. This study was supported by a grant of the Korea Health 21 R & D project, Ministry of Health & Welfare, Republic of Korea (HMP-98-D-7-0010).

[PA1-7] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Hypoglycemic Effect and Mutagenicity of JG-381

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JG-381, a racemic form of oxirane-2-carboxylate derivative, was examined for mutagenicity using various tests : the reverse mutation test on bacteria, chromosomal aberration test on cultured mammalian cells and micronucleus test on mice. Also the oral hypoglycemic effect of JG-381 was evaluated by measuring of plasma glucose in both normal and streptozotocin-induced diabetic rats. In the reverse mutation test on bacteria using Salmonella typhimurium strain TA98, TA100, TA102, TA1535, TA1537 with or without a metabolic activation system (S9 mix), JG-381 significantly increased reverse colonies in all test strains compared with the control. In the chromosomal aberration test using cultured Chinese Hamster Lung (CHL) cells, JG-381 increased the number of aberrant cells in the presence of S9 mix. In the micronucleus test, micronucleated polychromatic erythrocytes in the JG-381-treated mice were not significantly different from those of the vehicle-treated mice. These results indicate that JG-381 has mutagenic potential under this conditions. In normal rats single oral administration of JG-381 significantly lowered the level of plasma glucose in a glucose tolerance test. In contrast, in diabetic rats vivo four weeks treatment of JG-381 did not affect the level of plasma glucose.