Global Trends in Granule Use

By Eric Brand, L.Ac.

The creation of concentrated extract powders represents one of the most important developments in the history of Chinese herbal medicine. As technology has advanced, Chinese herbalists increasingly find themselves armed with a vast arsenal of convenient preparations that bring centuries of formulas and thousands of cooking hours into a space the size of a small closet. Leading this revolution of concentrated powders, liquids, and gelcaps are the "granules," which are concentrated dry extract powders that essentially place a full traditional pharmacy at the practitioner's fingertips. The versatility of granules has preserved some aspects of traditional methods while simultaneously inspiring dramatic changes of approach in Asia, and their convenience is quickly making them the most prominent method of herbal medicine delivery in the West.

Japanese Roots

Granule technology was originally pioneered in Japan, where it was created for Japanese Kampo. In Japan, most use of granules is based upon either biomedical or traditional applications of classical formulas, which are often used in an unmodified form. The vast majority of the formulas used in Japanese Kampo were created prior to the Song dynasty in China (around 960 CE), and formulas from the *Shang Han Lun* and *Jin Gui Yao Lue* are particularly prominent in modern clinical use. Practitioners rarely build formulas from single ingredients, instead preferring to employ whole formulas or combinations of formulas. While few Westerners have studied Japanese Kampo itself at depth, the technology that was created to maximize the Kampo approach has impacted Western practitioners tremendously.

From Japan, the technology spread first to Taiwan. Granules have become deeply integrated into healthcare in Taiwan over the past 30 years, and their prominence there has created an entirely new style of Chinese medicine. Indeed, many doctors feel that the most distinctive feature of Chinese medicine in Taiwan is its use of granules. This development was largely stimulated by the convenience of granules for patients, along with the fact that Taiwanese government insurance covers granule extracts exclusively when it comes to Chinese herbal medicine coverage. Granules are desirable for large scale healthcare because they are well-regulated and hygienic, and they are ideal for research because batches are consistent and traceable. Significantly, Taiwanese patients pay very little out of pocket for granules yet have to pay a fair sum out of pocket for raw herbs; this has created an entire culture of granule use, with the vast majority of patients using herbs in a concentrated extract form.

Taiwanese Methods

The Taiwanese method of using granules is relatively distinct because whole formulas are commonly combined together. With a repertoire of over 400 compound formulas on the shelf, Taiwanese doctors build complex combinations that boggle the young student mind, yet there is nothing haphazard about the construction of a well-crafted Taiwanese style formula if one understands the approach. Good doctors in Taiwan typically have a broad range of formula ingredients mastered, with a well-developed ability to see the relationships, similarities, and differences in each. A core formula at a higher dose typically

stands out at the center of the prescription, but instead of adding in just a few single herbs to accentuate certain directions, whole formulas may be added in. Here the formulas are used as a single principle, much as many of us add a single herb.

There are several reasons why compounding whole formulas together has become popular in Taiwan. Given the Japanese origin of the granule technology and the prominence of combining classical formulas in Japan, it seems reasonable to think that some of the initial inspiration for creating a wide range of whole formulas and combining them together may have been rooted in the technology's Japanese roots. However, the most important guiding factor today is the widespread belief in Taiwan that formulas that are cooked together are clinically superior to formulas that are created from scratch by combining single herb extracts.

Indeed, there are measurable differences in the final chemistry of the end product when medicinals are cooked together versus when they are combined from single extracts. Taiwanese doctors point to these differences and often strongly believe that the results of using whole formulas surpass the results of combining singles from scratch. While there have been studies in China that show no statistical differences between the clinical results of combining singles from scratch in comparison with whole formulas that have been cooked together, the vast majority of doctors in Taiwan prefer to use formulas that have been cooked together.

In addition to starting with whole formulas (often compounding two or three whole formulas together), Taiwanese doctors commonly add single herb extracts when customizing the prescription. Their insurance system pays for granules up to a dose of 6.0g, and the typical 6.0g dose is usually given three times per day for a total of 18g of concentrated extract powder per day. While the precise extraction ratios for each product are clearly stated on Taiwanese granule labels, most doctors think less in terms of calculating extraction ratios and replicating raw herb doses by weight, and focus more on the ratio of herbs and formulas within the daily target dose of 18g/day.

The dosage used by most doctors in Taiwan tends to fluctuate between 12–18g/day, with 18g being the most common for adults. Each granule product in Taiwan varies somewhat in terms of its concentration ratio, but a quick mathematical calculation shows that this concentrated powder dose is slightly lower than the typical daily dose given by Taiwanese doctors when they are dispensing raw herbs (often over 100g/day of crude medicinals). Despite this somewhat lower dose, granules are extracted more efficiently than herbs cooked at home, so it is reasonable to assume that they are at least slightly more potent than the equivalent amount of crude herbs. Furthermore, the use of whole formulas instead of just single herbs makes it slightly less of a straight mathematical equation, as the heat-clearing effect of a whole formula like *huang lian jie du tang* (Coptis Toxin-Resolving Decoction) is more powerful than the equivalent weight of singles like *huang lian* (coptis) or *zhi zi* (gardenia) alone.

Although most of the granule products in use in America are made in Taiwan, thus far relatively few practitioners are well-informed about the Taiwanese methods of using granules clinically. Because granules dominate the insurance-based healthcare system in Taiwan, doctors there have amassed a tremendous amount of experience with issues such as dosage and formula combining. However, while many practitioners in the US use their

products, few of us use their methods and dose ranges, making the results seen in Taiwan more difficult to replicate.

Common Approaches in Mainland China

In contrast to Taiwan, doctors in mainland China tend to combine whole formulas together much less, and primarily build formulas from scratch in a process identical to a normal raw decoction. While Taiwan has created a virtually new method of using herbal medicine based on their granule approach, granules in the mainland are largely an extension of the standard method of formula composition. In mainland China, whole formulas are less commonly available in a granule form, so nearly all prescriptions are made by combining singles. Rather than determining dose based upon a standard dose range of total extract powder, the dose is determined mathematically based on the raw herbal prescription.

While there are differences between mainland China and Taiwan in terms of their prescription composition when using granules, the biggest differences in the products themselves lie in their respective packaging and extraction technology. In mainland China, granules are often made from pure extract that is stored without filler, and the granules are packaged in single dose foil packs. In Taiwan, granules are made into a smooth flowing powder that is dispensed from small plastic bottles.

Granules that are made without filler must be packaged immediately to prevent clumping, which occurs rapidly if filler-free extract powder is exposed to air. The most common packaging method used in mainland China is a single dose foil pack that contains the concentrated equivalent of a standard daily dose of a given raw herb. Each herb has the potential to achieve a slightly different concentration, so the concentration ratio of each product (and the corresponding dose weight) varies. For an herb such as *yan hu suo* (corydalis), a 10:1 extract can be achieved, and the foil pack will contain 1g of extract because 10g of the raw product is used as an average daily dose. Another herb such as *pu gong ying* (dandelion) can only reach a 7.5:1 concentration, so a daily dose foil pack of *pu gong ying* contains 2g of extract, which is equivalent to 15g of the raw herb, again a typical daily dose.

The mainland Chinese method of using foil packs is convenient because a scale is not required, the formula can be easily modified, and ingredients can be subtracted if side-effects develop. However, the foil packs are slightly cumbersome because many packs must be opened with each daily dose, and there is more disposable waste associated with the foil packs.

As an alternative to the foil packs, some Chinese manufacturers have begun to produce products that dilute the pure concentrate with dextrin so that an even 5:1 consistency can be achieved. This allows the product to be exposed to air and stored in plastic bottles like the Taiwanese products.

Similarities and Differences in Technology

Both mainland Chinese granules and granules made in Taiwan share many basic characteristics. Reputable companies all capture and reintroduce essential oils, determine species identity with liquid chromatography, and evaluate potency by assessing marker chemicals in both the raw material and the finished product. The temperature is controlled,

and the ideal concentration ratio, water quantity, and cooking duration are determined by researching each product. Batch testing assesses the final product to ensure that heavy metals, bacteria, and fungi are all absent, and most companies test the dissolution time in water.

However, despite these common features, significant differences remain between the technology used in mainland China and Taiwan. In Taiwan, the herbal concentrate is reduced under a vacuum or forced air and low temperatures, and it is reduced to thick, viscous syrup that is then sprayed onto a carrier. The carrier is typically either pharmaceutical starch or finely ground crude herbs. Each herb achieves a different concentration ratio depending on how water soluble it is, as well as how sticky and rich it is by nature; these factors play a role in determining how much material can be extracted, and also influence the quantity of filler required to make the powder flow evenly.

By contrast, the mainland Chinese products are made into a dry extract without filler or with only a small amount of dextrin, and are immediately packaged in a sealed foil pack. Each foil pack contains the equivalent of a standard daily dose of the crude medicinal. This method does not allow for smooth flowing bulk powders that can be exposed to air for prolonged periods, so it is not suitable for the style of product required for the Taiwanese prescribing method. However, it is suitable for the mainland Chinese method of simply using concentrated powders to give a daily dose that equates to the normal raw decoction dose, and the foil packaging allows it to be conveniently dispensed.

Both the mainland and Taiwanese technologies offer unique advantages and disadvantages, but they produce slightly different final products. Taiwanese powders are often made into a relatively fine powder (*xi fen*), while mainland Chinese powders are often made into a slightly larger granule (*ke li*). The mainland products are often able to achieve a higher concentration ratio and tend to have less filler, but the Taiwanese products often tend to have a slightly stronger odor when the bottle it first opened. Additionally, the method of processing mineral medicinals often varies between the two regions, and the availability of herbs in a variety of *pao zhi* forms varies as well. Mainland China has a slightly wider selection of herbs with different types of *pao zhi* on the market, but Taiwan has a wider range of pre-made classical formulas available.

All of these factors illustrate the fact that the modern granule landscape is relatively diverse. Multiple styles abound, both in terms of formula composition as well as manufacturing styles, and each practitioner has a wide range of choice in determining which products and approaches are best for their clinical needs. Unfortunately, at present many Western practitioners have not deeply investigated the Asian trends in granule prescribing, and often remain uncertain on issues such as dosage calculation. Few practitioners realize that different technological methods are used in mainland China and Taiwan, and often fail to take these differences into account when determining dosage. As we move into a direction of clearer product labeling and increased cultural exchange, hopefully the West will begin to acquire more of the experience that our Asian colleagues have amassed in this fascinating field. Given the fact that granules are quickly becoming the most common form of herbal medicine in the Western clinic, it appears essential that we strive to better understand these products in terms of their dosage and clinical applications.

Mixing Singles vs. Using Whole Formulas

There are two major trends in formulation style when it comes to granule extracts. In Taiwan, most practitioners create a granule prescription by using one or more pre-made base formulas that have been decocted together, often with single herb additions. By contrast, in mainland China, most practitioners mix single herb extracts to create their desired formula and rarely start with pre-made base formulas when using granules. In the West, we tend to use a hybrid approach- some practitioners start from whole base formulas and others elaborate the formula purely based on singles.

These two broad approaches each have their adherents and arguments, and often people have a very strong opinion as to which method is superior. As in many situations where opinions run strong and clinical trends vary based upon region and culture, it is difficult to make any blanket proclamation that one method is inherently superior, though each practitioner tends to find their own preference and comfort zone. Given the fact that millions of patients have been successfully treated with both approaches, it seems reasonable to suggest that both have merit and clinical efficacy.

Part One: The Merits of Base Formulas

The case for using base formulas that have been cooked together is primarily based on the notion that preserving the interaction of the ingredients at the cooking stage is important. Historically, most formulas were administered by decoction and the herbs were decocted together. Thus, the historical evidence base of Chinese medicine presumes that the ingredients interact in the cooking process.

Many potential examples of herb interactions can be found in the traditional literature, such as the cooking of Da Huang with Gan Cao, the cooking of Wu Tou with honey, or the cooking of Fu Zi with Gan Cao and Gan Jiang (these combinations are thought to moderate the nature of the sovereign ingredient). Modern research has also demonstrated differences in the HPLC fingerprint between formulas that have been cooked together vs. mixed from singles, and, while the clinical significance of such chemical differences remains unclear, many users point to these differences as a reason to preserve the traditional interaction of the decoction process.

Individual constituents are extracted differently under different circumstances: For example, sour herbs will tend to lower the pH of the decoction, which will enhance the ability of alkaloids to enter solution. Many alkaline minerals will tend to raise the pH of the solution, which will cause fewer alkaloids to enter solution. Thus, it is quite possible that there will be a quantitative difference in the ephedrine alkaloids in a formula like Ma Huang Tang vs. a formula like Ma Xing Shi Gan Tang, even if the same amount of Ma Huang was present in each formula. While many traditional pill formulas such as Liu Wei Di Huang Wan do not assume interaction of ingredients as a decoction provides, a large number of classic decoction-based formulas such as Ma Xing Shi Gan Tang or Da Cheng Qi Tang are difficult to duplicate by mixing singles.

Beyond these traditional and chemical explanations, we find that some practitioners prefer mixing from base formulas because they like the aesthetic beauty of ancient prescriptions. Many ancient prescriptions are quite eloquent and balanced, and they have survived the test of time by gaining the respect of countless generations. Just as a chef notices that each dish needs to be cooked by adding certain spices at a certain stage, the traditional formula literature has given us a guide as to how we should prepare classic formulas. Preserving this knowledge and approach is a conservative way to minimize confounding variables while bringing the effects of an ancient medicine into the 21st century.

However, despite the above merits, there are a number of arguments to support the mixing of singles. Next, we will investigate the flip side of this issue by looking at the perspectives that support the mixing from singles. As mentioned above, both sides have their own merits, so the following section will play the devil's advocate.

Part Two: The case for mixing singles

Above is a summary of the main advantages of whole formulas that have been cooked together to form a granule extract. At present, the use of whole formulas in granule form is particularly widespread in Japan and Taiwan, while the use of single herb extracts to elaborate formulas from scratch is more common in China. Not surprisingly, each region has research and rationales that support each respective approach, so today's blog will focus on the advantages of mixing singles to provide an opposing perspective in the debate.

By any standard, we can clearly say that the patient numbers are adequate to show that both approaches have merit. According to data from Taiwan's electronic medical records, granules are used for approximately 30 million patient visits per year; this significant volume implies a strong evidence base for the efficacy of the Taiwanese approach. Not surprisingly, the numbers are quite high for the mainland Chinese side as well: over 1000 hospitals in mainland China use granules, and they have been given in over 200 million patient visits. Furthermore, even with the comparatively small numbers of patient visits that we have here in the U.S., we can clearly see that both practitioners that mix singles and practitioners that use whole formulas are satisfied with their respective results.

As we mentioned in the previous post, there are some compelling arguments for the use of whole formulas that have been cooked together. However, there are also a number of valid arguments for mixing singles. One of the core arguments in favor of mixing singles is that the prescription can be created without any unnecessary ingredients. When starting with a whole base formula, the practitioner can add ingredients but they cannot subtract ingredients (i.e., if one uses Liu Wei Di Huang Wan, there is no way to remove the Mu Dan Pi, for example). Another challenge with whole formulas is that one may have duplication of ingredients if multiple formulas are combined together. For example, if several formulas are used together and each formula has a low dose of Gan Cao, the cumulative dose of Gan Cao may be higher than the dose of the sovereign herbs in the principle formulas. Proponents of mixing singles tend to appreciate the versatility of building formulas from scratch because it keeps the formula limited to exactly the ingredients that the practitioner wants to include.

The strongest arguments in favor of mixing singles relate to practical aspects of an ideal supply chain and optimal techniques of extraction. In China, nearly 600 items are available in granule form, and many herbs come in multiple *pao zhi* choices. The largest Chinese

manufacturers tend to favor single herb extracts rather than formulas because single herbs are the only form of granules to be adopted on the Chinese hospital market. [Apparently the Chinese Pharmacopoeia is researching standards for whole formulas (marker constituent levels, TLC fingerprints for compound formulas, etc.), but at present official standards have only been formally developed in the mainland for single herb granule extracts.] Thus, the largest mainland Chinese suppliers have primarily based their QC standards and their research efforts around single herbs.

In mainland China, the vast scale of the population means that granule companies must source large amounts of raw materials. The largest granule companies tend to buy directly from the farms and original production regions, and they depend on the ability to secure an adequate supply of raw materials that meet their standards (in terms of constituents, growing region, grade, pesticide residues, heavy metals, etc). The large companies buy the herbs whole and apply most simple pao zhi techniques in-house before making granules, and they will typically produce the entire year's supply once the fresh new crop is ready. Most herbs are best if they are first dried, but dried herbs that are sent to sit around for months at the wholesale markets are often destined to degrade from oxidation, and all too often items that spoil easily are treated with sulfur for the wholesale market. Granule companies can avoid this degradation by producing the entire run from freshly dried whole herbs and they also gain the option to work with herbs that are best fresh instead of dried (such as Qing Hao).

Producing the entire year's batch of a given herb after harvest not only preserves freshness, it also allows a factory to more easily procure a consistent batch of raw materials from a single growing region or supplier. By contrast, the preparation of most whole formulas requires dried herbs from the open market, which opens up variables in terms of the freshness and growing conditions of the dried herbs. Each formula uses a small amount of any given single so there is less economy of scale (and often less thorough incoming raw material testing since each batch of raw materials is smaller and thus less economical to test); the herbs in the formula are also unlikely to come from the same harvest season so some will be more fresh than others.

Another argument in favor of mixing singles relates to the optimal conditions of extraction for any given medicinal. When decocting a whole formula together, one assumes that there is a beneficial interaction of ingredients that is potentially important for the preservation of the clinical effect. Many argue that the traditional method was a decoction and the historical evidence base thus depends on decocting medicinals together, but multiple other forms such as powders and pills have been used historically, and such formulas were not traditionally decocted together. Furthermore, in ancient times it would have been impractical to make a dozen separate decoctions instead of putting everything together in one of pot of water, so it may be that the standard decoction was done for practicality rather than assessed against an alternative method and selected based on merit.

When dealing with singles, one can do many experiments to find the ideal method of extraction for each medicinal, i.e., how much water, what temperature, what duration, which pao zhi methods, how many times the water should be changed, etc. When dealing with whole formulas, one can often make adjustments such as the pre-decoction of minerals but the general method, while tested by time, is somewhat generic and may be ideal for some medicinals in the formula but not ideal for others. When mixing singles, one lacks the

interaction of the ingredients in the cooking pot but one has a better ability to tailor the extraction method to suit the unique characteristics of each medicinal.

Most likely, the interaction of ingredients in the cooking process is very important in some situations and less important in others. For example, one Chinese clinical trial compared the effect of 10 formulas given by mixing single granules vs. decoctions and found no clinical differences in eight of the formulas but measurable differences in two of the formulas (the decoction surpassed the mixed granules for two of the formulas). In other words, the decoction process made a difference for 20% of formulas, but not all of them. One study revealed that the yield of puerarin from Ge Gen was higher in the single Ge Gen extract than it was when the Ge Gen was cooked in Ge Gen Qin Lian Tang; another study showed that the cardiotonic effects of Si Ni Tang cooked together were superior while its toxicity was 4.1 times lower than the toxicity of the mixed singles. Furthermore, a variety of novel chemicals have been discovered as a result of the decoction process, but their significance largely remains unexplored (one such compound is formed in Sheng Mai San, for example). New compounds not found in either herb alone are difficult and expensive to characterize, and it is even more difficult and expensive to produce, isolate, and examine their pharmacological effects.

By nature, studies assessing the mixture of singles vs. formulas that have been cooked together often yield contradictory results, and hardly any clinical studies have been done to compare granule formulas mixed from singles with *granule* formulas that were cooked together. In fact, very few places in the world use both 100% mixed singles and full formula granules side by side- in mainland China there are hardly any granule whole formulas on the market, and in Taiwan it is extremely uncommon for a practitioner to mix from singles without using any whole granule formulas as a base. In mainland China all the research is based on single granules compared to bulk herb decoctions, and in Taiwan all the granule use and research assumes the use of pre-made base formulas. In a sense, the hybrid system that has evolved in the West has characteristics of both approaches and represents yet another new direction.

At present, we have more questions than answers. My own personal preference is still to use formulas that have been cooked together whenever possible, but ultimately I think there are many valid questions to be explored and I believe it is important to minimize the tendency to make sweeping assumptions about the efficacy of any given granule approach. Granules are a new delivery method in Chinese medicine with unique strengths and limitations, and we need to work together to learn how to best harness their potential.

Understanding Dosage

Method One: Dosing Granules Based on Raw Herb Equivalence

5:1 Extracts

Products that have an even 5:1 concentration ratio are very easy to use, because the dosage can be easily calculated by simple division. If a raw formula calls for 10 grams of a given medicinal, 2 grams of the granule extract can be used.

When using 5:1 concentrates, many practitioners simply dose the granules at about 0.5-3.0 grams per medicinal per day. Usually, the total daily target dose for a compound formula will be about 12-20 grams, with about 12-15 grams per day being fairly typical.

15 grams of a 5:1 granule powder is equivalent to 75 grams of raw herbs. 75 grams is somewhat moderate for a raw herbal formula, as decoctions are commonly made with over 100 grams of raw herbs. However, there is a general consensus that the dosage can be reduced slightly from the equivalent raw herb dosage because the granule extraction process is more efficient than a home decoction. Thus, if 100 grams of raw herbs would be given to a particular patient as a home decoction, it would not be unreasonable to give 15-18 grams of 5:1 granules, which would equate to about 75-90 grams of raw herbs.

There is strong anecdotal support for the idea that granule doses can be reduced slightly from their precise raw herb equivalent. Many individual practitioners report that the results are satisfactory when using 12-18 grams of granules per day, which is mathematically a bit less than the same practitioners use in home decoctions (roughly equivalent to 60-90g/day instead of 80-120g/day). Additionally, research has begun to draw conclusions that support this clinical observation. One study demonstrated the increased efficiency of pressurized extraction techniques on constituents such as alkaloids and flavonoids, and at least one large-scale Chinese clinical trial has supported the idea that slight reductions in dosage may be appropriate when using granules.

To mix a prescription with 5:1 single medicinal extracts, simply write the prescription normally, with the standard raw decoction doses as a guide. Divide the raw doses by five to determine the granule dosage. Many practitioners round down, or use slightly less than the exact equivalent dose for the reasons listed above. However, the basic method still applies.

Method Two: Dosing Granules Based on a Total Target Dose

The easiest way to calculate granule dosage is to think about the target dose that is desired, and then dose the ingredients within the formula based on their relative importance and potency. Large formulas will tend to require higher doses, while small formulas can get by

with lower doses. Additionally, the dosing strategy changes slightly depending on whether single extracts or compound formulas are used.

Dosing formulas made from singles

In general, the total granule dosage should be between 10-18 grams per day. For children, the dosage often ranges from 3-10 grams per day, while severe and acute conditions can be treated with 15-25 grams per day. For the sake of simplicity, let us use an example based on an average patient that is being prescribed 10-18 grams per day.

First, consider the total amount that is going to be prescribed per day. If prescribing a formula with 15-18 ingredients, the total dose should be closer to 18 grams per day. If only 5-12 ingredients are used, a dosage of 10-18 grams is probably sufficient. If the case is mild or the patient is weak, the dosage should be on the low side. If the case is severe or the patient is large and robust, the dosage should be on the high side. As a rule of thumb, multiplying the number of ingredients by 1.5 should give a reasonable total daily dose.

Next, consider how many medicinals are in the prescription. If 18 grams will be prescribed and 12 ingredients are used, the average dose of each medicinal will be about 1.5 grams.

In any given formula, some items will be used at higher doses than others. Medicinals that are potent by weight or extreme in nature should be given at low doses, generally 0.3-1.5 grams per day. Examples include items such as Rou Gui (Cinnamomi Cortex), Ren Shen (Ginseng Radix), Fu Zi (Aconiti Radix Lateralis Praeparata), Sha Ren (Amomi Fructus), Chai Hu (Bupleuri Radix) and Wu Zhu Yu (Evodiae Fructus).

By contrast, medicinals that have a balanced nature and a relatively high standard dose in raw decoctions should be used at higher doses, typically 1-3 grams per day. Examples include items like Shu Di Huang (Rehmanniae Radix Praeparata), Shan Yao (Dioscoreae Rhizoma), Yi Yi Ren (Coicis Semen), Mu Li (Ostreae Concha), and Yu Zhu (Polygonati Odorati Rhizoma).

Items that have a moderate, mid-range dosage in decoctions are often used at a dose of 1-2 grams per day. Such items include Dang Gui (Angelicae Sinensis Radix), Bai Zhu (Atractylodis Macrocephalae Rhizoma), Bai Shao (Paeoniae Radix Alba), Ba Ji Tian (Morindae Officinalis Radix), etc.

Some items are used at different dosages for different purposes. For example, Chai Hu (Bupleuri Radix) is often used in low doses to raise yang in formulas such as Bu Zhong Yi Qi Tang (Center-Supplementing Qi-Boosting Decoction). In such applications, 0.3-0.8 grams of granule Chai Hu is generally sufficient. If Chai Hu is instead used to course the liver qi, slightly larger granule doses are typical, such as 0.5-1.5 grams. For treating lesser yang disease, even higher quantities would be called for, such as 1.5-3.0 grams. Similarly, Gan Cao

(Glycyrrhizae Radix) is generally used at a low dose as a courier to harmonize a formula (0.5-1.0 grams), but it can be used in high doses (2-3 grams) as a sovereign medicinal in a formula such as Zhi Gan Cao Tang (Honey-Fried Licorice Decoction).

Consider the following examples. In the first example, a small formula with only 8 ingredients is used. In this example, the daily target dose will be around 12 grams.

Medicinal	Granule dose	Notes	Typical raw dose
Ren Shen (Ginseng Radix)	1.2g	Potent by weight	3-10g
Fu Ling (Poria)	2.5g	Mild by weight	6-15g
Chen Pi (Citri Reticulatae Pericarpium)	1.0g	Potent by weight	3-10g
Gan Jiang (Zingiberis Rhizoma)	1.0g	Potent by weight	3-10g
Gan Cao (Glycyrrhizae Radix)	0.5g	Used to harmonize	3-6g
Bai Zhu (Atractylodis Macrocephalae Rhizoma)	1.8g	Moderate	3-15g
Huang Qi (Astragali Radix)	2.5g	Mild by weight	10-30g
Ban Xia (Pinelliae Rhizoma)	1.5g	Moderate	6-12g
Total	12g		

In this first example, the formula is relatively small. Consider the example below, with a larger formula of 12 ingredients. Here, the total daily target dose will be about 18 grams.

Medicinal	Granule dose	Notes	Typical raw dose
Ren Shen (Ginseng Radix)	1.0g	Potent by weight	3-10g
Fu Ling (Poria)	2.5g	Mild by weight	6-15g
Dang Gui (Angelicae Sinensis Radix)	1.2g	Moderate	6-15g
Bai Shao (Paeoniae Radix Alba)	1.5g	Moderate	6-15g
Zhi Gan Cao (Glycyrrhizae Radix Praeparata)	0.5g	Used to harmonize	3-6g
Bai Zhu (Atractylodis Macrocephalae Rhizoma)	1.5g	Moderate	3-15g
Shu Di Huang (Rehmanniae Radix Praeparata)	2.8g	Mild by weight	10-30g
Suan Zao Ren (Ziziphi Spinosi Semen)	1.5g	Moderate	6-15g
Ye Jiao Teng (Polygoni Multiflori Caulis)	2.0g	Mild by weight	10-30g
Chai Hu (Bupleuri Radix)	1.0g	Potent by weight	3-10g
Xiang Fu (Cyperi Rhizoma)	1.5g	Moderate	6-12g
Chuan Xiong (Chuanxiong Rhizoma)	1.0	Potent by weight	3-12g
Total	18g		

In a larger formula such as this one, there are many factors to pay attention to. The medicinals should always be in proportion to the patient's presentation. For example, if

blood vacuity is prominent, the relative doses of medicinals such as Shu Di Huang, Bai Shao, and Dang Gui should be relatively high. Within those three, Shu Di Huang will tend to be the highest because its raw dose standard is the highest. Bai Shao and Dang Gui can be used at similar dose ranges, but Dang Gui is somewhat prone to producing side-effects such as diarrhea if its dosage is too high.

The fundamental nature of each medicinal should always be taken into account. Shu Di Huang is rich and potentially stagnating, so its dosage should not be excessive in patients that are prone to dampness and diarrhea. Chuan Xiong and Chai Hu are relatively dry medicinals, so their dosage should not be too high for most cases. Fu Ling and Ye Jiao Teng are relatively weak medicinals by weight, so their dosage should be relatively high. Zhi Gan Cao here is used to harmonize here, so its dosage should be low. Medicinals such as Xiang Fu, Bai Shao, and Bai Zhu are here being used at a moderate dosage, not too high and not too low.

Dosage when combining formulas

If one is starting with base formulas, the dosing strategy changes slightly. Again, the total daily target dose will tend to be about 12-18 grams for the final prescription, but the quantities of each item within the formula will tend to be higher since whole formulas are used instead of single extracts.

When combining several formulas together that have similar principles, the dosage of both formulas can be reduced. For example, if Liu Jun Zi Tang (Six Gentlemen Decoction) and Bu Zhong Yi Qi Tang (Center-Supplementing Qi-Boosting Decoction) were used together, the dosage of each one could be reduced.

If one formula treats the main pattern and it is combined with a second formula that addresses a specific symptom or an auxiliary pattern, the main formula should be used at a dose of 8-12 grams and the auxiliary formula for the secondary pattern or symptom should be used at a dose of 1-6 grams. For example, to treat constipation due to liver depression, 12 grams of Xiao Yao San (Free Wanderer Powder) could be used with 4-6 grams of Ma Zi Ren Wan (Cannabis Seed Pill). In this instance, Xiao Yao San would be used to treat the root pattern of liver depression, while Ma Zi Ren Wan would be added to provide symptomatic relief for the constipation.

If two formulas are used with equal emphasis, they should have roughly similar doses, especially if they have a comparable number of ingredients. For example, the formula Si Ni San (Counterflow Cold Powder) is commonly combined with the formula Tong Xie Yao Fang (Painful Diarrhea Formula) to treat diarrhea and pain due to a wood-earth disharmony. Both of these formulas have the same number of ingredients and both may be equally important for the condition, so the dose of each one could be 6-8 grams.

If three or more formulas are used together, the dosage of each formula tends to be lower than it would be if only one base formula was used. If three or more formulas are combined, the dosage of each formula is often only 2-6 grams.

When using a whole formula as though it were a single medicinal addition, the dosage can be quite low. A single medicinal addition is usually added at a dose of 0.5-3.0 grams per day, and this same dose range could be used for a whole formula. For example, if one added Huang Lian Jie Du Tang (Coptis Toxin-Resolving Decoction) to a formula instead of adding a single medicinal such as Huang Lian (Coptidis Rhizoma), the whole formula could be added at a low dose such as 0.5 grams.

Example One:

A patient presents with diarrhea that is accompanied by tenesmus and pain. Upon examination, the patient is diagnosed with a wood-earth disharmony complicated by damp-heat. The following prescription is given:

Si Ni San (Counterflow Cold Powder) 6 grams
Tong Xie Yao Fang (Painful Diarrhea Formula) 6 grams
Huang Lian (Coptidis Rhizoma) 1 gram
Mu Xiang (Aucklandiae Radix) 1 gram

In this example, two compound formulas are used together, with two single medicinal additions. A total daily dose of 14 grams is used. Si Ni San and Tong Xie Yao Fang address wood-earth disharmony manifesting in painful diarrhea. Huang Lian and Mu Xiang are added here to eliminate tenesmus due to damp-heat.

Example Two:

A patient presents with constipation prior to menstruation. She experiences mood swings, irritability, painful menstruation, delayed menstruation, and breast distention. She is diagnosed with liver depression and mild blood stasis. She is prescribed the following formula:

Jia Wei Xiao Yao San (Supplemented Free Wanderer Powder) 8 grams
Tao He Cheng Qi Tang (Peach Kernel Qi4-Infusing Decoction) 2 grams
Qing Pi 0.8 grams
Yu Jin 1.0 grams
Xiang Fu 1.2 grams

Here, the patient is given a combination of two formulas with three single additions. The principle formula, Jia Wei Xiao Yao San, addresses the liver depression and irritability that is central to her diagnosis. The secondary formula, Tao He Cheng Qi Tang, frees the stool and

quickens the blood. Although Tao He Cheng Qi Tang contains Gui Zhi (Cinnamomi Ramulus) and is slightly warm, it is used at a relatively low dose here and its warm temperature is offset by the cool nature of Jia Wei Xiao Yao San. Qing Pi, Xiang Fu, and Yu Jin together strengthen the qi-moving nature of the formula and help to relieve the breast distention.

Conclusion

Dosage is a very important aspect of the clinical application of granules. Several different therapeutic approaches are prevalent and each method has its adherents. The use of granules is an emerging science, and it is essential to keep an open mind about the different strategies that are available.

All too often, practitioners view the issue of dosage with unnecessary rigidity. Some practitioners insist upon very strict mathematical calculations while others use broad estimates. Some practitioners dose their granules in a nearly identical fashion as they dose their decoctions, while others use granules in much lower dosages or use them with a totally different compounding style. At present, it is impossible to broadly assert the superiority of a single method because the landscape is too diverse and the various systems have not been extensively compared with one another in clinical trials.

The topic of granules is a fascinating subject precisely because it is largely unexplored in the academic world. Granules represent a multi-disciplinary field of research, and people with expertise in granules come from a variety of backgrounds. Some experts are chemists, some are clinicians, some are engineers, and some are entrepreneurs. Each expert has a particular viewpoint based on their own experience, but no one person has expertise in all the collective disciplines that affect granules.

Consequently, it is important to study widely and gain exposure to multiple styles and perspectives. At present, the world of granules is largely fragmented. For example, mainland China and Taiwan each have major experts and excellent factories, but both regions are largely unaware of the developments in their neighbor's backyard. Practitioners in both places broadly assert that the other region does it all wrong and boast that they alone have the correct approach. In truth, both sides make valid arguments and both regions have developed viable approaches that have proven to be clinically successful.

In many ways, the world of granules is influenced by the complex politics between mainland China and Taiwan. Invariably, if one travels regularly to both regions, one is stricken by the fact that there is significant regional prejudice on both sides of the water. There is generally insufficient academic exchange between the two regions, and their first real experience butting heads in the commercial world of granules is occurring for the first time right now, in overseas markets such as the USA, Canada, and Singapore. If a practitioner doesn't understand the complex history between these two regions, it is easy to be blinded by one-sided arguments.

The issues related to granule dosage are complex and multi-faceted. The field is new even in the Chinese world, and there are multiple perspectives to consider on many issues. Most people that gain exposure to the diverse landscape of methods used end up concluding that the situation with granule dosage is far from simple and has more than one right answer.

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