The March-April 2021 Newsletter of The GP-TCM Research Association

Contents of the GP-TCM RA Newsletter March-April 2021

Acknowledgements: The editors would like to thank Prof **Aiping Lu** (Hong Kong), Dr **Chi Zhang** (Beijing), Dr **Chris Chan** (Hong Kong), Prof **Clara Lau** (Hong Kong), Prof **Dean Guo** (Shanghai), Prof **Hubiao Chen** (Hong Kong), Prof **Jiqing Liu** (Shenzhen), Dr **Mei Wang** (Leiden), Prof **Pierre Duez** (Mons), Prof **Rudolf Bauer** (Graz), Prof **Zhongzhen Zhao** (Hong Kong), and the **WJTCM Editorial Office** (Beijing) for their great contributions.

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Highlights on Achievements of GP-TCM RA Members

Exosomal transfer of osteoclast-derived miRNAs to chondrocytes contributes to osteoarthritis progression. *Nature Aging*. 2021. Osteoarthritis (OA) is a prevalent aging-related joint disease lacking disease-modifying therapies. Here, we identified an

nature aging

ARTICLES

https://doi.org/10.1038/s43587-021-00050-6

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Exosomal transfer of osteoclast-derived miRNAs to chondrocytes contributes to osteoarthritis progression

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upregulation of circulating exosomal osteoclast (OC)-derived microRNAs (OC-miRNAs) during the progression of surgery-induced OA in mice. We found that reducing OC-miRNAs by Cre-mediated excision of the key miRNA-processing enzyme Dicer or blocking the secretion of OC-originated exosomes by short interfering RNA-mediated silencing of Rab27a substantially delayed the progression of surgery-induced OA in mice. Mechanistically, the exosomal transfer of OC-miRNAs to chondrocytes reduced the resistance of cartilage to matrix degeneration, osteochondral angiogenesis and sensory innervation during OA progression by suppressing tissue inhibitor of metalloproteinase-2 (TIMP-2) and TIMP-3. Furthermore, systemic administration of a new OC-targeted exosome inhibitor (OCExoInhib) blunted the progression of surgery-induced OA in mice. We suggest that targeting the exosomal transfer of OC-miRNAs to chondrocytes represents a potential

therapeutic avenue to tackle OA progression. Details: https://doi.org/10.1038/s43587-021-00050-6

International policies and challenges on the legalization of traditional medicine/herbal medicines in the fight against COVID-19. *Pharmacological Research*. 2021. The coronavirus disease 2019 (COVID-19) has now rapidly spread around the world, causing an outbreak of acute infectious pneumonia. To develop effective and safe therapies

Pharmacological Research 166 (2021) 105472

Contents lists available at ScienceDirect

Pharmacological Research

journal homepage: www.elsevier.com/locate/yphrs

Review

International policies and challenges on the legalization of traditional medicine/herbal medicines in the fight against COVID-19

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for the prevention and treatment of COVID-19 has become the major global public health concern. Traditional medicine (TM)/herbal medicines (HMs) have been used to treat multiple epidemics in human history, which brings hope for the fight against COVID-19 in some areas. For example, in China, India, and South Korea with traditional medication history and theory, the governments issued a series of guidelines to support TM/HMs in the medication of COVID-19. In contrast, other countries e.g. North American and European governments are typically silent on these practices, unless to warn of possible harm and overselling. Such difference is due to the discrepancy in culture, history and philosophical views of health care and medication, as well as unharmonized policies and standards in the regulation and legalization of TM/HMs among different areas. Herein, we reviewed the responses and scientific researches from seven selected countries on the policies and legalization of TM/HMs to treat COVID-19, and also analyzed the major challenges and concerns to utilize the traditional knowledge and resource. Details: https://doi.org/10.1016/j.phrs.2021.105472

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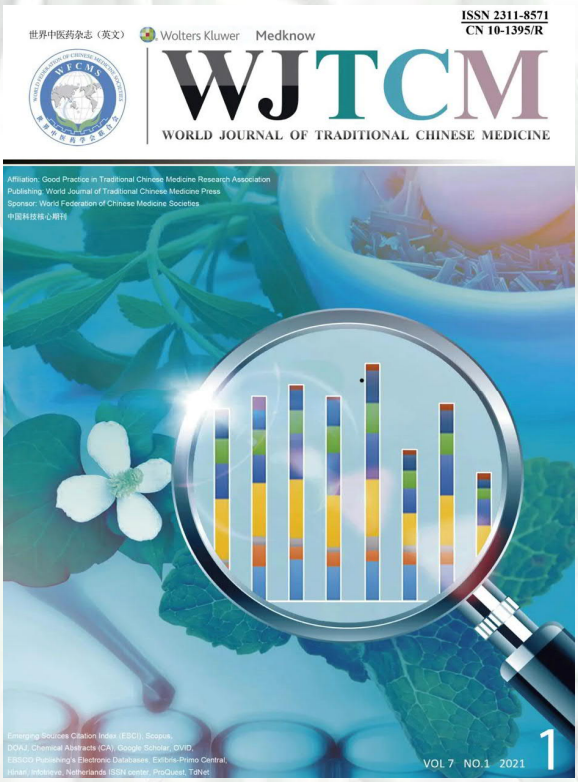
17 academic papers published in the official journal of GP-TCM RA have been online since Monday, March 8, 2021 as the contents of the Special Issue on Herbal Medicine Analysis and Quality Standards. Details: https://www.wjtcm.net/currentissue.asp?sabs=n



1. Quantitative analysis of eight ginsenosides in red ginseng using ginsenoside rg_1 as single reference standard (https://www.wjtcm.net/text.asp?2021/7/1/1/310931)
2. Simultaneous quantitative analysis of five components in *Angelica sinensis* and *Angelica acutiloba* acclimatized growing in Vietnam by high-performance liquid chromatography with photodiode array detector (https://www.wjtcm.net/text.asp?2021/7/1/6/310924)
3. Comprehensive metabolic profiling of modified gegen qinlian decoction by ultra-high-performance liquid chromatography-diode array detection-Q-exactive-orbitrap-electrospray ionization-mass spectrometry/mass spectrometry and application of high-performance thin-layer chromatography for its fingerprint analysis (https://www.wjtcm.net/text.asp?2021/7/1/11/310927)
4. Eleven absorbed constituents and 91 metabolites of chuanxiong rhizoma decoction in rats (https://www.wjtcm.net/text.asp?2021/7/1/33/310928)

5. A simple high-performance liquid chromatography method for the assay of flavonoids in Ginkgo biloba leaves (https://www.wjtcm.net/text.asp?2021/7/1/47/310933)
6. Comprehensive quality evaluation of shuxuening injection employing quantitative high-performance liquid chromatography fingerprint and chemometrics (https://www.wjtcm.net/text.asp?2021/7/1/54/310930)
7. Differentiation of belamcandae rhizoma and iridis tectori rhizoma by thin-layer chromatography and high-performance liquid chromatography (https://www.wjtcm.net/text.asp?2021/7/1/63/310938)
8. Rapid differentiation of aconiti kusnezoffii radix from different geographic origins using ultra-performance liquid chromatography coupled with time-of-flight mass spectrometry (https://www.wjtcm.net/text.asp?2021/7/1/71/310925)
9. Identification and determination of fructooligosaccharides in snow chrysanthemum (*Coreopsis tinctoria* Nutt.) (https://www.wjtcm.net/text.asp?2021/7/1/78/310936)
10. Ultra-high-performance liquid chromatograph with triple-quadrupole mass spectrometer quantitation of twelve phenolic components in different parts of *Sarcandra glabra* (https://www.wjtcm.net/text.asp?2021/7/1/86/310935)
11. Enzyme-linked immunosorbent assay and immunochromatographic strip for rapid detection of atrazine in three medicinal herbal roots (https://www.wjtcm.net/text.asp?2021/7/1/97/310937)
12. Discrimination of five species of *Panax* genus and their geographical origin using electronic tongue combined with chemometrics (https://www.wjtcm.net/text.asp?2021/7/1/104/310939)
13. Quantitative evaluation of the compatibility effects of aidi injection on the treatment of hepatocellular carcinoma using targeted metabolomics: A new strategy on the mechanism study of an anticancer compound in traditional Chinese medicine (https://www.wjtcm.net/text.asp?2021/7/1/111/310940)
14. Ultra-high performance liquid chromatography/ion mobility-quadrupole time-of-flight mass spectrometry and database-driven automatic peak annotation for the rapid profiling and characterization of the multicomponents from stephaniae tetrandrae radix (fang-ji) (https://www.wjtcm.net/text.asp?2021/7/1/120/310926)
15. Simultaneous determination and pharmacokinetics of tetrandrine, fangchinoline, and cyclanoline in rat plasma by ultra-high performance liquid chromatography-mass

spectrometry after oral administration of stephaniae tetrandrae radix extract (https://www.wjtcm.net/text.asp?2021/7/1/130/310929)

16. Gas chromatography–mass spectrometry for quantitative and qualitative analysis of essential oil from *Curcuma wenyujin* rhizomes (https://www.wjtcm.net/text.asp?2021/7/1/138/310932)
17. Network pharmacology evaluation method guidance (Draft) (https://www.wjtcm.net/text.asp?2021/7/1/146/310934)

Feature Stories

DNA milestone: One step closer to completing the tree of life for plants.

Understanding the evolutionary tree of life is the ultimate endeavour in biology, equivalent to constructing the periodic table in chemistry. Researchers at **Royal Botanic Gardens, Kew** are now well on the way to completing the tree of life for flowering plants by sequencing the DNA of one sixth of all genera. Kew scientists have achieved a major milestone in a vast project to complete the trees of life for plants and fungi. These trees of life, just like our own family tree, enable us to understand how different species are related to each other, and are vital for helping future species discovery, monitoring and conservation. One thing is clear: the pace of progress in unlocking the DNA secrets of the natural world is accelerating and it is now possible for science to address challenges that not so long ago would have seemed like science fiction.

These include the Earth Biogenome Project's "**moonshot for biology**" plan to catalogue the genetic code of all known species of complex life within 10 years, and the Darwin Tree of Life Project which is already underway with the aim to sequence the complete genomes of **all 70,000 British and Irish species.** All these projects are designed to provide a knowledge base to conserve, protect and restore biodiversity – and they would not be possible without the goldmine of resources stored in the world's natural history collections, including Kew. (Reported by Ben Hirschler)

Details: https://www.kew.org/read-and-watch/dna-tree-of-life-plants

HKBU-led research reveals hyocholic acids are promising agents for diabetes prediction and treatment. A series of studies led by researchers from Hong Kong Baptist University (HKBU) have revealed that hyocholic acid and its derivatives (collectively known as HCAs), a component of bile acids that facilitate fat digestion, are a promising risk indicator of type 2 diabetes. The strong efficacy of HCAs in regulating blood glucose levels and protecting against diabetes has also been uncovered. The findings open a window for the development of HCA-based predictive markers as well as anti-diabetic drugs. The research results have been published in the international scientific journals Cell Metabolism and Nature Communications. **High concentration of HCAs protects pigs from diabetes** Inspired by the traditional Chinese medical book Compendium of Materia Medica, which recorded the use of pig bile to treat excessive thirst, a condition known today as diabetes, Professor Jia Wei, Chair Professor of the School of Chinese Medicine at HKBU,

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ARTICLE

https://doi.org/10.1038/s41467-021-21744-w OPEN

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Hyocholic acid species as novel biomarkers for metabolic disorders

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led research teams to conduct a series of studies on the role of HCAs in glucose homeostasis and diabetes prevention. Diabetes is characterised by high blood glucose levels. Through a series of tests conducted on 55 humans, 32 mice and 12 pigs, Professor Jia's team confirmed that fasting blood glucose levels in pigs are significantly lower than that

of humans and mice. As HCAs constitute nearly 80% of bile acids in pigs, while the proportions in humans and mice are only about 2% and 3% respectively, **a negative correlation between HCAs and blood glucose levels was observed**. The result indicates the potential role of HCAs in the maintenance of stable glucose levels. This may explain why pigs, unlike humans, seldom suffer from diabetes despite their low physical activity levels and consumption of a calorie-rich diet. **HCAs correlate with diabetes and metabolic health** To analyse the correlation between the levels of HCAs and the occurrence of diabetes in humans, data was collected from two large-scale cohort studies, namely the Shanghai Obesity Study and the Shanghai Diabetes Study. The researchers examined the serum bile acid profiles of 1,107 participants of the Shanghai Obesity Study, which was published in 2013. The participants were divided into three groups: healthy lean, healthy obese and obese with type 2 diabetes. It was discovered that **the levels of serum HCAs were significantly lower in the healthy obese and obese with type 2 diabetes groups.** In another study, the serum bile acids of 132 participants of the Shanghai Diabetes Study were investigated. They were all healthy (at baseline) when they were enrolled in the study between 1998 and 2001. Ten years later, 86 of them had become metabolically unhealthy, while 46 remained healthy. Analysis showed that, compared with those who remained healthy ten years later, those who had become metabolically unhealthy had significantly lower baseline levels of serum HCAs, illustrating that levels of HCAs are a strong predictor of metabolic syndromes such as diabetes. **HCAs regulate blood glucose levels in animal models** Through a series of laboratory experiments, the researchers looked further into the mechanisms that underpin the key role that HCAs play in regulating blood glucose levels. In an animal model experiment, the researchers suppressed the synthesis of HCAs in the livers of a group of pigs by around 30%, and they found that their blood glucose levels increased by 30% when compared with the control group. HCAs were then given to the pigs, after which their blood glucose levels eased off. Another experiment conducted by the researchers focused on the effect of HCAs on glucagon-like peptide-1 (GLP-1). GLP-1 is a hormone produced by L-cells, a type of enteroendocrine cell that enhances insulin secretion and decreases blood glucose. In a laboratory setting, different kinds of bile acids, including HCAs, were applied to L-cells, at varying levels of concentration. Results showed that at a high concentration of 50 micromolar, HCAs were the most effective at stimulating GLP-1 secretion when compared with other types of bile acids. **The findings also revealed that HCAs regulate blood glucose levels by stimulating the secretion of GLP-1 and thus insulin production. Potential for diabetes prediction and treatment** "The results of our studies provide evidence of how HCAs help to regulate blood glucose levels, and they have revealed the mechanism of how it is achieved at a cellular level. HCAs demonstrate promising potential, and they could be developed into an agent for the prediction and treatment of type 2 diabetes," said Professor Jia. "As gut microbiota can regulate the metabolism of HCAs, targeting the intestines instead of the pancreas could be a prospective novel strategy for treating diabetes. We will further investigate how to increase the secretion levels of HCAs in diabetic patients by regulating the intestinal bacteria," he

added. Researchers from the Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Peking University, the Affiliated Drum Tower Hospital of Nanjing University Medical School, China Academy of Chinese Medical Sciences, China Agricultural University, Sichuan University and the University of Hawaii were also involved in the studies. Details: https://cpro.hkbu.edu.hk/en/press_release/detail/HKBU-led-research-reveals-hyocholic-acids-are-promising-agents-for-diabetes-prediction-and-treatment/

Selected Information on COVID-19

Prospective: Evolution of Chinese medicine to treat COVID-19 patients in China. *Frontiers in Pharmacology*. 2021. During the outbreak of the novel coronavirus disease (COVID-19), the Chinese government took a series of public health measures to tackle the outbreak and recommended six traditional Chinese medicine (TCM) evolved formulas, collectively referred to as “3-drugs-3-formulas”, for the treatment. In this prospective article, we will discuss how these six formulas evolved from TCM and what their underlying mechanisms of actions may be by evaluating the historical usage of the component formulas, the potential targeted pathways for the individual herbs used by STAR (signal transduction activity response) database from our laboratory, and the pathogenesis of COVID-19. Five of the six recommended formulas are administered orally, while the sixth is taken as an injection. Five classic categories of herbs in the six formulas including “Qing-Re”, “Qu-Shi”, “Huo-Xue”, “Bu-Yi” and “Xing-Qi” herbs are used based on different stages of disease. All five oral formulas build upon the core formula Maxingshigan Decoction (MD) which has anti-inflammatory and perhaps antiviral actions. While MD can have some desired effects, it may not be sufficient to treat COVID-19 on its own; consequently, complementary classic formulas and/or herbs have been added to potentiate each recommended formula’s anti-inflammatory, and perhaps anti-renin-angiotensin system (RAS)-mediated bradykinin storm (RBS) and antiviral effects to address the unique medical needs for different stages of COVID-19. The key actions of these formulas are likely to control systemic inflammation and/or RBS. The usage of Chinese medicine in the six formulas is consistent with the pathogenesis of COVID-19. Thus, an integrative systems biology approach—combining botanical treatments of conventional antiviral, anti-inflammatory or anti-RBS drugs to treat COVID-19 and its complications – should be explored. Details: https://doi.org/10.3389/fphar.2020.615287

Add-on Chinese medicine for coronavirus disease 2019 (ACCORD): A retrospective cohort study of hospital registries. *The American Journal of Chinese Medicine*. 2021. Chinese medicine (CM) was extensively used to treat COVID-19 in China. We aimed to evaluate the real-world effectiveness of add-on semi-individualized CM during the outbreak. A retrospective cohort of 1788 adult confirmed COVID-19 patients were recruited from 2235 consecutive linked records retrieved from five hospitals in Wuhan during 15 January to 13 March 2020. The mortality of add-on semi-individualized CM users and non-users was

compared by inverse probability weighted hazard ratio (HR) and by propensity score matching. Change of biomarkers was compared between groups, and the frequency of CMs used was analyzed. Subgroup analysis was performed to stratify disease severity and dose of CM exposure. The crude mortality was 3.8% in the semi-individualized CM user group and 17.0% among the non-users. Add-on CM was associated with a mortality reduction of 58% (HR = 0.42, 95% CI: 0.23 to 0.77, pp = 0.005) among all COVID-19 cases and 66% (HR = 0.34, 95% CI: 0.15 to 0.76, pp = 0.009) among severe/critical COVID-19 cases demonstrating dose-dependent response, after inversely weighted with propensity score. The result was robust in various stratified, weighted, matched, adjusted and sensitivity analyses. Severe/critical patients that received add-on CM had a trend of stabilized D-dimer level after 3–7 days of admission when compared to baseline. Immunomodulating and anti-asthmatic CMs were most used. Add-on semi-individualized CM was associated with significantly reduced mortality, especially among severe/critical cases. Chinese medicine could be considered as an add-on regimen for trial use. Details: https://doi.org/10.1142/S0192415X21500257

Seroprevalence and humoral immune durability of anti-SARS-CoV-2 antibodies in Wuhan, China: A longitudinal, population-level, cross-sectional study. *Lancet*. 2021. **Background** Wuhan was the epicentre of the COVID-19 outbreak in China. We aimed to determine the seroprevalence and kinetics of anti-SARS-CoV-2 antibodies at population level in Wuhan to inform the development of vaccination strategies. **Methods** In this longitudinal cross-sectional study, we used a multistage, population-stratified, cluster random sampling method to systematically select 100 communities from the 13 districts of Wuhan. Households were systematically selected from each community and all family members were invited to community health-care centres to participate. Eligible individuals were those who had lived in Wuhan for at least 14 days since Dec 1, 2019. All eligible participants who consented to participate completed a standardised electronic questionnaire of demographic and clinical questions and self-reported any symptoms associated with COVID-19 or previous diagnosis of COVID-19. A venous blood sample was taken for immunological testing on April 14–15, 2020. Blood samples were tested for the presence of pan-immunoglobulins, IgM, IgA, and IgG antibodies against SARS-CoV-2 nucleocapsid protein and neutralising antibodies were assessed. We did two successive follow-ups between June 11 and June 13, and between Oct 9 and Dec 5, 2020, at which blood samples were taken. **Findings** Of 4600 households randomly selected, 3599 families (78.2%) with 9702 individuals attended the baseline visit. 9542 individuals from 3556 families had sufficient samples for analyses. 532 (5.6%) of 9542 participants were positive for pan-immunoglobulins against SARS-CoV-2, with a baseline adjusted seroprevalence of 6.92% (95% CI 6·41–7·43) in the population. 437 (82.1%) of 532 participants who were positive for pan-immunoglobulins were asymptomatic. 69 (13.0%) of 532 individuals were positive for IgM antibodies, 84 (15.8%) were positive for IgA antibodies, 532 (100%) were positive for IgG antibodies, and 212 (39.8%) were positive for neutralising antibodies at baseline. The proportion of individuals who were positive for pan-immunoglobulins who had neutralising antibodies in April remained stable for the two follow-up visits (162 [44.6%] of 363 in June, 2020, and 187 [41.2%] of 454 in October–December, 2020). On the basis of data from 335 individuals who attended all three follow-up visits and who were positive for pan-immunoglobulins, neutralising antibody levels did not significantly decrease over the study period (median 1/5·6 [IQR 1/2·0 to 1/14·0] at baseline *vs* 1/5·6 [1/4·0 to 1/11·2] at first follow-up [p=1·0] and 1/6·3 [1/2·0 to 1/12·6] at second follow-up [p=0·29]). However, neutralising

antibody titres were lower in asymptomatic individuals than in confirmed cases and symptomatic individuals. Although titres of IgG decreased over time, the proportion of individuals who had IgG antibodies did not decrease substantially (from 30 [100%] of 30 at baseline to 26 [89.7%] of 29 at second follow-up among confirmed cases, 65 [100%] of 65 at baseline to 58 [92.1%] of 63 at second follow-up among symptomatic individuals, and 437 [100%] of 437 at baseline to 329 [90.9%] of 362 at second follow-up among asymptomatic individuals). **Interpretation** 6.92% of a cross-sectional sample of the population of Wuhan developed antibodies against SARS-CoV-2, with 39.8% of this population seroconverting to have neutralising antibodies. Our durability data on humoral responses indicate that mass vaccination is needed to effect herd protection to prevent the resurgence of the epidemic. Details: https://doi.org/10.1016/S0140-6736(21)00238-5

Effect and safety of Chinese herbal medicine granules in patients with severe coronavirus disease 2019 in Wuhan, China: A retrospective, single-center study with propensity score matching. *Phytomedicine*. 2021. **Background** Chinese herbal medicine (CHM) has been used for severe illness caused by coronavirus disease 2019 (COVID-19), but its treatment effects and safety are unclear. **Purpose** This study reviews the effect and safety of CHM granules in the treatment of patients with severe COVID-19. **Methods** We conducted a single-center, retrospective study on patients with severe COVID-19 in a designated hospital in Wuhan from January 15, 2020 to March 30, 2020. The propensity score matching (PSM) was used to assess the effect and safety of the treatment using CHM granules. The ratio of patients who received treatment with CHM granules combined with usual care and those who received usual care alone was 1:1. The primary outcome was the time to clinical improvement within 28 days, defined as the time taken for the patients' health to show improvement by decline of two categories (from the baseline) on a modified six-category ordinal scale, or to be discharged from the hospital before day 28. **Results** Using PSM, 43 patients (45% male) aged 65.6 (57–70) years from each group were exactly matched. No significant difference was observed in clinical improvement of patients treated with CHM granules compared with those who received usual (p = 0.851). However, the use of CHM granules reduced the 28-day mortality (p = 0.049) and shortened the duration of fever (4 days *vs*. 7 days, p = 0.002). The differences in the duration of cough and dyspnea and the difference in lung lesion ratio on computerized tomography scans were not significant. Commonly, patients in the CHM group had an increased D-dimer level (p = 0.036). **Conclusion** For patients with severe COVID-19, CHM granules, combined with usual care, showed no improvement beyond usual care alone. However, the use of CHM granules reduced the 28-day mortality rate and the time to fever alleviation. Nevertheless, CHM granules may be associated with high risk of fibrinolysis. Details: https://doi.org/10.1016/j.phymed.2020.153404

Pandemic burnout is rampant in academia. *Nature*. 2021. Remote working, research delays and childcare obligations are taking their toll on scientists, causing stress and anxiety. A year into the coronavirus pandemic, many in the academic scientific workforce are experiencing a state of chronic exhaustion known as burnout. Although it is not a medical condition and can occur in any workplace where there is stress, burnout is recognized by the World Health Organization as a syndrome. Its symptoms are physical and emotional, and include feelings of energy depletion or exhaustion; increased mental distance from and feelings of negativity or cynicism towards one's job; and a reduced ability to do one's work. At its core, burnout is caused by work that demands continuous, long-term physical,

cognitive or emotional effort. Indicators of the syndrome have risen sharply in some higher-education institutions over the past year, according to surveys in the United States and Europe. In a poll of 1,122 US faculty members that focused on the effects of the pandemic, almost 70% of respondents said they felt stressed in 2020, more than double the number in 2019 (32%). The survey, conducted last October by The Chronicle of Higher Education and financial-services firm Fidelity Investments in Boston, Massachusetts, also found that more than two-thirds of respondents felt fatigued, compared with less than one-third in 2019. During 2020, 35% felt angry, whereas just 12% said that in 2019. The results were released last month. More than half of people surveyed said they were seriously considering changing their career or retiring early. Emotional and other effects of pandemic-related burnout were worse for female faculty members: 75% of women reported feeling stressed, compared with 59% of men. By contrast, in 2019, that number was 34% for female respondents. Around eight out of ten women also indicated that their workload had increased as a result of the pandemic, compared with seven out of ten men. Almost three-quarters of female faculty members reported that their work–life balance deteriorated in 2020, compared with just less than two-thirds of male respondents. A similar survey in Europe offers an equally grim snapshot, showing a drastic increase in the rates of stress and mental-health concerns in the academic scientific workforce. Ominously, the pandemic's toll now also includes rampant career uncertainty.

As universities struggle with the economic fallout of repeated closures, burnout among academic researchers will probably continue for some time amid lay-offs or hiring freezes, say higher-education researchers. There are no quick or easy solutions to burnout, especially with no end in sight to its underlying structural causes; academic scientists are often largely left to muddle through as best they can. Details: https://doi.org/10.1038/d41586-021-00663-2

Recommended Reading

How Europe's €100-billion science fund will shape 7 years of research. *Nature.* 2021. As Horizon Europe issues its first call for grants, Nature reviews some big changes — from open science to goal-oriented 'missions'. Horizon Europe, the world's largest multinational research and innovation programme, has issued its first call for grant applications. Over the next seven years, the European Union's giant research-spending scheme will distribute a record €95.5 billion (US$116 billion) — including €5.4 billion from a COVID-19 recovery fund — to basic-science projects and cross-border research collaborations to be carried out by tens of thousands of researchers across 27 member states and more than a dozen other countries. Horizon Europe is an evolution, rather than a reinvention, of the EU's previous research programmes. Like its predecessor Horizon 2020, which ran from 2014 to 2020, it is a mixed bag of funding schemes. It includes grants for individual scientists in all fields, and for large multinational collaborations covering grand societal challenges such as health, climate change and the digital revolution. But Horizon Europe also includes new elements that reflect increasing attention to open science, equality, interdisciplinary research and practical applications. Here, Nature takes a look at some of the major changes.

- ✧ Funding reserved for priority areas
- ✧ A boost for basic research
- ✧ From lab to market
- ✧ Opening up
- ✧ Equality

EU policymakers and the European Commission have agreed to spend more than 3% of Horizon Europe money — around €3 billion — on widening the participation of member states that tend to win fewer grants. The scheme will continue to use tried-and-tested tactics, such as teaming leading research institutions with ones that are less well-established, providing special grants for top researchers in countries that joined the EU only recently, and training researchers to improve their grant-writing and project-management skills. However, it is unclear whether the headline Horizon Europe 'missions' will make fair allowance for scientists in poorer countries. "I do hope that the missions will not be geared for established players in rich countries," says Smith. "Smaller countries like Croatia have a lot to offer too. If implemented reasonably, the new concept has potential to narrow the East–West gap." Organizations participating in Horizon Europe will also have to submit plans to improve gender equality — another change from Horizon 2020. Starting in 2022, all Horizon Europe-funded research institutions will be expected to aim for gender balance among their research staff, enact recruitment and anti-harassment policies, and start to offer gender-equality training opportunities. Details: https://doi.org/10.1038/d41586-021-00496-z

Triptonide is a reversible non-hormonal male contraceptive agent in mice and non-human primates. *Nature Communications*. 2021. There are no non-hormonal male contraceptives currently on the market despite decades of efforts toward the development of "male pills". Here, we report that triptonide, a natural compound purified from the Chinese herb Tripterygium wilfordii displays reversible male contraceptive effects in both mice and monkeys. Single daily oral doses of triptonide induces deformed sperm with minimal or no forward motility (close to 100% penetrance) and consequently male infertility in 3–4 and 5–6 weeks in mice and cynomolgus monkeys, respectively. Male fertility is regained in ~4–6 weeks after cessation of triptonide intake in both species. Either short- or long-term triptonide treatment causes no discernable systematic toxic side effects based on histological examination of vital organs in mice and hematological and serum biochemical analyses in monkeys. Triptonide appears to target junction plakoglobin and disrupts its interactions with SPEM1 during spermiogenesis. Our data further prove that targeting late spermiogenesis represents an effective strategy for developing non-hormonal male contraceptives. Details: https://doi.org/10.1038/s41467-021-21517-5

Development status and prospects of international standardization of medical devices of traditional Chinese medicine. *Pharmacological Research*. 2021. As traditional Chinese medicine (TCM) becomes widely used in many countries around the world, global demand for intelligent and modernized medical devices of TCM is increasing. Medical devices of TCM have played an important role in diagnosis and treatment of disease. Standardization on medical devices of TCM cannot only be beneficial to ensuring the life safety of patients, but also to enhancing the effectiveness of diagnosis and treatment. This paper includes (1) classification and trends in medical devices of TCM; (2) status review on international standardization of medical devices of TCM; (3) key technical factors in developing international standards for medical devices of TCM and (4) prospects for international standardization development of medical devices of TCM. Details: https://doi.org/10.1016/j.phrs.2021.105485

Investigating the mechanisms of modified Xiaoyaosan (tiaogan-liqi prescription) in suppressing the progression of atherosclerosis, by means of integrative pharmacology and experimental validation. *Aging*. 2021. Atherosclerosis (AS)-related

diseases remain among the leading causes of death worldwide. Modified Xiaoyaosan (also called Tiaogan-Liqi prescription, TGLQ), a traditional Chinese medical formulation, has been widely applied in the treatment of AS-related diseases. The aim of this study was to investigate the underlying pharmacological mechanisms of TGLQ in acting on AS. A total of 548 chemical compounds contained in TGLQ, and 969 putative targets, were collected from the Computation Platform for Integrative Pharmacology of Traditional Chinese Medicine, while 1005 therapeutic targets for the treatment of AS were obtained from the DisGeNET, TTD and CTD databases. Moreover, the 63 key targets were screened by the intersection of the targets above, and by network topological analysis. Further functional enrichment analysis showed that the key targets were significantly associated with regulation of the immune system and inflammation, improvement of lipid and glucose metabolism, regulation of the neuroendocrine system and anti-thrombosis effect. The in vivo experiments confirmed that TGLQ could reduce plasma lipid profiles and plasma inflammatory cytokines, and also inhibit AS plaque formation, within the AS model ApoE-/- mice. The in vitro experiments validated the hypothesis that TGLQ could significantly reduce intracellular lipid accumulation, suppress the production of inflammatory cytokines of macrophages induced by oxidized-LDL, and inhibit the protein expression of heat shock protein 90 and toll-like receptor 4. This study identified a list of key targets of TGLQ in the treatment of AS by applying an integrative pharmacology approach, which was validated by in vivo and in vitro experimentation. Details: https://doi.org/10.18632/aging.202832

My most memorable mentors? Plants. *Nature*. 2021. **To nurture a thriving scientific community, look to the natural world for ideas.** I study how plants and bacteria stay in tune with the fast-changing environment to better survive and reproduce. As the seasons change from winter to spring, light cues signal lengthening days, prompting buds and new leaves to emerge. Shadows hint at the growth of neighbouring plants and can lead branches to extend or bend in a quest for full sunlight and maximal photosynthesis. As a Black woman professor, I am in the vast minority in my professional spaces. Even while publishing a stream of scientific papers, I have spent a lot of career time reflecting on how the conventional, transactional paths to scientific success can be at odds with nurturing a diverse community in my laboratory and discipline. Some of my most powerful personal lessons in how to thrive and help others to do so have come from the cress and cyanobacteria in my lab, and the corn and soya in university field plots. That plants with equal 'aptitude' grow and survive differently, depending on their environment, helps me think about how to help colleagues thrive. For instance, going from an observation, such as spotting yellow leaves on a tobacco plant, to listing its potential causes (overwatering, underwatering, nitrogen deficiency) might prompt ideas about, say, how to support graduate students. Are their presentation slides poorly prepared because of boredom, confusion, anxiety or overwork, or is the reason family or financial stress? Many scientists hesitate to apply the ideas that inspire their research and fuel their publications to their working lives and interactions. We've been trained not to. Instead, we're socialized to construct artificial barriers between scientific and personal insights. The use of the first person is discouraged. So is seeing plants or bacteria as instructive for human beings and society, as I explain in my book Lessons from Plants (2021). Consider the fascination that microbiologists feel for bacteria that do not grow under standard laboratory conditions. They don't blame the bacteria; instead, they try to find and supply the correct nutrients, temperature, light or other conditions that the microbes require to thrive. This is the sort of curiosity needed to learn what contributes to the success and growth of individuals, such as those from backgrounds

that are under-represented in research (B. L. Montgomery mSphere 5, e01046-20; 2020). Guided by this approach, in my lab, we avoid dictating strict guidelines, and focus instead on sharing general principles of success — for example, the importance of writing regularly rather than trying to pull together a manuscript in a rush, or putting it off so it never gets done. We then try to help each individual to discover the necessary framework (daily, weekly, monthly or perhaps quarterly writing) that works well for them personally to achieve a particular objective. Now consider the clear contradictions that exist between the reality of how science is conducted by teams, and how scientists celebrate individuals. We romanticize competition and put discovering something first above supporting and recognizing a community. Beyond individuals, arbitrary divides and silos exist between units or organizations, to the benefit of those in prized positions or with insider knowledge. So I reflect on why Indigenous peoples in the Americas have planted beans alongside corn and squash for thousands of years. The beans enrich the soil with nitrogen; the corn stalks support the twining beans and protect them from the pests and stress that the beans would be subject to if they grew along the ground; the squash suppresses weeds. Together, these crops are more productive, more resilient. The same applies to environments from wetlands to wild-flower meadows — strength lies in interactions. Such biological metaphors have made me unafraid to pursue collective success rather than focusing solely on rankings and prestige. So, in my lab, we regularly discuss the specific ways in which teamwork has advanced our research. Did one person's sharing of their experimental expertise lead to a breakthrough for another team member? To facilitate this culture, when I'm hiring, I deliberately look for individuals with demonstrated interest in collaborative effort. Increasingly, others are sharing their biologically inspired insights with me. One colleague compared surviving the stress of the COVID-19 pandemic to sporulation — the process by which bacteria or other organisms form a multilayered, dormant cellular structure in response to unfavourable or extreme environmental conditions, and wait until conditions are more favourable before they re-emerge. Another described the extra care and attention needed to mentor students and postdocs during the transition to working remotely as being akin to the transitional care needed when transplanting plants from one environment, such as pots in a greenhouse, to another, such as an open field. Some people tell me that I'm oversimplifying in thinking that plants can supply useful analogies for humans. They say such knowledge is simply not transferable. Others might counter that nature is about the survival of the fittest; that it, too, is a fierce contest for scarce resources, in which the most competitive wins. I say, let's apply all the cognitive tools we have to solving important challenges. Even though prevailing scientific norms demand that we remain personally distant from our subjects of study, I've been deeply inspired by mine and the metaphors they offer. Details: https://doi.org/10.1038/d41586-021-00961-9

Welcome New GP-TCM RA Life Members

New life members of GP-TCM RA (March-April 2021)

Life Members	
Prof Thomas Efferth	Johannes Gutenberg University
Prof Simon Ming-Yuen Lee	Macau University
Prof Lee-Yan Sheen	National Taiwan University
Prof Xuanbin Wang	Hubei University of Medicine
Dr Chris Chan	The University of Hong Kong

Invitation from Phytomedicine: Current Trends in Natural Products Applications in the Management of Lung Diseases

For more information, please visit: https://www.journals.elsevier.com/phytomedicine/call-for-papers/current-trends-in-natural-products-applications-in-the-mgmt

Special issue in Phytomedicine

Scope: Several traditional herbal remedies have been used throughout history for the treatment of symptoms related to lung diseases like asthma, COPD, lung cancer, pneumonia etc. The present work will provide an extensive overview of natural products affecting the most common lung diseases, their molecular targets, their role in drug discovery, and the current portfolio of available natural remedies. It will also contain knowledge about lung diseases and their herbal treatment strategies as well as a combination with nanoparticles. There are some following rules and guidelines for contributing authors:

1. Review articles have to be prepared systematically, e.g. according to the PRISMA criteria (= preferred reporting items for systematic review) (http://prisma-statement.org/).

Please be aware that ethnopharmacological and phytochemical information is not the main focus of Phytomedicine. We want to see the molecular biology explaining the mode of action of your compound/medicinal plant. Another important point is that in vivo data of animal experiments and clinical data of patients.

2. Original research manuscripts: The molecular functions of responsible genes and proteins as well as the signaling pathways must be investigated by Western blotting, real-time RT-PCR, fluorescence microscopy and other methods. Furthermore, as stated in the instruction for authors of Phytomedicine, the chemoprofiles of the plant extracts must be elucidated by HPLC-MS or related methods. Molecular docking results have to be verified by biochemical assays (microscale thermophoresis, isothermal calorimetry and surface plasmon resonance).

Of course, every article is subject to the external review process, and we cannot guarantee acceptance and publication. Even invited articles to have similar rejection rates than spontaneously submitted articles. This special issue will be very helpful for researchers who are working in this particular area. It's also very supportive of the global society particularly for those who are seeking their treatment through natural products.

Keywords: Asthma; Lung disease; natural products; Herbal; Artificial intelligence; Deep machine learnings; Bibliometric analysis.

Timeline: Submission portal will be opened on 4th Jan 2021. Submission portal will be closed 30th April 2021. Review process completed by September 2021**.** Submission Details:

To prepare the manuscript to submit it in the Journal PHYMED: please visit the link https://www.elsevier.com/journals/phytomedicine/0944-7113/guide-for-authors

Submission link: https://www.editorialmanager.com/phymed/default.asp

While submitting the manuscript in the Journal please choose the article type: management of Lung Disease

Invitation from Frontiers: Epithelial Plasticity and Complexity in Development, Disease and Regeneration

For more information, please visit: https://www.frontiersin.org/research-topics/18812/epithelial-plasticity-and-complexity-in-development-disease-and-regeneration

Epithelial plasticity, the ability of epithelial cells to reversibly change phenotype, is a fascinating phenomenon that has been extensively studied for decades. Phenotypic plasticity of the epithelium is a critical and common feature in embryonic development, inflammation/tissue repair, cancer and more recently stem cell differentiation. Most commonly epithelial plasticity refers to the conversion between epithelial and mesenchymal phenotype, processes known as epithelial-to-mesenchymal transition (EMT) and mesenchymal-to-epithelial transition (MET), the reverse process. Both processes are integral stages of many physiological processes and used by cells and tissues to adapt to various stimuli or cellular stress. EMT has been classically defined as a developmental program that is instrumental in early embryo patterning for many organs, characterized by epithelial cells losing cell-to-cell adhesion, epithelial tight junctions, and desmosomes. MET is regarded as the reversible biological process of EMT that involves losing mesenchymal signature and re-acquiring epithelial characteristics. In more recent years, an increasing number of studies have suggested novel aspects of epithelial biology which challenge the traditional classical definition of epithelium. Reports of sub-specialized epithelial, transit-epithelial and the conversion between epithelial sub-types in response to injury promote further investigation into the full complexity of epithelial plasticity and potential novel functions of conventional as well as non-conventional epithelial cells. Though the micro-environmental signals and the responding machineries enabling epithelial cells to change phenotype are yet to be fully identified, the importance of epithelial interactions such as epithelial-endothelial and epithelial-fibroblast crosstalk has been highlighted in inflammatory response, cancer progression and wound repair. In this Research Topic, we would like to call for submission of Original Research, Reviews, Mini-Reviews and Methods that address the fascinating and complex states of epithelial plasticity, their distinctions and function, in both human and various model organisms. We encourage contributions from developmental and cell biologists, biomaterial specialists, engineer, as well as experts in stem cell niches and tissue modelling. **The proposed Research Topic** aims to attract submissions related, but not limited, to the following areas:

• Plasticity, trans-differentiation, specialization, de-differentiation and re-differentiation of epithelial cells, including complete, partial or transient EMT and MET, and related mechanisms, functional implications and pharmacological interventions;
• Micro-environmental signals and regulatory mechanisms that orchestrate the interactions between epithelial and other cell types, e.g. endothelial cells, fibroblasts, pericytes, gamma delta T cells;
• Novel functions of conventional, unconventional and specialized epithelial cells, their interactions with the environments and innovative pharmacological implications;
• Tissue modelling and regenerative approaches utilizing epithelial plasticity, complexity and diverse functions.

Important Note: All contributions to this Research Topic must be within the scope of the section and journal to which they are submitted, as defined in their mission statements. Frontiers reserves the right to guide an out-of-scope manuscript to a more suitable section or journal at any stage of peer review.
Submission Deadlines: 30 April 2021 (Abstract); 27 August 2021 (Manuscript)
Manuscripts can be submitted to this Research Topic via the following journals:
Frontiers in Cell and Developmental Biology and Cell Adhesion and Migration

Invitation from the Official Journal of GP-TCM RA

WJTCM Call for papers: Systems Biology and Metabolomics of Traditional Chinese Medicine

Special Issue on

Systems Biology and Metabolomics of Traditional Chinese Medicine

CALL FOR PAPERS

Guest Editor
Prof. Xi-jun Wang

Guest Editor
Prof. Hai-tao Lu

Guest Editor
Prof. Toshiaki Makino

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/wjtcm

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Deadline for submission
May. 30, 2021

Intended publication date
October 30, 2021

WJTCM Call for papers: Diabetes and Vascular Disease with TCM

World Journal of Traditional Chinese Medicine (WJTCM)

The official journal of WFCMS and GP-TCM

Special Issue on

Diabetes and Vascular Disease with TCM

CALL FOR PAPERS

Guest Editor
Prof. Qiao-Bing Huang

Guest Editor
Prof. Zi-Lin Sun

Guest Editor
Prof. Jing Li

The diabetic incidence is increasing worldwide, with vascular disease as one of the common complications of diabetes, which is also one of the major causes of death of diabetic patients. The most common vascular diseases include cardio-cerebral vascular disease, renal, retinal, and skin microvascular lesions. The earliest Chinese medical classics "Huangdi's Classic on Medicine" has regarded Diabetes as "Xiaoke Lesion". Vascular complications could be classified into Jingmai (Meridians)-related syndromes in TCM, offering theoretic basis for its clinical treatment based on differentiation of signs.

We invite researchers home and abroad to contribute original research articles as well as reviews on the topic of Diabetes and Vascular Disease with TCM.

Potential topics include but are not limited to:

a. The new idea of TCM category of diabetic vascular complications

b. TCM treatment strategy of different diabetic vascular complications

c. The effect of promoting blood circulation and removing blood stasis (Huo-xue-hua-yu) in the treatment of diabetic vascular complications

d. Advanced development regarding diabetic vascular complications

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

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Manuscript Due
January 30, 2022

Intended publication date
March 25, 2022

WJTCM Call for papers: Biosynthesis-Driven Quality Design of Materia Medica

World Journal of Traditional Chinese Medicine (WJTCM)

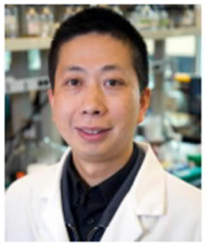
The official journal of WFCMS and GP-TCM

Special Issue on

Biosynthesis-Driven Quality Design of Materia Medica

CALL FOR PAPERS

Guest Editor
Prof. Wan-Sheng Chen



Guest Editor
Prof. Ji-Xun Zhan

Guest Editor
Prof. Shu-Juan Zhao

Biosynthesis and metabolic engineering together with molecular breeding provides an attractive approach to enhance the yield of effective components in medicinal plants and thus to improve or design the quality of Chinese Materia Medica, which is a great motivation for the sustainable development of the entire supply chain of traditional Chinese medicines.

We invite researchers home and abroad to contribute original research articles as well as reviews on the topic of biosynthesis-driven quality design of Chinese Materia Medica and other herbs.

Potential topics include but not limited to:

a. Elucidation and mapping of biosynthetic pathways of the effective components.

b. Metabolic engineering or regulation for the improvement of herbal quality.

c. Progress in understanding the biosynthesis of effective components.

d. Application of molecular breeding technology to medicinal plants.

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

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Manuscript Due Date
March 30, 2021

Intended Publication Date
June 25, 2021

WJTCM Call for papers: Qi Deficiency and Blood Stasis

World Journal of Traditional Chinese Medicine (WJTCM)

The official journal of WFCMS and GP-TCM

Special Issue on

Qi Deficiency and Blood Stasis

CALL FOR PAPERS

Guest Editor
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Guest Editor
Prof. Jian-Xun Liu

Guest Editor
Prof. Jing-Yuan Mao

Guest Editor
Prof. Ming-Jun Zhu

Qi deficiency and blood stasis is a common feature in coronary heart disease, cardiac hypertrophy, myocardial ischemia-reperfusion injury and heart failure, for which there is a lack of effective prevention and treatment methods in modern medicine. Some traditional Chinese medicine (TCM) has shown beneficial effect on heart diseases in clinic, and increasing clinical and basic studies have been carried out devoting to the mechanism behand these medicines, particularly focusing on their potential of tonifying Qi and promoting blood circulation, as well as the scientific essence of the Qi deficiency and Blood Stasis. In order to exchange the latest research results in this field, we have organized special issues of Qi deficiency and blood stasis, tonifying Qi and promoting blood circulation. Experts from this field are welcome to contribute original research articles or reviews.

Potential topics include but not limit to:

a. Reviews on Qi deficiency and blood stasis, tonifying Qi and promoting blood circulation

b. Clinical studies regarding Qi deficiency and blood stasis and tonifying Qi and promoting blood circulation

c. Basic studies regarding Qi deficiency and Blood Stasis and tonifying Qi and promoting blood circulation

d. Pharmacological mechanisms of tonifying Qi and promoting blood circulation

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

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Accept submission date:
July. 30, 2020-July, 25, 2021

Monthly Chinese Materia Medica Highlights

Water chestnut *(Eleocharis dulcis,* Cyperaceae*,* 荸荠*,* left) and
arrow head (*Sagittaria trifolia* subsp. *leucopetala,* Alismataceae*,* 慈姑*,* right)

Both water chestnut and arrow head are aquatic plants of high economic values. Their corms (swollen and solid underground stems) can be utilized as food/vegetable and folk Chinese medicinal material.

Widely cultivated in Asia (China, Korea, Japan, Vietnam, and Malaysia), Africa, and Australia, water chestnut is either eaten fresh or used to manufacture water chestnut juice and flour. As a folk Chinese medicinal, water chestnut (Eleocharitis Dulcis Rhizoma) clears heat, generates fluids, resolves phlegm, and reduces stagnation. It is indicated for thirst in febrile diseases, sore throat, phlegm-heat coughing, and food stagnation. Simply eating the fresh sweet corm or drinking its fresh juice represents a characteristic method of administration in Chinese materia medica.

Commonly cultivated in Asia (China, Korea, and Japan), arrow head is a delicious vegetable that contributes delicacy in some Asian cuisines. The fresh or dried corm (Sagittariae Rhizoma) is a folk Chinese medicinal that promotes blood circulation, cools blood, stops coughing, frees strangury, dissipates nodules, and resolves toxicity. It is indicated for postpartum disorder, coughing up blood in phlegm, urinary dribbling, furuncles and sores.

荸荠

多年草本岸边生
枣色为寒天作成
内白清纯才入口
又闻月下水流声

慈姑

多年草本花为白
箭叶常闻水里来
历尽千山谁觉苦
心存热血莫徘徊

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).