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薬物代謝工学部門は和漢薬の薬効，毒性発現に関与する代謝系の分子生物学的研究を発展させることを設置目的とし，① 和漢薬の薬効発現に関与する腸内細菌遺伝子の解析，② 薬物代謝機能調節遺伝子の解明とその応用，③ 腎毒性物質産生機構の分子生物学的解明とその制御に関する研究を課題として取りあげ，和漢薬の薬効発現機構，生体へのレスポンスなどの基礎的研究を通じて，和漢薬の科学的評価や臨床応用をはかることを目指している。主な研究題目を以下に示す。

1．天然物のバイオトランスフォーメイション
2．和漢薬の薬効発現に関与する腸内細菌遺伝子の解明
3．AIDS の予防 および 治療薬の開発
4．腎疾患における病態の解明と腎臓病治療薬の開発

本年度の主な研究を列挙すると：

1．ヒト腸内細菌による phorbol の変換を検討し，この化合物が 容易に開裂反応を経て種々の代謝物に変換されることを明らかにした。

2．HIV-インテグラーゼ阻害活性を指標に タイ薬用植物 50種のエキスを探索し，*Coleus parvifolius*, *Thevetia peruviana* などに強い酵素阻害活性を見出した。又，これらのエキスから阻害活性成分を単離し，その阻害様式を検討した。その他，180種のフラボン類のインテグラーゼ阻害活性を検討し，活性と活性相関を調べた。

3．中国少数民族使用薬物 および タイ薬用植物の抗ヘルペスウイルス活性を探索した。また，C型肝炎ウイルス由来の RNA ポリメラーゼ阻害活性もあわせ検討した。

4．増悪因子のラジカルの関与について，地楡，ソバ，薬用人参サポニン，丹参成分 magnesium lithospermate B，漢方方剤温脾湯の腎における役割を解析した。また糖尿病性腎症のモデルを構築し，漢方方剤の効果を究明した。

◇著　書　Books

1）服部征雄，中村憲夫：抗 HIV 活性を有する伝統薬物．『薬用植物・生薬開発の最前線』，佐竹元吉監修，株式会社シーエムシー，東京，2001，pp. 299–320.

2）Yokozawa T.: Role of the Active Dan Shen Component, Magnesium Lithospermate B, in the Kidney. "Molecular Aspects of Asian Medicines", edited by A. Mori and T. Satoh, PJD Publications Ltd., New York, 2001, pp.139-155.

◇原　著　Original papers

1）**Tezuka Y., Terazono M., Kusumoto T., Hatanaka Y., Kadota S., Hattori M., Namba T., Kikuchi T., Tanaka K., and Supriyatna S.: Helicterins A-F, six new dimeric (7.5', 8.2') -neolignans from the Indonesian medicinal plant *Helicteres isora*. *Helv. Chim. Acta*, 83: 2908-2919, 2000.**

（研究所年報 27巻 62頁 18 参照）

2）**Song S. J., Nakamura N., Ma C. M., Hattori M., and Xu S. X.: Five saponins from the root bark of *Aralia elata*. *Phytochemistry*, 56: 491-497, 2001.**

Five new saponins, 3-*O*-{ β-D-glucopyranosyl (1→2)-[β-D-glucopyranosyl 1→3)]- β-D-glucopyranosyl}oleanolic acid 28-*O*- β-D-glucopyranosyl ester (aralia-saponin V), 3-*O*-{ β-D-glucopyranosyl (1→2)-[β-D-glucopyranosyl (1→3)]- β-D-glucopyranosyl}echinocystic acid 28-*O*- β-D-glucopyranosyl ester (aralia-saponin VI), 3-*O*-{ β-D-glucopyranosyl (1→2)-[β-D-glucopyranosyl (1→3)]- β-D-glucopyranosyl}hederagenin 28-*O*- β-D-glucopyranosyl ester (aralia-saponin VII), 3-*O*-{ β-D-glucopyranosyl-(1→3)- β-D-glucopyranosyl -(1→3)-[β-D-glucopyranosyl- (1→2)]- β-D-glucopyranosyl}caulophyllogenin 28-*O*- β-D-glucopyranosyl ester (aralia-saponin VIII), 3-*O*-{ β-D-glucopyranosyl (1→2)-[β-D-glucopyranosyl(1→3)]- α-L-arabinopyranosyl}hederagenin 28-*O*- β-D-glucopyranosyl ester (aralia-saponin IX), were isolated from the root bark of *Aralia elata* (Miq.) Seem., together with four known compounds. Their structures were determined on the basis of chemical and spectroscopic methods.

3）**Ma C., Nakamura N., Min B., and Hattori M.: Triterpenes and lignans from *Artemisia caruifolia* and their cytotoxic effects on Meth-A and LLC tumor cell lines. *Chem. Pharm. Bull.*, 49: 183-187, 2001.**

One new triterpene, 3β-hydroxy-29-norcycloart-24-one (**1**), and four new lignans, caruilignans (**2-5**), together with six known compounds were isolated from the aerial part of *Artemisia caruifolia* Buch.-Ham. ex Toxb. Their structures were determined by various spectroscopic means. Most of the isolated lignans were moderately cytotoxic to Meth-A cells with ED_{50} values of 5-10 μg/ml, but not to Lowis lung carcinoma (LLC) cells. An oxime derivative of **1** showed more potent cytotoxic activity against Meth-A and LLC cells than the original triterpene **1** (see Fig. 1).

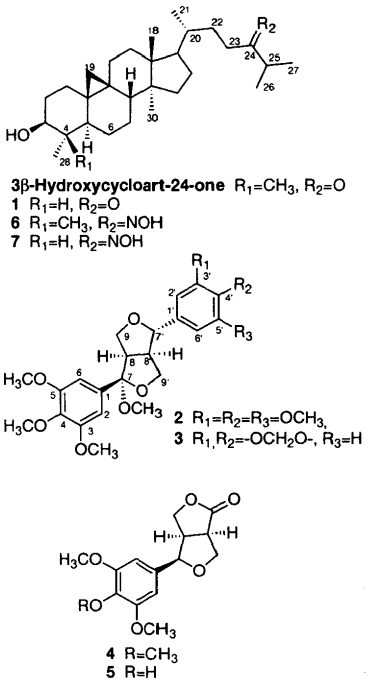

Fig. 1

4）**Min B., Tomiyama M., Ma C., Nakamura N., Hattori M.: Kaempferol acetylrhamnosides from the rhizome of *Dryopteris crassirhizoma* and their inhibitory effects on three different activities of human immunodeficiency virus-1 reverse transcriptase. *Chem. Pharm. Bull.*, 49: 546-550, 2001.**

Three new kaempferol glycosides, called crassirhizomosides A (**1**), B (**2**) and

C (**3**), were isolated from the rhizome of *Dryopteris crassirhizoma* (Aspidiaceae), together with the known kaempferol glycoside, sutchuenoside A (**4**). The structures of **1-3** were determined as kaempferol 3-α-L- (2,4-di-*O*-acetyl) rhamnopyranoside-7-α-L-rhamnopyranoside, kaempferol 3-α-L-(3,4-di-*O*-acetyl)rhamnopyranoside-7-α-L-rhamnopyranoside, and kaempferol 3-α-L-(2,3-di-*O*-acetyl)rhamnopyranoside-7-α-L-rhamnopyranoside, respectively, by chemical and spectroscopic means. Inhibitory effects of **1-4** and kaempferol on HIV reverse transcriptase-associated DNA polymerase (RNA-dependent DNA polymerase and DNA-dependent DNA polymerase) and RNase H activities were investigated.

5) **Zhao J., Yang X., and Hattori M.: Three new triterpene saponins from the seeds of *Aesculus chinensis*. *Chem. Pharm. Bull.*, 49: 626-628, 2001.**

Three new triterpenoid saponins were isolated from the seeds of *Aesculus chinensis*, and characterized as 22-tigloylprotoaescigenin 3-*O*-[β-D-glucopyranosyl (1→2)] [β-D-glucopyranosyl (1→4)]-β-D-glucopyranosiduronic acid (escin IVg, **1**), 22-angeloylproto-aescigenin 3-*O*-[β-D-glucopyranosyl (1→2)] [β-D-glucopyranosyl (1→4)]-β-D-glucopyranosid uronic acid (escin IVh, **2**) and 16-angeloyl-21-acetylproto-aescigenin 3-*O*-[β-D-glucopyranosyl (1→2)] [β-D-glucopyranosyl (1→4)]-β-D-glucopyranosid uronic acid (escin VIb, **3**), together with two known compounds, escin IIIa (**4**) and desacylescin I (**5**). Their structures were established on the basis of spectroscopic and chemical evidence.

6) **Meselhy R. M., Nishimoto E., Akao T., and Hattori M.: Transformation of shikonin by a cell-free extract of *Eubacterium* sp. A-44, a human intestinal bacterium. *J. Trad. Med.*, 18: 58-63, 2001.**

For the purpose of investigating the metabolic processes of shikonin (**1**) by human intestinal bacteria, we prepared a sonicated bacterial cell suspension and a crude enzyme preparation from *Eubacterium* sp. A-44, one of the intestinal bacteria capable of transforming **1** to various metabolites. After anaerobic incubation with the suspension for 1 hr, most of **1** was transformed to prometaboshikonin (**2**), and metaboshikonins I (**3**) and II (**4**). However, under aerobic conditions, the dimers, shikometabolins A (**5**) and B (**6**), were predominantly formed. In the presence of the crude enzyme preparation, formation of **2-4** was inhibited by oxygen, but markedly enhanced by the addition of NADH. On the other hand, formation of **5** and **6** was appreciably accelerated by the addition of NAD^+. In the absence of the crude enzyme preparation, NADH and/or NAD^+ showed no ability to transform **1** to the any metabolites, as in the case of a thermally inactivated preparation. Accordingly, the two different metabolic processes leading to compounds **2-4** and compounds **5** and **6** by *Eubacterium* sp. A-44 are concluded to be enzyme-dependent in the presence of NADH and NAD^+.

7) **Ma C., Nakamura N., Hattori M.: Inhibitory effects on HIV-1 protease of *tri-p*-coumaroylspermidine from *Artemisia caurifolia* and related amides. *Chem. Pharm. Bull.*, 49: 915-917, 2001.**

From a methanol extract of *Artemisia caruifolia*, which showed a moderate inhibitory activity on HIV-1 protease in a preliminary screening, N^1, N^5, N^{10}-tri-*p*-coumaroylspermidine and three dicaffeoylquinic acids were isolated. The former compound was found to appreciably inhibit HIV-1 protease. Of related amides which were chemically synthesized, N^1, N^5, N^{19}, N^{14}-tetra-*p*-coumaroylspermine and N^1, N^4, N^7, N^{10}, N^{13}-penta-*p*-coumaroyltetraethylenepentamine inhibited HIV-1 protease more potently than N^1, N^5, N^{10}-tri-*p*-coumaroylspermidine.

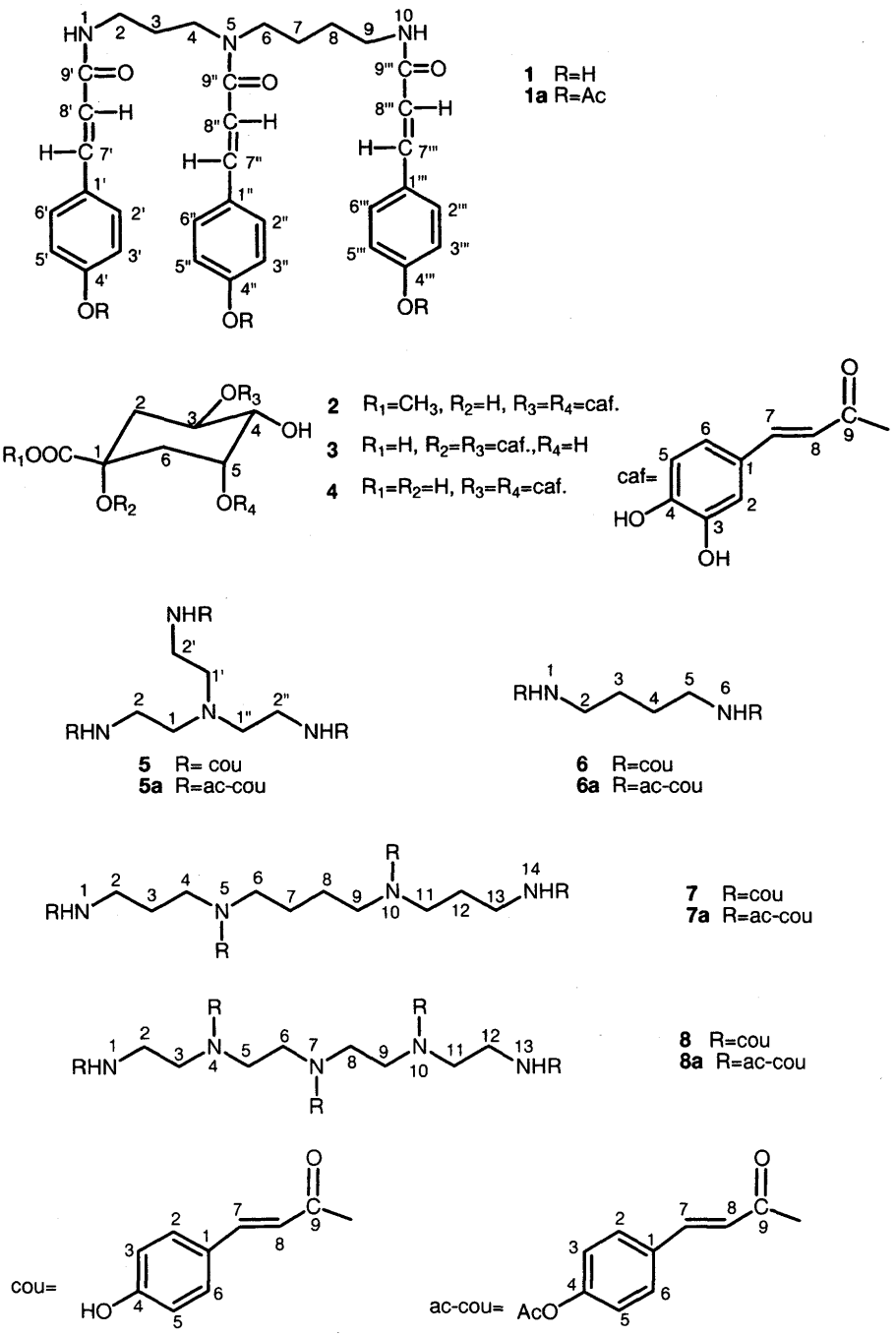

Fig. 2

8) **Abdel-Hafez A. A., Meselhy M. R., Nakamura N., Hattori M.: New paeonilactone-A adducts formed by anaerobic incubation of paeoniflorin with *Lactobacillus brevis* in the presence of arylthiols. *Chem. Pharm. Bull.*, 49: 918-920, 2001.**

During the course of preparing anticonvulsant paeonimetabolin-I adducts, new paeonilactone-A adducts: 9-phenylthiopaeonilactone-A, 9-(*o*-tolylthio)paeonilactone-A, 9-(*m*-tolylthio)paeonilactone-A, 9-(*p*-tolylthio) paeonilactone-A and 9-(2-naphthylthio)paeonilactone-A, were obtained along with expected paeonimetabolin-I adducts by anaerobic incubation of paeoniflorin from peony roots with *Lactobacillus brevis* in the presence of the aromatic thiols, phenylthiol, *o*-tolylthiol, *m*-tolylthiol, *p*-tolylthiol and 2-naphthylthiol. The structures of these compounds were determined by spectroscopic methods including 2D NMR.

9) **Abdel-Sattar E., Abdul-Aziz Al-Yahya M., Nakamura N., and Hattori M.: Penicillosides A-C, C-15 oxypregnane glycosides from *Caralluma penicillata*. *Phytochemistry*, 57: 1213-1217, 2001.**

The chloroform fraction of the defatted ethanol extract from the aerial parts of *Caralluma penicillata* yielded three new C-15 oxypregnane glycosides. The structures of the isolated compounds were established by a combination of spectroscopic methods.

10) **Murakami T., Kishi A., Matsuda H., Hattori M., and Yoshikawa M.: Medicinal foodstuffs. XXIV. Chemical constituents of the processed leaves of *Apocynum venetum* L.: absolute stereostructures of apocynosides I and II. *Chem. Pharm. Bull.*, 49: 845-848, 2001.**

Two new ionone glucosides, named apocynosides I and II, were isolated from the roasted leaves of *Apocynum venetum* L. together with nine known compounds. The absolute stereostructures of apocynosides I and II were determined by chemical and physicochemical evidence, which included the application of a modified Mosher's method and the circular dichroism helicity rule.

11) **Min S., Gao J., Nakamura N., Kim Y., and Hattori M.: Cytotoxic alkaloids and a flavan from the bulbs of *Crinum asiaricum* var. *japonicus*. *Chem. Pharm. Bull.*, 49: 1217-1219, 2001.**

A new pyrrolophenanthridone alkaloid, criasiacitidine A (**1**), was isolated from the bulbs of *Crinum asiaticum* var. *japonicum*, together with pratorimine (**2**), lycorine (**3**) and 4'-hydroxy-7-methoxyflavan (**4**). The structure of the new alkaloid was determined to be 4,5-etheno-9,10-dihydroxy-6-phenanthridone by spectroscopic means. The cytotoxicity of the isolated compounds **1**−**4** was evaluated *in vitro* against Meth-A (mouse sarcoma) and Lewis lung carcinoma (mouse lung carcinoma) tumor cell lines. Furthermore, lycorine (**3**) was examined for *in vivo* antitumor activity with LLC tumor cells.

12) **Gao J., Min B., Akao T., Meselhy R. M., Nakamura N., and Hattori M.: Enzyme immunoassay for the quantitative determination of ganoderic acid A from *Ganoderma lucidum*. *J. Trad. Med.*, 18: 154-160, 2001.**

For quantitative determination of ganoderic acid A (GAA, **1**), a major constituent of *Ganoderma lucidum*, a sensitive and specific enzyme immunoassay (EIA) system was developed; the side chain of GAA was extended by introducing a glycine moiety, and this compound was coupled with β-D-galatosidase (β-Gal) and bovine serum albumin (BSA) *via* an *N*-hydroxysuccinimide ester to give GAA-β-Gal (enzyme-labeled antigen, **5**) and GAA-BSA (immunogen, **6**), respectively. The anti-GAA antiserum, which had been elicited in rabbits by immunization with the GAA-BSA conjugate, possessed high affinity and specificity toward GAA, when the assay was carried out with a double antibody technique. A satisfactory standard curve for EIA of GAA was explored in a range of 0.1−1000 ng/tube. The antiserum of GAA was no cross-reactivity with GAA-related compounds isolated from *G. lucidum*, except for ganoderic acid γ (**11**) and ganolucidic acid A (**14**) with cross-reactivity of 52.4 and 12.9%, respectively, due to its close similarity in structure to GAA (ganoderic acid derivatives having a carbonyl group at C-3) . The plasma concentration of GAA after its intravenous or oral administration to rats was determined by the established EIA. The *AUC*s after intravenous administration of GAA were 32.8 ± 9.8 and 201.5 ± 38.7 μg min/ml at doses of 5 and 25 mg/kg, respectively. Following oral administration of GAA at doses of 5 and 50 mg/kg to rats, the plasma concentration of GAA rapidly reached a C_{max} (37 and 595 ng/ml) at 18.1 ± 2.5 and 18.0 ± 0.6 min, respectively, then decreased to 4.2 and 13.3 ng/ml at 480 min, respectively, indicating that GAA was rapidly absorbed into the body fluid from the gastrointestinal tract after the oral administration, and then decreased soon.

13) **Meselhy R. M., Nishimoto E., Akao T., and Hattori M.: Human intestinal *Bacteroides* spp. RHEIN-I and RHEIN-II capable of transforming rhein to rheinanthrone, induce rhein-**

dependent diarrhea in rats. *J. Trad. Med.*, 18: 169-176, 2001.

Two rhein-metabolizing bacteria were isolated from human feces. The biochemical and morphological characteristics of both isolates were typical of *Bacteroides* spp. and named strains RHEIN-I and RHEIN-II, respectively. Rhein was effectively metabolized to rheinanthrone by both strains. In conventional male Wistar rats, diarrhea was not induced after oral administration of rhein at a dose of 100 mg/kg (fecal water content of 71%), in spite of severe diarrhea with sennoside B at a dose of 40 mg/kg, increase of fecal water content to 89%. Also in Germ-free rats, rhein did not induce any diarrhea. Gnotobiote rats colonized with *B.* sp. strain RHEIN-I developed diarrhea (fecal water content increased to 85%) 11 hr after the oral administration of rhein. These findings indicate that rhein-transforming bacteria are responsible for the laxative effect associated with the ingestion of rhein and rhein containing preparations.

14) **Marpaung L., Nakamura N., Kakuda H., and Hattori M.: Absolute configuration of cipadesin and febrifugin from the seeds of *Cipadessa baccifera*. *Natural Med.*, 55: 220, 2001.**

Two tetranortriterpenoids, cipadesin and febrifugin, were isolated from the seeds of *Cipadessa baccifera.* Their absolute structures were elucidated by spectroscopic and X-ray method.

15) **Nawawi A., Nakamura N., Meselhy M. R., Hattori M., Kurokawa M., Shiraki K., Kashiwaba N., and Ono M.: *In vitro* antiviral activity of *Stephania cepharantha* against herpes simplex virus type-1. *Phytother. Res.*, 15:497-500, 2001.**

The antiviral activity of a MeOH extract of *Stephania cepharantha* (root tubers), its $CHCl_3$-soluble fraction (alkaloid fraction) and the major alkaloid FK-3000 (**1**) was investigated in BALB/c mice cutaneously infected with HSV-1 strain 7401H. At doses of 125 and 250 mg/kg body weight, p.o., the MeOH extract significantly delayed skin lesion on score 2 (vesicles in the local region), limited the development of further lesions on score 6 (mild zosteriform lesion), and prolonged the mean survival time of HSV-1 infected mice. After p.o. administration of the $CHCl_3$-soluble fraction at doses of 25 and 50 mg/kg or FK-3000 (**1**) at 10 and 25 mg/kg, similar results were obtained. Although the alkaloid improved survival of infected mice, it had a narrow therapeutic index.

16) **Min B., Kim Y., Tomiyama M., Nakamura N., Miyashiro H., Otake T., and Hattori M.: Inhibitory effects of Korean plants on HIV-1 activities. *Phytother. Res.*, 15: 481-486, 2001.**

In the search for novel anti-human immunodeficiency virus type 1 (anti-HIV-1) agents from natural sources, 49 MeOH extracts of Korean plants were screened for their inhibitory effects against RNA-dependent DNA polymerase (RT) and ribonuclease H (RNase H) activities of HIV-1 reverse transcriptase and HIV-1 protease, and anti-HIV-1 activity. Regarding the HIV-1 reverse transcriptase, *Agrimonia pilosa* (whole plant), *Cornus kousa* (stem and leaf), *Limonium tetragonum* (root) and *Mallotus japonicus* (stem) showed significant inhibitory activity on RT activity with 50% inhibitory activity (IC_{50}) of 8.9, 6.3, 7.5 and 11.9 mg/mL, respectively, whereas *Agrimonia pilosa* was also active against RNase H activity (IC_{50} = 98.4 mg/mL). Four plants, namely *Agrimonia pilosa* (whole plant), *Atractylodes japonica* (root), *Clematis heracleifolia* (whole plant) and *Syneilesis palmata* (whole plant), were appreciably active (<35%) against recombinant HIV-1 protease at a concentration of 100 μg/mL. *Crinum asiaticum* var. *japonicum* (root) showed significant anti-HIV-1 activity (ED_{50} = 12.5 μg/mL) with a favourable SI value of 16.

17) **Wang L., Meselhy M.R., Li Y., Nakamura N., Min B., Qin G., and Hattori M.: The heterocyclic ring fission and dehydroxylation of catechins and related compounds by *Eubacterium* sp. strain SDG-2, a human intestinal bacterium. *Chem. Pharm. Bull.*, 49: 1640-1643, 2001.**

A human intestinal bacterium, *Eubacterium* (*E.*) sp. strain SDG-2, was tested for its ability to metabolize various (3

R)- and (3*S*)-flavan-3-ols and their 3-*O*-gallates. This bacterium cleaved the C-ring of (3*R*)- and (3*S*)-flavan-3-ols to give 1,3-diphenylpropan-2-ol derivatives, but not their 3-*O*-gallates. Furthermore, *E.* sp. strain SDG-2 had the ability of *p*-dehydroxylation in the B-ring of (3*R*)-flavan-3-ols, such as (-)-catechin, (-)-epicatechin, (-)-gallocatechin and (-)-epigallocatechin, but not of (3*S*)-flavan-3-ols, such as (+)-catechin and (+)-epicatechin.

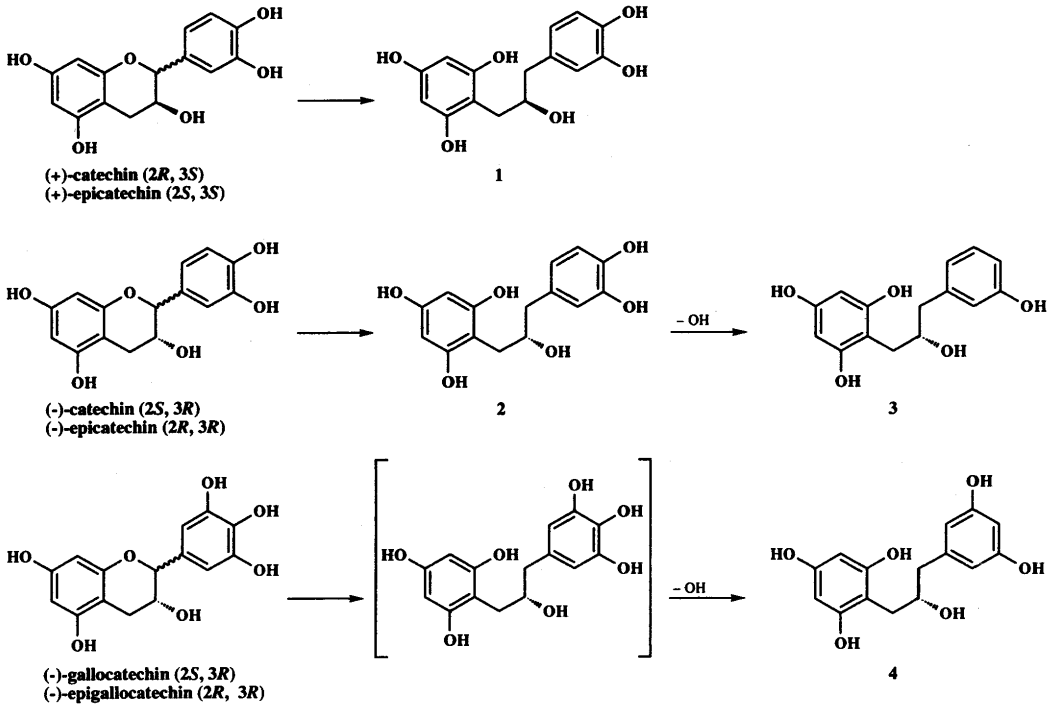

Fig. 3

18) **Wang L., Min B., Nakamura N., Qin G., Li C., and Hattori M.: Cytotoxic mono-tetrahydrofuran ring acetogenins from leaves of *Annona montana*. *Planta Med.*, 67: 847-852, 2001.**

Further studies on leaves of *Annona montana* led to isolation of one *iso-acetogenin*, montanacin G, three pairs of acetogenins, montanacins H-J and 34-*epi*-montanacins H-J, together with four known acetogenins, gigantetrocins A and B, annonacin and *cis*-annonacin. Montanacin G belongs to the *iso*-acetogenin group with a terminal 2,4-*trans*-ketolactone unit. Montanacins H-J and 34-*epi*-montanacins H-J contain the rare γ-hydroxy-γ-methyl-γ-lactone moiety. The cytotoxic activities of these compounds, together with previously reported acetogenins, montanacins B and C, were examined against Meth-A and LLC tumor cell limes *in vitro*.

19) **Quyang X., Takahashi k., Komatsu K., Nakamura N., Hattori M., Baba A., and Azuma J.: Protective effect of *Salvia miltiorrhiza* on angiotensin II-induced hypertrophic responses in neonatal rat cardiac cells. *Jpn. J. Pharmacol.*, 87: 289-296, 2001.**

The effect of the root of *Salvia miltiorrhiza* (SM) on angiotensin II (Ang II)-induced hypertrophic responses was examined in cultured neonatal rat cardiac cells (cardiomyocytes and non-cardiomyocytes). The methanol eluate fraction (SM2) of the water extract and the ethyl acetate-insoluble fraction (SM3) and its soluble fraction (SM4) partitioned from the methanol extract were prepared. Treatment with SM4 (5－80 μg/ml), not SM2 and SM3, for 24 h produced dose-dependent cytotoxicity against cardiac cells relative to the reduction in viability and the morphological injury of cardiomyocytes. SM2 or SM3 in the absence of Ang II affected neither hyperplastic nor hypertrophic growth of both cell types. However, SM3 (40 μg/ml) attenuated the positive chronotropic responsiveness of cardiomyocytes to Ang II (1 nM) stimulation, whereas Ang II-induced increase in non-cardiomyocyte number was decreased only by SM2 (40 μg/ml) treatment. Furthermore, SM3 suppressed Ang II-induced enlargement of

cell size by preceding Ang II-induced induction of immediate early response gene (*c-jun*) expression in cardiomyocytes, while SM2 decreased Ang II-indused DNA synthesis in non-cardiomyocytes. Moreover, three phenolic compounds and tanshinone IIA that differed quantitatively among three SM fractions were identified by reverse-phase high performance liquid chromatography. Thus, the present findings indicate that the root of SM is an effective inhibitor of Ang II action and has a plural effective constituent, which possess different pharmacological activities on Ang II-induced hypertrophy and hyperplasia in cultured neonatal rat cardiac cells.

20) **Supinya T., Miyashiro H., Hattori M., Yoshinaga T., Fujiwara T., Tomimori T., Kizu H., and Miyaichi Y.: Inhibitory effects of flavonoids on human immunodeficiency virus type-1 integrase. *J. Trad. Med.*, 18, 229-238, 2001.**

One hundred and eighty-three flavonoids were screened for their inhibitory effects on HIV-1 integrase (IN) using a multiplate integration assay (MIA). Of the tested flavonoids, 6-hydroxyluteolin, scutellarein, pedalitin, scutellarin, baicalein dimer, hypolaetin, 7-*O*-benzyl-6-hydroxyluteolin and baicalein showed appreciable inhibition with IC_{50} values of 0.4, 0.6, 1.3, 1.7, 2.0, 2.1, 3.0 and 3.6 μM, respectively. The potent inhibition was observed with flavonoids having at least one pair of vicinal hydroxyl groups and the activity was highly dependent on the number of vicinal hydroxyl groups. On the other hand, the inhibitory activity tended to be decreased by replacing a hydroxyl group with one of methoxyl, acetoxyl, isopropoxyl, isopentenyl, benzyloxyl, glucuronyl and glycosyl groups. No flavanones, flavanonols and chalcones examined in this experiment showed any significant inhibitory activity.

21) **Yokozawa T., Fujii H., Kosuna K., and Nonaka G.: Effects of buckwheat in a renal ischemia-reperfusion model. *Biosci. Biotechnol. Biochem.*, 65: 396-400, 2001.**

Experiments were done to find whether buckwheat extract ameliorates the renal injury induced by ischemia-reperfusion. In ischemic-reperfused control rats, the activities of antioxidative enzymes in renal tissue and blood and renal parameters deviated from the normal range, indicating dysfunction of the kidneys. In contrast, when buckwheat extract was given orally for 20 consecutive days before ischemia and reperfusion, the activities of the antioxidation enzymes superoxide dismutase, catalase, and glutathione peroxidase were higher, while thiobarbituric acid-reactive substance levels in serum and renal tissue were lower in the treated rats than in the controls. Decreased levels of urea nitrogen and creatinine in serum demonstrated a protective effect against the renal dysfunction caused by ischemia and recirculation. On the other hand, it was demonstrated that buckwheat extract had a protective effect on cultured proximal tubule cells subjected to hypoxia-reoxygenation, probably by preventing oxygen free radicals from attacking the cell membranes.

22) **Chen C.P., Yokozawa T., Sekiya M., Hattori M., and Tanaka T.: Protective effect of Sanguisorbae Radix against peroxynitrite-mediated renal injury. *J. Trad. Med.*, 18: 1-7, 2001.**

3-Nitrotyrosine, an oxidative product of protein that is produced *via* peroxynitrite ($ONOO^-$) nitration, was detected by HPLC analysis in plasma obtained from rats injected with lipopolysaccharide (LPS) and subjected to renal ischemia followed by reperfusion (LPS + ischemia-reperfusion), but not in rats subjected to sham-treatment. Rats pretreated with Sanguisorbae Radix extract orally for 30 days before LPS + ischemia-reperfusion, had lower 3-nitrotyrosine levels than rats without the pretreatment. Plasma levels of urea nitrogen and creatinine, indicators of renal dysfunction, were markedly lower in the animals pretreated with Sanguisorbae Radix extract than in those without the pretreatment. In addition, DNA fragmentation in renal tissues was significantly inhibited by administration of Sanguisorbae Radix prior to LPS + ischemia-reperfusion. These results suggest that Sanguisorbae Radix extract ameliorates oxidative damage caused by $ONOO^-$.

23) **Yokozawa T., Chen C. P., and Hattori M.: Confirmation that Luobuma ameliorates the deterioration of antioxidant defense in senescence-accelerated mice. *J. Trad. Med.*, 18: 27-32, 2001.**

To determine whether Luobuma extract ameliorates the deterioration in antioxidant defense with aging, the effect of Luobuma extract was investigated in senescence-accelerated mice (SAM). In comparison with AKR/N Slc mice, a strain consistent with SAM but exhibiting normal aging, SAM treated with extract showed a lower glutathione (GSH) and glutathione/glutathione disulfide (GSH/GSSG) ratio in the liver and kidney, and increased levels of malondialdehyde (MDA), a lipid peroxidation product. Administration of Luobuma extract increased the GSH level and GSH/GSSG ratio, and suppressed MDA production. On the other hand, the reduced activities of hepatic superoxide dismutase (SOD), glutathione peroxidase and glutathione reductase participating in the glutathione redox cycle were increased significantly by administration of Luobuma extract. A significant increase in renal SOD activity was also observed. In addition, the increased level of MDA in hepatic tissue was reduced in SAM given Luobuma extract. These findings indicate that Luobuma extract helps to ameliorate oxidative stress in SAM.

24) **Yokozawa T., Nakagawa T., and Terasawa K.: Effects of Oriental medicines on the production of advanced glycation endproducts. *J. Trad. Med.*, 18: 107-112, 2001.**

Advanced glycation endproducts (AGEs) are largely involved in the pathogenesis of diabetic nephropathy. It is apparent that inhibition of AGEs formation is important in preventing the occurrence and progression of nephropathy. Therefore, to seek possible AGEs inhibitors in Oriental medicines, we began our investigation with an *in vitro* evaluation system. Among the 12 Oriental medical prescriptions examined, Ompi-to inhibited AGEs formation to the greatest extent, followed by Tokaku-zyoki-to and Keishi-bukuryo-gan and Daio-botampi-to in that order. Among the 21 component galenicals examined, Rhei Rhizoma, Cinnamomi Cortex, Moutan Cortex and Paeoniae Radix all had a potent inhibitory action, indicating that Rhei Rhizoma, vascular system disturbance-eliminating drugs and tannin-containing crude drugs can all inhibit the formation of AGEs. These Oriental prescriptions and component galenicals proved to have more potent inhibitory activity than the positive control aminoguanidine.

25) **Huh J. I., Kim H. J., Kim J. W., Shim K. H., Kim Y. J., Lee K. H., Yokozawa T., Yu B. P., and Chung H. Y.: Influence of aging and dietary restriction on renal nitric oxide synthase. *Kor. J. Gerontol.*, 11: 28-33, 2001.**

Nitric oxide (NO) plays an important physiological roles: the control of vascular tone, the contraction of gastrointestinal organs, neurotransmission *via* activation of soluble guanylate cyclase (sGC), and also the gene transcription *via* activation or deactivation of many transcription factors, at the molecular level. The purpose of this study was to examine whether or not aging and dietary restriction (DR) could influence the activity of NO synthase (NOS) and NOS gene expression in rat kidney. To estimate the gene expression of endothelial NOS, we determined mRNA levels and protein levels with RT-PCR and western blot analyses, respectively. Renal NOS activity in DR rats showed a gradual increase up to 18 months of age, but only a slight decrease at 24 months of age in *ad libitum* (AL) rats. Furthermore, DR rats showed higher mRNA levels and protein amounts than AL rats at all ages studied. These results suggest that DR can provide a stimulus for the enhanced production of NOS and thereby DR possibly provides beneficial effects to vascular and renal function during aging.

26) **Yokozawa T., Rhyu D. Y., and Owada S.: Increase of radical in rats with adenine-induced renal failure is suppressed by Wen-Pi-Tang. *J. Trad. Med.*, 18: 147-153, 2001.**

We analyzed the free radical reaction in the body *in vivo* under the conditions of renal failure, using an L-band electron spin resonance apparatus. In rats with adenine-induced renal failure, the attenuation velocity of 3-carbamoyl-2,2,5,5-tetramethylpyrrolidine-N-oxyl was lowered in comparison with normal rats, indicating that they were in a state of augmented oxidation. In contrast, the attenuation velocity was higher in rats given Wen-Pi-Tang, showing

a shift toward reduction. In the kidney of rats given Wen-Pi-Tang, we also found that a significant decrease in glutathione disulfide (GSSG) level caused an increase in the glutathione/GSSG ratio. In addition, there were significant reductions of increased thiobarbituric acid-reactive substance level and decreased superoxide dismutase and increased glutathione peroxidase activities, suggesting a decreased hydrogen peroxide production, which presumably drove the glutathione redox cycle toward reduction. The results of the present study suggest the possibility that Wen-Pi-Tang exerts an antioxidant effect through regulation of the redox cycle.

27) **Nakagawa T., Yokozawa T., and Terasawa K.: A study of Kampo medicines in a diabetic nephropathy model. *J. Trad. Med.*, 18: 161-168, 2001.**

The effects of four Kampo medicines, Ompi-to, Hachimi-jio-gan, Keishi-bukuryo-gan and Sairei-to, were investigated in rats with diabetic nephropathy induced by subtotal nephrectomy and injection of streptozotocin. To evaluate their effects on the glycation reaction, excessive activity of the polyol pathway and oxidative stress (abnormal biochemical processes induced by persistent hyperglycemia), we determined levels of the major endproducts of these processes: advanced glycation endproducts (AGEs) and sorbitol in the kidney and lipid peroxidation in the serum. These three processes were all enhanced in rats with untreated diabetic nephropathy. Oral administration of all four medicines significantly lowered AGEs levels. The renal sorbitol concentration was significantly lowered in the Hachimi-jio-gan-, Sairei-to- and Keishi-bukuryo-gan-treated groups compared with the untreated control group. Serum lipid peroxidation was significantly lowered in the Keishi-bukuryo-gan, Ompi-to and Sairei-to groups, while creatinine clearance and urinary protein excretion (parameters of renal function) were ameliorated by Keishi-bukuryo-gan and Hachimi-jio-gan, respectively, indicating retardation of the progression of diabetic nephropathy. These results suggest the potential therapeutic usefulness of Kampo medicines as a treatment for diabetic nephropathy. It is believed that their actions may occur through different mechanisms.

28) **Yokozawa T., Tanaka T., and Kimura T.: Examination of the nitric oxide production-suppressing component in *Tinospora tuberculata*. *Biol. Pharm. Bull.*, 24: 1153-1156, 2001.**

The component of aqueous *Tinospora tuberculata* extract that inhibits nitric oxide (NO) production was examined using macrophages activated by the addition of lipopolysaccharide. The aqueous extract was partitioned with ethyl acetate. The aqueous layer was fractionated with a Diaion column. The residue of the aqueous extract was extracted with methanol, and partitioned with ethyl acetate. The ethyl acetate layer was found to be associated with a distinct decrease in the NO level and inducible NO synthase. On further fractionation, the subfraction of E-3 showed high anti-NO activity. *N-trans*-Feruloyltyramine isolated from E-3 was identified as exhibiting strong anti-NO activity. This compound is the most active component of *Tinospora tuberculata* with respect to the suppression of NO production.

29) **Hur J. M., Park S. J., Park J. G., Hwang Y. H., Park J. C., Yokozawa T., and Kim M. S.: Flavonoids from the leaves of *glycine max* showing anti-lipid peroxidative effect. *Nat. Product Sci.*, 7: 49-52, 2001.**

Anti-lipid peroxidative activity and phytochemical study on the leaves of *Glycine max* Meer. were investigated. The methanol extract of the leaves of *G. max* reduced the level of lipid peroxides induced by bromobenzene *in vitro*. From the leaves of this plant, apigenin, genistein 7-*O*-β-D-glucopyranoside, kaempferol 3-*O*-β-D-glucopyranoside, and kaempferol 3-*O*-sophoroside were isolated and characterized by spectral data.

30) **Yokozawa T., Nakagawa T., Wakaki K., and Koizumi F.: Animal model of diabetic nephropathy. *Exp. Toxic. Pathol.*, 53: 359-363, 2001.**

Injection of subtotally nephrectomized rats with streptozotocin produced metabolic abnormalities resembling

diabetic nephropathy in humans. These abnormalities were hyperglycemia, hypoinsulinemia, azotemia, hypertriglyceridemia and hypercholesterolemia, accompanied with an increase in glycosylated protein. Extraordinary changes in the urinary excretion of glucose and protein were also observed in rats that received streptozotocin treatment after subtotal nephrectomy. In addition, the level of creatinine clearance was significantly decreased. The pathological findings in the kidney of these rats revealed lesions of the glomerular capillary loops, mesangial area and Bowman's capsule. Coagulation was also found in the glomerular capillaries. Our results suggest that this rat model would be useful for studies of diabetic nephropathy.

31) **Yokozawa T., and Dong E.: Role of ginsenoside-Rd in cisplatin-induced renal injury: special reference to DNA fragmentation. *Nephron*, 89: 433-438, 2001.**

DNA of LLC-PK_1 cells cultured with cisplatin was fragmented to produce low-molecular-weight fragments. Agarose gel electrophoresis of the DNA revealed a ladder pattern characteristic of apoptosis, indicating the induction of apoptosis by cisplatin. However, the degree of apoptosis was lower in cells cultured with cisplatin in the presence of ginsenoside-Rd, and this was accompanied by suppressed leakage of lactic dehydrogenase into the culture medium. The ladder pattern was detected on electrophoresis of DNA in renal tissue samples obtained from rats given an intravenous injection of cisplatin. Such DNA fragmentation was less conspicuous in rats given ginsenoside-Rd orally for 30 days prior to cisplatin administration. Significant suppression of the DNA fragmentation was also demonstrated by densitometry, and measurement of urea nitrogen and creatinine in blood also showed a marked decrease in their respective levels in rats administered ginsenoside-Rd. The present findings suggest that ginsenoside-Rd ameliorates cisplatin-induced renal injury, a process in which apoptosis is plays a central role, and thereby causes restoration of renal function.

32) **Min B., Hattori M., Lee H., Kim Y.: Anticomplement activity of terpenoids from the spores of *Ganoderma lucidum*. *Planta Med.*, 67, 811-814, 2001.**

A new lanostane-type terpenoid, lucidenic acid SP1 (**1**), was isolated from a $CHCl_3$-soluble fraction of *Ganoderma lucidum* spores together with four other known compounds (**2-5**). The structure of lucidenic acid SP1 was determined to be 3β, 7β-dihydroxy-4,4,14α-trimethyl-11,15-dioxo-5α-chol-8-en-24-oic acid by spectroscopic means including 2D-NMR. Twelve tritepenes (**1-12**) isolated from *G. lucidum* spores were investigated *in vitro* for their anticomplementary 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 potency of these triterpene alcohols (**8-10**) in inhibiting CP activity was improved when the number of hydroxymethyl groups on the side chain moiety is increased. On the other hand, ganoderic acids **1-7**, which contain a carboxyl group in the side chain, and lucidumols A and B (**11,12**) had little activity on this system.

33) **Song Q.H., Toriizuka K., Iijima K., Yabe T., Yokozawa T., and Cyong J.C.: Effects of Hokoei-to (Pugongying-Tang), a Kampo formula, on monoamine content in brain regions and mitogenic activity of splenic lymphocytes in ovariectomized mice. *Am. J. Chin. Med.*, 29: 433-443, 2001.**

Hokoei-to (Pugongying-Tang) is onc of the Kampo formulae clinically used for gynecological disturbances such as lack of lactation and mammary swelling. We investigated the effect of Hokoei-to on the nervous and immune systems in ovariectomized micc as a climacteric disorder model. Hokoei-to suppressed the decrease of monoamines in the ventral hippocampus and dorsal hippocampus of ovariectomized mice. It was shown that the Hokoei-to could improve the metabolic turnover of dopamine. The mitogenic activity of lymphocytes in the spleen was reduced after ovariectomy; a suppression of this reduced activity was observed in the group given Hokoei-to.

◇総　説　Review paper

1）Yokozawa T., and Chen C.P.: Evidence suggesting a nitric oxide-scavenging activity for traditional crude drugs, and action mechanisms of Sanguisorbae Radix against oxidative stress and aging. *J. Amer. Aging Assoc.*, **24**: 19-30, 2001.

◇学会報告　Scientific presentation

1）久保山友晴，東田千尋，趙　静，服部征雄，小松かつ子：Ashwagandhaエキス中の神経突起伸展成分の同定－Withanolide A による軸索伸展作用－．日本薬学会第121年会，2001，3，27-30，札幌．

2）横澤隆子，柳　東泳，藤井　創，小砂憲一，野中源一郎：ソバの抗酸化作用．日本薬学会第121年会，2001，3，27-30，札幌．

3）関谷倫子，横澤隆子，黒川昌彦，服部征雄，白木公康：インフルエンザウイルス感染モデルにおける温脾湯の役割．日本薬学会第121年会，2001，3，27-30，札幌．

4）Atef A. Abdel-Hafez，中村憲夫，服部征雄：Biotransformation of phorbol by human intestinal bacteria．日本薬学会第121年会，2001，3，27-30，札幌．

5）孫　全忠，中村憲夫，角田広子，馬　超美，馮　挙，陳　道峰，服部征雄：*Kadsura longipedunculate* の新リグナン成分及びその HIV-1 プロテアーゼ阻害作用．日本薬学会第121年会，2001，3，27-30，札幌．

6）*Hattori M.: Recent studies on bitter principles of *Ganoderma lucidum* － Isolation of new Ganoderma triterpenes, their biological activity and pharmakokinetics －. 2001, 4, Auckland, New Zealand.

7）Park J. C., Park J. G., Hur J. M., Hatano T., Yoshida T., Miyashiro H., and Hattori M.: Anti-HIV-1 protease activity of Korean plant resources and bioactive tannins. 11th World Congress of Food Science and Technology, 2001, 4, Seoul, Korea.

8）Park J. G., Hur J. M., Park J. C., Shin D .Y., Park K. Y., Kim M. S., Miyashiro H., and Hattori M.: Inhibitory effects of extract and phenolic compounds from *Orostachys japonicus* on human immunodeficiency virus type 1 protease. 11th World Congress of Food Science and Technology, 2001, 4, Seoul, Korea.

9）Park J. G., Hur J. M., Rhyu D. Y., and Yokozawa T.: Radical-scavenging activity of some medicinal plants and phenolic compounds isolated from *Rosa rugosa* root on 1, 1-diphenyl-2-picrylhydrazyl radical. 11th World Congress of Food Science and Technology, 2001, 4, Seoul, Korea.

10）*Hattori M.: Application of biotechnology to the researches of traditional medicine. 2001 Nanjing International Symposium of Traditional Chinese Medicine and Pharmacy, 2001, 5, Nanjing China.

11）*Hattori M.: Development of anti-viral agents from natural sources. 5th International Symposium of Research Institute of Oriental Medicine-Eastern and Western Medical Appraaches on Intractable Diseases. 2001, 5, Kyong-Ju, Korea.

12）中川孝子，横澤隆子：漢方方剤の Advanced glycation endproducts（AGE）形成抑制作用．第44回日本腎臓学会学術総会，2001，5，東京．

13）柳　東泳，横澤隆子：パーオキシナイトライト由来腎障害モデルを用いた温脾湯の検討．第44回日本腎臓学会学術総会，2001，5，東京．

14）Supinya Tewtrakul，宮代博継，服部征雄，吉永智一，藤原民雄，富森　毅，木津治久，宮一諭起範：Inhibitory effects of flavonoids on human immunodeficiency virus type 1（HIV-1）integrase．日本薬学会北陸支部第104回例会，2001，6，金沢．

15）*横澤隆子：腎障害に対する地楡の役割と機序．第7回天然薬物研究方法論アカデミー，2001，8，大府．

16）中川孝子，横澤隆子，寺澤捷年，服部征雄：糖尿病性腎症における漢方方剤の作用．第18回和漢医薬学会大会ミニシンポジウム，2001，8，富山．

17）石田あい，横澤隆子，中川孝子，服部征雄：循環障害における黄連の役割：エンドトキシンショック並びに高脂血症モデルを用いた検討．第18回和漢医薬学会大会，2001，8，富山．

18)*Yokozawa T., Rhyu D. Y., and Kim D. W.: A study of buckwheat in a renal ischemia-reperfusion model. The VIII International Symposium on Buckwheat, 2001, 8, Chunchon, Korea.

19) 服部征雄：腸内嫌気性菌による反応の特色とその利用. 日本生薬学会第48回（2001年）年会, 2001, 9, 金沢.

20) 趙　静, 中村憲夫, 服部征雄, 東田千尋, 小松かつ子：Five new withanolide derivatives from the roots of *Withania somnifera*. 日本生薬学会第48回（2001年）年会, 2001, 9, 金沢.

21)*Yokozawa T.: The role of the active Dan Shen component, magnesium lithospermate B, in the kidney. 3rd International Congress of Nephrology on Integrated Traditional Chinese and Western Medicine. 2001, 9, Shanghai, China.

22) 中川孝子, 横澤隆子, 寺澤捷年：糖尿病性腎症における漢方方剤の役割. 第13回腎とフリーラジカル研究会, 2001, 9, 和歌山.

23) Kim H. Y., Yokozawa T., Cheigh H. S., and Choi J. S.: Antioxidant effect of isorhamnetin 3,7-di-*O*-β-D-glucopyranoside from mustard leaves (*Brassica juncea*) on oxidative stress in streptozotocin-induced diabetic rats. 第13回腎とフリーラジカル研究会, 2001, 9, 和歌山.

24)*Hattori M.: Biotransformation of epicatechin 3-*O*-gallate and epigallocatechin 3-*O*-gallate by human intestinal bacteria. 2001 International Conference on O-CHA (tea) Culture and Science, 2001, 10, Shizuoka.

25)*Yokozawa T., Nakagawa T., Shu S., and Juneja L. R.: Protective effects of green tea polyphenols against renal disease. 2001 International Conference on O-CHA (tea) Culture and Science, 2001, 10, Shizuoka.

26)*服部征雄：和漢薬成分の代謝：最近の進歩. 第22回和漢薬研究所特別セミナー, 2001, 10, 富山.

27)*Hattori M.: Metabolic activation of pro-estrogenic substances by human intestinal bacteria. International Symposium on Strategic Goals of Pharmacognostical Studies During the 21st Century, 2001, 10, Beijing.

28) Min B., Gao J., Hattori M., Kim Y., Bae K., Kim J., Kwon O., Oh S., Lee H.: Anti-complement of terpenoids from the spores of *Ganoderma lucidum*. 漢薬学会, 2001, 10, 淑明.

29) Min B., Gao J., Ahn E., Nakamura N., Hattori M., Lee H.: New triterpene aldehydes, lucialdehydes A-C, from *Ganoderma lucidum* and their cytotoxicity against murine and human tumor cells. 漢薬学会, 2001, 10, 淑明.

30) Park J. C., Hur J. M., Park J. G., Hwang Y. H., Choi D. R., Jung D. Y., Kim M. S., Kim S. N., Choi J. W., and Yokozawa T.: Antihepatotoxic activity and phytochemical study on *Rosa davurica*. International Symposium on Pharmaceutical Sciences Commemorating the 50th Anniversary of the Pharmaceutical Society of Korea, 2001, 10, Seoul, Korea.

31) Park J. C., Rhyu D. Y., and Yokozawa T.: Inhibitory effects of *Rosa rugosa* and *Zanthoxylum piperitum* on DPPH radical and their bioactive constituents. Korean Society of Medicinal Crop Science International Symposium 2001, 2001, 11, Daejeon, Korea.

32) 条美智子, 中村憲夫, 小松かつ子, 服部征雄, 黒川昌彦, 白木公康：抗 HSV 活性を指標とした中国少数民族薬物の探索. 日本薬学会北陸支部第105回例会, 2001, 11, 金沢.

33)*Hattori M.: Chemical and biological evaluation of the fruiting bodies of *Ganoderma lucidum*. The 8th International Symposium for Development of Advanced Materials from Resources Plants, 2001, 11, Kwangju, Korea.

34) Park J. C., Hyun K. H., Rhyu D. Y., and Yokozawa T.: Potent radical-scavenging compounds isolated from *Rosa davurica* on DPPH radical. International Symposium on Food, Nutrition and Health for 21st Century, 2001, 12, Seoul, Korea.

（＊印は 招待講演を示す）

◇講演会　Lectures

1）Hattori M.: Recent studies on metabolic transformation of natural products by human intestinal bacteria.

Dalian Institute of Chemical Physics, Chinese Academy of Science. 2001, 5, Dalian, China.

2）服部征雄：最近の霊芝研究，富山漢方会，2001，6，富山.

3）服部征雄：伝統医学に明日を求めて，韮山高等学校文化講演会，2001，11，韮山.

4）Hattori M.: Searching for anti-HIV agents among medicinal plants. 2001, 12, Chulalongkorn University, Bangkok.

5）Yokozawa T.: Action mechanisms of Sanguisorbae Radix against oxidative stress and aging. 2001, 10, Pusan National University, Pusan, Korea

◇その他　Others

1）服部征雄：エイズウイルスに効く伝統薬物をもとめて．第6回和漢薬研究所夏期セミナー，2001，8，富山.

2）Hattori M.: Metabolism of epicatechin 3-*O*-gallate and epigallocatechin 3-*O*-gallate by human intestinal flora. Proceedings of International conference on O-Cha (ter) culture and siences. Section III. Health and Benefits. pp. 38-41, 2001.

3）Yokozawa T., Rhyu D. Y., and Kim D. W.: A study of buckwheat in a renal ischemia-reperfusion model. Advances in Buckwheat Research, 583-586, 2001.

4）Chung H. Y., Soung D. Y., Kye I. S., Shim K. H., Kim Y. J., and Yokozawa, T.: Green tea tannin: potent peroxynitrite-scavengers. Proceedings of International Forum on Traditional Medicine, 201-212, 2001.

5）Yokozawa T., Nakagawa T., Shu S., and Juneja L. R.: Protective effects of green tea polyphenol against renal disease. Proceedings of 2001 International Conference on O-CHA(tea) Culture and Science, 22-25, 2001.

6）横澤隆子：老化促進モデルマウス（SAM）を用いての薬用人参サポニンRdの評価．The GINSENG REVIEW, No. 29, 5-8, 2001.

7）横澤隆子(代表)：抗酸化物としての羅布麻の探索．文部科学省科学研究費補助金（基盤研究C）研究成果報告書，2001，3.

8）横澤隆子(分担)：老化・老年病に対する栄養学的・薬理学的・分子遺伝学的手法による干渉に関する総合的研究．厚生科学研究費補助金長寿科学総合研究事業研究成果報告書，2001，3.

◇共同研究　Co-operative researches

1）小松かつ子：薬効解析センター，「痴呆脳に対するコーヒーの作用」

2）下遠野邦忠：京都大学ウイルス研究所，「C型肝炎RNAポリメラーゼ阻害活性を指標とした抗HCV剤の開発研究」

3）白木公康，小松かつ子：富山医科薬科大学医学部および和漢薬研究所，「抗ヘルペスウイルス作用を指標とした中国少数民族薬物の探索」

4）大竹　徹：大阪府立公衆衛生研究所，「天然からの抗エイズウイルス薬の開発」

5）木谷健一：国立療養所中部病院長寿医療研究センター，「抗老化薬に関する研究」

6）鄭　海泳：釜山大学校薬学大学，「抗酸化物に関する研究」

7）田中　隆：長崎大学薬学部，「活性成分に関する研究」

8）小砂憲一：アミノアップ化学，「機能性食品の開発研究」

◇研究費取得状況　Acquisition of research funds

1）日本学術振興会特別研究員奨励費「微生物を利用した新しい薬物の開発」（継続，服部代表）100万円.

2）文部科学省科学研究費基盤研究(A)(1)「高次脳機能障害モデルの作出，新規薬効評価法の確立と創薬」（継続，服部分担）50万円.

3）平成13年度教育研究学内特別経費「生薬配糖体の特性を生かした大腸送達性プロドラッグの創製 －潰瘍性大腸炎治療薬への展開－」（新規，服部分担）18万円.

4）平成13年度教育研究学内特別経費「アトピー性皮膚炎モデルにおける漢方方剤・食餌脂肪酸の有効性の作用機構および活性成分の検索」（新規，服部分担）18万円.
5）厚生省長寿科学総合研究費「老年・老年病に対する栄養学的・薬理学的・分子遺伝学的手法による干渉に関する総合的研究」（継続，横澤分担）250万円.
6）つくし奨学・研究基金「NO を中心としたラジカルの相互作用と和漢薬の関与」（継続，横澤代表）120万円.
7）2001年度日中医学協会助成金「糖尿病性腎症に有効な伝統薬物の探索」（新規，横澤代表）100万円.
8）興和生命科学振興財団「抗 HIV 活性を有するホルボールエステル類の探索研究」（新規，中村代表）100万円.
9）漢方医薬研究振興財団「C 型肝炎ウイルスの抗ウイルス剤の開発研究－HCV のポリメラーゼに対して阻害活性を示す中国少数民族薬物の探索－」（新規，中村代表）50万円.

◇学位および論文名　Academic degrees and theses

博士：Supinya Tewtrakul「Inhibitory effects of Thai medicinal plants, their constituents and related compounds on HIV-1 integrase」
修士：木村貴子「チベット生薬のエイズウイルス逆転写酵素及びC型肝炎ウイルスポリメラーゼ阻害作用について」
学士：平川暁子「霊芝苦味成分の細胞毒性及び抗腫瘍効果の検討」
　　山辺典子「糖尿病性腎症における八味地黄丸の影響」

◇研究室在籍者　Research member

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