

peroxidation and glutathione concentrations in rat liver. Male Sprague-Dawley rats were divided into two groups, one of which was fed a normal diet and the other a vitamin E-free diet. Each of these groups was divided further into three subgroups and treated with quercetin administered orally at either 2 or 20 mg/day or with vehicle for four weeks. The concentrations of  $\alpha$ -tocopherol in serum and liver increased following quercetin treatment, and these increases were significantly greater in rats maintained on a vitamin E-free diet. Quercetin significantly decreased the concentration of malondialdehyde (an indicator of lipid peroxidation) in the liver and this decrease was more pronounced in vitamin E-deprived rats than in those maintained on a normal diet (55-60% and 25-35% decrease in malondialdehyde concentrations, respectively). Quercetin treatment decreased the glutathione concentrations and glutathione reductase activity (40 and 34%, respectively) in the liver significantly and to a similar extent in vitamin E-deprived and undeprived rats. Collectively, these results suggest that quercetin may act not only as an anti-oxidant, but also as a pro-oxidant in rats.

[PA1-44] [ 2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function ]

### **Suppression of RelA/p65 Transactivation Activity by a Lignoid Manassantin isolated from *Saururus chinensis***

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In our search for NF- $\kappa$ B inhibitors from natural resources, we have previously identified two structurally related dilignans, manassantin A and B as specific inhibitors of NF- $\kappa$ B activation from *Saururus chinensis*. However, their molecular mechanism of action remains unclear. We here demonstrate that manassantin A and B are potent inhibitors of NF- $\kappa$ B activation by the suppression of transcriptional activity of RelA/p65 subunit of NF- $\kappa$ B. These compounds significantly inhibited the induced expression of NF- $\kappa$ B reporter gene by LPS or TNF- $\alpha$  in a dose-dependent manner. However, these compounds did not prevent the DNA-binding activity of NF- $\kappa$ B assessed by electrophoretic mobility shift assay as well as the induced-degradation of I $\kappa$ B- $\alpha$  protein by LPS or TNF- $\alpha$ . Further analysis revealed that manassantin A and B dose-dependently suppressed not only the induced NF- $\kappa$ B activation by overexpression of RelA/p65, but also transactivation activity of RelA/p65. Furthermore, treatment of cells with these compounds prevented the TNF- $\alpha$ -induced expression of anti-apoptotic NF- $\kappa$ B target genes Bfl-1/A1, a prosurvival Bcl-2 homologue, and resulted in sensitizing HT-1080 cells to TNF- $\alpha$ -induced cell death. Similarly, these compounds also suppressed the LPS-induced inducible nitric oxide synthase expression and nitric oxide production. Taken together, manassantin A and B could be valuable candidate for the intervention of NF- $\kappa$ B-dependent pathological condition such as inflammation and cancer.

[PA1-45] [ 2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function ]

### **Oxyresveratrol Derivative Compound DMPB Act as Potent Dipigment agent in Brown Guinea Pig Skin**

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This study with the object of reported to depigment agent, oxyresveratrol derivative, compound DMPB . Compound DMPB with a two methoxy groups and modified connection chain. It was synthesized in accordance with a simple combination process. Compound DMPB exhibits depigmentaion ability on ultraviolet B-induced hyperpigmentation of the brown guinea pig skin. In addition, this Compound exhibited 30% inhibitory effect of melanin generation without cell toxicity as a result of the treatment with 100 ppm in melan-a cells. Furthermore, we are conducted to evaluate the effects of compound DMPB on tyrosinase and dopachrome tautomerase activity and revelation for investigative the pathway of inhibit melanin production. The compound DMPB had no effect on the tyrosinase. But, it showed catalyzing effect of dopachrome transformation into 5,6-dihydroxyindole-2-carboxylic acid. Our result suggested that the pigment-lightening effects of the compound may

due to the dopachrome tautomerase stimulation.

[PA1-46] [ 2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function ]

### **Anti-inflammatory mechanism of melittin, a component of bee venom in Raw 264.7 cells and Synoviocyte**

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Bee Venom (BV) has been treated in inflammatory diseases such as rheumatoid arthritis (RA). Bee venom contains several biologically active non-peptide substances as well as two major known peptides; the hemolytic peptide melittin (50%) and the neurotoxic peptide apamin, and a number of minor peptides. Previous our study showed that BV blocked LPS and SNP-induced production of NO and PG through inactivation of NF- $\kappa$ B which regulates expression of COX-2 and iNOS. In this study, we investigated whether melittin, a major component of BV may play a critical role in the anti-inflammatory effect of BV. We investigated effect of melittin on lipopolysaccharide (LPS) and sodium nitroprusside (SNP)-induced induction of COX-2, cPLA2 and iNOS expression, and production of NO and PGE<sub>2</sub>, and activation of NF- $\kappa$ B in a murine macrophage cell line Raw 264.7 cell and synoviocytes. Similar to the effect of BV, melittin prevented LPS and SNP induced COX-2, cPLA2 and iNOS expression, and the production of NO and PGE<sub>2</sub> through inhibition of transcriptional and DNA binding activation of NF- $\kappa$ B. The inhibitory effect of melittin in some parameters tested was less extent compared to BV, but most of the inhibitory effects of melittin was comparable to the effect of BV, suggesting that melittin may be a causal effective component of anti-inflammatory effect of BV.

[PA1-47] [ 2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function ]

### **Effects of chlorhexidine digluconate on thickness of outer membranes isolated from Cultured Porphyromonas gingivalis.**

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To get a better insight into the biophysical mechanism of action of chlorhexidine digluconate, we examined the effect of chlorhexidine digluconate on the thickness of outer membranes isolated from cultured Porphyromonas gingivalis using energy transfer between the membrane surface fluorescent probe (1-anilinonaphthalene-8-sulfonic acid) and the hydrophobic fluorescent probe [1,3-di(1-pyrenyl)propane]. 1-Anilinonaphthalene-8-sulfonic acid quenches the monomer fluorescence of 1,3-di(1-pyrenyl)propane. The significant decreases the thickness of lipid bilayer of the outer membranes by chlorhexidine digluconate were observed even at 0.01, 0.1, 1, 2, 3, 4, and 5 mM. It is presumed that the decrease of membrane thickness was resulted, as discovered in another studies of ours, from the fact that chlorhexidine digluconate caused increase in the rate and range of the lateral and rotational mobility of the membrane lipid bilayer, increased annular lipid fluidity and then resulted in clustering of membrane proteins. Reduction in the membrane thickness causes interdigitation between inner and outer monolayers of the lipid bilayer and membrane expansion and in turn, the membrane expansion accompanies changes of the membrane properties and functions. It is presumed that chlorhexidine digluconate exhibits its specific pharmacological effect by the biophysical mechanism described above.

[PA1-48] [ 2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function ]

### **Differential regulation of phospholipase C $\gamma$ isoforms through Fc $\epsilon$ RI, high affinity IgE receptor**