

The September 2019 Newsletter of The GP-TCM Research Association Chinese National Day Special Edition



Editorials

 1.

A novel drug discovery strategy inspired by TCM philosophies



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Traditional Chinese medicine (TCM) *fufang* and the principle of *Jun-Chen-Zuo-Shi*

With only a small number of exceptions, TCM prescriptions comprise several herbs (and minerals or animal parts) to produce 'composite formulae' (*fufang*) based on the principle of *Jun-Chen-Zuo-Shi* [1]. It represents the basic theories behind the formulation of TCM treatments and guides the combination of different herbal medicines in *fufang*, based on the healing/pharmacological properties and constituents of each herb. The *Jun* (emperor) component is the principal phytocomplex targeting the major symptom of the disease. There are only a few varieties of *Jun* medicinals that are administered as a single formula, usually in large doses. The *Chen* (minister) herbs synergize with *Jun* to strengthen its therapeutic effects, and may also treat secondary symptoms. The *Zuo* (assistant) medicinal reduces or eliminates possible adverse or toxic effects of the *Jun* and/or *Chen* components, while also enhancing their effects and sometimes treating secondary symptoms. Finally, the *Shi* (courier) herbs facilitate delivery of the principal components to the lesion sites or facilitate the overall action of the other components.

Discovery of a universal effector compound in *Fufang Danshen* formulations

Fufang Danshen formulations (all contain *Salvia miltiorrhiza*) have a long history of application in China for treating cardiovascular and cerebrovascular diseases. Such formulations include *Danshenyin*, *Guanxin Danshenpian* and *Fufang Danshen Diwan* (Dantonic®). However, their compositions are complex and mechanisms of action still unclear.

Supported by successive grants from Chinese Ministry of Education, National Natural Science Foundation of China, and Project for Innovative Research Team of Research and Technology of Shaanxi Province, our team used mathematical modelling, advanced analytical equipment and metabolomics technologies to analyse active metabolite(s) of several *Danshen* formulations. Pharmacokinetic studies showed isopropyl 3-(3,4-dihydroxyphenyl)-2-hydroxypropanoate (IDHP) was preferentially found in heart and brain tissues, in agreement with the lesion sites expected to be targeted by this formulation according to TCM principles. Furthermore, synthetic IDHP was generated and shown to have significant anti-myocardial fibrosis [2], anti-myocardial ischemia and other effects [3], strongly suggesting that IDHP is a universal effector compound of these botanical formulations.

A simplified *Jun-Shi* Medicinal Compatibility Model

On the basis of this research, we extended our research on a selection of classic TCM herbal prescriptions with proven clinical safety and efficacy profile for over hundreds of years. As a strategy for drug discovery, we proposed a simplified *Jun-Shi* Medicinal Compatibility Model [4] to identify the phytochemicals from TCM formulations that reach the bloodstream and the pharmacological effects they may have in the body. We postulate that *Jun-Shi* medicinal pair also has the synergistic characteristics of a *fufang*, targeting the active phytochemicals to their designated sites of action. At the same time, the simpler composition of the *Jun-Shi* medicinal pair provides a less

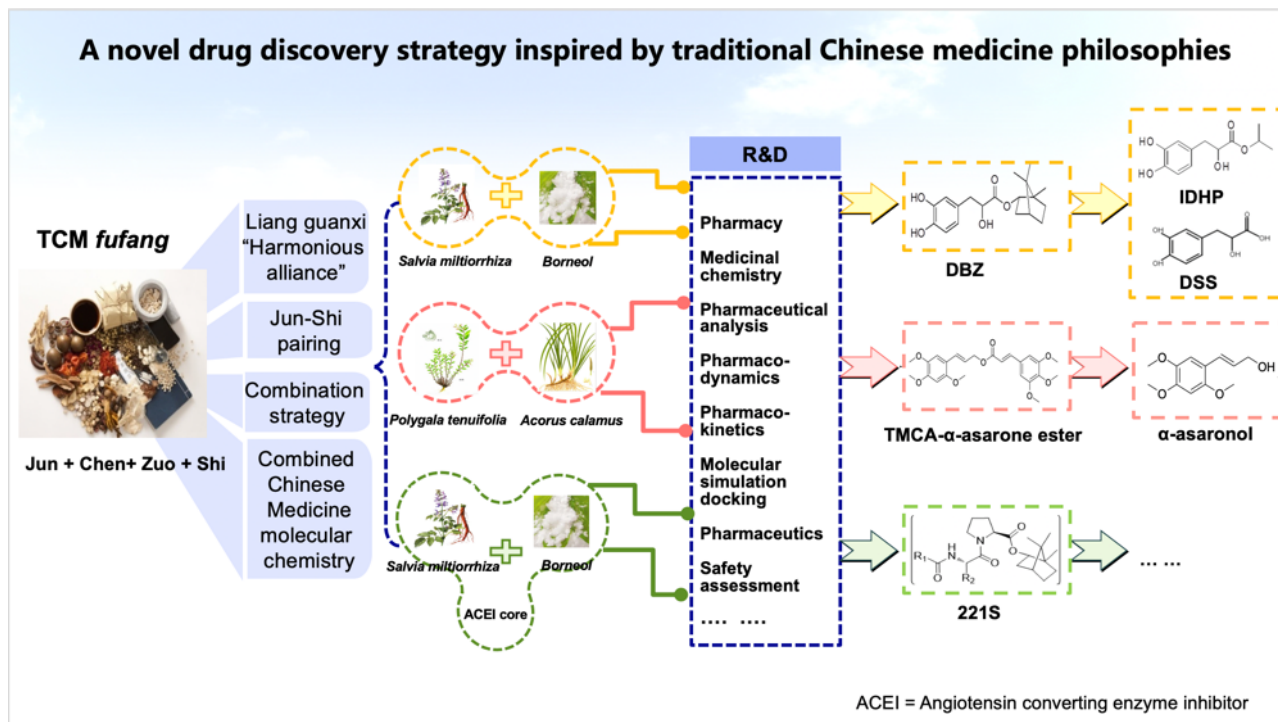


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complex formulation for scientific analysis, which should reduce the complexity and difficulty when seeking new drugs from TCM-related sources as illustrated by the following examples.

- Danshen (*Salvia miltiorrhiza*) series - Danshen-borneol; Danshen-Tan Xiang (sandalwood, *Santalum album*) and Danshen-Jiang Xiang (*Dalbergia odorifera* T. Chen);
- Guangzao (*Fructus Choerospondiatis*) series – Guangzao-borneol, Guangzao - Tan Xiang (*Santalum album*)
- Yuanzhi (*Polygala tenuifolia*) series - Yuanzhi – Shichangpu (*Acorus calamus*)



Design and synthesis of a novel synthetic small molecule angiogenesis stimulator inspired by botanical formulations for angina pectoris

As summarized in the diagram above, our team has systematically studied the “Jun herb” and “Shi herb” in these formulations. The role of the “Shi herb” is to increase the bioavailability of the main component(s) of “Jun herb” and enhance its/their affinity with the target organ(s). In the *Salvia miltiorrhiza*-Borneol pairing, Danshensu (DSS, 3,4-dihydroxyphenyllactic acid) was chosen as the active constituent of the “Jun herb”, while borneol was designated the active component of the “Shi herb”. Using engineered *E. coli*, we are now able to biosynthesize D-danshensu from L-DOPA [5]. With abundant supply of optically pure D-danshensu, we designed and synthesized tanshinol borneol ester (DBZ; 1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl-3-(3,4-dihydroxyphenyl)-2-hydroxypropanoate) by chemical combination of DSS and borneol (core effective components of Dantonin®) as well as a library of related compounds. We have obtained major funds for the creation of new small-molecule drugs such as DBZ and IDHP, leading to patent authorization in 58 countries and regions.

We used a network pharmacology approach to predict the molecular targets of DBZ, and validated its pro-angiogenic activities by cell culture and animal experiments [6]. In addition to biphasic modulation on proliferation and migration of three types of human endothelial cells, DBZ also promoted neovascularization in mice and partially reversed the vascular disruption in zebrafish induced by PTK787. Mechanistically, DBZ enhanced the cellular levels of VEGF, VEGFR2 and MMP-9, as well as activating Akt and MAPK signalling in endothelial cells. Selective inhibition of PI3K and MEK significantly attenuated its angiogenic effects. These data reveal, for the first time,

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that DBZ promotes multiple key steps of angiogenesis, at least in part through Akt and MAPK signalling pathways, and suggest it may be potentially developed further for treating myocardial infarction and other cardiovascular diseases. Paradoxically, we discovered in a separate study that DBZ can significantly reduce the formation of atherosclerotic lesions in ApoE^{-/-} mice by inhibiting inflammation and reducing macrophage infiltration into the vessel wall. In addition, it can affect the function of nuclear receptor LXR, inhibit lipopolysaccharide-induced macrophage migration, and inhibit oxidized low-density lipoprotein-induced formation of foam cells [7]. Therefore, DBZ has the potential to be developed for combating atherosclerosis in humans.

General applicability of *Jun-Shi* Medicinal Compatibility Model

Following this strategy, we used 3,4,5-trimethoxycinnamic acid (TMCA) from *Polygala tenuifolia* and asarone from *Acorus calamus* to synthesize TMCA- α -asarone ester, which is metabolized *in vivo* to generate α -asaronol. This novel compound displayed a broad spectrum of anticonvulsant activity and showed better protective indices and lower acute toxicity than its metabolic parent compound α -asarone [8]. To demonstrate the potential of "Combined Chinese Medicine molecular chemistry strategy", we fused ACEI core with DSS and borneol to produce a novel anti-hypertensive candidate 221S, with a better pharmacological profile than captopril.

In conclusion, the *Jun-Shi* Medicinal Compatibility Model can reduce the arbitrary nature of the drug discovery process and also improve its efficiency, as well as further enriching TCM theory and offering new perspectives on complex biomedical questions to resolve the unmet needs in global healthcare.

Acknowledgement. We thank Dr ZHAO Ye for her generous assistance with the diagram.

References

1. Fan TP *et al.* (2006) Angiogenesis: from plants to blood vessels. *Trends Pharmacol Sci.* **27**:297-309.
2. Yin Q *et al.* (2015) A metabolite of Danshen formulae attenuates cardiac fibrosis induced by isoprenaline, via a NOX 2/ROS/p38 pathway. *Br J Pharmacol.* **172**:5573-5585.
3. Wang SP *et al.* (2007) Vasorelaxant effect of isopropyl 3-(3, 4-dihydroxyphenyl)-2-hydroxypropanoate, a novel metabolite from *Salvia miltiorrhiza*, on isolated rat mesenteric artery. *Eur J Pharmacol.* **579**:283-288.
4. Zhao X *et al.* (2015) A novel drug discovery strategy inspired by traditional medicine philosophies. *Science* **347**: S38-S40.
5. Xiong T *et al.* (2019) Biosynthesis of D-danshensu from L-DOPA using engineered *Escherichia coli* whole cells. *Appl Microbiol Biotechnol.* **103**:6097-6105. DOI: 10.1007/s00253-019-09947-0.
6. Liao S *et al.* (2019) Tanshinol borneol ester, a novel synthetic small molecule angiogenesis stimulator inspired by botanical formulations for angina pectoris. *Br J Pharmacol.* **176**:3143-3160. DOI: 10.1111/bph.14714.
7. Wang J *et al.* (2017) DBZ (Danshensu Bingpian Zhi), a novel natural compound derivative, attenuates atherosclerosis in Apolipoprotein E-deficient mice. *Journal of the American Heart Association.* 6:e006297 DOI: 10.1161/JAHA.117.006297
8. He X *et al.* (2018) Anticonvulsant activities of α -asaronol ((E)-3'-hydroxyasarone), an active constituent derived from α -asarone. *Pharmacol Rep.* **70**(1):69-74. DOI: 10.1016/j.pharep.2017.08.004.



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NEW 2.

Is Angong Niu Huang Wan safe and effective for ischemic stroke treatment?



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In TCM, there are numerous formulas contain arsenic- and mercury-containing ingredients, namely realgar (arsenic sulfide, >90% As_4S_4) and cinnabar (mercuric sulfide, > 96% HgS). According to the 2015 Chinese pharmacopeia, there are 28 oral remedies containing realgar, 48 containing cinnabar, and more than 20 containing both realgar and cinnabar. The use of these heavy metal containing TCM formulas could be dated back to 2000 years ago and those heavy metal materials are still used by Asian countries presently. For example, Angong Niu Huang Wan (AGNHW) is one of the representative and classical realgar and cinnabar containing remedies, which named “one of the three treasures” in TCM practice. AGNHW is generally used as first aid TCM formula for emergency cases with the clinical symptoms like coma, seizure, high fever, etc. In modern TCM practice, AGNHW is often used for trauma brain injury and acute ischemic stroke and different infection diseases. However, the arsenical- and mercurial-containing ingredients in the formula raise great healthy concerns as these heavy metal components might cause severe health problems after consumption.

Two recent publications authored by Professor Jiangang Shen team from School of Chinese Medicine University of Hong Kong systematically addressed the questions whether arsenic and mercurial materials are necessary components contributing to the neuroprotective effects of AGNHW against cerebral ischemia-reperfusion injury and short term administration of AGNHW at regular doses would lead hepatic and renal toxicity and the accumulation of arsenic and mercury in the blood, liver, and kidney. They also evaluated the underlying neuroprotective mechanisms of AGNHW against cerebral ischemia/reperfusion injury.

According to the guideline of TCM practice, AGNHW is only used with one pill per day and daily used for 3-4 days. To address whether routine use of AGNHW would produce adverse drug reactions or toxic effects on patients, Professor Shen’s group previously searched PubMed, Embase, Cochrane library, TOXNET, and Chinese databases CNKI and Wanfang for articles published between January 1974 and January 2015. They found total reported 49 cases with adverse drug reactions (ADR) and adverse events (AE) from 10 articles, indicating the low risk of ADR/AE from AGNHW administration clinically [1]. The majority of ADR/AE was attributed to the improper use of AGNHW, such as use in children with overdosage or used with incompatible drugs. Following this literature study, they conducted well-designed animal experiments to assess its safety for the treatment of acute ischemic stroke [2-3]. They found that oral administration of AGNHW at the dose equivalent to human subjects to rats for 7 days caused slight increased levels of arsenic and mercury in the liver and the kidney respectively. With the increased dose of AGNHW, the level of heavy metals was proportionally elevated but no hepatic and renal toxicity was found in both normal rats and cerebral ischemic rats. The continuous consumption of AGNHW for 7 days did not affect hepatorenal functions in ischemic stroke rats. On a contrary, AGNHW promoted the recovery of animal body weight and liver functions. The experiments data suggest that short-term use of AGNHW with regular dose within one week should be relatively safe.

Furthermore, the studies have provided experimental evidence to support the use of AGNHW for ischemic stroke treatment. AGNHW treatment effectively promoted the recovery of the neurological functions, reduced infarct size and protected the blood-brain barrier (BBB) integrity in



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experimental stroke animal model due to its antioxidant and anti-inflammation properties. Furthermore, they found that the removing of arsenic and mercuric materials named realgar and cinnabar from the original formula would drop back the neuroprotective effects of AGNHW against cerebral ischemia-reperfusion injury. Interestingly, oral administration of realgar or cinnabar alone had no neuroprotective effects at all, suggesting the synergetic effects of the arsenic and mercuric materials with the herbal components against ischemic brain injury. Notably, realgar and cinnabar are in the sulfide forms of arsenic and mercury, which are the inert forms of the metal elements.

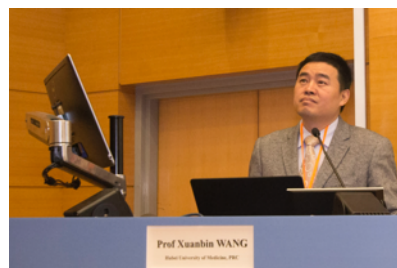
Notes for the readers: (1) Angong Niu Huang Wan has neuroprotective effects against acute ischemia brain injury; (2) Short term use of Angong Niu Huang Wan with one pill per day for one week should be safe without significant heavy metal accumulation and liver and renal toxicity; (3) Realgar and cinnabar, the mineral elements in the sulfide forms of arsenic and mercury, are necessary elements with synergetic actions with other herbal components for the neuroprotective effects of Angong Niu Huang Wan; (4) Long term use and/or overdose of Angong Niu Huang Wan should be avoided; (5) The well-designed randomized clinical trials are desirable to assess its efficacies and safety for the treatment of acute brain disorders.

References:

1. Zhao L, et al. Whether Metal Element-Containing Herbal Formula Angong Niu Huang Pill Is Safe for Acute Brain Disorders? *Biol Trace Elem Res.* 2015;**166**:41-8.
2. Tsoi B, et al. Neuroprotective Effects and Hepatorenal Toxicity of Angong Niu Huang Wan Against Ischemia-Reperfusion Brain Injury in Rats. *Front Pharmacol.* 2019;**10**:593.
3. Tsoi B, et al. Realgar and cinnabar are essential components contributing to neuroprotection of Angong Niu Huang Wan with no hepatorenal toxicity in transient ischemic brain injury. *Toxicol Appl Pharmacol.* 2019;**377**:114613.

Special Updates from the GP-TCM RA

Now 1. **Prof Xuanbin Wang appointed Deputy Newsletter Editor-in-chief.** We are pleased to announce that the BoD has recently appointed Prof. Xuanbin Wang (Hubei University of Medicine), to serve as another Deputy Editor-in-chief to report on events in mainland China. Together with Dr. Qihe Xu, Prof. Pierre Duez and Prof. Yuan-Shiun Chang, we look forward to a broader coverage of our newsletter in the future.



Now 2. **The newly set-up 7th Interest Group on “Good Clinical Practice Guidelines (GCPG)”**

We are pleased to announce the establishment of the 7th Interest Group on “Good Clinical Practice Guidelines (GCPG)”, with Vivian Wong as chair and a co-chair to be appointed in due course. We look forward to seeing the establishment of a framework for CPG development based on the best available evidence from both Chinese medicines and western medicines.



Special Features

Now 1. **Tu Youyou and other significant contributors to the P. R. China are honoured with medals and titles.** President Xi Jinping signs decree to recognize individuals ahead of country's 70th anniversary on Oct. 1. Scientist Tu Youyou, winner of the 2015 Nobel Prize for the discovery of artemisinin, was awarded a Medal of the Republic together with seven other role models...

<http://www.ecns.cn/news/2019-09-18/detail-1fznxzmn1176600.shtml>

<https://www.shine.cn/news/nation/1908280936/> (中文)

<https://mp.weixin.qq.com/s/vN954AerjDySMXVjL16NnQ> (中文)



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A video highlighting Tu and her contributions has been released by the State Administration of TCM to mark this milestone:

<http://www.nhc.gov.cn/wjw/spxw/201909/2bfe53de9635483b888b61da72540204.shtml> (中文)

2. Tingdong Zhang, Weidong Zhang and Wei Wang, experts in integrative Chinese medicine and modernisation of TCM, are honoured by Wu Jieping Award 2019.

<https://mp.weixin.qq.com/s/msxgDPU1IbZltaH8qFDQFQ> (中文)



3. The 9th Annual National Post-Graduate Student Research Training Forum was held at Nanjing University of Chinese Medicine in Nanjing 26-29 August 2019.



Written by Prof. Yin Lu, Director of Jiangsu Key Laboratory for Efficacy and Safety Evaluation of Chinese Materia Medica, School of Pharmacy, Nanjing University of Chinese Medicine. Photos are provided by Yushi Ding, a graduate student from Nanjing University of Chinese Medicine. Email: luyingreen@njucm.edu.cn

In order to give students a platform for learning and exchange, to facilitate students in training their own scientific ideas, and to recognize and solve problems in TCM research methodologically, my colleagues and I organized the four-day forum in Nanjing, sponsored by the Committee of TCM Pharmacology of Jiangsu Pharmacological Society, Jiangsu Key Laboratory for Efficacy and Safety Evaluation

of Chinese Material Medica, and the School of Pharmacy at Nanjing University of Chinese Medicine. Over three hundred participants from all over the country (Guangzhou University of Chinese Medicine, Shanghai Jiao Tong University, China University of Science and Technology, Huazhong University of Science and Technology, etc.) gathered at the Xianlin Campus of Nanjing University of Chinese Medicine for this forum. Professor Peng Cao, Dean of the School of Pharmacy, Nanjing University of Chinese Medicine gave the opening speech. Professor Min Hong, Head of Pharmacology Department from the same university, hosted the forum.

Invited speakers shared their experience and techniques in the study of TCM on topics including bioinformatics, histopathology, microbiota analysis, animal models for human diseases, CRISPR/Cas9-mediated gene editing, cell membrane chromatography, analysis of protein ubiquitination, academic writing, and application of software for academic use such as Endnote, the reference management software and Adobe Illustrator, the software for academic drawing. The forum was well received by the attendees. Excellent students were awarded certificates.



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For more information about this forum, please follow our official WeChat account 英文文献悦读 (中文) or visit <https://mp.weixin.qq.com/s/mTXPScNm5fbs1TXg3yn2aQ> (中文)



4. Traditional Chinese Medicine in Everyday Life. Written by: Prof. Zhongzhen Zhao, translated by: Elizabeth R. Qi.



The Palace Museum and Phoenix Television collaborated on the *Qingming Shanghe Tu* Digital Art Exhibit held at the AsiaWorld-Expo in Hong Kong. This special exhibition integrates art and culture with technology. They present the Song dynasty painting through dazzling 2D and 3D installations, allowing the audience to completely immerse into the details and historical background.

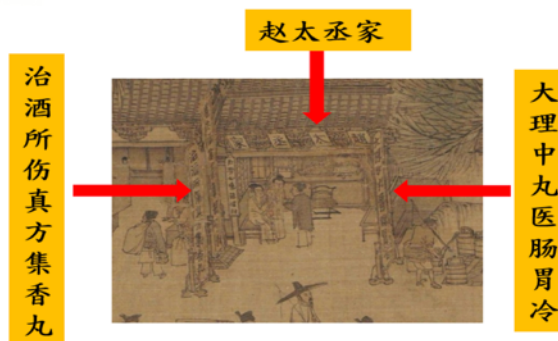
During the exhibition, Professor Zhao Zhongzhen was invited as a speaker and gave a special lecture: Searching for Chinese Medicine within the *Qingming Shanghe Tu*.



***Qingming Shanghe Tu*, or Along the River**

During the Qingming Festival, is a famous painting by Zhang Zeduan during the Northern Song dynasty. This painting is a bird's eye view of the old capitol of Bianliang with over 600 distinct animals and persons. This piece is a precious, historical artifact worth studying with aspects of medicine, history, and culture delicately portrayed in exquisite detail.

First, let's talk about the Home of Doctor Zhao, or Home of *Zhao Taicheng*, a www.gp-tcm.org/news-list/



The Home of Doctor Zhao

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traditional medicine clinic. *Taicheng* is an abbreviation for royal court doctor. The Home of Doctor Zhao probably belonged to a senior medical officer of the Song dynasty, and there were 48 doctors with this title during the rule of Emperor Huizong. This clinic is located close to the palace and may have been where court doctors work part-time during their free time. There is an empty chair in the middle of the clinic, suggesting the doctor has not arrived, but there are patients already waiting. Outside, there are three women with one standing, which may be the servant and one sitting down with a child. There is a possibility the women are at the doctor's because the child is ill.



Two advertisement banners can be seen in the picture: *Dalizhongwan Yichangweileng* and *Zhijiusuoshang Zhenfang Jixiangwan*. Loosely translated, one is a prescription for cold in the stomach and intestines and one is for injury caused by alcohol. Both of these ailments are considered to be the diseases of the rich. The painting showcases the peace and prosperity of the Song dynasty in contrast to the war and diseased time of Zhang Zhongjing and Hua Tuo. In the painting, we can see many restaurants and taverns as well as patrons vomiting after one too many drinks.

The Song dynasty was an era of medical advancement. Not only did they have a well-developed medical system but also a progressive pharmaceutical industry. During this time, patients could easily seek medical advice. The government also organized and published the *Taiping Huimin Heji Jufang*, which was the first official drug standard compiled by a government office. *Jixiangwan* and *dalizhongwan* could also be made in clinics and became popular formulations for medicine at the time.

Since ancient times, the Chinese medicine industry has had a saying: One, aromatics; two, tea; and third, medicinals. From this, we can see the importance of aromatics or *xiang*. In ancient times, the four major aromatics were agarwood, sandalwood, musk, and ambergris, also known as the Famous Four Aromatics. These aromatics are also valuable medicinals.

Agarwood has *qi* moving, pain-relieving, and kidney replenishing effects, and Southeast Asia was the original production area for agarwood. The aromatic agarwood is the result of the tree's innate self-defense mechanism against fungal infections and physical or chemical damage. This mechanism produces metabolites that condense into a resin-rich heartwood which allows agarwood can sink in water. This product is quite rare, and the demand was high. Therefore, agarwood was solidified as a precious commodity. *Xiang Gang*, or internationally known as Hong Kong, was named for it functioned as a port (*gang*) for aromatics (*xiang*), and the aromatic in question was agarwood.

Sandalwood is the heartwood of the tree. As a medicinal, sandalwood can move *qi*, relieve pain, dispel cold, and regulate the center. India was the original production region for sandalwood, which



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Liu's Aromatics Shop

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was also known as *laoshan* sandalwood or old mountain sandalwood. Later on, they also discovered sandalwood in Australia and called it *xinshan* sandalwood or new mountain sandalwood. Sandalwood is also found in Honolulu, Hawaii. In Chinese, Honolulu is also known as *tanxiang shancheng* or the city of sandalwood mountain.

Both agarwood and sandalwood can be used for medicine, for perfumes, or even for wood carvings; this makes these products expensive and highly sought after. There are pieces crafted from agarwood and sandalwood stored in the Palace Museum in Beijing and the National Palace Museum in Taipei.

Aromatic medicinals were a prominent part of trade during the Song dynasty. At the time, court officials and nobles were rewarded with items such as aromatics. This association only made aromatics even more luxurious and precious. Ever since ancient times, regardless whether it was the Han dynasty or the Tang dynasty, the source of Chinese medicinals have far exceeded its territories. In *Bencao Gangmu*, approximately 10% of the medicinals recorded were imported. The land-bound Silk Road exported Chinese silks to the West while the maritime Silk Road transported Chinese porcelain to the West. One of the most important imports from these trade routes were aromatics, including spices. In Fujian, Quanzhou, a pre-Song dynasty shipwreck was found with porcelain and silks onboard as well as black pepper, frankincense, sandalwood, and agarwood. This shipwreck illustrates the story of those who traveled the ancient maritime Silk Road and the commodities they traded. Even in ancient times, the Chinese have shipped and traded aromatics over thousands of miles.

Conclusion: Traditional Chinese medicine and Chinese folk customs are inextricably linked. This year we commemorated the 500th anniversary of Li Shizhen's birth. His masterpiece *Bencao Gangmu* is a scientific epic with very practical applications. *Bencao Gangmu* is about a day (everyday clothing, food, and shelter), a year (spring, summer, autumn, and winter), and a life (birth, aging, illness, and death) of a Chinese person. Chinese medicine and culture have been passed down over thousands of years, and millions of Chinese descendants incorporate it into their lives both at home and at every corner of the world.

5. Hong Kong TCM Community celebrated the 70th Anniversary of the founding of the People's Republic of China on 14th September 2019.



European Reports

1. Mervis J. Chinese ties don't faze European funders. *Science* 2019; 365:1068-1069. ...But government funding agencies in Europe and the United Kingdom harbor fewer suspicions about grantees who maintain robust ties with China. With smaller domestic research enterprises, they have long viewed foreign collaboration as a plus. "There is a lot less paranoia about China in the U.K.," says John Speakman, a Scottish physiologist who for the past 8 years has spent most of his time at the CAS Institute for Genetics and Developmental Biology in Beijing while retaining his position at the University of Aberdeen in the United Kingdom.

The European Union's flagship research program, Horizon 2020, does not require researchers to disclose any support from foreign sources, neither when they apply for a grant nor after they receive

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one. In addition, EU rules explicitly permit grantees to operate a second lab outside their home institution. And in the United Kingdom, an official from UK Research and Innovation (UKRI), the nation's main funding agency based in Swindon, explains that “any policies on researchers declaring overseas funding to their employers [are] set by that institution.”

Science found that no European funder has taken steps to address foreign influence that are comparable to what U.S. agencies have done over the past year...

<https://science.sciencemag.org/content/365/6458/1068.full>

Reports on China and China's International Cooperation

1. China to provide world's leading sci-tech journals. BEIJING, Aug. 16 (Xinhua). Chinese authorities have issued a guideline on promoting reform and development of the country's sci-tech journals. The guideline proposes approaches to achieve a goal of establishing world-leading sci-tech journals, stressing that sci-tech journals reflect a country's competitiveness and cultural soft power. It calls for efforts to enhance Chinese journals' management, market operation and international influence. The guideline was jointly issued by the China Association for Science and Technology, the Ministry of Science and Technology, the Ministry of Education and the Publicity Department of the Central Committee of the Communist Party of China.

http://www.xinhuanet.com/english/2019-08/16/c_138314185.htm

2. China encourages foreign sci-tech entrepreneurship. BEIJING, Aug. 12 (Xinhua). China supports foreign talent with permanent residence certificates to set up sci-tech enterprises, according to guidelines recently issued by the country's Ministry of Science and Technology. The guidelines, aimed to support innovation and development of small- and medium-sized enterprises (SMEs) in science and technology, said that foreign entrepreneurs will enjoy the same treatment as their Chinese counterparts. SMEs in science and technology are important forces in fostering new engines of growth and promoting high-quality development. The ability to innovate is their competitiveness, the guidelines said. Other favorable policies for SMEs include tax reduction, financial assistance and participation in major national sci-tech projects.

<http://www.chinadaily.com.cn/a/201908/12/WS5d51245da310cf3e35565434.html>

3. Beijing science awards add categories. China Daily 5th August 2019. Three categories have been added to Beijing's municipal science and technology awards for individuals, including one set aside for foreign talent, a first since the honors were established in 2002, officials said...

<http://www.ecns.cn/news/2019-08-05/detail-ifzmsrxe1262441.shtml>

4. China's top sciences academy to add new members. BEIJING, Aug. 9 (Xinhua) -- The Chinese Academy of Sciences (CAS), China's highest academic institution in natural sciences, has recently unveiled a list of 181 candidates for its new member selection. Among the list, 16 are female candidates, accounting for 9 percent of the total. The average age of the candidates is 55.5. Candidates are mainly from the CAS institutes, universities, enterprises and the military system.

The academy plans to enroll up to 71 new members this year, including six from the emerging and interdisciplinary subjects and five from the national defense and security areas, according to a notice issued January by the CAS. The emerging and interdisciplinary subjects refer to physical biology, chemical biology, bioimaging, environmental science, information and biomedicine and energy science. The selection will have several rounds of appraisals. Candidates A CAS academician title is the highest national academic achievement in science and technology and a lifelong honor. New members are selected every two years. are recommended by academicians and organizations.

http://www.xinhuanet.com/english/2019-08/09/c_138296536.htm



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NEW 5. Zhang Y. **New chip is brain for bikes as AGI creeps ever closer.** *China Daily* 3rd August 2019. Chinese scientists have unveiled an autonomous bicycle that can steer itself, avoid obstacles and respond to voice commands thanks to a newly developed chip called Tianjic that acts as the brains of the bike...

<http://www.chinadaily.com.cn/a/201908/03/WS5d44bf81a310cf3e35563aad.html>

NEW 6. **China announces major changes to its drug regulatory regime.** *Exology.com* 29 August 2019. Following years of discussion and debate, the 12th Session of the Standing Committee of China's National People's Congress passed the *Amendment of the Drug Administration Law of the People's Republic of China* on 26 August 2019 (the "Amendment"). Experts are calling this long-awaited Amendment, which comes into force on 1 December 2019, the second major systematic and structural amendment to China's drug-administration framework since the implementation of the last significant amendment in 2001. The Amendment boasts a total of 155 articles, including 51 new articles, four new chapters (Chapter II *Drug Research and Registration*, Chapter III *MAH*, Chapter VII *Drug Post-Marketing Management* and Chapter IX *Drug Storage and Supplement*), and significant changes to the law's previous articles. The key changes in the Amendment include:

<https://www.lexology.com/library/detail.aspx?g=f8b5a9a5-95cc-492d-918b-6ebd22423e39>

Post-Marketing Management: <https://page.weishang99.net/itver/n/374218/17602020496> (中文)

NEW 7. Jia L et al. **Dementia in China: epidemiology, clinical management, and research advances.** *Lancet Neurol* 2019. Published Online September 4, 2019 [http://dx.doi.org/10.1016/S1474-4422\(19\)30290-X](http://dx.doi.org/10.1016/S1474-4422(19)30290-X). China has the largest population of patients with dementia in the world, imposing a heavy burden on the public and health care systems. More than 100 epidemiological studies on dementia have been done in China, but the estimates of the prevalence and incidence remain inconsistent because of the use of different sampling methods. Despite improved access to health services, inadequate diagnosis and management for dementia is still common, particularly in rural areas. The Chinese Government issued a new policy to increase care facilities for citizens older than 65 years, but most patients with dementia still receive care at home. Western medicines for dementia symptoms are widely used in China, but many patients choose Chinese medicines even though they have little evidence supporting efficacy. The number of clinical trials of Chinese and western medicines has substantially increased as a result of progress in research on new antidementia drugs but international multicentre studies are few in number. Efforts are needed to establish a national system of dementia care enhance training in dementia for health professionals, and develop global collaborations to prevent and cure this disease.

[https://www.thelancet.com/pdfs/journals/laneur/PIIS1474-4422\(19\)30290-X.pdf](https://www.thelancet.com/pdfs/journals/laneur/PIIS1474-4422(19)30290-X.pdf)

<https://mp.weixin.qq.com/s/Esh-GCKmgbTYRjGsgFuyqQ> (中文)



Figure 1: The prevalence of dementia in people aged 60 years or older in China¹³

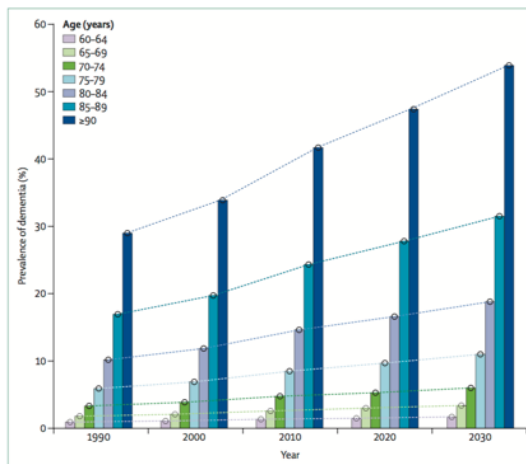


Figure 2: Estimated age-specific prevalence of dementia from 1990 to 2030 in China
The age-specific prevalence of dementia in China is shown with the data from 1990 to 2010 estimated by a systematic review,¹³ and the 2020 to 2030 predictions by Xu and colleagues.¹⁴

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8. R&D Report on China's Innovative Drug Industry.
huarui-boyuan WeChat 7th Sept. 2019:
<https://mp.weixin.qq.com/s/sdT7FC2KdqkDerErVealyg>



Acupuncture, TCM and Other Traditional Medicine

1. Li Y. A story on how fundamental research pushes acupuncture to the world stage. *Acupuncture Research* 2019;44(9). Dr Yongming Li commented on a new book by Prof Academician Jisheng Han and his colleague Prof. You Wan on Han's life, career and research on acupuncture.

<https://mp.weixin.qq.com/s/F0SHp3rZwhTgbFZ8hmYm4Q> (中文)

2. Jing X , Zhu B. Current Opportunities and Challenges in the Field of Acupuncture & Moxibustion. *Science & Technology Review. STReview WeChat* 28th August 2019.

<https://mp.weixin.qq.com/s/YjcHegD3BkAbNVRMpse3w> (中文)

3. Amended legislation on drug management to implement on 1st December 2019. *SATCM01 WeChat* 27th August 2019. This WeChat report from the official WeChat account of the State Administration of TCM introduces the changes of contents in this latest amended legislation.

<https://mp.weixin.qq.com/s/gZkFPy63nPJ6DLoUqzMCqg?> (中文)

4. A guideline of TCM treatment of coughing (2015).

<https://mp.weixin.qq.com/s/ME3Dab04jAhFb10eCESTww> (中文)

5. Xu J. Science, technology and innovation endow TCM with wings to fly. *satcm01 WeChat* 16th September 2019. This article summaries the main S&T achievements in the field of TCM since the founding of the People's Republic of China in 1949, to celebrate the 70th National Day of the New China. https://mp.weixin.qq.com/s/MzK_Smk0J59hYLIMKFHncA (中文)

6. Cong W, Xin Q, Gao Y. Reply to "Incidence and Etiology of Drug-Induced Liver Injury in Mainland China". *Gastroenterology.* 2019 Aug 20. pii: S0016-5085(19)41238-9. We read with interest the recent article published in *Gastroenterology* by Shen et al. , which reported findings of a retrospective study that determined the incidence and causes of drug-induced liver injury (DILI) in mainland China, and the leading cause of DILI was traditional Chinese medicines (TCM) or herbal and dietary supplements (HDS) (26.81%). Although this is the first large-scale estimate of DILI incidence and etiology in mainland China, there are still several critical issues inevitably making its conclusions to be reconsidered...

<https://www.sciencedirect.com/science/article/pii/S0016508519412389?via%3Dihub>

<https://mp.weixin.qq.com/s/OMqO3ee0fmjmUWs-td1YCw> (中文)

Omics in Progress

1. Marx V. A dream of single-cell proteomics. *Nature Methods* 2019;16: 809–812. As single-cell proteomics emerges, perhaps labs can avoid the need to infer protein levels from mRNA abundances...

<https://www.nature.com/articles/s41592-019-0540-6>

2. Campa CC et al. Multiplexed genome engineering by Cas12a and CRISPR arrays encoded on single transcripts. *Nature Methods* 2019;16: 887-893. A single transcript encoding Cas12a and an array of CRISPR RNAs enables multiplexed genome engineering, from multiple knockouts to transcriptional activation or repression to orthogonal transcriptional control and editing in the same sample...

<https://www.nature.com/articles/s41592-019-0508-6>

Other Recommended Readings

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1. Xie XS. Diseases Have No Borders, Neither Should Research! *Cell* 2019;178:1275-6.
In response to recent anti-Chinese sentiment in the US, Sunney Xie uses his own experiences to assert that American ideals should not be replaced by nationalism and populism and that everybody wins in Sino-US scientific collaborations, contrary to what Americans are led to believe—that China is the sole beneficiary...

[https://www.cell.com/cell/fulltext/S0092-8674\(19\)30853-0?dgcid](https://www.cell.com/cell/fulltext/S0092-8674(19)30853-0?dgcid)
http://newsen.pku.edu.cn/news_events/news/people/8751.htm

2. Asato S, Giordano J. Viewing “p” through the lens of the philosophy of medicine. *Philosophy, Ethics, and Humanities in Medicine* 2019;14:8. ...Indeed, Ronald Fisher’s introduction of the p-value in the 1920s was more for determining if the probability of outcomes would warrant evaluation and/or replication. We believe that there is (still) merit to Fisher’s view and intent. P-values can – and we assert, should - be seen as a threshold for either (1) the relative acceptability of research findings, or (2) prompting of further examination, assessment, and validation. Thinking logically, p-values were created by humans to test for chance happenings, which are, at least in part, produced by human error (and error in the use or function of tools and techniques created by humans). The research community may be facing an opportunity to broadly acknowledge the explicit obligation of science to be self-critical and self-revising, and through such a lens hold a mirror to itself and to medicine in examination of the ways that research outcomes are evaluated, regarded and used. We value that most surely as significant.

<https://www.linkresearcher.com/careers/b0c6af9a-bc61-49d8-9e32-7f2b25359f55> (中文)

3. Li W-Q et al. Effects of *Helicobacter pylori* treatment and vitamin and garlic supplementation on gastric cancer incidence and mortality: follow-up of a randomized intervention trial. *BMJ* 2019;366:15016.
Conclusion: *H pylori* treatment for two weeks and vitamin or garlic supplementation for seven years were associated with a statistically significant reduced risk of death due to gastric cancer for more than 22 years. *H pylori* treatment and vitamin supplementation were also associated with a statistically significantly reduced incidence of gastric cancer.

<https://www.bmj.com/content/366/bmj.l5016> (中文)



4. PNAS Editor writes on “Impact factor impacts on early-career scientist careers”
(Berenbaum MR. *PNAS* August 20, 2019 116 (34) 16659-16662).

www.pnas.org/cgi/doi/10.1073/pnas.1911911116
https://mp.weixin.qq.com/s/Z3vP3DwyDySV7AWYWp_9pQ (中文)

Invitation from Future Meetings

1. The 16th World Congress of Chinese Medicine will be held in Budapest, Hungary, in November 2019: World Congress of Chinese Medicine (WCCM), organized by World Federation of Chinese Medicine Societies (WFCMS), is a global academic event in the field of traditional Chinese medicine. It is convened annually and has been successfully organized 13 times in different countries. The 16th WCCM under the theme of the “Belt & Road TCM Academic Communications” will be held in Budapest, Hungary in November, 2019.

<https://www.medmeeting.org/MiniSiteEn/index/7888>
https://mp.weixin.qq.com/s/SpqrG4XwKKmOJC1QRZ_dWg (中文)

2. The 8th GP-TCM RA Annual Meeting will be held in Vytautas Magnus University, Kaunas, Lithuania. More information will be published in the near future.

<https://www.vdu.lt/en/vmu-will-host-the-annual-meeting-of-traditional-chinese-medicine/>

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3. **The 6th World TCM Summer Summit will be hosted by Hong Kong Registered Chinese Medicine Practitioners Association (HKRCMP).** For an introduction of HKRCMP and TCM in Hong Kong, please watch the film below.

https://drive.google.com/file/d/1KbPcYUMwS88YepXulryvfD_RPmPkyx7i/view


Invitation from Journals

1. **World Journal of Traditional Chinese Medicine: Sincere invitation for submissions.** World Journal of Traditional Chinese Medicine (ISSN 2311-8571, CN10-1395/R) is sponsored by WFCMS, and is the official journal of GP-TCM RA. WJTCM dedicates to report the research progress in clinical efficacy and action mechanism of Traditional Chinese Medicine, Chinese materia medica, acupuncture and moxibustion to doctors and biomedical researchers around the world, so as to provide new thoughts and methods for solving complex diseases and knotty diseases. To submit your manuscripts, or to read articles in the past issues, please visit: <http://www.wjtcn.net>

2. **Health-care reform in China: a *Lancet* call for papers.**

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(18\)33054-X/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)33054-X/fulltext)

Sounding Board:

 1. This column is reserved for comments, personal views, proposals for collaborations or any other features from our readers across the world. We look forward to hearing from you! Please get in touch with your editors: Dr Qihe Xu (qihe.xu@kcl.ac.uk), Prof Pierre Duez (pierre.duez@umons.ac.be) and Prof Yuan Shiun Chang (yschang0404@gmail.com).

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To Everyone who celebrates the 70th Anniversary of the founding of the People's Republic of China on 1st October, the GP-TCM RA wishes you a happy Chinese National Day!

