Review of the powder and decoction formulae in Traditional Chinese Medicine based on pharmacologically active substances and clinical evidence

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Supported by National Basic Research Program of China (Dose-Effect Relationship Study of Classical famous Prescription, No. 2010CB530601), Beijing Science Society Project (Common technology Demonstration and Research for Boiling Powders of Chinese Materia Medica, No. 212110200112010)

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Accepted: June 8, 2014

Abstract

Powder formulae are an indispensable part of prescription in Traditional Chinese Medicine. Powder formulae are characterized by good therapeutic efficacy and low dose used for their preparation. Analysis of the therapeutic application and material basis of pharmacological active substance in power formulae can enable the development of new powder formulae. This in turn can contribute to reduction of wastage of drug material, relief of shortage of herbal medicinal resources and sustainable development of Traditional Chinese Medicine.

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Key words: Powders; Decoctions; Drug prescriptions; Pharmacology; Medicine, Chinese traditional; Review

INTRODUCTION

Most crude drugs used in Traditional Chinese Medicine (TCM) are natural products. Some come from endangered species, which means their supply is very limited and the supply of some crude drugs is constrained by their exhaustibility. The use of powder formulae is an effective way to conserve these crude drug resources. Study indicates that the use of powder formulae can save up to two-thirds of each drug used compared with decoction formulae, while achieving identical therapeutic efficacy. Cai et al. conducted a retrospective review on the dosages of 28 processed herbal medicines commonly used in powder and decoction formulae created by herbalists from the Song to the Qing Dynasty (AD 1644-1911). They found that for all 28 drugs, the dosages used in powder formulae were smaller than those in decoction formulae. For the same processed medicine, the dosages in terms of powder were 20.9%-41.9% those in decoction. The ratio of dosages of the medicines used in powder to those in decoction formulae is 1:5 to 2:5. Therefore, research on traditional powder formulae could allow for further development of TCM therapeutics.

HISTORY OF POWDER FORMULAE IN TCM

Powder formulae in TCM consist of single or a few medicinal materials, and are the basis of dosage forms in both traditional and modern Chinese medicine. For example, traditional honeyed pills, water pills, and contemporary tablets in chunk or capsule form are all based on medicinal powders. As early as the Eastern
Han Dynasty (AD 25-220), the Treatise on Cold Pathogenic Diseases and Synopsis of Golden Chambers, compiled by Zhang Zhongjing, included more than 40 powder formulae. Powder formulae became more popular by the Five Dynasties (AD 907-979) and Song Dynasty (AD 960-1279), during which the use of powder formulae largely replaced that of decoction formulae. In the Shanghan Zongbing Lun, it was proposed that, "decoction formulae are prepared in powder form for direct consumption." The herbalist Li Shizhen of the Ming Dynasty (AD 1368-1644) compiled the compositions and indications of many medicinal formulae in the Compendium of Materia Medica. The book put great emphasis on the use of powder formulae, of which there are more than 3200 types. The powder formulae proposed by Zhang Zhongjing are categorized as orally or externally administered medication. Orally administered formulae are divided into blended type and decocted one. External formulae are divided into topical forms and suppositories. In powder formulae for blending, the drug powder is mixed with different fluids according, which facilitates oral administration. The fluids suggested by Zhang’s work include water, fermented vegetable infusion, wine, porridge, chicken egg yolk, and medicated infusion. In powder formulae for decoction, a suitable amount of drug powder is boiled with water before oral administration. This method proposed by Zhang combines the advantages of both powder and decoction formulae. Examples include decoction with Banxia (Rhizoma Pinelliae), Gajiang (Rhizoma Zingiberis) powder, Yiyiren (Semen Coicis), Fuzi (Radix Aconiti Lateralis Preparata), Baijiangcao (Herba Patriniae Scabiosaefoliae) powder. Topical powders are directly applied or rubbed on lesion sites. For example, the indication for cowherb seed powder is for "spreading on minor sores." For suppositories, the drug powder is wrapped inside cotton and then plugged into the lesion site. An example is the common Cnidium fruit powder used for treating genital coldness in women.

RESEARCH ON POWDER FORMULAE BASED ON PHARMACOLOGICALLY ACTIVE SUBSTANCES AND CLINICAL EVIDENCE

Herbal medicines

Herbal medicines containing insoluble or sparingly soluble active substances are not suitable or contraindicated in decoctions. Instead, they are pulverized for medical use. Examples include Hupo (Succinum), Ruxiang (Olibanum), Moyao (Myrrh), Anxixiang (Benzoinum), Suhexiang (Storax Liquidambaris Orientalis), Awei (Resina Ferulae), and Xuejie (Sanguis Draconis). These medicines have main active ingredients like resins and volatile oils. Resins are insoluble in water, and oils are lost during the decoction process. Qingdai (Indigo Naturalis) is a product formed by precipitation from water during processing, and nearly all constituents are insoluble in water. Bingpian (Borneolum Syntheticum) is the crystal obtained from the distillate of sambong leaves, and is volatile and labile in heat. Luhui (Aloe) are the concentrated and dried extracts of leaf fluid. Additionally, other herbal medicines that have volatile oils as their main active constituents are suitable for powder formulation for infusion. This is because the volatile components are largely evaporated during the decoction process, which diminishes their potency. Examples of these drugs include strongly fragrant herbs such as Doukou (Fructus Amomi Rotundus), Sharen (Fructus Amomi), Muxiang (Radix Aucklandiae), Jiangxiang (Lignum Dalbergiae Odoriferae), Tanxiang (Lignum Santali Albi), Rougui (Cortex Cinnamomi Cassia), Dingsxiang (Flo Syzygii aromatici), Xiao huixiang (Fructus Foeniculi), and Hujiao (Fructus Piperis Nigris). Some herbal medicines that contain coumarins with low water solubility and small amounts of volatile components are suitable for both decoction and powder formulae. However, powder formulae are more advantageous than decoction formulae. Examples include Baizhu (Rhizoma Atractyloidis Macrolepaleae), Cangzhu (Rhizoma Atractyloidis Lanceae), Houpu (Cortex Magnoliae Officinalis), Foshou (Fructus Citri Sativodactylos), Qianghuo (Rhizoma et Radix Notopterygii), Duhuo (Radix Angelicae Biserratae), Baizhi (Radix Angelicae Formosanae), Fangfeng (Radix Saposhnikoviae), Wuzhuyu (Fructus Evodiae Rutaceae), Chuanxiong (Rhizoma Chuanxiong), and Jianghuang (Rhizoma Curcumae Longae). Naphthoquinones found in Zicao (Radix Lithospermum) possess hemostasis, anti-bacterial, anti-viral, and anti-tumor effects, and are largely insoluble in water. Danshen (Radix Salviae Miltiorrhiza) contains hydrophilic phenolic acids and lipophilic phenanthrenequinones. The phenanthrenequinone tanshinone has therapeutic effects on tumors, cardiovascular diseases, bacterial infections, and inflammation. The choice of herbal medicines with both hydrophilic and lipophilic components for powder or decoction formulae depends on the clinical indication and the exact composition of active ingredients. Some herbal medicines containing soluble active substances are also suitable for powder formulae. Huanglian (Rhizoma Coptidis) contains water-soluble alkaloids, berberine, coptisine, palmatine, and jatrorrhizine. Sun et al. reported that when Huanglian (Rhizoma Coptidis) powders were dissolved in gastric juice, then berberine and jatrorrhizine dissolution was about 50% higher than that of its decoction. Wei et al. found that oral administration of Huanglian (Rhizoma Coptidis) powder facilitates intestinal absorption of not berberine but jatrorrhizine. Sanqi (Radix Notoginseng) contains water-soluble Panax notoginseng saponins (PNS). Han et al. found that PNS is poorly absorbed in small intestine after oral adminis-
tration. Low membrane permeability may be a more important factor for dominating absorption extent. In powder formulae, the drug particles are small and therefore easily absorbed during oral administration. Drugs are fast acting, have good therapeutic effects on digestive system diseases, and have a wide scope of application. For example, Rougui powder has pungent and warm properties, and can warm the stomach and kidney. Therefore, it can be used to treat abdominal or stomach pain caused by exposure to coldness with a dose of 0.6-1.5 g. The analgesic effect of Rougui powder can be augmented by combination with Yanhusu (Rhizoma Corydalis Yanhusuo) powder. Combination with Baishao (Radix Paeoniae Alba) powder can warm the middle energizer and calm the liver, thus treating abdominal colic. Combination with Huanglian powder can treat insomnia caused by flaring heart-fire or the breakdown of coordination between heart and kidney. Conversely, Hupo (Succinum) powder has sweet and mild properties, which can tranquilize the mind and heart, activate yang, and induce diuresis. A dose of 0.6-1 g can treat refractory insomnia, palpitation, or difficulty in diuresis. Sanqi powder is sweet and slightly bitter in flavor. Sanqi can stanch bleeding, relieve blood stasis, and relieve pain at a dose of 1.5-2.0 g. It is indicated for upper gastrointestinal tract bleeding, hemoptysis, hematuria, and chronic relapsing pain in the abdomen and chest from blood stasis. To treat upper gastrointestinal bleeding or hemoptysis, Sanqi (Radix Notoginseng) is combined with Baiji (Rhizoma Blettillae Striatae) while it is combined with Yanhusu for analgesia. A dose of 0.6-1.5 g can relieve symptoms including productive cough caused by chronic bronchitis and nausea and vomiting caused by gastritis and peptic ulcer. For resolving phlegm and cough suppression, prepared Banxia (Rhizoma Pinelliae) powder should be combined with Chuanbeimu (Pericarpium Citri Reticulatae) powder. For the management of nausea, vomiting, thirst, and yellow tongue coating, prepared Banxia (Rhizoma Pinelliae) should be combined with Huanglian (Rhizoma Coptidis) powder. Shi et al. used Baiji (Rhizoma Blettillae Striatae) powder in hemostasis during surgery. They found prominent effects on the reduction in bleeding during and after surgery, amount of blood transfusion needed after operation, operation time, and rinsing time after operation. For some herbal drugs, therapeutic efficacy could be improved by administration in powder formulae, while a decoction preparation can diminish the therapeutic effect. Representative examples include diuretics such as Fuling (Poria), Zexie (Rhizoma Alismatis); purgatives such as Dahuang (Radix et Rhizoma Rhei Palmatii). The powder of five ingredients with Fuling (Poria) was first proposed in Treatment and Diagnosis of Taiyang Diseases and Pulse Signs in Treatise on Cold Damage Disorders. This formula is mainly used in febrile disease with fluid retention, and edema caused by retention of dampness. Jin et al. compared the effectiveness of decoction and powder formulae of five ingredients with Fuling (Poria) in the treatment of edema in patients with nephrotic syndrome. The results showed that the powder formula was superior to the decoction formula in the relief of edema.

Animal parts

Those parts contain more protein and protein hydrolytic products, such as amino acids, animal peptide toxins, enzymes, and glycoproteins. Many clinically used animal parts include Shuizhi (Hirudo), Wugong (Scolopendra), Quanxie (Scorpio), Dilong (Pheretima Aspergillum), Tubiechong (Eupolyphaga), Jiangcan (Bombyx Batryticatus), and Mayi (Polyrhachis). A decoction preparation of animal parts would destroy their active ingredients, and some active ingredients are insoluble in water. Shuizhi (Hirudo) contain hirudin, heparin, histamine, 17 amino acids, and other peptides. Other small molecules found in Shuizhi (Hirudo) are pteridines, glycolipids, unsaturated fatty acids, and steroids. Wugong (Scolopendra) contain two toxins similar to apotxin, one of which is similar to histamine, while the other is a hemolytic protein. Other substances in centipedes are tyrosine, leucine, formic acid, cholic acid, and various trace elements. Scorpion bufotoxin is a protein toxin. Other compounds found in Quanxie (Scorpio) are trimethylamine, betaine, tauric acid, lecithin, and ammonium salts. Li et al. reported the extraction efficiency of active ingredients in Shuizhi (Hirudo) by various methods. Pepsin extraction yielded 80%, trypsin extraction yielded 38.75%, and water yielded 31%. Therefore, enzymatic extraction was most efficient. Meng et al. reported that the total protein yield and extract yield of Quanxie (Scorpio) was higher using homogenization compared with water reflux, alcohol reflux, or enzymatic extraction. However, these methods are not suitable for clinical prescription. The preferred method for medication is the preparation of powder formula for direct oral administration. Furthermore, gastrin, the spleen-invigorating and appetite-promoting substance in Jineijin (Endothelium Corneum Gigerianae Galli), is inactivated by heat. The use of Jineijin in powder formulae allows a smaller er dosage, and is therefore more efficient than decoction one. Qishe (Agkistrodon) and Wushaoshu (Zaocys) mainly contain proteins, lipids, and trace elements. Shell drugs including Guijia (Carapax et Plastrum Testudinis) and Biejsia (Carapax Trionycis) contain active ingredients such as animal gelatin, keratin, amino acids, and trace elements. The decoction process affects the extraction of these active ingredients. When decocted with other crude drugs, the active substances released from the shell may be partially adsorbed by the other drugs decoded together. Furthermore, the shell that is not completely dissolved during the decoction process is usually discarded, which would waste the valuable drug material.
To enhance the solubility of the shells, it should be pulverized to increase its surface area. This can facilitate dissolution and absorption in the stomach and increase availability on a per-weight basis. In prescriptions, the shell drug material can be prepared in powder form for infusion or decoction before oral administration. Chen et al. conducted a clinical trial with shell powder formulae, which demonstrated good therapeutic efficacies. Animal parts have migratory properties, and possess effects including expelling wind and excessiveness, removing blood stasis and opening collaterals, relieving obstructions in Qi and blood circulation, analgesia, and relieving edema. They are helpful for diseases caused by the obstruction of channels. Liu et al. used powder formulae consisting of animal parts [Sanqi (Radix Notoginseng), Dilong (Phereitima Aspergillum), Quanxie (Scorpio), and Wugong (Scolopendra)] for the treatment of nerve root cervical spondylosis. Compared with aconite-cinnamon granules for treating bone pain, the animal formulae demonstrated good therapeutic effects. Lyu reported the use of milkvetch-leech powder [Huangqi (Radix Astragali Mongolici) powder, Shuizhi (Hirudo) powder, and Danshen (Radix Salviae Miltiorrhizae) powder] for the treatment of chronic hepatitis in 30 patients. Eleven patients had completed clinical remission (36.6%), 15 had improved in clinical course (50%), and four patients saw no effects (13.3%). The total effective rate was 86.6%. A non-prescription Chinese medicine “capsule for reactivating heart and collaterals” contains animal parts such as powder of Shuizhi (Hirudo), Quanxie (Scorpio), Tubiechong (Eospolyphaga), and Wugong (Scolopendra). Qian et al. conducted a trial of these capsules for the treatment of stable angina. The total clinical effective rate was 85%.

Minerals
Minerals used in TCM include sulfides, carbonates, sulfates, mercury compounds, magnesium compounds, and calcium compounds. Most minerals are hard and heavy, and their active ingredients are sparingly soluble or insoluble in water. Nevertheless, they contain essential trace elements including iron, copper, zinc, manganese, molybdenum, and cobalt. To enhance their oral bioavailability, they are usually pulverized and then wrapped in a cloth bag during the decoction process. This process can enhance the release or dissolution of them. For external use, powder formulae can facilitate distribution and absorption on the applied site. Chishizhi (Halloysitum Rubrum) is composed of aluminum silicate, while Yuyuiliang (Limonitum) is composed of basic iron oxide. Both of these minerals are adsorptive anti-diarrhea drugs, and are suitable for oral administration in fine powders. Mangxiaojiao (Nalrii Sulfa) and Xuanmingfen (Natrii Sulfus Excisscatus) are composed of sodium sulfate. These minerals are highly water-soluble, and can be administered in decoction or infusion forms. One powder formula used for removing sum-

Precious medicinal materials
The precious medicinal materials are expensive, rare, or derived from endangered species. They can be administered as a decoction or fine powder. They have various pharmacologically active substances. Renshen (Radix Ginseng), Xiyangshen (Radix Panonis Quinqupellis), and Sanqi (Radix Notoginseng) contain saponins. Shihu (Herba Dendrobii Nobilis) and Chuanbeimu (Balbus Fritillariae Cirrhosa) mainly contain alkaloids. Lingyangjiao (Cornu Saigae Tataricae), Gejie (Gecko), Haima (Hippocampus Kelloggi), and Hailong (Solenogacthus) are all animal drugs. Chenxiang (Lignum Aquilariae Resinatun) contains volatile oils. According to the indications of precious medicinal materials documented in 2010 version of China Pharmacopoeia and the second edition of Chinese Materia Medica we compared the dosages of 14 processed precious medicinal materials used in powder or decoction formulae. From Table 1, it can be seen that dosages in powder formulae are usually 20%-50% of those in decoction formulae. Therefore, the use of powder formulae can reduce the amount of the drug consumed, lower the cost of drugs, and save the resources.

CONCLUSION
Generally, the properties of processed medicinal materials that are suitable for decoction include possession of
water-soluble active ingredients and heat-stability. However, the powder form is directly administered for medical purpose that have: heat-labile or water-insoluble ingredients; a high content of volatile oils; or precious, rare, or endangered animals and medicinal plants. The use of the pulverized medicinal materials can reduce the doses, save the resources. Some medical materials are suitable for both decoction and powder formulation. However, if they possess active ingredients that are not water-soluble, heat-labile, or poorly absorbed, then the use of powder formulation is encouraged. This can enhance bioavailability and reduce dosage. Animal bone and mineral drugs are hard and sparingly soluble and insoluble materials and decoctions of chunks of these drugs limits active substance release. Instead, these materials are pulverized and then wrapped in a cloth bag during decoction. This is known as a decoction powder formula. This can increase the drug suspension in the decoction and maximize therapeutic efficacy. It can also shorten the time needed for decoction.

**Research perspectives for powder formula of Traditional Chinese Medicine**

Clinical experience demonstrates that for some medicinal formulae used in powder form, an exceedingly small dosage can achieve the same therapeutic efficacy as full dosage decoction. Furthermore, for some formulae, the powder form can exhibit clinical effects that cannot be achieved by decoction.

Based on preliminary trials and literature review, Wang et al. proposed two mechanisms that explain the therapeutic efficacies of powder-form preferred formulae. First, during the decoction process, the components of individual drugs may react with each other to create new products. However, these chemical changes do not occur in powder formulae. Second, powder-form preferred formulae contain non-volatile and non-polar substances that are absent in decoction preparations. Decoctions lack the combination of non-polar substances compared with powder formulae. One reason for this is the loss of volatile components from evaporation during decoction. Additionally, water has a limited extraction capability for non-polar substances. Even when the solubility-enhancing effects between various solutes are taken into account, some non-volatile, non-polar molecules cannot be completely extracted from drug material. Therefore, if the active ingredients of the drug materials are non-volatile and non-polar, then that formula is only suitable for powder formulation.

Based on clinical efficacy and materialistic basis of drug material data, further research on novel powder formulae should be carried out. The understanding of scientific principles behind the preference for powder formulation over decoctions could significantly affect the conservation of drug material and improve the clinical efficacy of traditional Chinese herbal medicine. Increased understanding can also help to solve some questions encountered in current clinical practice. For example, the suitability of all or some animal parts in powder preparations should be investigated for dosage and clinical effects. This can help practitioners overcome problems with the use of animal parts in clinic, including the reluctance to prescribe because of toxicity or harshness, the difficulty in finding suitable dosages, or unanticipated clinical outcomes from inappropriate prescriptions. Systematic research on the preparation, qualification, and administration of powder formulae can ensure the standardization of manufacturing.

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**Table 1 Comparison of doses of Chinese herbs used in decoctions and powder formulae (g)**

<table>
<thead>
<tr>
<th>Chinese herb</th>
<th>Dose in decoction</th>
<th>Dose in powder form</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renshen (Radix Ginseng)</td>
<td>3-9</td>
<td>1-2</td>
</tr>
<tr>
<td>Xiyanghen (Radix Panaxis Quinquefolii)</td>
<td>3-6</td>
<td>1-2</td>
</tr>
<tr>
<td>Sanqi (Radix Notoginseng)</td>
<td>3-9</td>
<td>2-3</td>
</tr>
<tr>
<td>Dongchongxiacao (Cordyceps)</td>
<td>6-10</td>
<td>1-2</td>
</tr>
<tr>
<td>Shihu (Herba Dendrobii Nobilis)</td>
<td>6-15</td>
<td>2-6</td>
</tr>
<tr>
<td>Chuanbeimu (Bulbus Fritillariae Cirrhosae)</td>
<td>3-9</td>
<td>2-3</td>
</tr>
<tr>
<td>Tianma (Rhizona Gastrodiae)</td>
<td>6-10</td>
<td>2-3</td>
</tr>
<tr>
<td>Lingyangjiao (Corra Saiga Tataricae)</td>
<td>3-6</td>
<td>0.5-1</td>
</tr>
<tr>
<td>Gejie (Gecko)</td>
<td>5-10</td>
<td>1-2</td>
</tr>
<tr>
<td>Lingzhi (Ganoderma Lucidum)</td>
<td>6-12</td>
<td>1.5-3</td>
</tr>
<tr>
<td>Jinqianbaihushe (Buungaras Parvus)</td>
<td>2-5</td>
<td>1-1.5</td>
</tr>
<tr>
<td>Haima (Hippocampus Kelloggi)</td>
<td>3-9</td>
<td>1-1.5</td>
</tr>
<tr>
<td>Hailong (Solenognathus)</td>
<td>3-9</td>
<td>1.5-3</td>
</tr>
<tr>
<td>Chenxiang (Lignum Aquilariae Resinatum)</td>
<td>2-5</td>
<td>0.5-1</td>
</tr>
</tbody>
</table>
and quality assurance, and the rationalization of prescriptions.

In conclusion, further research and development of TCM herbal powder formulae and their processing and manufacturing can help save herbal medicine resources and improve imbalances in the supply and demand of drug materials. It can also allow the realization of clinical efficacy with minimal doses, and maximization of used drug materials. Promotion of the use of powder formulae can enable the rational use of herbal medicine resources in China, the balance of the ecosystem, and sustainable development of TCM.

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