The April 2020 Newsletter of The GP-TCM Research Association

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Editor-in-chief: Aiping Lu (lap64067611@126.com); executive editor: Ping Guo (s193231@hkbu.edu.hk); consulting editor: Qihe Xu (qihe.xu@kcl.ac.uk).

Hong Kong Baptist University (HKBU) today (24 March) offers over 5,000 sets of “HKBU Chinese Medicine Immunity Enhancement Remedy” for free to suitable frontline healthcare workers of the Hospital Authority (HA) as a token of appreciation for their effort in fighting the coronavirus outbreak. Each recipient can obtain a six-day course of the Remedy free of charge. The Chinese Medicine Immunity Enhancement Remedy is prescribed by the School of Chinese Medicine (SCM) and produced with herbal medicine ingredients free of any contaminants such as pesticides and heavy metals. This gift to frontline healthcare workers is made possible by the generous donation from the Philip K.H Wong Foundation and also with the support of the Tan Siu Lin Foundation. Free distribution of the HKBU Chinese Medicine Immunity Enhancement Remedy to HA frontline healthcare workers is yet another healthcare charitable initiative carried out by the University. Since February, it had collaborated with the Lions & Hong Kong Baptist University Chinese Medicine Charity Foundation, The Hong Kong Jockey Club Charities Trust, Fong’s Family Foundation and Fong Shu Fook Tong Foundation to distribute the herbal remedy to elders aged 65 or above, patients with chronic illnesses, residents of elderly care homes, families receiving Comprehensive Social Security Assistance (CSSA) and other people in need of help. Around 20,000 beneficiaries are getting the Remedy. Upon knowing that HKBU is distributing the herbal remedy for free to the needy, more donors come forward with Chinese medicines or donations to support this meaningful initiative. They include Jiangyin Tianjiang Pharmaceutical Industry Co Ltd, Mr Chung Po Yang, Mr Timothy Lam, Jr, Mrs Lee Siu Lun, Dr Ronald Lu and a senior Civil Engineering alumnus. (*The School of Chinese Medicine at HKBU is a member institution of GP-TCM RA*)

2. **PuraPharm manufacturing three traditional Chinese medicine formulas granules to help fight COVID-19**

In February 2020, China stepped into the key time of the COVID-19 epidemic control. PuraPharm (Nanning) Pharmaceutical Co., Ltd is commissioned by Lee Shau Kee Foundation Limited (under the Anti-COVID 19 Fund), manufacturing approximately 850,000 doses granules of three traditional Chinese medicine (TCM) prescriptions under special approval by leaders of the Food and Drug Administration of Guangxi Autonomous Region through opening a green channel. These prescriptions are recommended by the National Health Commission and the National Administration of Traditional Chinese Medicine and used for the prevention, treatment and recovery of COVID-19 infection with Qiwei Tang Granule (Seven Principle Decoction), Qingfei Paidu Granule (Lung Detoxifying Formula) and Kangfu Granule.
(Recovery Formula). These formulas granules were specifically designated for donation to 55 hospitals in the Hubei Province in China in connection with the COVID-19 epidemic situation and provided to more than 50,000 medical staffs and 40,000 patients.

**Introduction of TCM Prescription:**

**Qiwei Tang (Seven Principle Decoction):** is a prescription for prevention of COVID-19, which is developed by many experts in Hubei Provincial Hospital of TCM according to the clinical syndrome differentiation and treatment of patients, and experience in the prevention and treatment of SARS (Severe acute respiratory syndrome). It consists of seven herbs including HuangQi (Astragali Radix), with the effect of clearing heat, detoxifying dampness and drying, and enhancing immunity.

**Qingfei Paidu Tang (Lung Detoxifying Formula)** consists of 21 herbs, which made up of 4 optimized classical prescriptions of “ShiganTang”, “Wuling San”, “Xiaochaihu Tang” and “Sheganmahuang Tang”. It is suitable for the treatment of mild cases, moderate cases, severe cases of COVID-19 infection. As the recognized therapeutic prescription with positive curative effect of COVID-19 pneumonia, it is used in 10 provinces with 66 designated medical institutions, with an effective rate of 93.12%.

**Kangfu Granule (Recovery Formula)** is the suitable for the lung-spleen “Qi” deficiency pattern of convalescence of COVID-19. It consists of 9 herbs including FaBanxia (Pinellinae Rhizoma Praeparatum), with the effect of tonifying Qi and warming spleen, resolving dampness, accelerating the recovery from COVID-19 infection. According to the feedback from the medical institutions, using TCM prescription in the recovery period can obviously solving the symptoms, promote the absorption of lung inflammation to avoid causing some sequelae. *(Reported by Dr Hisayoshi Norimoto. Purapharma is a member institution of GP-TCM RA)*
More Information Related to COVID-19

1. We hope this book can provide references for other countries affected by the COVID-19, and also promote the experience exchange and cooperation in disease prevention, control, diagnosis and management, thus promote the development of global health together. Details: Guidance for Corona Virus Disease 2019: Prevention, Control, Diagnosis and Management. (ISBN 978-7-117-29817-9). [http://books.ipmph.com/books/detail/2035540.shtml]

2. A series of multifaceted public health interventions was temporally associated with improved control of the COVID-19 outbreak in Wuhan, China. These findings may inform public health policy in other countries and regions to combat the global pandemic of COVID-19. Details: Association of public health interventions with the epidemiology of the COVID-19 outbreak in Wuhan, China. JAMA. 2020. [https://jamanetwork.com/journals/jama/fullarticle/2764658]

3. Suspending intra-city public transport, closing entertainment venues and banning public gatherings were associated with reductions in case incidence. The national emergency response appears to have delayed the growth and limited the size of the COVID-19 epidemic in China, averting hundreds of thousands of cases by 19 February (day 50). Details: An investigation of transmission control measures during the first 50 days of the COVID-19 epidemic in China. Science. 2020. [https://science.sciencemag.org/content/early/2020/03/30/science.abb6105.full]

4. Even in the event of apparent elimination, SARS-CoV-2 surveillance should be maintained since a resurgence in contagion could be possible as late as 2024. Details: Projecting the transmission dynamics of SARS-CoV-2 through the postpandemic period. Science. 2020. [https://science.sciencemag.org/content/early/2020/04/14/science.abb5793.full]


7. There is a current outbreak of Coronavirus (COVID-19) disease. Details: All information from the World Health Organization. [https://www.who.int/health-topics/coronavirus#tab=tab_1VI](https://www.who.int/health-topics/coronavirus#tab=tab_1VI)

8. Pangolins should be considered as possible hosts in the emergence of novel coronaviruses and should be removed from wet markets to prevent zoonotic transmission. Details: Identifying SARS-CoV-2 related coronaviruses in Malayan pangolins. *Nature*. 2020. [https://www.nature.com/articles/s41586-020-2169-0](https://www.nature.com/articles/s41586-020-2169-0)

**Highlights on Academic Achievements of GP-TCM RA Members**

1. **Identification and characterization of N9-methyltransferase involved in converting caffeine into non-stimulatory theacrine in tea.** *Nature Communications*. 2020. [https://www.nature.com/articles/s41467-020-15324-7](https://www.nature.com/articles/s41467-020-15324-7)

Caffeine is a major component of xanthine alkaloids and commonly consumed in many popular beverages. Due to its occasional side effects, reduction of caffeine in a natural way is of great importance and economic significance. Recent studies reveal that caffeine can be converted into non-stimulatory theacrine in the rare tea plant *Camellia assamica* var. kucha (Kucha), which involves oxidation at the C8 and methylation at the N9 positions of caffeine. However, the underlying molecular mechanism remains unclear. Here, we identify the theacrine synthase CkTcS from Kucha, which possesses novel N9-methyltransferase activity using 1,3,7-trimethyluric acid but not caffeine as a substrate, confirming that C8 oxidation takes place prior to N9-methylation. The crystal structure of the CkTcS complex reveals the key residues that are required for the N9-methylation, providing insights into how caffeine N-methyltransferases in tea plants have evolved to catalyze regioselective N-methylation through fine tuning of their active sites. These results may guide the future development of decaffeinated drinks.

*(Corresponding author Rongrong He is a member of the Board of Directors of GP-TCM RA)*


NRBF2, a regulatory subunit of the ATG14-BECN1/Beclin 1-PIK3C3/VPS34 complex, positively regulates macroautophagy/autophagy. In this study, we report that NRBF2 is required for the clearance of apoptotic cells and alleviation of inflammation during colitis in mice. NRBF2-deficient mice displayed much more severe colitis symptoms after the administration of ulcerative colitis inducer, dextran sulfate sodium salt (DSS), accompanied by prominent intestinal inflammation and apoptotic cell accumulation.
Interestingly, we found that \textit{nrbf2}^{-/-} mice and macrophages displayed impaired apoptotic cell clearance capability, while adoptive transfer of \textit{nrbf2}^{+/+} macrophages to \textit{nrbf2}^{-/-} mice alleviated DSS-induced colitis lesions. Mechanistically, NRBF2 is required for the generation of the active form of RAB7 to promote the fusion between phagosomes containing engulfed apoptotic cells and lysosomes via interacting with the MON1-CCZ1 complex and regulating the guanine nucleotide exchange factor (GEF) activity of the complex. Evidence from clinical samples further reveals the physiological role of NRBF2 in maintaining intestinal homeostasis. In biopsies of UC patient colon, we observed upregulated NRBF2 in the colon macrophages and the engulfment of apoptotic cells by NRBF2-positive cells, suggesting a potential protective role for NRBF2 in UC. To confirm the relationship between apoptotic cell clearance and IBD development, we compared TUNEL-stained cell counts in the UC with UC severity (Mayo Score) and observed a strong correlation between the two indexes, indicating that apoptotic cell population in colon tissue correlates with UC severity. The findings of our study reveal a novel role for NRBF2 in regulating apoptotic cell clearance to restrict intestinal inflammation.

(Responding author Zhaoxiang Bian is the chairperson of GP-TCM RA Interest Group of Clinical Studies)

**Recommended Reading**

1. Subtype selectivity and functional bias are vital in current drug discovery for G protein-coupled receptors (GPCRs) as selective and biased ligands are expected to yield drug leads with optimal on-target benefits and minimal side-effects. Herein, we present an affinity mass spectrometry approach for screening herbal extracts to identify active ligands of a GPCR, the 5-HT2C receptor. Our study establishes an efficient approach to discovering novel GPCR ligands by exploring the largely untapped chemical space of natural products. Details: A novel G protein-biased and subtype-selective agonist for a G protein-coupled receptor discovered from screening herbal extracts. 
   \textit{ACS Central Science}. 2020. https://doi.org/10.1021/acscentsci.9b01125

2. As a single agent, only \textit{Phaseolus vulgaris} resulted in a statistically significant weight loss compared to placebo, although this was not considered clinically significant. No effect was seen for \textit{Camellia sinensis} or \textit{Garcinia cambogia}. Statistically, but not clinically, significant differences were observed for combination preparations containing \textit{C. sinensis}, \textit{P. vulgaris} or \textit{Ephedra sinica}. Of the herbal medicines trialled in ≤3
randomized controlled trials, statistically and clinically significant weight loss compared to placebo was reported for *Irvingia gabonensis*, *Cissus quadrangularis*, and *Sphaeranthus indicus* combined with *Garcinia mangostana*, among others, but these findings should be interpreted cautiously because of the small number of studies, generally poor methodological quality, and poor reporting of the herbal medicine interventions. There is currently insufficient evidence to recommend any of the herbal medicines for weight loss included in the present review. Details: Effectiveness of herbal medicines for weight loss: A systematic review and meta-analysis of randomized controlled trials. *Diabetes, Obesity, and Metabolism*. 2020. [https://doi.org/10.1111/dom.13973](https://doi.org/10.1111/dom.13973)

3. Twenty sessions of manual acupuncture was superior to sham acupuncture and usual care for the prophylaxis of episodic migraine without aura. These results support the use of manual acupuncture in patients who are reluctant to use prophylactic drugs or when prophylactic drugs are ineffective, and it should be considered in future guidelines. Details: Manual acupuncture versus sham acupuncture and usual care for prophylaxis of episodic migraine without aura: Multicentre, randomised clinical trial. *BMJ*. 2020. [https://doi.org/10.1136/bmj.m697](https://doi.org/10.1136/bmj.m697)
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Invitation from the Official Journal of GP-TCM RA
For more information, please visit: http://www.wjtcm.net/submitarticle.asp

1. WJTCM Call for papers: Herbal Medicine Analysis and Quality Standards.

World Journal of Traditional Chinese Medicine (WJTCM)
The official journal of WFCMS and GP-TCM

Special Issue on
Herbal Medicine Analysis and Quality Standards

CALL FOR PAPERS

Qualitative and quantitative determination of the effective components together with other workable approaches in traditional Chinese medicines and other herbal medicines is the reasonable and effective comprehensive quality control method, which is the fundamental basis for their quality standard setting and thereby to guarantee the clinical efficacy and safety of herbal medicines at large.

We invite researchers home and abroad to contribute original research articles as well as reviews on the topic of herbal quality.

Potential topics include but are not limited to:
a. Phytochemical analysis of complex herbal mixtures.
b. Development of state of the art analytical methods.
c. Tactics for herbal quality standard elaboration
d. Metabolic analysis of herbal drugs and herbal finished products.
e. Application of new quality control technology and methods in herbal industry.

Authors can submit their manuscripts via the Manuscript System at https://mc03.manuscriptcentral.com/wjtcm.
2. WJTCM Call for papers: Pharmacology and Toxicology of Herbal Medicine.

The special issue on Pharmacology and Toxicology of Herbal Medicine focuses on the biological effects and mechanisms of herbal medicine. It has a broad scope, covering basic research to clinical studies regarding pharmacology and toxicology.

We cordially invite researchers and experts to contribute original research articles as well as reviews on pharmacology and toxicology of herbal medicine.

Potential topics include but are not limited to:

a. Bioactive principles from herbal medicine,

b. Biological, pharmacological activities and mechanisms of herbal medicine,

c. Genomics, proteomics, metabolomics, pharmaconinformatics studies on herbal medicine,

d. Toxicology of herbal medicine.

Authors can follow the author instructions and submit their manuscripts via the Manuscript System at:

https://mc03.manuscriptcentral.com/wjtcm

Guest Editors

Hongxi Xu
Ph.D, Professor
Dean, School of Pharmacy
Shanghai University of Traditional Chinese Medicine, China
E-mail: xuhongxi88@gmail.com

Xuanbin Wang
Ph.D, Professor
Renmin Hospital
Hubei University of Medicine, China
E-mail: wangxb@hbu.edu.cn

Pulok Kumar Mukhrjee
Ph.D, Professor
School of Natural Product Studies
Jadavpur University, Kolkata, India
E-mail: pulokkm@gmail.com

Deadline for submission
January 30, 2021

Intended publication date
April 30, 2021
3. WJTCM Call for papers: Systems Biology and Metabolomics of Traditional Chinese Medicine

Traditional Chinese Medicines (TCMs) are evidenced to confer therapeutic actions by largely interacting with dysregulated multi-layers molecules that underlie diseases, which can be defined as the holistic characteristics of TCMs to treat different diseases.

The fact is that systems biology, and metabolomics have the robust-capacity to better understand the holistic characteristics by globally deciphering the complex interactions between TCMs and diseases associated with dysregulated molecules. Currently, they are widely used to address many key questions in TCMs involving chemical characterization, therapeutic efficacy, toxicology and metabolic features, etc.

We invite the scholars in the niches to contribute research articles, reviews, and perspectives to this special issue.

Potential topics include but are not limited to:

a. metabolomics of TCMs  
b. multiple omics of TCMs  
c. network pharmacology of TCMs  
d. systems biology of TCMs

Authors can submit their manuscripts via the Manuscript System at https://mc03.manuscriptcentral.com/wjtcem

Guest Editors

Xi-jun Wang  
Ph.D., Professor  
Heilongjiang University of Chinese Medicine, China  
E-mail: xijunw@sina.com

Hai-tao Lu  
Ph.D., Professor  
Shanghai Jiao Tong University, China  
E-mail: haitao.lu@sjtu.edu.cn

Toshiaki Makino  
Ph.D., Professor  
Nagoya City University, Japan  
E-mail: makino@phar.nagoya-cu.ac.jp

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May 30, 2021

Intended publication date  
October 30, 2021
4. WJTCM Call for papers: Processing of Chinese Medicinal Materials (Zhongyao Paozhi)

In traditional Chinese medicine (TCM) practice, one of the distinctive features is the use of processed Chinese medicinal materials (Yinpin). It is Zhongyao Paozhi, a unique pharmaceutical technique, that transforms raw Chinese medical materials into Yinpin. Zhongyao Paozhi plays a pivotal role in guaranteeing the clinical efficacy and safety of TCM therapies.

We invite researchers home and abroad to contribute original research articles as well as reviews on the topic of Zhongyao Paozhi.

Potential topics include but are not limited to:

a. Scientific basis of Zhongyao Paozhi.
b. Intelligentization of Zhongyao Paozhi.
c. Techniques of Zhongyao Paozhi.
d. Quality standards of adjuvant materials for Zhongyao Paozhi.
e. Quality markers of Yinpin.
f. Quality standards of Yinpin.

Authors can follow the author instructions and submit their manuscripts via the Manuscript System at: https://mc03.manuscriptcentral.com/wjtcm.

Guest Editors

Tu-ilin Lu
Ph.D, Professor
Department: Nanjing University of Chinese Medicine
e-mail: lutuling2005@126.com

Zhi-ling Yu
Ph.D, Professor
School of Chinese Medicine, Hong Kong Baptist University
zlyu@hkbu.edu.hk

Yuan-shiun Chang
Ph.D., Professor
College of Chinese Medicine, China Medical University
yschang@mail.cmu.edu.tw

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December 25, 2020
Elegant and beautiful moutan and peony are cultivated for ornamental (worldwide) and medicinal (mainly in China) purposes. In Chinese materia medica, the dried root bark of *Paeonia suffruticosa* (moutan cortex) clears heat, cools the blood, promotes blood circulation, and removes blood stasis. However, superb moutan cortex in commerce (produced in Anhui, Hunan, and Sichuan provinces) originates from *Paeonia ostii* (a small shrub with white flowers). The dried de-barked root of cultivated *Paeonia lactiflora* (paeoniae radix alba) nourishes the blood, regulates menstruation, pacifies the liver, relieves pain, preserves yin, and stops sweating. The dried intact root of wild *Paeonia lactiflora* (paeoniae radix rubra) has similar functions to that of moutan cortex.

The taxonomic treatment of plants in the genus of *Paeonia* has not yet been well established. Neither has the pharmacological mechanism of Chinese medicinals from this genus. Nevertheless, being a suffruticose (woody in the lower part of the stem) plant native to China, moutan is obviously different from peony. Peony is herbaceous (composed of non-woody tissue) and native to China, Japan, Korea, Mongolia, and Far East Russia.

The above colour photographs, English texts and Chinese poems are contributed by Prof Hubiao Chen (Hong Kong), Dr Ping Guo (Hong Kong) and Prof Jiqing Liu (Shenzhen), respectively. This column is advised by Prof Zhongzhen Zhao (Hong Kong).