

investigated. The total methanol extract of *B. platyphylla* var. *japonica* had protective effects against hydrogen peroxide ( $H_2O_2$ ) in the Chinese hamster lung fibroblast (V79-4) cell line and induced apoptotic cell death in human promyelocytic leukemia (HL-60) cells, a cancer cell line. *B. platyphylla* var. *japonica* extract significantly increased cell viability against  $H_2O_2$ . The extract also showed high 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity ( $IC_{50}$  2.4 mg/ml) and lipid peroxidation inhibitory activity ( $IC_{50}$  below 4.0 mg/ml). Furthermore, *B. platyphylla* var. *japonica* extract reduced the number of V79-4 cells arrested in  $G_2/M$  in response to  $H_2O_2$  treatment and increased the activities of several cellular antioxidant enzymes, including superoxide dismutase, catalase and glutathione peroxidase. Treatment with *B. platyphylla* var. *japonica* extract induced cytotoxicity and apoptosis in HL-60 cells, as shown by nucleosomal DNA fragmentation, increases in the subdiploid cell population, and fluorescence microscopy. *B. platyphylla* var. *japonica* extract gradually increased the expression of pro-apoptotic Bax and led to the activation of caspase-3 and cleavage of PARP. These findings suggest that *B. platyphylla* var. *japonica* exhibits potential antioxidant and anticancer properties.

[PC1-42] [ 2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function ]

### **Conformational Study of Pseudo-Proline Dipeptide in the Gas Phase and Solutions**

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We report here the results on N-acetyl-N"-methylamide of oxazolidine (Ac-Oxa-NHMe) calculated using the ab initio molecular orbital method with the self-consistent reaction field (SCRF) theory at the HF level of theory with the 6-31+G(d) basis set. The displacement of the  $\gamma$ -CH<sub>2</sub> group in proline ring by oxygen atom has affected the structure of proline, cis-trans equilibrium, and rotational barrier. The up-puckered structure is found to be prevalent for the trans conformers of the Oxa amide. The higher cis populations of the Oxa amide can be interpreted due to the longer distance between the acetyl methyl group and the 5-methylene group of the ring for the trans conformer of the Oxa amide than that of the Pro amide. The changes in charge of the prolyl nitrogen and the decrease in electron overlap of the C-N bond for TS structures seem to play a role in lowering rotational barriers of the Oxa amide compared to that of the Pro amide. The calculated preferences for cis conformers in the order of Oxa > Pro amides and for trans-to-cis rotational barriers in the order of Pro > Oxa amide in water are consistent with experimental results on Oxa-containing peptides. The pertinent distance between the prolyl nitrogen and the N-H amide group to form a hydrogen bond might indicate that this intramolecular hydrogen bond could contribute in stabilizing the TS structures of Oxa and Pro amides and play a role in prolyl isomerization

[PC1-43] [ 2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function ]

### **Involvement of Akt in mitochondria-dependent apoptosis induced by a naphthoquinone analog**

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Vitamin K-related analogs induce growth inhibition in various cancer cell lines. We report that 2,3-dichloro-5,8-dihydroxy-1,4-naphthoquinone (DDN), a naphthoquinone analog, induces mitochondria-dependent apoptosis in human promyeloid leukemic HL-60 cells. DDN induced cytochrome c release, cleavage of Bid, and activation of caspases -8, -9 and -3. Cleavage of Bid, the caspase-8 substrate, was inhibited by the broad caspase inhibitor zVAD-fmk, whereas cytochrome c release was not affected by zVAD-fmk. These results indicate that DDN induces activation of caspase-8 and subsequent processing of Bid downstream of cytochrome c release. DDN inhibited the activation of Akt detected by decreasing levels of phosphorylation. Overexpression of constitutively active Akt protected cells from DDN-induced apoptosis. Furthermore, Akt prevented release of cytochrome c in DDN-treated HL-60 cells. In conclusion, DDN-induced apoptosis in HL-60 cells is associated with mitochondrial signaling which involves cytochrome c release through the inhibition of Akt pathway.