Review Article

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Rhizoma polygonati from Mount Tai: nutritional value and usefulness as a traditional Chinese medicine, source of herbzyme, and potential remediating agent for COVID-19 and chronic and hidden hunger

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Abstract

Recently, traditional Chinese medicine-based treatment has succeeded in fighting coronavirus disease 2019 (COVID-19), and *Rhizoma polygonati* (Huangjing) has been one of the recommended components. Its processed products play antidiabetic, antiviral, antitumor, antioxidation, antifatigue, antiaging, and immune enhancement roles. The climate in Mount Tai is mild, and the dense forest is suitable for the growth of *Rhizome polygonati,* which has gradually evolved into a unique specie. Considering the important medicinal value and pleasant taste of Mount Tai-*Rhizoma polygonati,* various healthy and functional food products, controlled by quality markers with anti-COVID-19 potential, as well as emergency foods can be developed. The study aimed to review current evidence on the nutritional value of *Rhizoma polygonati* from Mount Tai and its usefulness as a traditional Chinese medicine, source of herbzyme, and potential remediating agent for COVID-19 and food shortage. Most recent findings regarding herbal nanomedicine have revealed that nanoscale chemical compounds are potentially efficient in drug delivery or nanozyme catalysis upon bioprocessing. Nanoflower structure is found in processed *Rhizoma polygonati* by self-assembly and has wide application in enzymatic events, particularly nanoscale herbzyme. The novel findings regarding Mount *Tai-Rhizoma polygonati* could enhance its novel applications in chronic and hidden hunger, clinical nanomedicine, and as an anti-COVID-19 agent.

Keywords: Chemical composition, Coronavirus disease 2019, Pharmacology, *Rhizome polygonati*

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1 Introduction

The recent outbreak of coronavirus disease 2019 (COVID-19) has culminated in a global pandemic, while traditional Chinese medicine, including *Rhizome polygonati* (Huangjing), has demonstrated efficacy in patient recovery. Over 60 varieties exist worldwide, with approximately half in China. There are different types of Huangjing, such as *Rhizome polygonati*, *Many-flower polygonati*, and *Dian rhizome polygonati*. *Dian rhizome polygonati* is distributed in Dali, Lijiang, and other areas in the western region of Yunnan Province. *Many-flower polygonati* is the dominant variety in the Jiuhua mountain area of Anhui and is related to named *Jiuhua rhizome polygonati*[1-2] In the Shandong province of Mount Tai, it is predominantly distributed in the mountainous areas of Tai'an, Culai, and Yimeng; however, its classification remains unclear as far as phylogenetic analysis is concerned. Mount Tai-*Rhizome polygonati* has the effects of invigorating *qi* and nourishing *yin*, strengthening the spleen, moisturizing the lungs, and benefiting the kidneys. It is used to treat a weak spleen and stomach, fatigue, dry lungs, cough diseases due to insufficient blood, and internal heat and thirst.

Mount Tai-*Rhizome polygonati* grows in shady slopes, stone walls, weeds, or rock gaps under trees. When rhizomes are administered as medicine, they have the effect of nourishing the spleen, lungs, *yin,and qi*. It is well-known as one of Mount Tai's four famous medicines with a long-recorded history[3-4]. Several legends and folktale stories exist regarding *Rhizome polygonati* use as an emergency and functional food due to its high content of polysaccharides and other nutrients. Moreover, recent nanotechnology has been applied to herbs, including *Rhizome polygonati,* in novel functional studies with the potential of wide application in future clinics. This study aimed to review current evidence on the nutritional value of *Rhizoma polygonati* from Mount Tai area, source of herbzyme its application as a traditional Chinese medicine, and potential remediating agent for COVID-19 and food shortage.

The literature review was performed by searching publications in PubMed, China National Knowledge Infrastructure, Google, Google scholar, Baidu. The most covered publications were from 2005 to 2020.

2 Cultivation of Mount Tai-Rhizome *polygonati*

Rhizome polygonati is a perennial herbaceous plant with the following characteristics: shade-loving, drought and cold resistance, poor adaptability, and strong habitat selectivity. Mount *Tai-Rhizome polygonati* is propagated using underground stems and seeds; however, the natural germination rate of its seeds is extremely low, which makes propagation under natural conditions mainly rely on underground stems[5]. The unique ecological habitat of Mount Tai-*Rhizome polygonati* renders the resource distribution sporadic, narrow, and scarce. Moreover, predatory mining and large-scale tourism cause the endangerment of wild resources and make resource recovery difficult. Sustained development brings heavy losses, and artificial cultivation techniques are required to increase production[6]. The flowering and fruiting periods of Mount *Tai-Rhizome polygonati, Many-flower polygonate,* and *Dian rhizome polygonati* are different[7].

The buds on the rhizome generally begin to germinate from October to November, and as the temperature decreases, the buds grow slowly and eventually stagnate[8-9]. In winter, Mount *Tai-Rhizome polygonati's* underground part dies and then germinates in the spring of the following year[8-9]. Under natural conditions, the seed germination rate of Mount *Tai-Rhizome Polygonati* is considerably low. Mount *Tai-Rhizome polygonati* seeds first form small bulbs, which differentiate into adventitious roots and buds, subsequently stay dormant for 30 to 40 d, and finally form seedlings. It is speculated that there are secondary dormancy phenomena, namely, seed dormancy and small bulb dormancy[9-10]. Studies have shown that seed dormancy can be overcome by refrigeration followed by 100 mg/L gibberellin treatment for 24 h[10]. Spring planting is the optimal planting time; nevertheless, it can also be planted in autumn from September to October[11]. For seed propagation, when the berries turn black in August, wet sand stratification should be immediately carried out[12-14].

Recent experiments have shown that wild Mount Tai-*Rhizome polygonati* can be reproduced using tissue culture in a Murashige and Skoog plant growth medium containing 4.0 mg/L 6-benzylaminopurine, 1.5 mg/L thidiazuron, and 1.0 mg/L 2,4-dichlorophenoxyacetic acid for proliferation, and the survival rate of transplanted test-tube seedlings after rooting can reach 90%[4]. Moreover, wild Mount Tai-*Rhizome polygonati* reproduction can be carried out by domestication using optimized soil and other environmental conditions[15-19] because the climate of Mount Tai experiences a significant vertical change, with the temperature at the base of the mountain averaging −3°C and peaking at −9°C in January and averaging 26°C and peaking at 18°C in July[19]. Annual precipitation increases with altitude, amounting to 1,132 mm at the mountain peak but only 22.6 mm at the bottom of the mountain[9] (Fig. 1) compared to that in other areas.

3 The natural products in Mount Tai-Rhizome *polygonati,* and nutritional values for potentially fighting chronic and hidden hunger

3.1 Trace elements

Trace elements are closely related to the following four properties of Chinese medicine: cold, cool, warm, and hot. Studies have discovered that Mount Tai-*Rhizome polygonati* is extremely rich in magnesium, iron, zinc, and calcium; however, the toxic presence of heavy metals such as Pb is significantly lower than that in fruits and satisfactorily safe[20-21]. Other elements of relatively high content include strontium, manganese, barium, boron, copper, titanium, cadmium, etc[20-21]. One study demonstrated that in an extract of Mount Tai-*Rhizome polygonate,* the first bench dissolution was approximately 30%, and the total dissolution of trace elements after leaching thrice was approximately 40%, suggesting the difficulty of dissolving all the trace elements[22-23]. The dissolution rate of Mg, Mn, Cr, Zn, Pb, and Fe is high, but rates of Cu and Ca are low[22-23]. Studies have shown that the actual potassium and sodium content in traditional Chinese medicine is similar to that in clinical drugs. However, that of other elements is quite different[22-23].

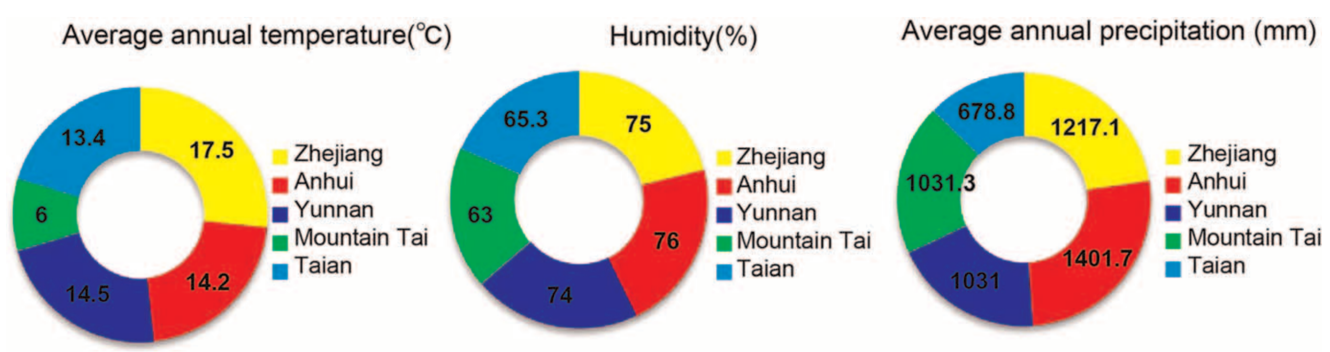

Figure 1. The average temperature, humidity, and precipitation of five different regions: Jinhua Zhejiang, Jiuhua Mountain Anhui, Kunming Yunnan, Mountain Tai, and Tai'an.

3.2 Natural products

Studies have demonstrated that the chemical constituents of Mount *Tai-Rhizome polygonati* mainly include polygonatum polysaccharides, steroidal saponins, anthraquinone compounds, alkaloids, lignin, vitamins, and a variety of useful amino acids and other compounds. Polygonatum polysaccharides are plant polysaccharides extracted from rhizomes, and they comprise the following three carbohydrates: glucose, mannose, and galacturonic acid in a ratio of 6:26:1, without obvious toxic side effects[24-25]. The component is affected by extraction time, times, and material-to-liquid ratio[26]. Studies have shown that it can inhibit the formation of hydroxyl radicals and liver homogenate lipid peroxidation with antioxidant effect[27]. The extraction methods included the use of a diethylaminoethyl cellulose-52 and Sepharose CL-6B column and hydrochloric acid deproteinization[28-30]. However, the large molecular weight of Polygonatum polysaccharides leads to poor water solubility, which is not conducive for absorption by organisms. Regarding function, it has been reported to reduce blood glucose levels[31] and fasting insulin levels in mice[32] or improving the symptoms, reducing hepatic cell steatosis, and improve myocardial fibrosis in diabetic rats[33-35]. Moreover, antiviral, antiaging, and anti-inflammatory effects as well as protection against chemical liver injury and improved immune response have been reported[36-39].

The aglycones of steroidal saponins, which are precursors of other saponins isolated from Polygonatum and *Dian rhizome polygonati,* vary considerably, especially diosgenin[40]. Li et al.[41] isolated six steroidal saponin compounds from *Dian rhizome polygonati,* which have anti-human immunodeficiency virus activity. Jin isolated 10 steroidal saponins from Hubei *Rhizome polygonati* and discovered that these compounds inhibit the proliferation of cervical cancer cells[42]. The volatile components of *Rhizome polygonati* mainly include furans, ketones, organic acids, olefins, alkanes, aldehydes, alcohols, and esters of which furans constitute the highest content[43]. *Rhizome polygonati* also contains 11 amino acids, including lysine[44]. In addition, a partial compound list is shown in Table 1.

Table 1

Partial and main chemical compounds in *Rhizoma polygonati* (https://www.symmap.org/detail/SMHB00185).

Compound name	Molecular formula	Molecular weight
Apigenin	$C_{15}H_{10}O_5$	270.25
Citral	$C_{10}H_{16}O$	152.26
Succinic acid	$C_4H_6O_4$	118.10
Beta-sitosterol	$C_{29}H_{50}O$	414.79
Diosgenin	$C_{27}H_{42}O_3$	414.69
Alpha-terpineol	$C_{10}H_{18}O$	152.31
Prunasin	$C_{14}H_{17}NO_6$	295.32
Isoliquiritigenin	$C_{15}H_{12}O_4$	256.27
Salicylic acid	$C_7H_6O_3$	138.13
Baicalein	$C_{15}H_{10}O_5$	270.25
Glucuronic acid	$C_6H_{10}O_7$	194.16
Liriodendrin	$C_{34}H_{46}O_{18}$	742.80
Neoliquiritin	$C_{21}H_{22}O_9$	418.43
Methylprotodioscin	$C_{52}H_{86}O_{22}$	1,063.38
Amygdalin	$C_{20}H_{27}NO_{11}$	457.429
Liensinine	$C_{37}H_{42}N_2O_6$	610.749
Neferine	$C_{38}H_{44}N_2O_6$	624.775
Higenamine	$C_{16}H_{17}NO_3$	271.32

3.3 Changes in chemical composition before and after processing: potential remediation of food shortages

Rhizome polygonati raw products reportedly can irritate the throat; thus, the plant needs to be processed to reduce potential discomfort. The pharmacological effects and effective ingredient content have been reported to change after processing[45]. With prolonged processing, the content of Polygonatum polysaccharides can be decreased[46-47]. Yang et al.[48] found that by simulating the "nine-times steamed and nine-times sun-dried" method during processing, the polysaccharide content in dried samples was reduced to approximately 12%. During the third steaming, the polysaccharide content of xanthine decreased to approximately 1%. Studies have shown that the polysaccharide content in raw *Rhizome polygonati* significantly decreased after processing, possibly owing to the conversion of monosaccharides[46-48]. However, the saponin content in xanthine was increased during the process. Yang et al.[48] discovered that the total-saponin content in *Rhizome polygonati* increased from 2% with "non-steaming" to approximately 14% after steaming for the fourth time, an increase of nearly seven times. Moreover, steroidal saponins produced secondary glycosides and aglycones after processing[49]. Additionally, 5-hydroxymethylglycolaldehyde levels increased, which relates to an immune system enhancement[50], whereas some essential-oil components, such as n-hexaldehyde, 1,7,7-trimethyltricycloheptane, camphene, 2-n-pentyl furan, and 4-diene, decreased[51]. The following oligosaccharides including D-sucrose, and raffinose, produced qualitative changes during processing and were hydrolyzed to their constituent monosaccharide or disaccharide[52-53]. Figure 2 summarizes the changes in chemical compounds during processing.

4 The pharmacological effects of Mount Tai-Rhizome *polygonati*

Several studies have reported the pharmacological effects of other types of *Rhizome polygonati,* such as antidiabetic, antiaging, blood-fat lowering, immune regulation, and infertility treatment functions, among others, though less prevalent in Mount Tai-*Rhizome polygonati.* Reference can be made to previously published reviews regarding other types of *Rhizome polygonati*[54]. The current study focused exclusively on Mount Tai-*Rhizome polygonati.*

4.1 Antiaging effect

A previous study demonstrated the function of Mount *Tai-Rhizome Polygonati* against lung cancer. In a study on urethane-induced lung cancer in mice, in which the mice were fed with Mount Tai-*Rhizome polygonati* by intragastric administration on eight occasions, lung adenocarcinoma was inhibited, thus enhancing the immunity of mice with lung cancer and improving their survival status[55].

4.2 Potential anti-inflammatory and antioxidant effects

Zhang et al.[55] discovered that in a mouse model of ear swelling/inflammation induced by xylene, Mount Tai-*Rhizome polygonati* could disrupt swelling, suggesting

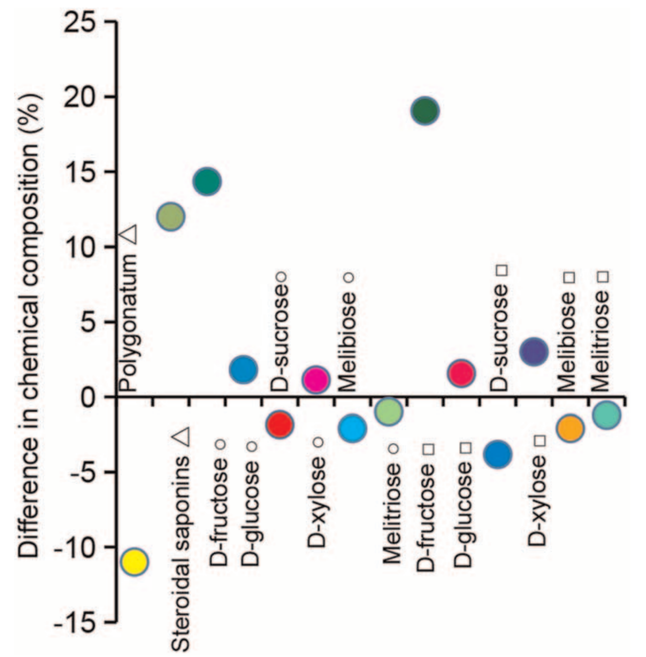

Figure 2. Differences in the chemical composition of *Rhizome polygonati* before and after processing (Δ –"nine-times steamed, nine-times sun-dried," ○-steamed, and □-stewed).

anti-inflammatory effects. Another study found that Mount *Tai-Rhizome polygonati* could significantly increase the thymus index in aging mice models and improve their immune function[56]. The researchers used D-galactose-induced-aging mouse models and found 30 g/kg of Mount Tai-*Rhizome polygonati* water extract, thus proving the plant's ability to significantly increase the superoxide dismutase content (oxidative defense system) and reduce the glutamate content in aging model mice[55]. Interestingly, in previous studies, 32 endophytic fungi with different colony morphology were isolated from the roots, stems, leaves, and fruits of wild Mount Tai-*Rhizome polygonati,* and the HJG3 extract had some antioxidant activity; however, the strains are yet to be identified[57-62]. Eleven endophytes were isolated from the wild *Rhizome polygonati* from Huangshan, including one species of the genus Bacillus[63-64]. The endophyte metabolite may also be used for antibacterial-induced inflammation or as an antioxidant by extraction of the chemical compound.

5 Medicinal values and drug development of Mount Tai-Rhizome *polygonati*

5.1 Chemical compounds in Mount Tai-Rhizome polygonati

The diosgenin content in Mount Tai-*Rhizome polygonati* is 0.19 mg/g[65-66], which is much higher than the average value of 0.0868 mg/g[67]. The diosgenin content may also be affected by different extraction methods. Studies have shown that the polysaccharide content of *Rhizome polygonati* in different geographical regions varies, and that in Mount Tai-*Rhizome polygonati* averages 13.19%[68-70]. In addition, Mount *Tai-Rhizome polygonati* is rich in various trace elements. According to previous reports[71-72], the content of iron, zinc, and magnesium in Mount Tai-*Rhizome polygonati* is as significantly high as that in food. Among these elements, zinc has a content of approximately 104.8 μg/g and magnesium that of 2,432.75 μg/g[71-72]. These elements play an important role in human metabolism.

5.2 Potent quality markers of Mount Tai-Rhizome Polygonati for medicinal values

Morphological and molecular markers are potentially useful in distinguishing the varieties. Therefore, these markers are widely used in *Rhizome polygonati* phylogenetic analysis and identification. Molecular markers, including restriction fragment length polymorphism, random amplified polymorphic DNA technology, simple-sequence repeat (SSR) markers, and other markers, are used in the morphological classification and traditional breeding of Polygonatum. Furthermore, DNA barcodes are mainly applied in classifying and identifying the systematic evolution of Polygonatum, genetic relationship, diversity analysis, etc[73-75]. Two molecular methods are commonly used, namely, DNA barcoding and molecular labeling, which are both applied to Polygonatum with universal Internal Transcribed Space 2 (ITS2) primers and DNA chips for a polymerase chain reaction, sequencing, and phylogenetic analysis[73-75]. Inter-SSR markers can effectively reveal the genetic diversity and accuracy of the genetic relationships among *Rhizome polygonati* species and can effectively distinguish the *Rhizome polygonati* species[76-79].

Rhizome polygonati is characterized by cold resistance and the affinity for a cool, wet environment. The Mount Tai area exhibits lower levels of humidity, average temperature, and average annual precipitation than other areas in which natural growth occurs (Fig. 1)[80-86]. In addition, the dense mountain forests in Mount Tai have natural geographical advantages for *Rhizome polygonati* plantations. The large-scale cultivation of Mount Tai-*Rhizome polygonati* may initially promote the development of the planting industry and increase farmers' income. Because *Rhizome polygonati* has important medicinal value, it can be directly processed into a Chinese medicinal decoction or an important ingredient of health products. Due to its sweet taste, it can be mixed with other nutrients to produce various nutritious food products.

5.3 Potential anti-COVID-19-drug development using Mount Tai-Rhizome polygonati

The recent COVID-19 pandemic has caused the large-scale infection, and traditional Chinese medicine has played essential roles in prevention, treatment, and recovery. *Rhizoma polygonati* has been used as a component in the complex receipt of more than 60% of anti-COVID-19 Chinese medicines, based on doctors' or official recommendations[87]. One example is that of the First Affiliated Hospital of Zhejiang University, as evidenced in a handbook of clinical treatment[88]. After rehabilitation and discharge during the recovery period, new coronary, lung, and spleen *qi* deficiency in patients are the main manifestations. Among many official recommendations for COVID-19 patients, *Rhizoma polygonati* use is included[89-91]. For example, for the recovery of lung fibrosis using traditional Chinese medicine to *qi* and phlegm, *qi* filling, and essence, the herbs of *Rhizoma polygonati,* Peach Kernel, Red Peony, Tangerine, and others are used to reduce fibrosis lesions and prevent further damage of lung function[90-91].

Recently, we reported the computer-based analysis of the molecular docking of potential *Rhizoma polygonati* chemical compounds in combating COVID-19 and identified certain high-ranked compounds which may bind to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) target proteins[92-93]. For example, (+)-syringaresinol-O-beta-D-glucoside potentially binds to the angiotensin-converting enzyme 2 (ACE2) of SARS-CoV-2, whereas diosgenin may bind to both ACE2 and RNA-dependent RNA polymerase based on calculation and computer modeling. All target genes of host cells are identified using computer modeling from the database[93]. Finally, in the future, relevant chemical compounds need to be identified to extract necessary drug-development chemicals.

5.4 Network pharmacology analysis of whole compounds in Rhizome polygonati suggesting the drug mechanisms

Network pharmacology has allowed us to identify all potential gene-protein-drug target networks and establish signaling pathways to explore specific disease targets. Using a traditional Chinese medicine database, we established a pharmacology network of *Rhizome polygonati* based on all current published and potential databases on compound analysis. The results demonstrated that *Rhizome polygonati* potentially target many kinases, including c-Jun, sarcoma, and mitogen-activated protein kinase, as well as the cell cycle and cell death (Fig. 3)[94-97]. Thus, to enhance the availability of the corresponding chemical compound for specific drug targets in precision medicine, environmental control of Mount Tai-*Rhizome polygonati* may be helpful.

5.5 Use of Mount Tai-Rhizome polygonati in nanomedicine: nanozymes and herbzyme

Nanotechnology has been applied in herbal medicine for efficient drug delivery, controlled release, and antibacterial infection[98]. Self-assembly can be achieved using natural products from herbs, and different chemical compounds have exhibited distinct assembly patterns[99]. We recently found that nanoscale Mount Tai-*Rhizome polygonati* extract can be self-assembled to form nanoflower after sun-dried and steam processing. The assembly is related to chemical compounds such as Polygonatum polysaccharides, based on computational modeling and calculation[100].

Moreover, nanoscale Mount Tai-*Rhizome polygonati* extract has nanozyme activity, including peptide digestion, related protease activity, and pH-dependent phosphatase activity. Although nanozymes have initially been considered to be metal nanoparticles, few studies have associated them with natural products, especially herbal particles[100]. The nanoparticles from Mount Tai-*Rhizome polygonati* extract are related to nanozyme activity under extreme pH conditions, suggesting the artificial enzymatic power that protein-based enzymes cannot exude[101] (Fig. 4). We proposed the term "herbzyme," which refers to a herb-derived natural nanozyme that has not undergone artificial synthesis or addition of metals. This would be a natural, green nanozyme.

In addition, at mild pH, nanoscale Mount Tai-*Rhizome polygonati* extract has exhibited biofuel- and phosphatase-enhancing functions by catalyzing the breakdown of p-nitrophenyl glucopyranoside to p-nitrophenol[102], which is consistent with our finding in which enzyme

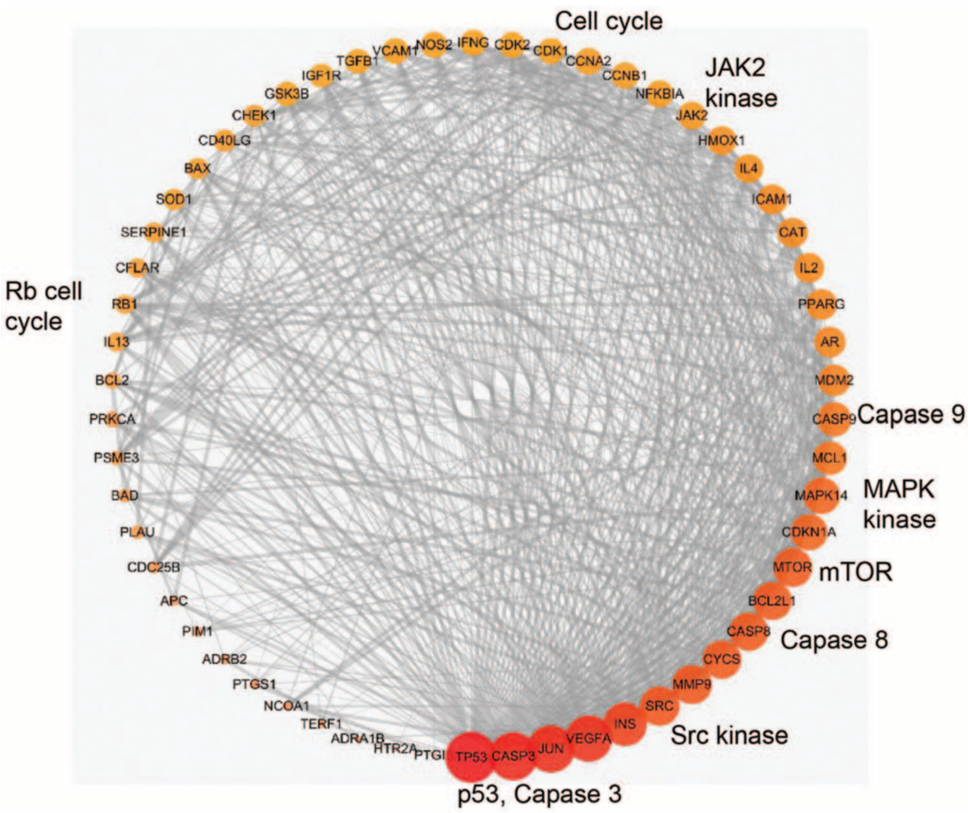

Figure 3. Pharmacology network of *Rhizome polygonati* based on all current published and potential databases on compound analysis. The network was established by TCMSP, Swiss Target Prediction databases, STRING database, and Cytoscape 3.7.2, without oral bioavailability or DL cutoff values, considering advanced potential drug delivery. DL: Drug-like; TCMSP: Traditional Chinese Medicine Systems Pharmacology.

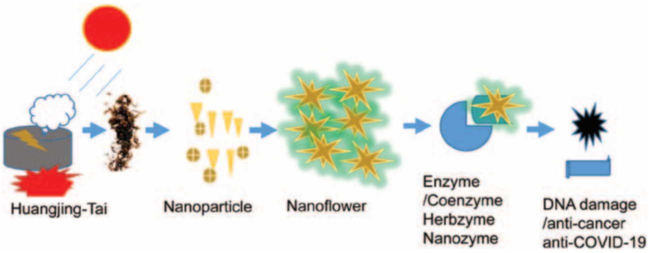

Figure 4. Flow chart for the mediated herbzyme production process using Mount *Tai-Rhizome polygonati* and other herbs. Nanoflower may be formed by self-assembly.

activity with cofactor or coenzyme potential was observed. This might have been due to the nanoparticle surface effect or other unknown effects.

6 Conclusions and future perspective

In summary, Mount Tai-*Rhizome polygonati* is uniquely characterized by its prolific growth in the Mount Tai environment; richness in trace elements; and pharmacological functions, namely, its antiaging, anti-inflammatory, and potent antibacterial effects. In addition, its processed water extract s potential surface effect, nanozyme characteristics, and other novel functions may allow us to critically consider the multiple facets of traditional Chinese medicine from its energy storage during processing, based on the energy theory of matters, and potentially through mechanisms of quantum theory at an atomic scale. Thus, further nanoscale, or even smaller, materials should be investigated in herbs. Finally, our finding regarding herbzyme is a breakthrough for the application of the processing of Mount-Tai *Rhizome polygonati* as a carrier of natural compounds through the combination of Western and Eastern medicine in clinical application. Mount Tai-*Rhizome polygonati* may be potentially useful both as a therapy drug, in drug delivery, in clinical application, and as an edible plant food in emergencies due to its high content of polysaccharides and other nutrients. Importantly, classification using genome studies should be carried out in the future to completely understand the metabolism and phylogenetic evolution of different types. Recently, research has made progress in sequencing the completed chloroplast genome of *Polygonatum sibiricum,* which is 152,960 bp long, is AT-rich, and comprises 1 6 genes, 90 of which are protein-coding[103]. A close relationship between *P. sibiricum* and *Polygonatum cyrtonema* has been shown in phylogenetic trees[103]. Thus, in future, whole-genome sequencing may reveal further knowledge to enhance the application in medicine and food. In addition, the metabolism pathways are being revealed to show more evidence that modifications or gene editing of the genome which is ongoing being studied may potentially uncover the secrets and applications in fighting hunger and can provide the new clues to be used for new generations of nutritional food[104].

Conflicts of interest statement

Yingqiu Xie is the editorial board member of this journal. Yingqiu Xie received financial support for research and consulting and Qian Wang received wages from Shandong Taishanghuangjing Biotechnology Co. Ltd.

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Author contributions

Yingqiu Xie supervised, designed the project, wrote the paper and drew the summary figure; Lazzat Nurtay wrote the draft, drew the figures; Qinglei Sun provided consulting, revision and comments; Zhongshan Cao and Cuiping Ma organized network pharmacology data; Qian Wang provided consulting, and comments; Chenglin Mu provided the figure of network pharmacology; Zongsuo Liang provided consulting, supervising, and comments; Amr Amin provided consulting, supervising and comments; Xugang Li provided revising, supervising and comments.

Ethical approval of studies and informed consent

Not applicable.

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References

[1] Le G, Wu PP, Chen LS. Research progress of high-yield cultivation techniques of Jiuhua *Rhizome polygonati*. *Anhui Sci Technol* 2013;26 (11):24–26.
[2] Chen XR, Chen L, Ma ZM. The medicinal value and development of Dian Rhizome polygonati. *Med Herald* 2003;22 (4):261–263.
[3] Wang GH, Wang Q, Shi YL. Taishan four famous medicines. *Shandong J Tradit Chin Med* 2006;25 (3):203–204.
[4] Mu XL, Zhang LM, Yang SX, et al. Study on tissue culture and rapid propagation technology of Taishan wild Rhizome polygonati. *Shandong Agric Sci* 2010;48 (1):12–13.
[5] Tian QJ, Zhao Z, Gu FG. Study on the phenological period of cultivated Rhizome polygonati. *Chin Med Mater* 2010;33 (2):168–169.
[6] Tian QJ, Zhao Z, Gu FG. Research on Rhizome polygonati cultivation technology. *Hubei Agric Sci* 2011;50 (4):772–776.
[7] Li ST, Kong Q, Che Y, et al. Study on resource distribution and applied cultivation of Taishan Rhizome polygonati. *China For Ind* 2016;7:115.
[8] Gong JH, Bi YW, Yang YH, et al. Study on the growth and development characteristics of rhizome winter buds in Taishan area. *Shandong Agric Sci* 2010;48 (1):43–44.
[9] Zong Y. Study on germination characteristics of rhizome of Taishan Rhizome polygonati. *Anhui Agric Sci Bull* 2009;15 (23):171–172.
[10] Sun WS, Chen WX, Zhu LX, et al. Effects of low temperature and gibberellin on germination characteristics of Taishan Rhizome polygonati seeds. *Shandong Agric Sci* 2019;51 (11):64–67.
[11] Gu ZW. Advances in research of cultivation techniques of Rhizome polygonati. *Qilu Pharm Aff* 2012;31 (6):358–359.
[12] Li S, Guo XJ, Su SX, et al. Study on high-yield and high-efficiency cultivation techniques of wild varieties of Rhizome polygonati. *China J Chin Mater Med* 1997;7 (22):398–401.
[13] Bi YW, Gong JH, Yang YH. Study on comprehensive cultivation techniques of Taishan Rhizome polygonati. *Chinese Agric Sci Bull* 2005;51 (12):280–282.

[14] Zhao Z, Pang YX, Yuan Y, et al. Advances in research on cultivation of medicinal plant Rhizome polygonati and several key issues in cultivation. *Guizhou Agric Sci* 2005;34 (1):85–86.
[15] Zhang Z. Taishan Rhizome polygonati and its high-yield cultivation. *Chin Local Prod* 1996;13 (6):11.
[16] Tian QJ, Zhao Z, Gu FG. Study on the phenological period of cultivated Polygonatum. *Chin Med Mater* 2010;33 (2):168–170.
[17] Yang J. Overview of the significance of introduction and domestication of medicinal plants. *World Latest Med Inform Dig* 2016;16 (A2):26–27.
[18] Zhang P. Artificial cultivation techniques of Taishan Rhizome polygonati. *Shandong Forest Sci Technol* 2002;32 (5):28–29.
[19] Li ST, Fan LG, Gao LX, et al. Habitat investigation and introduction of wild Rhizome polygonati from Taishan. *Spec Econ Anim Plants* 2016;19 (10):39–40.
[20] Yang ZX, Shi YL, Zhang ZY, et al. Study on the dissolution rate of some trace elements in the decoction of Taishan Rhizome polygonati Salvia miltiorrhiza Bupleurum bambusa. *Trace Elem Health Res* 1996;4:33–34.
[21] Zhang L, Xia ZL. Analysis and determination of trace elements in Taishan Rhizome polygonati. *China Med Herald* 2007;26:105–106.
[22] Lu JR, Li Z, Wu RT, et al. Study on the dissolution law of trace metal elements in Taishan Rhizome polygonati. *Food Sci Technol* 2006;25 (9):96–99.
[23] Wang SD, Song BS, Jin YL, et al. Analysis of trace elements and amino acids in rhizoma rhizome and fibrous roots. *Chin Pat Med* 2001;24 (5):59–60.
[24] Xu BB, Yu YJ, Wu F, et al. Review on the research of polysaccharides from rhizoma rhizome. *China Wild Plant Resour* 2015;34 (4):38–41. 46.
[25] Pang YX, Zhao Z, Yuan Y, et al. The chemical composition and pharmacological effect of rhizoma rhizome. *J Mt Agric Biol* 2003;11 (6):547–550.
[26] Gong JN, Yun CY, Wu J, et al. Study on extraction optimization and antioxidant activity of Polygonatum polysaccharide. *J Guizhou Norm Univ* 2019;37 (3):18–23.
[27] Yuan LR, Ye YL. Study on anti-oxidation effect of Polygonatum polysaccharide in vitro. *Strait Pharm* 2020;32 (2):18–21.
[28] Wang Y, Dong P, Jin CZ, et al. Composition of Polygonatum sibiricum polysaccharide and analysis of its antioxidant activity. *Genom Appl Biol* 2019;38 (5):2191–2199.
[29] Fang HL, Li XM, Li QQ, et al. Study on extraction of Polygonatum polysaccharide and its antioxidant effect. *Biochem Ind* 2018;4 (3):11–15.
[30] He XM, Li C, Li YZ, et al. Determination of Polygonatum sibiricum polysaccharide from different producing areas and study on its antioxidant activity in vitro. *J West Anhui Univ* 2018;34 (5):89–92.
[31] Wang QL, Tong XH, Li XD, et al. Effect of Polygonatum polysaccharide on STZ-induced type I diabetic mice. *J Yunnan Coll Tradit Chin Med* 2019;42 (1):1–7.
[32] Jia L, Shi J, Duan ZQ, et al. Effect of Polygonatum polysaccharide on glucose metabolism function in diabetic mice induced by high fat feed. *China Med Herald* 2017;14 (8):24–28.
[33] Wang Y, Peng GQ, Jiang XQ, et al. Study on the protective mechanism of Huangjing polysaccharide on diabetic rat model. *Chin Med Herald* 2017;23 (2):8–16.
[34] Zhang ZY, Wang GX, Chen TT, et al. Effect of rhizoma rhizome polysaccharide on myocardial fibrosis in diabetic rats. *China Pub Health* 2016;32 (6):807–810.
[35] Zhao HL, Xu Y, Zhao HY, et al. Effect of Polygonatum polysaccharide on the expression of SREBP-1c and SCD-1 protein in type 2 diabetic rats. *Pharmacol Clin Chin Mater Med* 2015;31 (1):106–109.
[36] Yan WL, Pu Q, Meng YW. Preparation of two polysaccharide derivatives of polygonatum and comparison of their antiviral activities. *Nat Prod Res Develop* 2000;5:60–65.
[37] Shi L, Meng YW, Li W. Pharmacological study of rhizoma rhizome and rhizoma rhizome polysaccharide. *Nat Prod Res Develop* 1999;3:67–71.
[38] Liu N. Study on the isolation, identification and immunomodulatory effect of Polygonatum polysaccharide. Shandong: Shandong Univ; 2017.
[39] Ye SF. Effects of rhizoma rhizome polysaccharide on thymus index, spleen index, T lymphocyte subsets and phagocytic function of exhausted exercise mice. *Genom Appl Biol* 2015;34 (1):60–65.
[40] Yang QX. Steroidal Saponins from Five Medicinal Liliaceous Plants. Diss, Kunming Kunming Institute of Botany. *Chinese Academy of Sciences* 1999.
[41] Li XC, Yang CR, Ichikawa M. Steroid saponins from Polygonatum kingianum. *Phytochemistry* 1992;31 (10):3559–3563.
[42] Jian JM. Chemical study on the composition of four lily cluster medicinal plants. Yunan: Kunming Inst Bot; 2003.
[43] Wang J, Yue YD, Tang F, et al. Analysis of volatile components before and after processing rhizoma rhizome. *China J Chin Mater Med* 2011;36 (16):2187–2191.
[44] Chen XR, Wang CJ, Li LX, et al. Advances in research on chemical constituents and pharmacology of Dian rhizoma rhizome. *Shi Zhen Natl Med* 2002;9:560–561.
[45] Zhang XX, Tang YT, Tang L, et al. Research progress of rhizoma rhizome's processing and quality analysis. *Mod Chin Doct* 2018;56 (22):165–168.
[46] Feng WS. Effect of Processing on Polysaccharide Content in Rhizoma Rhizome. Proceedings of the National Symposium on Research and Application of Polysaccharide Drugs of the Chinese Pharmaceutical Association. 2008;Professional Committee of Biochemical and Biotechnology Medicines of Chinese Pharmaceutical Association: Chinese Pharmaceutical Association, 44-147.
[47] Wang XD, Tian F, Shi GY, et al. Comparison of polysaccharide content in rhizoma rhizome from different places. *J Taishan Med Coll* 2008;9:657–658.
[48] Yang SX, Yang ZM, Chen YJ, et al. Changes of polysaccharide and saponin contents in rhizoma rhizome after "Nine Steamed Nine Made" process. *J Hunan Norm Univ* 2015;12 (5):141–144.
[49] Wang Q, Liu X, Xu M, et al. Study on the changes of steroidal saponins during the preparation of rhizoma rhizome. *Yunnan J Tradit Chin Med* 2017;38 (5):72–75.
[50] Zhong LY, Zhang Y, Huo HJ, et al. A Preliminary study on the changes of composition and drug effect of rhizoma rhizome before and after processing. *Chin Med Mater* 2011;34 (10):1508–1511.
[51] Wu QG, Hu YQ, Fan Z, et al. Research progress of the effect of processing on the chemical composition of rhizoma rhizome. *J Baotou Med Coll* 2018;34 (1):128–129. 133.
[52] Zhang YX, Zhou Q, Zhang XL, et al. Study on the changes and conversion mechanism of oligosaccharides and monosaccharides before and after rhizoma rhizome processing. *Chin Med Mater* 2020;2:318–322.
[53] Wang C, Song ZQ, Ning ZC, et al. Study on the Maillard reaction product of dichloromethane prepared by Huang Jing and its antioxidant activity. *Chin Herb Med* 2019;50 (3):604–610.
[54] Zhao P, Zhao C, Li X, et al. The genus Polygonatum: a review of ethnopharmacology, phytochemistry and pharmacology. *J Ethnopharmacol* 2018;214:274–291.
[55] Zhang C, Wei CF, Jia FL, et al. Study on Taishan rhizoma rhizome's effect on urethane-induced lung cancer and anti-inflammatory in mice. *J Taishan Univ* 2013;35 (3):113–116.
[56] Qi B, Ding T, Chang ZY, et al. Anti-aging effects of Taishan rhizoma rhizome on D-galactose-induced aging mice. *Shi Zhen Natl Med* 2010;21 (7):1811–1812.
[57] Li YL, Wang DC, Shi RJ, et al. Isolation, identification and antibacterial activity of endophytic fungi from Taishan rhizoma rhizome. *Chin Herb Med* 2013;44 (11):1490–1494.
[58] Yang HY, Huang QL, Liu ZL, et al. Isolation of an endophytic fungus from Taishan rhizoma rhizome and a preliminary study on its antioxidant activity. *J Taishan Med Coll* 2017;38 (10):1081–1083.
[59] Guo LD. Research progress of endophyte. *Mycobact Syst* 2017;38 (10):1081–1083.
[60] Wang YF. Research progress of plant endophytes. *Mod Hortic* 2019;11:23–24.
[61] Jiao R, He PF, Wang G, et al. Study on colonization ability of endophyte YN201728 and its effect of controlling tobacco powdery mildew. *J Nucl Agric* 2020;34 (4):721–728.
[62] Lan Q, Ji ZQ, Gu AG, et al. Preliminary study on insecticidal and bactericidal active substances in endophytic fungi of bitter vine. *J Northwest A & F Univ* 2004;10:79–84.
[63] Bai XH, Liu XL, Liu D, et al. Isolation, identification and antibacterial activity of an endophyte from rhizoma rhizome. *Nat Prod Res Develop* 2018;30 (5):777–782.
[64] Chi HR, Zhang YH, Zeng X, et al. Isolation, identification and antibacterial and promoting effects of endophytic bacillus Polygonatum. *Plant Protect* 2019;45 (4):122–131.

[65] Jiang CX, Zhang TJ, Chen CQ, et al. Research progress of rhizoma rhizome and prediction analysis of its quality markers. *Chin Herb Med* 2017;48 (1):1–16.

[66] Bi YW, Yang YH, Gong JH, et al. Determination of polysaccharide and diosgenin in rhizoma rhizome and Polygonatum. *J Changchun Univ Tradit Chin Med* 2010;26 (5):649–650.

[67] Zhou BZ. Study on the content of diosgenin in Dioscorea zingiberensis from different places. *Shanxi Agric Sci* 2017;63 (8):42–45.

[68] Li L, Tian LN, Ren ZX, et al. Research progress of structure analysis and functional activity of Polygonatum polysaccharide. *Chin J Exp Pharmacol* 2015;21 (15):231–234.

[69] Gao HL, Qu XL, Su YY. Ultrasonic extraction and content determination of polysaccharide in Taishan rhizoma rhizome. *J Taishan Med Coll* 2006;27 (2):151–152.

[70] Zhu YW, Zhu L, Chen QS. The Chemical Composition, Pharmacological Effect and Product Development of Rhizoma Rhizome. Compilation of papers of the 6th National Conference on Integrated Chinese and Western Medicine Nutrition. Chongqing: Nutrition Committee of Chinese Society of Integrated Traditional Chinese and Western Medicine; 2015.

[71] Zhang L, Xia ZL. Analysis and determination of trace elements in Taishan rhizoma rhizome. *China Med Herald* 2007;4 (26):105–106.

[72] Zhang L. Principal component analysis of trace elements in rhizoma rhizome from different places. *Trace Elem Health Res* 2009;26 (6):19–21.

[73] Hollingsworth PM, Forrest LL, Spouge JL. A DNA barcode for land plant. *Proc Natl Acad Sci USA* 2009;106 (31):12794–12797.

[74] Chen S, Yao H, Han J, et al. Validation of the ITS2 region as a novel DNA barcode for identifying medicinal plant species. *PLoS One* 2010;5 (1):e8613.

[75] Jiao J, Huang WL, Bai ZQ, et al. DNA barcoding for the efficient and accurate identification of medicinal Polygonati rhizome in China. *PLoS One* 2018;13 (7):e0201015.

[76] Štorchová H, Olson MS. The architecture of the chloroplast PsbA-trnH non-coding region in angiosperms. *Plant Syst Evol* 2007;268:235–256.

[77] Zhang HM. ISSR analysis of genetic diversity of rhizoma rhizome germplasm resources in Anhui Province. Anhui: Anhui Agric Univ; 2013.

[78] Vijayan K. Inter simple sequence repeat (ISSR) polymorphism and its application in mulberry genome analysis. *Int J Indust Entomol* 2005;2 (10):79–865.

[79] Jiao J, Jia XR, Liu P, et al. Species identification of Polygonati rhizoma in China by both morphological and molecular marker methods. *Plant Biol Pathol* 2018;341:102–110.

[80] Bi YW, Gong JH, Yang YH. The medicinal value and cultivation techniques of Taishan rhizoma rhizome. *Anhui Agric Bull* 2006;8:86–87.

[81] Bi YW, Gong JH, Yang YH. Research on artificial cultivation techniques of Taishan rhizoma rhizome. *Chin Med Res Inform* 2005;7 (9):33–36.

[82] Wang XJ, Zhu WH, Wang XL. Analysis on the meteorological features of fog weather in Mount Jiuhua. *J Anhui Agric Sci* 2012;40 (15):8655–8755.

[83] Sun J, Feng J, Duan W. Change in the urban heat island effect in Kunming. *Clim Environ Res (in Chinese)* 2015;20 (6):645–653.

[84] Zhejiang Meteorological Bureau. Available from: http://zj.cma.gov.cn/. Accessed 15 March, 2020.

[85] Tai'an Municipal Government. Available from: http://sd.cma.gov.cn/gslb/tasqxj/qxfw/. 2019. Accessed 15 April, 2020.

[86] Zhang Y, Yin HM. Comparative analysis on climate characteristics of Mountain Tai in Tai'an city. *Environ Sustain Develop* 2016;41 (5):217–219.

[87] Yang W, Liu M. Xinhua Polygonatum Becomes the "Loudi Element" to Help Fight the Epidemic. Sina.com. Available from: https://k.sina.com.cn/article_2687386043_a02e41bb02000rw26.html.from=news&subch=onews. Accessed 24 March, 2020.

[88] Zhejiang University - Handbook of COVID-19 Prevention and Treatment. Available from: https://video-intl.alicdn.com. Accessed 18 March, 2020.

[89] Chinese Forestry Society. Forest Medicinal Materials Play an Important Role in Fighting the Epidemic. Available from: http://www.csf.org.cn/News/noticeDetail.aspx?aid=48267. Accessed 17 April, 2020.

[90] Notice of Qingdao Municipal Health Commission on Issuing the " Guiding Opinions of Qingdao New Coronary Pneumonia Experts on Traditional Chinese Medicine Health Management." Available from: http://wsjkw.qingdao.gov.cn/n28356065/n32563120/n32563123/n32563126/200229124856749143.html. Accessed 28 February, 2020.

[91] Tongji Hospital of Huazhong University of Science and Technology. Five TCM coups for home rehabilitation of patients with new coronary pneumonia. Available from: https://www.hubei.gov.cn/zhuanti/2020/gzxxgzbd/fkkp/202003/t20200310_2177544.shtml. Accessed 10 March, 2020.

[92] Mu CL, Sheng YF, Wang Q, et al. Potential compound from herbal food of rhizoma polygonati for treatment of COVID-19 analyzed by network pharmacology and molecular docking technology. *J Funct Foods* 2021;77:104149.

[93] Mu CL, Sheng YF, Wang Q, et al. Dataset of potential Rhizoma polygonati compound-druggable targets and partial pharmacokinetics for treatment of COVID-19. *Data Brief* 2020;33:106475.

[94] Ru JL, Li P, Wang J, et al. TCMSP: a database of systems pharmacology for drug discovery from herbal medicines. *J Cheminform* 2014;6:13.

[95] Daina A, Michielin O, Zoete V. SwissTargetPrediction: updated data and new features for efficient prediction of protein targets of small molecules. *Nucleic Acids Res* 2019;47 (W1):W357–W364.

[96] Szklarczyk D, Gable AL, Lyon D, et al. STRING v11: protein-protein association networks with increased coverage, supporting functional discovery in genome-wide experimental datasets. *Nucleic Acids Res* 2019;47 (D1):D607–D613.

[97] Shannon P, Markiel A, Ozier O, et al. Cytoscape: a software environment for integrated models of biomolecular interaction networks. *Genome Res* 2003;13 (11):2498–2504.

[98] Dai L, Liu K, Si C, et al. Ginsenoside nanoparticle: a new green drug delivery system. *J Mater Chem B* 2016;4 (3):529–538.

[99] Li T, Wang P, Guo W, et al. Natural berberine-based chinese herb medicine assembled nanostructures with modified antibacterial application. *ACS Nano* 2019;13 (6):6770–6781.

[100] Gao L, Zhuang J, Nie L, et al. Intrinsic peroxidase-like activity of ferromagnetic nanoparticles. *Nat Nanotechnol* 2007;2 (9):577–583.

[101] Benassi E, Fan HY, Sun QL, et al. Generation of particle assemblies mimicking enzymatic activity by processing of herbal food: the case of rhizoma polygonati and other natural ingredients in traditional Chinese medicine. *Nanoscale Adv* 2021;3 (8):2222–2235.

[102] Kabulova A, Razbekova M, Xie YQ, et al. Nanoscale Huangjing extract from Mount Tai displays enzyme and biofuel enhancing activity: Potential in precision anti-cancer therapy [abstract]. *Cancer Res* 2020;80 (16.):

[103] Pan J, Lu W, Chen S, et al. Characterization of the complete chloroplast genome of Polygonatum sibiricum (Liliaceae), a wellknown herb to China. *Mitochondrial DNA B Resour* 2020;5 (1):528–529.

[104] Chen D, Han Z, Si J. Huangjing (Polygonati rhizoma) is an emerging crop with great potential to fight chronic and hidden hunger. *Sci China Life Sci* 2021;17:1–3.

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