

薬物代謝工学分野

Division of Metabolic Engineering

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◇研究目的

薬物代謝工学分野は和漢薬の薬効、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の役割の解明、(2) LC/MS/MS による和漢薬成分分析と薬物動力学的研究、(3) AIDS、C 型肝炎ウイルスに有効な天然薬物の探索、(4) 霊芝、樟芝などの担子菌類の薬効評価、(5) 内分泌調節作用を有する和漢薬の研究などを研究テーマとしている。

◇研究概要

I) 和漢薬の薬効発現に関与する腸内細菌の役割の解明

天然薬物中に多く存在する C-配糖体の腸内細菌による開裂反応を puerarin を用いて検討した。ヒトの糞便から単離した PUE 株は C-配糖体のグルコースの 6 位を重水素で置換した $[6\text{''}, 6\text{'''}-^2\text{H}_2]$ puerarin を代謝し daidzein と重水素を含むグルコースを生成することから加水分解的に C-C 結合を開裂していることが判明した。

II) LC/MS/MS による和漢薬成分分析と薬物動力学的研究

Swertia 属植物の LC/MS/MS による成分分析を行ない、含まれる成分を指標としたプロファイルを作成した。また主成分 swertiamarin を動物に経口的に投与し、含窒素代謝物 gentianine, (R)-gentianol, (S)-gentianol が生成することを証明した。

III) AIDS、C 型肝炎ウイルスに有効な天然薬物の探索

天然薬物中に存在するトリテルペンの A 環の開裂した化合物や化学的に合成した種々の類似化合物の HIV-1 プロテアーゼに対する阻害作用を検討した結果、これら化合物は相当するトリテルペンより強い阻害活性を示した。

IV) 霊芝、樟芝などの担子菌類の薬効評価

赤霊芝、紫芝から各種ラノスタン型トリテルペンを単離し、苦味活性、抗腫瘍活性を比較検討した。また、ベトナム産の黄芝から A 環の開裂した新規トリテルペンを単離し、HIV-プロテアーゼに対する阻害効果を調べた。

V) 内分泌調節作用を有する和漢薬の研究

当帰芍薬散の効果を下垂体摘出ラット、卵巢摘出ラットを用いて解析した結果、当帰芍薬散は視床下部における PACAP, PAC₁ を経由して性腺刺激ホルモンの分泌を促進していることが示唆された。

◇著書

- 1) 羅布麻茶の新しい薬効について. 「薬用食品の開発-薬用・有用植物の機能性食品素材への応用-Development of Medicinal Foods」吉川雅之監修, 83-91, シーエムシー出版, 東京, 2007.

◇原著論文

- 1) Jin J. S., Zhao Y. F., Nakamura N., Akao T., Kakiuchi N., and Hattori M.: Isolation and characterization of a human intestinal bacterium, *Eubacterium* sp. ARC-2, capable of demethylating arctigenin, in the essential metabolic process to enterolactone. *Biol. Pharm. Bull.*, 30: 904-911, 2007.

Abstract: Plant lignans, such as pinoresinol diglucoside, secoisolariciresinol diglucoside and arctiin, are metabolized to mammalian lignans, enterolactone or enterodiols, by human intestinal bacteria. Their metabolic processes include deglucosylation, ring cleavage, demethylation, dehydroxylation and oxidation. Here we isolated an intestinal bacterium capable of demethylating arctigenin, an aglycone of arctiin, to 2,3-bis(3,4-dihydroxybenzyl)butyrolactone (**1**) from human feces, and identified as an *Eubacterium* species (*E. sp.* ARC-2), which is similar to *Eubacterium limosum* on the basis of morphological and biochemical properties and 16S rRNA gene sequencing. By incubating with *E. sp.* ARC-2, arctigenin was converted to **1** through stepwise demethylation. Demethylation of arctigenin by *E. sp.* ARC-2 was tetrahydrofolate- and ATP-dependent, indicating that the reaction was catalyzed by methyltransferase. Moreover, *E. sp.* ARC-2 transformed secoisolariciresinol to 2,3-bis (3,4-dihydroxybenzyl)-1,4-butanediol by demethylation.

- 2) El-Halawany A. M., Chung M. H., Ma C. M., Komatsu K., Nishihara T., and Hattori M.: Anti-estrogenic activity of mansorins and mansonones from the heartwood of *Mansonia gagei* Drumm. *Chem. Pharm. Bull.*, 55: 1332-1337, 2007.

Abstract: Through an anti-estrogenic bioassay-guided fractionation of methanol extract of *Mansonia gagei*, three new coumarins, called mansorins I (**1**), II (**2**) and III (**3**) and a new naphthoquinone, mansonone I (**4**), were isolated. Their structures were determined based on their NMR data and CD spectroscopy. The anti-estrogenic activity of the fractions and the isolated compounds were investigated using a yeast two-hybrid assay method expressing estrogen receptors α (ER α) and β (ER β). In addition, an ER α competitor screening system (ligand binding screen) was used to verify the binding affinities of the isolated compounds to the estrogen receptor. 1,2-Naphthoquinones (mansonones) showed more binding affinities to ER in both assay systems. All the tested compounds showed higher binding affinities to ER β than to ER α in the yeast two-hybrid assay. Mansonones F and S showed the most potent estrogen binding and estrogen antagonistic effects.

- 3) El-Halawany A. M., Chung M. H., Nakamura N., Ma C. M., Nishihara T., and Hattori M.: Estrogenic and anti-estrogenic activities of *Cassia tora* phenolic constituents. *Chem. Pharm. Bull.*, 55: 1476-1482, 2007.

Abstract: Through an estrogenic activity bioassay-guided fractionation of the 70% ethanolic extract of *Cassia tora* seeds two new phenolic triglucosides, torachrysone 8-*O*-[β -D-glucopyranosyl(1 \rightarrow 3)-*O*- β -D-glucopyranosyl(1 \rightarrow 6)-*O*- β -D-glucopyranoside] (**1**) and toralactone 9-*O*-[β -D-glucopyranosyl-(1 \rightarrow 3)-*O*- β -D-glucopyranosyl-(1 \rightarrow 6)-*O*- β -D-glucopyranoside] (**2**), along with seven known compounds were isolated. The structures of the new compounds were elucidated on the basis of spectroscopic and chemical evidence. The estrogenic activity of the fractions and the isolated compounds were investigated using the estrogen-dependent proliferation of MCF-7 cells. In addition, the yeast two hybrid assay expressing estrogen receptor α (ER α) and β (ER β) and the ER α competitor screening assay (ligand binding screen) were used to verify the binding affinities of the isolated compounds to ER.

Furthermore, a naringinase pre-treatment of the 70% alcoholic extract of *Cassia tora* seeds resulted in a significant increase in its estrogenic activity. From the naringinase pre-treated extract six compounds were isolated, among which 6-hydroxymusizin and aurantio-obtusin showed the most potent estrogenic activity, while torachryson, rubrofusarin and toralactone showed a significant anti-estrogenic activity. Finally, the structure requirements responsible for the estrogenic activity of the isolated compounds were studied by investigating the activity of several synthetic compounds and chemically modifying the isolated compounds. The basic nucleus 1,3,8-trihydroxynaphthalen (T₃HN) was found to play a principal role in the binding affinity of these compounds to ER.

- 4) **Jin J. S., Kakiuchi N., and Hattori M.: Enantioselective oxidation of enterodiol to enterolactone by human intestinal bacteria. *Biol. Pharm. Bull.*, 30: 2204-2206, 2007.**

Abstract: In the course of our experiments on the metabolic conversion of lignans to the estrogenic substances enterodiol (END) and enterolactone (ENL) by human intestinal flora, we isolated two anaerobes, *Ruminococcus* sp. END-1 and strain END-2, capable of oxidizing END. The former selectively converted (–)-END to (–)-ENL, while the latter selectively converted (+)-END to (–)-ENL, indicating enantioselective oxidation by intestinal bacteria.

- 5) **Jin J. S., Zhao Y. F., Nakamura N., Akao T., Kakiuchi N., Min B. S., and Hattori M.: Enantioselective dehydroxylation of enterodiol and enterolactone precursors by human intestinal bacteria. *Biol. Pharm. Bull.*, 30: 2113-2119, 2007.**

Abstract: During the course of experiments on the transformation of lignans to phytoestrogenic substances, such as enterodiol (END) and enterolactone (ENL), a previously isolated bacterium, *Eubacterium* (E.) sp. strain SDG-2, capable of phenolic *p*-dehydroxylation in the biotransformation of secoisolariciresinol diglucoside to END and ENL, was concluded to be *Eggerthella* (Eg.) *lenta* (Eg. sp. SDG-2) on the basis of 16S rRNA gene sequence analysis. The bacterium could transform (+)-dihydroxyenterodiol (DHEND, **3a**) to (+)-END (**1a**), but not for (–)-DHEND (**3b**) to (–)-END (**1b**) under anaerobic conditions. By incubation of a mixture of (+)- and (–)-dihydroxyenterolactone (DHENL, **4a** and **4b**) with Eg. sp. SDG-2, only (–)-DHENL (**4b**) was converted to (–)-ENL (**2b**), selectively. On the other hand, we isolated a different bacterium, strain ARC-1, capable of dehydroxylating (–)-DHEND (**3b**) to (–)-END (**1b**) from human feces. Strain ARC-1 could transform not only (–)-DHEND (**3b**) to (–)-END (**1b**), but also (+)-DHENL (**4a**) to (+)-ENL (**2b**). However, the bacterium could not transform (+)-DHEND (**3a**) and (–)-DHENL (**4b**). Both bacterial strains demonstrated different enantioselective dehydroxylation.

- 6) **Tang J., Akao T., Nakamura N., Wang Z. T., Takagawa K., Sasahara M., and Hattori M.: *In vitro* metabolism of isoline, a pyrrolizidine alkaloid from *Ligularia duciformis*, by rodent liver microsomal esterase and enhanced hepatotoxicity by esterase inhibitors. *Drug Metab. Dispos.*, 35: 1832-1839, 2007.**

Abstract: Isoline, a major retronecine-type pyrrolizidine alkaloid (PA) from the Chinese medicinal herb *Ligularia duciformis*, was suggested to be the most toxic known PA. Its *in vitro* metabolism was thus examined in rat and mouse liver microsomes, and its toxicity was compared with that of clivorine and monocrotaline after i.p. injection in mice. Isoline was more rapidly metabolized by both microsomes than clivorine and monocrotaline and converted to two polar metabolites M1 and M2, which were spectroscopically determined to be bisline (a deacetylated metabolite of isoline) and bisline lactone, respectively. Both metabolites were formed in the presence or absence of an NADPH-generating system with liver microsomes but not cytosol. Their formation was completely inhibited by the esterase inhibitors, triorthocresyl phosphate (TOCP) and phenylmethylsulfonyl fluoride, but not at all or partially by cytochrome P450 (P450) inhibitors, α -naphthoflavone and proadifen (SKF 525A), respectively. These results demonstrated that both metabolites were produced by microsomal esterase(s) but not P450 isozymes. The esterase(s) involved showed not only quite different activities but also responses to different inhibitors in rat and mouse liver microsomes, suggesting that different key isozyme(s) or combinations

might be responsible for the deacetylation of isoline. Isoline injected i.p. into mice induced liver-specific toxicity that was much greater than that with either clivorine or monocrotalin, as judged by histopathology as well as serum alanine aminotransferase and aspartate aminotransferase levels. Isoline-induced hepatotoxicity was remarkably enhanced by the esterase inhibitor TOCP but was reduced by the P450 inhibitor SKF 525A, indicating that rodent hepatic esterase(s) played a principal role in the detoxification of isoline *via* rapid deacetylation *in vivo*.

- 7) **Yu Y. B., Nakamura N., Miyashiro H., and Hattori M.: Triterpenoids and flavonoids isolated from the leaves of *Alnus firma*. *Kor. J. Pharmacog.*, 38: 76-83, 2007.**

Abstract: In this study, three triterpenoids, two steroids and nine flavonoids were isolated from the leaves of *Alnus firma* Sieb. et Zucc. On the basis of spectroscopic evidence, the structures of these compounds were established as β -amyrin acetate, β -amyrin, β -sitosterol, alnustic acid methyl ester, β -sitosterol glucoside, pinocembrin, alnustinol, quercetin, quercetin-3-*O*- α -L-arabinofuranoside, quercetin-3-*O*- α -L-rhamnopyranoside, quercetin-3-*O*- β -D-glucopyranoside, myricetin-3-*O*- β -D-galactopyranoside, (+)-catechin and (-)-epicatechin.

- 8) **Yang L., Nakamura N., Hattori M., Wang Z., Bligh S. W. A., and Xu L.: High-performance liquid chromatography-diode array detection/electrospray ionization mass spectrometry for the simultaneous analysis of *cis*-, *trans*- and dihydro-2-glucosyl-oxycinnamic acid derivatives from *Dendrobium* medicinal plants. *Rapid Commun. Mass Spectrom.*, 21: 1833-1840, 2007.**

Abstract: sensitive, selective and reliable high-performance liquid chromatography (HPLC)-diode array detection (DAD)/electrospray ionization multi-stage mass spectrometry (ESI-MSⁿ) methods have been developed for the characterization of nine 2-glucosyloxycinnamic acid derivatives and quantitative analysis of three of the major 2-glucosyloxycinnamic acid, *cis*-melilotoside, *trans*-melilotoside and dihydromelilotoside, present in *Dendrobium* medicinal plants. The identities of the latter three major 2-glucosyloxycinnamic acids were confirmed by comparing their retention times, UV and mass spectra with those of the reference standards. The characteristic ESI-MSⁿ fragmentation patterns of the remaining six 2-glucosyloxycinnamic acid derivatives, which are similar to the three major compounds, have allowed the putative elucidation of their structures. The concentrations of the *cis*-, *trans*- and dihydromelilotosides were simultaneously determined by HPLC/ESI-MS² using the multiple reaction monitoring (MRM) mode in extracts of *Dendrobium* species. The method was validated with respect to the overall intra- and inter-day variation (RSD less than 8%) and the limits of quantification for the *cis*-, *trans*- and dihydromelilotosides were 0.09, 0.09 and 0.01 μ g/mL, respectively.

- 9) **Yang L., Han H., Nakamura N., Hattori M., Wang Z., and Xu L.: Bio-guided isolation of antioxidants from the stems of *Dendrobium aurantiacum* var. *denneanum*. *Phytother. Res.*, 21: 696-698, 2007.**

Abstract: Bio-guided fractionation of the stem of *Dendrobium aurantiacum* var. *denneanum* using a 1,1-diphenyl-2-picryl-hydrazyl (DPPH) radical scavenging assay, led to the isolation of three 2-glucosyloxycinnamic acid derivatives, namely, *cis*-melilotoside, *trans*-melilotoside and dihydromelilotoside, respectively. Their structures were elucidated through the analysis of uni- and bi-dimensional NMR, UV, IR and MS data. All these three compounds were first reported from the genus *Dendrobium* and exhibited potent antioxidant activities.

- 10) **Yu Y. B., Miyashiro H., Nakamura N., Hattori M., and Park J. C.: Effects of triterpenoids and flavonoids isolated from *Alnus firma* on HIV-1 viral enzymes. *Arch. Pharm. Res.*, 30: 820-826, 2007.**

Abstract: Triterpenoids and flavonoids isolated from *Alnus firma* S. Z. were found to inhibit HIV-1 virus replication and controlled its essential enzymes. In this study, the inhibition of HIV-1 viral replication and its essential enzymes, such as reverse transcriptase, protease and α -glucosidase, were observed using 18 Korean plant extracts. Among the extracts, the methanol extract of *Alnus firma* leaves showed potent inhibition against the HIV-1 induced cytopathic effect (CPE) in MT-4 cells on microscopic observation (the minimum concentration for complete inhibition of HIV-1 induced CPE, $IC_{50}=50\text{ }\mu\text{g/mL}$). Thus, 14 compounds were isolated and identified from the methanol extract of *Alnus firma* leaves. Of these compounds, alnustic acid methyl ester exhibited inhibition against HIV-1 protease, with an IC_{50} of $15.8\text{ }\mu\text{M}$, and quercetin, quercitrin and myricetin 3- O - β -D-galactopyranoside displayed inhibition against HIV-1 reverse transcriptase, all with IC_{50} values of $60\text{ }\mu\text{M}$. Based on these results, the viral replication inhibition of the methanol extract of *Alnus firma* leaves was adjudged to be acutely related to the protease inhibition activation of alnustic acid methyl ester as well as the reverse transcriptase inhibition activation of flavonoids.

- 11) **Chung M. H., Nakamura N., Tohda M., and Hattori M.: Effects of Tokishakuyakusan on hypothalamic pituitary adenylate cyclase-activating polypeptide (PACAP) and PACAP type I receptor (PAC_1) expression in hypophysectomized and ovariectomized rats. *J. Trad. Med.*, 24: 24-30, 2007.**

Abstract: The traditional Chinese medicine, Tokishakuyakusan (TS; Dang-Gui-Shao-Yao-San in Chinese), is frequently applied in obstetrics and gynecology departments in Japanese hospitals. The novel neuropeptide, pituitary adenylate cyclase-activating polypeptide (PACAP) that is transiently induced by the gonadotropin surge, plays an important role in the synthesis of estradiol and progesterone in ovarian granulosa cells. Here, we investigated the effect of TS on PACAP in hypophysectomized (HPX) or ovariectomized (OVX) female rats. The weight of the hypothalamus from HPX rats administered with oral TS for one week did not appreciably change. In contrast, TS decreased the weight of the hypothalamus that was increased by ovariectomy. Moreover, TS promoted the expression of PACAP and PACAP type I receptor (PAC_1) mRNA and protein in the hypothalamus of HPX and OVX rats. However, bone metabolism that was increased by removing the pituitary or ovaries was not suppressed. These findings suggest that TS promotes the secretion of gonadotropic hormone through the expression of hypothalamic PACAP, PAC_1 mRNA and PAC_1 protein.

- 12) **Chung M. H., Tohda M., and Hattori M.: Effects of Tokishakuyakusan on the ovary in hypophysectomized rats. *J. Trad. Med.*, 24: 31-38, 2007.**

Abstract: The prescription Tokishakuyakusan (TS; Dang-Gui-Shao-Yao-San in Chinese) is widely used in traditional Chinese medicine. Since delay of ovarian follicle maturation and fall of bone density are known in hypophysectomized (HPX) rats, we investigated the effects of TS on ovaries in HPX rats. Although TS did not recover the ovary weight decreased by hypophysectomy, it recovered the uterine weight. Two weeks after hypophysectomy, the expression of steroidogenic acute regulatory protein (StAR) mRNA was decreased, but recovered by administration of TS. On the other hand, the expression of pituitary adenylate-cyclase activating polypeptide receptor type I (PAC_1) and progesterone receptor (PR) mRNA was increased, but reduced by administration of TS. However, the expression of estrogen receptor α ($ER\alpha$) mRNA did not synchronize with PAC_1 mRNA and PR mRNA expression. Moreover, TS was demonstrated to promote the follicle maturation by histological analysis, and to decrease significantly the urinary deoxypyridinoline (DPD) level. These findings suggest that TS promotes the maturation of follicles and suppresses the bone metabolism associated with pituitary hormones.

- 13) **Ma C. M., Kully M., Khan J. K., Hattori M., and Daneshtalab M.: Synthesis of chrologenic acid derivatives with promising antifungal activity. *Bioorg. Med. Chem.*, 15: 6830-6833, 2007.**

Abstract: Derivatives of chlorogenic acid or its analogues were synthesized by coupling protected chlorogenic acid or its analogues with *p*-octyloxyaniline and selected amino acids. Most of the compounds exhibited significant potency against *Cryptococcus neoformans* and *Candida* species with low toxicity of brine shrimps. The 4,5-dihydroxyl groups in the quinic acid moiety were necessary for the activity and introduction of a free amino group increased the inhibitory activity against *Aspergillus fumigatus*.

◇学会報告 (*: 特別講演, シンポジウム, ワークショップ等)

- 1) Chung M. H., and Hattori M.: Female hormone secretion of Toki-shakuyaku-san (Japanese Traditional Medicine) and research on related gene expression changes: using ovariectomized rats. Pharmaceutical Sciences World Congress (PSWC2007), 2007, 4, 22-25, Amsterdam.
- 2) Hattori M.: Crucial roles of international bacteria in manifestation of medicinal effects by traditional Chinese medicines. Innovative Team Program in Beijing University. 21st Century COE Program in University of Toyama Joint Symposium, 2007, 6, 25, Beijing.
- 3) 陳 琮湜, 趙 宇峰, 中村憲夫, 赤尾光昭, 垣内信子, Min Byung-Sun, 服部征雄: 女性ホルモン様物質 enterolactone への代謝に関与する腸内細菌のエナンチオ選択性. 日本薬学会第 127 年会, 2007, 3, 28-30, 富山.
- 4) 佐藤直人, 高 江静, 馬 超美, 服部征雄: 紫芝 *Ganoderma sinense* の新規トリテルペノイド成分. 日本薬学会第 127 年会, 2007, 3, 28-30, 富山.
- 5) 危 英, 馬 超美, 服部征雄: *STAUNTONIA OBOVATIFOLIOLA* HAYATA SUBSP. *INTERMEDIA* からの新規トリテルペン成分の単離と同定. 日本薬学会第 127 年会, 2007, 3, 28-30, 富山.
- 6) 張 群, 左 風, 中村憲夫, 馬 超美, 服部征雄: LC/MS-MS を用いた, 霊芝由来のトリテルペン成分であるガノデリオール F のラット血液中における体内動態研究. 日本薬学会第 127 年会, 2007, 3, 28-30, 富山.
- 7) 鄭 美和, 服部征雄: 当帰芍薬散の下垂体摘出ラット卵巢に与える影響について. 日本薬学会第 127 年会, 2007, 3, 28-30, 富山.
- 8) 中村憲夫, 内山奈穂子, 小西天二, 小松かつ子, 服部征雄: タイ民族薬物の抗トリパノソーマ活性(2). 日本薬学会第 127 年会, 2007, 3, 28-30, 富山.
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- 10) 服部征雄: 複合薬物代謝研究の夜明け. 第 24 回和漢医薬学会大会, 2007, 9, 8-9, 富山.
- 11) 左 風, 和田明穂, 馬 超美, 中村憲夫, 服部征雄: Metabolism and disposition of antrocin C in rats: Extreme hepatic transformation and biliary excretion. 第 24 回和漢医薬学会大会, 2007, 9, 8-9, 富山.
- 12) 王 志剛, 馬 超美, 唐 淑含, 来田浩明, 服部征雄: Metabolism and pharmacokinetics of swertiamarin in rats. 第 24 回和漢医薬学会大会, 2007, 9, 8-9, 富山.
- 13) 鄭 美和, 古橋慶子, 鈴木佐和子, 服部征雄: 卵巢摘出ラットを用いた当帰芍薬散と 17 β -エストラジオールの作用差に関する研究. 第 24 回和漢医薬学会大会, 2007, 9, 8-9, 富山.
- 14) Christopher K., Lee J. S., and Hattori, M.: Hepatoprotective effects of Palauan medical plants. 第 24 回和漢医薬学会大会, 2007, 9, 8-9, 富山.
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- 16) Wei Y., Ma C. M., and Hattori M.: HIV protease and HCV protease inhibitory activity of triterpene derivatives. 日本生薬学会第 54 回年会, 2007, 9, 14-15, 名古屋.
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- 19) 中村賢一, 陳琮湜, 馬超美, 西畑友尋, 服部征雄: ヒト腸内細菌によるイソフラボン C-配糖体 Puerarin の代謝研究. 日本生薬学会第 54 回年会, 2007, 9, 14-15, 名古屋.
- 20) 陳琮湜, 中村賢一, 馬超美, 西畑友尋, 垣内信子, 服部征雄: Equol の産生に關与するヒト腸内細菌の単離とその特性について. 日本生薬学会第 54 回年会, 2007, 9, 14-15, 名古屋.
- 21) El-Halawany A. M., Chung M. H., Ma C. M., Komatsu K., Nishihara T., and Hattori M.: Anti-estrogenic activity of mansorins and mansonones from the heartwood of *Mansonia gagei* Drumm. 日本生薬学会第 54 回年会, 2007, 9, 14-15, 名古屋.
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- 3) Hattori M.: Pharmacological evaluation of herbal teas from the leaves of *Eucommia ulmoides* and *Apocynum venetum*. International Conference on Food Factors for Health Promotion. 2007, 11, 27-12, 1, Kyoto.
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◇ その他

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- 2) 服部征雄: 東洋人の知恵—伝統医学から学ぶ健康管理—. 医工連携フォーラム, 2007, 10, 10, 北見.
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- 5) 服部征雄: 和漢薬と腸内細菌のかかわりあい. 富山漢方会講演会, 2007, 11, 9, 富山.
- 6) 鄭美和: 当帰芍薬散の女性ホルモン様作用について. 富山漢方会講演会, 2007, 11, 9, 富山.

◇ 受賞

- 1) 服部征雄: 第 24 回和漢医薬学会大会学会賞
- 2) 服部征雄: 日本生薬学会第 54 回年会学会賞

◇ 共同研究

学内

- 1) 腸内嫌気性菌による生薬成分の代謝 富山大学薬学部 赤尾光昭
- 2) 抗 HSV 薬の開発研究 富山大学医学部 白木公康
- 3) 霊芝のかゆみ防止に対する効果 富山大学大学院医学薬学研究部 倉石泰

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- 1) 抗 HCV 薬の開発研究 慶応大学医学部 下遠野邦忠
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- 1) 抗 HSV 薬開発研究 チュラロンコン大学 Pornpen Pramyothin
- 2) アリストロキア酸誘導体の HPLC/MS/MS による分析 北京大学薬学院 蔡少青

◇ 研究費取得状況

- 1) 「既存添加物の成分と品質評価に関する研究」厚生労働科学研究費補助金（服部 分担）100 万円.
- 2) 「消化管をターゲットとした新しい和漢薬製剤の開発研究」富山県（継続，服部 代表）300 万円.
- 3) 「発芽玄米メシマコブの化学的，薬理学的研究及び一般メシマコブ菌糸体との比較」平成 19 年度笹川科学研究助成金（李 柱相）55 万円.

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修士論文：

鈴木 佐和子：経産リタイアラットにおける当帰芍薬散のエストロゲン様作用の解明 (3 月)

和田 明穂：台湾産樟芝菌糸体に含まれる Antrodin C のラットにおける代謝と体内動態
(3 月)

Kitalong Christopher : Hepatoprotective and HCV-protease inhibitory activity of Palauan medicinal
plants (9 月)

張 群：霊芝の抗腫瘍成分 Ganoderiol F の代謝，体内動態に関する研究 (9 月)

博士論文：

鄭 美和：当帰芍薬散の内分泌調節作用，および遺伝子発現変化に関する研究 (3 月)

Ali Mahmoud : エジプト及びタイ植物から単離したエストロゲン及び抗エストロゲン活
性を有するフェノール類 (9 月)

◇人事異動

鄭 美和：助教 (2007. 9. 1 採用)

Ali Mahmoud : COE 研究員 (2007.11.15 採用)

黒岩 純子：事務補佐員(2007. 7. 31 退職)