Nonsurgical treatment of chronic subdural hematoma with Chinese herbal medicine

A STROBE-compliant retrospective study

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Abstract
The aim of the study was to observe the efficacy of nonsurgical treatment with Chinese herbal medicine (CHM) for chronic subdural hematoma (CSDH). This study includes clinical results of a STROBE-compliant retrospective study.

Forty patients diagnosed with CSDH were recruited from outpatient. Different CHM prescriptions were dispensed for each patient based on syndrome differentiation until the patient had a stable neurologic condition for 2 weeks and/or CSDH completely resolved according to the computed tomography scan. Markwalder grading scale for neurologic symptoms and head computed tomography scan for hematoma volumes were performed before and after CHM treatment to evaluate efficacy.

Patients received uninterrupted CHM treatment for 2.81 ± 1.45 months (0.75–6 months). The hematoma volume significantly reduced from 73.49 ± 35.43 mL to 14.72 ± 15.94 mL (P < .001). The Markwalder grading scale scores of patients at the end of CHM treatment decreased significantly, from 1.3 ± 0.69 to 0.15 ± 0.36 (P < .001). Ninety percent of the patients showed >50% decrease in the hematoma volume and complete improvement in neurologic symptoms. The linear regression analysis suggested that change in hematoma was significantly related to the duration of CHM treatment (R² = 0.334; P < .001; Y = 25.03 + 11.91X). Leonurus heterophyllus Sweet (Yi-Mu-Cao, 90.5%), Semen persicae (Tao-Ren, 88.8%), and Acorus tatarinowii Schott (Shi-Chang-Pu, 86.2%) were the top 3 single Chinese herbs prescribed in CHM treatment.

The CHM treatment for CSDH based on syndrome differentiation with appropriate duration relieved neurologic symptoms quickly and promoted hematoma absorption effectively. It could be an effective nonsurgical therapy for CSDH.

Abbreviations: CHM = Chinese herbal medicine, CSDH = chronic subdural hematoma, CT = computed tomography, IL = interleukin, MGS = Markwalder grading scale, TCM = traditional Chinese medicine.

Keywords: Chinese herbal medicine, chronic subdural hematoma, Leonurus heterophyllus Sweet, nonsurgical treatment

1. Introduction
Chronic subdural hematoma (CSDH) is a common intracranial hemorrhagic disease, especially among the elderly population. It is an old blood collection between the cortical surface and the dura. The incidence of CSDH has increased as a result of an aging population and the increasing clinical use of anticoagulant and antiplatelet drugs. The incidence of CSDH is approximately 1 to 13 per 100,000 annually in the general population, while in people aged 80 years or older, the number rises up violently to 127.1 per 100,000.[1] Neurosurgical therapy is the current consensus on the treatment of radiologically confirmed CSDH. Surgical treatment of symptomatic CSDH can improve neurologic symptoms rapidly[2]; however, the high recurrence rate of about 25.6% in high-risk patients[3] is important to note. The mortality has increased from 11.1% to 13.5%[4] in surgically treated patients to 38.4%, independent of treatments, in patients aged 90 years or older.[5] Effective nonsurgical treatments are highly desirable owing to the high mortality and often complex medical problems in this age group. Though many studies have suggested agents including steroids, angiotensin-converting enzyme inhibitors, tranexamic acid, and atorvastatin as nonsurgical treatments for CSDH,[6–10] a clear evidence-based guideline is unavailable so far.

Chinese herbal medicine (CHM) and methods of arresting bleeding based on the traditional Chinese medicine (TCM) theory, such as improving blood circulation and arresting bleeding, benefiting qi and controlling blood, and warming meridians and arresting bleeding, have been used for treating hemorrhagic diseases for thousands of years and have an
indispensable important role in the adjuvant therapy of hemorrhagic diseases, including intracranial hemorrhage. Syndrome differentiation and treatment are the essence of TCM, and CHM treatment should be adjusted to fit individual clinical manifestations of patients, even if they may share the same medical diagnosis. To our best knowledge, few clinical data are available regarding the treatment of CSDH with CHM based on syndrome differentiation so far. The present study aimed to explore the short- and long-term efficacy of CHM treatment based on syndrome differentiation for CSDH.

2. Methods

2.1. Patients

This was a single-center, retrospective, observational study of CSDH patients who received CHM treatment at outpatient of the Department of Traditional Chinese Medicine, Beijing Tiantan Hospital, Capital Medical University, between June 2016 and October 2018. Ethics approval (KY 2019-330-01) for the present study was obtained from the Ethics Committee of Beijing Tiantan Hospital, Capital Medical University, China. All patients provided informed consent for their clinical records to be used for research purposes before enrollment.

Patients who fulfilled the following inclusion criteria were enrolled continuously: age ≥18 and <90 years old; diagnosed with CSDH using head computed tomography (CT) scans or magnetic resonance imaging; neurosurgeon made a judgment that cerebral hernia would not occur and surgical operation might not be performed in a short time; conservative treatment was adopted. Patients who met any of the following conditions were excluded: known hypersensitivity to CHM; history of TCM operation; hematoma caused by tumors, blood, and other known comorbidities; abnormal liver function; dysfunction of coagulation; and history of oral or intravenous steroid treatment in the last 2 weeks.

2.2. CHM treatment

Two attending TCM physicians and an experienced chief TCM physician diagnosed the syndrome differentiation cooperatively in the light of the Diagnostics of Traditional Chinese Medicine. There were 5 common syndromes in patients with CSDH and about 2 to 4 syndromes in different patients. The diagnostic criteria for syndromes and corresponding herbs were listed in Supplemental Tables 1, http://links.lww.com/MD/E703, and 2, http://links.lww.com/MD/E704. Based on the aforementioned syndrome differentiation and fundamental prescriptions, Chinese herbal prescriptions were made up and adjusted for each patient and the prescription might be modified at regular outpatient visits about every 4 weeks. Chosen herbs of the prescription were boiled to produce decoction. The decoction of one set of herbs was filled the following inclusion criteria were satisfied according to CT scans and complete resolution of symptoms.

2.3. Efficacy evaluation

All patients underwent head CT scan before and after CHM treatment. CT examination was performed using 64-slice spiral CT scanners (Discovery CT750HD; GE Healthcare Technologies, Milwaukee, WI). The hematoma volume (in milliliters) was calculated from CT using 3D slicer 4.8.1, an open-source software platform for medical image processing (https://www.slicer.org).

Neurologic functions were evaluated using Markwalder grading scale (MGS) before and after CHM treatment. The efficacy of CHM treatment was evaluated as “completely improved,” “significantly improved,” “partially improved,” and “not improved” by changes in neurologic symptoms and hematoma volume as follows: completely improved: hematoma absorption sufficient according to CT scans and complete improvement in neurologic symptoms; significantly improved: decrease in the hematoma volume of >50% but <100%, and partial or complete improvement in neurologic symptoms; partially improved: decrease in the hematoma volume of <50% and partial improvement in neurologic symptoms; and not improved: increase in the hematoma volume or a new CSDH, with aggravated neurologic symptoms.

2.4. Statistical analysis

The statistical analysis was performed using SPSS 22.0 (International Business Machines Corporation, Chicago, IL). According to the last observation carried forward principle, missing data during the treatment period were replaced with the last available data. After the test of normality, data of changes in the hematoma volume and MGS before and after CHM treatment were analyzed using the paired-sample t test. A linear regression analysis was conducted to explore a correlation between length of CHM treatment and changes in the hematoma volume. A P value <.05 was considered to be statistically significant.

3. Results

3.1. Baseline characteristics of the study population

A total of 40 patients with CSDH, including 30 males and 10 females, were enrolled retrospectively in the current study. The mean age was 66.83 ± 14.6 years (27-86 years). Eighteen patients (18/40, 45%) had recurrent CSDH after neurosurgical treatment. The demographics and clinical characteristics were summarized in Supplemental Table 3, http://links.lww.com/MD/E705.

3.2. Frequency of Chinese herbs used in CHM treatment for CSDH

In this study, 116 TCM prescriptions were made up for patients with CSDH who received CHM treatment, and an average of 12.2 ± 0.12 (9–16) Chinese herbs was included in a single prescription. Leonurus heterophyllus Sweet (Yi-Mu-Cao, 90.3%) was the most frequently single Chinese herb prescribed for patients with CSDH, followed by Semen persicae (Tao-Ren, 88.8%) and Acorus tatarinowii Schott (Shi-Chang-Pu, 86.2%). Details of the top ten single Chinese herbs most commonly prescribed by TCM physicians are shown in Table 1.

3.3. Efficacy evaluation of CHM treatment for CSDH

The treatment was stopped when CSDH completely resolved according to the CT scan and/or patients were in a stable...
neurologic condition. In this study, patients received CHM treatment for 2.81 ± 1.45 months (0.75–6 months) without interruption. After CHM treatment, the volume of hematoma significantly reduced from 73.49 ± 35.43 (12.2–168.8) mL to 14.72 ± 15.94 (0–55.35) mL (P < .001) (Fig. 1). The neurologic symptoms of enrolled patients were headache, dizziness, vertigo, tinnitus, barylalia, poor memory, gait disturbance, and weakness of limbs. During CHM treatment, none of the enrolled patients were switched to surgery or suffered deteriorated neurologic symptoms. The MGS scores of patients at baseline were 1.3 ± 0.69 (0–2). Among all patients, neurologic symptoms improved prior to complete hematoma absorption. The MGS scores of patients at the end of CHM treatment decreased significantly to 0.15 ± 0.36 (0–1) (P < .001) (Fig. 2). For efficacy evaluation of CHM treatment, 15 patients (37.5%) were assigned to the grade of “completely improved,” 21 patients (52.5%) were “significantly improved,” and 4 patients (10%) were “partly improved.” The CT scan images before, during, and after CHM treatment of 2 patients, cases 3 and 39, with complete improvement are shown in Figure 3.

3.4. Linear regression analysis of length of CHM treatment and change in the hematoma volume

The linear regression analysis of length of CHM treatment and change in the hematoma volume showed that change in hematoma volume was significantly related to the duration of CHM treatment (R² = 0.334; P < .001; Y = 25.03 + 11.91X) (Fig. 4).

3.5. Safety assessment

During the course of TCM therapy, no significant changes in blood cell counts, hematologic and liver functions, and drug allergy reaction were reported. None of the patients switched to surgery.

4. Discussion

The prevalence of CSDH has increased worldwide due to an aging population and the increasing clinical use of anticoagulant and antiplatelet drugs. Neurosurgical therapy is the current

| Table 1 | Top 10 single Chinese herbs prescribed in Chinese herbal medicine treatment for patients with chronic subdural hematoma. |
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| Leonurus artemisia Sweet | Yi-Mi-Cao | 105 | 90.5% |
| Semen persicae | Tao-Ren | 103 | 88.8% |
| Acorus tatarinowii Schott | Shi-Chang-Pu | 100 | 86.2% |
| Flos carthami | Hong-Hua | 92 | 79.3% |
| Achyranthes bidentata Radix | Huai-Nu-Xi | 91 | 78.4% |
| Astragalus membranaceus | Huang-Qi | 82 | 70.7% |
| Chuanxiong rhizoma | Chuan-Xiong | 81 | 69.8% |
| Parás cocos | Fu-Ling | 74 | 63.8% |
| Atractylodes macrocephala Koidz | Bai-Zhu | 51 | 44.0% |
| Hirudo | Zhi-Shui-Zhi | 50 | 43.1% |

Figure 1. The hematoma volumes of chronic subdural hematoma (CSDH) patients reduced significantly after Chinese herbal medicine treatment.

Figure 2. The Markwalder grading scale (MGS) scores of chronic subdural hematoma (CSDH) patients decreased significantly after Chinese herbal medicine treatment.
consensus on the treatment of radiologically confirmed CSDH. However, neurosurgical therapy is not suitable for the whole CSDH population because of relatively high recurrence rates, high hospitalization costs, surgical contraindication, and heavy psychologic burden of operation. Hence, effective and low-cost nonsurgical treatments are highly desirable.

To our best knowledge, few clinical data are available regarding the treatment of CSDH with CHM based on syndrome differentiation. This preliminary retrospective study investigated the clinical efficacy of TCM treatment based on syndrome differentiation for CSDH. Forty patients with CSDH received CHM treatment based on syndrome differentiation for 2.81 ± 1.45 months (0.75–6 months) without interruption. The data showed that the hematoma volume and neurologic symptoms of these patients improved significantly. At the end of CHM treatment, the hematoma volume of all enrolled patients with CSDH decreased and neurologic symptoms improved significantly compared with the baseline. None of the patients switched to surgery. Ninety percent of the patients showed a decrease in the hematoma volume of >50% and complete improvement in neurologic symptoms. One of the advantages of TCM treatments based on syndrome differentiation is to relieve the current symptoms of patients and improve their quality of life. The current study showed that CHM treatment could improve neurologic symptoms of patients with CSDH much earlier than hematoma absorption. The MGS scores decreased significantly at the end of CHM treatment than at the beginning.

The formation mechanism of CSDH has historically been considered as a result of head trauma; however, emerging recent evidence suggests that more complex processes are involved. The development and recurrence of CSDH is associated with localized inflammation (CSDH membrane and fluid formation), angiogenesis (formation of new immature vessels) and fibrinolysis (clot breakdown). It is believed that inflammation plays a pivotal role in the development of CSDH. A range of inflammatory cells and cytokines, both the pro- and anti-inflammatory molecules, mediate the inflammation in CSDH in some pathways. High levels of cytokines and chemokines such as interleukin (IL)-6, IL-8, IL-10, tumor necrosis factor-α, monocyte chemoattractant protein-1, and eotaxin-3 have been shown in CSDH fluid compared with serum. Localized inflammation induces disruption of the endothelial cell barrier, resulting in formation of new immature and “leaky” vessels. The high level of fibrin/bibibrinogen degradation products found in the CSDH fluid is considered to represent excessive fibrinolysis (clot breakdown) and therefore persistent bleeding.

In the present study, there was an average of 12.2 ± 0.12 (9–16) Chinese herbs were included in a single prescription and L. heterophyllus Sweet (Yi-Mu-Cao, 90.5%) was the most
frequently single Chinese herb prescribed for patients with CSDH. *L heterophyllus* Sweet is a common clinical Chinese medicine, with the effect of activating blood circulation and regulating menstruation, inducing diuresis to alleviate edema, and clearing heat and detoxification, according to the Pharmacopoeia of the People’s Republic of China (2015). Stachydrine and leonurine, the major bioactive alkaloid ingredients of *L heterophyllus* Sweet, have been demonstrated to exert protective effect against traumatic brain injury and endothelial injury, anti-inflammatory, anti-oxidative, and anti-apoptotic effects in vivo and ex vivo.[25,22–27] The second and third most commonly single Chinese herb prescribed for patients with CSDH are *S persicae* (Tao-Ren, 88.8%) and *A tatarinowii* Schott (Shi-Chang-Pu, 86.2%). Amygdalin is an effective monomer component of *S persicae*, which has the effects of anticooagulation, anti-inflammation, antineoplastic, and antitumor.[28] Modern pharmacologic studies have shown that extract of *A tatarinowii* Schott has a variety of biologic activities, such as antioxidant, anti-Alzheimer disease, antimicrobial, anticonvulsive, and antiepileptic effects.[29] Nevertheless, there is little evidence about the potential mechanism of Chinese herbs for CSDH. The high proportions of *L heterophyllus* Sweet, *S persicae*, and *A tatarinowii* Schott which included in a single prescription suggested that they may play a crucial role in promoting CSDH absorption. The novelty of our research was that it provided an innovative idea for herb screening, and further clinical experiments and pharmacologic research on the nonsurgical treatment of CSDH using TCM and Chinese herbs.

The linear regression analysis of length of TCM treatment and change in the hematoma volume was performed to explore the correlation between them. Data showed that the change in hematoma was significantly related to the duration of TCM treatment. It is well known that Chinese herbal formulas are advantageous in body regulation.[30,31] It is believed that appropriate TCM treatment and sufficient duration can improve the microenvironment of the body, redress disequilibrium among qi, blood, yin, and yang, reduce the excess syndrome, reinforce the deficiency condition, and promote the hematoma absorption gradually. The harmonization of qi, blood, yin, and yang can further prevent hematoma recurrence. Although CSDH is a neurosurgical disease, the vast majority of patients are elderly, often complicated with a variety of basic diseases. Surgery is a great test for patients’ body and mind, and the higher recurrence rate of surgery further reduces the benefits of patients. Our study shows that CHM treatment for CSDH is low-risk, convenient, and may improve neurologic symptoms as well as promote of hematoma absorption, which will be a beneficial choice as nonsurgical therapy.

This was a preliminary exploratory study with some unavoidable limitations. First, patient selection bias was likely because this was a retrospective study and the patients in our study were enrolled at outpatient and generally with relatively mild station. Second, the study was conducted in a single center, which also consequently limited its generalizability. Third, the Chinese herb prescription and treatment period of the patients was not equalized and evaluated, but our study may be more representative of actual clinical conditions. So prospective, randomized, controlled, and multicenter clinical trials with equalized CHM treatment should be carried out to estimate the efficacy of CHM for CSDH in the future. A number of studies have identified the beneficial effects of CHM[31,32], however, the exact mechanisms of action of CHM are still mostly unknown.

5. Conclusion
Collectively, the present retrospective study preliminarily suggested that CHM treatment based on syndrome differentiation was an effective nonsurgical therapy for CSDH. CHM treatment could relieve neurologic symptoms quickly and promote hematoma absorption effectively with few recurrences. Change in the hematoma volume was significantly correlated with CHM duration, indicating that appropriate and sufficient CHM treatment length was necessary for a favorable clinical outcome. The high proportions of *L heterophyllus* Sweet, *S persicae*, and *A tatarinowii* Schott that included in a single prescription suggested that they may play a crucial role in promoting CSDH absorption. This study may provide a preliminary basis for further clinical studies with regard to CHM treatment as a nonsurgical therapy for some neurosurgical diseases, including CSDH.

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References
[1] Karibe H, Kameyama M, Kawase M, et al. Epidemiology of chronic subdural hematomas [in Japanese]. No Shinki Geka 2011;39:1149–53.
[2] Kolias AG, Chari A, Santarius T, et al. Chronic subdural haematoma: modern management and emerging therapies. Nat Rev Neurol 2014;10:570–8.
[3] Shimamura N, Ogawara Y, Naraoka M, et al. Irrigation with thrombin solution reduces recurrence of chronic subdural hematoma in high-risk patients: preliminary report. J Neurotrauma 2009;26:1929–33.
[4] Santarius T, Hutchinson P. Chronic subdural haematoma: time to rationalize treatment. Br J Neurosurg 2004;18:328–32.
[5] Lee L, Ker J, Ng HY, et al. Outcomes of chronic subdural hematoma drainage in nonagenarians and centenarians: a multicenter study. J Neurosurg 2016;124:546–51.
[6] Sun TF, Boet R, Poon WS. Non-surgical primary treatment of chronic subdural haematoma: preliminary results of using dexamethasone. Br J Neurosurg 2005;19:327–33.
[7] Wiegell R, Hohenstein A, Schicklum L, et al. Angiotensin converting enzyme inhibition for arterial hypertension reduces the risk of recurrence in patients with chronic subdural hematoma possibly by an antiangiogenic mechanism. Neurosurgery 2007;61:788–92.
[8] Kagayama H, Toyooka T, Tsuzuki N, et al. Nonsurgical treatment of chronic subdural hematoma with tranexamic acid. J Neurosurg 2013;119:332–7.
[9] Thotakura AK, Marabathina NR. Nonsurgical treatment of chronic subdural hematoma with steroids. World Neurosurg 2015;84:1968–72.
[10] Jiang R, Zhao S, Wang R, et al. Safety and efficacy of atorvastatin for chronic subdural hematoma in Chinese patients: a randomized clinical trial. JAMA Neurol 2018;75:1338–46.
[11] Xu JH, Huang YM, Ling W, et al. Wen Dan Decoction for hemorrhagic stroke and ischemic stroke. Complement Ther Med 2015;23:298–308.
[12] Sun M, Zhang JF, Shan JZ, et al. Clinical observation of Danhong injection (herbal TCM product from Radix Salviae miltiorrhizae and Flos Carthami tinctori) in the treatment of traumatic intracranial hematoma. Phytomedicine 2009;16:683–9.
[13] Chang CC, Lee YC, Lin CC, et al. Characteristics of traditional Chinese medicine usage in patients with stroke in Taiwan: a nationwide population-based study. J Ethnopharmacol 2016;186:311–21.
[14] Li P, Tang T, Liu T, et al. Systematic analysis of tRNA-derived small RNAs reveals novel potential therapeutic targets of traditional Chinese medicine (Buyang-Huanwu-Decoction) on intracerebral hemorrhage. Int J Biol Sci 2019;15:895–908.
[15] Zhu W. Diagnostics of traditional Chinese medicine: China press of traditional Chinese medicine; 2017;1:139–214.
[16] Edlmann E, Giorgi-Coll S, Whitfield PC, et al. Pathophysiology of chronic subdural haematoma: inflammation, angiogenesis and implications for pharmacotherapy. J Neuroinflammation 2017;14:108.
[17] Prati A, Salvati M, Mamiero F, et al. Inflammation markers and risk factors for recurrence in 35 patients with a posttraumatic chronic subdural hematoma: a prospective study. J Neurosurg 2004;100:24–32.
[18] Stanisic M, Lyngstadaas SP, Pripp AH, et al. Chemokines as markers of local inflammation and angiogenesis in patients with chronic subdural hematoma: a prospective study. Acta Neurochir (Wien) 2012;154:113–20.
[19] Osuka K, Watanabe Y, Usuda N, et al. Eotaxin-3 activates the Smad pathway through the transforming growth factor beta 1 in chronic subdural hematoma outer membranes. J Neurotrauma 2014;31:1451–6.
[20] Li T, Wang D, Tian Y, et al. Effects of atorvastatin on the inflammation regulation and elimination of subdural hematoma in rats. J Neurol Sci 2014;341:88–96.
[21] Wang D, Li T, Wei H, et al. Atorvastatin enhances angiogenesis to reduce subdural hematoma in a rat model. J Neurol Sci 2016;362:91–9.
[22] Loh KP, Qi J, Tan BK, et al. Leonurine protects middle cerebral artery occluded rats through antioxidant effect and regulation of mitochondrial function. Stroke 2010;41:2661–8.
[23] Yin J, Zhang ZW, Yu WJ, et al. Stachydrine, a major constituent of the Chinese herb Leonurus heterophyllus Sweet, ameliorates human umbilical vein endothelial cells injury induced by anoxia-reoxygenation. Am J Chin Med 2010;38:157–71.
[24] Liu H, Zhang X, Du Y, et al. Leonurine protects brain injury by increased activities of UCP4, SOD, CAT and Bcl-2, decreased levels of MDA and Bax, and ameliorated ultrastructure of mitochondria in experimental stroke. Brain Res 2012;1474:73–81.
[25] Ohtsu A, Tanaka H, Seno K, et al. Palmitic acid stimulates interleukin-8 via the TLR4/NF-κB/ROS pathway and induces mitochondrial dysfunction in bovine oviduct epithelial cells. Am J Reprod Immunol 2017;77:
[26] Qi J, Wang JJ, Duan JL, et al. Leonurine improves age-dependent impaired angiogenesis: possible involvement of mitochondrial function and HIF-1α dependent VEGF activation. Front Pharmacol 2017;8:284.
[27] Yu N, Hu S, Hao Z. Beneficial effect of stachydrine on the traumatic brain injury induced neurodegeneration by attenuating the expressions of Akt/mTOR/Pi3K and TLR4/NF-κB pathway. Transl Neurosci 2018;9:175–82.
[28] Zhang X, Hu J, Zhou Y, et al. Amygdalin improves microcirculatory disturbance and attenuates pancreatic fibrosis by regulating the expression of endothelin-1 and calcitonin gene-related peptide in rats. J Chin Med Assoc 2018;81:437–43.
[29] Gao F, Zhou ZQ, Zou J, et al. Bioactive asarone-derived phenylpropanoids from the rhizome of Acorus tatarinowii Schott. J Nat Prod 2017;80:2923–9.
[30] Xiong X, Yang X, Liu Y, et al. Chinese herbal formulas for treating hypertension in traditional Chinese medicine: perspective of modern science. Hypertens Res 2013;36:570–9.
[31] Liu R, He SL, Zhao YC, et al. Chinese herbal decoction based on syndrome differentiation as maintenance therapy in patients with extensive-stage small-cell lung cancer: an exploratory and small prospective cohort study. Evid Based Complement Alternat Med 2015;2015:601067.
[32] Wang S, Long S, Wu W. Application of traditional Chinese medicines as personalized therapy in human cancers. Am J Chin Med 2018;46:933–70.