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Previously we reported that the methanolic extract of the leaves of *Pinus densiflora* Sieb. et Zucc. (Pinaceae) exerts radical scavenging effect on 1,1-diphenyl-2-picrylhydrazyl radicals. From this methanolic extract, (+)-catechin was isolated as one of active principles, together with the inactive components, dihydrokaempferol, and 1-*O*-benzoyl glucoside. In the course of continuous work on this plant, further antioxidant activity of *P. densiflora* was evaluated for potential to inhibit hydroxyl radicals, inhibit total reactive oxygen species generation in kidney homogenates using 2',7'-dichlorodihydrofluorescein diacetate (DCHF-DA), and scavenge authentic peroxynitrites. The methanolic extract of *P. densiflora* showed strong antioxidant activity in tested model systems, and thus fractionated with several solvents. The antioxidant activity potential of the individual fraction was in the order of ethyl acetate > *n*-butanol > water > dichloromethane fraction. The ethyl acetate soluble fraction exhibiting strong antioxidant activity was further purified by repeated silica gel and Sephadex LH-20 column chromatographies. An active lignan isolarisiresinol xylopyranoside, as well as two active flavonoids [kaempferol 3-*O*-β-galactopyranoside and its 6"-acetyl derivative], were isolated.

[PD2-29] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

New triterpene aldehydes, lucialdehydes A-C, from Ganoderma lucidum and their cytotoxicity against murine and human tumor cells

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Three new lanostante-type triterpene aldehydes, named lucialdehydes A-C (**1-3**), were isolated from the fruiting bodies of *Ganoderma lucidum*, together with ganodermanonol (**4**), ganodermadiol (**5**), ganodermanondiol (**6**), ganodermanontriol (**7**), ganoderic acid A (**8**), methyl ganoderic acid C1 (**9**) and ganoderic acid B8 (**10**). The structures of the new triterpenes were determined as (24*E*)-3β-hydroxy-5α-lanosta-7,9(11),24-trien-26-aldehyde (**1**), (24*E*)-3,7-dioxo-5α-lanosta-8,24-dien-26-aldehyde (**2**) and (24*E*)-3β-hydroxy-7-oxo-5α-lanosta-8,24-dien-26-aldehyde (**3**), respectively, by spectroscopic means. The cytotoxicity of the compounds isolated from the ganoderma mushroom was tested *in vitro* against Meth-A, Sarcoma 180, LLC and T-47D tumor cell lines. Lucialdehydes B-C (**2-3**), ganodermanonol (**4**) and ganodermanondiol (**6**) showed cytotoxic effect on tested tumor cells. Of the compounds, lucialdehyde C (**3**) exhibited LLC cells with ED_{50} values of 14.3, 10.7 and 14.0 μg/ml, respectively.

[PD2-30] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Seco-guaianolides from Artemisia iwayomogi and their inhibitions of nitric oxide synthesis in activated macrophages

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In activated macrophages the inducible form of nitric oxide synthase (iNOS) generates high amounts of the toxic mediator, nitric oxide (NO) that contributes to the circulatory failure associated with septic shock and inflammation. The inhibitors of i-NOS may have a role in the therapy of septic shock and inflammation. In a large-scale screening test for the searching for new i-NOS inhibitor from medicinal plants, two seco-guaianolide sesquiterpenes were isolated from *Artemisia iwayomogi* as active principles those inhibit the production of NO in lipopolysaccharide activated RAW 264.7 cells. Their structures were identified as 3β-hydroxy-1,10-dioxo-1,10-secoguaia-4,11(13)-dien-6βH-12,6-olide (**1**) and 3β-methoxy-1,10-dioxo-1,10-secoguaia-4,11(13)-dien-6βH-12,6-olide (**2**) by the analyses of

2-dimensional NMR spectral analyses. They showed dose-dependent inhibitions on NO syntheses and the IC50's were 3.1, 3.8 μg/ml, respectively. The spectral data and activity mechanism of these compounds will be discussed. These new inhibitors of iNOS may have potential in the treatment of endotoxemia and inflammation accompanied by the overproduction of NO.

[PD2-31] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Curcumin and its analogue, inhibitor of Farnesyl Protein Transferase, isolated from *Curcuma longa* L.

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Farnesyl-protein transferase(FPTase) catalyzes the farnesylation of Ras protein on the cysteine residue near the C-terminus, which is critical for triggering ras oncogene toward tumor formation. During the course of a screening program for inhibitors of FPTase from natural products, inhibitors were isolated from the roots of Curcuma longa L. Curcumin and its analogue were isolated from C. longa L. Curcumin exhibited strong inhibition activity against FPTase. FPTase inhibitors were purified by silica and LH-20 column chromatography. Structures of the compounds were determined by NMR and MS spectroscopy. FPTase inhibitory activity was measured against partially purified FPTase enzyme, prepared from rat brain, and biotin-YRASNRSCAIM acceptor peptide using a scintillation proximity assay method. The compounds were also evaluated for cytotoxicity against five human tumor cell lines.

[PD2-32] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Anti-complement of terpenoids from the spores of Ganoderma lucidum

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A new lanostane-type terpenoid, lucidenic acid SP1 (**1**), was isolated from a chloroform-soluble fraction of the spores of *Ganoderma lucidum* together with four known compounds (**2-5**). The structure of lucidenic acid SP1 was determined as 3β,7β-dihydroxy-4,4,14α-trimethyl-11,15-dioxo-5α-chol-8-ene-24-oic acid by spectroscopic means including 2D-NMR. The anticomplementary property of **1-5** was investigated *in vitro*. Furthermore, triterpenes (**6-12**) isolated from the same spores were tested for their anticomplemantary activity. Compounds **1-5** were inactive, whereas ganoderiol F (**8**), ganodermanondiol (**9**) and ganodermanontriol (**10**) showed a strong anticomplement activity against the classical pathway (CP) of the complement system with IC_{50} values of 4.8, 41.7 and 17.2 μM, respectively. The inhibitory potency of triterpene alcohols **8-10** on the CP activity increased accompanied by increase in terminal hydroxymethyl group of the side chain moiety. On the other hand, ganoderic acid **1-7**, which are present a carboxyl group in the side chain, and lucidumols A and B (**11-12**) were inactive on this system.

[PD2-33] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Isolation of Anti-Septic Shock Agents from Moutan Cortex

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