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城西国際大学

目 次

藥化学研究室	1
生物有機化学研究室	2
和漢医藥学研究室	3
藥物動態学研究室	5
藥理学研究室	8
臨床統計学研究室	14
分子細胞生物学研究室	17
機能生理化学研究室	20
臨床栄養学研究室	26
衛生化学研究室	27
製剤物性解析学研究室	29
医薬品評価科学研究室	33
藥品物理化学研究室	34
生藥学研究室	43
臨床藥学研究室	44

CONTENTS

Laboratory of Pharmaceutical Chemistry	1
Laboratory of Bioorganic Chemistry	2
Laboratory of Japanese-Oriental (Kampo) medicine	3
Laboratory of Drug Metabolism and Pharmacokinetics	5
Laboratory of Pharmacology	8
Department of Biostatistics	14
Laboratory of Molecular Cell Biology	17
Laboratory of Functional Physiological Chemistry	20
Laboratory of Applied Nutrition	26
Laboratory of Toxicology and Applied Pharmacology	27
Laboratory of Physicochemical Analysis and Pharmaceutics	29
Laboratory of Pharmaceutical Regulatory Science	33
Laboratory of Pharmaceutical Physical Chemistry	34
Laboratory of Pharmacognosy	43
Laboratory of Clinical Pharmacy	44

【学会発表】

田嶋公人、中村洋、亀井智代

グループディスカッション（ジクソー法）を用いた医薬品化学演習の授業デザイン
ー “くすりのかたちを見て考えることが楽しい” を引き出すためにー
第7回 日本薬学教育学会大会（オンライン開催，2022. 8）

【著書・訳書・総説・その他】

石崎幸 他（共訳）

世界アンチドーピング機構基準 2022年禁止表国際基準（日本語版）
日本アンチドーピング機構（JADA）2021年12月

【研究費の記録】

額賀路嘉（代表）、石崎幸（分担）

非共有結合性阻害剤の探索を目指したペニシリン認識酵素の構造解析
2022年度学長所管研究費（城西国際大学）

【学会発表】

亀井智代

「薬学部における若手教員の研究・教育活動の現状」 研究・教育活動に向き合う姿勢.
第7回日本薬学教育学会（オンライン，2022.8） シンポジウム講演

【原著論文】

J. Nutr. Sci. Vitaminol., 69, 63-67 (2023) *in press*

Weak Inhibitory Effects of Anthocyanins on Human Aldehyde Oxidase Activity: An in vitro study

Yuma Shibata¹⁾, Kaori Matsumoto²⁾, Tetsuya Hasegawa²⁾, Kosuke Ohara (大原厚祐)²⁾, Masayuki Akimoto^{1,2*)}

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Aldehyde oxidase (AO) plays an important role in metabolizing antitumor and antiviral drugs, including methotrexate, favipiravir and acyclovir. The consumption of blueberry fruits or their extracts, which contain large amounts of anthocyanins, has recently increased. The intake of large amounts of anthocyanins occurs through the frequent consumption of blueberries or their functional foods, which may result in unwanted interaction between anthocyanins and medicinal drugs. Therefore, the present study examined the inhibition of AO by anthocyanins, anthocyanidins, and blueberry extracts in human liver cytosol using a HPLC assay. A comparison of the 50% inhibitory concentration (IC₅₀) values of the test compounds showed that anthocyanidins slightly suppressed AO activity, whereas the inhibitory effects of anthocyanins and blueberry extracts were negligible. The inhibitory activity of the anthocyanins tested were approximately 60-to 130-fold weaker than that of the positive control menadione and were almost negligible. Furthermore they were approximately 2,000-fold less potent than that of raloxifene, a typical AO inhibitor, and, thus, unlikely to interfere with drug metabolism by AO. In addition, since the plasma concentration of anthocyanins after their administration were generally lower than IC₅₀ level, the inhibition of AO substrate metabolism by anthocyanins does not appear to be severe.

【学会発表】

大原厚祐, 芝田裕磨, 武井千弥, 松本かおり, 長谷川哲也, 秋元雅之

機能性表示食品の有用性・安全性に関するスクリーニング評価

第8回次世代を担う若手のためのレギュラトリーサイエンスフォーラム (東京, 2022. 8)

【原著論文】

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Weak Inhibitory Effects of Anthocyanins on Human Aldehyde Oxidase Activity: An in vitro study

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医薬品相互作用研究, 47 巻1号, 19-24 (2023)

ケトプロフェン貼付剤の先発医薬品及び後発医薬品の臨床における同等性の検討

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局所皮膚適用製剤の生物学的同等性試験は、“局所皮膚適用製剤の後発医薬品のための生物学的同等性試験ガイドライン”に基づき検証されている。しかし、薬物動態学試験だけでなく、残存量試験、などの複数の試験法が例示されており、現在臨床使用されている後発医薬品の生物学的同等性に関して比較可能なデータが十分ではない場合がある。本研究では、実際の臨床使用下で、ケトプロフェンテープ剤の先発医薬品及び後発医薬品からの薬物の吸収の同等性を評価することを目的とした。

ケトプロフェンテープの先発医薬品モーラス®テープ（先発A）と後発医薬品3製品（ケトプロフェンテープ「テイコク」：後発B，同「三和」：後発C，同「パテル」：後発D）を対象とした。患者が医師の指示通りに使用したケトプロフェンテープを回収した。残存量を測定し、残存率から推定累積吸収率を算出した。

75名から回収されたテープにより、先発A 18名、後発B 17名、後発C 17名、後発D 12名を解析対象とした。貼付時間12時間以上のケトプロフェン残存率は、後発医薬品Dは、先発医薬品Aに対し有意に高い値を示したが、後発医薬品B又はCは、先発医薬品Aとの相違はなかった。後発医薬品Dの累積吸収率は、Wagner-Nelson法によるケトプロフェンの累積吸収プロファイルより低い値を示した。テープ剤の後発医薬品には、動態学試験による生物学的同等性の検証がなされていない製品もあることから、患者に比較可能なエビデンスに基づいた情報提供を行うためにも、局所皮膚製剤の補完試験を実施していくことが必要である。

【学会発表】

大原厚祐，芝田裕磨，武井千弥，松本かおり，長谷川哲也，秋元雅之

機能性表示食品の有用性・安全性に関するスクリーニング評価

第8回次世代を担う若手のためのレギュラトリーサイエンスフォーラム（東京，2022.8）

【作成協力】

COVID-19の基礎知識

一般社団法人千葉県薬剤師会薬事情報センター

眞鍋知史，飯嶋久志，鷺尾夢香 作成

長谷川哲也，額賀路嘉，中野結菜，宮入菜穂，山口友美，日下唯奈 協力

http://www.c-yaku.or.jp/medical/221013_COVID-19.pdf

【原著論文】

Cell Tissue Res. 2023 Feb;391(2):287-303.

doi: 10.1007/s00441-022-03723-9. Epub 2022 Dec 14. PMID: 36513829.

Immunohistochemical characterization of transient receptor potential vanilloid types 2 and 1 in a trinitrobenzene sulfonic acid-induced rat colitis model with visceral hypersensitivity

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Transient receptor potential vanilloid type 2 (TRPV2) and type 1 (TRPV1) are originally identified as heat-sensitive TRP channels. We compared the expression patterns of TRPV2 and TRPV1 in the rat distal colon and extrinsic primary afferent neurons, and investigated their roles in visceral hypersensitivity in 2,4,6-trinitrobenzenesulfonic acid (TNBS)-induced colitis rats. Both TRPV2 and TRPV1 expressions in the colon, dorsal root ganglion (DRG), and nodose ganglion (NG) were significantly upregulated in the TNBS-induced colitis model. TRPV2 cell bodies co-localized with the intrinsic primary afferent marker NeuN and the inhibitory motor neuronal marker nNOS in the myenteric plexus. TRPV2 expressions were further detected in the resident macrophage marker ED2 in the mucosa. In contrast, no TRPV1-expressing cell bodies were detected in the myenteric plexus. Both TRPV2- and TRPV1-positive cell bodies in the DRG and NG were double-labeled with the neuronal retrograde tracer fluorescent fluorogold. Large- and medium-sized TRPV2-positive neurons were labeled with the A-fiber marker NF200, calcitonin gene-related peptide (CGRP), and substance P (SP) in the DRG while small-sized TRPV1-positive neurons were labeled with the C-fiber markers IB4, CGRP, and SP. TRPV2- and TRPV1-positive NG neurons were

labeled with NF200 and IB4. TNBS treatment increased p-ERK1/2-positive cells in TRPV2 and TRPV1 neurons but did not affect the TRPV2 and TRPV1 subpopulations in the DRG and NG. Both TRPV2 and TRPV1 antagonists significantly alleviated visceral hypersensitivity in TNBS-induced colitis model rats. These findings suggest that intrinsic/extrinsic TRPV2- and extrinsic TRPV1-neurons contribute to visceral hypersensitivity in an experimental colitis model.

【著書・訳書・総説】

田嶋公人、押 範之、長島瑞記、花島亜季、堀江俊治

胃運動減弱病態モデル動物へ導くア ril イソチオシアネートの生体作用：消化管粘膜における急性微細炎症の発生メカニズム

潰瘍 vol. 49-2022, p 1-5 (潰瘍学会賞受賞記念総説)

宮下祐真、田嶋公人、堀江俊治

逆流性食道炎・非びらん性胃食道逆流症モデルラットの食道痛覚過敏における transient receptor potential vanilloid I 発現知覚神経線維と免疫細胞の相互作用

潰瘍 vol. 49-2022, p 36-38

高石将大、田嶋公人、堀江俊治

炎症後過敏性腸症候群モデルマウスの結腸組織における一次知覚神経線維とマスト細胞の近接

潰瘍 vol. 49-2022, p 32-35

佐藤結梨、田嶋公人、北川礼代、柴田満咲、大川絵美、堀江俊治

抗がん薬白金製剤誘発悪心嘔吐モデルマウスにおけるパイカ行動に対する制吐薬の薬効評価

潰瘍 vol. 49-2022, p 49-51

中村 悠、田嶋公人、堀江俊治

酪酸誘起過敏性腸症候群モデルラットにおける温度感受性 TRP チャネルの発現変化と内臓痛覚過敏の関係

潰瘍 vol. 49-2022, p 30-31

中野結菜、田嶋公人、糸井直樹、道宗優也、齊藤栄樹、堀江俊治

デキストラン硫酸ナトリウムによる炎症後過敏性腸症候群モデルマウスにおける免疫細胞の動態解析—マスト細胞の関与—

潰瘍 vol. 49-2022, p 43-44

藤井瑤子、田嶋公人、大橋範之、並木隆雄、堀江俊治

麻酔下ラットにおける温度感受性TRPA1チャネル活性化薬アリルイソチオシアネートによる胃粘膜血流の増大反応—カルシトニン遺伝子関連ペプチドとアドレノメデュリンの役割—

潰瘍 vol. 49-2022, p 16-20

【特別講演・シンポジウムなど】

1. 堀江俊治、高石将大、中村 悠、川島孝浩、田嶋公人：炎症後過敏性腸症候群モデルマウスの結腸痛覚過敏における温度感受性TRPV1発現一次知覚神経の病態生理解析
第24回日本神経消化器病学会（旭川：2022年9月8日、9日）シンポジウム
2. 堀江俊治、田嶋公人、松本健次郎：消化管スパイスセンサーの機能と病態修飾：辛味は胃腸でも味わう
JPW2022（Japan Basic and Clinical Pharmacology Week 2022）（横浜：11月30日～12月3日）日本薬理学会・日本農芸化学会共催シンポジウム

【学会発表】

(a) 国際学会

Kimihito Tashima (田嶋公人), Hirokuni Okumi, Syunji Horie (堀江俊治):

Japanese Kampo formula Daikenchuto inhibits gastric acid secretion through activation of TRPV1 in conscious mice.

The 24th Japan-Korea Joint Seminar on Pharmacology, Japan-Korea Joint Session of the 96th Annual Meeting of the Japanese Pharmacological Society 第24回日韓薬理学合同セミナー (December 2, 2024, Yokohama) Poster presentation

(b) 国内学会

3. 藤井瑤子、田嶋公人、大橋範之、溝口淑子、並木隆雄、堀江俊治：麻酔下ラットにおける温度感受性TRPA1チャネル活性化薬アシルイソチオシアネートによる胃粘膜血流の増大反応—カルシトニン遺伝子関連ペプチドとアドレノメデュリンの役割—
第49回日本潰瘍学会（東京：2022年2月12日～13日）口頭発表
4. 中野結菜、田嶋公人、糸井直樹、道宗優也、斉藤栄樹、堀江俊治：デキストラン硫酸ナトリウムによる炎症後過敏性症候群モデルマウスにおける免疫細胞の動態解析—マスト細胞の関与—
第49回日本潰瘍学会（東京：2022年2月12日～13日）口頭発表
5. 中村 悠、田嶋公人、堀江俊治：過敏性腸症候群モデルラットの大腸組織における冷感受性TRPM8発現知覚神経細胞の増加と内臓痛覚過敏反応
第49回日本潰瘍学会（東京：2022年2月12日～13日）口頭発表
6. 高石将大、田嶋公人、堀江俊治：炎症後過敏性腸症候群モデルマウスの結腸組織における一時知覚神経線維とマスト細胞の近接
第49回日本潰瘍学会（東京：2022年2月12日～13日）口頭発表
7. 宮下祐真、田嶋公人、堀江俊治：逆流性食道炎モデルおよび非びらん性胃食道逆流症モデルラットの下部食道粘膜層及び筋層における熱感受性TRPV1チャネル発現神経の増加
第49回日本潰瘍学会（東京：2022年2月12日～13日）口頭発表
8. 佐藤結梨、田嶋公人、北川礼代、柴田満咲、大川絵美、堀江俊治：抗がん薬白金製剤誘発悪心嘔吐モデルマウスにおけるパイカ行動に対する制吐薬の薬効評価
第49回日本潰瘍学会（東京：2022年2月12日～13日）口頭発表
9. 田嶋公人、押 範之、長島瑞記、花島亜季、堀江俊治：ワサビ辛味成分アシルイソチオシアネート誘起胃運動減弱モデルにおける消化管運動改善薬の胃運動促進作用—胃腸運動改善薬の投与タイミングと摂食条件下の検討—
第49回日本潰瘍学会（東京：2022年2月12日～13日）口頭発表
*本発表で潰瘍学会賞を受賞

10. 堀江俊治：消化器領域で使われる漢方のメカニズム～基礎における3つの発見～
東京理科大学薬学部医療薬学教育研究支援センター 第3回薬剤師のためのスキルアップ講座（柏：2022年12月10日）
11. 堀江俊治：漢方の知恵と生薬薬理のサイエンス
日本薬剤師研修センター 2022年度漢方薬・生薬研修会（東京：2022年10月16日）
12. 田嶋公人、大橋範之、大重茉里奈、藤井瑤子、並木隆雄、堀江俊治：Allyl isothiocyanate-induced acute inflammation in the gastric mucosa leads to the impaired gastric motility in rodents: involvement of substance P and calcitonin gene-related peptide, but not mast cells
第96回日本薬理学会年会（横浜：2022年11月30日）ポスター発表

【研究費の記録】

堀江俊治（代表）：**機能性消化管疾患モデルのTRPチャネル起因消化管知覚過敏における神経免疫の関与（22K06633）**

2022～2024年度日本学術振興会科学研究費補助金（基盤研究C）

堀江俊治（代表）、田嶋公人：**炎症性腸疾患モデルマウスを対象とした、間葉系幹細胞培養上清又は微細藻類培養上清の、薬理作用の評価・検討**

城西国際大学・ロート製薬株式会社共同研究（2022～2024年）

堀江俊治（代表）、田嶋公人：**胃食道逆流症、機能性ディスペプシア、過敏性腸症候群の病態動物モデルにおける香辛料摂取による消化管有害反応の解析**

2022年度学長所管研究費研究奨励制度（共同研究助成）（城西国際大学）

堀江俊治（代表）：**軽度皮膚疾患病態動物モデルにおける皮膚トラブルの病因の病態生理学的および免疫組織化学的解明**

2022年度学長所管研究費研究奨励制度（個人研究助成）（城西国際大学）

田嶋公人（代表）、神谷貞浩：胆汁酸と免疫細胞による痛感過敏を伴う新規胃腸機能障害モデル動物の開発

2022年度学長所管研究費研究奨励制度（共同研究助成）（城西国際大学）

田嶋公人（代表）：白金製剤シスプラチンによる悪心嘔吐に対するステロイドの効果—アドレノメデュリンとカルシトニン遺伝子関連ペプチドの役割

2022年度学長所管研究費研究奨励制度（科研費研究助成）（城西国際大学）

【原著論文】

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Pharmacists' provision of sexual and reproductive health services: a cross sectional study

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Background: In many countries, pharmacists' scope of practice enables the delivery of professional pharmacy services related to sexual and reproductive health (SRH). Studies exploring practices and perspectives regarding a wide range of SRH professional pharmacy services and the extent to which pharmacists are involved in prescribing or administering injections are limited.

Objectives: This study aimed to explore SRH professional pharmacy services provided by pharmacists, evaluate pharmacists' self-reported confidence in providing SRH education and determine preferences for additional training.

Methods: A cross-sectional Web-based survey was administered to pharmacists working in community pharmacies in Alberta, Canada. The survey was sent via e-mail and was open for 8 weeks between June and August 2020. Descriptive statistics were used to analyze the data.

Results: Most of the 303 participants were female (66%) and received their first pharmacy degree in Canada (69%). Approximately two-thirds had additional prescribing authorization (APA), and 97% had injections authorization; 90% and 94% of participants reported administering injectable contraceptives and human papillomavirus vaccine, respectively, and more than 95% renewed prescriptions for oral contraceptives. Of the participants with APA, approximately 40% reported providing initial prescribing services for contraceptive products. Overall, participants reported confidence in providing SRH education for most topics. Most selected topics for additional training were related to sexually transmitted and blood-borne infections; sexual health concerns of lesbian,

gay, bisexual, transgender, queer or questioning; and abortion medications.

Conclusion: Pharmacists in Alberta reported providing a wide range of SRH services and are interested in expanding their SRH role. These findings highlight opportunities to improve access and reduce inequities in the delivery of SRH services through community pharmacies. However, pharmacists' training needs should be considered.

【著書・訳書・総説】

Shigeo Yamamura (山村重雄)

8.1.4 Roles and activities of the sports pharmacist in Japan, pp. 54-59, 8.2.2 Enquiries to sports pharmacists in Japan, pp. 60, Sports Pharmacy practice and education, A Global Overview 2022, FIP, <https://www.fip.org/file/5391>

山村重雄

カナダ薬剤師会雑誌情報 カナダ薬剤師会雑誌から 2022/1, 2022/2 2022/3 2022/4, 2022/5, 2022/6- 日本コミュニティーファーマシー協会
https://ja-cp.website/e-zine_category/cpj/

【特別講演・シンポジウムなど】

Shigeo Yamamura (山村重雄)

Activities of Japanese Sports Pharmacists in Community, FIP Webinar “Sports pharmacy: Global opportunities for pharmacists in the sports setting” , 12/8 (2022)
<https://www.fip.org/events?tab=2&eventCategory=&eventWhen=previous>

山村重雄

統計学や薬物動態学の知識を使って添付文書情報を患者ケアに応用する
イオンハピコム人材総合研修機構総合研修Ⅱ 2/13, 3/22 (東京) オンライン 2022

山村重雄

日常業務から研究のネタを
2021 なの花アカデミー (オンライン) 2/26 オンライン 2022

山村重雄

薬剤師のための情報収集活用術「薬剤師のための情報収集活用術」

総合研修 I -③ 6/16、6/23、6/30日（2022）オンライン

山村重雄

統計の基礎を学んで添付文書情報を解析してみよう

なの花アカデミー（オンライン） 9/19 2022

【学会発表】

末澤克己、アッセンハイマー慶子、篠原久仁子、浜田康次、大森由子、服部益治、山村重雄、島田光明、城戸真由美、乾 賢一、吉岡ゆうこ、**コロナ禍でのJACP※活動報告2020-2022※（一社）日本コミュニティファーマシー協会（2022/7）、第9回日本コミュニティファーマシーフォーラム、2022年7月（東京）**

鈴木知子、佐竹尚子、吉岡優子、浜田康次、山村重雄、佐藤透、和田耕治、池田俊也、**COVID-19流行下にて増加した薬剤師業務と関連するCOVID-19感染への恐れとうつ症状、第12回国際医療福祉大学学会学術大会2022年8月（オンライン）**

鈴木知子、佐竹尚子、吉岡優子、浜田康次、山村重雄、佐藤透、和田耕治、池田俊也、**COVID-19流行下に増加した薬剤師の健康不調、第32回日本産業衛生学会全国協議会2022年9月（オンライン）**

【研究費の記録】

山村重雄（代表） ケースシナリオを用いた「性と生殖に関する健康」サービス提供のための人材育成 令和4年度一般用セルフメディケーション振興財団 補助金（研究代表）

【原著論文】

Journal of Japanese Society for Extremophiles (2022), Vol.10, 2-9

Examination of the hearts of *Eptatretus burgeri* using histological analysis

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The heart creates positive and negative pressure in a regular rhythm to pump blood. The cardiac chambers seen in vertebrates are an advanced pump design. Many species, such as the hagfish, still have accessory pumps, but they are considered vestigial. Additionally, the processes by which the circulatory system develops in vertebrates, including heart development, are largely unknown. In this study, we examined the heart of hagfish (*Eptatretus burgeri*) using histological analysis. In *E. burgeri*, three types of hearts were observed: branchial, cardinal, and portal. Photomicrographs showed that there were many empty spaces in all three types. These hearts pump blood in and out of the sponge to absorb and discharge water. The cardinal heart near the brain in *E. burgeri* may be primitive because its cell structure is similar to that of skeletal muscle. Modern medical research and practices have largely concentrated on the molecular and physiological mechanisms underlying health and disease, whereas evolutionary medicine has focused on how evolution has shaped these mechanisms, which may influence disease risk. In this study, we investigated the hearts of *E. burgeri* to understand the origin of heart disease.

【学会発表】

西口慶一¹⁾、川名孝亮¹⁾、米谷将悟¹⁾、山崎広太¹⁾、田中秀樹¹⁾、神谷貞浩¹⁾、品川翔太²⁾、南澤宝美后²⁾、伊藤正紀^{2,3)}、芝清隆²⁾

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マイクロ遺伝子重合法を用いた新型コロナウイルス (SARS CoV-2) のエピトープペプチドワクチンの構築

第31・32回生物試料分析科学会合同年次学術集会 (四日市看護医療大学 (三重県), 2022.3.13)

田中秀樹¹⁾、山崎広太¹⁾、米谷将悟¹⁾、川名孝亮¹⁾、神谷貞浩¹⁾、松村聡²⁾、木内幸子²⁾、五郎丸 (新海) 美智子³⁾、黒田潤³⁾、渭原博⁴⁾、西口慶一¹⁾

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In silico を用いた新型コロナウイルス感染症ウイルス (SARS-CoV-2) のスパイクプロテインの解析

第31・32回生物試料分析科学会合同年次学術集会 (四日市看護医療大学 (三重県), 2022.3.13)

渭原博¹⁾、木内幸子¹⁾、谷あすか²⁾、西口慶一³⁾

- 1) 千葉科学大学危機管理学部
- 2) 東邦大学医療センター大橋病院臨床検査部
- 3) 城西国際大学薬学部

レチノール結合蛋白 (Retinol binding protein: RBP) のタイプ分類と生理的機能：文献調査による近年の研究

第6回日本ワンヘルスサイエンス学会 (東京都ヤマザキ動物看護大, 2022.9.2)

松原愛里¹⁾、西口慶一¹⁾、松本瑠華¹⁾、松崎美奈¹⁾、立石綾華¹⁾、植草瑠吾¹⁾、神谷貞浩¹⁾、
渭原博²⁾、木内幸子²⁾、五郎丸(新海)美智子³⁾、黒田潤³⁾

1) 城西国際大学薬学部

2) 千葉科学大学危機管理学部

3) 東邦大学薬学部

ヌタウナギ科のヌタ (slime) の性質とその美容効果について

第6回日本ワnhルヘルスサイエンス学会 (東京都ヤマザキ動物看護大, 2022.9.2)

【その他】

西口慶一 : 千葉県立東金高等学校

課題研究の授業

(千葉 2022. 5/6, 5/13, 5/27, 9/16, 11/25, 12/2)

西口慶一 : 千葉県立野田中央高等学校

系統別説明会: 薬学

(千葉 2022. 11. 24)

西口慶一 : 東京都立南葛飾高等学校

系統分野別 + 学費・奨学金ガイダンス: 薬学

(千葉 2022. 12. 14)

西口慶一

生物試料分析科学会 第44巻5号

編集後記

【原著論文】

日本予防医学会雑誌, 第16巻第2号pp21-26 発行年: 2022年04月30日

新型コロナワクチンの城西国際大学職域接種におけるワクチン接種動機と副反応の調査

佐々木英久¹、鈴木明子²、宮澤純子²、井上映子²、森健二¹、懸川友人¹、杉林堅次¹

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新型コロナワクチンの城西国際大学職域接種の対象者となった若年層において、副反応の発現背景と彼らの新型コロナワクチン接種の動機要因を調査した。対象は、モデルナ社製のmRNAワクチン接種を受け、アンケートに回答した学生に加えて、比較のために教職員、外部委託業者、外部関係者とした。調査項目は、年齢、性別、アレルギーの有無、COVID-19罹患歴の有無、新型コロナワクチン接種を決めた理由、副反応の有無、副反応の継続日数、新型コロナワクチン接種後の感想、副反応に対する対応方法とした。

新型コロナワクチンを接種することに決めた動機要因には、「COVID-19に罹患したくない」、「家族の勧め」、「テレビやインターネットなどの情報から」が多かった。接種後3日間の副反応頻度は、接種2回目の方が有意に高かった。副反応としては疼痛、発熱が高く、特に接種当日および翌日での38度以上の高熱の頻度が高く、接種2回目の解熱鎮痛薬の準備が重要であることが示唆された。また、副反応頻度は、男性より女性の方が、また、若年層である学生が高く、55歳以上となると有意に低くなった。さらに、副反応持続日数についても女性が有意に長かった。なお、大学生の2回目の新型コロナワクチン接種において特に発熱や疼痛が見られたが、副反応に関する正しい知識や対応方法を伝達したことで重篤な事象とならずに終えることができた。

日本予防医学会雑誌, 第16巻第2号 pp27-33 発行年: 2022年04月30日

千葉県東金市・山武市・大網白里市における薬局、病院、大学教員薬剤師の新型コロナワクチン接種業務の取り組みについて

佐々木英久¹⁾, 仲佐啓詳²⁾, 加瀬浩二³⁾, 小野珠美⁴⁾, 鈴木俊宏⁴⁾, 菊池健一⁴⁾, 懸川友人¹⁾, 杉林堅次¹⁾

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千葉県東金市・山武市・大網白里市にて、ワクチン集団接種の対応にあたった医師、看護師、行政担当者、薬剤師（薬局、病院、大学教員）にアンケート調査を実施し、ワクチン集団接種における薬剤師のあり方と勤務職種による違いについて検討することを目的とした。新型コロナワクチン接種業務全体の流れや習得度に関して、薬剤師は他の職種と比較して「上手くできた」割合が初回時50%と有意に低かったが（ $P < 0.01$ ）、直近時には90.9%に上昇した。また、ワクチン調製においても、初回時「上手くできた」割合が薬局薬剤師で低い傾向にあったが、直近では薬剤師の勤務職種間に差を認めなくなり、薬剤師間の話し合いや連携が寄与したことが示唆された。ワクチンの調製業務以外で薬剤師が行うべき業務として、接種後の経過観察や服用中の薬剤確認などがあげられ、ワクチン接種については薬剤師の前向きな意見が多かった。今回、薬局、病院の薬剤師だけでなく、大学の薬剤師が連携してワクチン調製業務を担ったことにより、勤務職種にかかわらず全ての薬剤師の習得度が高くなり、円滑なワクチン接種に貢献することができた。

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Computational and Crystallographic Analysis of Binding Structures of Inhibitory Compounds for HIV-1 RNase H Activity

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Chemotherapy of human immunodeficiency virus type-1 (HIV-1) has significantly developed over the last three decades. The emergence of drug-resistant variants is, however, still a severe problem. The RNase H activity of HIV-1 reverse transcriptase is an attractive target for a new class of antiviral drugs because there is no approved inhibitor. The nitro-furan-carbonyl and nitro-thiophene-carbonyl groups are potent scaffolds for the HIV-1 RNase H inhibitor. In this work, the binding structures of six inhibitory compounds were obtained by X-ray crystal analysis in a complex with a recombinant protein of HIV-1 RNase H domain. Every inhibitory compound was found to be bound to the catalytic site with the furan- or thiophene-ring coordinated to two divalent metal ions at the binding pocket. All the atoms in nitro, furan, carbonyl, and two metals were aligned in the nitro-furan derivatives. The straight line connecting nitro and carboxyl groups was parallel to the plane made by two metal ions and a furan O atom. The binding modes of the nitro-thiophene derivatives were slightly different from those of the nitro-furan ones. The nitro and carbonyl groups deviated from the plane made by two metals and a thiophene S atom. Molecular dynamics simulations suggested that the furan O or thiophene S atom and carbonyl O atom were firmly coordinated to the metal ions. The simulations made the planar nitro-furan moiety well aligned to the line connecting the two metal ions. In contrast, the nitro-thiophene derivatives were displaced from the initial positions after the simulations. The computational findings will be a sound basis for developing potent inhibitors for HIV-1 RNase H activity.

【特別講演・シンポジウムなど】

懸川友人, 茯苓由来トリテルペン pachymic acid の抗炎症作用機構の比較検討.

第37回生薬に関する懇談会（北里大学）、日本薬学会関東支部・（公社）東京生薬協会（東京，2022. 11）

懸川友人, 細胞の環境応答における翻訳調節.

エイチエスシー研究所 2022年11月研究会（東京（Zoom），2022. 11）

新倉雄一, 卵子の再生力を高める不妊治療薬「ペプチドX」

第416回FemTech特集, Morning Pitch（デロイト・トーマツ・ベンチャーサポート株式会社、野村證券株式会社）（東京，2022. 6）

新倉雄一, 卵からはじめるウイメンズヘルスケア

第1回MEDISOセミナーシリーズ～医療系ベンチャーの壁を超える～キックオフセミナー（厚生労働省，LINK-J共催）（東京，2022. 11）

【学会発表】

懸川友人, 石井洋佑, 菊池直也 ブラジル産プロポリスの抗ウイルス作用に寄与する含有成分の考察.

日本薬学会第142年会（名古屋，2022. 3）

蟹和美穂, 新垣知輝 2,6-二置換ピリジンによるタンパク質合成への影響の検討

日本薬学会第142年会（名古屋，2022. 3）

【メディア】

新倉雄一

あなたの「推し」の博士は？「日本の科学に金がない問題」解決のヒントは「推し活」にあり

BUSINESS INSIDER（Web，2022. 7）

新倉雄一

「高校生が創る高校生のためのオンライン大学校 Global Partners University」

グローバルパートナーズ株式会社（旧アリババマーケティング）（Web. 2022. 12）

- 生物好きの人見知り少年，生物学者に
- 毎日充実！仕事がアイデンティティ！
- 女性の社会進出を支える技術を解説！
- 女性が働きやすい環境を作りたい
- 知識にとらわれず，感性を研ぎ澄ませ

【研究費の記録】

Michiyoshi Nukaga（代表）

Cleveland VA Medical Research and Education Foundation

Exploring the activity of cefepime-VNRX-5133 and ceftibuten-(VNRX-7145->VNRX5236)
against multi-drug resistant pathogens.

額賀路嘉（代表）

2020-2023年度 科研費基盤研究(C)、課題番号20K07484

非共有結合性阻害剤の探索を目的としたペニシリン認識酵素のX線結晶解析

額賀路嘉（代表）、石崎幸、2022年度学長所管研究費

非共有結合性阻害剤の探索を目指したペニシリン認識酵素の構造解析

新倉雄一（代表）

「生殖細胞特異的なStra8活性化分子の同定と卵新生の制御」

令和2-4年度日本学術振興会科学研究費補助金 基盤研究(C)

新倉雄一（代表）、額賀路嘉、2022年度学長所管研究費

卵子の質をコントロールするStra8の構造機能相関研究

【公開講座】

額賀路嘉

2022年9月28日香取市民公開講座（香取市小見川市民センターいぶき館）
「新型コロナウイルスとそのワクチン」

【研究費報告】

2022年3月, Venatorx 社

Exploring the activity of cefepime-taniborbactam and ceftibuten-(VNRX-7145->VNRX-5236) against multi-drug resistant pathogens.

Krisztina M. Papp-Wallace², PhD, Scott A. Becka², BS, and Nukaga M. (額賀路嘉) ¹, PhD

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【著書・訳書・総説】

太田篤胤 (分担執筆著書)

3章 医薬品と食品の相互作用

食の機能と健康の科学 ―健康食品管理士/食の安全管理士テキスト― (平野和行・長村洋一 監修), 72-91, 日本食品安全協会, 三重 (2022年3月)

【教育講座・講演会】

太田篤胤

健康経営甲子園2022 (株)日本健康経営健主催 審査員講評 (ZOOM オンライン, 2022, 4)

太田篤胤

「健康寿命延伸に資する要因と機能性表示食品の役割を考える」 健康食品管理士会 関東支部研修会 (ZOOM オンライン, 2022, 6)

【学会発表】

扶川武志, 太田篤胤 ラットを用いたフラクトオリゴ糖とイヌリンのミネラル吸収促進作用の比較 日本栄養・食糧学会 第76回大会 武庫川女子大学 (兵庫, 2022. 6)

酒井健介, 加藤健志, 春日井亮太 主観的回復状況に及ぼす摂取エネルギーの影響 日本体力医会 第77回大会 (栃木, 2022. 9)

加藤健志, 春日井亮太, 酒井健介 レースパフォーマンスに及ぼす主観的回復と外的負荷量の影響 日本体力医会 第77回大会 (栃木, 2022. 9)

【原著論文】

YAKUGAKU ZASSHI, **142**, 1005-1014 (2022)

Repellent Activity of Vanillin Derivatives and Monoterpenes to Olive Weevil

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Olive weevils, *Pimelocerus (Dyscerus) perforatus* Roelofs, utilize olive trees as a host plant. The adult female uses an elongated snout to puncture the trunk and lay one egg a day, resulting in dozens of eggs over its lifetime. The hatched larvae grow by eating the olive trunk. When olive trees die due to feeding damage, olive productivity is seriously impaired. Since there is no effective pesticide for olive weevils so far, the authors aimed to develop a repellent for adult olive weevils from the viewpoint of integrated pest management. We prepared a measurable apparatus for the repellent action against olive weevils and screened chemical substances by using the apparatus. When the repellent activity was measured using vanillin and its derivatives, a clear repellent effect could be confirmed for two types of vanillin derivatives, such as o-vanillin, and 2-hydroxy-4-methoxybenzaldehyde. In addition, when the repellent activity against olive weevils was measured using monoterpenes, four types of acyclic monoterpenes, geraniol, β -citronellol, citral, and linalool, and three types of monocyclic monoterpenes, (-)-limonene, (+)-limonene, and (-)-menthol, and a bicyclic monoterpene, (1R)-(+)- α -pinene, were found to have dose-dependent repellent activity with statistical significance. In the future, it is expected that the formulation for applying the repellent substances to olive trees and the study of their practicality in olive fields will progress.

【研究費の記録】

光本篤史（代表）

農業用水汚濁水質分析依頼

両総土地改良区 委託研究

光本篤史（代表）

「東金市産オリーブのブランド確立プロジェクト」（業務委託）

東金市オリーブ組合

石田ゆかり、大橋優紀子、光本篤史（分担）

「年齢調整医療費を用いた医療費分析アプリケーションの構築と検証」

科学研究費基盤研究(C)

【原著論文】

Chemical and Pharmaceutical Bulletin, 70, 50-51 (2022)

Magnetic field-responsive pulsatile drug release using a magnetic fluid

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Ferrofluids are colloidal liquids with fine magnetic particles. They change shape and fluidity depending on the magnitude and direction of the external magnetic field. The magnetic field-responsive pulsatile release of a model drug, lidocaine hydrochloride (LID·HCl), was determined using a depot-type injection containing white petrolatum and/or hydrophilic cream with a magnetic fluid in various proportions. Drug release was confirmed using a self-made diffusion cell and the application of a moving magnet at the bottom of the preparation. Magnetic field-responsive LID release was observed only when using the white petrolatum preparation and depended on the concentration of the magnetic fluid. Magnetic field responsiveness was not observed in the preparation with only the hydrophilic cream. A greater magnetic field-responsive release was observed with a combination of white petrolatum and hydrophilic cream than with white petrolatum alone. These results may lead to the development of an injectable formulation that enables pulsatile administration of macromolecular drugs.

Chemical and Pharmaceutical Bulletin, 70, 716-719 (2022)

Effects of physicochemical properties of constituent ions of ionic liquid on its permeation through a silicone membrane

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Ionic liquids (ILs), defined as liquid salts composed of anions and cations, have the advantage of allowing constituent ions to be stably absorbed through biological membranes, such as skin. However, limited information is currently available on the effects of the physicochemical properties of constituent ions on the membrane permeation of ILs. Therefore, we herein investigated the effects of the polarity of constituent cations on the membrane permeation of each constituent ion from IL. Various ILs were prepared by selecting lidocaine (LID) as a cation and a series of *p*-alkylbenzoic acids with different *n*-octanol/water partition coefficients (*K*_{o/w}) as anions. These ILs were applied to a skin model, a silicone membrane, and membrane permeability was investigated. The membrane permeabilities of *p*-alkylbenzoic acids from their single aqueous suspensions were also measured for comparison. The membrane permeability of *p*-alkylbenzoic acid from the aqueous suspension increased at higher *K*_{o/w}. However, the membrane permeability of ILs was similar regardless of the *K*_{o/w} of the constituent *p*-alkylbenzoic acid. Furthermore, the membrane permeability of the counterion LID remained unchanged regardless of the constituent *p*-alkylbenzoic acid. These results suggest that even when the *K*_{o/w} of IL constituents markedly differs, the resulting IL does not affect membrane permeability.

Colloids and Surfaces B: Biointerfaces 220, 112916 (2022)

Chitosan-coated PLGA nanoparticles for transcutaneous immunization: Skin distribution in lysozyme-sensitized mice

Issei Takeuchi^{1,2}, Yuna Hidaka¹, Takeshi Oshizaka (押坂勇志)², Chihiro Takei², Kenji Mori (森健二)², Kenji Sugibayashi (杉林堅次)², Kimiko Makino¹

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The effect of transcutaneous immunization was studied using a combined system of poly(DL-lactide-*co*-glycolide) (PLGA) nanoparticles and iontophoresis (IP). Both hen egg-white lysozyme (HEL)-loaded PLGA nanoparticles coated with chitosan hydroxypropyltrimonium chloride and their fluorescent nanoparticles were prepared using an antisolvent diffusion method. Their mean volume diameters were 87.6 ± 38.9 nm and 84.9 ± 27.6 nm, respectively. It was suggested from the results of the *ex vivo* skin accumulation study using fluorescent nanoparticles that the HEL released from the nanoparticles to the skin surface was efficiently delivered to antigen-presenting cells. HEL-specific IgG1 and IgG2a titers were determined in an *in vivo* percutaneous immunoreactivity study using lysozyme-sensitized mice. As results, the group using nanoparticles and IP showed 1.33 times higher HEL-specific IgG1 titer than a sham treatment group. The HEL-specific IgG2a titer was 1.36 times higher in the nanoparticles and IP group than in the HEL solution and IP group. It was suggested from the quantification results of total IgE in serum that the combined use of PLGA nanoparticles and IP reduced the total IgE concentration. The level of cytokines may have decreased due to Th1 cell activation and relative suppression of Th2 cells. The cytokine level is presumed to be reduced by activation of Th1 cells and relative suppression of Th2 cells. The histamine amount in plasma and rectal temperature after the induction of anaphylactic shock using lysozyme-sensitized mice were also studied, which indicates that the combined use of PLGA nanoparticles and IP may provide the same therapeutic effect as an injection.

【著書・訳書・総説】

押坂勇志 (分担執筆著書), 森健二 (分担執筆著書)

第2部第2章 I 「医薬品添加物」, 第2部第2章 II 「製剤化」

製剤化のサイエンス 改訂11版 218-248, ネオメディカル, 東京 (2022年3月)

【特許】

森健二、武井千弥、押坂勇志、杉林堅次

製剤

日本公開特許 特開2022-39522 (2022年3月10日 公開)

【学会発表】

稲葉玲奈, 磯野真菜, 押坂勇志, 武井千弥, 竹内一成, 森健二, 杉林堅次

膜透過性に及ぼすイオン液体の影響に関する研究

日本薬学会第142年会 (名古屋, 2022.3)

山崎琴美, 武井千弥, 押坂勇志, 竹内一成, 森健二, 杉林堅次

通信機能を有するイオン液体型アンテナ装置の有用性評価に関する研究

日本薬学会第142年会 (名古屋, 2022.3)

竹内一成, 日高優那, 鈴木孝明, 押坂勇志, 武井千弥, 森健二, 杉林堅次, 牧野公子

食物アレルギーにおける経皮免疫療法のためのキトサン修飾PLGAナノ粒子

日本薬学会第142年会 (名古屋, 2022.3)

【研究費の記録】

押坂勇志 (代表), 森健二 (分担), 武井千弥 (分担)

Azone構造類似のイオン液体型アンテナ設計と薬物の経皮吸収促進効果 (21K06650)

令和3-令和5年度日本学術振興科学研究費補助事業 (基盤研究C)

押坂勇志 (分担), 森健二 (分担), 武井千弥 (分担)

化学物質の皮膚曝露後のin silico皮膚吸収性予測法の確立

日本化学工業協会 第9期「日化協LRI (長期自主研究)」

【著書・訳書・総説】

児玉庸夫（分担執筆著書）

第3部第2章第1節地域包括ケアの理念及び薬局と薬剤師の役割，第3部第2章第2節在宅医療及び居宅介護における薬局と薬剤師の役割，第3部第2章第3節学校薬剤師，第3部第2章第4節地域の保健、医療、福祉において利用可能な社会資源，第3部第2章第5節地域から求められる医療提供施設、福祉施設及び行政との連携.

2022-23年版 薬事関係法規・制度解説，薬事衛生研究会（編），薬事日報社，東京，pp 504-505，pp 506-508，pp 509-512，pp 513-514，pp 515-517.（2022年4月）

児玉庸夫（分担執筆著書）

第3章3.4 治験計画届出制度，第6章 製造販売後調査（市販後調査）.

医薬品開発入門第4版，古澤康秀（監修），じほう，東京，pp.77-83，pp.175-204.（2022年9月）

【原著論文】

Colloids and Surfaces B: Biointerfaces 220, 112916 (2022)

Chitosan-coated PLGA nanoparticles for transcutaneous immunization: Skin distribution in lysozyme-sensitized mice

Issei Takeuchi (竹内一成)^{1,2}, Yuna Hidaka¹, Takeshi Oshizaka², Chihiro Takei², Kenji Mori (森健二)², Kenji Sugibayashi², Kimiko Makino¹

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The effect of transcutaneous immunization was studied using a combined system of poly(DL-lactide-*co*-glycolide) (PLGA) nanoparticles and iontophoresis (IP). Both hen egg-white lysozyme (HEL)-loaded PLGA nanoparticles coated with chitosan hydroxypropyltrimonium chloride and their fluorescent nanoparticles were prepared using an antisolvent diffusion method. Their mean volume diameters were 87.6 ± 38.9 nm and 84.9 ± 27.6 nm, respectively. It was suggested from the results of the *ex vivo* skin accumulation study using fluorescent nanoparticles that the HEL released from the nanoparticles to the skin surface was efficiently delivered to antigen-presenting cells. HEL-specific IgG1 and IgG2a titers were determined in an *in vivo* percutaneous immunoreactivity study using lysozyme-sensitized mice. As results, the group using nanoparticles and IP showed 1.33 times higher HEL-specific IgG1 titer than a sham treatment group. The HEL-specific IgG2a titer was 1.36 times higher in the nanoparticles and IP group than in the HEL solution and IP group. It was suggested from the quantification results of total IgE in serum that the combined use of PLGA nanoparticles and IP reduced the total IgE concentration. The level of cytokines may have decreased due to Th1 cell activation and relative suppression of Th2 cells. The cytokine level is presumed to be reduced by activation of Th1 cells and relative suppression of Th2 cells. The histamine amount in plasma and rectal temperature after the induction of anaphylactic shock using lysozyme-sensitized mice were also studied, which indicates that the combined use of PLGA nanoparticles and IP may provide the same therapeutic effect as an injection.

Chemical and Pharmaceutical Bulletin, 70, 716-719 (2022)

Effects of physicochemical properties of constituent ions of ionic liquid on its permeation through a silicone membrane

Takeshi Oshizaka¹, Rena Inaba¹, Mana Isono¹, Chihiro Takei¹, Issei Takeuchi (竹内一成)¹, Kenji Mori (森健二)¹, Kenji Sugibayashi¹

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Ionic liquids (ILs), defined as liquid salts composed of anions and cations, have the advantage of allowing constituent ions to be stably absorbed through biological membranes, such as skin. However, limited information is currently available on the effects of the physicochemical properties of constituent ions on the membrane permeation of ILs. Therefore, we herein investigated the effects of the polarity of constituent cations on the membrane permeation of each constituent ion from IL. Various ILs were prepared by selecting lidocaine (LID) as a cation and a series of *p*-alkylbenzoic acids with different *n*-octanol/water partition coefficients (*K*_{o/w}) as anions. These ILs were applied to a skin model, a silicone membrane, and membrane permeability was investigated. The membrane permeabilities of *p*-alkylbenzoic acids from their single aqueous suspensions were also measured for comparison. The membrane permeability of *p*-alkylbenzoic acid from the aqueous suspension increased at higher *K*_{o/w}. However, the membrane permeability of ILs was similar regardless of the *K*_{o/w} of the constituent *p*-alkylbenzoic acid. Furthermore, the membrane permeability of the counterion LID remained unchanged regardless of the constituent *p*-alkylbenzoic acid. These results suggest that even when the *K*_{o/w} of IL constituents markedly differs, the resulting IL does not affect membrane permeability.

Molecules, 27, 6006 (2022)

Thermoresponsive polyphosphoester via polycondensation reactions: synthesis, characterization, and self-assembly

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Using a novel strategy, amphiphilic polyphosphoesters based on poly(oxyethylene H-phosphonate)s (POEHP) with different poly(ethylene glycol) segment lengths and aliphatic alcohols with various alkyl chain lengths were synthesized using polycondensation reactions. They were characterized by ¹H NMR, ¹³C {H} NMR ³¹P NMR, IR, and size exclusion chromatography (SEC). The effects of the polymer structure on micelle formation and stability, micelle size, and critical micelle temperature were studied via dynamic light scattering (DLS). The hydrophilic/hydrophobic balance of these polymers can be controlled by changing the chain lengths of hydrophilic PEG and hydrophobic alcohols. A solubilizing test, using Sudan III, revealed that hydrophobic substances can be incorporated inside the hydrophobic core of polymer associates. Loading capacity depends on the length of alkyl side chains. The results obtained indicate that these structurally flexible polymers have the potential as drug carriers.

In Vivo, 36, 2166-2172 (2022)

A mouse model for tuberculosis combined with inhalable imiquimod-PLGA nanocomposite particles based on macrophage phenotype

Teruki Nii^{1,2}, Shunsuke Takizawa³, Tomomi Akita^{3,4}, Chikamasa Yamashita^{3,4}, Issei Takeuchi (竹内一成)³⁻⁵, Kimiko Makino^{3,4}

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Background/Aim: In vivo models of tuberculosis are effective tools for developing new drugs. The objective of this study was to prepare in vivo models for tuberculosis by utilizing nanocomposite particles (NCPs) containing imiquimod-loaded poly(lactic-co-glycolic acid) nanoparticles. **Materials and Methods:** NCPs were prepared from dichloromethane with imiquimod and poly(lactic-co-glycolic acid) using a spray dryer. Mice were treated with NCPs in the lungs by inhalation, and then infection with *Mycobacterium bovis* bacille Calmette-Guerin was performed (treatment groups). The concentrations of the pro-inflammatory cytokines, tumor necrosis factor- α and interferon- γ were measured in bronchoalveolar lavage fluid using an enzyme-linked immunosorbent assay. **Results:** When animals were treated with NCPs, the concentrations of tumor necrosis factor- α and interferon- γ in bronchoalveolar lavage fluid were significantly higher than in animals not treated with NCPs. In addition, high bacterial counts and circular granuloma were observed. **Conclusion:** NCPs prepared in this study enhanced the level of inflammation in the lungs and support the preparation of in vivo models of tuberculosis

Anticancer Research, 42, 2847-2857 (2022)

Preparation of micelles encapsulating doxorubicin and their anticancer effect in combination with tranilast in 3D spheroids and *in vivo*

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Background/Aim: The objective of this study was to prepare doxorubicin encapsulated in micelles (DOX-micelles) using poly(hexadecanyloxyethylene glycol-lactate phosphate), which we recently synthesized, and to evaluate the anticancer effect of DOX-micelles *in vitro* and *in vivo*. **Materials and Methods:** To evaluate the anticancer effect of DOX-micelles *in vitro*, three-dimensional spheroids composed of B16 mouse melanoma cells and fibroblasts were prepared by changing the ratio of cancer cells to fibroblasts. In addition, for efficient doxorubicin treatment of the cells present in the center of the spheroids, tranilast, an anti-fibrotic drug was added to the spheroids before treatment with DOX-micelles, then the amount of doxorubicin and cell viability of spheroids were evaluated. Moreover, to assess the effects of the combination of DOX-micelles with tranilast *in vivo*, relative tumor volume was investigated in a mouse model of melanoma. **Results:** The mean diameter and doxorubicin content of DOX-micelles were 93.3 nm and 3.5%, respectively. When the ratio of cancer cells to fibroblasts was 20:80, spheroids with spherical and rigid shapes were obtained. In addition, the amount of doxorubicin in the spheroids was increased by tranilast treatment, and an efficient anticancer effect was also observed. The anticancer effect of the combination of tranilast and DOX-micelles was confirmed *in vivo*. **Conclusion:** Micelles encapsulating doxorubicin are promising for cancer therapy, and their anticancer effect is improved by tranilast pretreatment in 3D spheroids *in vivo*.

Bio-Medical Materials and Engineering, 33, 2159-168 (2022)

Effects of lower alcohols on nanocomposite particles for inhalation prepared using O/W emulsion

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Background: Inhalable nanocomposite particles using O/W emulsions were studied. The effect of the composition of the dispersed phase on the nanoparticles in the nanocomposite particles was reported, however, the effect on the inhalation characteristics of nanocomposite particles has not been investigated. Objective: The aim of this study was to study the effects of lower alcohols in the dispersed phase of O/W emulsions on inhalable nanocomposite particles. Methods: Nanocomposite particles were prepared using a spray dryer from O/W emulsion. A mixed solution of dichloromethane and lower alcohols in which rifampicin (RFP) and poly(L-lactide-co-glycolide) were dissolved was used as a dispersed phase, and an aqueous solution in which arginine and leucine were dissolved was used as a continuous phase. Results: We succeeded in preparing non-spherical nanocomposite particles with an average diameter of 9.01–10.91 μ m. The results of the fine particle fraction (FPF) measurement showed that the higher the hydrophobicity of the lower alcohol mixed in the dispersed phase, the higher the FPF value. The FPF value of the nanocomposite particles was significantly increased by using ethanol and 1-propanol. Conclusions: The results were revealed that mixing 1-propanol with the dispersed phase increased the amount of RFP delivered to the lungs.

Anticancer Research, 42, 1801-1811 (2022)

Poly(alkyloxyethylene-lactate phosphate) for delivery of doxorubicin: synthesis and characterization

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Background/Aim: Serious side effects are associated with the use of doxorubicin. Nanoparticles as carriers for anticancer drugs are useful for reducing side effects and improving therapeutic effects. In this study, a polymer for preparing doxorubicin-containing nanoparticles was developed. Using a novel strategy, a biodegradable poly(oxyethylene glycol lactate H-phosphonate) based on dimethyl H-phosphonate and poly(ethylene glycol)-lactate (PEG-lactate) was synthesized. Materials and Methods: Poly(hexadecanyloxyethylene - lactate phosphate) was obtained via chlorination of poly(oxyethylene glycol - lactate H-phosphonate) with trichloroisocyanuric acid and the addition of 1-hexadecanol. The polymer was characterized by ¹H NMR and ³¹P NMR. Results: The results of ¹H NMR and ³¹P NMR showed that the polymer was successfully synthesized, and the yield was 46.9%. Conclusion: Poly(hexadecanyloxyethylene - lactate phosphate) has potential as a drug carrier.

【著書・訳書・総説】

竹内一成

半固形製剤の物性評価

製剤機械技術学会誌, 31 (2022) 68-74.

【学会発表】

星野友希, 西川元也, 草森浩輔, 竹内一成, 牧野公子

乾癬治療を目的とした PLGA-PEG-PLGA トリブロックコポリマーを用いたタクロリムス含有ナノ粒子の開発

東京理科大学薬学部 DDS シンポジウム 2022 (東京, 2022. 12)

藤原成海, 竹内一成, 草森浩輔, 西川元也

アトピー性皮膚炎治療を目的とした cyclosporine A 含有ナノ粒子の開発

東京理科大学薬学部 DDS シンポジウム 2022 (東京, 2022. 12)

藤原成海, 竹内一成, 草森浩輔, 西川元也

アトピー性皮膚炎マウス皮膚における cyclosporine A 含有 PLGA-PEG-PLGA ナノ粒子の浸透性

第66回日本薬学会関東支部大会 (横浜, 2022. 9)

稲葉玲奈, 磯野真菜, 押坂勇志, 武井千弥, 竹内一成, 森健二, 杉林堅次

膜透過性に及ぼすイオン液体の影響に関する研究

日本薬学会第142年会 (名古屋, 2022. 3)

山崎琴美, 武井千弥, 押坂勇志, 竹内一成, 森健二, 杉林堅次

通信機能を有するイオンフォレーシス装置の有用性評価に関する研究

日本薬学会第142年会 (名古屋, 2022. 3)

竹内一成, 日高優那, 鈴木孝明, 押坂勇志, 武井千弥, 森健二, 杉林堅次, 牧野公子

食物アレルギーにおける経皮免疫療法のためのキトサン修飾 PLGA ナノ粒子

日本薬学会第142年会 (名古屋, 2022. 3)

竹内一成

半固形製剤の物性評価

一般社団法人製剤機械技術学会, 招待講演 (オンライン開催, 2022. 8)

【研究費の記録】

竹内一成 (代表), 西川元也 (分担)

**PLGA-PEG ブロックコポリマーを用いた難治性皮膚疾患治療のための経皮DDS
(22K06553)**

令和4-令和6年度日本学術振興科学研究費補助事業 (基盤研究C)

牧野公子 (代表), 竹内一成 (分担)

経皮免疫治療のための高分子キャリアを用いたナノ DDS 製剤の開発 (19K07030)

平成31-令和3年度日本学術振興科学研究費補助事業 (基盤研究C)

【著書・訳書・総説】

奥山恵美（分担執筆）

パートナー生薬学 改訂第4版（木内文之・小松かつ子・三卷祥浩 編），
南江堂，東京（2022年2月）

【原著論文】

日本予防医学会, 16(2), 21-26 (2022)

Investigation of coronavirus infectious disease 2019 vaccination palpitations and adverse events in a young population at Josai International University

Hidehisa Sasaki¹⁾, Akiko Suzuki²⁾, Junko Miyazawa²⁾, Eiko Inoue²⁾, Kenji Mori¹⁾, Tomohito Kakegawa¹⁾, Kenji Sugibayashi¹⁾

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We investigated the adverse reactions and motivations for vaccination in a young group of Josai International University students with the coronavirus infectious disease 2019 (COVID-19) vaccine. The subjects were students, faculty, staff, and external parties who received the COVID-19 vaccine moderna intramuscular injection and responded to the questionnaire. The survey items included age, sex, allergies, history of COVID-19, reasons for decision to vaccinate, adverse reactions, medications used for adverse reactions, and post-vaccination impressions. The most common motivating factors for vaccination were as follows: “I do not want to get COVID-19,” “family recommendation,” and “information on television or internet.” The frequency of adverse reactions was significantly higher in the second dose of vaccination for all adverse reactions and in women and younger age groups, and significantly lower in those aged ≥ 55 years. Additionally, the duration of adverse reactions was significantly longer in women. The correct knowledge of adverse reactions to the COVID-19 vaccine and how to respond to them was communicated to the students, which resulted in no serious events.

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Approaches to coronavirus disease vaccination by community pharmacies, hospitals, and university faculties pharmacists in Togane, Sammu, and Oamishirasato Cities, Chiba

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This study aimed to examine the role of pharmacists in mass vaccination by conducting a questionnaire survey of doctors, nurses, administrators, and pharmacists (working at community pharmacies, hospitals, and university faculties) who were engaged in mass vaccination in Togane, Sammu, and Oamishirasato cities, Chiba. Regarding the overall coronavirus disease vaccination service and degree of achievement of professional collaboration, the percentage of pharmacists who “successfully completed” the service was 50% per the first survey, which was significantly lower than that of other professionals ($P < 0.01$); however, it increased to 90.9% per the final survey. Regarding the preparation of vaccines for administration by pharmacists, the percentage of “well done” responses in the first survey tended to be lower among pharmacists working in pharmacies than among those working in hospitals and university faculties; however, there was no difference between the percentage of professionals per the final survey. The tasks that pharmacists should perform other than vaccine preparation include post-vaccination follow-up and confirmation of medications taken. Nonetheless, there were many positive comments about pharmacists’ vaccination service. By having pharmacists from pharmacies, hospitals, and universities collaborate on vaccine preparation, pharmacists from all fields could increase their mastery and contribute to efficient vaccination.

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Effects of treatment with sodium/glucose cotransporter 2 inhibitors on Diabetic nephropathy

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A 30-month retrospective study was conducted to elucidate the effect of sodium/glucose cotransporter (SGLT) 2 inhibitors, an antidiabetic agent for type 2 diabetes mellitus, on the progression of diabetic nephropathy.

A total of 279 diabetic outpatients routinely visiting Secomedic Hospital with an eGFR of 59 mL/min or less were divided into two groups, 199 patients treated with SGLT2 inhibitors (empagliflozin, dapagliflozin, and luseogliflozin) and 80 non-treated patients. All patients were observed for 30 months. The degree of improvement in renal function was evaluated by dividing the patients into G3a, G3b, and G4 stages of chronic kidney disease (CKD) severity at the start of the study. The results revealed no differences in blood pressure or HbA1c between the two groups. In all renal function severities, there was a significant increase in serum creatinine levels in the non-treated group than in the SGLT2 inhibitor-treated group. The change in serum creatinine levels of all three drugs showed an invariant trend, with no significant differences between the three groups. Female patients ($P<0.05$) and those with high HDL-C ($P<0.05$) had a trend toward improvement in serum creatinine levels after six months of treatment with SGLT2 inhibitors.

The present results suggest that SGLT2 inhibitors suppress the progression of diabetic nephropathy regardless of the severity of renal function.

【著書・訳書・総説】

佐々木英久（分担執筆著書）

第58章「副甲状腺機能異常症（亢進症/低下症）」，第60章「アジソン病」，第61章「アルドステロン症」，第62章「尿崩症」，第63章「その他の内分泌系疾患」，第64章「糖尿病」，第65章「脂質異常症」，第66章「高尿酸血症・痛風」

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【その他】

溝口優，教材「肺炎の薬物治療」，学研メディカルサポート「看護師の特定行為研修」，東京，2022.9

【学会発表】

高野樹奈，座間未来，伊藤奈津江，山崎章江，土屋大樹，富田健二，富田勲，溝口優，三浦剛，佐々木英久：調剤薬局の在宅医療における保険点数の妥当性について．第55回日本薬剤師会学術大会，仙台，2022.10

小林悠大，藤澤遼，玉井祐馬，濱島健斗，溝口優，三浦剛，長澤宏之，佐々木英久：4種DPP-4阻害薬投与糖尿病患者の肝腎機能が血糖降下作用に与える影響について．第55回日本薬剤師会学術大会，仙台，2022.10

齋藤凌，溝口優，三浦剛，武田美佳，大橋綾子，佐々木英久：高齢者糖尿病患者に対する血糖コントロール目標値の適正調査について（第二報）．第55回日本薬剤師会学術大会，仙台，2022.10

田原知華，中村夢伽，玉井祐馬，濱島健斗，溝口優，三浦剛，長澤宏之，佐々木英久：糖尿病腎症患者に対する経口血糖降下薬SGLT2阻害薬の投与効果（第二報）．第55回日本薬剤師会学術大会，仙台，2022.10

玉井祐馬，田原知華，濱島健斗，溝口優，三浦剛，佐々木英久，長澤宏之：糖尿病腎症患者に対するSGLT2阻害薬の投与効果の比較（第二報）．第55回日本薬剤師会学術大会，仙台，2022.10