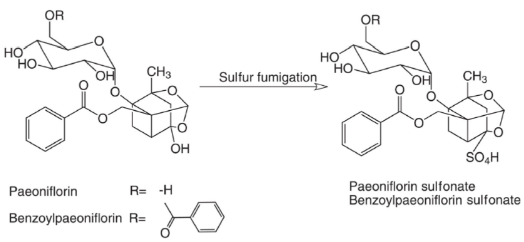
RIVER HERBS

長江中藥

Organic & Lab-tested Chinese Herbs
有機&檢測中藥

Bai Shao 白芍



1 hour of sulfur dioxide exposure from fumigation reduced peoniflorin (a marker of BaiShao therapeutic strength) by 40%, forming a new inactive peoniflorin-sulfonate derivative. *Wang et al (2005) Simultaneous LC determination of major constituentsin red and white peony root.Chromatographic 62, 581-588*

1小時的硫磺熏蒸致使芍藥苷（白芍的藥物有效活性成分）損失40%，使之形成了不具藥物活性的芍藥苷磺酸鹽衍生物。

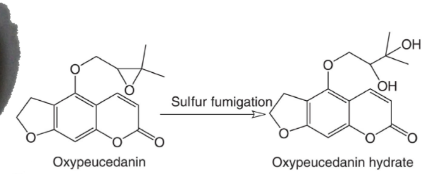
Are you under-dosing your patients?
您給病人用藥夠量嗎?

HangZhou Food & Drug Administration reported 60-70% of herbs currently on the market have been fumigated with sulfur (Oct, 2011).
杭州市食品藥品監督管理局2011年10月的一份報告指出，目前市場上經由硫磺熏蒸的中藥材的比例高達60-70%。

Bai Zhi 白芷

Sulfur fumigation of BaiZhi had 60% loss of imperatorin and almost total loss of oxypeucedanin (key bioactive compound). *Wang et al (2009) Study of the destructive effect to inherent quality of Angelicae dahuricae radix (Baizhi) by sulfur-fumigated process using chromatographic fingerprinting analysis. J. Phar. Biomed. Anal. 49, 1221-1225*

白芷經硫磺熏蒸損失60%的前胡素和幾乎全部的氧化前胡素（關鍵生物活性化合物）



Heavy Metal, Pesticide & Sulfur Contamination

重金屬，農藥&硫污染

Raw Chinese herbs containing sulfur preservatives isn't just a source of potential adverse reactions, more importantly it significantly reduces the therapeutic potency. Presence of heavy metals found in Chinese herbs, which bio-accumulates in our body can cause irreversible health effects. Pesticides residues are extremely common in Chinese medicine. These three impurities directly lead the public to question the safety of Chinese herbs. As practitioners ourselves, we are very concerned about the safety and efficacy of Chinese medicine. We are optimistic that through education and advocacy the safety and efficacy of lab-tested and organic Chinese herbs, will restore the credibility and integrity of Chinese medicine among practitioners and patients. A recent study found 16 out of 17 randomly sampled raw BaiShao (Peony Radix) contains the inactivated sulfur-altered version of the therapeutic ingredient paeoniflorin. When 7 different compound formula containing Bai Shao from 7 different manufacturers were tested, all 7 contained the inactivated sulfured version of paeoniflorion. For more information on the wide problem of impurities in Chinese herbs, please consult the scientific papers that we' ve enclosed for your reference. Please visit us at www.riverherbs.ca and Facebook: River Herbs for more information about the safety and efficacy of Chinese herbs. Together we can improve the credibility and integrity of the Chinese herbal industry.

中藥含硫不單單直接影響身體，更影響到藥的療效。更不用說無法被代謝，只會在身體裡積聚的重金屬，對人體造成的傷害是無法逆轉的。農藥殘留問題更是普遍。三大因素直接導致公眾質疑中藥的安全性。作為從業者，我們非常關注中草藥的安全和療效。我們樂觀地相信，通過教育和宣傳使用更為安全和有效的中藥材（經過實驗室檢測的或有機的中藥材），將恢復醫生和患者之間的誠信。最新的一項研究發現，隨機抽樣的17種白芍樣本中的16種，含被硫化過的原有效成份芍藥苷的變體，大大降低了白芍的藥效。同時測試了來自7個不同生產廠家，均含有白芍的7個不同的複合配方，7種樣品均含有芍藥苷的無效硫化版本。更多中藥相關問題的信息，可以參考我們附錄上的科學研究論文，及我們公司網站 www.riverherbs.ca 上有關中藥材安全和辨別的視頻。

RIVER HERBS

About Us — Who we are

River Herbs stocks a wide selection of dried medicinal herbs. Our herbs are of the highest lab-tested quality (undetected pesticide and sulfur) and we select cultivated organic or wild-crafted herbs whenever possible. Our staff works under the supervision of registered TCM practitioners. We offer dispensing service and customized decoction in our YorkSafe (York Region Public Health Inspection) compliant facility. River Herbs is dedicated to providing unique, professional and friendly service for medical practitioners and their patients across Canada and the United States.

關於我們 — 公司簡介

長江中藥有限公司備有大量精選中藥材。我們選用最高品質的測驗藥材(無農藥殘留和硫磺)，只要有可能我們都選擇有機或野生栽培的藥材。我們的工作人員完全在註冊中醫師的監督下操作。我們在通過YorkSafe食品安全認證和GMP設計認證的設施裡，提供配藥服務和訂製煎劑服務。在加拿大和美國境內，長江中藥專門為醫生和病人提供獨特的，專業的和友好的服務。

What we do
經營範圍

Wholesale

River Herbs is proud to be the authorized Canadian distributor for Nuherbs Co., who shares our value and vision to promote health and wellness, and be the trusted source practitioners can rely on to provide lab-tested and organic herbs.

批發

長江中藥很榮幸成為Nuherbs的加拿大授權經銷商，Nuherbs和我們擁有相同的價值觀和願景：促進公眾健康和保健；成為中醫執業人員獲取實驗室檢測和有機中藥材可以信賴的來源。

Dispensing

We are a full-service TCM herbal medicine dispensary, located in the heart of Markham (Canada' s high-tech capital). Practitioners and patients can order custom formulas in dried or decoction format. We created our own web-based e-commerce platform, River Order System (ROS), to enable medical professionals the option of ordering and delivering custom formulas to and from anywhere in the world. As herbalists ourselves, ROS was specifically designed to ensure prescription writing and refilling is easy for the practitioner and convenient for their patients.

配藥

我們是一家提供全面服務的中醫藥房，位於Markham市中心（加拿大高科技首都）。醫生和患者可以預訂訂製處方， 並可以要求我們提供煎煮服務或只是配藥。我們創建了自己的基於網絡的電子商務平台，長江預訂系統（ROS），使醫療專業人員無論在世界任何一個角落都可以訂購和快遞訂製的處方藥。對於中醫來講，長江預訂系統是經過專門設計，以確保處方填寫和藥物續訂過程簡單便捷，更方便地為醫生和病人服務。

Decoction

At River Herbs, herbs are cooked on-site in computerized stainless steel pressure cookers at 125 ° C using sterile water that fulfill USP standards. After it is prepared, the medicinal liquid is packaged into retort pouches at high temperature, in a negative pressurized environment to prevent contamination.

煎煮

長江中藥的草藥通過計算機控制的不銹鋼壓力鍋，在125℃下用過濾反滲透無菌水煎煮，完全符合USP（美國藥典）標準。草藥煮妥後，藥液是在高溫下打包成袋，在負壓力的環境下包裝，以防止可能產生的污染。

Products

Our organic and lab-tested Chinese herbs in medicinal grade and they are available in wholesale quantities and pricing. We also dispense custom formulas in dried or decoction format to practitioners and patients. In addition, we provide classical and customized herbal tea and nutritious soup base for everyday use.

產品

我們批發醫藥級品質的經實驗室測驗的和有機藥材。我們也給中醫師和病人提供來單抓藥或是訂製煎煮的服務。另外，我們提供經典的或是個性化的花草茶，以及家庭日常需要的養生湯底。

Please contact River Herbs at 905-305-6868

Visit us at www.riverherbs.ca

33-11 Fairburn Drive,
Markham, Ontario
Canada L6G 0A4

Email: info@riverherbs.ca

Tel: 905-305-6868

Fax: 905-305-6685

請聯繫我們

長江中藥 905-305-6868

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電話：905-305-6868

傳真：905-305-6685

About our supplier

Nuherbs Co. supplies pharmacopeia-grade, geo-authentic, conventional and organic Chinese herbs since 1979. Herbal identity of every ingredient is confirmed macroscopically and chemically, when there is a method provided in the Chinese Pharmacopeia. Each lot of every herb is tested for pesticide residues, heavy metals, micro bacteria and other quality indices. Our emphasis on quality extends to the farms that we source from proper processing of each herb to the proper storage of the botanicals in our California warehouse.

Made at GMP internationally certified facilities. (Good Manufacturing Practices) In addition to the laboratory testing required by the different GMPs, nuherbs Co. conducts additional testing for contaminants such as heavy metals, mircobacteria, and pesticide residues.

Dual testing is done by independent laboratories in the United States and the factory' s in-house laboratories in China. This is one of the few companies that does dual testing.

Pharmacopeia Grade - meets or exceeds standards of Chinese Pharmacopeia guidelines. Simply put, the quality of pharmacopeia herbs is better than commonly used food grade herbs to ensure they deliver their intended effect.

關於我們的供應商

Nuherbs Co.從1979年起提供藥典級，道地的常規和有機中草藥。每味藥材根據中國藥典中所提供的方法驗明了其宏觀藥性和化學性質。每批次的每味草藥都經過了農藥殘留，重金屬，微生物等質量指標的測試。我們強調質量，同樣的理念延展到我們對每個藥草的來源基地的選擇和監督，以及我們在加利福尼亞保存草藥的倉庫。

GMP國際認證的設施生產製造。除了由不同的GMP（良好生產規範）要求的實驗室測試，Nuherbs進行了進一步的測試：污染物如重金屬，微生物和農藥殘留。

雙重測試。由美國獨立的實驗室和中國工廠內部實驗室完成。我們是為數不多的做雙測試的公司之一。

藥典級 - 達到或超過了中國藥典公佈的標準。簡單地說，藥典級藥材的質量比常用的食品級藥材高，這樣才能保證藥材能達到預期的效果。

Poney Chiang Ph.D R.Ac R.TCMP
President, River Herbs
Chair of Herbal Medicine, Ontario College of TCM
Adjunct Professor, Faculty of Health, York University

Dr. Poney Chiang graduated with a PhD from the Institute of Medical Science at the University of Toronto. He completed a 4 year professional Masters in Oriental Medicine from the Pacific College of Oriental Medicine in New York and over 1000 hours of formal discipleship in a medical lineage that once consulted for the Forbidden City and Taiwanese presidential palace. His areas of interest are dermatology and neurology.

Poney has authored articles in Medical Acupuncture, European Journal of Oriental Medicine and Oriental Medicine Newsletter and regularly appears on local television (OMNI News) as an expert in Chinese medicine. He has been an invited speaker to Asian Integrative Medicine Symposium, Contemporary Medical Acupuncture Symposium and American Academy of Medical Acupuncture Symposium.

Poney has been teaching since 2008 and is the Chair of the Department of Herbal Medicine at the Ontario College of Traditional Chinese Medicine. He founded River Herbs in 2013 to provide regulated practitioners with high quality herbs that meet organic and lab-tested standards in an effort to elevate public trust in the safety of Chinese medicine. Poney is also the program director for the Neuro-Meridian Integrative Acupuncture Certificate Program at the Canadian College of Naturopathic Medicine.

江澈博士
長江中藥有限公司，董事長
安省中醫學院，中藥系主任
約克大學，健康學院，兼職教授
醫學博士，註冊針灸師，註冊中醫師

江澈博士畢業於多倫多大學的醫學科學研究所，並獲得博士學位。他在紐約的太平洋東方醫學院完成了4年的醫學碩士學位，並跟隨紐約老中醫曹維鳴醫師承襲方脉傳授5年（曹維鳴醫師是前台灣總統府中醫顧問吳海峰醫生的入室弟子）。他感興趣的領域是皮膚科和神經科。江澈博士撰寫的文章發表於《醫學針灸》，《歐洲東方醫學》和《東方醫學通訊》，他作為中國醫學的專家還經常出現在當地電視台（OMNI新聞）。他曾多次受邀在亞洲中西醫結合治療研討會，當代醫學針灸研討會和美國科學院醫學針灸學術研討會上發表演講。

江澈博士自2008年開始任教，現在是安省中醫學院中藥系主任。他於2013年創立了長江中藥，為執牌行醫的中醫師提供經實驗室檢測過的和有機的高品質中藥材，致力於提高公眾對中醫藥安全的信任。江澈博士同時也是加拿大自然療法醫學院，神經經絡針灸結合療法証書培訓科目的創始人。

Organic Items–有機品種

2015 价格 / 磅
Price / lb

Bai Xian Pi (Organic) – Dictamni Cortex – 有機白蘚皮	$21.79
Bai Zhu (Organic) – Atractylodis Macrocephalae Rhizoma – 有機白朮	$14.53
Ban Xia (Fa) (Organic) – Pinellia ternata – 有機法半夏	$38.14
Ban Xia (Jiang) (Organic) – Pinelliae Ternatae Rhizoma(Ginger Preparatum) – 有機姜半夏	$38.14
Cang Er Zi (Organic) – Xanthii Sibirici Fructus – 有機蒼耳子	$7.26
Cang Zhu (Organic) – Atractylodis Rhizoma – 有機蒼朮	$12.71
Chai Hu (Organic) – Bupleuri Radix – 有機柴胡	$31.78
Chi Shao (Organic) – Paeonia rubra Radix – 有機赤芍	$14.53
Dang Shen (Organic) – Codonopsis Pilosulae Radix – 有機黨參	$38.14
Fu Ling (Organic) – Poria – 有機茯苓	$11.80
Gou Qi Zi (Organic) – Lycii Fructus – 有機枸杞子	$19.98
Huang Qin (Organic) – Scutellariae Radix – 有機黃芩	$11.80
Jing Jie (Organic) – Schizonepetae Herba – 有機荊芥	$11.80
Ku Shen (Organic) – Sophorae Flavescentis Radix – 有機苦參	$8.17
Long Dan Cao (Organic) – Gentianae Radix – 有機龍膽草	$24.52
Mu Tong (Chuan) (Organic) – Clematidis Armandii Caulis – 有機川木通	$9.08
Nu Zhen Zi (Organic) – Ligustri Lucidi Fructus – 有機女貞子	$7.26
Sang Ji Sheng (Organic) – Taxilli Herba – 有機桑寄生	$9.08
Suan Zao Ren (Chao) (Organic) – Semen Zizyphi Spinosae – 有機炒酸棗仁	$58.17
Suan Zao Ren (Organic) – Zizyphi Spinosae Semen – 有機酸棗仁	$53.80
Wei Ling Xian (Organic) – Clematidis Radix – 有機威靈仙	$12.71
Wu Wei Zi (Organic) – Schisandrae Chinensis Fructus – 有機五味子	$21.79
Xuan Shen (Organic) – Scrophulariae Ningpoensis Radix – 有機玄參	$9.08
Yi Yi Ren (Organic) – Coicis Semen – 有機薏苡仁	$8.17
Yin Chen Hao (Organic) – Artemisiae Herba – 有機茵陳蒿	$9.99
Yin Yang Huo (Organic) – Epimedii Herba – 有機淫羊藿	$12.71

***Price subject to change without notice**
價格如有變更，恕不另行通知
Please contact us for additional herbs, we can source them and even make PaoZhi herbs!
如有其他藥材需求請與我們聯繫，我們甚至可以為您炮製藥材！

Lab-tested Items–檢測品種

2015 价格 / 磅
Price / lb

Ba Ji Tian – Morindae Officinalis Radix – 巴戟天	$19.07
Ba Ji Tian (Yan Chao) – Radix Morindae Officinalis – 巴戟天（鹽炒）	$29.06
Bai Hua She She Cao – Hedyotidis Diffusae Herba – 白花蛇舌草	$9.99
Bai Ji Li – Tribuli Fructus – 白蒺藜	$8.17
Bai Qian – Cynanchi Stauntonii Radix or Rhizoma – 白前	$14.53
Bai Shao (Chao) – Paeoniae Lactiflorae Radix (Preparatum) – 白芍 (炒)	$15.44
Bai Shao (Sheng) – Paeoniae Lactiflorae Radix – 白芍 (生)	$13.62
Bai Xian Pi – Dictamni Radicis Cortex – 白鮮皮	$19.07
Bai Zhi– Angelicae Dahuricae Radix – 白芷	$11.80
Bai Zhu (Chao) – Atractylodis Macrocephalae Rhizoma(Preparatum) – 白朮(炒)	$16.34
Bai Zhu (Sheng) – Atractylodis Macrocephalae Rhizoma – 白朮 (生)	$13.62
Ban Lan Gen – Isatidis Seu Baphicacanthi Radix – 板藍根	$11.80
Ban Xia (Fa) – Pinellia ternata – 法半夏	$36.32
Ban Xia (Jiang) – Pinelliae Ternatae Rhizoma(Ginger Preparatum) – 半夏 (姜)	$36.32
Bu Gu Zhi – Psoraleae Fructus – 補骨脂	$9.08
Cang Er Zi – Xanthii Sibirici Fructus – 蒼耳子	$5.45
Cang Zhu – Atractylodis Rhizoma – 蒼朮	$9.99
Chai Hu – Bupleuri Radix – 柴胡	$31.78
Chan Tui – Periostricum Cicadae – 蟬蛻	$51.76
Chen Pi – Pericarpium Citri Reticulatae – 陳皮	$19.07
Chi Shao – Paeoniae Lactiflorae Radix – 赤芍	$11.80
Chuan Xiong – Ligustici Radix – 川芎	$12.71

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杜仲
Dù Zhòng

Lab-tested Items-檢測品種

2015 价格 / 磅
Price / lb

Chuan Xiong (Jiu Zhi) - Ligusticum chuanxiong - 川芎（酒製）	$13.62
Dan Shen - Salvia miltiorrhizae Radix - 丹參	$9.99
Dan Shen (Wild) - Salvia Miltiorrhiza Radix - 丹參（野）	$9.99
Dang Gui - Angelicae sinensis Radix - 當歸	$19.98
Dang Shen - Codonopsitis Pilosulae Radix - 黨參	$31.78
Di Fu Zi - Kochiae Fructus - 地膚子	$5.45
Du Huo - Angelicae Pubescentis Radix - 獨活	$10.90
Du Zhong - Cortex Eucommiae Ulmoidis - 杜仲	$13.62
E Zhu - Curcuma Zedoaria Rhizoma - 莪朮	$9.99
Fang Feng - Saposhnikoviae Divaricatae Radix - 防風	$17.25
Fu Ling - Poria - 茯苓	$10.12
Gan Cao - Glycyrrhizae Uralensis Radix - 甘草	$14.53
Ge Gen - Puerariae Radix - 葛根	$8.17
Gou Qi Zi - Lycii Fructus - 枸杞子	$18.86
Gui zhi - Cinnamomi Cassiae Ramulus - 桂枝	$7.26
Han Lian Cao - Ecliptae Herba - 旱蓮草	$6.36
He Huan Pi - Albizziae Julibrissin Cortex - 合歡皮	$7.26
Hong Hua - Flos Carthami Tinctorii - 紅花	$27.24
Hou Po - Magnoliae Officinalis Cortex - 厚樸	$11.80
Huai Hua Mi - Sophorae Japonicae Flos - 槐花米	$14.53
Huang Bai - Phellodendri Cortex - 黃柏	$9.08
Huang Lian - Coptidis Rhizoma - 黃連	$31.78

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Lab-tested Items–檢測品種

2015 价格 / 磅
Price / lb

Huang Qi (Sheng) – Astragali Radix – 黃耆 (生)	$19.98
Huang Qin – Scutellariae Baicalensis Radix – 黃芩	$11.80
Huo Ma Ren (Chao) – Cannabis Semen (Preparatum) – 炒火麻	$7.26
Ji Xue Teng – Spatholobi Caulis – 雞血藤	$6.36
Jie Geng – Platycodi Grandiflori Radix – 桔梗	$23.61
Jin Yin Hua – Lonicerae Japonicae Flos – 金銀花	$43.61
Jing Jie – Seu Flos Schizonepetae Tenuifoliae Herba – 荊芥	$9.99
Ku Shen – Sophorae Radix – 苦參	$6.36
Lian Qiao – Forsythiae Suspensae Fructus – 連翹	$19.07
Long Dan Cao – Gentianae Radix – 龍膽草	$20.88
Mai Men Dong – Tuber Ophiopogonis Japonici – 麥門冬	$21.79
Mu Dan Pi – Moutan Radicis Cortex – 牡丹皮	$14.53
Mu Tong (Chuan) – Clematidis Armandii Franch – 木通 (川)	$9.99
Mu Xiang – Aucklandiae Radix – 木香	$9.08
Niu Xi (Chuan) – Cyathulae Radix – 牛膝（川）	$11.80
Niu Xi (Huai) – Achyranthis Bidentatae Radix – 牛膝 (懷)	$9.08
Nu Zhen Zi – Ligustri Lucidi Fructus – 女貞子	$5.75
Qian Cao Gen – Et Rhizoma Rubiae Radix – 茜草根	$24.52
Qian Hu – Peucedani Radix – 前胡	$21.79
Qiang Huo – Et Radix Notopterygii Rhizoma – 羌活	$43.58
San Leng – Sparganii Stoloniferi Rhizoma – 三棱	$9.99
San Leng (Cu) – Sparganium Stoloniferum Rhizoma – 三棱（醋）	$10.90

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Lab-tested Items–檢測品種

2015 价格 / 磅
Price / lb

Sang Bai Pi – Mori Albae Folium – 桑白皮	$9.08
Sang Ji Sheng – Taxilli Herba – 桑寄生	$6.36
Sha Ren – Amomi Fructus – 砂仁	$54.48
Sha Shen (Bei) – Glehniae Radix – 沙參 (北)	$16.34
Shan Yao – Dioscoreae Oppositae Radix – 山藥	$19.98
Shan Zha – Crataegi Fructus – 山楂	$6.62
Shan Zhu Yu – Corni Officinalis Fructus – 山茱萸	$17.25
Sheng Di Huang – Rehmanniae Radix – 生地黄	$9.08
Sheng Ma – Cimicifugae Rhizoma – 升麻	$9.08
Shi Chang Pu – Acori gramini Rhizoma – 石菖蒲	$14.53
Shu Di Huang – Rehmanniae Radix – 熟地黄	$9.99
Suan Zao Ren – Zizyphi Spinosae Semen – 酸棗仁	$52.66
Suan Zao Ren (Chao) – Semen Zizyphi Spinosae – 酸棗仁（炒）	$56.71
Tao Ren – Persicae Semen – 桃仁	$24.52
Tian Hua Fen – Trichosanthis Radix – 天花粉	$10.90
Tu Fu Ling – Smilacis Glabrae Rhizoma – 土茯苓	$9.99
Wei Ling Xian – Clematidis Radix – 威靈仙	$9.99
Wu Wei Zi – Schisandrae Chinensis Fructus – 五味子	$19.07
Xia Ku Cao – Spica Prunellae Vulgaris – 夏枯草	$11.80
Xian Mao – Curculiginis Rhizoma – 仙茅	$13.03
Xiang Fu (Zhi) – Cyperus Rhizome – 香附（製）	$9.08
Xing Ren – Pruni Armeniacae Semen – 杏仁	$11.80

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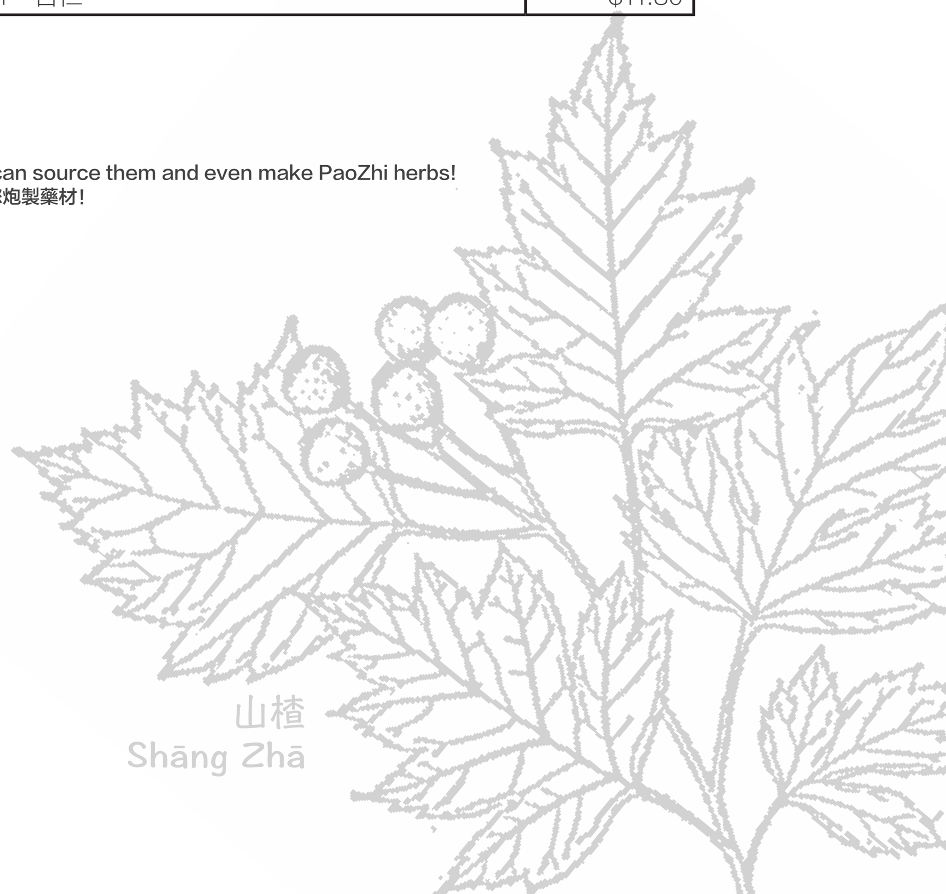

Lab-tested Items–檢測品種

2015 价格 / 磅
Price / lb

Xuan Shen – Scrophulariae Ningpoensis Radix – 玄参	$6.92
Yan Hu Suo – Corydalis Rhizoma – 延胡索	$24.52
Ye Jiao Teng – Polygoni Multiflori Radix – 夜交藤	$7.21
Yi Mu Cao – leonuri Herba – 益母草	$5.45
Yi Yi Ren (Sheng) – Coicis Semen – 薏苡仁 (生)	$10.99
Yi Yi Ren(Chao) – Coicis Semen(Preparatum) – 薏苡仁 (炒)	$8.66
Yi Zhi Ren – Alpiniae Oxyphyllae Fructus – 益智仁	$19.07
Yin Chen Hao – Artemisiae Herba – 茵陳蒿	$8.17
Yin Yang Huo – Epimedii Herba – 淫羊藿	$11.58
Yu Jin – Curcumae Domesticae Rhizoma – 鬱金	$13.03
Yuan Zhi (Zhi) – Plygalae Tenuifoliae Radix(Preparatum) – 遠志 (製)	$33.60
Ze Xie – Alismatis Rhizoma – 澤瀉	$11.80
Zhi Ke (Chao) – Citri Aurantii Fructus (Preparatum) – 枳殼 (炒)	$9.99
Zhi Shi (Chao) – Immaturus Citri Aurantii Fructus(Preparatum) – 枳實 (炒)	$8.17
Zhi Zi (Shan) – Gardeniae Jasminoidis Fructus – 梔子 (山)	$12.71
Zi Wan – Asteris Radix – 紫菀	$10.12

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Sample certificate of analysis for lab-tested herbs

CERTIFICATE OF ANALYSIS

Latin Name:	Radix Angelicae Sinensis		
Botanical Source:	*Angelica sinensis (Oliv.) Diels*	**Pinyin Name:**	Dang Gui
Plant Part Used:	Root	**Batch No.:**	130301H003
MFTD Date:	June. 14, 2013	**Batch Quantity:**	3500kg
Retest Date:	June. 14, 2018	**Issue Date:**	June. 22, 2012
Testing Reference:	Quality Standard of Radix Angelicae Sinensis	**Origin:**	China

Test				
Analysis	**Specification**	**Results**	**Test Methods**	**Detection Limits**
Identity	Macroscopical Complies	Complies	Visual & Organoleptic, CP2010	/
	Microscopical Complies	Complies	CP2010	/
	TLC Positive	Positive	TLC, CP2010	/
Impurity	<1%	Complies	Appendix IX A, CP2010	/
Water	<12.0%	11.9%	Appendix IX H, CP2010	/
Total Ash	<7.0%	6.4%	Appendix IX K, CP2010	/
Acid-insoluble ash	<2%	1.1%	Appendix IX K, CP2010	/
Ethanol Extractives	>45.0%	51.7%	Appendix X A, CP2010	/
Assay				
Ferulic acid ($C_{10}H_{10}O_4$)	>0.05%	0.09%	HPLC	/
Heavy Metals				
Lead (Pb)	<5ppm	1.06ppm	AAS, Euro Pharm	0.05ppm
Cadmium (Cd)	<1ppm	0.03ppm	AAS, Euro Pharm	0.01ppm
Mercury (Hg)	<0.1ppm	0.02ppm	AAS, Euro Pharm	0.01ppm
Pesticides Residue				
Organophosphorpestizide	Euro Pharm	Negative	GC, Euro Pharm	0.01ppm
Organochlorpestizide	Euro Pharm	Negative	GC, Euro Pharm	0.01ppm
Pyrethroide	Euro Pharm	Negative	GC, Euro Pharm	0.05ppm
Piperonylbutoxid	Euro Pharm	Negative	GC, Euro Pharm	0.1ppm
Microbiological Tests				
Total Plate Count	$<10^7$cfu/g	$1.0*10^4$cfu/g	Appendix XⅢ C, CP2010	1cfu/g
Yeast & Mold	$<10^5$cfu/g	$1.0*10^3$cfu/g	Appendix XⅢ C, CP2010	1cfu/g
E. Coli	Negative	Negative	Appendix XⅢ C, CP2010	1cfu/g
Salmonella	Negative	Negative	Appendix XⅢ C, CP2010	Absent in 10g
Conclusion	This product complies with specifications.			
Package	Plastic bag			
Storage	Preserve in a ventilated dry place, protected from mould and moth.			
Shelf Life	5 years when stored properly.			

Remarks: This is a computer print out of the certificate of analysis and is valid without signature.

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Sample certificate of analysis for organic herbs

CERTIFICATE OF ANALYSIS

Latin Name:	Organic Radix Paeoniae Rubra		
Botanical Source:	*Paeonia lactiflora Pall.*	**Pinyin Name:**	You Ji Chi Shao
Plant Part Used:	Root	**Batch No.:**	121101BH028
MFTD Date:	Nov. 02, 2012	**Batch Quantity:**	1500kg
Retest Date:	Nov. 02, 2017	**Issue Date:**	Nov. 28, 2012
Testing Reference:	Quality Standard of organic Radix Paeoniae Rubra	**Origin:**	China

Test				
Analysis	**Specification**	**Results**	**Test Methods**	**Detection Limits**
Identity	Macroscopical Complies	Complies	Visual & Organoleptic, CP2010	/
	Microscopical Complies	Complies	CP2010	/
	TLC Positive	Positive	TLC, CP2010	/
Impurity	<1.0%	Complies	Appendix IX A, CP2010	/
Water	<13.0%	11.6%	Appendix IX H, CP2010	/
Heavy Metals				
Lead (Pb)	<5ppm	0.66ppm	AAS, Euro Pharm	0.05ppm
Cadmium (Cd)	<1ppm	0.03ppm	AAS, Euro Pharm	0.01ppm
Mercury (Hg)	<0.1ppm	0.02ppm	AAS, Euro Pharm	0.01ppm
Pesticides Residue				
Organophosphorpestizide	Euro Pharm	Negative	GC, Euro Pharm	0.01ppm
Organochlorpestizide	Euro Pharm	Negative	GC, Euro Pharm	0.01ppm
Pyrethroide	Euro Pharm	Negative	GC, Euro Pharm	0.05ppm
Piperonylbutoxid	Euro Pharm	Negative	GC, Euro Pharm	0.1ppm
Microbiological Tests				
Total Plate Count	$<10^7$cfu/g	$1.5*10^4$cfu/g	Appendix XⅢ C, CP2010	1cfu/g
Yeast & Mold	$<10^5$cfu/g	$2.0*10^3$cfu/g	Appendix XⅢ C, CP2010	1cfu/g
E. Coli	Negative	Negative	Appendix XⅢ C, CP2010	1cfu/g
Conclusion	This product complies with specifications.			
Package	Plastic bag			
Storage	Preserve in a ventilated dry place, protected from mould and moth.			
Shelf Life	5 years when stored properly.			

Remarks: This is a computer print out of the certificate of analysis and is valid without signature.

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Heavy Metal and Pesticide Content in Commonly Prescribed Individual Raw Chinese Herbal Medicines

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Abstract

Heavy metal and pesticide contamination has previously been reported in Chinese Herbal Medicines (CHMs), in some cases at potentially toxic levels. This study was conducted to determine general patterns and toxicological significance of heavy metal and pesticide contamination in a broad sample of raw CHMs. Three-hundred-thirty-four samples representing 126 species of CHMs were collected throughout China and examined for arsenic, cadmium, chromium, lead, and mercury. Of the total, 294 samples representing 112 species were also tested for 162 pesticides. At least 1 metal was detected in all 334 samples (100%) and 115 samples (34%) had detectable levels of all metals. Forty-two different pesticides were detected in 108 samples (36.7%), with 1

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to 9 pesticides per sample. Contaminant levels were compared to toxicological reference values in the context of different exposure scenarios. According to a likely scenario of CHM consumption, only 3 samples (1%) with heavy metals and 14 samples (5%) with pesticides were found with concentrations that could contribute to elevated background levels of contaminant exposure. According to the most conservative scenario of CHM consumption, 231 samples (69%) with heavy metals and 81 samples (28%) with pesticides had contaminants that could contribute to elevated levels of exposure. Wild collected plants had higher contaminant levels than cultivated samples. Cadmium, chromium, lead, and chlorpyrifos contamination showed weak correlations with geographic location. Based on our assumptions of the likely mode of consumption of raw CHMs, the vast majority (95%) of the 334 samples in this study contained levels of heavy metals or pesticides that would be of negligible concern. However, given the number of samples with detectable contaminants and the range between the more likely and more conservative scenarios of contaminant exposure, more research and monitoring of heavy metals (especially cadmium and chromium) and pesticide residues (especially chlorpyrifos) in raw CHMs are advised.

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Article

Detection of Sulfur-Fumigated Paeoniae Alba Radix in Complex Preparations by High Performance Liquid Chromatography Tandem Mass Spectrometry

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Abstract: Detection of sulfur-fumigated Paeoniae Alba Radix (PAR) in different complex preparations is challenging due to the relatively lower content of PAR and interference from more complicated components in complex preparations with different multiple constituent herbs. In this study, a high performance liquid chromatography-triple-quadrupole tandem mass spectrometry method was developed for detecting sulfur-fumigated PAR in different complex preparations. Paeoniflorin, the major component of PAR, and paeoniflorin sulfonate, the characteristic artifact transformed from paeoniflorin during sulfur-fumigation of PAR, were used as chemical markers. Multiple reaction monitoring (MRM) scan was employed to maximize sensitivity and selectivity. Through optimizing full mass scan and daughter ion scan conditions, two mass transitions were selected and employed respectively for unequivocal identification of paeoniflorin and paeoniflorin sulfonate. The detection limits for paeoniflorin and paeoniflorin sulfonate using MRM were much lower than those detected with UV 270 nm. Paeoniflorin and paeoniflorin sulfonate could be simultaneously detected in different commercial PAR-containing complex preparations without interference of other components using the established method, indicating that the newly established method was selective and sensitive enough for screening sulfur-fumigated PAR in commercial complex preparations.

The representative chromatograms are shown in Figures 4 and 5, and the results are summarized in Table 1. It was found that paeoniflorin and paeoniflorin sulfonate were simultaneously detected in sixteen of seventeen commercial PAR samples and all seven PAR-containing complex preparations collected, and no other peaks interfered with the detection of these two compounds even in seven different complex preparations. Further more, the ion intensity ratios of two mass transitions for paeoniflorin sulfonate (*m/z* 543→*m/z* 259 *vs.* *m/z* 543→*m/z* 213**)** and paeoniflorin (*m/z* 449→*m/z* 327 *vs.* *m/z* 449→*m/z* 165) were calculated to be 6.52 ± 0.29 (RSD 4.4%) and 0.50 ± 0.048 (RSD 9.6%) respectively in seventeen raw materials, whereas 5.55 ± 0.52 (RSD 9.3%) and 0.53 ± 0.03 (RSD 6.2%) respectively in seven complex preparations, suggesting that there were a little matrix effects on ionization of two marker compounds in raw materials and complex preparations. All these results suggested that the established method had high selectivity for the identification of sulfur-fumigated PAR, and is a universal method for screening sulfur-fumigated PAR in complex preparations with different constituent herbs.

Figure 5. Representative chromatograms of different PAR-containing complex preparations by MRM scan. (**A**) XYW (JPACM-02-06) ion transition *m/z* 543→*m/z* 259; (**B**) XYW (JPACM-02-06) ion transition *m/z* 543→*m/z* 213; (**C**) XYW (JPACM-02-06) ion transition *m/z* 449→*m/z* 327; (**D**) XYW (JPACM-02-06) ion transition *m/z* 449→*m/z* 165; (**E**) MRW (JPACM-02-05) ion transition *m/z* 543→*m/z* 259; (**F**) MRW (JPACM-02-05) ion transition *m/z* 543→*m/z* 213; (**G**) MRW (JPACM-02-05) ion transition *m/z* 449→*m/z* 327; (**H**) MRW (JPACM-02-05) ion transition *m/z* 449→*m/z* 165. **1**: paeoniflorin; **2**: paeoniflorin sulfonate.

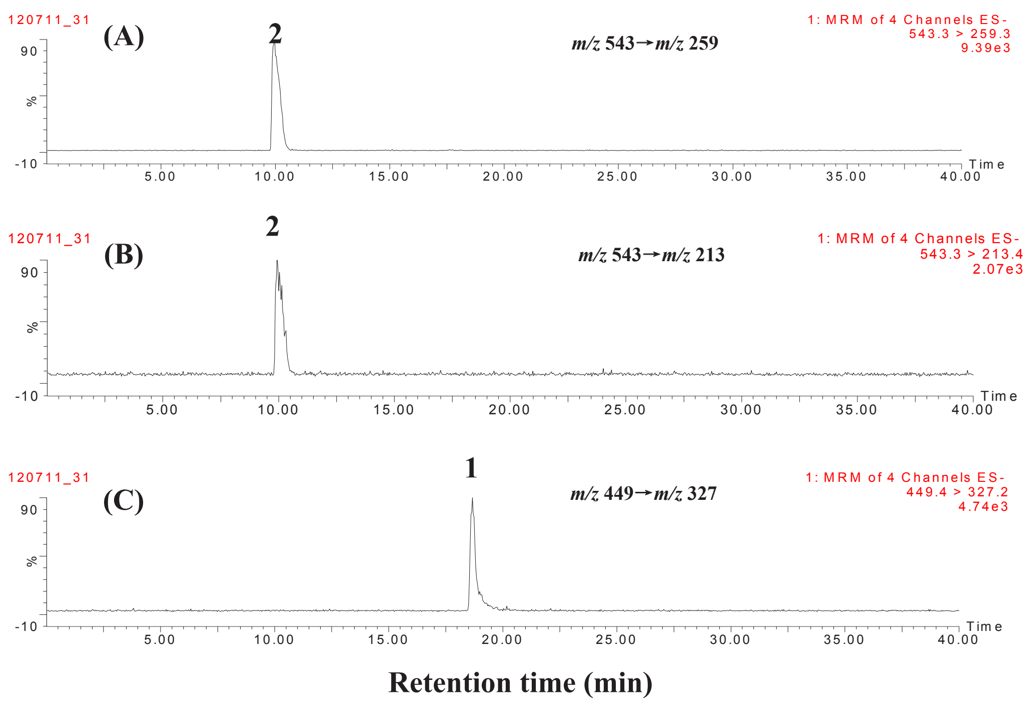
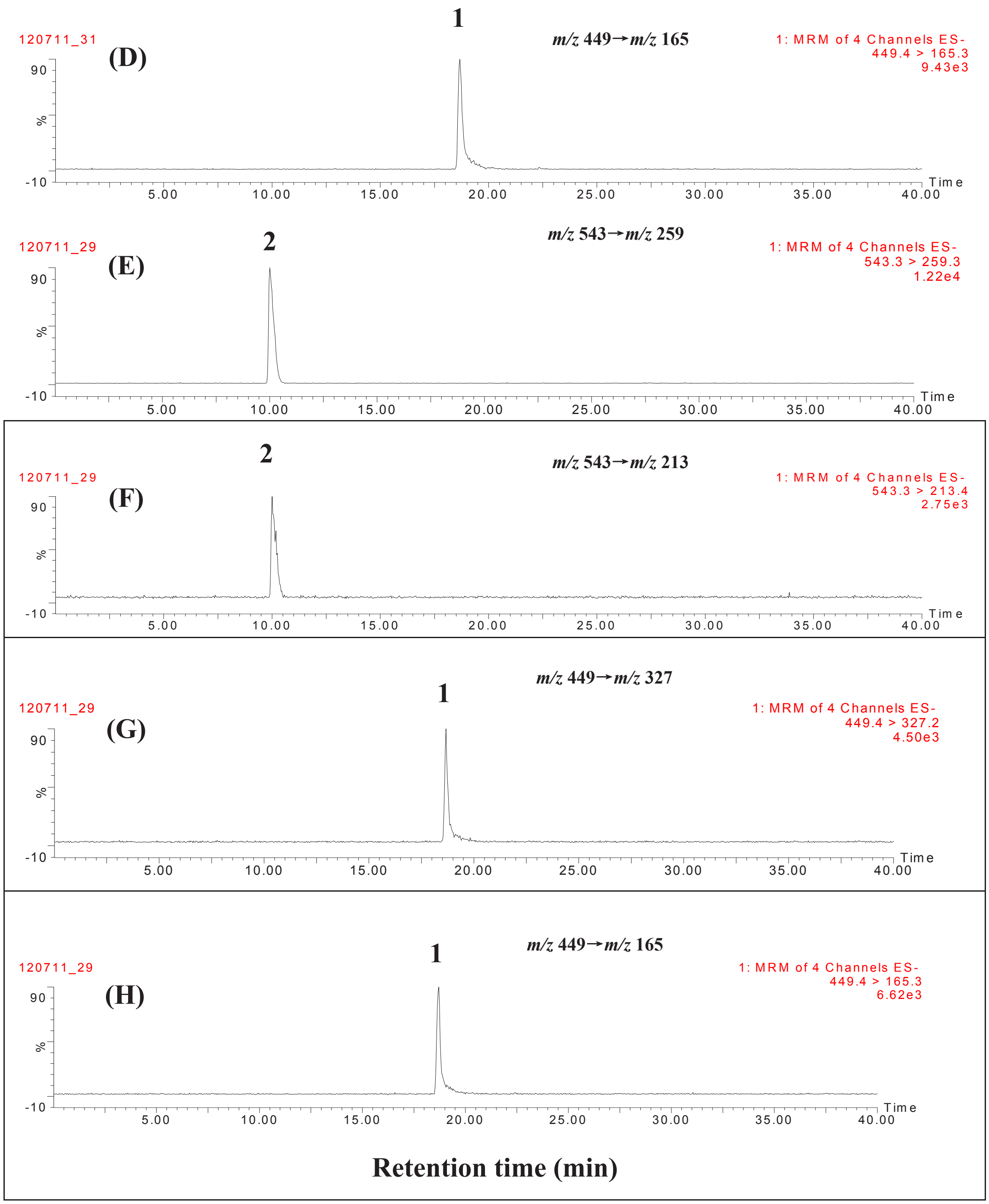


Figure 5. *Cont.*



It was also found from Table 1 that paeoniflorin sulfonate was widely detected in the investigated PAR samples and its complex preparations collected from different localities and producers. So it could be concluded that sulfur-fumigation is currently still a common process method in post-harvest handling of PAR. Therefore it is recommended that SFDA of China should strengthen the enforcement to prohibit PAR being sulfur-fumigated, so that PAR-containing complex preparations could be effectively and safely used in clinical medications.

Table 1. Detection of paeoniflorin sulfonate in PAR and PAR-containing complex preparations.

PAR			
Sample code	**Collection locality**	**Collection time (year-month)**	**Result**
JPACM-01-01	Bozhou, Anhui province	2009-01	−
JPACM-01-02	Bozhou, Anhui province	2009-01	+
JPACM-01-03	Shangqiu, Henan province	2009-01	−
JPACM-01-04	Shangqiu, Henan province	2009-01	+
JPACM-01-05	Jiang county, Shanxi province	2009-01	−
JPACM-01-06	Jiang county, Shanxi province	2009-01	+
JPACM-01-07	Bai Xin Pharmacy, Nanjing	2009-10	+
JPACM-01-08	Bao Feng Tai Ping Pharmacy, Nanjing	2009-10	+
JPACM-01-09	Hua Yue Pharmacy, Nanjing	2009-10	+
JPACM-01-10	Lao Bai Xing Pharmacy, Nanjing	2009-10	+
JPACM-01-11	Lao Bai Xing Pharmacy, Nanjing	2009-10	+
JPACM-01-12	Xian Sheng Pharmacy, Nanjing	2009-10	+
JPACM-01-13	Xian Sheng Pharmacy, Nanjing	2009-10	+
JPACM-01-14	Zhi Lin Pharmacy, Nanjing	2009-10	+
JPACM-01-15	Tian Shi Pharmacy, Nanjing	2009-10	+
JPACM-01-16	Hong Ji Tang Pharmacy, Jinan	2010-02	+
JPACM-01-17	Jian Lian Pharmacy, Jinan	2010-02	+
JPACM-01-18	Shen Nong Ben Cao Pharmacy, Jinan	2010-02	+
JPACM-01-19	Qi Lu Yi Kang Pharmacy, Jinan	2010-02	+
JPACM-01-20	Bozhou Chinese Yinpian company, Bozhou	2009-11	+
JPACM-01-21	Bozhou county, Anhui province	2009-11	−
JPACM-01-22	Bozhou county, Anhui province	2009-11	+
JPACM-01-23	Fu Shun Pharmacy, Liaoning province	2010-02	+
PAR-containing complex preparations			
Sample code	**Preparation names (herbs contained)**	**Producer**	**Result**
JPACM-02-01	SJWTKL * (Evodiae Radix, Murrayae Folium et Cacumen, Zanthoxyli Radix, Aucklandiae Radix, Astragali Radix, Poria, Rehmanniae Radix, Paeoniae Radix Alba)	SJYY #	+
JPACM-02-02	QZWTKL (Bupleuri Radix, Corydalis Rhizoma, Aurantii Fructus, Cyperi Rhizoma, Paeoniae Radix Alba, Glycyrrhizae Radix et Rhizoma Praeparata Cum Melle)	LNBXSY	+
JPACM-02-03	YWKL (Astragali Radix Praeparata Cum Melle, Codonopsis Radix, Citri Reticulatae Pericarpium, Cyperi Rhizoma, Paeoniae Radix Alba, Dioscoreae Rhizoma, Mume Fructus, Glycyrrhizae Radix et Rhizoma)	ZDQCBYY	+
JPACM-02-04	WKLJN (Paeoniae Radix Alba, Bletillae Rhizoma, Notoginseng Radix et Rhizoma, Glycyrrhizae Radix et Rhizoma, Poria, Corydalis Rhizoma, Sepiae Endoconcha, Belladonna Extract)	KHYY	+
JPACM-02-05	MRW (Cannabis Semen, Armeniacae Semen Amarum, Rhei Radix et Rhizoma, Aurantii Fructus Immaturus, Magnoliae Officinalis Cortex, Paeoniae Radix Alba)	NJTRT	+

Table 1. *Cont.*

PAR-containing complex preparations			
Sample code	**Preparation names (herbs contained)**	**Producer**	**Result**
JPACM-02-06	XYW (Bupleuri Radix, Angelicae Sinensis Radix, Paeoniae Radix Alba, Atractylodis Macrocephalae Rhizoma, Poria, Glycyrrhizae Radix et Rhizoma Praeparata Cum Melle, Menthae Haplocalycis Herba, Zingiberis Rhizoma Recens)	HNSWXZY	+
JPACM-02-07	XLJN (Scorpio, Bombyx Batryticatus, Sargassum, Scolopendr, Curcumae Radix, Prunellae Spica, Eupolyphaga Steleophaga, Laminariae Thallus Eckloniae Thallus, Agrimoniae Herba, Hirudo, Astragali Radix, Paeoniae Radix Alba, Pheretima, Hedyotidis Herba , Ostreae Concha)	JSSZXYJHYY	+

+: Detectable; −: Undetectable; *: Abbreviated names of PAR-containing complex preparations; #: Abbreviated names of drug companies

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Sulfur fumigation processing of traditional Chinese medicinal herbs: beneficial or detrimental?

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Majority of traditional Chinese medicine (TCM) herbs need to undergo post-harvesting processing to convert raw material into the form readily used for prescription. In general, processing procedures are either according to China Pharmacopeia or based on traditional methods. Recently sulfur fumigation is increasingly used to replace traditional sun-drying for its pesticidal and anti-bacterial properties in a cheap and convenient manner. However, to date information on effects of sulfur fumigation on herbal safety and efficacy are limited. This article addresses potential destructive effects of sulfur fumigation on herbal efficacy and and safety through reviewing currently available information. Since recently increased numbers of studies have demonstrated that sulfur fumigation-induced dramatic changes in chemical profiles of various sulfur-fumigated herbs, consequent alteration of efficacy, and/or potential incidence of toxicity are suspected. Therefore comprehensive investigations on effects of sulfur fumigation on toxicity, chemical profiles, pharmacokinetics, and bioactivities of TCM herbs are timely to provide scientific basis for standardization and regulation of this currently common but potentially harmful processing method.

Keywords: sulfur fumigation,TCM herb processing, sulfur fumigation-induced chemical alteration, pharmacokinetic alteration, toxicity of sulfur dioxide, toxicity of sulfiting agents

INTRODUCTION

In the traditional Chinese medicine (TCM) practice, a personalized Chinese Materia Medica, usually in a mixed form, is prescribed to individual patients (Chan, 1995; Ye and He, 2010). The prescribed mixed form is called compound formula (Fufang) and commonly taken orally as an aqueous decoction. The compound formula consists of a complementary combination of various TCM materials, including medicinal herbs, animals, and minerals, which contain multiple bioactive compounds and interact synergistically with each other for enhanced efficacy at multiple targets (Tomlinson et al., 2000; Kan et al., 2008). Among Chinese Materia Medica used, TCM herbs are predominant. In China, the use of TCM remains the first-line treatment for many minor illnesses and chronic diseases. Recently, there is an increasing number of people worldwide who are using alternative medications especially TCM, and believe their therapeutic and safe values (Bent and Ko, 2004). For instance, it has been reported that up to 20% of cancer patients used herbal medicine to complement conventional chemotherapy regimens, enhance the immune system, improve general health, and reduce adverse effects from the conventional chemotherapy (Chiu et al., 2009; Damery et al., 2011). Studies also showed that 78% of patients admitted to hospital for acute cardiovascular dis- eases used natural health products, and of them 20% used herbal products and 9% consumed TCM herbs (Alherbish et al., 2011).

Despite the surging popularity of TCM herbs, there are still many uncertainties surrounding its use. Often, not all of the bioactive and/or toxic constituents are identified in TCM herbs, so it complicates the process of delineating the mechanisms of beneficial action and adverse effects/toxicities, and therefore makes their quality control to be extremely difficult and challenging (Wang et al., 2009a). In general, medicinal herbs used in most Western countries are fresh or simply dried. Whereas, most of the TCM herbs have to be processed after harvesting by using physical and/or chemical methods to convert the raw materials to the readily used herbal forms called decoction pieces (Yinpian), which are then suitable for prescription or clinical usage (Zhao et al., 2010). Unfortunately, in addition to the numerous factors, such as herbal plant species, growing environment, harvesting time, storage condition, and contamination, which may significantly affect quality of TCM herbs (Tomlinson et al., 2000; Deng, 2002; Bent and Ko, 2004), unique and different post-harvesting processing methods, such as stir-frying, steaming, and calcining, for the same and different herbs, certainly cause more variations for the quality control of TCM herbs (Zhao et al., 2010). To make the situation even more complicated and problematic, some uncontrolled or poorly controlled processing procedures, such as the recently emerged sulfur fumigation, are often used by herbal farmers, producers, and manufactories in China. Recently, sulfur fumigation processing has attracted more attention due to its potential detrimental effect on the safety and efficacy of sulfur-fumigated TCM herbs. This article reviews the current situation and problems of sulfur fumigation of TCM herbs with emphasis on altercations of chemical profiles, pharmacokinetics, bioactivities, and even adverse effects/toxicities of TCM herbs caused by sulfur fumigation.

CONVENTIONAL PROCESSING METHO DS

According to the principles of TCM, the main purpose of processing is to increase the efficacy and/or reduce the toxicity of TCM herbs. In addition, processing may be used to improve the odor or flavor of the herb, enhance the solubility of specific components in the herb, increase the purity by reduction of contaminants, and

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preserve the active ingredients (Zhao et al., 2010; Chang et al., 2011; Zhan et al., 2011). As early as 200 BC, TCM herbs were processed by burning and soaking in wine as documented in the Chinese "52 Bing Fang" (Prescriptions for 52 Diseases; Zhao et al., 2010). Currently 15 processing methods are recorded in Pharmacopeia of People's Republic of China (PRC; State Pharmacopoeia Committee, 2010). Some common processing methods, including slicing, steaming, boiling, stir-frying, calcining, and soaking in wine or vinegar, have been previously reported in few review articles, and thus are not described in details here (Chan, 1995; Bent and Ko, 2004; Wang et al., 2009a; Zhao et al., 2010).

One of the major post-harvesting factors affecting the efficacy and safety of TCM herbs are discrepancies in processing methods. Many studies demonstrated that various common processing methods drastically changed the chemical profile of TCM herbs. For instances, processing of Ligusticum Chuanxiong Rhizome (Chuanxiong, Ligusticum chuanxiong Hort., Umbelliferae) by sun drying and stir-frying remarkably increased the contents of several bioactive ingredients, including senkyunolides I and H, riligustilide, levistolide, and ferulic acid, but significantly reduced contents of three major constituents, senkyunolide A, z-ligustilide, and coniferyl ferulate in the herb via processing-induced hydroxylation, dimerization, and hydrolysis reactions (Li et al., 2007), although the former two major ingredients are also bioactive (Chan et al., 2007). Similarly, soaking Angelicae Sinensis Radix (Danggui, Angelica sinensis [Oliv.] Diels, Umbelliferae) in yellow wine increased and reduced quantities of ferulic acid and z-ligustilide, respectively (Zhan et al., 2011). Previously, several articles have reported and reviewed the general practice of the conventional processing methods recommended by Pharmacopeia of PRC and its beneficial effects of enhancing efficacy and reducing adverse effect/toxicity of TCM herbs via the alteration of chemical profiles of the herbs (Yu et al., 2005; Li et al., 2010a; Shaw, 2010; Zhao et al., 2010; Chang et al., 2011). Therefore, the details of these conventional processing methods are not described in this article.

SULFUR FUMIGATION PROCESSING

Traditionally, the roots and rhizomes of herbs were dried naturally under sun or in the shade, but in recent decades, this practice has been replaced by sulfur fumigation, a faster and cheaper method. Generally, herbs are placed in the upper levels of a closed chamber and sulfur powder is burned at the bottom of the chamber overnight. Sulfur dioxide is released into the chamber during this process and may penetrate into the herb (Wang et al., 2009b). Moreover, some herbal farmers even sprinkle sulfur powder on to the herbs to infiltrate sulfur into the herbs. Herbs are often treated by sulfur fumigation to decrease drying time, ward off insects, prevent molding and bacterial contamination, and give the herb a more pleasing white color (Upton, 2003; Wang et al., 2009b). Alternatively, herbs may be treated directly with sulfiting agents, such as sodium or potassium sulfite, and bisulfite or metabisulfite to protect the herb's moist appearance and maintain its color and freshness (Kim et al., 2000; Hayes et al., 2005). Although Pharmacopeia of PRC has prohibited sulfur fumigation for bleaching and processing all TCM herbs since 2005, there are no objectives of quantitative standards or well-defined regulations for acceptable levels of sulfur dioxide in herbs. Therefore, farmers continue to use this method to dry herbs with a higher profit margin and consumers are using the sulfur-fumigated herbs without awareness of their potential toxicity and possibly reduced or even no efficacy.

TOXICITY ARISING FROM SULFUR FUMIGATION AND SULFITING AGENTS

Exposure to sulfur dioxide seriously compromises human health. It has been reported that workers who performed sulfurization of apricots reported "asthma-like" symptoms such as itchy eyes, shortness of breath, cough, runny or stuffed nose, scratchy throat, and reduced pulmonary function when exposed to mean sul- fur dioxide concentrations of 342 ppm in a 1-h period (Koksal et al., 2003). In controlled human exposure studies, asthmatic subjects had increased airway resistance and decreased forced expiratory volume after being exposed to 400 ppb sulfur dioxide for 5–10 min while exercising and showed cough, chest tightness, throat irritation, and other respiratory symptoms (Goodman et al., 2010). Sulfur dioxide forms sulfuric acid upon contacting with moist membranes and irritates the eyes, mucous membranes, and skin. Sulfuric acid also inhibits pulmonary particle clearance and induces mild bronchoconstriction, which is exacerbated in asthmatic patients (Komarnisky et al., 2003).

Sulfiting agents may lead to mild, moderate, and severe adverse events in the sulfite-sensitive asthmatic population (Lester, 1995), and specifically, dermatological symptoms (such as urticaria, angioedema, swelling), respiratory symptoms (such as dyspnea, wheezing, and bronchoconstriction), and gastrointestinal symptoms (such as nausea, vomiting, and diarrhea) have been clinically reported (Lester, 1995; Timbo et al., 2004; Vally et al., 2009). In more severe cases, sulfiting agents induced hypotension, cyanosis, shock, seizures, loss of consciousness, and even death (Yang and Purchase, 1985; Lester, 1995). Although the exact mechanism of sulfiteinduced toxicity is unknown, it has been suggested that sulfite is a strong nucleophilic anion that reacts with immunological molecules (Gunnison and Jacobsen, 1987). Sulfite-sensitive asthmatics may have reduced levels and activity of sulfite oxidase, an enzyme mediating the oxidation of sulfite to sulfate, leading to higher susceptibility to sulfite intoxication (Yang and Purchase, 1985; Torun et al., 1989; Lester, 1995).

It has been reported that long-term inhalation of sulfur dioxide reduced lung function, increased oxidative stress, bronchial inflammation, and increased risk of lung cancer developed, and consumption of sulfur dioxide-containing herbs also caused clinical incidences of lung, liver, and kidney damage, blindness, skin rashes, asthma, and breathing difficulties (Nafstad et al., 2003; Rusconietal., 2011). However, it is currently unknown whether these toxicities of sulfur-fumigated herbs originate only from the residual sulfur dioxide on the herb and/or from the chemical changes of the key compounds induced by sulfur fumigation in the herb. Although no extensive studies have been conducted on the safety of sulfurfumigated herbs, it is suspected that long-term consumption of these herbs may be hazardous to health. Therefore, not only acceptable levels of sulfates or sulfites in the processed herbs need to be defined, the concentration of sulfur dioxide generated in and around the fumigation chamber also needs to be determined and governed to ensure the levels of sulfur dioxide, a common air pollutant, are at an acceptable level that will not induce harm to humans. In addition, understanding the

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impact of the chemical changes of the key ingredients in the herbs induced by sulfur fumigation on the safety of the sulfur-fumigated herbs is also timely and crucially important.

CHEMICAL ALTERATION BY SULFUR FUMIGATION

As summarized in **Table 1**, although limited information on the chemical changes induced by sulfur fumigation are available, the sulfur fumigation-induced alteration of chemical profiles of TCM herbs has been evidenced undoubtedly. Several studies investigated chemical changes of Paeoniae Radix Alba (Bai Shao, Paeonia lactiflora Pall., Paeoniaceae) after sulfur fumigation. In the sulfurfumigated Bai Shao, the amount of peoniflorin, a chemical marker for quality control of the herb, remarkably reduced, while a new compound peoniflorin sulfonate (**Figure 1A**) was found, which was further proved to be generated from the reaction of peoniflorin with sulfur dioxide in a mimic reaction even at room temperature (Wang et al., 2005). It has been demonstrated that almost 40% of peoniflorin was converted to peoniflorin sulfonate as early as 1 h after such reaction (Wang et al., 2005). Similarly, treating the herb with sodium bisulfite caused a reduction of peoniflorin content along with the formation of peoniflorin sulfonate (Hayes et al., 2005). Likewise, a reaction of pure peoniflorin with sodium bisulfite also yielded peoniflorin sulfonate (Hayes et al., 2005). In another study, two sulfonated components, namely peoniflorin sulfonate and benzoylpaeoniflorin sulfonate (**Figure 1A**), were formed in the sulfur fumigated-Bai Shao, while contents of the corresponding peoniflorin and benzoylpaeoniflorin were sig- nificantly decreased comparing with non-sulfur-fumigated herb (Cheng et al., 2010a).

The effect of sulfur fumigation on chemical profile of Angelicae Dahuricae Radix (Bai Zhi, Angelica dahurica [Fisch. ex Hoffm.] Benth. et Hook. f., Apiaceae) was also reported (Wang et al., 2009b). HPLC fingerprinting analyses were performed to analyze and compare chemical profiles of the sun-dried herb obtained from a cultivation base in China in operation under good agricultural practices (GAP) guidelines and from commercial sources that were confirmed to be sulfur-fumigated using sulfite residue testing. The results revealed that contents of the major furocoumarins were significantly reduced and at least 60% of imperatorin and almost all of oxypeucedanin was lost due to sulfur fumigation (Wang et al., 2009b). To further confirm these chemical changes, the herb was directly treated with sulfur dioxide in a mimic processing procedure. The results illustrated that contents of three major furocoumarins, namely imperatorin, isoimperatorin, and oxypeucedanin, were significantly decreased and converted to xanthotoxol, bergaptol, and oxypeucedanin hydrate, respectively (**Figure 1B**) were formed (Wang et al., 2009b).

A recent study on white ginseng (Shengshaishen), the processed Ginseng Radix et Rhizoma (Ren Shen, Panax ginseng C.A. Meyer, Araliaceae) also demonstrated the same processing problem. Some commercially available white ginseng samples, which should be processed by air-drying according to Pharmacopeia of PRC, were found to be also sulfur fumigated. A sensitive UPLC–Q-TOF– MS/MS method used to analyze chemical profiles of both white ginseng and its decoction form (Du-Shen-Tang) revealed that contents of various ginsenosides were reduced and two ginsenoside sulfonate derivatives (**Figure 1C**) were found in both samples, however, the sulfonate substitution positions in these derivatives have not been definitively elucidated yet (Li et al., 2010b).

The aforementioned studies and their findings provided evidence to reveal one of the key problems with sulfur fumigation. Sulfur fumigation may cause significant quantitative and qualitative changes of herbal bioactive ingredients, resulting in remarkable decrease or even disappearance of the bioactive compounds along with generation of new sulfonate derivatives. Consequently, not only pharmacokinetics and pharmacological activities of bioactive components are likely very different between sulfurfumigated herbs and conventionally processed herbs, changes in the undersigned bioactivities produced by sulfonate derivatives, which can be beneficial or harmful, may also occur inevitably in sulfur-fumigated herbs.

Table 1 | Effects of sulfur fumigation or reaction with sulfiting agents on chemical constitution and pharmacokinetics of various TCM herbs.

Herb	Processing	Chemical alteration	Pharmacokinetic alteration	Reference
Paeoniae Radix Alba (Bai Shao)	Sulfur fumigation	Formation of peoniflorin sulfonate (9–16 mg/g herb) and benzoylpaeoniflorin sulfonate (0.16–0.43 mg/g herb)	Oral absorption of peoniflorin sulfonate was slower than that of peoniflorin. Benzoylpaeoniflorin sulfonate but not benzoylpaeoniflorin was present in blood circulation after oral administration	Cheng et al. (2010a,b)
	Reaction with sodium bisulfite	Formation of peoniflorin sulfonate	N.A.	Wang et al. (2005)
	Sulfur fumigation	Almost all of peoniflorin converted to peoniflorin sulfonate	N.A.	Hayes et al. (2005)
Angelicae Dahuricae Radix (Bai Zhi)	Sulfur fumigation	Loss of major furocoumarins: i.e., at least 60% loss of imperatorin, and significant loss of isoimperatorin and oxypeucedanin	N.A.	Wang et al. (2009b)
Ginseng Radix et Rhizoma (Ren Shen)	Sulfur fumigation	Formation of two ginsenoside sulfonates	N.A.	Li et al. (2010b)

N.A., data not available.

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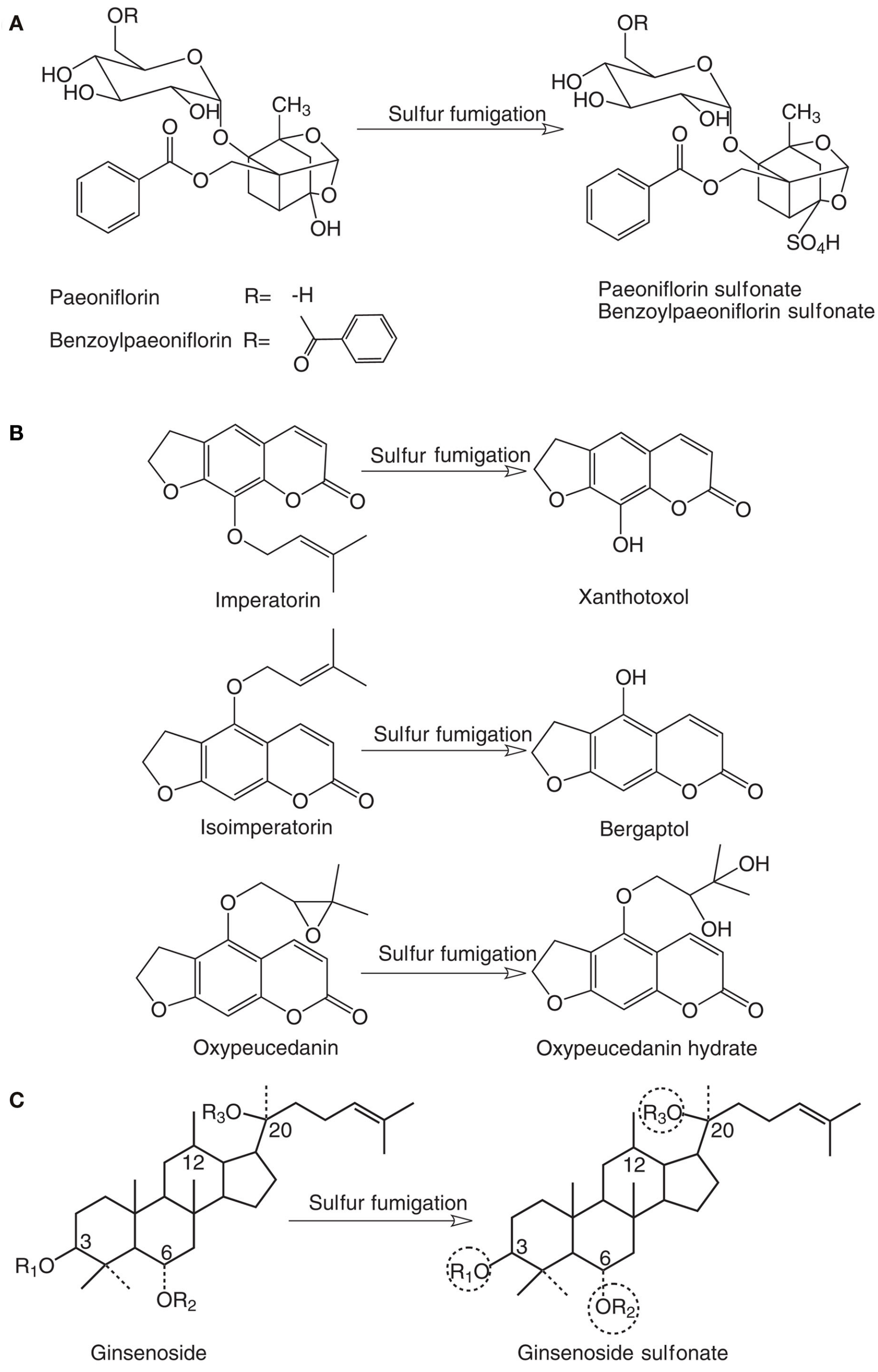

FIGURE 1 | Chemical alterations after sulfur fumigation in (A) Paeoniae Radix Alba (Bai Shao); (B) Angelicae Dahuricae Radix (Bai Zhi); and (C) Ginseng Radix et Rhizoma (Ren Shen). R1, R2, and R3 represent different sugar moieties, and one of these circled sugar moieties were replaced with SO_3H group after sulfur fumigation.

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PHARMACOKINETIC ALTERATION BY SULFUR FUMIGATION

It is reasonable to hypothesize that the chemical profiling changes in the sulfur-fumigated herbs may result in pharmacokinetic alteration of herbal bioactive ingredients. However, to date, there is limited information in this regard and only one study examined pharmacokinetics of two main bioactive ingredients of Bai Shao, namely peoniflorin and benzoylpaeoniflorin, and also directly compared them with their sulfonate derivatives in mice via oral administration at 110 mg/kg, although it did not compare pharmacokinetic fates of these ingredients after oral administration of sun-dried and sulfur-fumigated herbs (Cheng et al., 2010b). Compared with their parent compounds, both sulfonates had better metabolic stability as no metabolites of the sulfonates were found, which were suggested by the authors to be due to the replacement of hydroxyl group with sulfone group in the structures. The absence of the hydroxyl group prevented cleavage of the hemiketal–acetal system that normally occurs during metabolism to form peonimetabolins. For instance, owing to the better metabolic stability of the sulfonate derivative, peoniflorin had a significantly shorter half life ($t_{1/2\beta}$: 112.3 ± 48.36 vs 247.1 ± 65.35 min, $p < 0.05$) than its sulfonate derivative. Moreover, it was unexpected that the oral absorbability of the sulfonate was significantly enhanced (C_{max}:5.01 ± 2.21 vs 4.36 ± 1.13 μg/ml, $p < 0.05$) with a delayed absorption profile (T_{max}: 30.0 ± 0.0 vs 56.0 ± 8.9 min, $p < 0.05$) comparing with that of peoniflorin, and sulfonate derivative had a significantly higher oral bioavailability ($AUC_{0-\infty}$: 633.1 ± 173.7 vs 519.1 ± 155.6 μg·min/ml, $p < 0.05$) than peoniflorin. Similarly, benzoylpaeoniflorin sulfonate significantly improved oral bioavailability ($AUC_{0-\infty}$: 1486.7 ± 499.5 μg·min/ml), while benzoylpaeoniflorin was not absorbed because it was not detected in all plasma samples collected within 0–8.5 h after administration (Cheng et al., 2010b). However, whether such improvement of oral bioavailability and delay of absorption of sulfonate derivatives are common or unique in specific cases and whether systemic exposure of sulfonate derivatives affects herbal efficacy and/or toxicity are unknown and demands further systematic investigation.

BIOACTIVITY ALTERATION BY SULFUR FUMIGATION

It is also logical to suspect that the significant alteration of chemical profiles in sulfur-fumigated herbs will lead to significant changes in pharmacokinetic profiles of herbal bioactive components, and thus inevitably affect herbal efficacy and safety. However, to date only very limited information on the sulfur fumigation-induced changes of chemical and pharmacokinetic profiles are available, whereas, the impacts of sulfur fumigation on herbal pharmacological activities and adverse effects/toxicities due to the alteration of the chemical profiles have not been explored. Various researchers have expressed their views and concerns on the potential influences of sulfur fumigation on bioactivity and toxicity of TCM herbs. For instance, in the aforementioned study of Bai Zhi, based on the results of significant loss of the major active furocoumarins in sulfur-fumigated herb, the authors expected that herbal antiinflammation and anti-tumor activities, which were produced by furocoumarins, would be drastically reduced or even diminished (Okuyama et al., 1990; Ban et al., 2003). Nevertheless, no single published report has demonstrated the effects of chemical changes caused by sulfur fumigation on efficacy and safety of the processed herbs yet. Therefore, investigation in this regard is timely and warranted.

CURRENT ISSUES WITH SULFUR FUMIGATION AND PERSPECTIVES

Rigorous efforts have been made and are also continued to ensure good quality control in growth, harvesting, formulation, packaging, and marketing of TCM herbs and their compound formulae. However, information about standardized post-harvesting processing procedures is scarce due to the empirical and subjective nature of processing in its long history of practice. Although there is a general national standard for processing well-known TCM herbs, the standards differ among provinces and locations in China (Bent and Ko, 2004; Zhao et al., 2010). Often, processing is not considered as one of the major sources responsible for the lack of herbal efficacy and/or incidence of adverse effect/toxicity, and the public is unaware of how their consumed TCM herbs were processed and to what extent the quality of such herbs was affected (Shaw, 2010; Zhao et al., 2010). In recent years, particularly triggered by the prevalence of sulfur fumigation to process TCM herbs, increasing number of scientists are paying close attention to beneficial and detrimental effects of processing on the bioactivities of TCM herbs, and public consensus and media urge the need of implementing higher vigilance and tighter control of processing methods to increase safety, bioactivity, and credibility of TCM herbs (Deng, 2002; Bent and Ko, 2004; Shaw, 2010; Ye and He, 2010; Zhao et al., 2010). At the second Annual Meeting of the Specialty Committee of TCM Pharmaceutical Analysis of WFCMS & International Conference on TCM Pharmaceutical Analysis (July 1st–3rd, 2011) in Chengdu, China, the potential effects of sulfur fumigation were addressed by several presentations, indicating the need for further studies in this area. Recently, China State Food and Drug Administration (SFDA) announced recommendations in that 11 TCM herbs, namely Achyranthis Bidentatae Radix (Niu Xi, Achyranthes bidentata Bl., Amaranthaceae), Asparagi Radix (Tian Dong, Asparagus cochinchinensis [Lour.] Merr., Liliaceae), Atractylodis Macrocephalae Rhizoma (Bai Zhu, Atractylodes macrocephala Koidz., Asteraceae), Bletillae Rhizoma (Bai Ji, Bletilla striata (Thunb.) Reichb. f., Orchidaceae), Codonopsis Radix (Dang Shen, Codonopsis pilosula (Franch.) Nannf., Campanulaceae), Dioscoreae Rhizoma (Shan Yao, Dioscorea opposita Thumb., Dioscoreaceae), Gastrodiae Rhizoma (Tian Ma, Gastrodia elata Bl., Orchidaceae), Kansui Radix (Gan Sui, Euphorbia kansui T.N. liou ex T.P. Wang, Euphorbiaceae), Paeoniae Radix Alba (Bai Shao, Paeonia lactiflora Pall., Paeoniaceae), Puerariae Thomsonii Radix (Fenge, Pueraria thomsonii Benth., Leguminosae), and Trichosanthis Radix (Tian Hua Fen, Trichosanthes kirilowii Maxim., Cucurbitaceae), are allowed to be processed by sulfur fumigation, but should have sulfur dioxide residual amount less than 400 ppm (400 mg/kg), while a residue limit

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of 150 ppm (150 mg/kg) is allowed for all other TCM herbs with prohibited sulfur fumigation (State Food and Drug Administration, 2011). However, scientific evidence supporting the rational for such residue limitations is unavailable. Currently, this recommendation is open for public opinion for future establishment of new regulations if public consensus is reached.

In addition to measuring sulfur dioxide residues, it is timely to develop suitable, convenient, and sensitive analytical methods for the determination of qualitative and quantitative changes in chemical components caused by sulfur fumigation, in order to assess (1) whether the herb has been sulfur fumigated; (2) which herbal bioactive components have changed after sulfur fumigation; (3) how the components have changed structurally; and (4) how much of the components have changed in terms of formation of new compounds and degradation of existing compounds. Furthermore, in vivo investigation of sulfur-fumigated herbs, including chemical and metabolite profiling, needs to be systematically conducted together with pharmacokinetic, bioactivity, and toxicity studies in parallel to acquire a better understanding of the effects of sulfur fumigation on efficacy and safety of TCM herbs. Only until the solid evidences have been obtained from the systematic and scientific studies, appropriate regulations governing which TCM herbs should not (processing-induced harm) or should (processing-induced benefit or no change) be processed by sulfur fumigation with well-controlled procedures can be established.

Nevertheless, the aforementioned quality control of postharvesting processing is one of many crucial steps, such as GAP on herbal farms, good manufacturing practice (GMP) in herbal manufacturing, and good warehousing practice (GWP) for storage and distribution, for the assurance of good quality of TCM herbs. This task is extremely challenging and needs tremendous efforts from close collaborations among various parties including government authorities, regulatory agencies, TCM farmers, pharmaceutical industry, consumers, and scientists. Such collaborative work will boost local and international credibility of TCM herbs, and ultimately result in the production and sale of safer TCM herbs with higher efficacy for public health.

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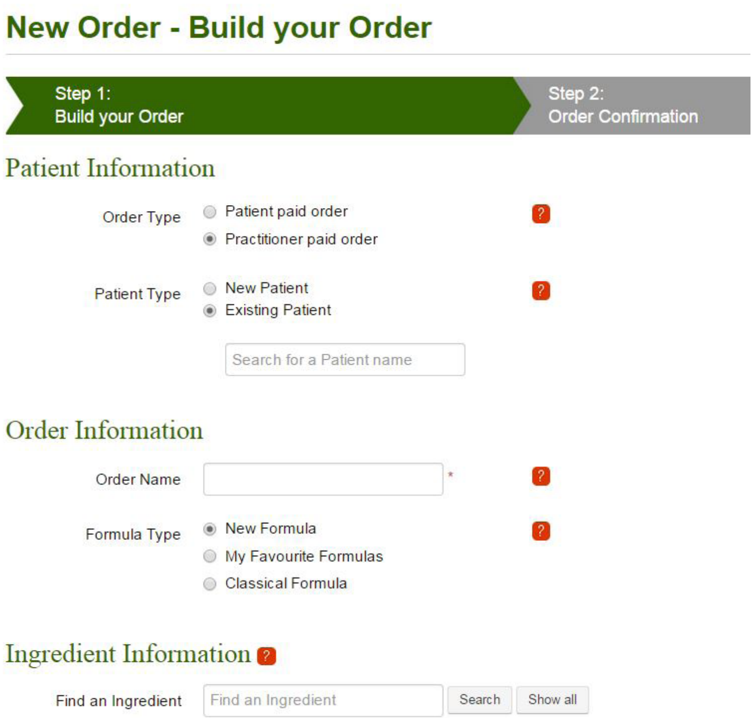

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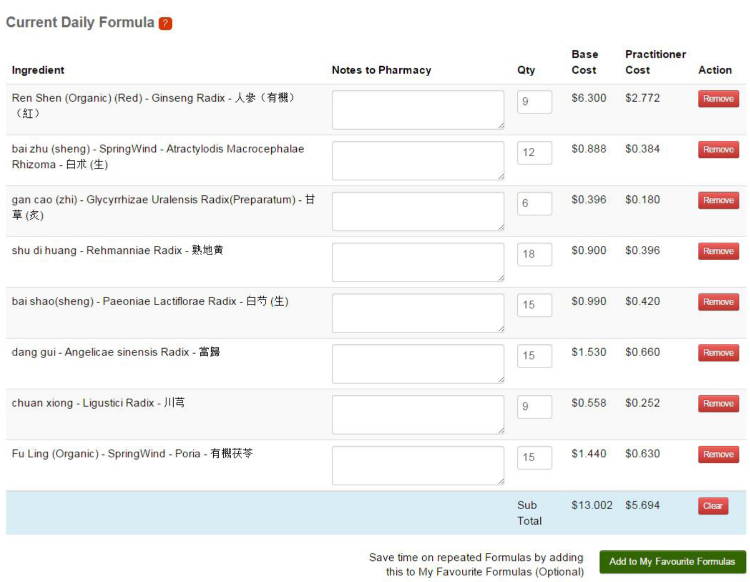

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bai zhu (sheng) - SpringWind - Atractylodis Macrocephalae Rhizoma - 白朮 (生)		12	$0.888	$0.384	Remove
gan cao (zhi) - Glycyrrhizae Uralensis Radix(Preparatum) - 甘草 (炙)		6	$0.396	$0.180	Remove
shu di huang - Rehmanniae Radix - 熟地黃		18	$0.900	$0.396	Remove
bai shao(sheng) - Paeoniae Lactiflorae Radix - 白芍 (生)		15	$0.990	$0.420	Remove
dang gui - Angelicae sinensis Radix - 當歸		15	$1.530	$0.660	Remove
chuan xiong - Ligustici Radix - 川芎		9	$0.558	$0.252	Remove
Fu Ling (Organic) - SpringWind - Poria - 有機茯苓		15	$1.440	$0.630	Remove
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