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A substantial body of evidence indicates that reactive oxygen intermediates (ROIs) are implicated in pathogenesis of diverse human diseases, including cancer, diabetes, and neurodegenerative disorders. Recent studies have revealed that moderate amounts of intracellular ROIs can cause cell death via apoptosis while their excessive cellular accumulation leads to necrotic death. Cell death is regulated by plenty of functional genes and their protein products. Bcl-2 which is an integral inner mitochondrial membrane protein blocks cell death induced by a wide variety of toxicants. In the present work, we have investgated the possible protective role of *bcl-2* on oxidative death induced by hydrogen peroxide and beta-amyloid in cultured PC12 cells. Hydrogen peroxide is a typical ROI produced by xenobiotic redox molecules. It is also generated under normal physiological conditions and is recognized as an important messenger mediating the intracellular signaling in response to external stimuli. Beta-Amyloid is a peptide accumulated in the certain brain regions of patients with Alzheimer disease, and is known to exert its toxicity through ROI generation. When PC12 cells were treated with hydrogen peroxide or beta-amyloid, they underwent apoptotic death as determined by morphological features, internucleosomal DNA fragmentation and positive *in situ* terminal end-labeling (TUNEL staining). Transfection of PC12 cells with the anti-apoptotic *bcl-2* gene protected these cells from oxidative damage caused by either hydrogen peroxide or beta-amyloid. PC12 cells overexpressing *bcl-2* exhibited relatively high constitutive DNA binding and transcriptional activities of NF-kappa B, compared with the vector-transfected control cells. In addition, sustained NF-kappa B activation was observed in the *bcl-2*-overexpressing cells after treatment with hydrogen peroxide or beta-amyloid. Western blot analyses revealed that *bcl-2* transfected PC12 cells exhibited the higher level of p65, the functionally active subunit of NF-kappaB, in the nucleus than did the vector-transfected controls. In contrast, the cytoplasmic inhibitor IkappaB-alpha was present to a lower level in the cells overexpressing *bcl-2*. These results suggest that the ubiquitous eukaryotic transcription factor NF-kappa B plays a role in cell survial against oxidative stress.
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[OD-1] [04/21/2000 (Fri) 11:10 - 11:25 / Rm B113, Bldg 26]

Computer Graphics: Theoretical Study of DNA-Intercalation

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Most DNA-intercalators bind to DNA bases, cytidines and guanidines, which are affected by hydrogen-bonding, electrostatic energy and Van der Waals energy in the DNA.
Generally, the study of DNA-intercalation has been carried out with NMR analysis, Gel-electrophoresis and so on. By the computer-aided molecular modeling, we inserted anticancers, 9 types of the Ellipticin derivatives which are already well-known as DNA-intercalators, into the DNA centers of a form (CGCG)2- DNA and b form (CGCG)2- DNA and then DNA-drug complexes were formed via docking. After energy minimization for the complexes, we observed whether hydrogen bonding was made up or not.
At the results, the existing DNA-intercalators formed hydrogen bonding with a form (CGCG)2- DNA but didn't with b form (CGCG)2- DNA.

[OD-2] [04/21/2000 (Fri) 11:25 - 11:40 / Rm B113, Bldg 26]

Facile Construction of Oxaphenalene Skeleton by peri Ring Closure. Total Synthesis of Mansonone F

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Mansonone F and Biflorin which are the members of the naturally occurring ortho-naphthoquinone consist of the unusual oxaphenalene skeleton. Biflorin, the first oxaphenalene natural product, was found to have antibiotic properties. More interestingly, mansonone F of a tricyclic sesquiterpenoid has been reported as a phytoalexin which is accumulated in the heartwood of the genus Ulmus in response to infections. Recently, mansonone F has been also isolated from the root bark of Ulmus davidiana which has been traditionally used as a medicinal plant for the infection diseases in Korea. In addition, the highly potent anti-MRSA activities of mansonne F comparable to that of vancomycin have been disclosed in our laboratory. However, the paucity of natural mansonone F as well as its inherent structural constraint has limited the optimization of its biological properties by structural modification and its therapeutic application. These reasons prompted us to develop a practical and divergent synthetic route to mansonone F .
The total synthesis of mansonone F has been accomplished via 10 step sequence, starting from the readily available 5-methoxy-1-tetralone. The key part of this synthesis involves an efficient preparation of 1,6-dimethyl-5-alkoxynaphthalene as a divergent cyclization precursor and its facile conversion to the oxaphenalene skeleton by peri ring closure.
This concise and practical synthetic procedure, providing a variety of substituents at C3, C6 and C9 positions, offers a useful synthetic route to the important anti-MRSA drug prospect.

[OD-3] [04/21/2000 (Fri) 11:40 - 11:55 / Rm B113, Bldg 26]

Kalopanaxsaponin A Is a Basic Saponin Structure for the Antitumor Activity of Hederagenin Monodesmosides

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Hederagenin (1), delta-hederin (2), kalopanaxsaponin A {3, hederagenin 3-O-alpha-L-rhamnosyl (1-2)-alpha-L-arabinoside}, kalopanaxsaponin I {4, hederagenin 3-O-beta-D-xylosyl (1-3)-alpha-L-rhamnosyl (1-2)-alpha-L-arabinoside} and sapindoside C {5, hederagenin 3-O-beta-D-glucosyl (1-4)-beta-D-xylosyl (1-3)-alpha-L-rhamnosyl (1-2)-alpha-L-arabinoside} were isolated from a saponin fraction of the MeOH extract of Kalopanax pictus Nakai (Araliaceae). 1 disaccharide (3), 1 trisaccharide (4), 1 tetrasaccharide (5) showed significant cytotoxicity on several tumor cell lines in contrast to no cytotoxicity of 1 monosaccharide (delta-hederin). We found that 3 commonly named also alpha-hederin is a basic structure of most 1 monodesmosides for the cytotoxicity. When the mice were treated with 37.5 mg/kg and 75 mg/kg of 3 or 15 mg/kg of cisplatin, a significant antitumor activity was obtained against colon cancer (% T/C of 124-169) and lung cancer (% T/C of 175.5-205), respectively. Throughout the cytotoxicities of 3 derivatives on several tumors, many saponins such as 1 disaccharides bearing (1-2) glycoside linkage and their serial saponins were suggested to have significant anti-tumor effect.

[OD-4] [04/21/2000 (Fri) 11:55 - 12:10 / Rm B113, Bldg 26]

Inhibitory Effect of Gyrophora esculenta on α-Glucosidase

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Diabetes mellitus is classified into insulin-dependent diabetes mellitus(IDDM) and noninsulin-dependent diabetes mellitus(NIDDM). It makes serious problems caused by its subsequent complications rather than by its own symptoms. α-Glucosidases are the key enzymes for these carbohydrate digestion. Therefore, α-glucosidase inhibitors could prevent and improve the