The Flagship Remedy of Chinese Medicine: Reflections on the Toxicity and Safety of Aconite

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The most dreaded poison has become the best medicine.
GIOVANNI ANTONIO SCOPOLI

Wolfsbane and Leopard Killer:Mythology's Cardinal Toxin

The toxic properties of aconite, perhaps more than that of any other medicinal substance, loom large in the lore surrounding this plant in both East and West. According to Greek mythology, the botanical species Aconitum napellus originated from the slavering mouth of Cerberus, the three-headed dog with deadly bite that guarded the gates to the underworld. The vanquishing of this toxic animal was Hercules' 12th and most difficult labor. Because of its poisonous potential, later Western sources variously referred to the aconite plant as leopard killer, woman killer, brute killer, dog killer, and wolfsbane. According to Dioscorides, the term wolfsbane originated from the practice of mixing the unprocessed roots of the plant with raw flesh for the purpose of killing wolves. Not surprisingly, assassination stories involving aconite as a poisonous draft are numerous in the history of Western herbalism.[1] In contrast, the medicinal applications of aconite were not fully explored until the 18th century when the Viennese physician Anton Stoerck published his clinical observations about the benefits of the "internal use of aconite in humans" in 1762.[2]

Chinese herbalism, in contrast, has held aconite in extremely high regard as a medicinal substance. For 2,000 years, it has been called the "king of all

1 John S. Haller, "Aconite: A Case Study in Doctrinal Conflict and the Meaning of Scientific Medicine," in *Bulletin of the New York Academy of Medicine* 1984, 60/9:889.

2 Anton Stoerck, "Libellus, quo demonstrator: Stramonium, Hyosciamum, Aconitum non solum tutopose exhiberi usu interno hominibus, rerum et ea esse remedia in multis morbis maxime salutifera " (Vindobonae, 1762).

herbs" in relevant texts. But even in the context of ancient Oriental alchemy, where toxic metals and other potent substances were routinely incorporated into herbal prescriptions, the toxic properties of this plant were acknowledged. The *Shen Nong bencao jing* (Shen Nong's Classic of the Materia Medica), China's classic materia medica from the 2nd century CE, states clearly: "If [aconite] sap is condensed by simmering, it is called Shewang (Shooting Net) and used to kill wild animals."[3] The 5th century Daoist hermit Tao Hongjing elaborates further: "When the sap of the raw [aconite] vine is extracted by mortaring it to a pulp, and then concentrating it by simmering, the paste yielded from this process is called Shewang. Arrows dipped into it can be used by hunters to shoot wild animals; when hit by such an arrow, an animal will fall to the ground after 10 steps. If a human is struck by such an arrow, s/he will die as well, unless the poison is swiftly neutralized by an antidote."[4] Aconite antidotes can be found China's earliest extant medical texts, the so-called Mawangdui Bamboo Tablets unearthed from a grave from the 2nd century BCE. They are recorded in a specialty chapter entitled "On Aconite Poisoning." [5]

From a modern biochemical perspective, the toxicity of aconite is directly related to several alkaloids found in the raw plant material, the most dangerous of which is aconitine:

> All parts of the [aconite] plant contain highly toxic cardiotoxins, the C19-diterpenoid alkaloids such as aconitine, mesaconitine and hypaconitine. These alkaloids activate voltage-sensitive sodium channels in the heart and other nervous tissues which then become refractory to further stimulation. Onset of symptoms such as numbness of the mouth and tingling of the hands and feet is rapid, usually within 10 minutes of ingestion. Other symptoms include nausea, vomiting, dizziness, hypotension, ventricular tachycardia, torsades de pointes and heart block which can lead to death. The lethal dose is estimated to be approximately 2 mg of aconitine.[6]

Progenitor of Life: "The King of All Medicinal Substances" in Chinese Medicine

Although aconite's toxic properties have been described in both Eastern and Western sources, the medicinal properties of Aconitum carmichaelii (Fuzi and Chuanwu/Wutou) and Aconitum kusnezoffii (Caowu) have been honored in China for more than 2,000 years. The influential Daoist text *Huainanzi* stated during the 2nd century BCE: "There is no substance on earth that is more toxic than Chicken Poison (*jidu*; an ancient term for Chuanwu/Wutou aconite), yet a good physician collects it and stores it away to be used for medicinal purposes."[7]

While the poisonous properties of unprocessed aconite are widely acknowledged and cautioned against in the context of traditional Chinese herbalism, they are understood to result from an extreme concentration of life engendering *yang qi*. In its unprocessed state it can be too intense and thus bring about death. Similar

3 See Shen Liansheng, ed., *Shen Nong bencao jing zhongyao caise tupu* (A Colored Illustration of the Herbs in Shen Nong's Classic of the Materia Medica), (Beijing: Zhongyiyao Chubanshe, 1996), p. 472.

4 Tao Hongjing, *Mingyi bielu* (Supplementary Records of Famous Physicians), quoted in Li Shizhen, *Bencao gangmu*, Wutou section (Hongkong: Siku Quanshu Dianziban edition).

5 See the chapter "Du wu;" translated in Donald Harper, *Early Chinese Medical Literature: The Mawangdui Transcripts* (London: Routledge, 1998).

6 Debbie Shaw, "Toxicological Risks of Chinese Herbs," in *Planta Medica* 2010, 76:2014. See also Thomas Y. K. Chan, "Aconite Poisoning," in *Clinical Toxicology* 2009, 47/4:279-285.

7 See chapter 9 of Liu An, *Huainanzi*, in *Baizi quanshu* (An Encyclopedia of the 100 Masters), (Shanghai: Zhejiang Renmin Chubanshe, 1991), 8 vols., vol. 5, no page numbers; for an English translation of the *Huainanzi*, see John S. Major, Sarah A. Queen, Andrew Seth Meyer, and Harold D. Roth, trs. and eds., *The Huainanzi: A Guide to the Theory and Practice of Government in Early Han China* (New York: Columbia University Press, 2010).

to a lightning strike—an expression of the power of the unbridled life force in most ancient cultures—raw aconite was seen as dangerous when one was exposed to it directly.

Of the many designations given to the aconite plant in ancient China, many have become synonymous with the concept of "medicine" itself. The earliest names for aconite reflect its positive and life-engendering qualities, such as Jin 堇 (Fertile Earth), Gen 茛 (Consolidator), and Jian 建 (Life-Force Builder; a direct reference to the 6 central stars of the Dipper and Hexagram 1). Even the common modern term, Fuzi 附子 (originally 付子), reflects this etymological direction. While referencing the unique shape of the root, "Seedlings Attached to the Sides (of the mother root)," the term Fuzi can also be translated functionally, namely as "Recharging the Essence Seed."

Herbal Alchemy: The Traditional Science of Eliminating Aconite Toxicity

Since the toxic effect of raw aconite can be buffered or eliminated altogether by various alchemical methods, early Chinese medical texts focus much attention on processes involving the production of processed aconite. This includes procedures involving special growing and harvesting techniques, special processing techniques, as well as herb combining techniques that blend the processed root with other foods and medicinal substances to safeguard against negative side effects.

Examples of traditional efforts intended to harness the medicinal benefits of aconite while reducing its toxicity are the following:

1) **Terroir—the Science of Defining Appropriate Growing Location**

Ancient Chinese herbalists espoused a distinct concept of space referred to as *daodi yaocai* (herbs grown in the proper location). In the case of no other herb is the aspect of this earth-centered science more adamant than with the Aconitum carmichaelii plant. Li Shizhen and other ancient authorities of the Chinese materia medica invariably state that "the best Fuzi is produced in Mianzhou in the region of Shu (the northern part of today's Sichuan province). Although aconite plants can also be found in other areas, they are unsuitable for treating disease."[8] A Song dynasty account gives a description of this particular region that is still known for producing China's only "genuine" aconite:

> Mianzhou (today's Mianyang in Sichuan Province) is the ancient region formerly called Guanghan. Its land is divided into eight administrative districts, among which only the county of Zhangming (today's Jiangyou) produces Fuzi. Zhangming consists of 20 townships, among which only Chishui, Lianshui, Huichang, and Changming are suitable for the cultivation of this particular crop. The total arable land in all four townships amounts to a bit more than 520 Qing (approximately 320 acres). 50% of this land is set aside to yield rice, 30% is used for beans and other staple crops, and only 20% is reserved for the cultivation of Fuzi.[9]

Jiangyou County borders the Fujiang, a river that originates on the Tibetan Plateau and seasonally replenishes the local earth with Himalayan silt. The earth in Jiangyou is thus particularly rich in naturally occurring minerals and metals, which apparently benefit both the safety and efficacy of

8 See, for instance, the Fuzi entry in Zhang Zhicong, *Bencao chongyuan* (Honoring the Source Knowledge of the Materia Medica, fl. 1674), (Beijing: Zhongguo Zhongyiyao Chubanshe, 1996), p. 108.

9 Yang Tianhui, "Zhangming fuzi ji" (Notes from my Visit to the Fuzi Growing Area of Zhangming County, 1099), reprinted in Tao Zongyi's 14th century database, *Shuofu* (A Collection of Treatises), (Hongkong: Siku Quanshu Dianziban edition).

the medicinal uses of the aconite plants cultivated here. The local roots grow three times as big in comparison to those grown in other regions. Possibly, the unique soil composition of the Jiangyou region also has a unique effect on the essential relationship between the plant's toxic alkaloids and its medicinal properties.

2) Traditional Growing Techniques

It has become an established tradition in the Jiangyou region, where aconite has been cultivated as a medicinal plant for more than 2,000 years, to transplant wild aconite seedlings from the mountains to local fields situated along the Fujiang river. This transplantation happens just after the winter solstice, and the ensuing process of labor intensive cultivation culminates in a harvest of the aconite roots just before the summer solstice. In this manner, the systematic cultivation of genuine aconite used to be tied to not only a very specific location in space, but also a very specific temporal environment. It was grown at time when only the life-giving *yang qi* was present in nature. Here is a description of these time honored growing practices from the 11th century account of a local mandarin:

> The peasants prepare the land for cultivation by clearing the fields at the appropriate time of year, then plant it with a jumbled mixture of dill (Anethum graveolens), shephard's purse (Capsella bursa-pastoris) and wheat grass. Once these fertilizer crops have begun to sprout robustly, they are plowed under, leaves and roots and all, until the land looks clear again. Only then the aconite seedlings are planted. For each Mu of land 10 pieces of cattle are used, applying 50 Hu (approximately 450 gallons) of their dung as fertilizer. … Once the spring rains have passed, causing the crop stalks to grow tall, weeds are cultivated to form a protective ground cover around them, to keep the gradually intensifying rays of the sun out. The amount of labor required for this type of crop is thus 10 times the effort applied to other fields. [10]

3) Traditional Detoxification—Aconite Processing Techniques

The Chinese materia medica contains about 70 recorded types of post-harvest processing techniques aimed at reducing the toxic potential of aconite. The toxic effect of aconite stems from its alkaloids, especially aconitine. Since this ingredient is very sensitive to heating, the processes of roasting, boiling or in most recent times, pressure-steaming can eliminate most alkaloids.[11] Ancient Chinese texts specify that before heating the aconite tuber should be peeled with bamboo knives. This highly labor-intensive technique has been virtually abandoned in the contemporary production of medicinal aconite.

In addition, the so-called Fire Spirit School of Sichuan herbalism, comprised of a long lineage of physicians that specialize in the treatment of chronic and recalcitrant diseases with processed Fuzi, emphasizes that the salt used for preservation of the aconite tubers after the harvest needs to be eliminated completely before they are brought to market. After the harvest, the unprocessed aconite root will decay rapidly (within a week) unless it is immediately immersed in brine. Brine immersion will embalm the root during the time when the entire year's harvest is waiting for the typical step-by-step detoxification process consisting of skin removal and the application of heat. Traditional *paozhi* techniques specify that all brine is removed from the raw aconite slices before steaming or baking them, by soaking and rinsing them repeatedly in basins of fresh water. Seasoned Fire School

10 Ibid.

11 Debbie Shaw, "Toxicological Risks of Chinese Herbs," 76:2014.

practitioners, i.e. the contemporary scholar-physicians Drs. Lu Chonghan and Liu Lihong, have observed that industrial aconite production during the last two decades has flooded the market with high salt content aconite slices. To most kidney deficient patients, this significant salt residue in most pharmacy grade aconite (70% in most contemporary aconite products) is harmful and may be partially responsible for some of the side effects associated with aconitine alkaloids in the pharmacological literature. In addition, it has become common practice in recent years to remove the root peel by immersion in hydrochlorid acid, defying the stringent alchemical experience of aconite detoxification garnered during the last two millennia.

4) Inter-Herbal Alchemy: Herb Combination Techniques

The combination of herbs into formulas with high alchemical integrity—low toxicity, high efficacy, and food-grade tolerability—is an outstanding feature of traditional Chinese herbalism. The so-called *jun-chen-zuo-shi* (emperor, minister, assistant, servant) principle of Chinese prescription science prominently features the concept of combining herbs for maximum effect and low toxicity.

In the *Lü shi chunqiu* (The Annals of Lü Buwei), an important historical text from the 3rd century BCE, we find the following passage that illustrates the early adaptation of this concept: "Among the medicinal grasses there are the pungent weeds (*xin*) and the toxic vines (*lei*)—by themselves they will kill you, but when combined properly they benefit health and longevity. In this way, even the 10,000 aconite toxins won't be able to kill."[12]

Li Shizhen, the esteemed Ming dynasty author of China's definitive materia medica, added 1,800 years later: "Aconite is thus commonly used in combination with the herbs Gancao (licorice), Renshen (ginseng), and Shengjiang (fresh ginger). All of these have the effect to control the inherent toxicity of aconite and harness its power for righteous medicinal purposes."[13] This effect has been confirmed by modern scientific studies: "Processing with Glycirrhiza species (Gancao) or Zingiber species (Ganjiang) has been shown to further reduce the aconitine alkaloids by enhancing hydrolysis."[14]

In addition, the science of traditional Chinese phytotherapy prefers to tie the concept of herbal toxicity (*duxing*) to the alchemical interaction of a patient's constitution with a particular substance rather than to a quantitative assay of biochemical ingredients. The life work of veteran toxicologist Prof. Li Zulun from the Pharmacology Dept. of Chengdu University of TCM is of particular interest in this context. His doctoral dissertation, the first in the field of modern TCM, concluded that the concept of absolute toxicity does not exist in Chinese medicine, where "toxic effects" are always related to an alchemical reaction between an herb and the constitutional terrain of the person who imbibed it. The local peasants from the aconite growing region in Jiangyou, for instance, know that some people can eat a small piece of raw aconite root on a given day without experiencing any ill effects, while the same action may cause another person's death. In addition to proper growing and processing techniques, it is therefore the diagnostic science of correct pattern differentiation that is the main key to avoid toxic reactions.

12 See chapter 25 of *Lü shi chunqiu* (Mr. Lü's Spring and Autumn Annals), in *Baizi quanshu* (An Encyclopedia of the 100 Masters), (Shanghai: Zhejiang Renmin Chubanshe, 1991), 8 vols., vol. 5, no page numbers.

13 Li Shizhen, *Bencao gangmu*, Fuzi section.

14 Debbie Shaw, "Toxicological Risks of Chinese Herbs," 76:2014.

Buying Safe Aconite: Realities of the Modern Marketplace

In modern times, the first three of these traditional requirements for safe medicinal aconite are absent in 95% of the Fuzi and Wutou brought to market in both Chinese and Western pharmacies. Most of today's aconite originates from Shaanxi Province, although it is often shipped to Sichuan to receive a "genuine Jiangyou aconite" stamp on its packaging and get distributed from there. In addition, modern growing techniques in Shaanxi and Yunnan do not follow the labor-intensive traditional growing practices cultivated for the last 2,000 years in northern Sichuan.

Most importantly, the majority of aconite tubers sold today are improperly processed. After the harvest, the roots are often immersed in hydrochlorid acid or other chemicals to remove the peel. The brine content of most aconite produced today, moreover, tends to be in the 70% range.

Following the example of Fire School masters such as Drs. Lu Chonghan and Liu Lihong, Classical Pearls commenced direct cooperation with a local aconite processing facility in Jiangyou 4 years ago. This cooperation has contributed to a local revival of traditional growing and processing techniques. The aconite seedlings are brought down from the mountains around the winter solstice, grown among corn plants in the ancient fields adjacent to the river, and harvested just before the summer solstice. Local peasants are then contracted to hand-peel and cut the large aconite tubers into slices with bamboo knives, then soak and rinse them repeatedly until all of the salt content has been removed, before finally pressure steaming and drying the pieces.

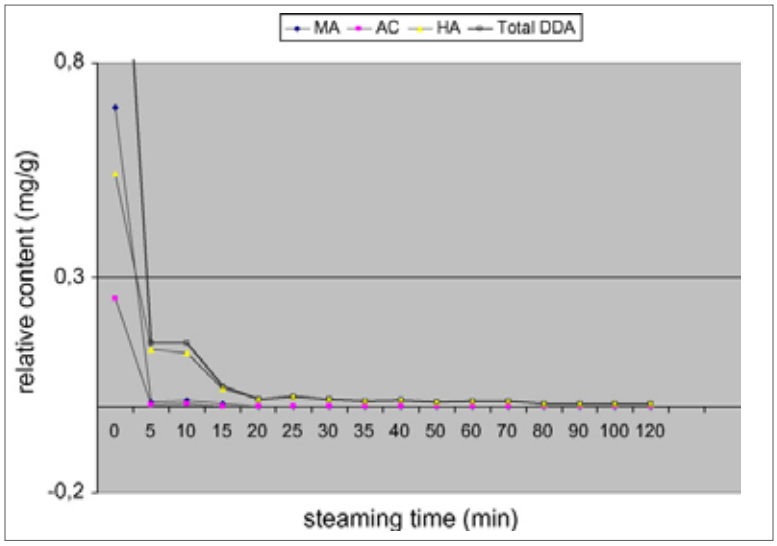


Fig. 1: Reduction of dieter diterpene alkaloids (DDAs), including the toxic alkaloid aconitine, during processing of aconite roots by pressure-steaming technique[15]

Generally, processed aconite slices should be boiled for 1-2 hours before adding the remaining ingredients of a Chinese herbal formula for further decoction. This process intends to expose the root slices to an additional application of heat before the decoction is imbibed, to further decrease any leftover aconitine to levels that are absolutely safe. Even without this last boiling process, Classical Pearl's traditionally grown and processed aconite slices contain "undetectable levels" of aconitine according to an independent German/Chinese lab.

15 Judith Singhuber, Ming Zhu, Sonja Prinz, and Brigitte Kopp, "Aconitum in Traditional Chinese Medicine—A Valuable Drug or an Unpredictable Risk," in *Journal of Ethnopharmacology* 2009, 126:18-30.

Fig. 2: HPLC chromatogram of aconitine (CRS)[16]

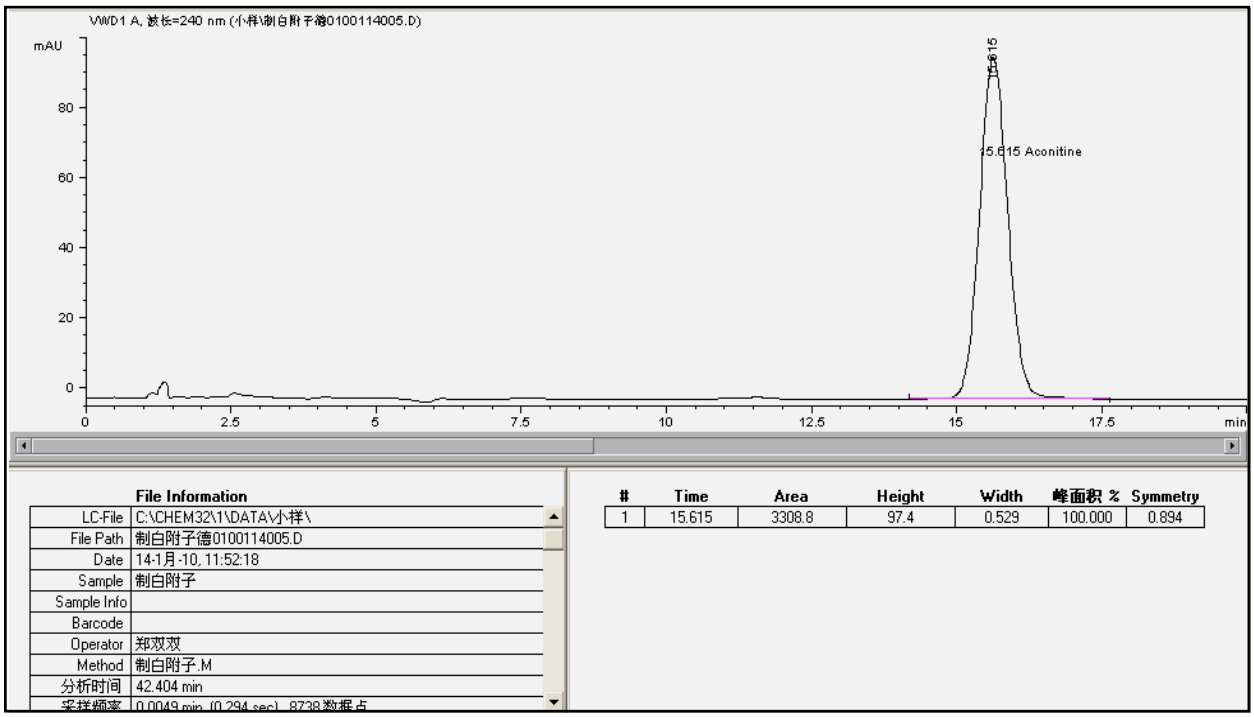
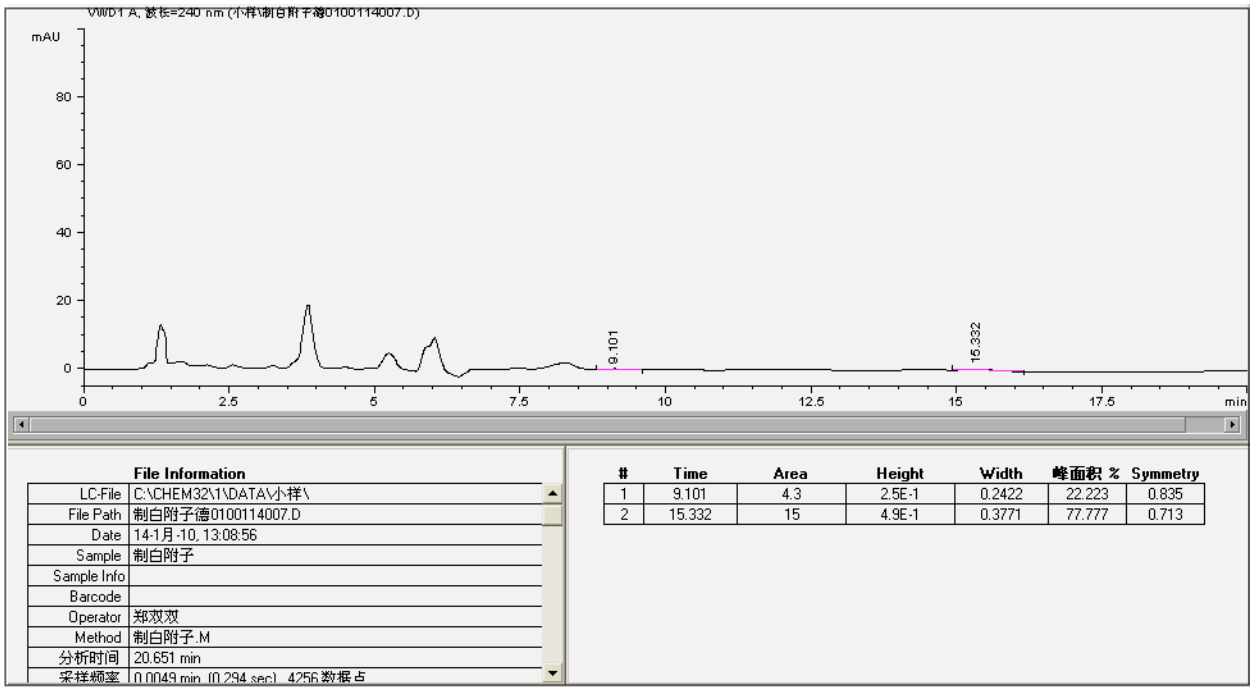


Fig. 3: HPLCS chromatogram of traditionally grown and processed Radix Aconiti Lateralis Praeparata[17] used by Classical Pearls



16 Chinaherb Pharmacognosy Technology Co., LTD., "Analysis Report of Chinese Materia Medica: Radix Aconiti Lateralis Praeparata (附子 Fuzi), Report #HBY100301." (Yantai: 2010), p. 4.

17 Ibid.

Nevertheless, the processed aconite slices used for the production of Classical Pearls' Fuzi, Wutou and Caowu granules as well as the company's relevant patent formulas have been subjected to a process of 3 hours of soaking and 2 hours of boiling. To date, Classical Pearls has introduced about 7 tons of this type of traditionally grown and processed aconite to the Western market. During this time, the company has not received a single incident report involving severe side effects induced by aconite. In contrast, it did receive a host of case reports involving improvement in chronic conditions that had not responded favorably to other treatment methods.

The Classical Pearls enterprise can serve as a successful example that proves the efficacy of ancient alchemical processing techniques, and restores one of the most powerful herbs of the Oriental material medica available for safe therapeutic use in modern times. It is the declared goal of the Classical Pearl enterprise to contribute to an evolving trend in the responsible processing and trading of Chinese herbs.

It is advisable, however, that the prescription of aconite belongs to the domain of a licensed health care professional who has been trained in the therapeutic prescription of Chinese herbs. Whatever direction the ongoing discussion on aconite may take in the future, the young profession of Chinese medicine should be wary to throw out the proverbial baby with the bath water. Many contemporary decisions that have led to a ban of natural substances have been based on irrational fears, and often incorporated no clinical knowledge of the subject matter. In the case of properly processed Fuzi, Wutou/Chuanwu and Caowu it serves nobody to ignite yet another cycle of ill informed aconite hysteria, described so aptly by the scholar-physician Zhang Zhicong more than 300 years ago:

> There are many doctors who regard Fuzi as a type of vicious poison for the duration of their entire career. They go around telling people: "You can't take Fuzi—if you do, it will cause you to become wild and crazy and bleed from every orifice in your body; it will cause fire symptoms to engulf your body, and toxic sores to erupt everywhere; it will cause your organs to rot internally, and if you take it this year, the effects of toxic degeneration will become visible next year." Alas! Under these circumstances, how does one ever dare to use Fuzi when it is indicated? Disregard income and reputation and excuse oneself from treatment? Humble oneself and recommend another doctor as better suited? This will then end in a situation where the patient gets this medicine prescribed today and that medicine tomorrow, until the patient's spirit becomes severely degenerated. If at that time one returns to the right type of treatment, it will be too late—even if you have the elixir of immortality in your possession, nothing will be able to save the patient then.[18]

As a scholar of ancient Chinese medical texts and a clinician specializing in the use of phytotherapy for chronic and recalcitrant diseases, I cannot stress enough the enormous significance of aconite as a core symbol of Oriental medicine. Aconite is both a cultural icon—an emblem for the profession of Chinese medicine—and one of the most effective herbs for the alternative treatment of difficult diseases such as pain, endocrine dysfunction, auto-immune disease and cancer. Any cry for the removal of processed aconite from the list of legally accessible substances equals the denial of the profession of Chinese medicine itself.

In conclusion, it is pertinent to point out that virtually all research about the toxic dangers of aconite involve the raw unprocessed form of aconite, which is an entirely different substance in comparison to properly grown and processed Fuzi, Wutou, and Caowu. As a recent paper investigating the facts on the topic of aconite toxicity states clearly: "Poisoning from Aconitum spp is mainly due to incorrect use—

18 See Zhang Zhicong's Fuzi entry in *Bencao chongyuan*, p. 109.

either use of poorly processed roots resulting in overdose of the alkaloids or due to poor directions for use, for example, ingestion of liniments prepared for topical use only."[19]

Economic and political pressures have led to an abandoning of traditional growing and processing techniques involving Aconitum carmichaelii during the last 20-30 years. Most undesirable side effects can be avoided by strict adherence to the traditional knowledge that has surrounded the safe therapeutic usage of this herb for the last 2,000 years. While it may be advisable to cast a closer regulatory eye on some naturally occurring medicinal substances with toxic potential, in the case of aconite I strongly recommend that any future attempt to limit its therapeutic use focuses on mandating maximum allowable levels of the toxic alkaloid aconitine rather than an outright ban of the aconite root itself. As an international team of researchers recently concluded in their assessment of aconite safety:

> The current development of fingerprint assays, in particular HPLC, has set a good basis to conduct an appropriate quality control for TCM crude herbs and their ready-made products. Therefore, a stipulation for a maximum level of DDA content of *Aconitum* is highly desirable in order to guarantee the clinical safety and its low toxicity in decoctions.[20]

While traditional processing methods have proven themselves over millennia, the advent of modern biochemical testing methods gives us an additional safeguard to ensure the proper use of this pivotal medicinal substance.

19 Debbie Shaw, "Toxicological Risks of Chinese Herbs," 76:2014.

20 Singhuber et. al, 2009.