Review

The formation of \textit{daodi} medicinal materials

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\textbf{A R T I C L E  I N F O}

\textbf{Article history:}
Received 12 December 2011
Received in revised form 27 January 2012
Accepted 27 January 2012
Available online 5 February 2012

\textbf{Keywords:}
Daodi medicinal material
Historical change
Materia medica (bencao)

\textbf{A B S T R A C T}

\textit{Daodi} medicinal material is produced and assembled in specific geographic regions with designated natural conditions and ecological environment, with particular attention to cultivation technique, harvesting and processing. The quality and clinical effects surpass those of same botanical origin produced from other regions. It is thus widely recognized and has long enjoyed a good reputation. Based on literature, market and field investigation on daodi medicinal materials, the historical background and reasons behind the formation and the development of daodi medicinal material are analyzed. This review clarifies the concept and rationalizes the formation of daodi medicinal material.

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1. Introduction

The term “\textit{daodi} medicinal material” refers to a concept that has been widely recognized in the Chinese medicinal industry for centuries. Although it is also known as authentic and superior medicinal herbal, authentic medicinal, genuine medicinal material, geo-herb, geo-authentic medicinal material, and top-geoherb (Hu, 1989; Huang et al., 2007; World Health Organization, 2007; Xiao et al., 2007; Huang et al., 2010; Zhao et al., 2012), the Pinyin transliteration \textit{daodi} medicinal material has gradually become an accepted specialized technical term just like yin, yang, and qi. “\textit{Daodi} medicinal material” is a customary term that is synonymous with high-quality medicinal product. It is famous not unlike the horrific phrase “lao zhong yi” (literally “old Chinese medicine doctor”), which is used to describe famous senior practitioners of Chinese medicine (Zhao, 2011).

“\textit{Daodi} medicinal material” is defined as “medicinal material that is produced and assembled in specific geographic regions with designated natural conditions and ecological environment, with particular attention to cultivation technique, harvesting and processing. These factors lead to quality and clinical effects surpass those of same botanical origin produced from other regions, and thus is widely recognized and has long enjoyed a good reputation.” Among the 500 commonly used Chinese medicinal materials, about 200 are recognized as having \textit{daodi} medicinal material specifications. The consumption of these 200 \textit{daodi} medicinal materials accounts for 80% of the total consumption of medicinal materials in China (Pan, 2011).

The word “\textit{dao}” (in \textit{“daodi”}) was an ancient Chinese unit of measurement for the division of administrative districts. In the Tang Dynasty (618–907 C.E.), the nation was divided into 10 “\textit{dao}” according to landscapes in the \textit{Zhenguan} Years, and was later
increased to 15 dao in the Kaiyuan Years. Conceptually similar to the present day organizational system of provinces, the deep influence of these names can still be seen in the modern day Chinese names given to areas of Japan and the Korean peninsula, such as Hokkaido (bêhaidao). The word “di” (in “daodi”) broadly refers to “earth”, “land” or “soil”, as in geography, regions, topography, and landforms.

2. The clinical practice of Chinese medicine is the basis of the formation of daodi medicinal material.

Chinese medicine has accumulated abundant clinical experience regarding the use of medicinal substances over a long period of time, and superior quality medicinal varieties have emerged from this tradition. It can be understood in the way that there would be no concept of “daodi medicinal material” without the clinical experience of Chinese medicine.

Clear records related to daodi medicinal material can be found throughout the historical literature. In China, books that record the sources and applications of medicinal substances are known as bencao (materia medica). Materia medica texts of past dynasties primarily describe 3 aspects of a Chinese medicinal: medicinal materials, medicinal properties, and medicinal principles. Within the context of medicinal materials, production regions are given great importance. The Eastern Han Dynasty (25–220 C.E.) text The Divine Husbandman’s Classic of Materia Medica (Shen nong ben cao jing) was the first text to discuss the importance of production regions; it states: “Each medicinal material has laws for its production region, authenticity, and freshness.” Although at that time it only recorded basic descriptions such as “grows in mountain valleys, river valleys, or marshes,” many medicinal names are rich with connotations of production regions. Examples include the medicinals ba dou (Crotonis fructus), ba ji tian (Morindae officinales radix), shu jiao (Zanthoxyl pericarpium), qin pi (Fraxini cortex), qin jiao (Gentianae macrophyllae radix), and wu zhu yu (Evodiae fructus), “Ba,” “Shu,” “Wu,” and “Qin” were names of regions that were in use before and after the ancient Western Zhou Dynasty (c. 1100–771 B.C.E.), and the names of these regions reflect the geographic origin of the medicinals listed above. During the Northern and Southern Dynasties period (420–589 C.E.), the text Collection of Commentaries on the Classic of the Materia Medica (Ben cao jing ji zhu) started to record specific production regions for medicinals. The text clearly stated that “the places where all medicinals come from have specific boundaries,” and it began to use terms such as “the best” (zui jia) and “surpasses” (wei sheng) to describe correlations between appearance, production region, and quality. For example, under the description of licorice root (gan cao), it states that specimens with “a red cortex, an uneven fracture, and a firm texture” . . . . are the best.

Newly Revised Materia Medica (Xin xiu ben cao), a materia medica commissioned by the government of the Tang Dynasty, stated: “If medicinal material is not produced from its native environment, the effect will be different.” The Tang dynasty text Formulas Worth a Thousand Gold Pieces (Qian jin fang), written by the so-called “King of Medicine,” Sun Simiao, began to use “dao”, the unit of measurement for the division of administrative districts, to summarize production regions; thus, Sun’s text contains the original concept that would later become known as “daodi”. In the first volume of Formulas Worth a Thousand Gold Pieces (Qian jin fang), the section of “using medicinals” states: “Ancient doctors depended on medicinals produced from the proper production areas. Therefore, if they treated ten patients, they achieved results in nine. Although contemporary doctors understand the pulse and prescriptions, they are not familiar with the proper production regions, harvest time, and quality of medicinal materials. Therefore, they only achieve results in five or six cases out of ten.” This suggests that one can achieve excellent treatment results only by using daodi medicinal materials. In the Song Dynasty (960–1279 C.E.) text Extension of the Materia Medica (Ben cao yan yi), we find the clear statement: “All medicinals must be chosen from suitable production regions” (Association of Chinese Culture Research, 1999).

Commissioned by the government of the Ming Dynasty (1368–1644 C.E.), Essentials of Materia Medica Distinctions (Ben cao pin hui jing yao) recorded 1809 medicinals and featured with 1371 illustrations. The entry “daodi” was formally listed under the heading of “land” (di) for 268 botanical medicinals specifying their daodi production regions. Under this entry, specialized terms that express various nuances were used to describe the superiority of medicinals and their production areas (Cao, 2004) (Fig. 1). Thus, the text Essentials of Materia Medica Distinctions (Ben cao pin hui jing yao) started to document daodi medicinal material as a professional terminology, and established its scale and basic varieties. Later on, the phrase “good daodi medicinal materials” appeared in the famous masterpiece opera “The Peony Pavilion: Exploration of Medicine” by Tang Xianzu (Tang, 2002). This has made the term “daodi medicinal material” spread far and wide among common people in China.

In modern times, daodi medicinal material is recognized as one of the most valuable parts of ancient materia medica (Hu, 1995). In the first modern monograph on daodi medicinal material, 159 daodi medicinal materials (including 131 botanical, 20 zoological, and 8 mineral substances) are classified into 8 categories according to the production regions: chuan (Sichuan), guang (Guangdong/Guangxi), yun (Yunnan), gui (Guizhou), nan (Southern China), bei (Northern China), zhe (Zhejiang), and huai (Henan) (Hu, 1989). Collecting and distributing centers for daodi medicinal materials have also been formed in different areas of China (Zhao et al., 1990).
3. The superior germplasm resource is the internal factor of the formation of daodi medicinal material.

China is vast in territory with diversified landforms and mountain ranges, and hence diverse weather. This diversity of natural ecosystems provides abundant botanical and zoological germplasm resources. This is the internal factor of the formation of the daodi medicinal materials (Zhao et al., 2012).

There is a famous Chinese saying that states; “plant melons and you get melons; grow beans and you get beans”. Indeed, the special characteristics of a plant are determined by genetics. Ancient people sometimes mentioned the differences of medicinal materials produced from the north and south. Beyond the concept of growing region, these differences are actually related to different plant species in taxonomy. For example, many people get confused because the fresh Dioscorea rhizoma (shan yao) sold in vegetable markets is large and flat. It looks different than the traditional product seen in herbal stores. In reality, Dioscorea rhizoma (shan yao) has been divided into edible and medicinal varieties since the Ming Dynasty. Dioscorea rhizoma (shan yao) used in medicine is distributed in a relatively northern region, and its botanical origin is Dioscorea opposita Thunb. Medicinal materials (known as “huai shan yao”) produced from plantation sites at Wuzhi County and Wen County of Henan province are believed to be superior in quality, especially a specific type in commerce known on the market as tie gun shan yao. Dioscorea rhizoma (shan yao) used in food is distributed in southern provinces. Its botanical origins are complicated, involving Dioscorea japonica Thunb., Dioscorea alata L., Dioscorea persimilis Prain et Burk., and Dioscorea fordii Prain et Burk. (Lou and Qin, 1995; Xu and Xu, 1997).

Chinese medicine has been used for an exceptionally long time. Chinese medicinals are characterized by diverse and complex origins. In the Chinese Pharmacopoeia (2010 edition), 616 medicinal materials are recorded and over 25% of them (157) are derived from two or more sources. Although these medicinal materials share similar Chinese names, they are derived from different plant species. Examples include: bei cang zhu (Atractylodes chinensis (DC.) Koidz.) and nan cang zhu (Atractylodes lancea (Thunb.) DC.), bei da hong (Rheum palmatum L., Rheum tanguticum Maxim. ex Balf.) and nan da hong (Rheum officinale Baill.), bei wu wei zi (Schisandra chinensis (Turcz.) Baill.) and nan wu wei zi (Schisandra sphenanthera Rehd. et Wils.), guan hong bai (Phellodendron amurense Rupr.), and chuan hong bai (Phellodendron chinense Schneid.), nei meng hong qi (Astragalus membranaceus (Fisch.) Bge. var. mongolicus (Bge.) Hsiao) and mo jia hong qi (Astragalus membranaceus (Fisch.) Bge.), zi cao (Arnebia guttata Bunge) and xin jiang zi cao (Arnebia euchroma (Royle) Johnst.), chai hu (Bupleurum chinense DC.) and nan chai hu (Bupleurum scorzonerifolium Willd.), jin yin hua (Lonicera japonica Thunb.) and shan yin hua (Lonicera macranthoides Hand.-Mazz., Lonicera hypoglauca Miq., Lonicera confusa DC., Lonicera fulvotomentosa Hsu et S.C. Cheng), chuan hou po (Magnolia officinalis Rehd. et Wils.) and ri ben hou po (Magnolia obovata Thunb.).

4. Suitable geographic conditions are the external factor of the formation of the daodi medicinal material.

It is well-known that environmental factors such as topography, soil, climate, humidity, and light directly influence the secondary metabolites (many of which are bioactive constituents) of plants. Ancient people said that “tangerine plants grown south of the Huai river produce tangerines, but if they grow north of the Huai river they produce bitter oranges; the leaves are similar but the flavor of the fruit is different.” Ancient observers recognized that different environments not only produce changes in appearance, they also produce differences in medicinal nature.

The Chinese medicinal chuan xiong (Ligusticum chuanxiong Hort.) has the word “chuan” in its name because its daodi medicinal material is produced in Sichuan province. It is principally cultivated in regions of Sichuan such as Dujiangyan and Pengzhou, which have the largest output and the longest history of medicinal use. However, in a cultivar known as fu xiong (Ligusticum chuanxiong Hort. cv. Fuxiong) that is mainly cultivated in Jiangxi province, genetic variations have arisen: this cultivar goes a long time without flowering and rarely sprouts. Although fu xiong also has large and fleshy rhizomes, it contains less volatile oil and ligustazine than Sichuan-cultivated chuan xiong (Fang and Zhang, 1984).

Time has brought great changes to the environment of China over the past two thousand years. Natural selection and survival of the fittest have resulted in a number of changes in terms of varieties, growing regions, and natural resources for some daodi medicinal materials. For example, the present production center of Notoginseng radix (san qi) is in Yunnan’s Wenshan region, although the Tianzhu region of Guangxi province was its original production center. Similarly, Poria (fu ling) historically came from the wild in Yunnan province, hence the name “yun ling”; now the dominant medicinal material comes from Huber’s Luotian region and is called “jiu zhi he fu ling” (Sun et al., 2009).

The case of Ginseng radix (ren shen) is one of the most classic examples. Prior to the Song dynasty, ginseng was found in a wide region that included Shanxi, Hebei, and provinces of north-east China. Extant illustrations of “lu zhou ren shen” provide evidence that ginseng plants of the Araliaceae were growing in the Luzhou region in former times (the area is now known as Shanxi’s Changzhi region). The Northern and Southern Dynasties (420–589 C.E.) text Miscellaneous Records of Famous Physicians (Ming yi bie lu) stated that Ginseng radix (ren shen) produced in Shanxi’s Shandang region was of high quality. However, due to overharvesting and environmental changes, Ginseng radix (ren shen) of Shanxi province was exhausted early on. By the time of the Qing dynasty, the daodi production region assigned to Ginseng radix (ren shen) had already moved to northeastern China. In the years of the “Great Leap Forward” (1958–1959), people in mainland China attempted to cultivate ginseng on Hainan Island in southern China. However, the roots grown in Hainan were large but almost completely lacking in active constituents, ending up nearly useless beyond the appearance.

5. Advancement in cultivation techniques promotes the development of the daodi medicinal material.

China is a great agrarian nation. The experience in crop cultivation that ancient Chinese people accumulated was applied to the cultivation of medicinal plants early on. Thus, why did it take until the Ming Dynasty before daodi medicinal materials advanced in scale and scope?

Looking back at history, during the Southern Song and Yuan Dynasties (1127–1368 C.E.) central China was continually ravaged by war, and was said to be “without the sound of a cock’s crow for a thousand miles”. Following this era, the Ming Dynasty government implemented immigration policies that greatly speeded the development of agriculture in central China. The achievements of this era were summarized by works such as Xu Guangqi’s Comprehensive Text of Agricultural Policy (Nong zhen quan shu) and Song Yingxing’s science and technology work Exploitation of the Works of Nature (Tian gong kai wu). This great advancement of agriculture allowed cultivation experience to accumulate over many years, and cultivation techniques of medicinal plants gradually matured. The botanical origins used as daodi medicinal materials thus changed to be principally based on cultivated species.
Achyrantthis bidentatae radix (niu xi), Rehmanniae radix (di Huang), Dioscoreae rhizoma (shan hua), and Chrysanthemi flos (ju hua), known as the “four famous medicinal materials of Henan”, are representative masterpieces of this era. Records of the cultivation techniques of Rehmanniae radix (di Huang) can be found as early as the Tang dynasty text Formulas Worth a Thousand Gold Pieces (Qian Jin Fang). From the Ming dynasty onward, it was generally recognized that Rehmanniae radix (di Huang) cultivated in Huaqingfu (modern day Henan province) was of particularly high quality. Li Shizhen of the Ming dynasty noted that “ancient people cultivated [Rehmanniae radix (di Huang)] from seed, contemporary people cultivate it from roots.” This asexual cultivation method of Rehmanniae radix (di Huang) is used up to the present day. Nowadays, the species cultivated in this region remains exceptional in quality. It produces large, high-yielding roots with high levels of the active constituent catalpol (Li et al., 2002; Qiu et al., 2010). It is also strongly resistant to drought, waterlogging, disease, and insect damage. People have gradually forgotten about Shanxi’s Xianyang and Tongzhou and Jiangsu’s Yangcheng and Jiangning, which were known prior to the Song dynasty as traditional production areas of Rehmanniae radix (di Huang).

Daodi medicinal materials are not fixed and unchanging. In cooperation with universities and research institutes, pharmaceutical manufacturers have involved in “Good Agricultural Practice (GAP) for Traditional Chinese Medicinal Materials”, which has been enforced by the Chinese government since 2002 (Fig. 2). This has expanded production regions for daodi medicinal materials and allowed new daodi medicinal materials to emerge. For example, Sichuan is traditionally considered to be the daodi production region for Salviae miltiorrhizae radix et rhizoma (dan shen). Sichuan is the largest producer of this traditional daodi medicinal material, which has been cultivated in Sichuan’s Zhongjiang County for over 100 years. Nonetheless, modern herbal companies have now established large-scale standardized plantation sites for Salviae miltiorrhizae radix et rhizoma (dan shen) in Shangluo of Shaanxi province. Similarly, Zhejiang province (especially the regions Lin’an and Chun’an) is the traditional daodi production region of Corni fructus (shan zhu yu), but some herbal companies have now established standardized plantation sites in Henan and Shaanxi provinces as well (Zhao et al., 2012).

6. Traditional Chinese medicinal processing produces special characteristics of the daodi medicinal material

Chinese medicinal processing (pao zhi) is a pharmaceutical technique that meets different therapeutic, dispensing, and pharmaceutical requirements based on traditional Chinese medicine (TCM) theory. The use of processed Chinese medicinals makes TCM different from other oriental and western herbal medicines (Zhao et al., 2010). Only after raw Chinese medicinal materials have undergone certain treatments of processing into decoction pieces, can they then be in clinical application. In the Chinese Pharmacopoeia (2010 edition), a total of 591 raw medicinal materials are recorded. Among them, standards for decoction pieces of 446 raw medicinal materials are established, involving 672 individual decoction pieces. It has been clarified in the Chinese Pharmacopoeia (2010 edition) that medicinal properties, channel tropisms, functions, indications, usage, and dosage are attributed specifically to decoction pieces.

In addition to the enhancement of efficacy and the reduction of toxicity of Chinese medicinals, the application of medicinal processing has produced special features in some famous daodi medicinal materials. For example, four processed products of Aconiti lateralis radix praeparata (fu zi) are listed in the Chinese Pharmacopoeia (2010 edition): black sliced aconite lateral root (hei shun pian), white sliced aconite lateral root (bai fu pian), desalted sliced aconite lateral root (dan fu pian) and blast-fried sliced aconite lateral root (pao fu pian) (Fig. 3). Additionally, in the daodi production region of Aconiti lateralis radix praeparata (fu zi) at Jiangyou, Sichuan, there are additional processed forms that enjoy international fame, such as blast-fried aconite lateral root (pao fu zi), cooked sliced aconite lateral root (shou fu pian), planed sliced aconite lateral root (bao fu pian), and yellow sliced aconite lateral root (huang fu pian).

The famous Asini corii colla (e jiao) produced from donkey hide in Shandong province is another highly developed example. In ancient times, Asini corii colla (e jiao) was made from ox hide. Miscellaneous Records of Famous Physicians (Ming yi bie lu) clearly stated that “e jiao is produced in Dongping prefecture from ox hide and comes from Dong’e.” In fact, the efficacy of donkey hide-produced e jiao versus that produced from ox hide was a subject of debate all the way up to the time of Li Shizhen’s Compendium of Materia Medica (Ben cao gan mu). The debate finally reached its conclusion when Compendium of Materia Medica (Ben cao gan mu) proclaimed e jiao from donkey hide to be a “sacred medicine” (Association of Chinese Culture Research, 1999). From that point on, the item produced from ox hide became known as huang ming jiao, and that produced from donkey skin became known as e jiao.

Naturally, the creation of e jiao from donkey hide is not as simple as a basic boiling process. Rather, it is a refined process that is quite particular. Deposited in the museum of Chinese Medicine at Hong Kong Baptist University, a treasured instruction detailing e jiao in the Daoguang years of the Qing Dynasty (1821–1850 C.E.) describes the entire process of making e jiao. The instruction not only details the water used to make e jiao as well as the raising of the donkey and the selection of the hide, but also outlines a strict sequence of using silver pots and gold shovels. The instruction also mentions that the use of counterfeit forms would damage health.
and addresses common formulas for the use of e jiao in gynecology (Fig. 4).

For a thousand years, e jiao was known as “nine dynasties tribute gelatin” because it achieved a great reputation due to its excellent clinical effect. Originally reserved as a valuable item for officials and eminent people, nowadays it has become an item used by common people. At present, the provinces of Shandong and Anhui are key areas for raising donkeys, and donkey skin from countries such as Afghanistan, Australia, and South Africa has entered the Chinese market to guarantee the production supply for e jiao.

7. The naturalization of medicinal substances from outside China enriches daodi medicinal material resources

Some medicinal substances that come from outside of China are among the daodi medicinal materials used in Chinese medicine. In some cases, medicinal substances from outside of China that are unused or under-appreciated in their own countries are favored in China, and have been introduced and raised in China to enrich China’s treasure house of daodi medicinal materials.

Aucklandiae radix (mu xiang) was originally produced in India and Myanmar, and was historically called guang mu xiang because it was imported into China via Guangzhou. Later on, it was successfully cultivated in China’s Yunnan province and produced good quality medicinal material called yun mu xiang. The output of medicinal material has continually increased and the quality is high. Research result showed that the total amount of costunolide and dehydrocostus lactone contained in Aucklandiae radix (mu xiang) produced in Yunnan was much higher than that specified in the Chinese Pharmacopoeia (Liang and Gao, 2005). As a result, yun mu xiang has already become known as a daodi medicinal material of Yunnan province that is sold throughout China and distributed overseas. Certified GAP plantation sites have also been established at Lijiang in Yunnan province.

Saffron was originally produced in Southern Europe, and it is cultivated in Spain, France, Greece, Italy, and India. Historically, it was imported into China via Tibet. Known as Croci stigma (xi hong hua) in China, it began to become incorporated into Chinese medical practice in the Ming Dynasty. In TCM, Croci stigma (xi hong hua) moves the blood, dissipates blood stasis, cools the blood, and resolves toxicity. It is extremely expensive because it takes 160,000 flowers to produce a single kilogram of saffron. Nowadays, it has also been successfully cultivated in Shanghai, Jiangsu, and Zhejiang provinces in China. Certified GAP plantation sites have also been established at Baoshan in Shanghai.

While Chinese ginseng (Panax ginseng C. A. Mey.) had already been used for thousands of years, American ginseng (Panax quinquefolius L.) was asleep in virgin forests of North America. In 1702, a French priest Father Jartoux observed the use of Chinese ginseng in Manchuria. He provided a detailed physical description and a description of the environment where Panax ginseng grew in China. Fascinated by his information, another priest Father Joseph Francois Lafitau in North America (French Canada) discovered American Ginseng near Montreal in 1716 (Persons, 1994). Later on, American ginseng from Canada was brought to China and became a valued item in the imperial court. Nowadays, American ginseng is successfully cultivated in China on a large scale. Certified GAP plantation sites have also been established at Jingyu in Jilin province.

8. Prospects for future research

Over centuries of treating disease and attempting to preserve health, ancestors of the Chinese people developed a unique and comprehensive medical system, known as traditional Chinese
medicine (TCM). This is valuable cultural heritage left to the Chinese by their ancestors. China also has abundant natural resources of medicinal materials, which are the material basis for the application of TCM theory in preventing and treating disease. As the essence of Chinese medicinal materials, *daodi* medicinal material has been playing an important role in treating disease and preserving health for thousands of years. As an outcome of cultural heritage and natural resources, *daodi* medicinal material has undergone changes and development during the past millenia.

Although *daodi* medicinal material has long enjoyed a good reputation both in the medicinal industry and TCM clinical practice, its superior quality has not yet been adequately elucidated by modern science and technology. At present, adulterations in the market have seriously damaged the reputation of *daodi* medicinal material. Furthermore, lacking of scientific guidance to its production has a negative influence on the preservation and sustainable utilization of *daodi* medicinal material. The scientific community has realized the importance of systematic research on *daodi* medicinal material. Multidisciplinary measures have been adopted to explore scientific and practical methodology for the research of *daodi* medicinal material. The past 20 years’ research efforts and outcomes from 1980 have been summarized. It has been suggested future research should focus on the following aspects of *daodi* medicinal material: (1) the authentication of the species and production areas; (2) the establishment and implement of commercial specification criteria; and (3) standardized plantation and processing (Xiao et al., 2009). In February 2011, the 390th session of Xiangshan Science Conference discussed systematic studies of the attributes and contributing factors of *daodi* medicinal material. According to this conference, the following 3 aspects should be reinforced in the future research: (1) the application of quantitative genetics methods to explore the genetic basis of medicinal material in order to reveal the molecular mechanism of the formation of *daodi* medicinal material; (2) the application of omics and systems biology to elucidate the contributing factors of *daodi* medicinal material; (3) the application of geographic authentication and protection of the intellectual property rights of *daodi* medicinal material based on its biological, chemical and pharmacological features (Pan, 2011).

Recently, research on *daodi* medicinal material has been listed as one of the key projects sponsored by the national natural science foundation of China and the above-mentioned research efforts are in progress. Nevertheless, clarifying the concept and understanding the formation as well as historical changes of *daodi* medicinal material are prerequisites for its further research.

**Acknowledgments**

Some photographs were kindly provided by Dr. Hubiao Chen and further processed by Ms. Lailai Wong.

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