potential β-lactamase inhibitors. Among them 1,1-Dioxo-6-bromo-6-[(2-bromo, 3-phenyl) allylidene] penicillanic acid effectively inhibited Enterobacter cloacae β-lactamase(IC50 = 0.007mM/ml).
In this study, three inhibitors from this series were docked into Enterobacter cloacae β-lactamase with computer docking program, QXP. The docking results demonstrated that a new inhibitor with high biological activity proven experimentally docked well into the active site of the enzyme but the inhibitors with no activities were not docked. It provided potential binding modes for the new inhibitor to the target enzyme. The docking results of E and Z isomers of 1,1-Dioxo-6-bromo-6-[(2-bromo, 3-phenyl) allylidene] penicillanic acid showed that more prevalent Z isomer docked well into the active site, while the E isomer did not. This result suggests that the biologically active stereoisomers may be selected by the docking study.

[PC1-8] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Properties of Polyphenoloxidase and Antioxidant Enzyme in the Leaves of Erechitites hieracifolia

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Polyphenoloxidase activity in the leaves of Erechitites hieracifolia was estimated by Warburg's manometric method. The enzyme was most reactive toward chlorogenic acid followed by caffeic acid. Diethydithiocarbamate and potassium cyanide were shown powerful inhibition rate to the polyphenoloxidase from the leaves of Erechitites hieracifolia. Electrophoretic isoenzyme banding pattern of SOD, POD and CAT were observed by native PAGE. We confirmed antioxidant activity of its methanol extract by DPPH radical scavenging method.

[PC1-9] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Inhibitory effect of some natural product on tyrosinase activity in vitro

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To indentify inhibitors of melanogenesis, we compared the effect of 4 natural products on mushroom tyrosinase, human melanocytic tyrosinase activity and melanin content. The cytotoxicity of the component were also tested on cultured mouse melanoma cells.
Each extract significantly inhibited tyrosinase activity in vitro and B 16 melanoma cell lines. In B 16 cell lines, watermelon's inner shell extract inhibited tyrosinase activity as strong as kojic acid at 0.105g/ml concentration. Each extract were strong inhibitors of tyrosinase activity in B 16 mouse melanoma cell lines at less than 0.1g/ml concentration.
These result show that extract of watermelon's inner shell,lettuce,morning glory's seed,ginko could be developed as skin whitening component of cosmetics.

[PC1-10] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Inhibitory Effects of Isoquinoline Alkaloids on Proinflammatory Cytokines.

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Inhibitory effects of isoquinoline alkaloids on proinflammatory cytokines of tumor necrosis factor(TNF-α), interleukine-1β(IL-1β), interleukine-5(IL-5) have been estimated. Among 11 kinds of isoquinoline alkaloids (tetrahydopapaverine, salsolinol, berberine, coralyne chloride, hydrastine, laudanosine, pamatine chloride, noscapine, papaverine, ethaverine, and tetrahydropapaveroline) tested, 9 samples exhibited inhibitory effects on the IL-5 bioactivity with an IC50 value of 7.5 uM by tetrahydropapaverine, 3.5uM by salsoline, 0.9 uM by berberine, 0.3 uM by coralyne chloride, 24 uM by laudanosine, 15.8 uM by pamatine chloride, 1.4 uM by papaverine, 1.4 uM by ethaverine, and 1.6 uM by tetrahydropapaveroline. However, the compounds have no inhibitory effects on TNF-α and IL-1β bioactivities. Experiments to know effects on IL-3, IL-4 and IL-6 are in progress.

[PC1-11] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Celastrol, a quinone methide triperpenoid, suppresses NF-kB Activation by inhibiting phosphorylation of IkBa

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Celastrol, a quinone methide triterpenoid, was isolated as a NF-kB inhibitor from Celastrus orbiculatus by activity-guided fractionation. This compound dose-dependently inhibited the induced NF-kB reporter gene expression and DNA-binding activity of NF-kB in different cell lines by various stimuli without affecting DNA-binding activity of AP-1 transcription factor. Preincubation of celastrol completely blocked the induced degradation and phosphorylation of IkBa protein by LPS, TNF-a, or PMA. Moreover, celastrol suppressed the induced NF-kB activation by overexpression of NEKK-1, NIK, or IKK-a, but not by p65, suggesting that celastrol suppressed the induced NF-kB activation by preventing phosphorylation of IkB, possibly through inhibiting kinase activity of IkB kinase complex. To verify that celastrol is a NF-kB inhibitor, we investigated its effect on some NF-kB target genes expressions. Celastrol prevented not only LPS-induced mRNA expression of iNOS and TNF-a, but also TNF-a induced expression of Bfl-1/A1, a prosurvival bcl-2 homologue. Consistent with these results, this compound significantly suppressed the production of NO and TNF-a in LPS-stimulated RAW264.7 cells, and increased the cytotoxicity of TNF-a in HT-1080 cells. Taken together, this study extends our understanding on the molecular mechanisms underlying the antiinflammatory activities of celastrol and celastrol-containing extracts that are used in traditional oriental medicine. Furthermore, celastrol could be an interesting lead compound for the modulation of NF-kB-dependent pathological conditions such as inflammatory diseases and cancer.

[PC1-12] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Mechanism of Cinnanaldehyde induced-apoptosis in human leukemia HL-60 cells

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In the previous report, we found that cinnamaldehyde, isolated from the stem bark of Cinnamomum cassia, induced cytotoxicity and apoptosis. These effects were completely prevented by pretreatment with antioxidant N-acetyl-L-cystein (NAC). Cinnamaldehyde activated various caspases, such as caspase-3, caspase-8 and caspase-9 activities, and induced the release of cytochrome-c from mitochondria into the cytosol. Bid, a death agonist member of the Bcl-2 family, was processed following exposure of cells to cinnamalehyde. These data suggest that cinnamaldehyde induced apoptosis of HL-