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◇研究目的 Aims of the research projects

本部門は、化学的手法を応用する和漢薬の基礎研究として、天然薬物を中心とする生理活性分子の医薬化学的及び生物有機化学的研究を行っている。この目的で、天然薬物の成分単離、構造解析、合成等の、和漢薬成分に関する化学的研究を行う。さらに、その過程で構造が明らかとなる天然薬物成分につき、その構造・活性相関、構造・機能相関の化学的解明に取り組んでいる。 本年度の主な研究課題は下記の通りである。

◇研究概要 Research projects

I. 天然薬物成分の科学的研究 東南アジア(インドネシア、ネパール、ベトナム、タイ、ミャンマー等)の薬用植物

Ⅱ. 和漢薬成分の医薬化学

- 1. 羅布麻, プロポリスから単離した生理活性成分の合成
- 2. 肝臓病や骨粗鬆症に有効な天然薬物成分の開発研究
- 3. マトリックスメタロプロテアーゼ産生阻害を有する天然薬物成分の研究
- 4. 紅豆杉の活性成分の研究

Ⅲ. 漢方製剤の品質評価法

- 1. 通関丸, 桃核承気湯, 当帰飲子など
- 2. 基源植物,修治生薬のLC-MSによる評価

IV. 和漢薬成分の生物有機化学的研究

ベルベリン、ベトナム人参、CAPE類縁体、キナ酸誘導体、カリクシン類、花椒成分など

V. 天然薬物調査

ベトナム, ミャンマー, ブラジルなど

上記の研究課題によって得られた本年度の成果(原著及び学会報告)は下記の通りである。

◇著 書 Books

1)「和漢薬の辞典」(分担),富山医科薬科大学和漢薬研究所(編集),難波恒雄(監修),朝倉書店,東京, 2002年 6 月 (門田, 手塚).

◇原著論文 Original papers

1) Yuan Z., Tezuka Y., Fan W., Kadota S., and Li X.: Constituents of the Underground Parts of Glehnia littoralis. Chem. Pharm. Bull., 50, 73-77 (2002).

Abstract: From the underground parts of Glehnia littoralis F_R. S_{CHMIDT} ex M_{IQUEL} (Umbelliferae), twenty-six compounds, including two new lignan glycosides [glehlinosides A (1) and B (2)], a new neolignan glycoside [glehlinoside C (3)], a new phenylpropanoid glycoside [4- $[\beta$ -D-apiofuranosyl-(1 \rightarrow 6)- β -D-glucopyranosyloxy]-3-methoxypropiophenone (4)], were obtained and their structures were determined by analysis of their spectral data. The DPPH radical scavenging assay disclosed quercetin (8), isoquercetin (9), rutin (10), chlorogenic acid (11), and caffeic acid (24) as the major antioxidative constituents in this crude drug.

2) Awale S., Tezuka Y., Shimoji S., Taira K., and Kadota S.: Secoorthosiphols A-C; Three Highly Oxygenated Secoisopimarane-type Diterpenes From *Orthosiphon stamineus*. *Tetrahedron Lett.*, 43, 1473-1475 (2002).

Abstract: Three new highly oxygenated 2,3-secoisopimarane-type diterpenes, named secoorthosiphols A (1), B (2) and C (3), have been isolated as extremely minor constituents from the aerial parts of the *Orthosiphon stamineus* from Okinawa. A unique unprecedented structural feature of such a ring A opened system in newly isolated compounds was encountered for the first time in isopimarane-type diterpenes. Secoorthosiphol C (3) represents the first example of a biogenetically unique and unconventional secoisopimarane-type diterpene having a cyano group.

3) Banskota A. H., Nagaoka T., Sumioka L. Y., Tezuka Y., Awale S., Midorikawa K., Matsushige K., and Kadota S.: Anti-proliferative activity of the Netherlands propolis and its active principles in cancer cell lines. *J. Ethnopharmacol.*, 80, 67-73 (2002).

Abstract: The MeOH extract of the Netherlands propolis showed promising antiproliferative activity toward highly metastatic liver murine colon 26-L5 carcinoma with an EC₅₀ value of $3.5 \,\mu$ g/mL. Further, antiproliferative activity-guided purification of the MeOH extract led us to isolate four flavonoids (1-4), seven cinnamic acid derivatives (5-11) and two new glycerol derivatives (12, 13), whose structures were elucidated on the basis of spectral analysis. The isolated compounds were tested for their antiproliferative activity against murine colon 26-L5, murine B16-BL6 melanoma, human HT-1080 fibrosarcoma and human lung A549 adenocarcinoma cell lines. The benzyl (9), phenethyl (10) and cinnamyl caffeates (11) possessed potent antiproliferative activities with EC₅₀ values of 0.288, 1.76 and 0.114 μ M, respectively, toward colon 26-L5 carcinoma. These caffeates were considered to be active constituents of the Netherlands propolis in their antiproliferative activity. The antioxidative activity of these caffeates may play an important role in their antiproliferative activities.

4) Awale S., Tezuka Y., Banskota A. H., Kouda K., Tun K. M., and Kadota S.: Four Highly Oxygenated Isopimarane-Type Diterpenes of *Orthosiphon stamineus* from Myanmar. *Planta Med.*, 68, 286-288 (2002).

Abstract: Four highly oxygenated isopimarane-type diterpenes, named orthosiphols O, P and Q and nororthosiphonolide A, have been isolated from the aerial parts of *Orthosiphon stamineus* from Myanmar, together with three known diterpenes, orthosiphols D and E and orthosiphonone A. Their structures were determined on the basis of extensive spectral analysis. All the isolated compounds displayed mild antiproliferative activities against highly liver metastatic colon 26-L5 carcinoma and human HT-1080 fibrosarcoma cell lines

5) Akihisa T., Wijeratne E. M. K., Tokuda H., Enjo F., Toriumi M., Kimura Y., Koike K., Nikaido T., Tezuka Y., and Nishino H.: Eupha-7,9(11),24-trien-3β-ol ("Antiquol C") and Other Triterpenes from *Euphorbia antiquorum* Latex and Their Inhibitory Effects on Epstein-Barr Virus Activation. J. Nat. Prod., 65, 158-162 (2002).

Abstract: The structures of three triterpene alcohols isolated from the latex of *Euphorbia antiquorum* were established to be eupha-7,9(11),24-trien-3 β -ol (2; antiquol C), 19(10 \rightarrow 9)abeo-8 α ,9 β ,10 α -eupha-5,24-dien-3 β -ol (3; antiquol B), and 24-methyleupha-8,24(24¹)-dien-3 β -ol (4; euphorbol) on the basis of spectroscopic methods. Componds 3 and 4 have previously been assigned the erroneous structures of 10 α -cucurbita-5,24-dien-3 α -ol and 24-methyleupha-8,24(24¹)-dien-3 β -ol, respectively. Compounds 2-4 and four other known compounds isolated from the latex, euphol (1), lemmaphylla-7,21-dien-3 β -ol (5), isohelianol (6), and camelliol C (7), showed potent inhibitory effects on Epstein-Barr virus early antigen (EBV-EA) activation induced by the tumor promoter 12- α -detradecanoylphorbol-13-acetate (TPA).

6) Awale S., Tezuka Y., Wang S., and Kadota S.: Facile and Regioselective Synthesis of Phenylpropanoid-Substituted Flavan-3-ols. *Org. Lett.*, 4, 1707-1709 (2002).

Abstract: A highly efficient, facile, one-pot regioselective synthesis of a series of phenylpropanoid-substituted flavan-3-ols is described. The mechanism involves dienone-phenol rearrangement followed by a Michael-type reaction.

7) Usia T., Banskota A. H., Tezuka Y., Midorikawa K., Matsushige K., and Kadota S.: Constituents of Chinese Propolis and Their Antiproliferative Activities. *J. Nat. Prod.*, 65, 673-676 (2002).

Abstract: Two new flavonoids, 3-O-[(S)-2-methylbutyroyl]pinobanksin (1) and 6-cinnamyl-chrysin (2), were isolated from the EtOAc-soluble fraction of the MeOH extract of Chinese propolis, along with 12 known compounds (3-14). The structures of the isolated compounds were elucidated on the basis of spectroscopic and chemical analyses. The isolated compounds were tested for their antiproliferative activity toward five different cancer cell lines. Benzyl caffeate (13) and phenethyl caffeate (14) showed potent antiproliferative activity toward tested cell lines with a selective activity toward colon 26-L5 carcinoma cell line (EC₅₀ values: 13, 1.01; 14, 0.30 μ M).

8) Ueda J., Tezuka Y., Banskota A. H., Tran Q. L., Tran Q. K., Harimaya Y., Saiki I., and Kadota S.: Antiproliferative Activity of Vietnamese Medicinal Plants. *Biol. Pharm. Bull.*, 25, 753-760 (2002).

Abstract: Methanol, methanol-water (1:1) and water extracts were prepared from seventy-seven Vietnamese medicinal plants and tested for their antiproliferative activities against human HT-1080 fibrosarcoma cells. Among them, fifteen extracts including seven methanol extracts of Caesalpinia sappan, Catharanthus roseus, Coscinium fenestratum, Eurycoma longifolia, Hydnophytum formicarum and Streptocaulon juventas (collected at two areas), six methanol-water (1:1) extracts of Cae. sappan, Cat. roseus, Co. fenestratum, H. formicarum and S. juventas (at two areas), and two water extracts of Cae. sappan and S. juventas exhibited antiproliferative activities in a concentration-dependent manner. Their antiproliferative activities against human cervix HeLa adenocarcinoma, human lung A549 adenocarcinoma, murine colon 26-L5 carcinoma, murine Lewis lung carcinoma (LLC) and murine B16-BL6 melanoma cells were then examined. Co. fenestratum showed selective activity against lung carcinoma and/or lung metastatic cell lines, A549, LLC and B16-BL6, while H. formicarum and S. juventas showed selective activity against human tumor cell lines, HeLa and A549. Characteristic morphological change and DNA fragmentation indicated the antiproliferative activity to be due to the induction of apoptosis.

9) Tran Q. L., Adnyana I K., Tezuka Y., Harimaya Y., Saiki I., Tran Q. K., and Kadota S.: Hepatoprotective Effect of Majonoside R2, The Major Saponin from Vietnamese Ginseng (*Panax vietnamensis*). Planta Med., 68, 402-406 (2002).

Abstract: The hepatoprotective effect of majonoside R_2 (MR2), the major saponin constituent from Vietnamese ginseng (*Panax vietnamensis*, Araliaceae), was evaluated *in vivo* on D-galactosamine (D-GalN)/lipopolysaccharide (LPS)-induced hepatic apoptosis and subsequent liver failure in mice. Pretreatment of mice with MR2 (50 or 10 mg/kg, intraperitoneal) at 12 and 1 h before D-GalN/LPS injection significantly inhibited apoptosis and suppressed following hepatic necrosis. Importantly, the elevation of serum tumor necrosis factor-alpha (TNF- α) level, an important mediator for apoptosis in this model, was significantly inhibited by MR2 at a dose of 50 mg/kg. On the other hand, MR2 was found to protect primary cultured mouse hepatocytes from cell death by inhibiting apoptosis induced by D-GalN/TNF- α in vitro, as evidenced by DNA fragmentation analysis. These findings suggested that MR2 may have protected the hepatocytes from apoptosis via an inhibition of TNF- α production by activated macrophages and a direct inhibition of apoptosis induced by TNF- α .

10) Awale S., Tezuka Y., Banskota A. H., Shimoji S., Taira K., and Kadota S.: Norstaminane- and Isopimarane-type Diterpenes of *Orthosiphon stamineus* from *Okinawa*. *Tetrahedron*, 58, 5503-5512 (2002).

Abstract: Nine novel highly-oxygenated and structurally diverse diterpenes, named norstaminolactone A (1), norstaminols B and C (2 and 3), secoorthosiphols A-C (4-6) and orthosiphols R-T (7-9) have been isolated from the aerial part of *Orthosiphon stamineus* cultivated in Okinawa Prefecture, Japan. Norstaminolactone A (1) is the first representative of a biogenetically unusual norstaminane-type diterpene bearing a nitrogen atom. Norstaminol C (3) possessed a framework presumed to be biosynthesized from the staminane-type diterpene. Secoorthosiphols A-C (4-6) possessed an unprecedented structural feature of the opened ring A system, encountered for the first time in isopimarane-type diterpenes. Secoorothosiphol C (6) also represents the first example of biogenetically unique and unconventional secoisopimarane-type diterpene bearing a cyano group. Norstaminolactone A (1) showed a potent antiproliferative activity with an IC₅₀ value of 2.16 μ g/mL against highly liver metastatic colon 26-L5 carcinoma cell line.

- 11) Hasegawa H., Suzuki R., Nagaoka T., Tezuka Y., Kadota S., and Saiki I.: Prevention of Growth and Metastasis of Murine Melanoma through Enhanced Natural-Killer Cytotoxicity by Fatty Acid-Conjugate of Protopanaxatriol. *Biol. Pharm. Bull.*, 25, 861-866 (2002).
- 12) Mook-Jung I., Kim H., Fan W., Tezuka Y., Kadota S., Nishijo H., and Jung M. W.: Neuroprotective effects of constituents of Oriental crude drugs, *Rhodiola sacra*, *R. sachalinensis* and Tokaku-joki-to, against beta-amyloid toxicity, oxidative stress and apoptosis. *Biol. Pharm. Bull.*, 25, 1101-1104 (2002).

Abstract: We tested the constituents of two *Rhodiola* plants, *Rhodiola sacra* S. H. Fu and *R. sachalinensis* A. Bor, and an Oriental crude drug, Tokaku-joki-to, for their neuroprotective effects. Of the 58 compounds tested, six had considerable protective effects against beta-amyloid-induced cell death, and two of the six compounds protected neurons from H₂O₂-induced cell death. These results suggest that some of the tested compounds protect neurons from beta-amyloid toxicity based on antiapoptotic and antioxidative activity.

13) Nagaoka T., Banskota A. H., Tezuka Y., Saiki I., Kadota S.: Selective Antiproliferative Activity of Caffeic Acid Phenethyl Ester Analogues on Highly Liver-Metastatic Murine Colon 26-L5 Carcinoma Cell Line. *Bioorg. Med. Chem.*, 10, 3351-3359 (2002).

Abstract: Caffeic acid phenethyl ester (CAPE, 2) and its twenty analogues (1, 3-21) were prepared. These esters were tested by MTT assay on growth of murine colon 26-L5 carcinoma, murine B16-BL6 malonoma, murine Lewis lung carcinoma, human HT-1080 fibrosarcoma, human lung A549 adenocarcinoma, and human cervix HeLa adenocarcinoma cell lines. It was found that CAPE analogues possessed selective antiproliferative activity toward highly liver-metastatic murine colon 26-L5 carcinoma cell line. Among them, 4-phenylbutyl caffeate (4), (Z)-8-phenyl-7-octenyl (10a) and (E)-8-phenyl-7-octenyl (10b) caffeate showed the most potent antiproliferative activity (EC₅₀ value, 0.02 μ M). In addition, CAPE (2) induced DNA fragmentation at concentrations of 1 to 10 μ g/ml towards murine colon 26-L5 carcinoma cells.

14) Tominaga K., Higuchi K., Hamasaki N., Hamaguchi M., Takashima T., Tanigawa T., Watanabe T., Fujiwara Y., Tezuka Y., Nagaoka T., Kadota S., Ishii E., Kobayashi K., and Arakawa T.: In vivo activation of novel alkyl methyl quinolone alkaloids against *Helicobacter pyroli*. J. Antimicrob. Chemother., 50, 547-552 (2002).

Abstract: Previously purified and isolated compounds of novel alkyl methyl quinolone alkaloids (AM quinolones) from Gosyuyu (Wu-Chu-Yu), a Chinese herbal medicine, have a strong and highly selective antibacterial activity against *Helicobacter pylori in vitro*. To clarify the antibacterial mechanism(s) of AM quinolones, we examined the effects of AM quinolones on respiration of *H. Pylori in vitro*. One week after treatment with AM quinolones alone (2, 10 or 20 mg/kg/day, orally) or combinations of AM quinolones and omeprazole (30 mg/kg/day) for *H. Pylori* (1×10^8 cfu)-infected Mongolian gerbils, we checked viable *H. pylori* and myeloperoxidase (MPO) activity in the gastric tissues. AM quinolones decreased the number of *H. pylori* and inhibited *H. pylori* respiration in a dose-dependent manner. AM quinolones decreased the number of viable *H. pylori* (AM quinolones alone: $46.0\pm22.6 \times 10^4$, $17.3\pm4.9\times10^4$ and $8.1\pm6.6\times10^4$ cfu/stomach, respectively; and combinations of AM quinolones and omeprazole: $8.0\pm5.6\times10^4$, $4.2\pm2.5\times10^4$, and $5.5\pm2.7\times10^4$ cfu/stomach) compared with the vehicle-treated group (control: $359.9\pm180.3\times10^4$ cfu/stomach). AM quinolones significantly decreased MPO activity of *H. pylori*-inoculated gastric tissues. These findings suggest that AM quinolones have a potent antibacterial effect against *H. pylori* through respiratory inhibition, and reduced bacterial growth *in vivo*. AM quinolones might be nobel therapeutic agents for *H. pylori* eradication.

15) Banskota A. H., Usia T., Tezuka Y., Kouda K., Nguyen N. T., and Kadota S.: Three New C-14 Oxygenated Taxanes from the Wood of Taxus yunnanensis. *J. Nat. Prod.*, 65, 1700-1702 (2002).

Abstract: Three new C-14 oxygenated taxane-type diterpenes, hongdoushans A-C (1-3), were isolated from the wood of *Taxus yunnanensis* together with four known diterpenes and two lignans. The absolute stereochemistry of the 2-methylbutyryloxy group attached at C-14 of the taxane skeleton was determined to be S by GC analysis of methyl ester of 2-methylbutyric acid obtained after alkaline hydrolysis of 1 and 4 followed by treatment with CH₂N₂. The complete stereostructure of the known compound $2\alpha,5\alpha,10\beta$ -triacetoxy- 14β -[(S)-2-methylbutyryloxy]-4(20),11-taxadiene (4) was established for the first time. The isolates obtained were evaluated for their antiproliferative activity towards murine colon 26-L5 carcinoma and human HT-1080 fibrosarcoma cell lines.

16) 金 辰彦, 門田重利, Banskota A. H., 山村重雄, 百瀬弥寿徳, 佐治大介, 石井権二: モルモット摘出回腸標本におけるステビア発酵エキスの抗 histamine 作用. 応用薬理, 62, 105-109 (2002).

Abstract: Stevia rebaudiana Bertoni is a shrub growing originally in Paraguay. The leaves of this plant contain stevinoside, a sweet constituent which is 300 times as sweet as sucrose. Recently, this extracts is clinically useful for IgE related disease, atopic dermatitis or allergic dermatitis. Therefore, we studied the effects of stevia fermenting

extracts (*Stevia rebaudiana* Bertone) on histamine-induced contractions in isolated ileum from guinea pig. Two stevia extracts (A and C) inhibited the histamine-induce contractions. However, stevia extracts B, D and E did not affect on the histamine-induced contraction. Our results show stevia fermenting extracts having antihistaminic effect (H₁ receptor).

17) Nishiyama T., Ogura K., Nakano H., Kaku T., Takahashi E., Ohkubo Y., Sekine K., Hiratsuka A., Kadota S., Watabe T.: Sulfation of Environmental Estrogens by Cytosolic Human Sulfotransrerases. *Drug Metabol. Pharmacokin.*, 17, 221-228 (2002).

Abstract: It is known that in humans taking soy food, the phytoestrogens, daidzein (DZ) and genistein (GS), exist as sulfates and glucuronides in the plasma and are excreted as conjugates in urine. To investigate which human sulfotransferase (SULT) isoforms participate in the sulfation of these phytosetrogens, the four major cytosolic SULTs, SULT1A1, SULT1A3, SULT1E1, and SULT2A1, occurring in the human liver were bacterially expressed as His-tagged proteins and chromatographically purified to homogeneity in the presence of Tween 20 and glycerol as highly efficient agents for stabilizing the recombinant enzymes. All the SULTs showed sulfating activety toward both DZ and GS. However, k_{cat}/K_m values of 0.3 and 0.7 μ M for GS and 1.9 and 3.4 μ M for DZ, respectively. DZ and GS strongly inhibited the sulfation of the endogenous substrate, β -estradiol, by SULT1E1 in a non-competitive manner with K_i values of 14 and 7 μ M, respectively, suggesting that these phytoestrogens might affect tissue levels of β -estradiol in the human. The phenolic endocrine-disrupting chemicals, bisphenol A (BPA), 4-n-nonylphenol (NP), and 4-t-octylphenol (t-OP), were used as substrates to investigate the possible participation of human SULTs in their metabolism for excretion. High k_{cat}/K_m values were observed for the sulfation of BPA by SULT1A1, NP by SULT1A1 and SULT1E1, and t-OP by SULT1E1 and SULT2A1.

◇総 説 Review papers

1) 手塚康弘: 東南アジア産薬用植物の生物活性成分に関する研究. Natural Medicines, **56**, 78-83 (2002).

◇学会報告 Scientific presentation

- 1) Arjun H. Banskota, Tepy Usia, 手塚康弘, 幸田恭治, 門田重利: Chemical Constituents and Isolation of Two New Taxanes from the Wood of *Taxus yunnanensis*. 日本薬学会第122年会, 2002, 3/26-28, 千葉.
- 2) 幸田恭治, 手塚康弘, Arjun H. Banskota, 門田重利:新規 diarylheptanoid 類の MS/MS スペクトル. 日本薬学会第122年会, 2002, 3/26-28, 千葉.
- 3) 王 淑敏, 手塚康弘, Suresh Awale, Arjun H. Banskota, Tran Le Quan, 門田重利: 沱茶の成分研究. 日本薬学会北陸支部第106回例会, 2002, 6/15, 富山.
- 4) 李 建平, Arjun H. Banskota, 手塚康弘, Mohan B. Gewali, 門田重利: *Hematoxylon campechianum* および *Artemisia vulgaris* の血糖降下作用. 日本薬学会北陸支部第106回例会, 2002, 6/15, 富山.
- 5) Jun Yin, Yasuhiro Tezuka, Kyoji Kouda, Quan Le Tran, Tatsuro Miyahara, Yasutaro Mikami, Yingjie Chen, Shigetoshi Kadota: solation of six new saponins from antiosteoporotic fraction of *Dioscorea spongiosa*. 第19回和漢医薬学会大会,2002,8/31-9/1,千葉.
- 6) 岩田 宏, Tepy Usia, 手塚康弘, 門田重利, 平塚 明, 渡部 烈:生薬エキス83種類によるヒト肝シトクロムP450 (CYP3A4, CYP2D6) の阻害. 第19回和漢医薬学会大会, 2002, 8/31-9/1, 千葉.
- 7) Arjun H. Banskota, Jianping Li, Nhan Trung Nguyen, Yasuhiro Tezuka, Quan Le Tran, Shigetoshi Kadota: Secoisolariciresinol, a Potent Hypoglycemic Agent from the Wood of *Taxus yunnanensis*. 第19回和漢医薬学会大会, 2002, 8/31-9/1, 千葉.

- 8) Myint Myint Than, Arjun H. Banskota, Yasuhiro Tezuka, Quan Le Tran, Kiyoshi Midorikawa, Katsumichi Matsushige, Shigetoshi Kadota: Constituents of Water Extract of Brazilian Propolis, Their Biological Properties and Botanical Origin. 第19回和漢医薬学会大会, 2002, 8/31-9/1, 千葉.
- 9) 長岡武馬, Arjun H. Banskota, 手塚康弘, 松繁克道, 小泉桂一, 播磨谷優子, 済木育夫, 門田重利: プロポリス成分 CAPE 及びその類縁体による癌転移の抑制. 第19回和漢医薬学会大会, 2002, 8/31-9/1, 千葉.
- 10) 長谷川秀夫,長岡武馬,手塚康弘,門田重利,済木育夫:人参トリオール系サポニン代謝物の脂肪酸抱合物による抗腫瘍効果の発現. 第19回和漢医薬学会大会,2002,8/31-9/1,千葉.
- 11) 上田純也, 手塚康弘, Arjun H. Banskota, Quan Le Tran, Qui Kim Tran, 播磨谷優子, 済木育夫, 門田重利:ベトナム産薬用植物 Streptocaulon juventas の成分研究. 日本生薬学会第49回年会, 2002, 9/5-6, 福岡.
- 12) Suresh Awale, 手塚康弘, 下地清吉, 平良一彦, 門田重利: Highly Oxygenated Novel Diterpenes of *Orthosiphon stamineus* from Indonesia. 第46回香料・テルペンおよび精油化学に関する討論会 (46th TEAC)・国際精油シンポジウム (ISEO) 合同大会, 2002, 10/18-21, 徳島.
- 13) 殷軍,幸田恭治, 手塚康弘, Quan Le Tran, 陳英傑, 門田重利: The study of anti-osteoporotic constituents from *Dioscorea hypoglauca*. 2002 International Osteoporotic Conference, 2002, 10/20-22, 上海.
- 14) 岩田 宏, Tepy Usia, 手塚康弘, 門田重利, 平塚 明, 鎌滝哲也, 渡部 烈: 漢方薬を構成する生薬 によるヒトシトクロムP450の阻害. 第17回日本薬物動態学会年会, 2002, 11/20-22, 東京.
- 15) 緑川 淑, Banskota A. H., 手塚康弘, 松繁克道, 門田重利: プロポリスの基源植物. 第54回北陸質量分析談話会, 2002, 12/7, 金沢.

◇その他 Others

- 1) 門田重利: 拠点大学交流事業に参加, 講演 (Chulabhorn Research Institute; Prince of Songkla University). 2002, 12/22-28, タイ.
- 2) 手塚康弘: 和漢薬の化学的研究と質量分析. 日本電子第24回 MS ユーザーズミーティング(東京), 2002, 11/26-27, 東京.
- 3) 手塚康弘: 和漢薬の化学的研究と質量分析. 日本電子第24回 MS ユーザーズミーティング (大阪), 2002, 12/2, 大阪.

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大学院後期 1 年: Tepy Usia (2002, 4~), 岩田 宏(2002, 4~), Mai Thanh Thi Nguyen (2002, 10~)

大学院後期2年:殷 軍, Nhan Nguyen Trung, 王 淑敏 (2002, 4/10, 一身上の都合により退学),

李 建平 (2002, 5/10, 一身上の都合により退学)

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◇学位(修士・博士)取得者 Academic degrees and theses

課程博士 (2002年3月):

Tran Le Quan: Biologically Active Saponin Constituents from Vietnamese Ginseng Plants

課程修士(2002年3月):

Tepy Usia: Chemical Constituents of Chinese Propolis and Their Antiproliferative Activities