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The 11th Joint Seminar on Biomedical Sciences

Toho University, Kunming Medical University, Chiang Mai University and Prince of Songkla University

Variety and Controversy to Creativity

November 13-15, 2019

Deevana Plaza Krabi Aonang,
Krabi, Thailand

11th Joint Seminar on Biomedical Sciences

(11thJSOBMS)

"Variety and Controversy to Creativity"

November 13–15, 2019

Deevana Plaza Aonang, Krabi, Thailand

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Welcoming Speech
by PSU President

Asst. Prof. Dr. Niwat Keawpradub
President, Prince of Songkla University

Honorable Keynote Speakers,
Distinguished Participants,
Colleagues and Friends,

On behalf of Prince of Songkla University, it is my great pleasure to welcome you all to the beautiful province of Krabi and to the 11th Joint Seminar on Biomedical Sciences "Variety and Controversy to Creativity," held here at Deevana Plaza Krabi Aonang.

As we know, this seminar is a milestone event among Kunming Medical University, Toho University, Chiang Mai University and Prince of Songkla University, with one of its key roles to establish and maintain close collaboration, both academic and cultural with institutions within our region. Therefore, I am certain that this 11th Joint Seminar on Biomedical Sciences is a great opportunity for all participating physicians, researchers, and lecturers to share knowledge and exchange experiences in their specializations.

The contribution and engagement from all of us is essential for the continuity of this joint seminar and highlight the importance of exchanging and sharing up-to-date experiences in order to develop our healthcare service, educational system, as well as our research collaboration.

I would like to welcome you all again to this auspicious joint seminar, and I sincerely hope that you will enjoy the event coupled with your stay here in the beautiful scenery of Krabi.

Thank you.

Welcome Remarks
by Dean

Assoc. Prof. Dr. Nimit Worakul
Dean, Faculty of Pharmaceutical Sciences,
Prince of Songkla University

Dear Colleagues and Friends,

On behalf of the Faculty of Pharmaceutical Sciences, Prince of Songkla University, it is with great pleasure that I welcome you to the 11th Joint Seminar on Biomedical Sciences. This seminar has a rich history of international collaboration among Toho University, Kunming Medical University, Chiang Mai University, and Prince of Songkla University, and we look forward to deepening these relationships and connections. We are confident that collaborations like this can build a better tomorrow.

The theme of the 2019 seminar is "Variety and Controversy to Creativity," an exciting topic engaging both the researcher and the healthcare provider. Topics have been chosen to address issues and ideas among all disciplines represented, including medicine, pharmaceuticals, nursing, and sciences. Symposium topics such as aging, cancer, and environmental-related issues have been selected to create stimulating discussion which leads to positive advancement in these areas. Our keynote speakers have prepared lectures on innovative topics, and we welcome contributions of papers for both oral and poster presentation. Our hope is that you leave this event feeling reenergized and ready to invest your newfound knowledge and rekindled passion in the biomedical field.

Finally, I would like to welcome you all again and thank you very much for coming.

Welcome Remarks
by Dean

Assoc. Prof. Puttisak Puttawibul, M.D.
Dean, Faculty of Medicine, Prince of Songkla University

It is my great honor and pleasure to extend a very warm welcome on behalf of Faculty of Medicine to all honorable delegates, from Kunming Medical University Toho University Chiang Mai University and Prince of Songkla University, to this conference.

The 11th Joint Seminar on Biomedical Sciences (11th JSOBMS) offers us the occasion to create research and share ideas for all researchers, also to update and discuss their works. It is also an opportunity for future research networking and technological collaboration.

I would also like to express my deep appreciation to our distinguished guest speakers and all participants. I trust that The 11th Joint Seminar on Biomedical Sciences (11th JSOBMS) will be a great benefit for all participants. In closing, I want to mention that we have arranged for our participants to experience Thai cuisine at its best, in Southern Thailand. We have also scheduled an excursion to four Islands, all the most beautiful islands in Krabi that you will find enjoyable and relaxing. Again, thank you for your attendance.

Program Schedule

11th Joint Seminar on Biomedical Sciences (11thJSOBMS) **"Variety and Controversy to Creativity"**
13–15 November 2019 Deevana Plaza Aonang, Krabi, Thailand

Symposium Topics:

1. Cancer
2. Complementary and alternative medicine
3. Infectious diseases
4. Health informatics/Big data/ Bioinformatics
5. Medical innovation and technology
6. Environmental-related issue/Marine biology
7. Aging societies
8. Health Science Education

A. Tentative program

Day 0	Tuesday, 12 November 2019 (Pre-Seminar)	
18:00	**Dinner on arrival at Deevana Plaza Aonang (Coupon)**	*(dress code: casual)*

Day 1	Wednesday, 13 November 2019
08:00–08:20	**Registration**
08:20–08:45	**Welcome remarks** Assoc. Prof. Puttisak Puttawibul and Assoc. Prof. Dr. Nimit Worakul Dean, Faculty of Medicine and Faculty of Pharmaceutical Sciences, PSU
	Opening speech Asst. Prof. Dr. Phichit Rerngsangvatana Vice President, Prince of Songkla University (PSU)
08:45–09:00	**Opening Ceremony**
09:00–09:30	**Keynote Lecture: Cancer** Differential Cellular Response for the BRCA1-Defective and BRCA1-Competent Breast Cancer Cells to Anticancer Ruthenium(II)-AreneComplex, RAPTA-EA1 Assoc. Prof. Dr. Adisorn Ratanaphan (PSU)

	Symposium I: Cancer **Chairpersons:** Dr. Tavitiya Sudjaritruk (CMU) & Dr. Ninghui Zhao (KMU)
09.30–09.50	Economic Evaluation of Temozolomide for Newly Diagnosed Glioblastoma in Thailand according to MGMT promoter methylation Asst. Prof. Dr. Thara Tunthanathip (PSU)
09.50–10.10	Recurrence Analysis in Endometrial Cancer Asst. Prof. Dr. Chalong Cheewakriangkrai (CMU)
10.10–10.30	**Coffee break**
	Symposium I: Cancer (cont.)
10.30–10.50	Fluvastatin Prevents Lung Adenocarcinoma Bone Metastasis by Triggering Autophagy Asst. Prof. Dr. Zuozhang Yang (KMU)
	Symposium II: Complementary and alternative medicine **Chairpersons:** Prof. Yukiko Katagiri (TOHO) & Prof. Dr. Teerapol Srichana (PSU)
10.50–11.10	Application of Complementary and Alternative Medicine in Common Ear, Nose and Throat (ENT) Disorders Asst. Prof. Dr. Warangkana Arpornchayanon (CMU)
11.10–11.30	Metabolomics Approach towards the Stability of Andrographis Herb Assoc. Prof. Dr. Anuchit Plubrukarn (PSU)
11.30–11.50	Discovery of anti-HIV diterpenoids from medicinal plants of Thymelaeaceae and Euphorbiaceae families Assoc. Prof. Wei Li (TOHO)
11.50–12.10	Comparison of Orthosis and Exercise Training for Adolescent Idiopathic Scoliosis Assoc. Prof. Dr. Wei Liu (KMU)
12.10–13.30	**Lunch and networking**
	Keynote Lecture: Infectious diseases
13.30–14.00	Novel Technologies and Diagnostic Methods in AMR Era Prof. Kazuhiro Tateda (TOHO)
	Symposium III: Infectious diseases **Chairpersons:** Dr. Hao Zou (KMU) & Asst. Prof. Dr. Chalong Cheewakriangkrai (CMU)
14.00–14.20	Severe Dengue infection: an experience in Songklanagarind Hospital Assoc. Prof. Kamolwish Laoprasopwattana (PSU)
14.20–14.40	Subclinical peripheral arterial disease among Thai adolescents living with HIV Dr. Tavitiya Sudjaritruk (CMU)
14.40–15.00	Trends and Predictors of internalized and personal stigma among HIV and non-HIV patients and occupational stigma among healthcare providers in South of China Assoc. Prof. Jing Li (KMU)

15.00–15.30	**Coffee break**
	Symposium IV: Environmental-related issue/Marine biology **Chairpersons:** Assoc. Prof. Dr. Anuchit Plubrukarn (PSU Rx) & Assoc. Prof. Atsuko Saito (TOHO)
15.40–16.00	How scientific professionals solved the complicated little known health problems associated with the lethal box jellyfish: 2008–2019. Prof. Dr. Lakkana Thaikruea (CMU)
16.00–16.20	Quality of Life–Environmental Impact Level: Case study of people living in the Khun Tat Wai and Pa Ching Sub-district Administrative Organizations, Amphoe Chana, Songkhla Province Asst. Prof. Dr. Thitiworn Choosong (PSU)
16.20–16.40	Polycyclic Aromatic Hydrocarbons in Marine Environments of the Pacific Coast of Japan: Influence of the 2011 Tsunami and Fire Asst. Prof. Dr. Mayu Onozato (TOHO)
16.40–17.00	Effects of ground uplift, constructionofan artificial tidal flat and tsunami seawalls on marine life and local residents following the 2011 Great East Japan Earthquake Prof. Kenji Okoshi (TOHO)
18.30–20.30	**Welcome Dinner** *at Deevana Plaza Hotel* *(dress code: smart casual)*

Day 2	**Thursday, 14 November 2019**
	Keynote Lecture: Medical innovation and technology
08.30–09.00	Mission to the Moon: Building up Health Tech Innovation Ecosystem in Chiang Mai Asst. Prof. Dr. Surat Tanprawate (CMU)
	Symposium V: Medical innovation and technology **Chairpersons:** Prof. Yuichi Hori (TOHO) & Asst. Prof. Dr. Thitiworn Choosong (PSU)
09.00–09.20	A Nutraceutical for Cancer Prevention Made from Garcinia cowa Leaf Extract with Rice Bran Oil Assoc. Prof. Dr. Pharkphoom Panichayupakaranant (PSU)
09.20–09.40	Evaluation of the myocardial microcirculation and systolic function in patients with Ischemia and No Obstructive Coronary Artery Disease (INOCA) by myocardial contrast echocardiography and speckle tracking imaging Asst. Prof. Dr. Yu Wang (KMU)
09.40–10.00	Nanoparticles-based microfluidic chips for liquid biopsy Dr. Soracha (Thamphiwatana) Dechaumphai (PSU)
10.00–10.20	**Coffee break**

	Keynote Lecture: Health informatics
10.20–10.50	Cancer trend in Thailand Assoc. Prof. Hutcha Sriplung (PSU)
	Symposium VI: Health informatics **Chairpersons:** Chairpersons: Assoc. Prof. Dr. Pharkphoom Panichayupakaranant (PSU Rx) & Assoc. Prof. Wei Li (TOHO)
10.50–11.10	Medical informatics for improvement on health working process in Chiangmai University hospital Asst. Prof. Krit Khwanngern (CMU)
11.10–11.30	Gene expression analysis for drug repursposing in osteosarcoma Dr. Rawikant Kamolphiwong (PSU)
11.30–11.50	Influence of social support network on drug use among clients of methadone maintenance treatment clinics in Kunming Assoc. Prof. Ling Shen (KMU)
11.50–13.00	**Lunch and networking**
	Keynote Lecture: Aging societies
13.00–13.30	The application of environmental interventions in the prevention of falls in community-dwelling older people Dr. Lei Wang (KMU)
	Symposium VII: Aging societies **Chairpersons:** Prof. Dr. Lakkana Thaikruea (CMU) & Prof. CAI Le (KMU)
13.30–13.50	Synthesis and Evaluation of new Coumarin Derivatives as Acetylcholinesterase Inhibitors Assoc. Prof. Dr. Luelak Lomlim (PSU)
13.50–14.10	Integrated Care for Dementia: A Geriatric Medical Center Model Asst. Prof. Surat Tanprawate (CMU)
14.10–14.30	Aging and ovarian function Prof. Yukiko Katagiri (TOHO)
14.30–14.50	Association among activities of daily living, instrumental activities of daily living and health-related quality of life in Yi elderly of Yunnan province Dr. Lingyun Ran (KMU)
14.50–16.30	**Posters session** *(and Coffee break)*
17.30–20.30	**Farewell dinner** *at Aonang Villa Hotel*

Day 3	Friday, 15 November 2019
	Symposium VIII: Health Science Education **Chairpersons:** Assoc. Prof. Kamolwish Laoprasopwattana (PSU) & Asst. Prof. Dr. Warangkana Arpornchayanon (CMU)
09.00–09.20	Transforming Health Professional Education: PSU Experience Asst. Prof. Dr. Kanyika Chamniprasas
09.20–09.40:	Report on the usage of the video lecture delivery (VLD) system Prof. Naoki Hiroi (TOHO)
09.40–10.00	Dynamic Risk Assessment System for Drug User in Community-Based Drug Rehabilitation Program in Yuxi China Assoc. Prof. Wei Liu (KMU)
10.00–10.20	**Poster award announcement and closing ceremony**
10.20–10.40	**Coffee break**
10.40–11.40	**Panel discussion on future collaboration & research *(only representative)***
11.00–11.45	**Business meeting (Representative of Denka Seiken)**
12.00–13.00	**Luncheon networking**
	Special event
13.00	Excursion (For pre-registered guests)

History of Collaboration among
KMU, TU, PSU and CMU

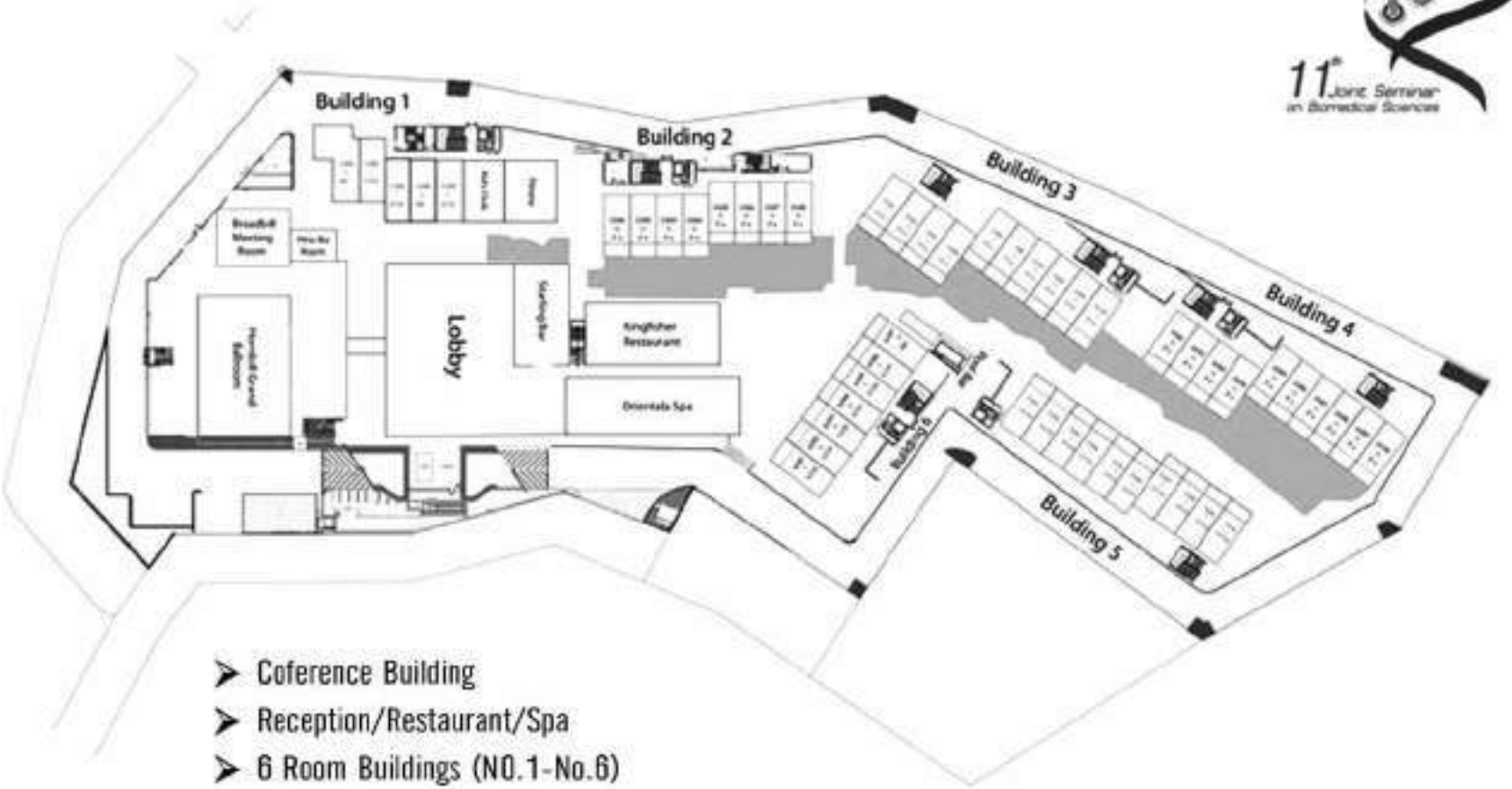
October 22–23, 1993	The 1st Joint Seminar on Pharmacological Research (PSU/TU) in **Phuket, Thailand**
October 13, 1997	The 2nd Joint Seminar on Pharmacological Research (PSU/TU) at PSU campus in **Hat Yai, Songkhla, Thailand**
October 14–16, 2001	The 3rd Joint Seminar on Biomedical Science between PSU and TU based on MOU at TU campus in **Tokyo, Japan**
October 11–12, 2004	The 4th Joint Seminar on Biomedical Science among PSU, CMU, KMU and TU in **Chiang Mai, Thailand**
October 26–27, 2006	The 5th Joint Seminar on Biomedical Science among PSU, CMU, TU and KUMS in **Kunming, P.R. China**
October 12–13, 2009	The 6th Joint Seminar on Biomedical Science among PSU, CMU, KMU and TU in **Tokyo, Japan**
October 13–16, 2011	The 7th Joint Seminar on Biomedical Science among KMU, TU, CMU and PSU in **Hat Yai, Songkhla, Thailand**
October 14–17, 2013	The 8th Joint Seminar on Biomedical Science among PSU, CMU, TU and KMU at Kunming Medical University, **P.R. China**
November 4–6, 2015	The 9th Joint Seminar on Research Clusters: A Step Toward Future Collaboration among TU, KMU, PSU and CMU in **Chiang Mai, Thailand**
November 15–17, 2017	10th Anniversary Joint Seminar on Biomedical Sciences: "From Cluster to Fusion/Creation and Beyond" among CMU, PSU, KMU and TU in **Tokyo, Japan**

11th Joint Seminar on Biomedical Sciences (11thJSOBMS)

"Variety and Controversy to Creativity"

DEEVANA PLAZA
Krabi-Aonang

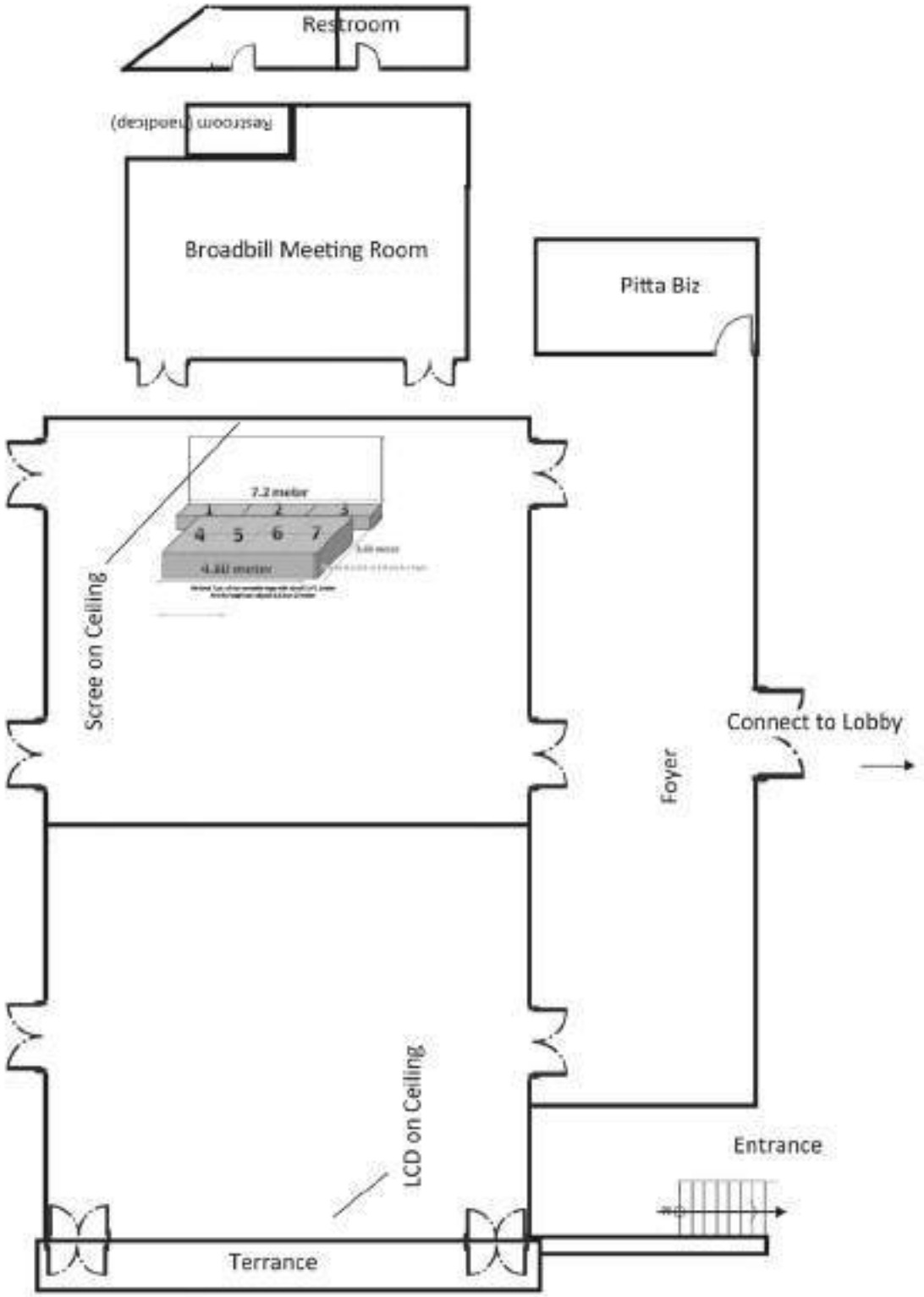
11th Joint Seminar in Biomedical Sciences



- Coference Building
- Reception/Restaurant/Spa
- 6 Room Buildings (NO.1-No.6)
- Fitness Center and Kids Corner
- 3 Regular Swimming Pools and 1 Kid Pool

Floor plan

11th Joint Seminar on Biomedical Sciences (11th JSOBMS)



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Abstracts

for Oral presentation

11th Joint Seminar on Biomedical Sciences
(11th JSOBMS)
"Variety and Controversy to Creativity"

Kunming Medical University
Chiang Mai University
Toho University
Prince of Songkla University

JHSMR Journal of Health Science and Medical Research

Fluvastatin Prevents Lung Adenocarcinoma Bone Metastasis by Triggering Autophagy

Yang Zuozhang

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Abstract

Objective: to investigate the relationship between autophagy induced by Fluvastatin through the P53/AMPK/mTOR pathway and bone metastasis of human lung adenocarcinoma cells, and the changes of proteins and genes related to the pathway and autophagy through cell and animal experiments.

Material and Methods: Wound healing assay and Transwell migration assay were used to evaluate the effect of fluvastatin on cell migration of SPC-A-1 and A549. The influence of fluvastatin on the invasion of SPC-A-1 and A549 cells of lung cancer was detected by Matrigel invasive assay. To study the effect of fluvastatin on bone metastasis of SPC-A-1 cells of lung cancer in nude mice. By Western Blot detecting autophagy marker proteins: LC3Ⅱ/Ⅰ and Beclin 1 expression; The formation of autophagosomes was detected by fluorescent staining with single MDC. By transfection with pgfp-lc3 plasmid, SPC-A-1 and A549 cell lines stably transferred pgfp-lc3 were screened and stimulated with fluvastatin. GFPLC3 fusion protein was used to tracer the formation of autophagosomes under fluorescence microscope. Autophagy inhibitors were used to inhibit the autophagy activity of spc-a-1 and A549 cells to test whether fluvastatin had lost its inhibitory effect on the migration and invasion of lung cancer cells. Tumor autophagy was inhibited in nude mice to observe whether fluvastatin inhibited the bone metastasis of lung cancer. After the treatment of SPC-A-1 and A549 cells with fluvastatin, the P53 mRNA was detected by RT-PCR and the protein expression level of P53 was detected by Western Blot, and the expression changes of LC3 and beclin-1 were detected at the same time. P53 inhibitor and siRNA were used to interfer the expression of P53 to observe whether it was accompanied by the expression changes of LC3 and beclin-1. Western Blot was used to determine whether fluvastatin inhibited mTOR phosphorylation to determine whether fluvastatin induced autophagy was mtor-dependent. Mevalonate was added to observe whether fluvastatin could antagonize mTOR inhibition. Western Blot was used to detect whether fluvastatin could promote the activation of RAS, phosphorylation of PI3K, erk1/2,

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AMPK, Akt, bcl-2, eIF2 alpha protein, and up-regulated expression of Agt12 and P53 genes. SiRNA was used to interfere PI3K, Akt, AMPK, RAS, erk1/2, bcl-2, eIF2 alpha, Agt12 and P53 genes, respectively, to detect the influence of these genes on fluvastatin induced autophagy, and to clarify the importance of these genes in fluvastatin induced autophagy. The method of autophagy detection is the same as above. Through the use of P53 inhibitor pifithrin-alpha (PFT alpha) and siRNA interference with P53 expression, the changes of AMPK and mTOR expression levels were observed to clarify the mutual regulatory relationship among the three.

Results: fluvastatin can inhibit the migration, invasion and growth of lung adenocarcinoma cells in vitro, inhibit bone metastasis in mice, and induce autophagy and up-regulate the expression of P53. The use of autophagy inhibitor 3-ma and P53 inhibitor PFTa can reduce the ability of fluvastatin to resist bone metastasis in vivo and in vitro. Among them, the down-regulated expression of P53 can reduce the level of fluvastatin induced autophagy.

Conclusion: fluvastatin can inhibit bone metastasis of human lung adenocarcinoma cells in vitro and in vivo, and the mechanism may be related to autophagy induced by P53/AMPK/mTOR pathway.

Keywords: fluvastatin, lung adenocarcinoma, bone metastasis, autophagy

JHSMR Journal of Health Science and Medical Research

Comparison of Orthosis and Exercise Training for Adolescent Idiopathic Scoliosis

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Abstract

Objective: To compare the effects of spinal orthosis and exercise training on patients with adolescent idiopathic scoliosis (AIS), and their impact on psychological status and quality of life.

Material and Methods: From July, 2017 to February, 2018, 55 AIS patients aged ten to 16 years were enrolled. According to the individual's choice, they were divided into exercise group (n = 25) and orthosis group (n = 30). The Cobb angle, apex vertebral rotation (AVR), trunk shift (TS) and apex vertebral translocation (AVT) were measured before intervention, three months and six months after intervention. They were also evaluated with Scoliosis Research Society Patient Questionnaire-22 (SRS-22) before intervention and six months after intervention.

Results: Six months after intervention, the scores of function/activity level, pain, self-image/appearance and treatment satisfaction were better in the exercise group than in the orthosis group (t > 2.137, P < 0.05). Three months and six months after intervention, the Cobb angles were significantly smaller in both groups (t > 4.461, P < 0.001); six months after intervention, the Cobb angle was smaller in the orthosis group than in the exercise group (t = 2.548, P < 0.05). Three months and six months after intervention, the TS, AVR and AVT were better in both groups (t > 2.338, P < 0.05); six months after intervention, they were better in the orthosis group than in the exercise group (t > 2.259, P < 0.05).

Conclusion: Single exercise training has good therapeutic effect on AIS patients with Cobb angle ranged 25°~40°, and the improvement in the aspect of psychological status and survival quality is better than that of orthotics treatment, however, but improvement in the aspect of deformity indexes of idiopathic scoliosis is inferior to that of orthotics treatment.

Keywords: adolescent idiopathic scoliosis, orthosis, exercise training, psychological status

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Trends and Predictors of Internalized and Personal Stigma Among HIV and Non-HIV Patients and Occupational Stigma Among Healthcare Providers in South of China

Jing Li[1], Jing You[2], Tian Lu[3], Sawitri Assanangkornchai[4] and Virasakdi Chongsuvivatwong[4]

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Abstract

Background: HIV/AIDS-related stigma is a major barrier for equal access to healthcare service. The aim was to explore trends and predicators of internalized, personal and occupational stigma among HIV, non-HIV patients and healthcare providers.

Material and Methods: A cross-sectional study was conducted from January to September 2015 in Kunming, China. The parallel scales (internalized and personal stigma scales) including two factors: guilt/blaming and being refused/refusing were used among HIV and non-HIV patients, respectively. Another scale (occupational stigma) containing three factors: blaming, professionalism and egalitarianism was conducted among healthcare providers. All of them were ranked from 1 "strong disagree" to 4 "strong agree", and responses were summed to obtain three total scores (M±SD). Multiple linear regressions were conducted to explore time and associations with socio-economic factors separately.

Results: Scores of internalized, personal and occupational stigmas were 25.7(5.6), 23.4(4.4) and 32.3(8.8). There was a significant change of occupational stigma by time among healthcare providers. However, the trends of internalized and personal stigma were not significant. Age, ethnic group, marital status and occupation were significantly associated with internalized stigma among HIV patients. Ethnic group, marital status and household income were associated with feeling "refused", while gender, marital status, occupation and education were associated with feeling "guilty". For non-HIV patients, religious affiliation, marital status and education were significantly associated

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with personal stigma. Marital status and education were associated with "refusing", while religious affiliation, marital status, education and household income were significantly associated with "blaming". Age, gender and education were significantly associated with occupational stigma.

Conclusion: Occupational stigma was tended to change by time compared to internalized and personal stigma, which appeals to interventions among healthcare providers. Additionally, marital status and education level were the stronger predictors for reduction of HIV/AIDS stigma toward service equality.

Keywords: Internalized stigma, Personal stigma, Occupational stigma, Marital status, Education

JHSMR Journal of Health Science and Medical Research

Evaluation of the Myocardial Microcirculation and Systolic Function in Patients with Ischemia and No Obstructive Coronary Artery Disease (INOCA) by Myocardial Contrast Echocardiography and Speckle Tracking Imaging

Yu Wang, Ying Rao, Wenjuan Song, Xuejuan Ma, Liping Liu, Ying Gu, Yue Sun and Yue Zhao

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Abstract

Objective: To investigate the myocardial microcirculation and systolic function in patients with ischemia but no obstructive coronary artery disease by myocardial contrast echocardiography (MCE) and two-dimensional speckle tracking echocardiography (2D-STE).

Material and Methods: Forty patients with chest pain in cardiology, but no obstructive coronary artery and with diagnosis as INOCA were included in the case group, who all were enrolled from the First Affiliated Hospital of Kunming Medical University from February 2018 to March 2019, and other 35 healthy individuals were randomly assigned to control group. All subjects underwent MCE and 2D-STE in order to obtain myocardial contrast score (MCS) and left ventricular global longitudinal peak systolic strain (GLS).

Results: Compared with the control group, E value, E/A value decreased in INOCA group, the difference was statistically significant ($P < 0.05$). GLS was significantly reduced in INOCA group compared to control group ($P < 0.05$). MCS decreased in INOCA group and the difference was statistically significant ($P < 0.05$). Bland-Altman plot analysis demonstrated that GLS of left ventricular myocardium had good inter-observer and intra-observer consistency.

Conclusion: MCE combined with the 2D-STE can evaluate the changes of myocardial microcirculation and systolic function sufficiently in INOCA patients and have the prospect of clinical application.

Keywords: Ischemia and no obstructive coronary artery disease, Myocardial contrast echocardiography, Speckle tracking imaging, Microcirculation

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Influence of Social Support Network on Drug Use Among Clients of Methadone Maintenance Treatment Clinics in Kunming

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Abstract

Background: To explore drug use behavior of clients attending Methadone Maintenance Treatment (MMT) programs and its relationship with the clients' social network characteristics by cross-sectional study. It visited 324 consecutive MMT clients in four MMT clinics in Kunming, China

Material and Methods: A structured, self-completed questionnaire on background characteristics and existing social network. Current drug use was assessed by urine test for opiate metabolites after questionnaire visiting with every MMT client. All data analyses were performed using the R language. The association between client's social network characteristics and their own current drug use behavior is analysed using multiple logistic regression adjusting for socio-demographic characteristics. Adjusted odds ratios (AOR) with 95% confidence intervals (CI) are obtained to give the strength of the associations

Results: 324 MMT clients reported having 1,275 members in their social network. MMT clients were more likely to concurrently use heroin while attending MMT if their social network had any of the following characteristics: any member had a high level of influence on them (AOR = 6.47, 95% CI = 2.86,14.65) and any member joined them in using drugs (AOR = 1.94, 95% CI = 1.04,3.63). Having a social network member who could provide emotional support (AOR = 0.11, 95% CI = 0.03,0.35), and having a social network member with a high level of closeness (AOR = 0.28, 95% CI = 0.09, 0.90) were associated with a decreased odds of heroin use.

Conclusion: Among clients attending MMT clinics in Kunming, social networks who could provide MMT clients with emotional support and a close relationship were significant factors for reducing the risk of concurrent drug use. Behavioral interventions should address the role of family and social network members in providing support to these clients.

Keywords: social, support, network, drug use, MMT

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The Application of Environmental Interventions in the Prevention of Falls in Community-Dwelling Older People

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Abstract

Fall is not an independent disease. It is a common and often serious symptom of senile syndrome. It is a result of the decline in physiological function of the elderly and the interaction between chronic diseases and the environment. Environmental intervention is an important intervention in occupational therapy to prevent falls. There is no uniform standard for home modification in falls prevention, but some researchers have been exploring and researching this area over the years. This review summarizes the current research progress of environmental interventions to prevent falls in the community in order to identify the existing problems of environmental interventions and the new directions of falls prevention. This will also help to explore the establishment of home-based environment modification standards, to develop comprehensive strategies of falls prevention, and in the future to promote the development of occupational therapy in preventing falls.

Keywords: environmental interventions, falls, fall prevention, community, the elderly

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Association Among Activities of Daily Living, Instrumental Activities of Daily Living and Health-Related Quality of Life in Yi Elderly of Yunnan Province

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Abstract

Background: The health-related quality of life (HRQoL) of the elderly population of Yi ethnic minority, which is the seventh largest nationality in China, has been rarely reported. This study was designed to explore the HRQoL of the elderly Yi ethnicity and association between their HRQOL and functional abilities.

Material and Methods: A total of 291 Yi ethnic residents were randomly recruited from 12 rural counties in Yunnan province and divided into different age groups. Local residents in Yunnan province and the elderly from Hangzhou were the counterparts. The MOS 36-Item Short Form Health Survey (SF-36), activities of daily living (ADL), instrumental activities of daily living (IADL) scales were utilized to evaluate the HRQoL and functional ability. One-way ANOVA was used to statistically compare the ADL and IADL among different age groups. The influential variables on HRQOL were analyzed by multiple linear regression analysis. Pearson correlation analysis was used to analyze the association among HRQoL, ADL and IADL.

Results: The HRQoL of the elderly Yi minority was significantly lower than those of local residents in Yunnan province and the elderly counterparts in Hangzhou. The IADL ability of the elderly Yi minority was low, whereas they could perform most items of ADL. ADL, IADL, and education level were positively associated with HRQoL, whereas age, chronic diseases, and the frequency of medication use were negatively correlated with HRQoL.

Conclusion: The HRQoL and functional capacity of the elderly Yi ethnic minority were lower compared with their counterparts in Yunnan province and Hangzhou. The low level of IADL indicated that the elderly Yi participants had a high risk of cognitive impairment. Much attention should be diverted to influential factors of the HRQoL.

Keywords: Health-related quality of life, Elderly, Yi ethnic minority, ADL, IADL

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Dynamic Risk Assessment System for Drug User in Community-Based Drug Rehabilitation Program in Yuxi China

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Abstract

Background: Dynamic risk assessment system for drug user in the context of mobile internet has been established to effectively assess risk status of drug users and timely respond in community-based rehabilitation program. We aimed to test the system in terms of App function, acceptance and satisfaction of user.

Material and Methods: A rapid assessment was conducted with key informant interview, real-time testing the App and existing data in the system in Yuxi Yunnan China.

Results: The system is functioning well and the App is acceptable and easy to use. 265 clients registered in the program, in which 46.4% is low risk, 21.5% middle risk and 32.1% high risk. The risk score measured by APP is a crucial element, which is consisted of historical records of criminal detention and performance of community-based rehabilitation for participants in the program. The historical background includes number of detentions and length of criminal detention, accounting for 30% risk score; while community-based rehabilitation performance accounting for 70% in which methadone taking days and urinate test are core indicators. Dynamic risk score ranges 0-100 points, the low risk level is 0-40 points, 41-65 points for middle risk and 66-100 points for high risk.

Conclusion: The Dynamic risk assessment system not only facilitates multi-sectoral collaboration to prevent and control risk of drugs and social problems, but also encourages participants to mediate risk behaviors, reduce harms and stay clean. Further improvement of the APP is still in progress. The APP has drawn attention to experts from domestics and international for field-study.

Keywords: risk assessment, community rehabilitation, APP, drugs

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Recurrence Analysis in Endometrial Cancer

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Abstract

Recurrence of cancer after treatment is one of the major health problems in women with gynecologic malignancy. Most patients with cancer recurrences have a poor prognosis. Understanding the patterns and prognostic factors that may predict early development of recurrent disease is very important and may guide a choice of adjuvant therapy subsequently.

Endometrial cancer is the most common gynecological malignancy in western countries, however, the number of patients is increasing in Asian populations. After primary treatment, about 10.0–15.0% of tumors relapse and the majority (80.0–90.0%) of recurrences take place within 2–3 years. We demonstrate some clinicopathological factors that associated with recurrent disease from cancer database analysis that could implement for clinical cancer care and surveillance.

Keywords: endometrial cancer, recurrences analysis, prognostic factors

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Application of Complementary and Alternative Medicine in Common Ear, Nose, and Throat (ENT) Disorders

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Abstract

Background: The use of complementary and alternative medicine (CAM) seems to benefitfor various ENT diseases, however scientific proof is still needed.A number ofrandomized controlled trials (RCT) have beenconducted in the Pharmacology Department since 2012.

Objective: To collectthe clinical efficacy of CAM used forcommon ENT disordersin recentRCTs fromthe Pharmacology Department, CMU

Material and Methods: Retrospective data collection of 5 RCT studies from 2012 to 2019 was done, involving 298 patientsof acute rhinitis, allergic rhinitis (AR), post-sudden sensorineural hearing loss (SNHL), and tinnitus.

Results: For acute rhinitis, patients who inhaled hot steam alone or with shallot or eucalyptus felt significant reliefof nasal congestion, compared to pre-inhalation. Greatest improvementoccurred after shallot inhalation but nasal airflowresistanceremained unchanged. For AR, when oral shallot was added to cetirizine,the use of shallot (3 g per day) for 2 weeks significantly improved sneezing, itchy nose and eyescompared to placebo.Likewise,reduction of nasal symptoms especially itchy nose and sneezing scores were greater in Lingzhi extract (1.4 g per day) than placebo in AR patients. For post-sudden SNHL,improvement of hearing thresholds (>10 dB) was found in 38.5% of patients received 12 sessions of electroacupuncture (EA) within 4 weeks, compared with 8.7% of controls. Tinnitusscores werestatistically decreased after EA.

Conclusion: Clinical effectiveness of CAM had been shown in RCT studies for acute rhinitis, AR, post-sudden SNHL, andtinnitus, especially whenused as adjunctive treatment.

Keywords: complementary and alternative medicine, acute rhinitis, allergic rhinitis, tinnitus, sensorineural hearing loss

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Subclinical Peripheral Arterial Disease Among Thai Adolescents Living with HIV

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Abstract

Background: To identify prevalence and associated factors of subclinical peripheral arterial disease (PAD), using non-invasive measurements, among Thai perinatally HIV-infected adolescents (PHIV).

Material and Methods: A multicenter, cross-sectional study was conducted in two pediatric HIV centers in Thailand (Chiang Mai and Bangkok). PHIV aged 10-25 years who received antiretroviral therapy (ART) for >12 months, and age- and sex-matched HIV-uninfected controls were enrolled (ratio 3:1). PAD was assessed by ankle-brachial index (ABI) and cardio-ankle vascular index (CAVI). ABI≤0.9 in any extremities indicates arterial occlusion, whereas CAVI≥9.0 reflects arterial stiffness. PHIV having abnormal ABI and/or CAVI without clinical symptoms of PAD were defined as having subclinical PAD. Logistic regression analysis was performed to identify associated factors of subclinical PAD in our PHIV.

Results: During January to March 2017, 150 HIV-infected and 50 HIV-uninfected adolescents were enrolled. The median age was 18.0 years (IQR:14.7-20.5), and half (50.0%) were female. Thirty-one adolescents (16.0%) were overweight, 25 (13.0%) had systemic hypertension, 3 (2.0%) had hyperglycemia, and 41 (21.0%) had hypo-HDL cholesterolemia. Among PHIV, 65 (43.0%) received protease inhibitor-based regimen at enrollment, and median ART duration was 12.8 years (IQR:9.2-14.2). The median current CD4 T-cell was 28.0% (IQR:24-32.0%), and 82.0% had

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HIV RNA <50 copies/mL. Subclinical PAD was documented in 20 adolescents (10.0%; 95.0%CI:6–15.0%), of whom 17 (11.0%; 95%CI:7–18.0%) were HIV–infected, and 3 (6.0%; 95%CI:1–17.0%) were HIV–uninfected adolescents (P=0.28). In multivariable analysis, female sex and hyperglycemia were significantly associated with subclinical PAD in our HIV–infected adolescents (P<0.05).

Conclusion: Despite a low prevalence of subclinical PAD in our Thai PHIV, serial monitoring of arterial diseases should be considered, particularly among adolescents with risk factors.

Keywords: adolescent living with HIV, ankle–brachial index; arterial occlusion, arterial stiffness, cardio–ankle vascular index, peripheral arterial disease

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How Scientific Professionals Solved the Complicated Little Known Health Problems Associated with the Lethal Box Jellyfish: 2008–2019

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Abstract

Background: In 2008 the situation of the lethal box jellyfish was complicated for several reasons, including the refusal to acknowledge the box jellyfish envenomation's existence, conflict of interest, misdiagnosis, politically sensitivity, traditional treatments which could lead to death, and the lack of effective first aid, laboratory facility and expert. Communities and stakeholders play a vital role in dealing with the stings as stings can kill people within 2–10 minutes.

Objective: 1) To prove the existence of lethal box jellyfish; 2) To assess the magnitude of problem; 3) To develop knowledge of detection, treatment, and prevention; 4) To implement prevention measures.

Material and Methods: Two medical epidemiologists formed a leading team to investigate and develop an innovative solution to deal with problem. The solution based around 5 key strategies. These were: knowledge sharing, early warning and rapid response, effective intervention, ensuring sustainability, and evidence-based management.

Results: In the period from 2008 to 2019, the study achieved the following outcomes: lethal jellyfish envenomation affirmation, establishment of toxic jellyfish networks and surveillance systems, development of new knowledge and innovation (stinger net, vinegar station, educational warning signs, vacuum sticky tape technique for identification of toxic jellyfish classes), discovering new box jellyfish species, policy contribution, and solving outbreaks. There has been no fatal case since 2016.

Conclusion: The strategies involved scientific investigation and research and combined the findings with local knowledge. The findings from these works have helped develop new knowledge, have been used for practical innovation, policy, and risk communications in all target audiences.

Keywords: box jelly fish, risk communication, evidence-based management, envenomation

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Mission to the Moon: Building Up Health Tech Innovation Ecosystem in Chiang Mai

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Abstract

According to the Thai government's ambitious Thailand 4.0 program is a concerted effort at encouraging investment and innovation, and the tech community is paying attention. Health Technology Innovation is one of the key area to drive economic growth and fill the gap of health care system.

Chiang Mai is one of the city that the government aims to develop the innovation in health care system because of welcoming culture, reasonable cost of living and sophisticated technological infrastructure. The Ecosystem of health care innovation including biotechnology, health tech start up, herbal research development, and medical tourism has been developed for the past 2 years. The startup, and health innovation program by the Northern Science and Technology Park including incubation, and funding program were granted. In2019, National Innovation Agency (NIA) signed MOU with Chiang Mai University to develop area based healthcare innovation district named "Suandok Health Innovation District" to build up infrastructure, business opportunity and grooming health tech start up.

In the Faculty of medicine, the Medical CMU Health Innovation Center (MED CHIC) was established to organize the healthcare innovation in the strategic process, and transform research to industrial scale. MED CHIC Innovation Day, Digital Health Project, and Spin-Out Project were example of the Health Tech Innovation activities. The products and innovation technologies such as Smile Migraine, Suandok Music Therapy Application, EV car for disable, and CPR model, were demonstrated as a success cases.

Keywords: health tech innovation, innovation ecosystem, Chiang Mai

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Integrated Care for Dementia: A Geriatric Medical Center Model

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Abstract

Background: The number of people living with dementia is significantly high. Caring dementia people needs multidimensional care including mental, physical, psychosocial, and spiritual as a holistic approach. Geriatric Medical Center is the hospital which aims to integrate multidisciplinary care process and team to manage the common problem in elderly including dementia. We set up the integrated model for dementia care and tracking the result.

Objective: To demonstrate the model for dementia care using integrated approach and overview the benefit and result.

Results: Three hundred and thirty nine patients diagnosed as dementia visited Geriatric Medical Center. Alzheimer's disease (80.0%) is the main diagnosis following by Vascular dementia, and other cause of dementia. The model for dementia were set up including screening and followed up dementia patients with standard measurement, cognitive training, set standard guideline for dementia medication treatment, family member meeting, and leisure activity in patients with dementia. Over 75.0% of the patient follow-up with the integrated care model showed good all dimension result.

Conclusion: Integrated care model for dementia showed promising result and should be applied to all patient with dementia.

Keywords: dementia, multidimensional care, alzheimer's disease

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Discovery of Anti-HIV Diterpenoids from Medicinal Plants of Thymelaeaceae and Euphorbiaceae Families

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Abstract

Background: Natural products (NPs) and NP-derived compounds present major opportunities for the inhibition and elimination of human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS). Approaches to combat HIV are hindered by its ability to hide in an inactive state inside certain immune cells and avoid drug treatment. Viral rebound occurs if combination antiretroviral treatment is discontinued. Thus, latent HIV reservoirs must be eliminated. "Shock-and-Kill" strategies involve two steps: first, reactivating latent virus hidden in immune cells using latency reversing agents and second, targeting the reactivated cells for clearance by the immune system and cytopathic effects.

Objective: Medicinal Plants belonging to Thymelaeaceae and Euphorbiaceae families contain characteristic diterpenoids, which share large chemical diversity and show potent biological activities. Our investigations aimed to discover novel anti-HIV diterpenoids from medicinal plants of Thymelaeaceae and Euphorbiaceae.

Methods and Results: In continuation of our biological screening program on Euphorbiaceae and Thymelaeaceae plant extracts for discovery of anti-HIV natural products, the extracts from *Stellera chamaejasme* and *Euphobia kansui* roots showed the strongest selective inhibition of HIV replication. Herein, we report the screening, bioassay-guided isolation, and semi-synthesis of bioactive diterpenoids from the extracts as potent anti-HIV agents. The most promising diterpenoids were selected to be further investigated for their potential as an anti-HIV latency drug candidate. Among these diterpenoids, gnidimacrin and 3-(2-naphthoyl)ingenol, were identified as the most promising candidate for development of new effective anti-HIV agents that can inhibit HIV-1 infection and reactivate latent HIV-1.

Keywords: anti-HIV, diterpenoids, gnidimacrin

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Novel Technologies and Diagnostic Methods in AMR Era

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Abstract

Appearance and spreading of antibiotic resistance (AMR) in bacteria are becoming a world-wide problem. Particularly, community-acquired AMR, such as CA-MRSA and ESBL producers, is in a spot light. Infection control in addtion to appropriate antibiotic uses may be a key factor for prevention of AMR issues. Prompt results in microbiological testing, ideally within 30 min (before prescription of antibiotic), are necessay for wise decision making, antibiotic use or not-use. In this point of view, ordinary PCR techniques are not sufficient, and probably more quick methods are required in recent AMR era. Several diagnostic companies are developing new instruments and technologies to make diagnosis of several infectious diseases. Especially, etiological diagnosis of sepsis and meningitis are hot topics, because suffered individuals are in risk of severe damage and/or death. One of the examples of quick diagnostic methods is an immune-chromatography targeting a variety of pathogenic antigens, such as polysaccharide and ribosomal proteins. Another is nucleic acid amplification-dependent chromatographic approaches. By using these methods, several infectious diseases will be made diagnosis within 30 min. In this presentation, recent progress of novel and unique diagnostic technologies will be reviewed. Further, advantages of these techniques, how we can use these methods for our patients, will be discussed with audiences.

Keywords: antibiotic resistance, AMR era, diagnostic methods

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Polycyclic Aromatic Hydrocarbons in Marine Environments of the Pacific Coast of Japan: Influence of the 2011 Tsunami and Fire

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Abstract

Background: The Great East Japan Earthquake of 11 March 2011 was a magnitude 9-class earthquake. The earthquake epicenter was off the Pacific coast of the Tohoku district in northern Japan, strong shaking across extensive areas of eastern Japan, and triggered extremely destructive tsunamis along the east coast of several prefectures. In tsunami-devastated regions, sediments and marine life along the coast may be at risk of exposure to organic pollutants, including polycyclic aromatic hydrocarbons (PAHs) that have been re-suspended from benthic sediments by the disturbance. The parts of Thailand and Indonesia facing the Andaman Sea were heavily damaged by the Great Sumatra-Andaman Earthquake occurred in December 2004. There are few reports on the accumulation behavior of chemical substances in marine organisms. Thus, we investigated the concentration, composition, and distribution of PAHs in sediments and bivalves from some intertidal sites along the coast.

Material and Methods: Surface sediments and bivalves were collected in 2013. The preparation for collected samples and PAHs analysis using GC-MS were the same as those reported previously (Onozato *et al. Polycycl Aromat Comp.* 28: 462–71, 2008).

Results: The total PAH concentrations in sediments were within the ranges of 21–1447μg kg-1-dry. The PAHs detected at each sites were derived from combustion rather than oil/fuel pollution. Total PAH concentrations were 244, 301, and 370 μg kg-1-dry for clams, mussels, and oysters, respectively.

Conclusion: Although the sampling sites were extensively damaged by the tsunamis and fires in 2011, PAH concentrations remained low, indicating minimal influence of the tsunami on PAH pollution. Assessment of the sediments showed that contamination levels were too low to cause any effects on intertidal benthos, and the concentrations present in bivalves would have negligible effects on human health through dietary intake. In addition, the PAHs levels in sediment and bivalves determined in this study were lower than world standard levels.

Keywords: Great East Japan Earthquake, Pacific coast of Tohoku, polycyclic aromatic hydrocarbons, sediment, bivalve

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Effects of Ground Uplift, Construction of an Artificial Tidal Flat and Tsunami Seawalls on Marine Life and Local Residents Following the 2011 Great East Japan Earthquake

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Abstract

Eight years have passed since the Great East Japan Earthquake occurred. I divided the process of the earthquake into four main events—the initial earthquake including liquefaction, subsequent tsunamis, land subsidence and ground uplift—and examined the impact of each event on marine life. Under the influence of lamd subsidence, the young oysters born in the summer of 2011 were attached 50 cm or more above where the parent generation was attached. However, in 2016, due to the influence of the ground uplift, oysters attached to the top of the rock began to die. Mass colonization of Manila clams occurred after the artificial tidal flat was created and the clam fishing industry was reopened. The new seawalls were constructed seaward of the previous seawalls. High seawalls break the continuity of nature between land and sea. From the viewpoint of disaster prevention, a seawall is necessary, but it will cause great damage to tourism and residents' lifestyles because the sea is hardly visible.

The Great Sumatra-Andaman Earthquake occurred in 2004. The tsunamis had a major impact on tropical reef organisms, while the earthquake in Japan had an impact on temperate species, but reports on the impact of earthquakes and tsunamis that occurred five years prior to the Japan Earthquake on the coastal environment and marine life are very useful precedents. During the joint survey of the Phang-Nga coast in 2017, we aimed to clarify the differences and commonalities between the reef area and the Rias coast area. The survey confirmed that large chunks of coral, moved by the tsunamis from the outer edge of the reef, were numerous in the shallow lagoon. Fifteen years after the Indian Ocean earthquake, land plants have not yet grown on the tops of coral clumps struck by the tsunamis. In Japan, it is known that a large tsunami in Meiwa occurred in 1771. Even after 250 years, many coral blocks are seen on Miyakojima Island. Land plants are growing on some of the large coral outcrops that were struck. The case of Japan indicates that it may take a long time for corals to weather and to deposit sediments in coral hollows, and it serves as a reference for estimating future changes in Thailand. The difference between the two countries is clearly seen in the seawalls built after the earthquake. In Thailand, instead of creating seawalls, tsunami evacuation towers were built along the coast of the Andaman Sea.

Keywords: earthquake, tsunami, marine life, seawall construction, coral reef

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Aging and Ovarian Function

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Abstract

The ovaries and testis are gonadal, which have two main functions. One is a hormone-secreting organ, and the other is a reproductive organ that produces oocyteor spermatozoa involved in the next generation. Although gonadalfunction decaysbecause of aging, lower hormone levels can be compensated by hormone replacement. On the other hand, the function as a reproductive organ cannot be compensated especially oogenesis because that was completed before birth. In female, by the 5th month of gestation, approximately 7 million oocytes are produced and are completed. Thereafter, the first meiosis occurs and the development stops after growing into the primary oocyte. It decreases to 2 to 3 million at birth, 300 to 400,000 at the first menarche, and 200,000 by reproductive age. Meiosis resumes after puberty, oocyte maturation and ovulation occur. The decrease in oocytes is accelerated from the late 30s.

Since all oocytes are produced in the fetal period, chromosomal desegregation tends to occur due to aging at the time of resumption of meiosis, and the risk of chromosomal aberrations such as monosomy and trisomy increases.As a result, infertility increases due to arrest of early embryonic development or implantation failure. Although assisted reproductive technology (ART) has developed and spread, it is not universal and clinical results depend on the female age. In the aging of female who want to have offspring, we will present the ovarian insufficiency and ART

Keywords: ovarian function, aging, ART, meiosis, offspring

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Report on the Usage of the Video Lecture Delivery (VLD) System

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Abstract

Background: With the implementation of the 2016-curriculum in TOHO University, we have started operating the video lecture delivery (VLD) system to encourage active learning.

Purpose: To analyze the effects of this system on student's learning behavior, we surveyed the system usage status.

Material and Methods: As of March 31, 2019, we calculated video recording rates for all lectures, and analyzed the viewing log of students. In addition, as of April 2018, we conducted a questionnaire survey on the usage of this system for 2nd graders (completed the 1st grade) and 3rd graders.

Results: The cumulative recording rate of lectures in the 1st grade increased with each year, reaching around 90%. The number of viewing history also increased year by year, and the number in 2018 was 6307. The cumulative recording rate for the 2nd grade was about 80%. Viewers in both 2017 and 2018 were almost the same, and the number in 2018 was 2000. As for the 3rd grade in 2018, the first year of 2016-curriculum, was 49%, and viewers were 432. The number of viewers significantly decreased in subjects with a low recording rate (less than 70%) compared with subjects with a high one (80% or more). According to the questionnaire, about 90% of the students answered that this system is "Beneficial/Mostly Beneficial". As the opinion of the free description, many students pointed out problems in recording such as unrecorded lectures.

Conclusion: While the VLD system is considered to be a useful educational support tool for students, some points need to be improved.

Keywords: video lecture delivery (VLD) system, educational support tool, active learning

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Differential Cellular Response for the *BRCA1*-Defective and *BRCA1*-Competent Breast Cancer Cells to Anticancer Ruthenium(II)-Arene Complex, RAPTA-EA1

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Abstract

Background: The ruthenium(II) complex with an arene-tethered ethacrynic acid ligand, RAPTA-EA1, has been reported to overcome drug resistance that developed due to the current use of platinum drugs. However, the exact mechanism of action of RAPTA-EA1 remains largely unexplained.

Objective: We have further studied the effect of RAPTA-EA1 on *BRCA1*-deficient HCC1937 breast cancer cells and compared its effects on *BRCA1*-proficient MCF-7 breast cancer cells.

Material and Methods: *BRCA1*-deficient HCC1937 and *BRCA1*-proficient MCF-7 breast cancer cells were treated with the ruthenium(II)-arene complex, RAPTA-EA1. Cellular proliferation was evaluated by a MTT assay. Cellular uptake of ruthenium was measured by ICP-MS. Cell cycle progression and apoptotic cell death were assessed using a flow cytometer. Expression of *BRCA1* mRNA and BRCA1 protein was quantitated by a real-time RT-PCR and Western blotting.

Results: Differences in cytotoxicity were correlated with the differential accumulations of ruthenium and the induction of apoptosis. The ruthenium-based compound caused dramatically more damage to the *BRCA1* gene in the *BRCA1*-deficient HCC1937 cells than to the *BRCA1*-proficient MCF-7 cells. The ruthenium complex decreased the expression of *BRCA1* mRNA in the *BRCA1*-proficient cells, while in contrast, its expression increased in the *BRCA1*-deficient cells. However, the expression of the *BRCA1* protein was significantly decreased in both types of breast cancer cells.

Conclusion: The results presented here have demonstrated a differential cellular response for the *BRCA1*-deficient and *BRCA1*-proficient breast cancer cells to RAPTA-EA1. These findings have provided more insight into the actions and development of the ruthenium-based compounds for use for the treatment of breast cancer.

Keywords: ruthenium, breast cancer, cytotoxicity, cellular uptake, *BRCA1* Expression

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Economic Evaluation of Temozolomide for Newly Diagnosed Glioblastoma in Thailand According to IDH1 Status

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Abstract

Background: Glioblastomas (GBM) is the most common primary brain tumor in adults. Temozolomide (TMZ) is the alkylating agent to have demonstrated a significant survival benefit in patients with GBM. However, TMZ has a high cost than adjuvant radiotherapy alone.

Objective: The objective of this work was to determine the cost-effectiveness analysis of concomitant TMZ with radiotherapy (TMZ/RT) compared with radiotherapy alone (RT) according to IDH1 mutation.

Material and Methods: A retrospective study was conducted to collect relevant data from 173 patients. Effectiveness of TMZ was estimated with the survival analysis and propensity score adjustment. The incremental cost-utility ratio (ICUR) between TMZ/RT and RT is a statistic used in cost-utility analysis by IDH1 mutation.

Results: By survival analysis with propensity score adjustment, TMZ/RT was associated with a significantly better prognosis (HR 0.36, 95%CI 0.21-0.60). For cost-utility analysis, ICUR of IDH1-wildtype GBM was ฿ 2,790,472/QALY while ICUR of IDH1-mutant GBM was ฿ 8,653,652/QALY. With the willingness-to-pay threshold of Thailand (฿160,000/QALY), TMZ/RT is not cost-effectiveness therapy and is not comparable to that of the standard therapy for patients with GBM in Thailand.

Conclusion: Although TMZ/RT was significant to increase median survival time, this therapy is hard to implicate into the national health system because of the limited willingness-to-pay threshold.

Keywords: glioblastoma, cost-effective analysis, health-technology assessment, temozolomide, propensity score

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Metabolomics Approach Towards the Atability of Andrographis Herb

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Abstract

Background: Widely recognized as an alternative medicine for the symptomatic treatment of common cold, Andrographis Herb (the aerial parts of A*ndrographis paniculata*) has otherwise a short half-life, and an impractical and problematic stability.

Objective: To establish the degradation profiles of Andrographis Herb in a real time manner using a metabolomics approach.

Material and Methods: A ^{1}H NMR-based metabolomics analysis was performed on the raw materials of Andrographis Herb from three suppliers stored at the ambient conditions over a six-month period.

Results: Principal component analysis revealed the rapid decomposition of diterpene lactones in Andrographis Herb and suggested that 14-deoxy-11,12-didehydroandrographolide, a decomposition product of andrographolide, be used as a stability marker.

Conclusion: Using the ^{1}H NMR-based metabolomics workflow, the degradation of the chemical composition in Andrographis Herb was determined. With an estimated shelf life (t90%) of three-five months, we recommended that the products of Andrographis Herb shall be regulated simultaneously with both lower and upper limits, e.g., 6-10% of total lactone contents. A triturated product manufactured with initial lactones contents of 10% would allow a practical shelving period of 12 months.

Keywords: andrographis herb, *Andrographis paniculata*, andrographolide, metabolomics, stability

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Severe Dengue Infection: An Experience in Songklanagarind Hospital

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Abstract

Dengue viral infection (DVI) is a common cause of morbidity and mortality in tropical countries. Severe dengue is defined as dengue patients with dengue shock syndrome (DSS) and/or organ failure/dysfunction. In this narrative review, we describe our previous studies of risk factors and outcomes of severe DVI. Of the 238 children with severe DVI, 30 (12.6%) subsequently died. Nearly one-third of the severe DVI patients had at least one organ failure, with acute respiratory failure (ARF), acute kidney injury (AKI), acute liver failure (ALF), and/or hematologic failure (severe bleeding) in 18.5, 17.2%, 16.4%, and 18.5% of the cases, respectively. Patients with ARF and severe bleeding had an 82% fatality rate, but patients without these two risk factors together had a 99% survival rate. Patients with non-DSS-caused organ failure have a good prognosis. Obese children are at higher risk of developing severe DVI and subsequent organ failure, notably AKI and ALF. Prolongation of prothrombin time (PT>15 seconds) is the major risk factor for severe bleeding. In our review, we found PT had a high correlation with transaminase enzymes. Taken together, these various factors suggest that ALF plays a key role in hemorrhage in DVI patients by causing decreased synthesis and increased consumption of coagulation factors. Further studies on how to prevent or to improve ALF are needed in patients with severe DVI, since the liver is the target organ of dengue virus and patients with ALF who subsequently develop severe bleeding have a poor prognosis.

Keywords: risk factors, severe dengue, dengue shock syndrome, dengue hemorrhagic fever, organ failure

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Quality of Life–Environmental Impact Level: Case Study of People Living in the Khun Tat Wai and Pa Ching Sub–District Administrative Organizations, Amphoe Chana, Songkhla Province

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Abstract

Background and Rationale: Nowadays, the changing global environment from industrial development impacts the quality of human life. A good quality of life assessment appropriate for a community situation can give important information for community development in the future. Thus, this study aimed to investigate the level of quality of life among people living in Khun Tat Wai and Pa Ching Sub–district Administrative Organizations, Amphoe Chana, Songkhla Province who are affected by a changing environment from industrial development such as a biomass power plant.

Objective: To investigate the level of quality of life and the factors related to quality of life among people living in Khun Tat Wai and Pa Ching Sub–district Administrative Organizations, Amphoe Chana, Songkhla Province.

Material and Methods: The study design was a cross–sectional study with qualitative and quantitative methods. The participants were the people living in the Khun Tat Wai and Pa Ching Sub–district Administrative Organizations, Amphoe Chana, Songkhla Province. For the quantitative study, 479 samples were selected by accidental sampling from the village that was selected by purposive sampling. The data were collected from October 8, 2018 to November 13, 2018. The quantitative data were analyzed using descriptive statistics and ordinary regression analysis.

Results: The quality of life levels of both sub–districts were measured by WHOQOL–BREF–THAI and the results of all perceptions of the quality of life questionnaire were at moderate levels. From the content analysis of the focus group of Pa Ching Sub–district, the attitude of environmental effects on living showed the effects of pollution, especially water pollution and the unwanted rubber–like odor, and the effect of drug addiction. The environmental effects at Khun Tat Wai Sub–district were dust, smoke, and water pollution.

Conclusion: The industrial culture is affecting the environmental quality of life due to air and water pollution resulting in dramatically reduced crop production and the production of unpleasant odors.

Keywords: quality of life – environmental impact, case study

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Nanoparticle-Based Microfluidic Device for Liquid Biopsy

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Abstract

Circulating tumor cells (CTCs) are cancer cells that escape from the primary, or metastatic lesions to the peripheral bloodstream. The number of CTCs in the blood of patients with cancer is a strong indicator for the progress of the disease. CTCs assay can be used in clinical practice for diagnostic, prognosis as well as therapy monitoring in the care of cancer patients. CTCs detection from blood for cancer diagnostic is called: liquid biopsy. Cellsearch® is a CTCs detection device which has been the only device approved by the FDA for metastatic breast cancer patients. However, its cell capture efficiency needs improvement for clinical translation. Microfluidic platforms and nanostructures have the potential to enhance cell capture efficiency. Herein, we therefore aim to develop a multivalent nanoparticles-enabled microfluidic device for circulating tumor cells detection. Microfluidic chips were designed and successfully fabricated as herringbone and pillar structures, using soft lithography techniques. Biomarkers-conjugated nanoparticles were then functionalized on the surface within the microfluidic channel. MCF-7 breast cancer cells, EpCAM overexpressed cells, are used for validation. The devices, with both herringbone and pillar structures, improved mixing properties and enhanced the surface interactions between both biomarkers and targeted cells. The fabrication processes along with flow rates were optimized. Cell capture efficiency was increased to ~ 80-92%, with the device functionalized with nanoparticles. To summarize, the combination of CTCs biomarkers-conjugated nanoparticles, with the microfluidic chip enhanced CTCs detection efficiency, and sensitivity of the device. It is a promising platform for clinical translation in the future.

Keywords: Circulating tumor cells (CTCs), Microfluidic, Nanoparticles, Liquid biopsy, Cancer

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A Nutraceutical for Cancer Prevention Made from Garcinia Cowa Leaf Extract with Rice Bran Oil

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Abstract

Background: Chamuangone, a polyprenylated benzophenone has been isolated from *Garcinia cowa* leaves, and showed various biological activities, i.e. antibacterial, leishmanicidal and anticancer activities. n-Hexane has been reported to be the most suitable solvent for extraction of chamuangone. However, the use of hexane as a solvent for herbal extraction was limited in pharmaceutical industrial applications due to its toxicities. Therefore, the present study focused on investigating the use of vegetable oils as alternative green solvents for extraction of chamuangone using a microwave assisted extraction. In addition, the extraction processes were optimized to obtain the chamuangone enriched *G. cowa* leaf extract. Cytotoxicity of the standardized chamuangone extract against human cancer cell lines was also determined.

Material and Methods: Microwave assisted extraction (MAE) and HPLC were used for extraction and standardization. The cytotoxic activity was determined using sulforhodamine B (SRB) assay.

Results: The chamuangone enriched extract was obtained using rice bran oil as the alternative green solvent and standardized to contain 2.0 mg/mL chamuangone. In addition, the extract contained some natural antioxidants, including α-tocopherol (76.7 mg/100 g), γ-oryzanol (67.1 µg/mL cycloartarnyl ferulate, and 85.6 µg/mL 24-methylene-cyloartarnyl ferulate), and antioxidant capacity determined as ascorbic acid (258.7 mM AAE/g). The extract exhibited cytotoxic activity against human lung adenocarcinoma (A549), human breast adenocarcinoma (MCF-7), and human colorectal adenocarcinoma (HT-29) cell lines, with IC50 values of 15.3, 15.9 and 12.8 µg/mL, respectively, and was nontoxic to human gingival fibroblasts (HGF) at a concentration of 50 µg/mL.

Conclusion: These findings indicates that the chamuangone extract with rice bran oil may be considered as a novel functional food in cancer chemoprevention.

Keywords: *Garcinia cowa*, chamuangone, anticancer, antioxidant, green extraction

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Synthesis and Evaluation of New Coumarin Derivatives as Acetylcholinesterase Inhibitors

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Abstract

Background: Alzheimer's disease (AD) is one of the most important neurodegenerative disorder that globally affect older people. Reduction of acetylcholine (ACh) level in the brain is considered as the main pathophysiology of AD. ACh activity is terminated via hydrolysis of the ACh molecule by acetylcholiesterase (AChE) enzyme. Acetylcholinesterase inhibitors (AChEIs) blocks AChE function and ACh level is then increased. AChEIs are the key agents currently used for AD drug therapy.

Objective: In this research, new coumarin derivatives were synthesized and evaluated for acetylcholinesterase inhibitory activity.

Material and Methods: AChE inhibitory activity of the synthesized compounds was determined using Ellman's method. Inhibition mode of the selected compound was indicated by kinetic study. Molecular docking was performed to investigate ligand-enzyme binding interactions. Druglikeness properties of the compounds were anticipated by ADMET analysis. HEK-293 cells were used for cytotoxicity evaluation. Results: The coumarin derivatives exhibited potent AChE inhibitory activities at micromolar level. The most active compound inhibited AChE in the noncompetitive mode. Molecular docking study revealed binding interactions between the coumarin with both catalytic anionic (CAS) and peripheral anionic (PAS) sites of AChE. It did not induce cytotoxic effect against HEK-293 cells.

Conclusion: The coumarin derivatives can be promising lead compounds for development of anti-Alzheimer's agents.

Keywords: acetylcholinesterase inhibitor, coumarin, molecular docking, ADMET analysis, cytotoxicity

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Abstracts

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"Variety and Controversy to Creativity"

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Gaq Promoted Antioxidative Ability of Neural Cells by Activating Nrf2 and Inhibiting NF-kB

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Abstract

Gastrodia elate (Order: Orchidaceae, Family: Gastrodieae, Genus: Gastrodia) has been used as a traditional herbal medicine for over 2000 years, and is recorded to have sedation, antidepressant and cognition enhancing properties. Gastrodin (GAS) is the major and bioactive component in Gastrodia elate. The protective effects of gastrodin in physiological and pathologic conditions are discussed in this review. GAS's metabolism and bioavailability are briefly introduced. This is followed by molecular mechanisms of effects of GAS on the brain, including glutamatergic transmission, monoamine transmission, GABA, apoptosis, autophagy, inflammation, neural stem cells and neurore-generation. The molecular mechanisms of the neuroprotective effects of gastrodin in Alzheimer's disease (AD), major depression, Parkinson's disease (PD), epilepsy, cerebral ischemia, cerebral trauma, memory and cognition impairment, spinal cord injury and pain are presented. Further more, the protective effects of GAS on cardiovascular system and other systems are involved. It is hoped that this discussion will stimulate more studies on the use of gastrodin in physical illness.

Keywords: gastrodin, bioavailability, alzheimer's disease

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The Addictive Possibility of Cannabidiol (CBD) in SD Rat

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Abstract

Objective: Cannabidiol (CBD), one of the major components of cannabis, which has been reported had potential therapeutic effect on some neurodegenerative diseases. However, there are few reports on the addiction of cannabinol. The present study was using conditioned place preference (CPP) protocol to investigate whether CBD has addictive effect on Sprague Dawley rat. And collect experimen tal evidences for the interventional treatment of neurodegenerative diseases in the future.

Material and Methods: Full spectrum of cannabidiol (CBD), which concentration was 67.6%(V/V), was provided by Hempson Bio-Tech Co., Ltd. The protocol of the biased procedure of conditioned place preference (CPP) was used. In detail, the rats were put into a CPP system and adaptation for 3 days. And then, the rat's preference chamber was confirmed. Then, the rat of CBD groups were given the difference dosage (50 mg/kg or 100 mg/kg) of CBD by intragastric administration for continuously 10 days. And methamphetamine (10 mg/kg) or morphine hydrochloride (10 mg/kg) were performed via intraperitoneal administration as positive control groups, and hemp seed oil was performed via intraperitoneal administration as a negative control. The periods of methamphetamine, morphine hydrochloride, or hemp seed oil administed was the same as the CBD groups. On the eleventh day, the addictive effects of rats were evaluated by CPP protocol.

Results: Compared with the methamphetamine group and morphine group, there were no siginificant CPP effect in the low-dose CBD group (50 mg/kg) and the high-dose CBD group (100 mg/kg), the difference were significant (P<0.05). Morever, there was no siginificant difference when comparing the CPP effects of the hemp seed oil group with the low-dose CBD group (50 mg/kg) or high-dose CBD group (100 mg/kg) group (P>0.05).

Conclusion: After 10 days of intragastric administration of different doses of CBD, eg, 50 mg/kg or 100 mg/kg, SD rat did not induce significant addictive effect. The data suggested the CBD has not petential addictive effect on the SD rat.

Keywords: cannabidiol, neurodegenerative diseases, conditioned place preference

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The Extraction and Detection Methods for Cannabidiol: The Current Situation in China

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Abstract

Objective: Cannabidiol is one of the main chemical constituents in cannabis plant, and its medical application value is closely related to its purity. Therefore, it is necessary to understand the advantages and disadvantages of the extraction and detection methods of cannabidiol. The paper reviewed the extraction and detection methods of cannabidiol in current China, so as to provide evidence for further studies.

Material and Methods: Literature retrieval was carried out using three terms, which are Cannabidiol, extraction, and detection. in Wanfang data and knowledge service platform, China national knowledge infrastructure, PubMed and Web of science. In Chinese database, the search term is limited to the title, abstract or keyword item for retrieval. In PubMed and Web of science, the following queries were used: "Cannabidiol/isolation and purification" [Mesh] (PubMed), ("Cannabidiol/analysis" [Mesh]) AND "Cannabidiol/chemistry" [Mesh](PubMed), and TS=(Cannabidiol AND [isolation OR purification]) (Web of Science). The retrieval results were sorted out and summarized.

Results: In terms of the extraction methods of cannabidiol, the materials used for extraction mainly include the hemp plants and flowers and leaves, which were firstly dried, ground and crushed, and then the powder was extracted. The extracted reagents and conditions included N-hexane, alcohol, oil, subcritical water extraction, supercritical CO_2 extraction, etc. The filtrate with cannabidiol was obtained after extraction and concentrated by a rotary evaporator or a

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film evaporator. The cannabidiol enrichment was obtained by distilling the concentrated solution. The cannabidiol was purified by column chromatography or recrystallization from the cannabidiol enrichment. Subcritical water extraction method could harvest a concentration up to 99.7% of CBD, which could be used as a standard. Methods for detecting cannabidiol included HPLC, RP-HPLC, GC-MS, GC-MS/MS, LC-MS/MS, UPLC-MS/MS, and UPLC/PDA-QDA, etc. For some of which national standards have been issued.

Conclusion: Cannabidiol extracted from ru cannabis plant has high purity, and its detection methods were highly sensitive, which could meet the requirement of medical application.

Keywords: cannabidiol, extraction, detection

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Socioeconomic Differences in Prevalence and Behaviors of Smoking in Rural Southwest China

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Abstract

Background: China is both the world's largest tobacco manufacturer and consumer, accounting for one-third of the world's tobacco production and consumption. This study examines how prevalence and behaviors of smoking differ by socioeconomic status among rural southwest Chinese adults.

Material and Methods: A cross-sectional survey was conducted including 7,743 adults aged ≥35 years in rural regions of Yunnan Province, China from 2016 to 2018. Information on individual socioeconomic status (SES), ethnicity, and self-reported smoking behaviors was collected utilizing a standardized questionnaire. The individual socioeconomic position (SEP) index was constructed using principal component analysis. Multivariate logistic regression models were used to analyze the association between individual SES variables and the prevalence and behaviors of smoking.

Results: In the study population, the overall prevalence rate of current smokers was 33.5%. Males had a markedly higher prevalence of current smokers than females (62.6% vs. 4.8%, $P<0.01$). Of these smokers, 74.5% began smoking during adolescence, 88.8% had never attempted to quit smoking, and 81.1% reported smoking in public places. Those with low levels of education and/or low SES status were more likely to use tobacco as well as more likely to start smoking, and regularly smoke, during adolescence ($P<0.01$). Participants with poor access to medical services had a higher prevalence of current smoking than their counterparts ($P<0.01$). Han ethnicity, good access to medical services, and high SEP were positively associated with the probability of having attempted to quit smoking at least once, while a high level of education and high SEP were negatively associated with the probability of smoking in public places ($P<0.01$).

Conclusions: Disparities in prevalence and behaviors of smoking exist across a diversity of indicators of individual SES in rural southwest China. Future tobacco cessation interventions should focus on men, ethnic minorities, and those with low education levels, poor access to medical services, and low SEP.

Keywords: smoking, behaviors, socioeconomic status, China

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Effect of Shock Wave on NMJ and Muscle Morphology in Rabbits

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Abstract

Objective: To evaluate the bilateral change of AChE, nAChR and the orphological changes of muscle tissue when only one leg are accept the Extracorporeal Shock Wave (radial Extracorporeal Shock Wave Treatment, rESWT) processing.

Material and Methods: 63 male New Zealand rabbits weighing 2 +/- 0.2 kg. The strength of rESWT was determined in 3 rabbits by pre-experiment, and then the remaining 60 rabbits were subjected to a shock of 1.5 bar and frequency of 10Hz for 2000 times with the largest position of the left calf triceps muscle abdomen slightly laterally. Divided into six groups, Japanese photoelectric meb-9100k EMG was used to record the lateral head compound muscle action potential of bilateral gastrocnemius muscle under anesthesia on the day of the treatment of the rESWT and at week 1, 2, 4, 6 and 8 after the treatment. Comparing the amplitude and latency of the two sides, One sample was taken from each group and repeated electrical stimulation was performed on the lateral head of bilateral gastrocnemius muscle. The attenuation of amplitude after different frequency stimulation was recorded. Immediately remove the lateral cephalic tissue of bilateral gastrocnemius muscle after EMG examination. Morphological changes of muscle tissue were observed by HE staining after frozen section. The mean optical density was measured after AchE staining, and nAChR was counted after immunohistochemical staining.

Results: The action potential amplitude of the experimental side of the first three groups of rabbits (on the day of treatment and the first and second weeks after treatment) decreased significantly compared with that of the control side ($P<0.05$). The amplitude of action potential on the experimental side was not significantly different from that on the control side. There was no significant difference in the latent period of bilateral action potential between all experimental rabbits, and no obvious morphological abnormality of muscle tissue was found in HE staining. The mean optical density of AchEon the experimental side of the first five groups of rabbits was significantly higher than that on the control side ($P<0.05$). The mean optical density of AchE on the experimental side decreased slowly after the first week of

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treatment, and there was no statistically significant difference between the mean optical density of AchE on the experimental side and the control side at 8 weeks after treatment (P>0.05); Compared with the first 5 groups, the AchR count on the experimental side was significantly decreased (P<0.05), but gradually increased from the day of shock wave treatment to 8 weeks after treatment, and there was no statistically significant difference in AchR count between the experimental side and the control side at 8 weeks after treatment (P>0.05).

Conclusion: The effect of rESWT on the maximal hypertrophy of the triceps crus muscle abdomen at a strength of 1.5 bar and a frequency of 10Hz for 2000 shocks can reduce the amplitude of its complex muscle action potential, but the effect duration is short and has no significant impact on the muscle tissue morphology. AchE significantly increased and AchR significantly decreased in a short period of time, suggesting that the treatment of this intensity rESWT reduced the number and degree of stimulation received by muscle cells in a short period of time, thereby reducing the generation of action potential.

Keywords: muscle action potential, extra corporeal shock ware, AchE

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Dual-Task Balance and Mobility Training Reduces Cognitive-Motor Interference and Falls in Chronic Stroke: A Randomized Controlled Trial

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Abstract

Background and Purpose: Functional community ambulation requires the ability to perform a mobility and cognitive task simultaneously (dual-tasking). This single-blinded randomized controlled study aimed to examine the effects of dual-task exercise in chronic stroke patients.

Material and Methods: Eighty-four chronic stroke patients (24 women; age: 61.2±6.4 years; time since stroke onset: 75.3±64.9 months) with mild to moderate motor impairment (Chedoke-McMaster leg motor score: median=5; interquartile range=4-6) were randomly allocated to the dual-task balance/mobility training group, single-task balance/mobility group, or upper-limb exercise (control) group. Each group exercised for three 60-minute sessions per week for 8 weeks. The dual-task interference effect was measured for the time to completion of three mobility tests (forward walking, Timed-up-and-go, and obstacle-crossing), and for the correct response rate during serial-3-subtractions and verbal fluency task. Secondary outcomes included the Activities-specific Balance Confidence Scale, Frenchay Activities Index, and Stroke-specific Quality of Life Scale. The above outcomes were measured at baseline, immediately after, and 8 weeks after training. Fall incidence was recorded for a 6-month period post-training.

Results: Only the dual-task group exhibited reduced dual-task walking time post-training [forward walking combined with verbal fluency (9.5%, p=0.014), forward walking with serial-3-subtractions (9.6%, p=0.035), and the timed-up-and-go with verbal fluency (16.8%, p=0.001)]. The improvements in dual-task walking were largely maintained at the 8-week follow-up. The dual-task cognitive performance showed no significant changes. The dual-task program reduced the risk of falls and injurious falls by 25.0% (95%CI: 3.1-46.9%, p=0.037) and 22.2% (95%CI: 4.0-38.4%, p=0.023), respectively during the 6-month follow-up period compared with controls. There was no significant effect on other secondary outcomes (p>0.05).

Conclusion: The dual-task program was effective in improving dual-task mobility, reducing falls and fall-related injuries in ambulatory chronic stroke patients with intact cognition. It had no significant effect on activity participation or quality of life.

Keywords: cerebrovascular accident, rehabilitation, mobility limitation, exercise, accidental falls

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Tim-3 Modulation of CXCR3 Expression on NK Cells in Primary Biliary Cholangitis Mice

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Abstract

Objective: To investigate the regulation of T cell immunoglobulin domain and mucin containing molecule (Tim)-3 on the expression of CXCR3 in NK cells, and to reveal the regulatory role of Tim-3 in the pathogenesis of PBC.

Material and Methods: PBC animal models were established to observe the expression of Tim-3 and its natural ligand Gal-9 in liver and spleen. Serum soluble Tim-3 levels were measured. Mononuclear cells from spleen, liver and peripheral blood were extracted and the distribution of NK cells and CXCR3 + NK cells were analyzed with flow cytometry. The changes of CXCR3 + NK cells were observed after blocking and activating Tim-3 pathway.

Results: The expressions of Tim-3 and Gal-9 were abnormal in liver and spleen of PBC mice. However, the level of serum soluble Tim-3 was decreased. The frequencies of $Tim\text{-}3^+$ and $CXCR3^+$ NK cells in peripheral blood were increased significantly. The $Tim\text{-}3^+$ cells were increased in liver, and no significant difference was found in CXCR3+NK cell subsets. $CXCR3^+$ NK cells decreased when Tim-3 pathway activated, While $CXCR3^+$ NK cells increased significantly when Tim-3 pathway blocked.

Conclusion: Tim-3/Gal-9 pathway is involved in the pathogenesis of PBC, which could down-regulate the expression of CXCR3 on NK cells.

Keywords: tim-3, Gal-9; NK cells, CXCR3, primary biliary cholangitis

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Clinical and Basic Research in Functional Neurosurgery

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Abstract

Aim: Research on functional extrauterine diseases from clinical and basic aspects.

Material and Methods: Deep brain stimulation was used to treat Parkinson's disease, dystonia, and essential tremor. The best indications and targets for DBS treatment were sought, and remote program control and independent intellectual property product development were carried out. Targeting drugs 6-OHDA and transgenic animals to find targets for neuroprotective drugs in Parkinson's disease.

Results: There is a certain understanding of DBS treatment and program control in clinical work. In the Parkinson model, gastrodin treatment can increase the activity of dopamine neurons and decrease the expression of α-synuclein. After adding gastrodin, it can enhance its chemotactic behavior.

Conclusion: Clinical and basic research on functional neurosurgical diseases is needed to better study the occurrence, development and treatment of diseases.

Keywords: functional neurosurgery, Parkinson's disease, clinical research, basic research

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The Number of Regional Lymph Node Metastasis Associate with the Overall Survival in Distal Cholangiocarcinoma

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Abstract

Purpose: To investigate the relationship between the number of lymph nodes retrieved and lymph node metastasis and prognosis of patients with distal cholangiocarcinoma (DCC).

Material and Methods: Clinicopathological data of patients with DCC who confirmed by postoperative pathology after radical surgery in the Second Affiliated Hospital of Kunming Medical University (Yunnan, China) from July 2015 to December 2017 were analyzed retrospectively. Univariate and multivariate analyses were performed to determine the risk factors and independent risk factors influencing the prognosis of DCC patients.

Results: Carbohydrate antigen 125 (CA 125), neutrophiltolymphocyte ratio (NLR), perineural invasion, vascular invasion, fat invasion, the number of regional lymph node metastasis, the American Joint Committee on Cancer (AJCC) stage and recurrence were the risk factors influencing the prognosis of DCC patients. Among the 8 risk factors, NLR, the number of regional lymph node metastasis and recurrence were independent risk factors influencing the prognosis of DCC patients.

Conclusion: The number of regional lymph node metastasis is an independent risk factor for patients with DCC, and the number of total lymph node retrieved had no definite effect on the prognosis of DCC patients. If the regional lymph node metastasis counts are more than 3 nodes, continuous large-scale lymphadenectomy is meaningless to improve the overall survival rate of DCC patients.

Keywords: distal cholangiocarcinoma, lymph node metastasis, overall survival, prognosis

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G6PD Promotes Glucose Uptake in NSCLC via the STAT3/GLUT1 Axis and Suggests a Poor Prognosis

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Abstract

Objective: To study the relationship between G6PD and prognosis in non-small cell patients, and to explore the effect of G6PD on glucose uptake in non-small cell lung cancer cells and its molecular mechanism.

Material and Methods: Forty-six patients with non-small cell lung cancer (NSCLC) and benign pulmonary nodules were enrolled in this study. The correlation between G6PD expression and SUVmax and SUVmean was statistically analyzed. The expression of G6PD in lung cancer and paracancerous tissue engineering chips was evaluated by immunohistochemistry using lung cancer and paracancerous tissue engineering chips. The relationship between G6PD expression level and overall survival and progression-free period was analyzed. The expression of G6PD was detected in lung cancer cells, and the G6PD knockdown lung cancer stable cell line (A549-G6PDko) and the stable transgenic cell line overexpressing G6PD (A549-G6PDko-G6PDover) were detected by CRISPR/Cas9. The glucose uptake capacity of A549, A549-G6PDko and A549-G6PDko-G6PDover cells was detected, and the expression of STAT3 and GLUT1 in three cells was detected. The nude mice bearing tumor model of the above three cells was constructed by subcutaneous transplantation tumor model, and the tumor formation time, growth rate and metabolism were detected.

Results: 1. SUVmax and SUVmean were significantly higher in patients with NSCLC than in benign pulmonary nodules (SUVmax: 6.3±1.1 vs 3.2±1.1, P=0.03; SUVmean: 5.5 vs 2.7, P=0.01; patients with non-small cell lung cancer) Vs. patients with benign nodules in the lungs; and G6PD expression levels were positively correlated with SUVmax. 2. The overall survival and disease-free progression of patients with high expression of G6PD in NSCLC were significantly reduced (OS: 8.2±2.3 vs 12±3.2, P=0.003; PFS: 3.2±1.1 vs 5.8±2.1, P=0.04; G6PD high vs G6PD low in

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NSCLC). 3. G6PD was highly expressed in lung cancer cells, and glucose uptake in lung cancer A549 cells knocked down by G6PD was decreased (83.3±22.11 vs 228.32±32.29, P=0.0038, A549-G6PDko vs A549), accompanied by STAT3 (0.47±0.21 vs 1.02±). 0.13, P=0.043, A549-G6PDko vs A549) and GLUT1 (0.43±0.09 vs 1.08±0.12, P=0.022, A549-G6PDko vs A549) decreased expression; after overexpression of G6PD, glucose uptake of A549 cells increased (33.13± 8.29 vs 188.43±22.37, P=0.027, A549-G6PDko vs A549-G6PDko-G6PDover) and STAT3 (1.03±0.11 vs 3.37±0.82, P=0.003, A549-G6PDko vs A549-G6PDko-G6PDover) and GULT1 (1.04±) 0.13 vs 2.02±0.37, P=0.029, A549-G6PDko vs A549-G6PDko-G6PDover) increased expression levels; inhibition of STAT3 activity in both cell lines found that knockout or overexpression of G6PD did not affect GLUT1 expression. 4. The tumor-bearing model of nude mice showed that the tumorigenic ability of mice knocked out of G6PD was significantly decreased with decreased metabolism (SUVmax 3.38±1.09 vs 5.78±2.11, P=0.022, A549-G6PDko vs A549); mice overexpressing G6PD The tumorigenic ability increased and the metabolism increased (SUVmax 2.48±0.93 vs 6.89±1.79, P=0.003, A549-G6PDko vs A549-G6PDko-G6PDover).

Conclusion: 1. Overexpression of G6PD in patients with NSCLC suggests a poor prognosis. 2. G6PD regulates NSCLC glucose uptake via the STAT3/GLUT1 axis.

Keywords: glucose uptake, non-small cell lung cancer, G6PD

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A New Community Accessible, Practical Specimen Preparation Technique to Assist in Fighting a Deadly Jellyfish Health Threat

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Abstract

Background: Box jellyfish can cause fatalities. In Thailand, communities play a vital role in surveillance and control measures as stings can kill people within 2–10 minutes. For early warning and rapid response, a cheap practical tool and technique for identifying classes of toxic jellyfish is needed.

Objective: 1) To develop a new simple and inexpensive technique for collecting and transferring toxic jellyfish specimens and for the identification of nematocysts (Vacuum sticky tape (VST) for identification of toxic jellyfish class–VST). 2) To compare the quality of outcome of VST technique to those of existing standard preparation method (the Wet Mount technique).

Material and Methods: The VST technique used glossy finish transparent sticky tape to collect tentacles of box jellyfish (Collecting), sticky tape that wrapped tentacles (without air bubble) were sent via postal mail (Transferring), and VST was attached on the glass microscope slide and examined under a fluorescence microscope with 20X, 40X, and 100X objective lenses (nematocyst identification). The quality of the picture of nematocyst identification from VST were compare to the Wet Mount technique.

Results: There was no significant difference as regards quality of image in the identification of the type of toxic jellyfish between two techniques. In addition the VST technique is easier to prepare and transfer the sample to the nematocyst identification site.

Conclusion: The VST is a new cheap practical technique inform and improve the toxic jellyfish surveillance system. In addition, it will contribute to new knowledge of the toxic jellyfish in Thailand.

Keywords: vacuum stick tape, box jelly fish, nematocyst, vacuum technique, wet mount preparation

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Minilaparotomy, Cyfra 21-1, and Other Predicting Factors for Suboptimal Cytoreductive Surgery in Advanced Epithelial Ovarian Cancer: A Pilot Study

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Abstract

Background: Standard treatment of advanced epithelial ovarian cancer is primary cytoreductive surgery following by chemotherapy. Removing all macroscopic tumor gains the maximal survival benefit. Neoadjuvant chemotherapy isan alternative treatment in patients having medicallyunfit for surgery or the probability of suboptimal cytoreductive surgery. Unfortunately, there are no reliable assessment tools predicting suboptimal surgery.

Objective: To find candidate predicting factors for suboptimal primary cytoreductionfrom clinical data, serum biomarkers, CT/MRI imaging, and minilaparotomy decision in patients with clinically-advanced epithelial ovarian, fallopian tube, and peritoneal cancer.

Material and Methods: Women with clinically suspiciousforadvanced-stage ovariancancer were recruited. Clinical data, abdominopelvic CT/MRI and serum CA125, HE4 and Cyfra 21-1 were collected preoperatively. Minilaparotomyhad been done to predict the probability of suboptimal surgery before the wound was extendedas routine andprimary debulking surgery was done. Residual tumor status wasrecorded. All datawas used to initially examine the trend of predictive value for suboptimal surgery.

Results: Fourteen patients were included,twelvepatients were primary ovarian or fallopian tubecancer, while another twowere finally diagnosed colorectal cancer with ovarian metastasis.Fifty-seven percentachieved optimal primary cytoreductive surgery. By using exact logistic regression, rectosigmoid invasion from abdominal CT, Cyfra 21-1, HE4, and minilaparotomy were significantly associated with suboptimal cytoreductive surgery.

Conclusion: Probable candidate predicting factors in clinically-advanced ovarian, fallopian tube, and peritoneal cancer were rectosigmoid invasion from abdominal CT, Cyfra21-1, HE4, and minilaparotomy.These factors will be used further for study size estimation and prognostic model design in further study.

Keywords: minilaparotomy, cyfra 21-1, cytoreductive surgery, ovarian cancer

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Study on Supply, Demand and Distribution of Physicians in JAPAN: The Case of Pediatricians and Obstetricians/Gynecologists

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Abstract

Background: In Japan, the introduction of new resident training system in 2004 triggered the "sense of physician shortage". This study picked up the pediatrician obstetrics/gynecology (OB/G) case, which seemed to be especially serious and made clear the past 20 years' trend of supply, demand and distribution of pediatrician and OB/Gs in Japan using governmental statistics.

Material and Methods: We selected the number of outpatient and total length of stay in hospitals as proxies of demand for pediatricians, and the number of deliveries and Caesarean sections (C-section) as proxies of demand for OB/Gs. As for the supply side, the number of both departments' physicians was calculated. In addition, we measured the situation of geometrical mal-distribution using Gini coefficient (0<Gini coefficient<1, the larger coefficient means the more severe mal-distribution).

Results: Since 2008 the demand for pediatricians was almost stable. As for the demand for OB/Gs, the number of deliveries had been decreasing consistently, however the number of C-sections was stable. The number of pediatricians and OB/Gs had increased gradually since 2008, however, the growth rates were lower than that of all physicians. Gini coefficient of both departments' physicians had increased since 2006.

Conclusion: As for demand for OB/Gs, the number of deliveries has been decreasing, however, the proportion of complicated deliveries seems to be increasing because of increase of late child bearing. On other hand, the supply of OB/Gs was not sufficient, and the problem of geographical mal-distribution of pediatricians and OD/Gs have become more severe.

Keywords: health manpower, pediatrician, obstetrician/gynecologist, physician shortage

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Fangotherapy, Using Maturated Mud with Hot Spring Water, for Medical Treatment ~ Pain Relieving Effect ~

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Abstract

Background and Objectives: Fangotherapy is one of the popular treatments using peloids maturated with hot spring water in Europe. Our research focused on Fango found in Abano, Italy, and modified into "Japanese style Fango" named Biofango® made by natural hot spring water with maturated peloids. We already presented the data of hyperthermia and the medical benefits of Biofango® treatment as warm-temperature effect and produce a milder burden on the body compared with only hot spring water or with hot tap water. And, stress and skin beauty, and the pain reduction effect of chronic pain were evaluated on Biofango® treatment. In this presentation, the usefulness of Biofango® treatment, especially for pain relieving effect for osteoarthritis on the knee, was assessed.

Material and Methods: The pain relief effect of osteoarthritis on the knee by Biofango® treatment were investigated using crossover study with randomly selecting 2 groups (A group; Biofango® group, B group; usual treatment destination group) of 43 men and women (over 50 years old) who had osteoarthritic knee disease. Pain Visual Analog Scale (VAS), Performance in the 30-sec Chair-Stand Test (CS-30), Timed Up and Go Test (TUG) and Health-related QOL (SF-36) were described after treatment of Biofango®.

Results and Conclusion: Fangotherapy shows a beneficial thermal effect in the previous reports. In this presentation, there was no difference in the treatment order and no carryover effect. VAS, CS-30, TUG, QOL showed significant improvement effect compared to usual treatment, and pain reduction effect was recognized.

Keywords: Fango (Biofango®) treatment, hot spring, pain relieving effect, osteoarthritic knee disease

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Consideration of Treatment Strategy Against DIC Caused by Aortic Dissection

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Abstract

Background: The frequency of DIC with aortic dissection is approximately 4 %. This DIC is local DIC occurring due to abnormal bloodstream in false lumen and vascular endothelial injury. As a result, PLT and a coagulation factor are consumed chronically at this state.

Objective: This time, 3 cases of DIC caused by aortic dissection are to be reported based on my experience.

Material and Methods: Three cases of DIC caused by aortic dissection had TEVAR. I evaluated the treatment effect from change over time of the DIC score before and after operation.

Results: Consideration: There are multiple treatment strategies against the DIC with aortic dissection. All 3 cases demonstrated improvement of the DIC by TEVAR, so that it is considered that TEVAR is an effective treatment for the DIC. However, the third patient had ITP by a lot of PLT transfusion for a long period of time. Therefore, I believe that it is beneficial to provide surgical treatment for aortic dissection with the DIC as soon as possible.

Keywords: Aortic dissection, DIC, TEVAR

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Carbapenemase Gene Acquisition of IncN-pST5 Plasmid Carrying *Bla*$_{CTX-M-2}$

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Abstract

Background: A CTX-M-2-group enzyme was the first detected extended-spectrum β-lactamase in Japan at 1993. Incompatibility group N (IncN) plasmids belonging to the plasmid multilocus sequence type (pST) 5 and carrying both carbapenemase gene both *bla*$_{IMP-1}$ and *bla*$_{CTX-M-2}$ and both *bla*$_{IMP-6}$ and a *bla*$_{CTX-M-2}$, named pMTY14373_IncN (GenBank accession no. AP018557.1) and pKPI-6 (AB616660.2), respectively, have reported in Japan at 2014.

Objective: The objective of this study was comparative analysis of among pMTY14373_IncN, pKPI-6, and an estimated their common ancestor plasmid sequence.

Material and Methods: *E. coli* TUM2255 strain isolated from boiler stool in 2004 that was positive for *bla*$_{CTX-M-2}$ and IncN plasmid by draft whole-genome sequenced by MiSeq (illumina) was sequenced using MinION (oxford nanopore technologies). Sequenced reads data of MiSeq and MinION were *de novo* assembly using Unicycler.

Results: *E. coli* TUM2255 strain harboring an IncN plasmid belonging pST5 carrying *bla*$_{CTX-M-2}$ named pMTY2255_IncN was completely sequenced. The nucleotide sequence of pMTY2255_IncN highly resembled that of pMTY14373 and pKPI-6 except for the contents of gene cassettes of a class 1 integron which contained blaIMP-1 or *bla*$_{IMP-6.}$

Conclusion: pMTY2255_IncN is considered to be a common ancestor of pMTY14373 and pST-5 IncN, and to have acquired *bla*$_{IMP-1}$ or *bla*$_{IMP-6}$ at different genetic events, respectively.

Keywords: carbapenemase-producing enterobacteriaceae, carbapenemase, plasmid, whole-genome sequencing

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A Survey about Research Ethics Education in Japanese Medical Schools

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Abstract

Background: In Japan, doctors may be involved in medical research without holding a doctorate. Educating undergraduate students about research ethics is therefore necessary. However, there is currently no report about the state of research ethics education in Japanese medical schools.

Objective: This study investigates how research ethics education is currently conducted in Japanese medical schools.

Material and Methods: We designed an anonymous questionnaire survey aimed at the research ethics educational supervisors of 82 medical schools. The questions were concerned with the respondents' role in relation to research ethics education, their teaching goals and methods for each grade, and the difficulties they encountered in their program.

Results: We received responses from 23 medical schools (recovery rate: 28%) and discarded three answers from schools which did not have a research ethics educational supervisor. Fourteen respondents explicitly mention the protection of human subjects as one of their educational goals, and nine mention research integrity. That topics vary between the different schools. Most schools conduct their ethics education by the fourth grade, but two schools conduct it in the fifth grade. Twelve schools provide ethics education over several years. It often consists of lectures and case studies, but some schools have also introduced e-learning. The issues encountered by the schools include the need for human resources and teaching materials, and the low motivation of students.

Conclusion: Although the recovery rate was low, we were able to partly assess the current state of research ethics education for medical students in Japan.

Keywords: research ethics, medical school, education, survey

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Antibacterial Effects of Antibiotic-Bonded Vascular Grafts Comparison of Rifampicin, Colistin, Vancomycin, and Daptomycin

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Abstract

Background: The prosthetic graft infections can be life-threatening. This study used a previously described *in vitro* vascular graft infection model to evaluate infection resistance in vascular grafts treated with rifampicin.

Objective: To evaluate antibacterial effects of antibiotic-bonded vascular grafts in vitro.

Material and Methods: Vascular grafts were immersed in several antibiotic solutions (rifampicin, colistin, vancomycin, or daptomycin). After *Pseudomonas aeruginosa* PAO1 or *Staphylococcus aureus* N315 were inoculated to the graft exterior, the number of colony-forming units (CFU) inside and outside the grafts was measured over time.

Results: For grafts immersed in rifampicin, CFU values outside the grafts decreased over time and inside the grafts did not increase when grafts were exposed to a 10^6 CFU/ml concentration of PAO1 or N315. However, at 10^8 CFU/ml, CFU values increased over time outside and inside the grafts. In PAO1 testing, grafts treated with colistin resisted the pathogen in the tested area, and grafts treated with both colistin and rifampicin had even greater resistance. In N315 testing, vancomycin-treated grafts had some resistance to infection, but daptomycin-treated grafts did not.

Conclusion: Rifampicin-bonded grafts have a strong antibacterial effect when the concentrations of pathogens are low. Colistin-bonded grafts are effective against *P. aeruginosa* infection and vancomycin-bonded grafts are effective against *S. aureus infection.*

Keywords: rifampicin-bonded vascular graft, colistin, vancomycin, *Pseudomonas aeruginosa, Staphylococcus aureus*

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Actual Status of Health Communication Using the Municipal National Health Insurance Data in Japan

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Abstract

Background: In recent years, local municipalities in Japan have been required to utilize the municipal National Health Insurance (NHI) data, such as medical receipts or health examination results which they own, for health services. In order to plan and conduct these health services effectively and locally, health communication with residents (providing information related to local health condition and promoting decision-making) is essential. However, there is little knowledge about how to utilize municipal NHI data for health communication.

Objective: The purpose of this study is to investigate the actual status and effects of health communication using the municipal NHI data by nationwide survey.

Material and Methods: We conducted semi-structured interviews for three municipalities and designed a self-administered questionnaire survey for all local municipalities (n=1,741) in Japan. This study was conducted as part of the interdisciplinary joint research project in Toho University.

Results: From the results of the interviews, we identified five possible health services and situations which related to health communication with residents as follows: community organizations (developing health promotion volunteers), group health education (holding health classes), individual health guidance, explanatory meeting on the results of health examination, residential meeting (e.g. for health promotion planning). Based on these findings, we designed the questionnaire to ask how the municipal NHI data are used for health communication in the above services and situations, and whether these activities worked effectively. The questionnaire survey will be conducted in October 2019 and a part of primary data will be showed at the conference.

Keywords: Health Communication, Health Service, National Health Insurance Data, Local Municipalities

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In Vivo Characterization of Rate-Dependent Change in QT Interval of *Microminipig* Assessed by Atrial Electrical Pacing: Development of Correction Formulae of QT Interval

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Abstract

Background: QT interval on electrocardiogram has been known to be shortened in a heart rate-dependent manner. Electropharmacological studies on *microminipig* have been extensively performed, in which the correction formulae for humans and dogs have been empirically used to eliminate the rate-related influences on the QT interval. However, it is still unknown how much the conventional correction formulae can appropriately correct the QT interval of *microminipig*.

Objective: We tried to develop correction formulae for microminipigs, which were compared with the conventional ones for humans and dogs.

Material and Methods: The QT interval was measured at atrial pacing cycle length (CL) of 400, 500, 600, 750 and 1000 ms in the halothane-anesthetized *microminipig* (n=5). Based on the basal heart rate of the animal (80 bpm), slope constant α values in the QT-interval correcting formulae were calculated to estimate the QT interval at a CL of 750 ms (80 bpm) from the QT/RR relationship under other pacing CLs.

Results: The following correction formulae were established for the halothane-anesthetized *microminipigs.* Linear equation: $QTc=QT-0.2072(CL-750)$. Non-linear equation: $QTc=QT/(CL/750)^{0.4007}$. Both slope constant α values; namely, 0.2072 in the former and 0.4007 for the latter, were closer to that for humans than that for dogs.

Conclusion: These new correction formulae can better correct the QT interval of the halothane-anesthetized *microminipig* compared with the conventional correction formulae for humans and dogs. Moreover, analysis of slope constant α values indicates that the rate-dependent change in the QT interval of *microminipig* would better mimic that of humans than that of dogs.

Keywords: *microminipig*, experimental animal model, electrophysiology, QT interval, correction formula

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Electrophysiological Characterization of *Microminipig* as a Laboratory Animal for Pharmacological Study by Analyzing Bepridil-Induced Cardiovascular Responses

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Abstract

Background: *Microminipig* is an extraordinarily small-sized miniature pig, weighing approximately 7 kg at 6 months. We have characterized *microminipig* as an *in vivo* laboratory animal in comparison with dogs. However, information is still limited regarding physiological and pharmacological contributions of IKs and ICaT in the *in situ* heart of *microminipig.* Bepridil can suppress I_{CaT}, I_{CaL}, I_{Ks}, I_{Kr}, and I_{Na} with IC_{50} values of 0.4-10, 0.5, 6.2, 13.2 and 30 μmol/L, respectively.

Objective: To clarify physiological roles of IKs and ICaT in *microminipig*, we examined *in vivo* cardiovascular effects of bepridil.

Material and Methods: Experiments were performed using male *microminipigs* of approximately 10 kg under general anesthesia (n=4). Bepridil in doses of 0.3 and 3 mg/kg was intravenously infused over 10 min.

Results: The low dose hardly altered any of these variables. The high dose increased the heart rate at 5 min followed by a decrease for 15-60 min, and also increased the $LVdP/dt_{max}$ at 10 min, whereas it decreased the mean blood pressure and left ventricular end-diastolic pressure for 5-10 min. The high dose prolonged the QRS width and QT interval for 10-60 min, and QTcF and $J\text{-}T_{peak}c$ for 5-60 min, whereas it shortened the $T_{peak}\text{-}T_{end}$ at 10 min followed by prolongation for 20-30 min. No significant change was observed in the PR interval.

Conclusion: *Microminipig* may be less sensitive for ICaT inhibitory action of bepridil, whereas they are more responsive to I_{Na}, I_{Kr} and I_{Ks} suppression than dogs. This information may be useful to apply *microminipig* to electropharmacological study.

Keywords: *microminipig*, I_{CaT} inhibitory action, I_{Ks} suppression

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Real-Time Evaluation of Systemic-Ocular Microcirculation Using Laser Speckle Flowgraphy in White Rabbits

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Abstract

Backgroud: The activity of the sympathetic nervous system has been reported to be correlated with the ocular blood flow.

Objective: To establish systemic-ocular microcirculation using laser speckle flowgraphy (LSFG) in white rabbits and investigate the circulatory response to a systemic adrenaline load.

Material and Methods: We used six normal adult male New Zealand white rabbits. Heparinized arterial cannulas were placed in the right brachial arteries for measurement of blood pressure while the blood flow rates of the right femoral artery and the left common carotid artery were measured using laser Doppler to determine blood flow volume in each artery. Mean blur rate (MBR) of the retinal vessels and choroid area were measured using LSFG-rabbit™ (Softcare, Fukuoka, Japan), developed for animals. Continuous intravenous adrenaline (100-1000 ng/kg) was administered for 10 minutes, and changes in each index were observed.

Results: The MBR increased in the retinal vessels and choroid area in a dose-dependent manner with the adrenaline load. The Δ mean blood pressure showed a significant correlation (R=0.37 to 0.77) with each area of ΔMBR. The Δ carotid blood flow volume showed a significant negative correlation with Δ retinal blood vessel MBR at 100-300 ng/kg dose and the Δ femoral arterial blood flow volume showed a significant positive correlation with Δ choroid area of MBR at each dose.

Conclusion: We successfully demonstraited a real-time evaluation system for systemic-ocular microcirculation using LSFG in white rabbits. A systemic adrenaline load caused an increase in MBR, associated with elevation in blood pressure.

Keywords: systemic-ocular microcirculation, laser speckle flowgraphy, mean blur rate

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Analysis of Ocular Blood Flow Waveforms in Model Rat with Retinopathy of Prematurity Using Laser Speckle Flowgraphy-Micro

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Abstract

Background: The most representative model of human ROP is the rat oxygen-induced ischemic retinopathy (OIR) model. As a result of the addition of BS (Beat Strength) to the analysis items covered by the Laser Speckle Flowgraphy (LSFG) -Micro system, it is now possible to analyze blood flow waveforms even in small animals. BS/MBR, obtained by dividing BS by the ocular blood flow value (Mean blur rate (MBR), is believed to be positively correlated with peripheral vascular resistance (PVS).

Objective: The object of this study is to reveal the BS/MBR relationship between room air rats (RmA) and those with oxygen-induced retinopathy (OIR).

Material and Methods: BS values in 16 previously reported cases involving 50/10 OIR model rats and 17 cases involving reared in room air rats (RmA) were analyzed and reevaluated. Blood flow was measured for subjects with age in days (P) at 14 (P14) and 18 (P18). BS/MBR values were compared between the 2 OIR and RmA groups.

Results: The BS/MBR at P14 (OIR vs. RmA: 0.64±0.16 vs. 0.41±0.17; p=0.0004) and P18 (OIR vs. RmA: 0.4±0.12 vs. 0.28±0.12; p=0.0089) were recorded.

Conclusion: Although BS/MBR decreased in both the OIR and RmA groups by P18, both BS and MBR values were significantly higher in the OIR group. Blood flow waveform analysis was possible even in small animals such as rats, and BS values may be considered to be useful in examining vascular resistance. (246 words)

Keywords: ocular blood flow, retinopathy, laser speckle flowgraphy

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Evaluation for Lytic Spectrum against Various *Legionella* Strains of *Legionella* Induced Phage

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Abstract

Background: Aspiration of *Legionella* spp. contaminated aerosols are a major cause of *Legionella* infections. Source control of infection in the environment is important for the reduction of *Legionella* diseases.

Objective: The objective of this study was evaluation and molecular characterization of *Legionella* temperate phage derived from prophage of *Legionella* spp. chromosome.

Material and Methods: A total of 16 stored bacterial strains in our laboratory, *L. pneumophila* serogroups 1 to 11, 13, *L. longbeachae*, *L. bozemanii*, *L. micdadei*, and *L. sainthelensi*, were used as hosts of prophage. Prophages were induced by 0.5 mg/L of mitomycin C. Crude lysate including Temperate phage was prepared by filtration using the 0.2 μm filter of fully culture supernatant using buffered yeast extract (BYE) broth and then polyethylene glycol precipitation. Lysis activity and spectrum of temperate phages for *Legionella* spp. strains were evaluated by spot test on BYE agar. To characterize of temperate phage derived from phage lysogenic *Legionella* spp., which crude temperate phage genome was analyzed by shotgun metagenomic sequencing using a next-generation sequencer MiSeq (Illumina).

Results: The samples considered to contain temperate phages were named MTS (mitomycin C treated sample) 1 to 16 in the order of strains-description. MTS1-7,9 and 15 lysed 3-10 kinds of *Legionella* strains. Ongoing phage genome analysis has now detected intact prophage genome sequence from MTS1 and MTS2.

Conclusion: Some *Legionella* phage including MTY1 and MTY2 showed broad spectrum for different serogroups of *L. pneumophila* and species of *Legionella*.

Keywords: bacteriophage, mitomycin C, shotgun metagenomic sequencing

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Estimation of the Social Burden of Stroke of Each Prefecture in Japan by Comprehensive Cost of Illness Method

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Abstract

Background: Aging speed varies among regions resulting in the difference of medical demands. Therefore, redistribution of medical resources in response to local medical demands is important. Medical demands should be estimated taking the incidence and the social burden of diseases into account. We tried to estimate the medical demands for each prefecture in Japan, taking stroke as an example.

Material and Methods: We used the C-COI (Comprehensive Cost of Illness) method to calculate the burden of stroke for each prefecture. The C-COI method developed from the COI method accounts for the burden of the long-term care (LTC), whose proportion is significant in chronic conditions. The C-COI includes direct medical costs, morbidity costs, mortality costs, direct LTC cost (public LTC insurance), and family burden of LTC. All data sources were government statistics (2013 or 2014).

Results: The national value of C-COI per capita was 49,603 JPY, of which the LTC burden was 27,017 JPY. There were big differences among prefectures; the largest was 67,086 JPY in Kagoshima, and the smallest was 38,650 JPY in Saitama. Components of C-COI differed by prefectures.

Conclusion: This study demonstrated that it was possible to calculate the social burden of stroke of each prefecture using C-COI methods. There was a big difference in total cost and proportions of components among prefectures. This result suggested that each prefecture has a different situation related to stroke: incidence and mortality, acute medical care, recovery rehabilitation, LTC, etc. The results of this study will contribute to future medical policy decision-making in Japan.

Keywords: health economics, aging, community medicine, long term care, stroke

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Syntheses of 4-OH and 5-OH Imidacloprids

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Abstract

4-OH and 5-OH imidacloprids, important metabolites of neonicotinoid insecticides, were synthesised in 4 steps starting from Smethylisothiourea sulfate. The structure of 4-OH imidacloprid was determined by X-ray crystallographic analysis. This is the first example of the synthesis of both metabolites independently.

Background: Imidacloprid is the first commercial example of the neonicotinoid insecticides, which are a widely used class of insecticides and extremely effective against a large variety of insects. Neonicotinoid insecticides including 1act selectively on nicotinic acetylcholine receptors (nAchR). They are taken up by plants and transported to all organs including flowers, pollen and nectar as well as any fluid produced by the plant. There are increasing concerns about the impact of these systemic neonicotinoid insecticides on nontarget organisms such as honey bees and humans. Since some metabolites of neonicotinoid insecticides have been proven to possess a variety of toxicities, it is also important to evaluate the biological effect and presence in the environment of metabolites of neonicotinoid insecticides. In this work, we report the syntheses of 4-OH and 5-OH imidacloprids which are important metabolites of 1 in addition to imidacloprid olefin. Chemical syntheses Figure 1. Imidacloprid and its important metabolites. of 2 and 3 have not been reported to date except for the microbial oxidation of 1 producing 3. Figure 2. Crystallographic structure of 2·H_2O. Scheme 1. Synthesis of 4-OH imidacloprid and 5-OH imidacloprid.

Results: Based on reported procedures, S-methylisothiourea sulfate was nitrated using fuming HNO_3 and H_2SO_4 to give 6. Compound 6 was reacted with 5-aminomethyl-2-chloropyridine smoothly in warm ethanol to give intermediate 8 (Scheme 1). N-Allylation of8with allyl bromide using NaH under cooling conditions in DMF gave 9a and 9bin 45% yield and 19% yield, respectively. Although these allylation reactions produced a mixture of regioisomers in moderate selectivities, this synthetics routeenabled the synthesis of both 4-OH and 5-OH imidacloprids independently. From 9a, Lemieux-Johnson oxidationusing sodium periodate and a catalytic amount of osmium tetroxide caused the oxidative cleavage of the olefin group followed by the cyclization of resulting aldehyde 10 to produce 4-OH imidacloprid. The structure of

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2 was unambiguously determined by X-ray crystallographic analysis. Additionally, 5-OH imidacloprid was synthesized from 9bby a similar method. 1H and 13C NMR spectra of synthetic 3exhibited good agreement with those reported in the literature.

Conclusion: We have synthesized 4-OH and 5-OH imidacloprids, which are important metabolites of imidacloprid. The structure of 2 was determined by X-ray crystallographic analysis. This is the first example of the synthesis of both 2 and 3 independently.

Keywords: neonicotinoid insecticides, 4-OH and 5-OH imidacloprids, metabolitse

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Comprehensive Evaluation of Antioxidant Effects of Japanese Kampo Medicines

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Abstract

Background: Oxidative stress due to the overproduction of reactive oxygen species plays an important role in the pathogenesis of various diseases. Many Kampo medicines are applied to oxidative stress-related diseases, but the relationship between their clinical effects and antioxidant effects has not been clarified.

Objective: In this study, we aimed to comprehensively evaluate the antioxidant effects of 147 oral formulations of Japanese Kampo medicines.

Material and Methods: Firstly, the antioxidant activities of 147 formulations of Kampo medicines were evaluated using in vitro three kinds of radical scavenging assays, namely, DPPH assay, SOD assay, and the oxygen radical absorption capacity assay. Then, three out of 147 formulations of Kampo medicines were selected for further investigation of the intracellular antioxidant activities, against H_2O_2-induced oxidative stress in HepG2 cells using DCFH-DA assay. Finally, the three Kampo medicines were evaluated in vivo antioxidant effects in mice using biological antioxidant potential (BAP) test.

Results: Three Kampo medicines tested, namely, Tsudosan, Daisaikoto, and Masiningan, showed the most potent in vitro antioxidant activities. The results of DCFH-DA assay demonstrated that all three Kampo medicines significantly inhibited H_2O_2-induced oxidative stress in HepG2 cells. Moreover, Tsudosan significantly increased the serum BAP values when orally administrated to mice, indicating that it also had in vivo antioxidant activity.

Conclusion: Tsudosan was identified as a Kampo medicine with potent antioxidant activity, which may be one of the mechanisms closely correlated to its clinical usage against blood stasis.

Keywords: Kampo, antioxidant, daisaikoto, Tsudosan, Masiningan

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Tigliane Diterpenoids From *Wikstroemia Scytophylla*

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Abstract

Background: The plants of *Wikstroemia* species (Thymelaeaceae) biosynthesize highly functionalized diterpenoids with excellent biological activities. *Wikstroemia scytophylla* Diels. is an evergreen shrub mainly distributed in Yunnan, Sichuan and Tibet of P.R. China. Previous chemical investigations of this plant were quite limited, and have reported the isolation of guaiane-type sesquiterpenes, tigliane-type diterpenoids, flavonoids, and lignans.

Objective: In continuation of our investigations for discovery of novel biological diterpenoids from plants of Thymelaeaceae family, the present study aimed to the isolation and structure elucidation of new terpenoids from W. scytophylla.

Material and Methods: The whole plants of *W. scytophylla* were collected in Yunnan Province, P.R. China. The plants were extracted with MeOH, and the extract was partitioned with EtOAc and H_2O. The EtOAc fraction was further separated by ODS column chromatography. The final purification was carried out by preparative RP-HPLC. The chemical structures of isolated compounds were elucidated by various spectroscopic and physicochemical analyses.

Results: Five tiglinane-type diterpenoids were isolated from the extract by multiple column chromatographic methods. Two compounds were previous known compounds and were identified as Dapholosericin A and Stelleracin C. Three new compounds were named as Wikstrocins A-C.

Keywords: Tiglinane, diterpenoid, *Wikstroemia scytophylla*

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Identification and Comparison of Steroidal Glycosides from *Polygonatum* Species by LC-ESI-MS Analysis

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Abstract

Background: The plants belonging to the genus of Polygonatum (Liliaceae) are perennial herbaceous plants widely distributed in East Asia and Europe. Polygonatum species has a long history of using as traditional medicines and function foods both in Europe and Asia. The steroidal glycosides were reported to be their major bioactive constituents.

Objective: In this study, we performed an LC-ESI-MS analysis to identify the steroidal glycosides in four Polygonatum species, namely, P. falcatum, P. macranthum, P. odoratum and P. sibiricum, which are cultivated in Japan.

Material and Methods: A fast and simple method based on liquid chromatography coupled with electrospray ionization mass spectrometry (LC-ESI-MS) was developed to systematically analyze and identify the steroidal glycosides in Polygonatum species. The dried rhizomes were extracted with methanol, then analyzed by a Shimadzu LCMS-8040 triple quadrupole liquid chromatography mass spectrometry in selected ion monitoring (SIM) and full-scan modes.

Results and Disscussion: A total of 37 steroidal glycosides were identified, which included 22 known glycosides and 15 previously undescribed steroidal glycosides, on the basis of their chromatic and mass fragmentation patterns. Four species showed similar chemical compositions of steroidal glycosides but also have some interspecific differences. Biosynthetically, *P. falcatum* and *P. macranthum* contained steroidal glycosides with higher oxidation level in their sapogenin parts, and the sugar moieties were also different from *P. odoratum*. On the contrary, no steroidal glycosides were identified from *P. sibiricum*.

Keywords: LC-MS, Steroidal glycosides, Genus *Polygonatum*

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Determination of Organic Pollutants in Environmental Samples from Tokyo Bay, Japan

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Abstract

Background: In this study, two kinds of organic pollutants, surfactants and polycyclic aromatic hydrocarbons (PAHs), in the coast of Tokyo Bay were analyzed by LC–MS and GC–MS. Surfactants are present in detergents and disinfectants, and are able to accumulate in marine environment through untreated waste water. PAHs consist of multiple benzene rings and originate from burning fossil fuels and oil spillage. Some PAH are carcinogenic and tend to accumulate in bottom sediment due to their hydrophobic properties. These pollutants were quantified and analyzed on distribution and accumulation by location.

Material and Methods: Environmental samples, surface water, sediment and shellfish, were collected from four coasts around Tokyo Bay and their adjacent rivers. Cationic surfactants (CS), anionic surfactants (AS) and nonionic surfactants (NS) were analyzed using LC–MS (2010EV, Shimadzu). Eight types of PAHs, phenanthrene (Phe), anthracene (Anth), fluoranthene (Flu), pyrene (Pyr), chrysene (Chry), benzo[*b*]fluoranthene ([*b*]flu), benzo[*a*]pyrene ([*a*]pyr) and perylene (Pery), were quantified using GC–MS (QP2010, Shimadzu).

Results: CS showed accumulation from surface water to sediment and shellfish, possibly because of its low biodegradability. AS results showed less accumulation and NS were not detected in most samples. Comparison with results from 2003 to 2018 indicated surfactant contentin river water hasbeen decreasingwhile covering area of wastewater treatment has been increasing. Results showed values varied between locations for all pollutants with a higher PAHs content in sediment at highest densely populated areas near the Tokyo metropolitan area.

Keywords: surfactants, polycyclic aromatic hydrocarbons, Tokyo bay

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Public Participation for Health Promotion

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Abstract

Background: In 2000, the Japanese government announced that municipalities need to implement a health promotion plan and recommended to involve citizens in the planning and implementation stages. However, public participation is limited to a few citizens. Recently, within the environment and urban planning field, meetings in where citizens are invited via random selection is gathering attention to involve "everyday citizens" into the policy making process. This methodology could work positive in health-related issues.

Objective: The purpose of this study is to introduce the methodology of Jumin-Kyogikai (residential meeting by randomly selected citizens) and explore the possibilities of its adaptation in the field of health promotion through a case study of Ohta city, Gunma prefecture, Japan.

Material and Methods: We analyzed the protocol and report of Jumin-Kyogikai and conducted semi-structured interviews for administrative officer in Ohta city. This study was conducted as part of the interdisciplinary joint research project in Toho University.

Results: The meetings of Jumin-Kyogikai were held 4 times during July and October 2017 and 50 citizens were participated. The participants discussed about the recommendation for the reform plan for health policies. From the interviews, it was suggested that improving health related policy requires local concerns and local communication. For example, one of the participants started her own activities for her mother in the city, because she realized that such kind of services does not exist within the city.

Conclusion: The research supports the view that the methodology contributes to the planning process and implementation process.

Keywords: health communication, public participation, randomly selected, communication

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Fluorescence Enhancement of Nitroarenes and Its Analytical Application

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Abstract

Nitroarenes such as nitropyrenes and nitrobenzanthrones have been receiving a considerable amount of attention, because of their mutagenic activity and wide occurrence in the environment. They are especially abundant in exhaust gas and particles from vehicle engines and in smoke and soot from factories. It has been pointed out that inhaling polluted air induces lung cancer with high probability. Nitroarenes are reduced to amino compounds and then detected by HPLC with FLD or chemiluminescence detector (CLD), attaining high analytical sensitivity. In addition, nitroarenes can be also detected sensitively by means of gas-chromatography / tandem-mass- spectrometry with negative ion chemical ionization. These methods, however, require additional and expensive equipment and/or troublesome pretreatment is also necessary before the analysis. In 2017, it was found that 1-NP and 3-NBA in ethanol solutions give rise to the fluorescence enhancement. This prompted us to apply the fluorescence enhancement to the analysis of nitroarenes. In the study, we investigated the fluorescence enhancement of ethanol solutions of 1-NP and 3-NBA, which are important in environmental health-risk assessment, and examined its application to quantitative analysis of the two compounds by HPLC-FLD. The chemical species causing the enhancement are also discussed on the basis of the data of LC/MS measurements and molecular orbital calculations.

Keywords: Nitroarene, 1-nitropyrene, 3-nitrobenzanthrone, HPLC-FLD, LC/MS

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A Search for Intergenerational Exchange with a Focus on Daily Life Support

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Abstract

Background: Japan has seen an increase in single elderly people living alone, as well as child abuse due to lack of support. As a strategy to prevent isolation of both sides, the development of a mechanism to promote intergenerational exchange would potentially be effective. In this study we extracted the needs of parents, as well as the ways in which the elderly generation can support parents.

Material and Methods: We searched the CiNii database for documents published by 2015, using the keywords 'life support" and "childcare support". Nineteen studies were included for analysis. In addition, individual interviews were conducted with the three corporations that support child-rearing on the issues when elderly people support the generation of child-raisin

Results: The literature review showed that parents were in need of 1 a one-day nursery service, 2 child transfers, caring for their older children, 3 nursery services when their child was ill, and 4 housework support. The interviews revealed that older people who support younger generation parents tend to impose their own parenting views on them and they are less aware of personal information leaks.

Conclusion: For intergenerational exchanges focusing on daily life support. It is necessary to change the attitude of the elderly generation from a critical one of "the recent parents do not conform to the norm" to a more permissive one. Many elderly people may need to receive training to change their attitudes before engaging in such services.

Keywords: intergenerational exchange, daily life support, child-rearing

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Serum D-and L-Lactate, Pyruvate, and Glucose Levels in Individuals with at-Risk Mental State and Correlations with Clinical Symptoms

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Abstract

Background: Little information exists on the peripheral metabolite levels in individuals with at-risk mental state who meet the criteria for a high-risk state of psychosis. Here, we aimed to investigate serum levels of glucose, pyruvate, and d- and l-lactate, which may act as signalling molecules for learning and memory in neuronal cells.

Material and Methods: High performance liquid chromatography or commercial kits were used to assess serum metabolites in individuals with attenuated psychosis symptoms of at-risk mental state (n=24, men=12) who were not receiving antipsychotics. The metabolite levels of these individuals were compared with those of age- and sex-matched healthy individuals (controls, n=23 men=11). Correlations between the metabolites and clinical symptoms of at-risk mental state were also examined.

Results: Individuals with at-risk mental state had higher serum glucose levels than did controls (P=2.18 × 10-3), while no significant difference in pyruvate levels were observed between the groups. Individuals with at-risk mental state had significantly lower serum l-lactate levels than did controls (P=6.31×10^{-5}), while no differences in d-lactate levels were observed. Furthermore, a negative correlation was identified between serum l-lactate levels and Positive and Negative Syndrome Scale negative symptoms scores (r=-0.5651, P=4.01×10^{-3}) in individuals with at-risk mental state.

Conclusion: We found that, compared with controls, individuals with at-risk mental state have reduced serum l-lactate levels, which may predate psychosis onset, and may be involved in the related cognitive impairments.

Keywords: at-risk mental state, glucose, L-lactate, pyruvate, schizophrenia

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Vascular Complications from CAG/PCIs Comparing Day Cases and In-Patient Cases at Songklanagarind Hospital: A Retrospective Study

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Abstract

Background: Cardiovascular catheterization is a procedure for diagnosis and/or treatments (CAG/PCIs) of coronary artery diseases. Songklanagarind Hospital has initiated the day-case CAG/PCIs program since 2009. However, the incidence and risk factors of vascular complications post procedure had not been reported and studied.

Objective: To compare the incidence and the risk factors of vascular complications between patients undergone CAG/PCIs as outpatients (day case) and those as inpatients.

Material and Methods: We performed a retrospective chart review of the patients, visiting the Naradhiwas Rajangarin Heart Center from October 2014 to September 2018. We included patients, aged 18 years or older who undergone the CAG/PCIs. The patients, referred to and from the other hospitals were excluded. The main outcome were vascular complications defined as 1) bleeding with significant blood loss during the procedure or 2) Hematoma 24 hours or 1 month after the procedure. The Wilcoxon's rank sum and chi-squared test were used to assess the risk factors.

Results: Of all 784 patients undergone CAG/PCIs, 387 were day cases and 397 were inpatients. The incidence of vascular complications was not differed significantly between the day cases (1.30%, 95% CI: 0.72%-1.87%) and inpatients (1.80%, 95% CI: 1.10%-2.42%) We found that the risk factors of vascular complications were percutaneous coronary interventions and using a vascular closure device to remove the introducer sheath.

Conclusion: Performing CAG/PCIs as day case did not increase the risks of complications post-procedure. Patients undergone PCI or with vascular closure devices used should be monitored closely for the vascular complications.

Keywords: cardiovascular catheterization, day case, vascular complication

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A Microfluidic Based Electrochemical Sensor for Clinical Monitoring

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Abstract

Background: Next-generation clinical monitoring requires fast, precise analysis techniques to give the clinician relevant chemical data in real-time. Real-time chemical measurement is most easily achieved using microdialysis (as the sampling probe is FDA approved). The integration of an electrochemical sensor into a microfluidic chip has increased attention, which allows the achievement of real-time chemical monitoring due to low consumption of analytes, short-time analysis, low cost, and compact size. In this study, dopamine used as a model is a neurotransmitter responsible for regulating a wide variety of vital life functions such as brain's function and Parkinson's disease.

Objective: This study aims to develop a microfluidic-based electrochemical sensor for dopamine detection under a continuous flow system.

Material and Methods: A microfluidic chip with typically 250 μm in width and 100 μm in depth channels was fabricated using Polydimethylsiloxane (PDMS). The performance of a microfluidic chip integrated with a modified screen-printed electrode was investigated in different dopamine concentration using a computer-controlled microfluidic platform by uProcess software.

Results: The result revealed that our microfluidic-based electrochemical sensor was successfully employed to determine dopamine continuously. The microfluidic-based dopamine sensor exhibited a linear range from 2 to 10 μM with the detection limit (LOD) of 230 nM. Also, the microfluidic-based electrochemical sensor for dopamine monitoring could overcome the problem of fouling.

Conclusion: Expectedly, this novel platform can be a powerful tool which allows us to monitor dynamic changes of dopamine and other analytes in real-time, especially when incorporated with microdialysis probe.

Keywords: microfluidic device, continuous monitoring, amperometric technique

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Predictors of Clinical Outcome Among Thai Patients with Atrial Fibrillation–Associated Acute Ischemic Stroke

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Abstract

Background: Although atrial fibrillation (AF) is a poor prognostic factor in general acute ischemic stroke patients, studies regarding specific predictors among AF–associated acute ischemic stroke (AF–stroke) subgroup are limited in number.

Objective: We aim to identify predictors of 3–month death among an AF–stroke subgroup.

Material and Methods: This retrospective cohort study was conducted at a university hospital in Thailand. Patients with AF–stroke admitted between 2012 and 2017 were enrolled into the study. We collect the baseline characteristics, clinical presentations, complications, and outcomes measured by the modified Rankin scale.

Results: Among 118 AF–stroke patients, the mortality rate was 26.27%. The predominant characteristics of the death group compared to the survived group were older age, higher CHA2DS2–VASc and NIHSS scores, higher number of overall hospital complications, and acute kidney injury (AKI). The independent predictor of 3–month death was developing AKI during hospitalization (adjusted OR=3.122 95% CI=1.635–15.365, p=0.031,). In contrast, receiving treatment with an oral anticoagulant prior to the stroke episode was a protective factor (adjusted OR=0.090, 95% CI=0.008–0.979, p=0.048).

Conclusion: Developing AKI during hospitalization was the independent predictor of 3–month death among AF–stroke patients.

Keywords: acute ischemic stroke, predictor, atrial fibrillation, mRS, acute kidney injury

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Gut Microbiome Study in Pediatric Patients with Short Bowel Syndrome Receiving Alternate Gastrointestinal Prophylactic Antibiotics

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Abstract

Background: Gut microbiome in human is attributed as a vital organ. Unbalanced microbial ecosystem in the small intestine accounts for the development of small intestine bacterial overgrowth (SIBO) which is a common unwanted condition in pediatric patients with short bowel syndrome (SBS). For the reason, gut prophylaxis using alternate antimicrobial agents is practiced in these cases. However, the effectiveness of the prophylaxis in terms of controlling microbial composition has not been well studied.

Objective: This study aimed to explore the change of the gut microbial composition in pediatric patients with SBS before taking prophylactic antibiotics and after taking each phase of cyclic antibiotics.

Material and Methods: Pediatric patients with SBS under 10 years taking oral alternate metronidazole and trimethoprim-sulfamethoxazole as '10-day cyclic protocol' were involved in this study. Stool specimens collected from these patients were analyzed for bacterial phyla, using the Illumina 16s metagenomic sequencing.

Results: Fecal specimen from 3 SBS patients were studied. The gut microbial composition was found to change prominently in each alteration of treatment. *Firmicutes* spp. and *Proteobacteria* spp. were 2 dominant phyla within the feces of SBS patients. The average of gut microbiome among these patients was calculated. Obviously, in antibiotic-free condition, Firmicutes was the predominant phylum (70 %), followed by Proteobacteria (25%) and other phyla was 5%, whereas the percentage of Proteobacteria became significantly higher following 10 days of antimicrobial use (65 % comparing to 35% of Firmicutes).

Conclusion: Prophylactic cyclic antibiotics treatment is effective in controlling bacterial ecosystem in pediatric SBS patients.

Keywords: gut microbiome, short bowel syndrome, antibiotics

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Effect of the Different Molar Ratio of Colistin on the Surface Properties of Sodium Deoxycholate Sulfate

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Abstract

Background: Colistin is currently used as the last line for multidrug-resistant gram-negative bacteria treatment, but its usage clinically is hinder by its nephrotoxicity. Sodium deoxycholate sulfate (SDS) as the newly developed amphiphilic carrier has been proven to decrease nephrotoxicity for several peptide drugs. Thus development toward colistin to produce better formulation should be necessary.

Objective: In this study, we attempt to see surface properties of SDS relative to different molar ratio with colistin sulfate.

Material and Methods: The measurements were carried out using dynamic light scattering. The different molar ratio of colistin to SDS was titrated from 100:1 to 100:19, followed by size and zeta potential measurement. We also calculate the isoelectric point (pI) of colistin sulfate using ChemAxon software.

Results: The results showed that the increasing ratio of colistin in SDS-Colistin also increases the zeta potential of the nanoparticle from -65 to -28.13. The particle size and PDi showed a slight decrease from 411 to 345 d.nm and 0.82 to 0.34 respectively, in increased ratio. The calculation of colistin pI resulted in pH 10.4.

Conclusion: Therefore, these results suggest that the surface charges of Colistin-SDS can be affected by the different drug to carrier molar ratio. The result can lead to the optimal design of colistin-SDS formulation in future development.

Keywords: colistin, sodium deoxycholate sulfate, zeta potential

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Size and Surface Charges of Polymyxin B in an Amphiphilic Carrier 'Sodium Deoxycholate Sulfate'

Sunisa Kaewpaiboon, Pornvichai Temboot and Teerapol Srichana

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Abstract

Background: Polymyxin B (PMB) is a cyclic peptide that currently used as a last-line therapy against the multidrug-resistant (MDR) Gram-negative bacteria. However, nephrotoxicity is a major drawback of PMB for continuous treatment. New formulation using lipid-based carrier has been introduced to overcome this problem.

Objective: Recently, sodium deoxycholate sulfate (SDCS) based formulations showed lower nephrotoxicity than the PMB. Thus, the PMB micelles based on SDCS have been developed.

Material and Methods: The critical micelle concentration (CMC) was evaluated using a pendant drop tensiometer and dynamic light scattering.

Results: We found that surface tension revealed CMC at 24.97 and 21.52 μM for PMB and SDCS, respectively. The titration of PMB with SDCS exhibited CMC at mole ratio of 1:45 (PMB:SDCS). Before CMC, PMB without SDCS showed larger size diameter (275.10 d.nm) with high polydispersity index (0.967) and zeta-potential approximately 7.74 mV. At the CMC, PMB micelles showed size average 203.05 d.nm and zeta-potential approximately -16.50 mV with lower polydispersity index 0.114.

Conclusion: These finding could provide crucial data for further development of PMB micelles.

Keywords: polymyxin B, sodium deoxycholate sulfate, critical micelle concentration, surface tension

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The Antibacterial Activity of Mupirocin Nanoparticle-Loaded Hydrogel in Methicillin-Resistant *Staphylococcus Aureus*

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Abstract

Background: Mupirocin is commercially available as a cream and ointment, the indications include prophylaxis in ulcers, operative wounds, burn wounds and treatment of skin infections. However, the disadvantages of those formulations are greasiness, stickiness, and viscosity temperature variations.

Objective: The novelty of this study is a loading of mupirocin nanoparticles into the hydrogel (MLH). That is expected to enhance the antibacterial activity of mupirocin.

Material and Methods: This study investigated the antimicrobial activity of MLH against methicillin-resistant *Staphylococcus aureus* (MRSA) in comparison with mupirocin (pure drug) by minimum inhibitory concentration (MIC) test using broth microdilution method and minimum bactericidal concentration (MBC) using colony culture plating directly the content of wells with concentrations higher than the MIC value. MIC and MBC were confirmed by flow cytometry. The live-cells count was compared after exposure with the MIC and MBC of MLH at five times interval (0, 6, 12, 18 and 24 h) on MRSA. The fluorescein diacetate was employed to monitor cell viability before measurements were made using a flow cytometer.

Results: The results indicated that MIC and MBC of MLH were 0.30 µg/ml and 2.44 µg/ml, respectively. The live-cell counts obtained during 24 h showed a decrease in the number of viable bacteria. At 24 h the viable bacteria of MIC and MBC are 44-49% and 0.2-1.8%, respectively. These two techniques offer considerable advantages in antimicrobial activity studies. This can be further developed for use in the clinic for early susceptibility testing.

Keywords: mupirocin nanoparticles, loaded hydrogel, flow cytometer, methicillin-resistant *Staphylococcus aureus*

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Development of Nanodispersion-Based Sildenafil Pressurized Metered-Dose Inhalers

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Abstract

Background: Sildenafil is a selective phosphodiesterase type-5 inhibitor used to treat pulmonary arterial hypertension (PAH). When taken orally, sildenafil has low bioavailability, a moderate onset of action, and dose-dependent adverse systemic reactions.

Objective: Inhaled sildenafil formulation could enable an effective drug targeting to the lungs, provide a rapid onset of action, help avoid gastrointestinal tract issues, reduce the dose of sildenafil, have fewer adverse systemic reactions, and provide a non-invasive method for delivering sildenafil into the pulmonary system.

Materials and Methods: In this study, the nanodispersion-based sildenafil metered-dose inhaler (MDI) has been developed by using poloxamer 188 (P188) as a stabilizer. The physical and chemical stability, delivered dose uniformity, in vitro aerosol characteristics, electrical charge profile, and in vitro cytotoxicity and inflammatory effect of the formulations were assessed.

Results: The optimal formulation was stable and well-uniform after storage at room temperature for 6 months. The MDI formulation had suitable aerosol characteristics for inhaled products, was non-toxic to respiratory epithelial cells, and did not induce the inflammatory responses of alveolar macrophages. The study found that P188 possesses the ability to prevent the growth of sildenafil citrate monohydrate crystals in hydrofluoroalkane-based formulations. P188 also affected mass median aerodynamic diameter (MMAD) and electrical charge of the MDI formulations. With increased P188 concentration, both MMAD and large negatively-charged particles increased.

Conclusion: The study provided a basis for the development of sildenafil MDI as a potential candidate for the treatment of PAH.

Keywords: sildenafil, metered-dose inhaler, aerosol particle size distribution, poloxamer, pulmonary arterial hypertension

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The Interaction of Amphotericin B Lipid-Based Nanomicelles with Cholesterol and Ergosterol: An Insight into Affinity and Selectivity

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Abstract

Background: Amphotericin B (AmB) is one of the most effective and commonly used as an antifungal against invasive fungal diseases. AmB presents higher activity in cells containing ergosterol (fungi) than cholesterol (mammalian) confers them "selectivity" and enables their therapeutic use. However, AmB has severe side effects, including hemolysis and nephrotoxicity.

Objective: Our previous works, AmB carried with sodium deoxycholate sulfate (SDCS) have been developed and shown that enhanced antifungal activity, reduced hemolysis and lower nephrotoxicity than conventional AmB. However, the improved potency and reduced toxicity of this AmB formulation are still not known.

Material and Methods: Here, we evaluated the affinity and specificity of AmB-SDCS nanomicelles to cholesterol and ergosterol (human and bacterial cell membrane components in respective order) using spectroscopic techniques.

Results: Both UV-Vis and fluorescence spectroscopy experiments revealed that AmB and Fungizone® preferred to bind with cholesterol better than ergosterol. While AmB-SDCS nanomicelles exhibited similar binding affinity to cholesterol and ergosterol. The rate of binding constant of cholesterol to ergosterol (Kbcho/Kbergo) is ~180, ~80, and ~1 times for AmB, Fungizone®, and AmB-SDCS nanomicelles, respectively. From these data, the orders of affinity to cholesterol are AmB standard > Fungizone® > AmB-SDCS nanomicelles.

Conclusion: These results could provide insight into the mechanism of AmB-SDCS nanomicelles on binding affinity and selectivity to fugal cells.

Keywords: amphotericin B, sterol, selectivity, spectroscopy

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The Efficacy of Anti-Tuberculosis Dry Powder Aerosols for Treatment of TB Patients

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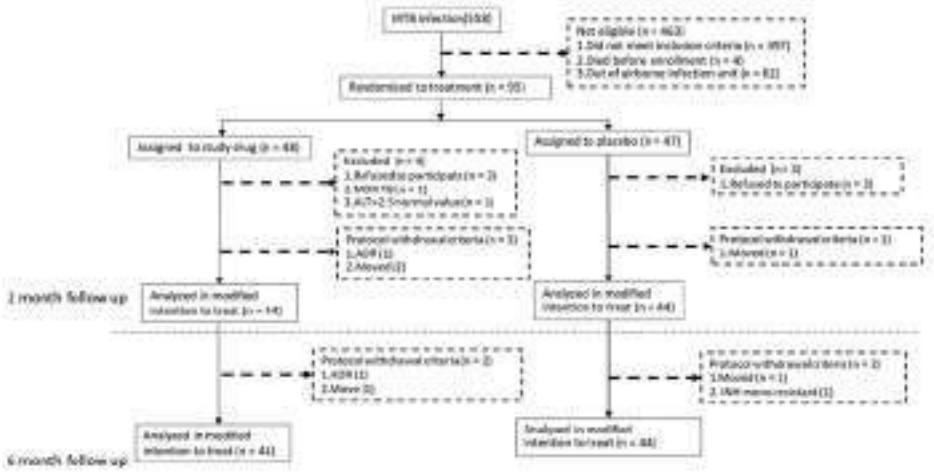
Abstract

Objective: The anti-tuberculosis dry powder was prepared as nano-particulate system for inhaling into the respiratory system. The clinical trial was studied in TB patients. To evaluate efficacy and safety of oral anti-tuberculosis drugs plus anti-tuberculosis dry powder inhaler in treatment of pulmonary TB compared to oral anti-tuberculosis drugs plus placebo.

Material and Methods: This clinical trial was carried as the following diagram.



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Results: The results revealed that the primary outcomes of study groups are not different from the control groups. It is important to note that the sputum conversion from positive to negative in the study groups was significantly higher than the control groups during 4 weeks and 6 weeks. After that there was no difference between the two groups. The cough and chest X-ray gave a clear evidence of significant lower in study group.

Keywords: lung tuberculosis, anti-tuberculosis, efficacy, adverse effects

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Groin Dressing Post Cardiovascular Catheterization: Pressure Dressing vs Transparent Film at Songklanagarind Hospital: A Retrospective Study

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Abstract

Background: After Cardiovascular catheterization puncture site care is usually done with pressure dressing in many institutions due to the belief that is should prevent the vascular complication as bleeding, hematoma. Songklanagarind Hospital performed a new of dressing using Transparent film dressing since 2017. However, the incidence of vascular complications had not been reported and studied.

Objective: To compare the incidence of vascular complications between patients with the pressure dressing and transparent film dressing applied to the femoral artery puncture wound.

Material and Methods: We performed a retrospective chart review of the patients, after sheath removal at the Naradhiwas Rajangarin Heart Center from May 2017 to September 2018. We included patients, aged 18 years or older who undergone manual compression (MC) method for hemostasis. Vascular closure device used were excluded. The main outcome were vascular complications defined as 1) bleeding with significant blood loss during the procedure or 2) Hematoma 24 hours or 1 month after the procedure. The Wilcoxon's rank sum and chi-squared test were used.

Results: Of all 419 patients undergone MC, 208 were transparent film and 211 were pressure dressing. The incidence of vascular complications was not differed significantly between the transparent film (0.48%, 95% CI: 0.00-0.96) and pressure dressing (1.89%, 95% CI: 0.95-2.83)

Conclusion: Performing Transparent film dressing did not increase the vascular complications post-procedure. Patients undergone pressure dressing difficult assessment the vascular complications.

Keywords: cardiovascular catheterization, transparent film dressing, pressure dressing, vascular complication

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Development of Microfluidic Devices for Cell Culture Using Stereolithography (SLA) 3D Printing Technology

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Abstract

Background: Microfluidic technology, which offer the possibility of handling small volume of samples in a microchannel, has become an emerging and powerful tool for various biomedical and clinical applications such as cancer screening, high-throughput drug testing, and point-of-care diagnostics. Among different applications, the use of microfluidics for cell culture has attracted much interest due to the cost and complexity of conventional process. However, fabrication of microfluidic devices is often complicated, time consuming, requires expensive equipment and cleanroom facilities. In this study, we therefore focused on the feasibility of creating 3D microfluidic device for cell culturing using stereolithography (SLA) 3D printing as a simple, cost effective and precise methodology.

Objective: This study aims to develop of a rapid prototype of cell culture on a chip using microfluidic technology and applications of stereolithography (SLA) 3D printing.

Material and Methods: The microchannels was designed using CAD software. The models were printed Stereolithography (SLA) 3D printer. The 3D printed molds were washed with isopropanol after printing and then they were cured by UV light. Then the Polydimethylsiloxane (PDMS) was poured into the master mold. Channel dimension profile of 3D printed mold and PDMS replica were inspected by using a Scanning Electron Microscope (SEM).

Results: According to the accuracy of the printed mold, characterized by SEM, there was no difference between the dimension profiles, including radius and channel parts, of the CAD design and the printed mold. The width of radius and channel exhibited acceptable errors with less than 1.5% and 4%, respectively. Interestingly, these reusable molds can be printed within 10 mins, at an average cost of 0.5 US$, which lead to fast prototyping and cost effective production. Conclusion: (SLA) 3D printing technology represents a powerful, simple, rapid, and cost-effective method to fabricating highly complex microfluidic devices.

Keywords: (SLA) 3D Printing, microfluidics chip, cell culturing

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We would also like to extend special thanks all those who contributed to the 11th JSOBMS both direct and indirect support.

Organizing Committee of the 11th JSOBMS
November 2019

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The journal's former title: Songklanagarind Medical Journal

Owner: Prince of Songkla University

Aims and scope: Journal of Health Science and Medical Research is an online, quarterly peer reviewed scientific journal published by Prince of Songkla University. This journal aims to publish original article, review article, case reports in all aspects of basic and applied medical and health sciences. Manuscripts submitted to Journal of Health Science and Medical Research will be accepted on the understanding that the author must not have previously submitted the paper to another journal or have published the material elsewhere. The journal does not charge for submission, processing or publication of manuscripts and even for color reproduction of photographs.

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Guideline for Authors

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Manuscript types

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They are invited by Editor-in-Chief of JHSMR and should be written in English and structured as follows: Introduction, Main text, Conclusion, and References. Editorial should not be less than 2,000 and cannot exceed 3,000 words total (counting from Introduction to Conclusion), and should keep references to a minimum.

2. Special article

These articles are invited by Editor-in-Chief of JHSMR. They should be written in English and structured as follows: Abstract, Introduction, Main text, Conclusion, and References. Abstract should be less than 250 words. Special articles should not be less than 2,000 and cannot exceed 3,000 words total (counting from Introduction to Conclusion).

3. Original article

These form the large majority of papers published by the JHSMR. There is 3,500 words and 40 references limit while efforts should be made to keep manuscripts as succinct as possible. Full reports should include separate sections entitled Abstract, Introduction, Material and Methods, Results, Discussion and Conclusion. The abstract should contain no more than 250 words. The following sections should be included after the text: Acknowledgments, Financial Support, and Disclosures regarding real or perceived conflicts of interest.

4. Case report

This format can be used for submission of important preliminary observations, technique modifications, or data that do not warrant publication as a full paper. Short reports should contain no sub-headings, and be no more than 2,000 words in length, with no more than 100 words in the abstract, 2 tables and/or figures, and 15 references.

5. Review article

The JHSMR will consider reviews on relevant topics in medicine, medical education, medical innovation and related areas. Typically reviews will be submitted by leading authorities in a field. We encourage mini-reviews, providing concise reviews of focused topics in no more than 3,000 words 6 tables and/or figures and no limit reference. The abstract should contain no more than 250 words. The larger reviews will be considered.

Manuscript preparation

Prepare your manuscript using a word processing program and save it as a .doc file using Microsoft Word. For items that accompany the text (letters, figures, copyright forms, etc.), you may upload the following file types: .xls, .ppt, .gif, .pdf, .jpg, .eps, .png, and .tif.

Cover letter and signatures

All manuscripts should be accompanied by a cover letter with the following information:

1. The title of the paper

2. A brief description of the significance of the paper to the readers of the JHSMR

3. A statement confirming that the material is original, has not already been published, and has not and will not be submitted for publication elsewhere as long as it is under consideration by the JHSMR

4. Written disclosure of any relationships or support which might be perceived as constituting a conflict of interest

5. Name and signature of corresponding author

Authorship

There is no limit to the number of authors that may be listed.

Manuscript formatting

1. Spacing: The text should be in 11 or 12 point type, fully double-spaced, leaving a margin of 1 inch on all sides. Continuous line numbers (NOT restarting with each page) should be included throughout the manuscript and pages should be numbered consecutively.

2. Title page: This should include, in the following sequence, the title, a list of all authors, and author institutions, identified by superscripts in Arabic numerals. The corresponding author should be denoted by an asterisk, with address, e-mail, and phone number in a footnote. The running title should be limited with 40 words. The key words should be at least of 3 words.

3. Title: The manuscript title should be as succinct as possible. Titles should generally not include abbreviations and not be longer than 60 characters (including spaces).

4. Abbreviations: Abbreviations are commonly overused, compromising the clarity of manuscripts. Authors are advised to keep abbreviations to a minimum, using them when they are clearer than long terms (e.g. PCR, DNA), but avoiding them when possible when they are non-standard and idiosyncratic. Terms should be spelled out with first usage in both the abstract and text, with the abbreviation following in parentheses. After this first usage, the abbreviation must be used consistently. Plurals of abbreviations do not require apostrophes.

5. Drug names: Proprietary names of drugs may not appear in the title but may be used in conjunction with the generic name when the drug is first mentioned in the abstract, and again when first mentioned in the text. Thereafter, use only the generic name.

6. Names of organisms: Genus and species should be italicized. After the first usage the genus should be abbreviated with a single letter (e.g. *E. coli*). For different species within a genus, the genus should be spelled out with the first usage of each.

7. Figures: Figures should be numbered in Arabic numerals and cited in the text. It should be noted that a fee is required for color illustrations in print, but authors can choose black & white in print. All figures should contain a brief legend. The size should be 5x7 itches with at least of 300 dpi.

8. Tables: Tables should be serially numbered in Arabic numerals and cited in the text. Each table should be placed on a separate page at the appropriate point in the text or at the end of the manuscript.

9. References: References should be cited by consecutive numbers in the text. The numbers should appear in superscripts that appear after closing punctuation. First 6 authors should be listed. If there are more than 6 authors, list the first 6 authors followed by "et al.". Abbreviate journal names as in PubMed, with journal name and volume number in italics. References should be from peer-reviewed publications.

Examples of references

1. Journal

- Hanprasertpong J, Geater A, Jiamset I, Padungkul L, Hirunkajonpan P, Songhong N. Fear of cancer recurrence and its predictors among cervical cancer survivors. J Gynecol Oncol 2017;28:e72.
- Rujirojindakul P, Liabsuetrakul T, McNeil E, Chanchayanon T, Wasinwong W, Oofuvong M, et al. Safety and efficacy of intensive intra-operative glycaemic control in cardio-pulmonary bypass surgery: a randomised trial. Acta Anaesthesiol Scand 2014;58:588-96.

2. Supplement

- Lofwall MR, Strain EC, Brooner RK, Kindbom KA, Bigelow GE. Characteristics of older methadone maintenance (MM) atients [abstract]. Drug Alcohol Depend. 2002;66(Suppl 1):S105.

3. Book

- Fealy S, Sperliny JW, Warren RF, Craig EV. Shoulder anthroplasty: complex issues in the primary and revision setting. New York: Thieme; 2008.

4. Chapter

- Waltzman SB, Shapiro WH. Cochlear implants in adults. In: Valente M, Hosfond-Dunn H, Roeser RJ, editors. Audiology treatment. 2nd ed. New York: Thieme; 2008;p.361-9.

5. Patent

- Tintara H, inventor; Prince of Songkla University, assignee. Amniotomy training model. Thai petty patent 7488. September 18, 2012.

6. Journal article on the Internet

- Sanders GD, Bayoumi AM, Holodniy M, Owens DK. Cost-effectiveness of HIV screening in patients older than 55 year of age. Ann Intern Med [serial on the Internet]. 2008 Jun [cited 2008 Oct 7]; 148(12). Available from: http://www.annals.org/cgi/reprint/148/12/889.pdf

7. Monograph on the Internet

- Field MJ, Behrman RE. Where children die: improving palliative and end-of-life case for children and their families [monograph on the Internet]. Washington: National Academy Press; 2003 [cited 2008 Sep 26]. Available from: http://nap.edu/openbookphp?record_id=10390&page=1

8. Homepage/Website

- Cancer-Pain.org [homepage on the Internet]. New York: Association of Cancer Online Resources, Inc.; c2000-01 [cited 2008 Oct 3]. Available from: http://www.cancer-pain.org/

Contact

E-mail: manager@jhsmr.org, offices@jhsmr.org

Other websites

Thai Journals Online: https://www.tci-thaijo.org/index.php/jhsmr


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Variety and Controversy to Creativity

NOVEMBER 13-15, 2019

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