化学応用部門

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本部門では，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。即ち，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いて，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。

Ⅰ．天然薬物成分の単離，構造解析，合成，作用

1）升麻，人参，丹参等の和漢生薬

2）インドネシア，スリランカ等の薬用植物

3）麝香から単離した新規成分ムスクライド類の合成及び誘導体化

Ⅱ．薬物・生体高分子相互作用系の生物有機化学

1）構造・機能相関解析に有用な独自の化学的手法の開発

2）イオンチャンネル，オピオイドレセプター等の機能性生体高分子の構造生物学

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

Ⅰ．天然薬物成分の単離，構造解析，合成，作用

1）Potent Antihepatotoxic Activity of Dicaffeoyl Quinic Acids from Propolis
Basnet P., Matsushige K., Hase K., Kadota S., Namba T., *Biol. Pharm. Bull.*, 19, 655－657 (1996).

Hepatoprotective activity guided chemical analyses led to the isolation of two dicaffeoyl quinic acid derivatives, methyl 3,4-di-*O*-caffeoyl quinate and 3,4－di－*O*－caffeoyl quinic acid from water extract of propolis, and their structures were determined by the use of 2D NMR. These compounds were stronger antihepatotoxic agents than glycyrrhizin.

2）Four Di-*O*-caffeoyl Quinic Acid Derivatives from Propolis. Potent Hepatoprotective Activity in Experimental Liver Injury Models
Basnet P., Matsushige K., Hase K., Kadota S., Namba T., *Biol. Pharm. Bull.*, 19, 1479-1484 (1996).

The water extract of propolis (PWE) showed a strong hepatoprotective activity against CCl_4-toxicity in rats and D-galactosamine (GalN)/lipopolysaccharide (LPS)-induced liver injury in mice. The PWE also showed a significant hepatoprotective activity against CCl_4-induced liver cell injury in cultured rat hepatocytes. The *in vitro* hepatoprotective activity guided fractionation and chemical analysis led to the isolation of four dicaffeoyl quinic acid derivatives from the PWE. The structure of these isolates was determined to be methyl

3,4-di-*O*-caffeoyl quinate, 3,4-di-*O*-caffeoyl quinic acid, methyl 4,5-di-*O*-caffeoyl quinate, and 3,5-di-*O*-caffeoyl quinic acid by spectroscopic methods. These compounds were more potent hepatoprotective agents than glycyrrhizin at a concentration of 10 μg/ml and methyl 3,4-di-*O*-caffeoyl quinate was the most potent among the four compounds in the cultured hepatocytes. Quinic acid alone did not show hepatoprotective effects in cultured rat hepatocytes against CCl_4-toxicity. On the other hand, chlorogenic acid or caffeic acid alone was found to be less potent than the dicaffeoyl quinic acid derivatives.

3) Potent Free Radical Scavenging Activity of Dicaffeoyl Quinic Acid Derivatives from Propolis
Matsushige K., Basnet P., Kadota S., Namba T., *J. Trad. Med.*, 13, 217-228 (1996).

We evaluated the free radical scavenging activity of the water, methanol and chloroform extracts of propolis in DPPH free radical and xanthine-XOD generated superoxide anion assay systems. The water extract of propolis (PWE) showed a strong free radical scavenging activity. The free radical scavenging activity guided fractionation and chemical analysis led to the isolation of four dicaffeoyl quinic acid derivatives from the PWE. The structures of these isolates to be methyl 3,4-di-*O*-caffeoyl quinate, 3,4-di-*O*-caffeoyl quinic acid, methyl 4,5-di-*O*-caffeoyl quinate, and 3,5-di-*O*-caffeoyl quinic acid by spectroscopic methods. These compounds showed more potent free radical scavenging activity than the most commonly used antioxidants such as vitamin C, vitamin E and caffeic acid. Quinic acid alone did not show free radical scavenging activity. Chlorogenic acid or caffeic acid was found to be less potent than dicaffeoyl quinic acid derivatives. Dicaffeoyl quinic acid also showed an inhibitory activity on nitrite formation on lipopolysaccharide (LPS)-induced murine macrophages, J774.1.

4) Propolis Protects Pancreatic β-cells Against the Toxicity of Streptozotocin (STZ)
Matsushige K., Basnet P., Hase K., Kadota S., Tanaka K., Namba T., *Phytomedicine*, 3, 203-209 (1996).

Propolis is a glue, prepared by honeybees from plant materials to stick their hives on the beehive wall. It has gained popularity in Japan as a healthy drink and people believe that propolis can cure inflammation, heart diseases and even diabetes and cancer. We have evaluated the β-cell protective effect of propolis against the toxicity of streptozotocin (STZ) in rats. The water extract of propolis (PWE) completely protected β-cell destraction against STZ toxicity. The protective effect of PWE was found to be almost equal to that of nicotinamide. PWE also inhibited the interleukin-1β) (IL-1β) generation from human leucocytes. The free radical scavenging activity together with IL-1β and nitric oxide (NO) synthase inhibitory activities are thought to be the prime factors for the protective effect of PWE against STZ toxicity.

5) Hepatoprotective Effects of Traditional Medicines. Isolation of the Active Constituent from Seeds of *Celosia argentea*
Hase K., Kadota S., Basnet P., Namba T., Takahashi T., *Phytother. Res.*, 10, 387-392 (1996).

The hepatoprotective effects of water extracts from twelve crude drugs were investigated. Among them, the water extracts of *Cassia obtusifolia, Celosia argentea, Cucurbita moschata and Curcuma aeruginosa* showed a significant protective effect on carbon tetrachloride induced liver injury in rats and D-galactosamine (D-GalN)/lipopolysaccharide (LPS) induced liver injury in mice. The water extract of *C. argentea* was found to be the most effective. The hepatoprotective activity guided fractionation of this extract led to the isolation of an active constituent. This component was named as celosian, and was found to be an acidic heteroglycan (molecular weight : 1.9×10^5) containing 4 % of proteins.

6) Hepatoprotective Effects of *Panax notoginseng* : Ginsenosides-Re and -Rg_1 as Its Active Constituents in D-Galactosamine/lipopolysaccharide-induced Liver Injury
Prasain J. K., Kadota S., Basnet P., Hase K., Namba T., *Phytomedicine*, 2, 297-303 (1996).

The hepatoprotective effects of the methanol and water extracts of the roots of *Panax notoginseng*

were studied on various animal models. The methanol and water extracts of *Panax notoginseng* showed a significant activity in carbon tetrachloride-induced liver injury in rats. However, the methanol extract was found to be more active. The hepatoprotective effects of the methanol extract was further evaluated using D-galactosamine as well as heat-killed *Propionibacterium acnes*/lipopolysaccharide-induced liver injury models. Two major isolates from the methanol extract, ginsenosides-Re and -Rg_1, showed a significant hepatoprotective effect on D-galactosamine/lipopolysaccharide-induced liver injury in mice.

7) Antioxidative Effects of Phenylethanoids from *Cistanche deserticola*
Xiong Q., Kadota S., Tani T., Namba T., *Biol. Pharm. Bull.*, 19, 1580-1585 (1996).

The acetone-H_2O (9 : 1) extract from the stem of *Cistanche deserticola* showed a strong free radical scavenging activity. Nine major phenylethanoid compounds were isolated from this extract. They were identified by NMR as acteoside, isoacteoside, 2'-acetylacteoside, tubuloside B, echinacoside, tubuloside A, syringalide A 3'-α-rhamnopyranoside, cistanoside A and cistanoside F. All of these compounds showed strong free radical scavenging activities than α-tocopherol on 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical and xanthine-xanthine oxidase (XOD) generated superoxide anion radical (O_2^-). Among the nine compounds, isoacteoside and tubuloside B, whose caffeoyl moiety is at 6'-position of the glucose, showed an inhibitory effect on XOD. We further studied the effects of these phenylethanoids on the lipid peroxidation in rat liver microsomes induced by enzymatic and non-enzymatic methods. As expected, each of them exhibited significant inhibition on both ascorbic acid/Fe^{2+} and ADP/NADPH/Fe^{3+} induced lipid peroxidation in liver microsomes, which were more potent than α-tocopherol or caffeic acid. The antioxidative effect was found to be potentiated by an increase in the number of phenolic hydroxyl groups in the molecule.

8) The Effect of Traditional Medicines on Bone Resorption Induced by Parathyroid Hormone (PTH) in Tissue Culture : A Detailed Study on Cimicifugae Rhisoma
Li J. X., Kadota S., Li H. Y., Miyahara T., Namba T., *J. Trad. Med.*, 13, 50-58 (1996).

Thirty-four MeOH and water extracts of natural crude drugs were screened for their inhibitory activities on bone resorption induced by parathyroid hormone (PTH) in bone organ culture. Thirteen MeOH extracts and nine water extracts showed significant inhibitory activities. Among these, the MeOH extract of *Cimicifuga heracleifolia* KOMAROV and *C. foetida* L. showed a potent inhibitory activity, so that MeOH extracts of these two species were further fractionated into hexane, EtOAc, *n*-BuOH, and water soluble fractions. Each fraction and sixteen triterpenoids isolated from EtOAc and *n*-BuOH fractions were performed for the bone resorption assay. On the basis of a structure-activity relationship analysis of inhibitory activity on bone resorption, the triterpenoids were considered to contribute to the inhibitory activity of Cimicifugae Rhizoma on bone resorption.

9) Effect on Cultured Neonatal Mouse Calvaria of the Flavonoids Isolated from *Boerhaavia repens*
Li J., Li H., Kadota S., Namba T., Miyahara T., Khan U. G., *J. Nat. Prod.*, 59, 1015-1018 (1996).

A MeOH extract from the whole plant of *Boerhaavia repens* was found to inhibit bone resorption induced by parathyroid hormone (PTH) in tissue culture. Systematic separation of the MeOH extract afforded one new and two known flavonoid glycosides, namely, eupalitin 3-*O*-β-D-galactopyranosyl-(1 → 2)-β-D-glucopyranoside (**1**), eupalitin 3-*O*-β-D-galactopyranoside (**2**), and 6-methoxykaemferol 3-*O*-β-D-(1 → 6)-robinoside (**3**). The structure of the new compound **1** was determined using spectroscopic techniques. The inhibitory activity of these substances toward bone resorption induced by PTH was evaluated, and compounds **1** and **2** were found to exhibit significant activity.

10) Michael-Type Addition of Illudin S, a Toxic Substance from *Lampteromyces japonicus*, with Cysteine and Cysterin-Containing Peptides *in Vtro*

Tanaka K., Inoue T., Tezuka Y., Kikuchi T., *Chem. Pharm. Bull.*, 44, 273-279 (1996).

Reaction of illudin S with cysteine derivatives (cysteine methyl ester, glutathione and a peptide, Cys-Asp-Pro-Gly-Tyr-Ile-Gly-Ser-Arg) were investigated. In the reaction with cysteine methyl ester, four products (P1, P2, P3, P4) were obtained and their structures were determined, on the basis of MS and NMR data, to be adducts of the mercapto group of cysteine methyl ester with the α,β-unsaturated carbonyl group of illudin S. In the reactions with glutathione and the peptide, two addition products in each case were identified by liquid chromatography-tandem mass spectrometry (LC-MS/MS) and NMR analyses. The structures of these adducts also indicated that the α,β-unsaturated carbonyl group in illudin S behaves as a Michael acceptor for the mercapto group in cysteine.

11) Studies on the Metabolites of Mycoparasitic Fungi. V. Ion-Spray Ionization Mass Spectrometric Analysis of Trichokonin-II, a Peptaibol Mixture Obtained from the Culture Broth of *Trichoderma koningii*
Huang Q., Tezuka Y., Hatanaka Y., Kikuchi T., Nishi A., Tubaki K., *Chem. Pharm. Bull.*, 44, 590-593 (1996).

The sequence of a peptide, trichokonin-II (TK-II), obtained from the culture broth of *Trichoderma koningii* OUDEMANS, was examined by ion-spray ionization mass spectroscopy (ISI-MS), including the collision-induced dissociation (CID) techique. TK-II was considered to be a mixture of three peptaibols, TK-IIa, TK-IIb, and TK-IIc.

12) Furostanol Glycosides from Bulbs of *Allium chinense*
Peng J.-P., Yao X.-S., Tezuka Y., Kikuchi T., *Phytochemistry*, 41, 283-285 (1996).

Two new furostanol saponins named chinenosides II and III, were isolated along with seven known compounds, from the bulbs of *Allium chinense* G. Don by a combination of silica gel, Diaion HP-20, and octadesylsilanized (ODS) silica gel column chromatographies and preparative HPLC. On the basis of chemical and spectroscopic evidence, the structures of chinenosides II and III were determined to be 26-*O*-β-glucopyranosyl 3β,26-dihydroxy-(25R)-5α-furost-20 (22)-en-6-one 3-*O*-β-xylopyranosyl-(1→4)-[α-arabinopyranosyl(1→6)]-β-glucopyranoside and 26-*O*-β-glucopyranosyl 3β,26-dihydroxy-(25R)-5α-furost-20(22)-en-6-one 3-*O*-α-arabinopyranosyl(1→6)-β-glucopyranoside, respectively.

13) Metabolism of Illudin S, a Toxic Substance of *Lampteromyces japonicus*: Urinary Excretion of Mercapturic Acids in Rat
Tanaka K., Inoue T., Tezuka Y., Kikuchi T., *Xenobiotica*, 26, 347-354 (1996).

1) The urinary excretion of the mercapturic acids of illudin S after oral administration to rat has been studied. 2) From LC-MS/MS analysis of methanolic extracts of lyophilized rat urine, stereoisomeric mercapturic acids were detected. 3) The mercapturic acids excreted 3 days following administration amounted to approximately 0.39-0.73 % of the administered dose. 4) *In vitro* glutathione conjugation of illudin S by subcellular fractions was also examined. 5) No significant increases in the formation of glutathione adducts were observed in any subcellular fractions examined.

14) Biogenetically Important Quinonemethides and Other Triterpenoid Constituents of *Salacia reticulata*
Dhanabalasingham B., Karunaratne V., Tezuka Y., Kikuchi T., Gunatilaka A. A. L., *Phytochemistry*, 42, 1377-1385 (1996).

Phytochemical investigation of the outer root bark of *Salacia reticulata* var. β-diandra (Celastraceae) has resulted in the isolation, along with salacenonal, several known celastroloids and friedooleanane triterpenoids. Details of the structural elucidation and ^{1}H and ^{13}C NMR spectral assignments of these compounds are presented and their biogenetic significance is discussed.

15) A Dioxoaporphine and Other Alkaloids of Two Annonaceous Plants of Sri Lanka
Wijeratne E. M. K., Hatanaka Y., Kikuchi T., Tezuka Y., Gunatilaka A. A. L., *Phytochemistry*, 42, 1703-1706 (1996).

A new 4,5-dioxoaporphine alkaloid, 8-methoxyouregidione, along with artabotrine, ouregidione, liriodenine, oxocrebanine, oxobuxifoline, ather-

ospermidine and lanuginosine have been isolated from *Artabotrys zeylanicus*. Investigation of *Xylopia championii* afforded *O*-methylmoschatoline and dicentrinone.

16) A New Triterpene Ester from *Eriobotrya japonica*
Shimizu M., Uemitsu N., Shirota M., Matsumoto K., Tezuka Y., *Chem. Pharm. Bull.*, 44, 2181-2182 (1996).

A new triterpene ester, 3-*O*-*trans*-feruloyl euscaphic acid, was isolated from the leaves of *Eryobotrya japonica*. The structure of this compound was elucidated by means of chemical and spectroscopic studies.

17) New Furostanol Glycosides, Chinenoside IV and V, from *Allium chinense*
Peng J., Yao X., Tezuka Y., Kikuchi T., and Narui T., *Planta Med.*, 62, 465-468 (1996).

Further studies on water-soluble components in the bulbs of *Allium chinense* G. Don have led to the isolation of two new furostanol saponins, chinenoside IV (**1**) and V (**2**). On the basis of chemical evidence and spectral analyses [^{1}H-, ^{13}C-NMR (DEPT), ^{1}H-^{1}H COSY (COSY45 and p-type), ^{1}H-^{1}H relay-COSY, ^{1}H-^{13}C COSY, HMBC, and FAB-MS], the structure of **1** was established as 26-*O*-β-glucopyranosyl-3β,26-dihydroxy-23-hydroxymethyl-25(*R*)-5α-furost-20(22)-en-6-one 3-*O*-β-xylopyranosyl(1→4)-[α-arabinopyranosyl-(1→6)]-β-glucopyranoside and that of **2** to be 26-*O*-β-glucopyranosyl-3β,26-dihydroxy-23-hydroxymethyl-25(*R*)-5α-furost-20(22)-en-6-one 3-*O*-α-arabinopyranosyl(1→6)-β-glucopyranoside, respectively.

II. 薬物・生体高分子相互作用系の生物有機化学

1) Synthesis and Characterization of Novel Photoreactive Naltrexone Analogs as Isomeric Carbene-Generating Probes for Opioid Receptors
Hatanaka Y., Nakamura N., Wakabayashi M., Fujioka T., Kikuchi T., *Heterocycles*, 43, 519-522 (1996).

A convenient synthesis of *m*- and *p*-CF_3-diazirinylbenzoic acid was developed. A pair of novel photoaffinity probes bearing these diazirines on a naltrexyl framework bind reversibly with high affinity at μ-, δ-, and κ-receptors.

2) Synthesis of a Carbon-Linked CMP-NANA Analog and Its Inhibitory Effects on GM3 and GD3 Synthases
Hatanaka Y., Hashimoto M., Hidari K. I.-P. J., Sanai Y., Nagai Y., Kanaoka Y., *Heterocycles*, 43, 531-534 (1996).

A carbon-liked analog of cytidine monophospho-*N*-acetylneuraminic acid (CMP-NANA) was synthesized as the degradation resistant inhibitor for sialytransferases. The compound is the first example of synthetic CMP-NANA analog that exhibited inhibitory effects on the activity of GM3 and GD3 sythases.

3) Synthesis and Characterization of a Carbene-Generating Biotinylated Lactosylceramide Analog as a Novel Chromogenic Photoprobe for GM3 Synthase
Hatanaka Y., Hashimoto M., Hidari K. I.-P. J., Sanai Y., Tezuka Y., Nagai Y., Kanaoka Y., *Chem. Pharm. Bull.*, 44, 1111-1114 (1996).

A new biotinylated lactose derivative bearing a nitro-substituted chromogenic diazirine was synthesized. The biotinyl group within the structure enabled to perform a convenient assay of GM3 synthase based on avidin-biotin technology and Km values of this biotinylated photoprobe were determined as 40 μM and 49 μM using bovine brain and rat liver Golgi as the enzyme source, respectively. Furthermore, the sialylation of lactosylceramide, natural acceptor substrate for GM3 synthase, was competitively inhibited by this synthetic analog. The reagent could be a useful chromogenic photoprobe for GM3 synthase.

4) Photocrosslinking of β-1,4-Galactosyltransferase
Hatanaka Y., Hashimoto M., Kanaoka Y., *Photomedicine and Photobiology*, 18, 119-120 (1996).

Photochemical crosslinking reaction using a novel photoreactive *N*-acetylglucosamine derivative, *N*-[2-[2-[2-(2-biotinlaminoethoxy)ethoxy]-ethoxy]-4-[3-(trifluoromethyl)-3*H*-diazirin-3-yl]-benzoyl]-*N*4-[2-(acetylamino)-2-deoxy-β-D-glucopyranosyl]-L-aspartamide (BDGA), was

applied for the specific biotinylation of acceptor binding-site of β1, 4-galactosyltransferase (GalT). The introduction of BDGA for photoaffinity labeling of bovine GalT has facilitated the subsequent steps of photolabeled product analysis based on the specific manipulation of photochemically attached biotinyl residue. The quantitative chemiluminescent analysis revealed a presence of progressive decrement phenomenon in the yield of specific photolabeling with lowering the incubation temperature from 37°C to 20°C or 4°C.

5) Synthesis and Characterization of a Carbene-Generating Biotinylated *N*-Acetylglucosamine for Photoaffinity Labeling of β-1,4-Galactosyltransferase
Hatanaka Y., Hashimoto M., Nishihara S., Narimatsu H., Kanaoka Y., *Carbohydr. Res.*, 294, 95-108 (1996).

A photoreactive *N*-acetylglucosamine derivative, *N*-[2-[2-[2-(2-biotinylaminoethoxy)ethoxy]-4-[3-(trifluoromethyl)-3*H*-diazirin-3-yl]-benzoyl]-*N*4-[2-(acetylamino)-2-deoxy-β-D-glucopyranosyl]-L-aspartamide (BDGA), was synthesized as a carbene-generating biotinylated probe for UDP-galactose : *N*-acetylglucosamine β1,4-galactsytransferase (GalT). The photoaffinity labeling experiments of bovine GalT with BDGA at various conditions were examined based on the quantitative chemiluminescent detection of biotinyl residue which was photochemically introduced onto the GalT protein. A progressive decrement in the yield of specific photolabeling with lowering the incubation temperature from 37°C to 20°C or 4°C was observed. The amount of photoincorporation was also decreased when UMP was not included in the incubation mixture. Using a crude protein mixture of recombinant human GalT, a band corresponding to the glutathione S-transferase fusion GalT protein was also specifically visualized. Furthermore, combined use of BDGA photolabeling with an immobilized avidin was found to be effective for the selective retrieval of photolabeled GalT from a reaction mixture containing a large amount of unlabeled GalT protein. The results we have obtained clearly demonstrate that the covalent biotinylation using the carbene-generating photoaffinity reagent BDGA would be useful for the analysis of acceptor substrate binding sites within GalT protein.

6) Diazirine-Based Photoaffinity Labeling : Chemical Approach to Biological Interfaces
Hatanaka Y., Nakayama H., Kanaoka Y., *Reviews on Heteroatom Chem.*, 14, 213-243 (1996).

The technique of photoaffinity labeling has become increasingly appreciated as a powerful chemical methodology for the detailed structural analysis of ligand binding domains. This review describes our recent approach to the development of photoreactive groups, the design of novel photoprobes, and their application to ion channel probing and glycobiology.

Ⅲ. その他の原著論文

1) Blepharocalyxins A and B, Novel Diarylheptanoids from *Alpinia blepharocalyx*, and Their Inhibitory Effects on NO Formation in Murine Macrophages
Kadota S., Prasain J. K., Li J. X., Basnet P., Dong H., Tani T., Namba T., *Tetrahedron Lett.*, **37**, 7283-7286 (1996).

2) Suppression of Hepatitis B Virus Surface Antigen Secretion by Traditional Plant Medicines
Goto W., Kusumoto I. T., Kadota S., Namba T., Kurokawa M., Shiraki K., *Phytother. Res.*, **10**, 504-507 (1996).

3) Ameliorating Effects of Dan-Shen Methanol Extract on Cognitive Deficiencies in Senescence-Accelerated Mouse
Arima T., Baba I., Hori H., Kitamura Y., Namba T., Hattori M., Kadota S., Nomura Y., *Kor. J. Gerontol.*, **6**, 14-21 (1996).

4) Syringin 4-*O*-β-Glucoside, a New Phenylpropanoid Glycoside, and Costunolide, a Nitric Oxide Synthase Inhibitor, from the Stem Bark of *Magnolia sieboldii*
Park H.-J., Jung W.-T., Basnet P., Kadota S., Namba T., *J. Nat. Prod.*, **59**, 1128-1130 (1996).

5) Processing of *Nux Vomica*. VII. Antinociceptive Effects of Crude Alkaloids from the Processed and Unprocessed Seeds of *Strychnos*

nux-vomica in Mice
Cai B.-C., Nagasawa T., Kadota S., Hattori M., Namba T., Kuraishi Y., *Biol. Pharm. Bull.*, **19**, 127-131 (1996).

6) アピセラピーとしてのプロポリスと漢薬露蜂房の比較本草学的考察
松繁克道，門田重利，難波恒雄，薬史学雑誌，**31**, 183-199 (1996).

7) Effects of Alkaloids from *Corydalis decumbens* on Contraction and Electrophysiology of Cardiac Myocytes
Kadota S., Sun X.-L., Basnet P., Namba T., Momose Y., *Phytother. Res.*, **10**, 19-22 (1996).

8) Protective Effect of Celosian, an Acidic Polysaccharide, on Chemically and Immunologically Induced Liver Injuries
Hase K., Kadota S., Basnet P., Takahashi T., Namba T., *Biol. Pharm. Bull.*, **19**, 567 - 572 (1996).

◇ 学会報告

Ⅰ．天然薬物成分の単離，構造解析，合成，作用

1) 有馬　隆，松野純子，堀妃登美，難波恒雄，服部征雄，門田重利，野村靖幸：老化促進モデルマウス（SAM）の空間認知機能障害に対するLithospermate Bの作用．第12回SAM（老化促進マウス）研究会，1996，3，京都．

2) 金　東郁，横澤隆子，服部征服，門田重利，難波恒雄：羅布麻（*Apocynum venetum* L.）に関する研究－高cholesterol食投与ラットを用いての検討－．日本薬学会第116年会，1996，3，金沢．

3) 長谷耕二，門田重利，難波恒雄：青葙子の実験的肝障害に対する抑制効果．日本薬学会第116年会，1996，3，金沢．

4) 李　慧英，李　建新，門田重利，難波恒雄，宮原龍郎，瀬戸　光，呉　翼偉：伝統薬物による抗骨粗鬆活性成分の研究（II），接骨木 *Sambucus sieboldiana* BLUME ex GRAEBN.（茎）について．日本薬学会第116年会，1996，3，金沢．

5) 松繁克道，Basnet Purusotam, 長谷耕二，門田重利，難波恒雄：Pancreatic β-Cells Protective Effect of Propolis Against the Toxicity of Streptozotocin（STZ）．日本薬学会第116年会，1996，3，金沢．

6) 熱娜卡斯木，長谷耕二，門田重利，難波恒雄：丹参の肝臓保護活性成分Lithospermate Bに関する研究．日本薬学会第116年会，1996，3，金沢．

7) Jeevan Kumar Prasain, 門田重利，Basnet Purusotam, 長谷耕二，難波恒雄：Studies on Hepatoprotective Effect of *Panax notoginseng*, Ginsenosides-Re and Rg as its Active Constituents. 日本薬学会第116年会，1996，3，金沢．

8) 百瀬弥寿徳，山村重雄，手塚康弘，畑中保丸：トリココニンの心筋Ca^{2+}チャネル活性化作用について．第69回日本薬理学会年会，1996，3，長崎．

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