化学応用分野 Division of Natural Products Chemistry

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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．薬物代謝酵素阻害活性を有する天然物成分の研究
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。

◇ 原著論文 Original papers

1) **Awale S., Tezuka Y., Banskota A. H., and Kadota S.: Siphonols A-E: Novel Nitric Oxide Inhibitors From *Orthosiphon stamineus* of Indonesia. *Bioorg. Med. Chem. Lett.*, 13, 31-35 (2003).**

Abstract: From the methanolic extract of *Orthosiphon stamineus*, four novel highly oxygenated isopimarane-type diterpenes named siphonols A-D (**1-4**) and a novel biogenetically interesting norisopimarane-type diterpene named siphonol E (**5**) were isolated. The new compounds **1-3** and **5** showed more potent inhibitory effects on the nitric oxide (NO) production in lipopolysaccharide (LPS)-activated macrophage-like J774.1 cells than a positive control N^G-monomethyl-L-arginine (L-NMMA). Siphonols A-E (**1-5**) represent the first examples of isopimaranes oxygenated at C-20.

2) **Li H., Miyahara T., Tezuka Y., Tran Q. L., Seto H., and Kadota S.: Effect of Berberine on Bone Mineral Density in SAM P6 as a Senile Osteoporosis Model. *Biol. Pharm. Bull.*, 26, 110-111 (2003).**

Abstract: The effects of berberine in senescence accelerated mice P6 (SAMP6) were investigated to learn whether the alkaloid affects bone mineral density (BMD). Oral administration of berberine (10 mg/kg/d) to male and female mice for 22 weeks resulted in an increase in BMD in both sexes. A decreased concentration of deoxypyridinoline (Dpd) in urine was only observed in female mice. There was no effect on body or tibia weight or on the concentration of procollagen type I carboxyterminal extension peptide (PICP) in serum.

3) **Awale S., Tezuka Y., Banskota A. H., Adnyana I K., and Kadota S.: Nitric Oxide Inhibitory Isopimarane-type Diterpenes from *Orthosiphon stamineus* of Indonesia. *J. Nat. Prod.*, 66, 255-258 (2003).**

Abstract: A methanolic extract of *Orthosiphon stamineus* yielded six new highly-oxygenated isopimarane-type diterpenes, orthosiphols U-Z (**1-6**), and 15 previously reported diterpenes. The isolated diterpenes all showed significant dose-dependent inhibitory effects on the nitric oxide (NO) production in lipopolysaccharide (LPS)-activated macrophage-like J774.1 cells. Orthosiphols A (**7**), B (**8**), D (**9**), and X (**4**) showed more potent inhibitory activities than a positive control N^G-monomethyl-L-arginine (L-NMMA), and **1** displayed the strongest activity with an IC_{50} value of 6.4 μM.

4) **Awale S., Tezuka Y., Banskota A. H., Adnyana I K., and Kadota S.: Highly-Oxygenated Isopimarane-type Diterpenes from *Orthosiphon stamineus* of Indonesia and Their Nitric Oxide Inhibitory Activity. *Chem. Pharm. Bull.*, 51, 268-275 (2003).**

Abstract: From the methanolic extract of Indonesian *Orthosiphon stamineus,* nine new highly-oxygenated isopimarane-type diterpenes [7-*O*-deacetylorthosiphol B (**1**), 6-hydroxyorthosiphol B (**2**), 3-*O*-deacetylorthosiphol I (**3**), 2-*O*-deacetylorthosiphol J (**4**), siphonols A-E (**5-9**)] have been isolated together with nine known diterpenes [orthosiphols H (**10**), K (**11**), M (**12**) and N (**13**); staminols A (**14**) and B (**15**); neoorthosiphols A (**16**) and B (**17**); norstaminol A (**18**)]. Their structures were determined based on the spectroscopic data. The isolated diterpenes inhibited nitric oxide (NO) production in lipopolysaccharide (LPS)-activated macrophage-like J774.1 cells. Compounds **4-7**, **9**, **10**, **14**, and **17** showed inhibitory activities more potent (IC_{50}, 10.8-25.5 μM) than a positive control N^G-monomethyl-L-arginine (L-NMMA; IC_{50}, 26.0 μM).

5) **Than M. M., Banskota A. H., Tezuka Y., Midorikawa K., Matsushige K., and Kadota S.: Inhibitors of nitric oxide (NO) production in murine macrophage-like J774.1 cells from Brazilian propolis. *J. Trad. Med.*, 20, 22-29 (2003).**

Abstract: Water and MeOH extracts of Brazilian propolis showed dose-dependent inhibition toward nitric oxide (NO) production in lipopolysacchalide (LPS)-activated murine macrophage-like J774.1 cells. From the water extract, 17 phenolic compounds were isolated and among them 15 are new for the water extract of propolis. Moreover, methyl *p*-hydroxydihydrocinnamate (**9**) and 1-(4-hydroxyphenyl)butane-1,3-dione (**11**) were isolated, for the first time, from propolis. Labdane-type diterpenes, flavonoids and some phenolic compounds possessed potent NO inhibitory activity. Coniferyl aldehyde (**23**) and dimeric coniferyl acetate (**33**) showed the strongest NO inhibition with IC_{50} values of 18.0 and 27.1 μM, respectively, which were stronger than the positive control, N^G-monomethyl-L-arginine (L-NMMA; IC_{50}, 44.5 μM).

6) **Awale S., Tezuka Y., Banskota A. H., and Kadota S.: Inhibition of NO Production by Highly-Oxygenated Diterpenes of *Orthosiphon stamineus* and Their Structure-Activity Relationship. *Biol. Pharm. Bull.*, 26, 468-473 (2003).**

Abstract: Nitric oxide (NO) has been implemented in various pathological processes. In the present study, 47 highly-oxygenated isopimarane-type and novel carbon framework staminane-type diterpenes isolated from *Orthosiphon stamineus* of Indonesia, Okinawa, Myanmar and Vietnam were evaluated for their inhibitory activity in NO production by lipopolysaccharide (LPS)-activated macrophage-like J774.1 cells. All the isolated diterpenes showed concentration-dependent inhibition of NO production in LPS-activated macrophage-like J774.1 cells, and based on the results, their structure-activity relationships were established.

7) **Nagaoka T., Banskota A. H., Tezuka Y., Midorikawa K., Matsushige K., and Kadota S.: Caffeic Acid Phenethyl Ester (CAPE) Analogues: Potent Nitric Oxide Inhibitors from the Netherlands Propolis. *Biol. Pharm. Bull.*, 26, 487-491 (2003).**

Abstract: The MeOH and water extracts of the Netherlands propolis were tested for their inhibitory activity towards nitric oxide (NO) production in lippolysaccharide (LPS)-activated murine macrophage-like J774.1 cells. Both of the extracts possessed significant NO inhibitory activity with IC_{50} values of 23.8 and 51.5 μg/ml, respectively . Then 13 phenolic compounds obtained form the MeOH extract showing stronger NO inhibition were examined on their NO inhibitory activities. Caffeic acid phenethyl ester (CAPE) analogues, *i.e.*, benzyl caffeate, CAPE and cinnamyl caffeate, possessed most potent NO inhibitory activities with IC_{50} values of 13.8, 7.64 and 9.53 μM, respectively, which were two- to four-fold stronger than positive control N^G-monomethyl-L-arginine (L-NMMA; IC_{50}, 32.9 μM). Further study on the synthetic analogue of CAPE revealed that both of 3-phenylpropyl caffeate (**18**; IC_{50}, 7.34 μM) and 4-phenylbutyl caffeate (**19**; IC_{50}, 6.77 μM) possessed stronger NO inhibitory activity than CAPE (**10**) and that elongation of alkyl side chain of alcoholic parts of caffeic acid esters enhanced the NO inhibitory activity. In addition, it was found that CAPE analogues having longer carbon chain (> C_5) in alcoholic part showed toxic effects toward J774.1 cells. This NO inhibitory effect may directly correlate with anti-inflammatory properties of the Netherlands propolis.

8) **Awale S., Wang S., Tezuka Y., Banskota A. H., Tran Q. L., and Kadota S.: Antioxidative and Antihepatotoxic Principles of Tuocha. *J. Trad. Med.*, 20, 45-50 (2003).**

Abstract: Tuocha is one of the special varieties of fermented compressed tealeaves, praised for its important health benefits, such as antiaging, lowering cholesterol, enhancing immune function, lowering of blood pressure, reducing heart attacks etc. In present study, we carried out fractionation and isolation of the active constituents, guided by 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity. In addition, antioxidative and antihepatotoxic potency on D-galactosamine (D-GalN)/tumor necrosis factor-alpha (TNF-α)-induced cell death in primary cultured mouse hepatocytes was also examined. Our study revealed that, tuocha is rich in antioxidants such as phenolics, lignans, flavanoides and flavan-3-ols, and showed a good understanding between structure and activity relationship.

9) **Banskota A. H., Li J., Tezuka Y., and Kadota S.: Hypoglycemic effect of *Aemotoxylon campechanum* on streptozotocin (STZ)-induced diabetic rats. *J. Trad. Med.*, 20, 57-61 (2003).**

Abstract: Hypoglycemic activity of *Aemotoxylon campechanum* was examined in STZ-induced diabetic rats. The water extract of *A. campechanum* lowered fasting blood glucose level of STZ-induced diabetic rats significantly and dose-dependently. The water extract further divided into MeOH and H_2O-soluble fractions. The MeOH-soluble fraction showed the strongest hypoglycemic effect, which lowered fasting blood glucose level by 37% at a dose of 100 mg/kg (*i.p.*). The water extract and the MeOH-soluble fraction were found to be more effective in lowering the blood glucose level of diabetic rats than the mixtures of tolbutamide (200 mg/kg) and buformin (1 mg/kg) used as positive control, which lowered blood glucose level by 35.1%. The active fraction led to isolation of five guainane-type sesquiterpenes and a coumarin derivative.

10) **Nagaoka T., Banskota A. H., Tezuka Y., Harimaya Y., Koizumi K., Saiki I., and Kadota S.: Inhibitory Effects of Caffeic Acid Phenethyl Ester Analogues on Experimental Lung Metastasis of Murine Colon 26-L5 Carcinoma Cells. *Biol. Pharm. Bull.*, 26, 638-641 (2003).**

Abstract: We have previously examined the antiproliferative activity of caffeic acid phenethyl ester (CAPE) and its 20 analogues against six tumor cell lines, and found that CAPE analogues possess selective antiproliferative activity towards the murine colon 26-L5 carcinoma cell lines. To extend our study, the effects of CAPE analogues on the metastatic development of murine colon 26-L5 carcinoma cell in the lung were examined. The oral administration of CAPE (5 mg/mice/d) for 7 d after tumor inoculation decreased the tumor weight and the number of tumor nodules in the lung by 50% and 50%, respectively, compared to the control, while CAPE (5 mg/mice/d) administered for 7 d before tumor inoculation showed no significant effect. Beside CAPE, 4-phenylbutyl caffeate, 8-phenyl-7-octenyl caffeate, 2-cyclohexylethyl caffeate and *n*-octyl caffeate at and oral dose of 2mg/mice/d caused a 55%, 43%, 55%, and 35% reduction of the tumor nodules in their lung metastasis formation, respectively. These results further elaborate the possibility of CAPE and its analogues to become a new class of chemopreventive agents for the treatment of colon cancer metastasis.

11) **Tran Q. L., Than M. M., Tezuka Y., Banskota A. H., Watanabe H., Zhu S., Komatsu K., Thet M. M., Swe T., Maruyama Y., and Kadota S.: Wild ginseng grows in Myanmar. *Chem. Pharm. Bull.*, 51, 679-682 (2003).**

Abstract: Ginseng, the underground parts of plants of *Panax species,* has been used in oriental traditional medicine for centuries. Unfortunately, because of extensive exploitation over thousands of years, the natural source of these species has been almost exhausted. Recently, we have found a wild ginseng growing in Myanmar. Here, by a combination of chemical composition study and gene sequence analysis, we unambiguously demonstrate that the wild ginseng is actually *P. zingiberensis,* commonly known as ginger ginseng. This ginseng was an indigenous to the southwestern China. However, now it is seriously threatened to brink of extinction and is put on the highest level of protection in China. Therefore, an appropriate protection measure is highly recommended to preserve this valuable resource, since this Myanmar ginseng might turn out to be the last *P. zingiberensis,* which could ever be seen in the planet.

12) **Yin J., Kouda K., Tezuka Y., Tran Q. L., Miyahara T., Chen Y., and Kadota S.: Steroidal Glycosides from the Rhizomes of *Dioscorea spongiosa*. *J. Nat. Prod.*, 66, 646-650 (2003).**

Abstract: A water extract of the rhizomes of *Dioscorea spongiosa,* which showed anti-osteoporotic activity, was examined, and four new pregnane glycosides, named spongipregnolosides A-D (**1-4**), and two new cholestane glycosides, named spongiosides A (**5**) and B (**6**), were isolated together with 15 known glycosides. Their structures were determined on the basis of spectroscopic analysis and chemical methods. Among the isolated compounds,

spongioside A (**5**), hypoglaucin G (**7**), methylprotodioscin (**8**), and (*R*)-oct-1-en-3-yl *O*-α-L-arabinopyranosyl-(**1**→**6**)-α-D-glucopyranoside (**9**) showed potent inhibition against bone resorption induced by parathyroid hormone in bone organ culture system.

13) **Tran L. Q., Tezuka Y., Ueda J., Nguyen N. T., Maruyama Y., Begum K., Kim H.-S., Wataya Y., Tran Q. K., and Kadota S.: In vitro antiplasmodial activity of antimalarial medicinal plants used in Vietnamese traditional medicine. *J. Ethnopharmacol.*, 86, 249-252 (2003).**

Abstract: Among 42 extracts, prepared from 14 medicinal plants used in Vietnamese traditional medicine to treat malaria, 24 were found to have antiplasmodial activity by inhibiting the growth of the chloroquine-resistant *Plasmodium falciparum* strain FCR-3 with EC_{50} values less than 10 μg/ml. Each medicinal plant possessed at least one active extract. The methanol extract of *Coscinium fenestratum* had the strongest antiplasmodial activity with EC_{50} value of 0.5 μg/ml. Activity-guided fractionation led to identification of berberine as the major active constituent.

14) **Banskota A. H., Tezuka Y., Nguyen N. T., Awale S., Nobukawa T., and Kadota S.: DPPH Radical Scavenging and Nitric Oxide Inhibitory Activities of the Constituents from the Wood of *Taxus yunnanensis*. *Planta Med.*, 69, 500-505 (2003).**

Abstract: The H_2O, H_2O/MeOH (1:1) and MeOH extracts of the wood of *Taxus yunnanensis* possessed significant DPPH radical scavenging and nitric oxide (NO) inhibitory activities. Chemical investigation of these extracts led us to isolation of nineteen compounds, i.e., five lignans, two simple phenolics, and twelve taxane-type diterpenes. Isotaxiresinol and secoisolariciresinol, two major lignans of the wood, possessed potent DPPH radical scavenging activities with IC_{50} values of 21.7 and 28.9 μM, respectively. Similarly, coniferyl aldehyde, taxusin, 10-desacetyltaxuyunnanine C, hongdoushan A, and 2α,5α,10β-triacetoxy-14β-[(*S*)-2-methylbutyryloxy]-4(20),11-taxadiene showed potent NO inhibitory activity with IC_{50} values of 18.0, 22.1, 28.5, 15.0 and 26.4 μM, respectively, which were either equal or lower than the positive control N^G-monomethyl-L-arginine (L-NMMA) with an IC_{50} value of 28.5 μM.

15) **Banskota A. H., Attamimi F., Usia T., Linn T. Z., Tezuka Y., Kalauni S. K., and Kadota S.: Novel norcassane-type diterpene from the seed kernels of *Caesalpinia crista*. *Tetrahedron Lett.*, 44, 6879-6882 (2003).**

Abstract: Three novel norcassane-type diterpenes were isolated from a CH_2Cl_2 extract of the seed kernels of *Caesalpinia crista* together with four known cassane-type diterpenes. All the new compounds represent unprecedented carbon framework. Norcaesalpinin A (**1**) and B (**2**) had 17-norcassane skeleton, while norcaesalpinin C (**3**) had 16-norcassane skeleton. Their structures were elucidated on the basis of spectral analysis.

16) **Ueda J., Tezuka Y., Banskota A. H., Tran Q. L., Tran Q. K., Saiki I., and Kadota S.: Antiproliferative Activity of Cardenolides Isolated from *Streptocaulon juventas*. *Biol. Pharm. Bull.*, 26, 1431-1435 (2003).**

Abstract: Sixteen cardenolides, two hemiterpenoids, two phenylpropanoids and a phenylethanoid isolated from the roots of *Streptocaulon juventas* (LOUR.) MERR. were examined for their antiproliferative activity toward three human-derived (HT-1080 fibrosarcoma, lung A549 adenocarcinoma, cervix HeLa adenocarcinoma) and three murine-derived (colon 26-L5 carcinoma, Lewis lung carcinoma, B16-BL6 melanoma) cell lines. The cardenolides selectively and strongly inhibited proliferation of the HT-1080 (IC_{50} values, 0.054-1.6 μM) and A549 (IC_{50}, 0.016-0.65 μM) cell lines. The characteristic morphological changes and ladder-like DNA fragmentation in those cells treated with the cardenolides indicated the antiproliferative activity was due to the induction of apoptosis.

17) **Midorikawa K., Banskota A. H., Tezuka Y., Matsushige K., Message D., Huertas A. A. G., and Kadota S.: Buds of *Baccharis dracunculifolia*: potent source of biologically active caffeoylquinic acids and labdane-type diterpenes of Brazilian propolis. *J. Trad. Med.*, 20, 187-194 (2003).**

Abstract: Porpolis is a complex mixture of sticky substances collected by honeybees form various plants. It is interestingly but challenging task to search botanical origin of individual components present in propolis. Liquid chromatography mass-spectrometry (LC-MS) analysis of both Brazilian propolis and *Baccharis dracunculifolia* were performed. The water extracts of propolis and *B. dracunculifolia* and both contain 3,4-di-*O*-caffeolyqiuic acid (**28**), 3,5-di-*O*-caffeoylquinic acid (**31**) and chlorogenic acid (**32**), which were known for hepatoprotective components of Brazilian propolis. Moreover, 27 individual compounds were identified in *B. dracunculifolia* including labdane-type diterpenes, prenylated compounds, flavonoids and cinnamic acid derivatives, which were reported form Brazilian propolis. The plant source of 19 individual components of Brazilian propolis was, for the first time, established to be *B. dracunculifolia.* Thus, *B. dracunculifolia* was appeared to be vital source of Brazilian propolis including caffeoylquinic acid, labdane-type diterpenes and penolic components.

18) **Nguyen N. T., Banskota A. H., Tezuka Y., Nobukawa T., and Kadota S.: Diterpenes and sesquiterpenes from the bark of *Taxus yunnanensis. Phytochemistry,* 64, 1141-1147 (2003).**

Abstract: Two taxane-type diterpenes, 10β-acetoxy-2α,5α,7β,9α-tetrahydroxytaxa-4(20),11-dien-13-one and 2α-acetoxy-9α-benzoyloxy-5α,7β,10β,15-tetrahydroxy-11(15→1)-abeotaxa-4(20),11-dien-13-one, and two new drimane-type sesquiterpenes, 1β-acetoxy-7-drimen-11α-ol-12,11-lactone and 1β-acetoxy-11,12-epoxy-6-drimen-8α,11α-diol, were isolated from the bark of *Taxus yunnanensis* together with 35 known taxane-type diterpenes, a known drimane-type sesquiterpene and a known flavanone.

19) **Ueda J., Tezuka Y., Banskota A. H., Tran Q. L., Tran Q. K., Saiki I., and Kadota S.: Constituents of Vietnamese Medicinal Plant *Streptocaulon juventas* and their Antiproliferative Activity against the Human HT-1080 Fibrosarcoma Cell Line. *J. Nat. Prod.*, 66, 1427-1433 (2003).**

Abstract: The methanolic extract of roots of *Streptocaulon juventas* (Asclepiadaceae), having shown strong antiproliferative activity against highly metastatic human HT-1080 fibrosarcoma cell line, was subjected to activity-guided isolation to yield 16 cardenolides including five new ones, acovenosigenin A 3-*O*-β-digitoxoside (**1**), digitoxigenin gentiobioside (**2**), digitoxigenin 3-*O*-[*O*-β-glucopyranosyl-(1→6)-*O*-β-glucopyranosyl-(1→4)-3-*O*-acetyl-β-digitoxopyranoside] (**3**), digitoxigenin 3-*O*-[*O*-β-glucopyranosyl-(1→6)-*O*-β-glucopyranosyl-(1→4)-*O*-β-digitalopyranosyl-(1→4)-β-cymaropyranoside] (**4**), and periplogenin 3-*O*-(4-*O*-β-glucopyranosyl-β-digitalopyranoside) (**5**), and two new hemiterpenoids, (4*R*)-4-hydroxy-3-isopropylpentyl rutinoside (**6**) and (*R*)-2-ethyl-3-methylbutyl rutinoside (**7**), together with two known phenylpropanoids and a known phenylethanoid. The isolated cardenolides strongly inhibited the proliferation of HT-1080 cell line (IC_{50} values, 54-1600 nM).

20) **Tran Q. L., Tran Q. K., Kouda K., Nguyen N. T., Maruyama Y., Saiki I., and Kadota S.: A survey on agarwood in Vietnam. *J. Trad. Med.*, 20, 124-131 (2003).**

Abstract: Agarwood is a one of the most valuable minor forest products of the Southeast Asian tropical forests. In Vietnam agarwood is produced from the heartwood of rarely available natural *Aquilaria crassna* trees (Thymelaeaceae). In our field work in Vietnam, a natural *A. crassna* was found in Khanh Hoa Province. Information on agarwood exploitation and production were also gathered by interviewing the local people. The result showed that part of the local people earn their living by dealing with agarwood, but due to over exploitation the natural resource

for this valuable plant has declined dramatically in the past decades, while the demand for the resource remains constant or even increases. The cultivation of *A. crassna* has been started in several places in the country as an initiative for conserving this endangered but economically important plant species.

◇総　　説　Review papers

1）Kadota S., Tezuka Y., Prasain J. K., Ali M. S., Banskota A. H.: Novel Diarylheptanoids of *Alpinia blepharocalyx*. *Current Topics in Medicinal Chemistry,* 3, 203-225 (2003).

2）Banskota A. H., Tezuka Y., Tran Q. L., Kadota S.: Chemical Constituents and Biological Activities of Vietnamese Medicinal Plants. *Current Topics in Medicinal Chemistry,* 3, 227-248 (2003).

3）緑川　淑，A. H. Banskota，手塚康弘，松繁克道，門田重利：ブラジル産プロポリスの品質評価に関する研究．ミツバチ科学（Honeybee Science），24，15-20（2003）．

◇学会報告　Scientific presentations

1）Arjun H. Banskota，手塚康弘，Nhan Trung Nguyen, Suresh Awale，信川高寛，門田重利：Antioxidative properties of the wood of *Taxus yunnanensis*. 日本薬学会第123年会，2003，3，長崎.

2）Thein Zaw Linn, Faisal Attamimi, Tepy Usia, Arjun H. Banskota，手塚康弘，門田重利：Novel cassane- and norcassane-type diterpenes from the seed kernels of *Caesalpinia crista*. 日本薬学会第123年会，2003，3，長崎.

3）長岡武馬，Arjun H. Banskota，手塚康弘，緑川　淑，松繁克道，門田重利：Inhibitors of nitric oxide production in LPS-activated murine macrophage-like J774.1 cells from the Netherlands propolis. 日本薬学会第123年会，2003，3，長崎.

4）Suresh Awale，手塚康弘，Arjun H. Banskota，門田重利：Inhibition of nitric oxide production by highly-oxygenated diterpenes of *Orthosiphon stamineus* and their structure-activity relationship. 日本薬学会第123年会，2003，3，長崎.

5）岩田　宏，Tepy Usia，手塚康弘，門田重利，平塚　明，渡部　烈：五味子（Shisandrae fructus）成分によるチトクロムP450（CYP3A4）の阻害作用．日本薬学会第123年会，2003，3，長崎.

6）殷　軍，幸田恭治，手塚康弘，Quan Le Tran，門田重利，陳　英傑：Novel Diarylheptanoids from the Rhizomes of *Dioscorea spongiosa* and Their Antiosteoporotic Activity. 日本薬学会北陸支部第108回例会，2003，7，金沢.

7）Mai Thanh Thi Nguyen, Suresh Awale，手塚康弘，小林光夫，張　建雄，門田重利：New staminane- and isopimarane-type diterpenes from *Orthosiphon stamineus* of Taiwan. 日本薬学会北陸支部第108回例会，2003，7，金沢.

8）Nhan Trung Nguyen, Arjun H. Banskota，手塚康弘，信川高寛，門田重利：New diterpenes and sesquiterpenes from the bark of *Taxus yunnanensis*. 日本薬学会北陸支部第108回例会，2003，7，金沢.

9）Thein Zaw Linn, Faisal Attamimi, Arjun H. Banskota，手塚康弘，門田重利：New cassane- and 17-norcassane-type furanoditerpenoids from the seed kernels of *Caesalpinia crista*. 日本薬学会北陸支部第108回例会，2003，7，金沢.

10）岩田　宏，金子哲也，Tepy Usia，手塚康弘，門田重利，平塚　明，足立伊佐雄，渡部　烈：五味子（Shisandrae fructus）に含まれるチトクロム P450 3A4（CYP3A4）阻害成分の同定．第20回和漢医薬学会大会，2003，8，熊本.

11）殷　軍，幸田恭治，手塚康弘，Quan Le Tran，宮原龍郎，陳　英傑，門田重利：*In vivo* Antiosteoporotic Effects of *Dioscorea spongiosa* and Its Constituent, Methyl Protodioscin. 第20回和漢医薬学会大会，2003，8，熊本.

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6）平良一彦：琉球大学，「*Orthosiphon stamineus* に関する研究」，2002，2～
7）平塚　明：東京薬科大学，「和漢薬が関与する薬物相互作用に関する研究」，2002，4～

◇研究費取得状況　Acquisition of research funds

1）厚生労働省がん研究助成（分担：門田重利）「がん生物学に基づく新しい治療法に関する研究」
2）厚生労働省科学研究費（分担：門田重利）「数種の食用油に含まれる微量有害因子に関する研究」
3）平成15年度研究拠点形成費補助金（COE）（フェロー）「東洋の知に立脚した個の医療の創生」

◇研究室在籍者　Research members

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大学院博士前期2年：Thein Zaw Linn
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大学院博士後期2年：Tepy Usia，岩田　宏，Mai Thanh Thi Nguyen
大学院博士後期3年：殷　軍，Nhan Nguyen Trung，上田純也（～2003，12）
受託研究員：　緑川　淑
外国人客員研究員：　Faisal Attamimi (2003，3/25～6/20)，Sanit Thongnest (2003，7/1～8/30)，史　麗穎 (2003，12/22～2004，3/31)
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◇学位（修士・博士）取得者　Academic degrees and theses

課程博士（2003年3月）：
Suresh Awale：「Highly-Oxygenated Diterpenes of *Orthosiphon stamineus* and Their Niric Oxide Inhibitory Activity」
長岡武馬：「オランダ産プロポリス成分 Caffeic Acid Phenethyl Ester (CAPE) 及びその類縁体の抗腫瘍活性に関する研究」
課程博士（2003年12月）：
上田純也：「ベトナム産薬用植物 "Ha thu o trang" (*Streptocaulon juventas*) の細胞増殖抑制活性成分に関する研究」
修士（2003年3月）：
Myint Myint Than：「Chemical Constituents of Brazilian Propolis and Myanmar Medicinal Plants」

◇人事異動

幸田恭治：本学文部技官　退職
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