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◇研究目的

和漢薬や天然薬物（特にアジアの伝統薬物）から，膵臓癌，糖尿病，抗マラリア，骨粗鬆症，痛風などに有用な医薬シーズを探索すること，ならびに，和漢薬や天然薬物が薬物代謝酵素に及ぼす影響を解明することを目的とする。

◇研究概要

Ⅰ）伝統薬物から栄養飢餓状態で殺細胞作用を有する物質の探索

国立がんセンターとの共同研究で，膵臓癌 PANC-1 細胞株を用い，低栄養状態（IMEM）で PANC-1 に対する殺細胞活性を示し，通常培地（DMEM）では細胞の成育に活性を示さないような薬物を天然資源より探索している。その結果，牛蒡子より PANC-1 細胞株に対する選択的な細胞毒性を有する Arctigenin を見出し，in vivo の動物実験でも有効性を確認した。また，独活からも新規活性物質 Angelmarin を構造決定し，報告した。

Ⅱ）天然薬物から酵母 Ca^{2+} シグナル伝達阻害物質の探索と医薬への応用

広島大学で開発したポジティブスクリーニング法を用いて，新規医薬シーズ開発を目的に研究を行っている。中国及び東南アジア産生薬によるスクリーニングを行い，これまで約 1000 サンプルの試験を終え，25 検体に阻害活性を見い出している。この中で，ベトナム産 *Combretum quadrangulare* から単離した Methyl quadrangularate O に活性を見出し，詳しい作用機序を検討中である。

Ⅲ）東南アジア産薬用植物から抗マラリア活性物質の探索

現代のマラリア流行地は，ほぼ熱帯・亜熱帯に限定され，それら地域では多剤耐性マラリアに有効な新しい抗マラリア薬が必要とされている。我々は東南アジア等で抗マラリア薬として用いられている薬用植物エキスについて多剤耐性マラリアに対する活性のスクリーニングを行い，活性を示した薬用植物中の活性物質を単離・構造解析を行っている。現在，インドネシアおよびミャンマー産薬用植物 *Caesalpinia crista* について抗マラリア作用を検討し，その活性物質を構造解析した。

Ⅳ）天然薬物の薬物代謝酵素阻害に関する研究

通常，和漢薬を始めとする天然薬物は合成医薬品と併用されている事から，天然薬物が“薬物代謝酵素（シトクローム P450，CYP）”に及ぼす影響（薬物間相互作用）を系統的に検証しておく事が，天然薬物の有効利用の上で必要とされる。我々は，漢方生薬及びインドネシア・ジャムウ生薬について CYP3A4 及び CYP2D6 阻害活性を検索し，強い阻害活性を示した生薬について，その活性成分の解明を行っている。本年は，CYP2D6 阻害活性を示した漢方生薬 "黄柏" および "黄連"，CYP2D6 に対する代謝依存的阻害

（mechanism-based inhibition）を示したジャムウ生薬 *"Piper cubeba"*，CYP3A4 に対する mechanism-based inhibition を示したジャムウ生薬 *"Foeniculum vulgare"* の活性成分について検討した。

Ⅴ）骨粗鬆症に有効な天然薬物成分の開発研究

紅豆杉の含有リグナン isotaxiresinol が抗骨粗鬆活性を有することを pQCT を用いた in vivo 動物実験で証明し報告した。また，中国で臨床的に骨粗鬆症の治療薬に用いられている 19 種の方剤について，破骨細胞に類似した細胞を用いたアッセイ系等で科学的評価を行い Bu-Shen-Jian-gu-Tang（補腎健骨湯）に活性を見出し報告した。

Ⅵ）ベトナム産生薬の Xanthine Oxidase 阻害活性物質の研究

痛風治療薬の開発を目的に，ベトナム産生薬（98 種）について Xanthine Oxidase 阻害作用を指標にスクリーニングした。阻害作用の強かった *Caesalpinia sappan* から活性物質の構造を決定した。

Ⅶ）脳由来神経因子（BDNF）の発現制御物質の探索

沈香よりラット脳由来細胞において記憶・学習に関係することが明らかになっている脳由来神経因子 (BDNF) の発現制御作用を有する新規セスキテルペンを単離，構造解析し報告した。

Ⅷ）フィールド調査

ミャンマーの伝統医師との聞き取り調査ならびにベトナムのプーコック島，ニントン省の少数民族チャンパ族の伝統薬や使用生薬や処方等を調べ調査記録として報告した。

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

1) **Yin J., Tezuka Y., Subehan, Shi L., Nobukawa M., Nobukawa T., and Kadota S.: *In vivo* anti-osteoporotic activity of isotaxiresinol, a lignan from wood of *Taxus yunnanensis*. Phytomedicine, 13: 37–42, 2006.**

Abstract: Isotaxiresinol, the main lignan isolated from the water extract of wood of *Taxus yunnanensis*, was investigated for its effect on bone loss, on serum biochemical markers for bone remodeling and on uterine tissue, using ovariectomized (OVX) rats as the model of postmenopausal osteoporosis. After oral administration of isotaxiresinol (50 and 100 mg/kg/d) for 6 weeks, bone mineral content (BMC) and bone mineral density (BMD) in total and cortical bones were increased as compared to those of OVX control rats, and decreases of three bone strength indexes induced by OVX surgery were prevented. Serum biochemical markers for bone remodeling revealed that isotaxiresinol slightly increased bone formation and significantly inhibited bone resorption without side effect on uterine tissue. These results suggest that isotaxiresinol may be useful for treatment of postmenopausal osteoporosis, especially for prevention of bone fracture induced by estrogen deficiency.

2) **Usia T., Iwata H., Hiratsuka A., Watabe T., Kadota S., and Tezuka Y.: CYP3A4 and CYP2D6 inhibitory activities of Indonesian medicinal plants. Phytomedicine, 13: 67–73, 2006.**

Abstract: Thirty samples of Indonesian medicinal plants were analyzed for their capacity to inhibit *in vitro* metabolism by human cytochrome P450 3A4 (CYP3A4) and CYP2D6 with a radiometric assay. The MeOH-soluble fractions of 25 samples, prepared from water extracts, demonstrated inhibitory activity more than 50% on the metabolism mediated by CYP3A4, and 21 samples on the metabolism mediated by CYP2D6. Among the MeOH-soluble fractions, *Piper nigrum* leaf showed the highest inhibitory activity against CYP3A4 (91.7%), and *Punica granatum* against CYP2D6 (98.1%). The water extracts of which MeOH-soluble fraction showed inhibitory activity more than 70% were fractionated with EtOAc. From the EtOAc-soluble fractions, *Curcuma heyneana* (67.0%), *Pi. cubeba* (75.0%), *Pi. nigrum* fruit (84.0%), *Pi. nigrum* leaf (85.8%), and *Zingiber aromaticum* (75.3%) demonstrated inhibitory activity more than 50% on the metabolism mediated by CYP3A4, but only *Pi. nigrum* fruit (72.8%) and *Pi. nigrum* leaf

(69.1%) showed strong inhibitory activity against CYP2D6. For samples that showed more than 70% inhibition, their IC_{50} values were determined. The most potent inhibitory activity against CYP3A4 (IC_{50} value of 25μg/ml) was found for the extract of *Pi. nigrum* leaf, while that of *Catharanthus roseus* showed the most potent inhibitory effect against CYP2D6 (IC_{50} value of 11 μg/ml). These results should indicate once more the possibility of potential medicinal plant-drug interactions.

3) **Banskota A. H., Nguyen N. T., Tezuka Y., Nobukawa T., and Kadota S.: Hypoglycemic effects of the wood of *Taxus yunnanensis* on streptozotocin-induced diabetic rats and its active components. Phytomedicine, 13: 109–114, 2006.**

Abstract: Hypoglycemic effects of the H_2O and MeOH extracts of the wood of *Taxus yunnanensis* were examined in streptozotocin (STZ)-induced diabetic rats. The H_2O extract significantly lowered the fasting blood glucose level by 33.7% at a 100 mg/kg dose on intraperitoneal administration. From the active H_2O extract of the wood, three lignans, *i.e.*, isotaxiresinol (**1**), secoisolariciresinol (**2**) and taxiresinol (**3**), were isolated as major components. These lignans were further tested for their hypoglycemic effects on the same experimental model. At a dose of 100 mg/kg (*i.p.*), isotaxiresinol (**1**) reduced the fasting blood glucose level of diabetic rats by 34.5%, while secoisolariciresinol (**2**) and taxiresinol (**3**) reduced by 33.4% and 20.9%, respectively. The blood glucose lowering effects of **1** and **2** were stronger than the mixture of tolbutamide (200 mg/kg) and buformin (1 mg/kg) used as a positive control, which lowered fasting blood glucose level by 24.0%.

4) **Nguyen M. T. T., Awale S., Tezuka Y., Ueda J., Tran Q. L., and Kadota S.: Xanthine oxidase inhibitors from the flowers of *Chrysanthemum sinense*. Planta Med., 72: 46–51, 2006.**

Abstract: From the MeOH extract of the flowers of *Chrysanthemum sinense*, a new flavone glucoside, acacetin 7-*O*-(3-*O*-acetyl-*β*-D-glucopyranoside), has been isolated together with 27 known compounds including flavonoids, caffeoylquinic acid derivatives, phenolics, and a monoterpenoid glucoside. Their structures were elucidated on the basis of spectroscopic data. Compounds and displayed significant xanthine oxidase inhibitory activity in a concentration-dependent manner, and compounds and showed more potent inhibitory activity, with IC_{50} values ranging from 0.13 to 2.31μM, than that of a positive control allopurinol (IC_{50}=2.50μM). The kinetic study indicated that and displayed competitive-type inhibition like that of allopurinol, while displayed a mixed-type inhibition.

5) **Awale S., Nakashima E. M. N., Kalauni S. K., Tezuka Y., Kurashima Y., Lu J., Esumi H., and Kadota S.: Angelmarin, a novel anti-cancer agent able to eliminate the tolerance of cancer cells to nutrient starvation. Bioorg. Med. Chem. Lett., 16: 581–583, 2006.**

Abstract: The CH_2Cl_2-soluble extract of *Angelica pubescens* was found to kill PANC-1 cancer cells preferentially under nutrition starvation at a concentration of 50μg/ml, with virtually no cytotoxicity under nutrient-rich conditions. Further bioassay-guided fractionation and isolation led to the isolation of a novel compound named angelmarin as the primary compound responsible for the preferential cytotoxicity; the compound exhibited 100% preferential cytotoxicity against PANC-1 cells at a concentration of 0.01 μg/ml.

6) **Awale S., Lu J., Kalauni S. K., Kurashima Y., Tezuka Y., Kadota S., and Esumi H.: Identification of arctigenin, as an antitumor agent having the ability to eliminate the tolerance of cancer cells to nutrient starvation. Cancer Res., 66: 1751–1757, 2006.**

Abstract: Tumor cells generally proliferate rapidly and the demand for essential nutrients as well as oxygen always exceeds the supply due to the unregulated growth and the insufficient and inappropriate vascular supply. However, cancer cells show an inherent ability to tolerate extreme conditions, such as that characterized by low nutrient and oxygen supply, by modulating their energy metabolism. Thus, targeting nutrient-deprived cancer cells may be a novel strategy in anticancer drug development. Based on that, we established a novel screening method to discover anticancer agents that preferentially inhibit cancer cell viability under the nutrient-deprived condition. After screening 500 medicinal plant extracts used in Japanese Kampo medicine, we found that a CH_2Cl_2-soluble extract of *Arctium lappa* exhibited 100% preferential cytotoxicity under the nutrient-deprived condition at a concentration of 50μg/mL with virtually no cytotoxicity under nutrient-rich condition. Further bioassay-guided fractionation and isolation led to the isolation of arctigenin as the primary compound responsible for such preferential

cytotoxicity; the compound exhibited 100% preferential cytotoxicity against nutrient-deprived cells at a concentration of 0.01μg/mL. Furthermore, arctigenin was also found to strongly suppress the PANC-1 tumor growth in nude mice, as well as the growth of several of the tested pancreatic cancer cell lines, suggesting the feasibility of this novel antiausterity approach in cancer therapy. Further investigation of the mechanism of action of arctigenin revealed that the compound blocked the activation of *Akt* induced by glucose starvation, which is a key process in the tolerance exhibited by cancer cells to glucose starvation.

7) **Awale S., Linn T. Z., Tezuka Y., Kalauni S. K., Banskota A. H., Attamimi F., Ueda J., and Kadota S.: Constituents of *Caesalpinia crista* from Indonesia. Chem. Pharm. Bull., 54: 213–218, 2006.**

Abstract: Ten new furanocassane-type diterpenes named, caesalpinins H–P (**1**–**9**) and norcaesalpinin F (**10**), were isolated from the CH_2Cl_2 extract of the seed kernels of *Caesalpinia crista*, together with 13 known diterpenes. Their structures were determined based on the spectroscopic analysis. Among the isolated compounds, caesalpinin N (**7**) represents the first example of furanocassane-type diterpene possessing an aldehyde group at C-14.

8) **Ueda J., Imamura L., Tezuka Y., Tran Q. L., Tsuda M., and Kadota S.: New sesquiterpene from Vietnamese agarwood and induction effect on brain-derived neurotrophic factor mRNA expression *in vitro*. Bioorg. Med. Chem., 14: 3571–3574, 2006.**

Abstract: Agarwood, one of the valuable non-timber products in tropical forest, is a fragrant wood, whose ethereal fragrance has been prized in Asia for incense in ceremony, as well as sedatives in traditional medicine. We separated the 70% EtOH extract of Vietnamese agarwood, which showed significant induction effect on brain-derived neurotrophic factor (BDNF) mRNA expression in rat cultured neuronal cells, to isolate a new compound and a 2-(2-phenylethyl)chromone derivative. The new compound was determined to be a spirovetivane-type sesquiterpene, (4*R*,5*R*,7*R*)-1(10)-spirovetiven-11-ol-2-one, by spectroscopic data and showed induction effect of BDNF mRNA.

9) **Subehan, Usia T., Iwata H., Kadota S., and Tezuka Y.: Mechanism-based inhibition of CYP3A4 and CYP2D6 by Indonesian medicinal plants. J. Ethnopharmacol., 105: 449–455, 2006.**

Abstract: Thirty samples of Indonesian medicinal plants were tested for their mechanism-based inhibition on cytochrome P450 3A4 (CYP3A4) and CYP2D6 via erythromycin *N*-demethylation and dextromethorphan *O*-demethylation activities in human liver microsomes. From screening with 0 and 20 min preincubation at 0.5 mg/ml of methanol extracts, five plants (*Cinnamomum burmani* bark, *Foeniculum vulgare* seed, *Strychnos ligustrina* wood, *Tinospora crispa* stem, and *Zingiber cassumunar* rhizome) showed more than 30% increase of CYP3A4 inhibition, while three (*Alpinia galanga* rhizome, *Melaleuca leucadendron* leaf, and *Piper nigrum* fruit) showed more than 30% increase of CYP2D6 inhibition. In these eight plants, *Foeniculum vulgare* seed, *Cinnamomum burmani* bark, and *Strychnos ligustrina* wood showed time-dependent inhibition on CYP3A4 and *Piper nigrum* fruit and *Melaleuca leucadendron* leaf on CYP2D6. Among these, four plants other than *Melaleuca leucadendron* revealed NADPH-dependent inhibition. Thus, *Foeniculum vulgare*, *Cinnamomum burmani*, and *Strychnos ligustrina* should contain mechanism-based inhibitors on CYP3A4 and *Piper nigrum* contain that on CYP2D6.

10) **Kalauni S. K., Awale S., Tezuka Y., Banskota A. H., Linn T. Z., Asih P. B., Syafruddin D., and Kadota S.: Antimalarial Activity of Cassane- and Norcassane-Type Diterpenes from *Caesalpinia crista* and Their Structure–Activity Relationship. Biol. Pharm. Bull., 29: 1050–1052, 2006.**

Abstract: Malaria is one of the most life-threatening infectious diseases worldwide and claims millions of people's lives each year. The appearance of drug-resistance *Plasmodium falciparum* has made the treatment of malaria increasingly problematic, and thus, it is a dire need to search the new alternatives of current drugs. In the present study, 44 cassane- and norcassane-type diterpenes isolated from *Caesalpinia crista* of Myanmar and Indonesia were evaluated for their antimalarial activity against the malaria

parasite *Plasmodium falciparum* FCR-3/A2 clone *in vitro*. Most of the tested diterpenes displayed antimalarial activity, and norcaesalpinin E (**28**) showed the most potent activity with an IC_{50} value of 0.090μM, more potent than the clinically used drug chloroquine (IC_{50}, 0.29μM). Based on the observed results, a structure-activity relationship has been established.

11) **Awale S., Linn T. Z., Than M. M., Swe T., Saiki I., and Kadota S.: The healing art of traditional medicines in Myanmar. J. Trad. Med., 23: 47–68, 2006.**

Abstract: Traditional medicines are an integral part of people's culture and are used extensively by the peoples in developing countries for their primary health care. A rich heritage of traditional medical knowledge and the use of plants as medicines still exist in Myanmar which have been inherited from earlier generations. However, many areas in Myanmar are now experiencing rapid changes. Traditional knowledge as well as plants that the traditional healers rely upon are being lost at an alarming rate. Therefore, it is important that immediate steps be taken to protect the important source of traditional knowledge as well as medicinal plant diversity. This paper highlights information and observations on the art of healing performed by the traditional medicine practitioners in Myanmar, their success stories, together with an inventory of some medicinal plants, and traditional knowledge pertaining to their use, including preparation and administration.

12) **Nguyen M. T. T., Tran Q. L., Nakashima E. M. N., Awale S., and Kadota S.: Investigation on traditional medicine at Phu Quoc Island and Nihn Thuan Province in Vietnam. J. Trad. Med., 23: 69–82, 2006.**

Abstract: Vietnam is a tropical Southeast Asian country possessing a broad range of natural resources and a long history of traditional medicine system. In this investigation report, we highlight the practice of traditional medicine and the use of herbal drugs to treat common diseases and interview with local traditional medicine practitioners at Phu Quoc Island and Ninh Thuan Province in Vietnam. The results indicated that the Phu Quoc islanders possess abundant indigenous knowledge and experiences on the use of plants as herbal medicine along with a widespread myth that says the wild plants on the mountain in Phu Quoc Island are more therapeutically active than the plants of the garden. In Ninh Thuan Province, Cham community possess their own specific traditional medicine system and some medicinal plants used for the treatment of common diseases only exist with Cham name. Therefore, taxonomical study, evaluation, standardization and regulation of medicinal plants must be enhanced in these places, in order to promote the scientific development of traditional medicine.

13) **Subehan, Usia T., Kadota S., and Tezuka Y.: Alkamides from *Piper nigrum* L. and Their Inhibitory Activity against Human Liver Microsomal Cytochrome P450 2D6 (CYP2D6). Nat. Prod. Commun., 1: 1–7, 2006.**

Abstract: Drug–herb interaction through inhibition of cytochrome P450 alters the pharmacological response and/or toxicities of drug used concomitantly. In our screening, *Piper nigrum* L. was observed to inhibit cytochrome P450 2D6 (CYP2D6) in human liver microsomes. Thus, the MeOH extract of this plant was investigated for their chemical constituents and 19 alkamides including a new pipercyclobutanamide were isolated. Their structures were elucidated on the basis of spectroscopic analyses. The isolated compounds were tested for their inhibition on human liver microsomal dextromethorphan *O*-demethylation activity, a selective marker for CYP2D6, and pipercyclobutanamide A (**17**) showed the most potent inhibition with an IC_{50} value of 0.34 μM. The result demonstrated the potential of drug–alkamides interaction on concomitant consume of white pepper with the drugs being metabolized by CYP2D6.

14) **Subehan, Usia T., Kadota S., and Tezuka Y.: Mechanism-based Inhibition of Human Liver Microsomal Cytochrome P450 2D6 (CYP2D6) by Alkamides of *Piper nigrum* L. Planta Med., 72: 527–532, 2006.**

Abstract: Nineteen alkamides isolated from *Piper nigrum* L. were tested for their mechanism-based inhibition on human liver microsomal dextromethorphan *O*-demethylation activity, a prototype marker for cytochrome P450 2D6 (CYP2D6). All compounds increased their inhibitory activity with increasing preincubation time. Among them, **15** and **17** showed more than 50% decrease of the CYP2D6 residual activity after 20 min preincubation. Further investigations on **15** and **17** showed that the characteristic

time- and concentration-dependent inhibition, which required a catalytic step with NADPH, was not protected by nucleophiles, and was decreased by the presence of a competitive inhibitor. The kinetic parameters for inactivation (k_{inact} and K_I) were 0.028 min^{-1} and 0.23 μM for **15** and 0.064 min^{-1} and 0.71 μM for **17**, respectively, which were stronger than the known mechanism-based inhibitor, paroxetine (a positive control). Thus, **15** and **17** are potent mechanism-based inhibitors of CYP2D6.

15) Shi L., Tezuka Y., Subehan, Ueda J., Miyahara T., Yin J., Nobukawa T., and Kadota S.: Inhibitory effect of Kampo medicines on bone resorption *in vitro* and preventive effect on bone loss *in vivo*. J. Trad. Med., 23: 92–100, 2006.

Abstract: The inhibitory activities of 19 Chinese formulae on osteoclast formation and bone resorption *in vitro* were investigated. The inhibitory activity on osteoclast formation was evaluated using a mouse bone marrow cell culture in which osteoclast-like multinucleated cells were formed in the presence of parathyroid hormone (PTH). The inhibitory activity on bone resoption was evaluated using PTH-induced resorption of ^{45}Ca from ^{45}Ca-prelabeled neonatal mouse parietal bone. Among the 19 Chinese formulae, nine showed a strong inhibitory activity on osteoclast formation at a concentration of 50 μg/ml, and three of the nine also showed a strong inhibitory activity on bone resorption. Among these three formulae, Bu-Shen-Jian-Gu-Tang (補腎健骨湯) showed the most promising activity in a dose-dependent manner on the inhibition of bone resorption. A further *in vivo* experiment in ovariectomized (OVX) model rats using peripheral quantitative computed tomography (pQCT) revealed its preventive effect on bone loss.

16) Awale S., Linn T. Z., Than M. M., Thet M. M., Swe T., Saiki I., and Kadota S.: An amazing cow's urine therapy practice in Myanmar. J. Trad. Med., 23: 178–183, 2006.

Abstract: The medical practice of Myanmar traditional medicine is shrouded with mystery. Many of the customs perpetuated through the ages had their roots in the religious beliefs. In some parts of Myanmar, the traditional knowledge which dates back to Buddhist era is still preserved and practiced as a holistic method of treatment. This paper highlights an amazing cow's urine therapy practice performed by the traditional medicine practitioners of Buddhist culture in Myanmar.

17) Zaidi S. F. H., Awale S., Kalauni S. K., Tezuka Y., Esumi H., and Kadota S.: Diterpenes from "Pini Resina" and their Preferential Cytotoxic Activity under Nutrient-Deprived Condition. Planta Med., 72: 1231–1234, 2006.

Abstract: In the course of our search for anticancer agents based on a novel anti-austerity strategy, we found that the 70% EtOH extract of "Pini Resina" showed 100% preferential cytotoxicity at the concentration of 50μg/mL. Further bioassay-guided fractionation and purification led to the isolation of 15 compounds including one new compound 7-oxo-13α-hydroxyabiet-8(14)-en-18-oic acid (**1**). Their structures were elucidated on the basis of spectroscopic analysis. Among the isolated compounds, methyl abieta-8,11,13-trien-18-oate (**7**) showed the most potent preferential cytotoxicity at 10μg/mL under nutrient-deprived condition.

18) Ueda J., Awale S., Tezuka Y., Shimamura E., Hirai K., Nobukawa T., Sato A., and Kadota S.: Growth Inhibitory Activity of Wood of *Taxus yunnanensis* and its Liquid Chromatography Fourier-Transform Mass Spectrometry Analysis. Planta Med., 72: 1241–1244, 2006.

Abstract: The wood of *Taxus yunnanensis* (Taxaceae) showed growth inhibitory activities against human cancer cell lines, such as cervical HeLa adenocarcinoma. The morphological changes indicated that the cellular growth inhibitions were caused by apoptosis. To determine the active components, *T. yunnanensis* wood was analyzed by using a liquid chromatography–Fourier-transform MS (LC/FT-MS) technique. As a result, taxane-type diterpenes, such as 10-deacetylcephalomannine and 10-deacetyltaxol, were found to be present in amounts consistent with the growth inhibitory activity.

19) Koyama J, Morita I, Kobayashi N, Hirai K, Simamura E, Nobukawa T, and Kadota S.: Antiallergic activity of aqueous extracts and constituents of *Taxus yunnanensis*. Biol. Pharm. Bull., 29: 2310–2312, 2006.

◇学会報告　(*: 特別講演、シンポジウム、ワークショップ等)

1) 三宅克典，岡田泰典，上田純也，手塚康弘，宮川都吉，門田重利：東南アジアの天然薬物から Ca^{2+}シグナル伝達阻害物質の探索．日本薬学会第 126 年会，2006，3，仙台．
2) Syed F. Haider Zaidi, Suresh Awale, Surya K. Kalauni, 手塚康弘，江角浩安，門田重利：Diterpenes from "Pini Resina" and thier preferential cytotoxic activity under nutrient-deprived conditions. 日本薬学会第 126 年会，2006，3，仙台．
3) Surya K. Kalauni, Suresh Awale, 手塚康弘，Puji Budi Setia Asih, Din Syafruddin, 門田重利：Antimalarial activity of cassane- and norcassane-type diterpenes from *Caesalpinia crista* and their structure–activity relationship. 日本薬学会第 126 年会，2006，3，仙台．
4) 守川耕平，岩田　宏，門田重利，手塚康弘：黄連および黄柏中の薬物代謝酵素 CYP2D6 阻害活性成分について．日本薬学会第 126 年会，2006，3，仙台．
5) 大沼友和，岩田　宏，西山貴仁，小倉健一郎，手塚康弘，平塚　明：生薬エキス 77 種類によるヒト肝シトクロム P450 (CYP1A2) の阻害．日本薬学会第 126 年会，2006，3，仙台．
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