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The Mechanism of DNA Strand Scissions Induced by Brazilin : Involvement of Reactive Oxygen Species and Cu(II)/Cu(I) Redox Cycling

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Brazilin is the phenolic compound isolated from the *Caesalpinia sappan*. This compound has shown a wide range of physiological properties, such as hypoglycemic, anticonvulsant, vasorelaxing, and immunomodulating effects. In this study, we have found that brazilin induced DNA strand scissions in the presence of Cu(II) and this DNA cleavages were mediated by reactive oxygen species. DNA strand scissions were dependent on concentrations of brazilin and Cu(II), and incubation time. Cu(I) was found to be an essential intermediate from the result of experiment that neocuproine was employed as a selective Cu(I) sequestering agent. Stoichiometric analysis indicated that five Cu(II) ions were reduced by one brazilin molecule. Analysis of linear dichroism showed that brazilin intercalates DNA with a shortening effect of DNA length only in the presence of Cu(II). Resolution of brazilin-induced DNA fragment on a sequencing gel with Maxam-Gilbert sequencing reactions showed that brazilin did not show the sequence specificity of DNA strand scissions. These results suggest that DNA strand scissions may be induced by a oxygen radical reactions. To find out exact reactive oxygen species, DNA strand scissions were investigated in the presence of various reactive oxygen scavengers. Results suggest that copper-peroxide complex, which have a reactivity similar to that of singlet oxygen or a bound hydroxyl radical, may play a major role in the DNA strand scission induced by brazilin.

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Inhibitory effects of natural products on lipopolysaccharide-stimulated PGE2 and nitric oxide production in RAW 264.7 cells

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Prostaglandins (PGs) and NO (nitric oxide) are important elements to keep homeostasis and host defense system in human beings. When PGs and NO are overproduced by cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS), respectively, they can cause chronic inflammation, tissue damage, and carcinogenesis. On this line, we are interested in finding agents that can inhibit the production of PGs and NO from natural products for developing anti-inflammatory and cancer chemopreventive agents.

In this study, we investigated the effects of the extracts derived from rice germinated *Phelinus linteus*, eugenol conjugated chitosan (ECC), Cordyceps, HBT (the combinations of 9 plant extracts: *Saururus chinensis*, *Cuscuta chinensis*, *Polypora cordata*, *Lonicera japonica*, *Cassia obtusifolia*, *Glycyrrhiza glabra*, *Poria cocos*, *Stevia rebaudiana*, *Salvia officinalis* extracts), and the fractions of *Phelinus linteus* (EtOH, EtOAc, H₂O, Hexane, and crystal) on LPS (lipopolysaccharide)-stimulated RAW 264.7 for the inhibition of iNOS and COX-2 activity

determining NO and PGE₂, respectively. As a result, HBT inhibited LPS-stimulated PGE₂ and NO production in a dose-dependent manner. ECC also inhibited PGE₂ production. In addition, we investigated the growth inhibitory effects of HBT, Cordyceps, and the extracts of *Phelinus linteus* (PL) on human lung cancer cells (A549). HBT, the fractions of PL (EtOH and Hexane), and the extract of Cordyceps showed the growth inhibition against A549 cells. These findings show that eugenol conjugated chitosan (ECC), *Phelinus linteus* (PL), the fractions of PL, and HBT might be potential lead candidates for developing cancer chemopreventive and/or anti-inflammatory agents.

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Effect of *Polygonum cuspidatum* on renal function

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Polygonum cuspidatum has been used as treatments of dermatitis, inflammation, hyperlipidemia and diuretics in folk remedies. In order to evaluate the urinary effect of *Polygoni cuspidati Radix*, its MeOH extract was administered in rats. We determined the total urine volume, chemical parameters (urea nitrogen, creatinine, uric acid), electrolytes (sodium, potassium, chloride) in serum and urine. *Polygoni cuspidati Radix* showed increase in urine volume and electrolytes.

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Pharmacological screening of *Alnus japonica* and isolation of active constituent

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An extract of *Alnus japonica* (Betulaceae) cortex has been traditionally used for purifying blood, and curing feces containing blood, enteritis, diarrhea, alcoholism and cut wounds. In the preliminary test was carried out for determining whether it has the novel pharmacological activity, the butanol fraction showed significant inhibitory effect on carrageenan-induced paw edema as an acute inflammation, adjuvant-induced arthritis as a chronic inflammation, HCl-ethanol-induced gastric lesion and aspirin-ligation gastric ulcer. Carrageenan-induced paw edema test was performed with sub-fractionations to determine what constituent has anti-inflammatory activity. Active component is estimated as a flavonoid from H-NMR and C-NMR data, and specifications will be further studied with other spectrometric identification methods.

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Fertility effect of chronically administered CBNU-1 on male rats

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