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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