Multi-elements characteristic and potential risk of heavy metals in MOUTAN CORTEX from Anhui Province, China

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Received: 20 August 2021 / Revised: 5 April 2022 / Accepted: 11 July 2022 / Published online: 6 August 2022
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Abstract
To ensure the quality and safety of herbs, the content of 54 elements in MOUTAN CORTEX (MC) was determined by the ICP-AES and ICP-MS, and the health risks of Cu, As, Cd, Pb, Hg and rare earth elements (REEs) were assessed. These herbs were collected from 5 producing areas in Anhui Province, China, namely Wuhu, Tongling, Bozhou, Xuancheng and Chizhou. The multi-elements fingerprint identification of MC in Anhui Province was established. The total amount of macro-elements from Wuhu and Tongling is significantly lower than Bozhou. Among all MC from 5 producing areas, the highest content is Ca. Except for Bozhou, the content of macro-elements and REES in the other 4 origins of MC is from highest to lowest: Ca > K > Mg > Al > Fe > Na and Ce > La > Nd > Y > Pr > Er > Yb > Eu > Ho > Th > Tm > Lu. The chemical forms of Cd in MC from Bozhou with the highest percentage were P_{H2O} of high toxicity and migration, while the other 4 regions were P_{NaCl} of low activity and mobility. There was a great difference in the content of inorganic elements and chemical forms of Cd between the MC produced from the plain (Bozhou) and the hilly areas (Wuhu, Tongling, Chizhou and Xuancheng). Except for Cd, the content of Cu, As, Pb and Hg in MC did not exceed the limit. The results of PTWI_{Fact} and ADI for Cd and REEs showed that MC herbs did not pose a risk to human health.

Keywords MOUTAN CORTEX (MC) · Element distribution · Producing area · Heavy metals · Cadmium · Risk assessment

Introduction
Chinese herbal medicines (CHMs) are a practical product of the treatment of diseases for thousands of years and a treasure of Chinese national culture. In particular, Lianhua Qingwen Capsule and other Chinese medicines have outstanding clinical efficacy in the fight against coronavirus disease 2019 (COVID-19) (Xiao et al. 2020), and CHMs have attracted more enthusiastic attention from people all over the world.

There are 12,807 kinds of CHMs in China, including 11,146 kinds of medicinal plants. The global herbal medicine market was worth 93.15 billion USD in 2015 and is estimated to grow to 5 trillion USD by 2050 (Zhao et al. 2014; Li et al. 2016; Rai et al. 2005). In recent decades, mining, sewage irrigation and fertilizer use are deteriorating the soil environment and heavy metals (Pb, As, Cr, Cd, Zn, Hg, Cu, Ni, etc.) accumulate in plants (Akram. et al. 2018; Tauqeer et al. 2022). Cases of heavy metals exceeding standard in CHMs often occur (Wang et al. 2019). In order to ensure the efficacy and safety of CHMs, the quality control of CHMs has become an urgent issue to be solved.

Previous researches were limited to using multiple index organic active ingredients to evaluate the quality of CHMs (Chinese Pharmacopeia Commission 2020; Wang et al. 2016). However, with the rapid development of inorganic chemistry and the continuous deepening of researches on pharmacological active substances of CHMs, it has found that inorganic elements are important components of plant secondary metabolites, which affect the quality and efficacy of CHMs (Guo et al. 2014). Cd in plants can interfere with Fe metabolism and reduce the availability of Fe in plants,
Promoting circulation and removing stasis (Chinese Pharmacopoeia Commission 2020). The annual output of MC in China is between 400 to 2500 tons (Lu et al. 2014), and some famous Chinese patent medicines (e.g., Liuwei Dihuang Wan, Jiawei Xiaoyao Wan and some famous Chinese patent medicines (e.g., Liuwei Dihuang Wan, Jiawei Xiaoyao Wan and Yiganning Keli) contain MC. The quality control research of MC has developed from the outward shape, color, smell and other appearance properties to its internal material basis. Presently, More researches have focused on the organic components of MC (paeonol, paeniflorin, total glycoside, polysaccharide, etc.), which play an essential role in pharmacological effects of lowering blood sugar, liver protection, analgesia and anti-inflammation and anti-tumor (Zhu et al. 2018; Saahene et al., 2018; Du et al. 2021; Pourmohammadi et al. 2022). However, the less research has been done on inorganic elements.

CHMs have regional characteristics. Herbs grown in specific regions have better clinical efficacy and are called Daodi herbs, while herbs produced in other regions also meet the efficacy requirements and they are also used in clinical practice. The Daodi herbs of MC are produced in Phoenix Mountain at the junction of Tongling and Wuhu in Anhui Province, commonly known as “Fengdanpi” (Peng et al. 2017; Pan 1989). By introducing seedlings, they are planted all over China. In order to explore the influence of environmental differences in the quality of MC herbs, an experiment with comprehensive information on the inorganic elements and the chemical forms of heavy metals in MC was conducted as follows: (1) revealing the distribution characteristic of macro-elements and trace elements in MC from different producing areas for origin tracing; (2) exploring the speciation of heavy metals in MC for understanding bioavailability; and (3) clarifying the potential health risks of consuming this herb. This research provides the basis for the safety evaluation, the identification of Daodi medicinal materials and more reasonable quality evaluation standard of MC.

Materials and methods

Reagents and instrument

All the reagents used in the experiment were Guaranteed Reagent (GR) grade, which were purchased from Sinopharm Chemical Reagents Co., LTD. Ultrapure water (resistivity > 18.2 Ω·cm) was prepared using the Milli-Q Synthesis Purification System (Merck Millipore, German). All glass containers were soaked in 10% HNO₃ for 12 h, boiled with 20% HNO₃ and then rinsed with ultrapure water repeatedly for use. The concentrations of macro-elements and trace elements in the samples were determined by ICP-AES (Thermo Fisher iCAP-6300-Duo, USA) and ICP-MS (Thermo Fisher ICP Q, USA) in Nanjing Center of China Geological Survey. All powder samples were treated with microwave digester (MDS-8G, Shanghai Xinyi Microwave Chemical Technology Co., Ltd, China). Water bath thermostatic oscillator (SHA-C, Changzhou Guoyu Instrument Manufacturing Co. LTD, China) and Centrifuge (Thermo Fisher MULTI-FUGE-X1R, USA) were used for chemical form extraction. The Certified Reference Material (CRM) Astragalus (GBW 10,028, GSB-19) was purchased from Institute of geophysical and geochemical exploration (Langfang, China) to verify the accuracy of the method.

Sample collection

In this research, 66 MC samples were collected from Tongling (Daodi-producing area), Wuhu (Daodi-producing area), Xuancheng, Chizhou and Bozhou (main producing area) in Anhui Province, China (Fig. 1) (Tongling and Wuhu each have 5 sampling sites, and the other 3 regions each have 4 sampling sites, and each sample site collected 3 batches of samples). The junction of Tongling and Wuhu is Phoenix Mountain which is the Daodi-producing area of MC. Tongling is located on the south bank of the Yangtze River (Tao et al. 2011). The landform of Tongling is mainly in...
low hilly areas. It is located in the middle latitude region and belongs to the subtropical humid monsoon climate, with abundant water and heat resources. Tongling is rich in mineral resources, with a copper mining history of more than 3000 years, and is an important non-ferrous metal smelting base in China (Ou et al. 1997). Wuhu, Xuancheng and Chizhou are hilly areas along the Yangtze River. Bozhou is located in Huaibei Plain, which belongs to the warm temperate semi-humid monsoon climate. Bozhou is the top of China’s four major medicinal materials production areas, and the planting area of medicinal materials has exceeded 666.7 km², accounting for about 1/10 of the planting area of medicinal materials in China. At present, most of MC herbs on the market come from Bozhou. *Paeonia suffruticosa* Andr. Can be excavated after 3–5 years of cultivation, and the roots are usually dug out from October to November. Wash, remove the fibrous roots, cut longitudinally with a knife, remove the wood core and dry to get the medicinal material of MC.

**Sample preparation**

After being washed with tap water and ultrapure water, all collected MC samples are dried in an oven at 40 °C to a constant weight. Next, broken into fine powder and passed through the No.5 sieve prescribed by the Chinese Pharmacopoeia (R40/3 series of National Standard) (Chinese Pharmacopoeia Commission 2020).

The 0.5 g MC sample was accurately weighed and poured into a Teflon digestion vessel, and then 8 mL of concentrated HNO₃ and 2 mL of concentrated H₂O₂ were added, mixed them well and left for 12 h. Cover the inner lid, place it in the microwave digestion instrument and digest it according to the set digestion program (S2). Each MC sample to be digested was parallel three times. Before the digestion solution is transferred to a 25 mL volumetric flask, it evaporates at 100 °C for about 30 min, then the digestion solution is volume fixed with ultrapure water to the scale line and shaken well for measurement. Blank control solution of reagent was prepared by the same method. In addition, a CRM *Astragalus* standard reference material (GBW 10,028, GSB-19) was digested and determined using the same method. The elemental concentrations of all MC samples and standard reference materials were determined using ICP-MS and ICP-AES.

**Extraction of Cd chemical forms**

The chemical forms of Cd were analyzed for all MC herbs from 5 producing areas. According to some optimized step-by-step extraction method designed by Zhao et al. (2015) and Xin et al. (2014) (Table 1), different chemical forms of Cd in MC samples were successfully obtained. Each CM sample was tested three times in parallel and blank at the same time.

The 2 g MC sample was accurately weighed and added to 20 mL ethanol and was vibrated at 30 °C on the oscillator for 24 h, then centrifuged at 5000×g for 10 min to obtain supernatant I. The precipitation was mixed with 20 mL ethanol again, vibrated for 4 h and centrifuged at 5000×g for 10 min to obtain supernatant II. The obtained precipitates were extracted step by step with other extractants (The extraction agents are ultrapure water, 1 mol/ L NaCl, 2% HAc and...
0.6 mol/L HCl). The supernatant I and II extracted at each step were mixed and dried at 80 °C to a constant weight. Added digestion solution (HNO3-to-H2O2 ratio: 4:1) and left for 12 h and digested it at 120–180 °C until it was clear and transparent, then kept the volume to 100 mL for testing. The following 4 extraction steps for supernatant digestion are the same. After the extraction steps were completed, the digestion method of the last step residues was the same as that of MC medicinal materials. The concentration of different chemical forms of Cd was determined by ICP-MS.

**Method validation**

ICP-AES and ICP-MS operating conditions, working parameters of Microwave Digester and standard solution preparation methods were presented in S2. The linear equation of the standard curve, the linear ranges, the LODs and the LOQs for each element are presented in S3. The correlation coefficients of 54 elements in the linear range are 0.99–1.000, which shows a good linear relationship and indicates a good linear relationship. The accuracy of the method was verified by A CRM Astragalus standard reference material (GBW 10,028, GSB-19). As shown in S4, the recovery rate is in the range of 80% (I) – 124% (Br), indicating that the measured value is close to the standard value. Meanwhile, the precision of the method was verified by calculating the relative standard deviation (RSD%) of the replicates. The value was less than 5%, indicating that the two instruments had good stability during the testing process.

**Risk assessment methods**

To assess the health risks of people who take MC regularly, we used the PTWI of Cd to evaluate potential adverse health effects. Calculation formula shows as follows (Zuo et al. 2016; Lei et al. 2015; Zhu et al. 2013):

\[
\text{PTWI} = \frac{\text{Ci} \times \text{IR} \times \text{ED}}{\text{BW}}
\]

In the above formulas, PTWI is the tolerable weekly intake per kilogram of body weight (ug.kg⁻¹). Ci is the average metal concentration in the MC (mg.kg⁻¹), IR is the maximum dose of CHMs intake for an adult prescribed by the Chinese Pharmacopoeia 2020 (g.person⁻¹.day⁻¹) (Chinese Pharmacopoeia Commission 2020), BW represents the average adult weight, which is 62.5 kg (Lei et al. 2015). MC cannot be used for a long time, and general clinical medication is stopped after seven consecutive days. ED is the exposure cycle (7d). The limit for Cd is 0.6 mg.kg⁻¹ (specified by WHO) (Zuo et al. 2016; Geneva: Joint FAO/WHO Expert Committee on Food Additives 2010).

To assess the risk of rare earth elements (REEs) in MC to human health, the health risk method recommended by the United States Environmental Protection Agency (USEPA) was used, and the calculation model is as follows (Yuan et al. 2019):

\[
\text{ADI} = \frac{\text{Ci} \times \text{IR} \times \text{EF} \times \text{ED}}{\text{BW} \times \text{AT}}
\]

ADI is the lifetime average daily pollutant intake (mg.kg⁻¹.d⁻¹), and Ci is the concentration of REEs in the MC (mg.kg⁻¹), IR is the daily intake (kg.d⁻¹), EF is the exposure frequency (90 d.a⁻¹) (Zuo et al. 2016), ED is the exposure cycle (70 a), BW is the body weight, and the standard body weight (62.5 kg) is generally adopted. AT is lifetime time (365 × 70 d) (Li et al. 2013a, b).

**Table 1** Method for extracting chemical forms of Cd

| Extraction step | Chemical form                        | Extracting agent | Extracted substance | Digestion conditions |
|-----------------|-------------------------------------|------------------|---------------------|----------------------|
| 1               | Inorganic (PEtOH)                   | 80% ethanol      | Inorganic metals giving priority to nitrate, chloride and aminophenol metals | HNO₃-to-H₂O₂ ratio: 4:1 |
| 2               | Water-soluble (PW₂O)                | Ultrapure water  | Water-soluble metals associated with organic acids and M(H₂PO₄)₂ | HNO₃-to-H₂O₂ ratio: 4:1 |
| 3               | Pectate and protein-integrated (PSA₃)| 1 mol/L NaCl     | Pectate and protein-integrated metals | HNO₃-to-H₂O₂ ratio: 4:1 |
| 4               | Insoluble heavy metal phosphates (PHₐ₃)| 2% acetic acid (HAc) | Insoluble MHPO₄, M₃(PO₄)₂ and other metal-phosphate complexes | HNO₃-to-H₂O₂ ratio: 4:1 |
| 5               | Oxalate (PHCl)                      | 0.6 mol/L HCl    | Metal-oxalate complexes | HNO₃-to-H₂O₂ ratio: 4:1 |
| 6               | Residual form (PR)                  | –                | Residues            | 8 mL HNO₃ and 2 mL H₂O₂ |
Results and discussion

Multi-elements characteristic and fingerprint

The concentrations of 54 elements in the studied MC samples were expressed as mean (c) ± standard deviation (SD) of the sampling sites, the means and RSDs% of all the studied elements were calculated for further analysis whether there were differences in the levels of each element from different regions. Data of K, Na, P, Ca, Mg, Al, S, Si, B, Fe, Mn, Zn, Ba, Sr and Cu were obtained by ICP-AES, and the rest elements were determined by ICP-MS. Internal standard solution (Rh) was used during the ICP-MS determination. According to the average content of 54 elements from different producing areas, we established the multi-elements distribution fingerprint of MC herbs using Origin 9.0, as shown in Fig. 2. These elements are divided into 4 groups: (a) K, Ca, Mg, Na, Al, Fe, S and P are at the above 100 mg·kg⁻¹; (b) Sc, Y, La, Ce, Pr, Nd, Sm, Eu, Gd, Tb, Dy, Ho, Er, Tm, Yb and Lu are rare earth elements (REEs); (c) As, Cd, Hg, Pb and Cu are heavy metals and toxic elements that must be monitored according to “Green Trade Standards of Importing & Exporting Medicinal Plants & Preparations” (WM2-2001); (d) Ba, V, Mo, Sr, Li, I, Zn, Mn, B, Ti, Si, Co, Sb, Sn, Rb, Ni, Cs, U, Be, Bi, Tl, Th, Ge, Br and Cr are the remaining elements to be studied.

The content of K, Ca, Mg, Na, Al, Fe, S and P is above 100 mg·kg⁻¹ in Table 2 and Fig. 2, accounting for 98.79% of the total amount (27,306 mg·kg⁻¹, S5). The RSDs% values were all higher than 48, indicating significant differences in the levels of each element from different regions. The herbs of Chizhou got the highest K (11,812 mg·kg⁻¹) and Ca (25,369 mg·kg⁻¹) while the lowest content of K (3364 mg·kg⁻¹) and Ca (8370 mg·kg⁻¹) was in Tongling and in Xuancheng, respectively. The Na content in Bozhou sample (890 mg·kg⁻¹) is extremely high, which is 10.08 times of that in Tongling sample (89 mg·kg⁻¹). The herbs of Bozhou got the highest Mg (2832 mg·kg⁻¹), but was only 824 mg·kg⁻¹ in herbs of Wuhu. The Fe content is the highest in the herb produced in Bozhou (744 mg·kg⁻¹), which is 4.4 times the lowest in Wuhu (170 mg·kg⁻¹). Al is an element that accumulates in the body and causes chronic toxicity. The highest Al content in Chizhou was 1254 mg·kg⁻¹, while the Al content in Wuhu was only 286 mg·kg⁻¹. P and S are non-metallic elements, and their contents are in the range of 805 mg·kg⁻¹ (Wuhu) ~ 2214 mg·kg⁻¹ (Chizhou) and 412 mg·kg⁻¹ (Wuhu) ~ 1325 mg·kg⁻¹ (Bozhou), respectively. The contents of K, Ca, Mg, Na, Al, Fe and P in MC from different producing areas were close to those of other reports (Liu et al. 2017; Zhu et al. 2020). In short, the content of K, Mg, Al, Fe, Na, S and P of the MC herbs from Tongling and Wuhu is much lower than those from other regions in Group (a). Except Bozhou, the contents of metal elements in other origins are arranged in the following order: Ca > K > Mg > Al > Fe > Na, and Ca is the most abundant element of all MC herbs.

The concentration of elements in Group (b), (c) and (d) are significantly lower than the group (a). Therefore, RSDs% of the studied elements below 50 are considered to have little difference in origin. In group (b), 16 REEs (Sc, Y and Lanthanide, Pm was excluded) are determined in Table 3 and Fig. 2, and all REEs are found in all MC herbs. The content of REEs (i.e., Eu, Tb, Y, Pr, La, Nd, Th, Sm, Dy, Ho and Gd) displayed similar levels as the RSDs% is 25–52. The highest and lowest contents of REEs were Wuhe and Bozhou, which got 5.094 mg·kg⁻¹ and 2.000 mg·kg⁻¹, respectively. The abundance of even atomic number elements was higher than that of their odd atomic number neighbors (Fig. 2), which conforms to the law of Oddo–Harkins (Markert 1987). The ratio of light to heavy rare earth elements (LREEs/HREEs = Σ([La]−[Eu])/Σ([Gd]−[Lu]+ Y + Sc)) is between 3.807 and 5.504, indicating the enrichment of LREEs in all MC samples. Except for Bozhou, the contents of REEs in the other four production areas of MC are as follows: Ce > La > Nd > Y > Pr > Er > Yb > Eu > Ho > Tb > Tm > Lu. These results can not only see the differences between MC growing in the plain and hilly areas, but also can be used for the identification of MC.

For heavy metals and toxic elements (Table 4 and Fig. 3), the content of Pb, Cu and Cd had remarkable different as the RSDs% are 65, 56 and 67, while As and Hg are slightly less affected by origin. The highest content of As and Hg is 0.223 mg·kg⁻¹ and 0.004 mg·kg⁻¹, respectively. The content of Pb was the highest in Wuhu (2.897 mg·kg⁻¹) and the lowest in Bozhou (0.457 mg·kg⁻¹). The content of Cu varied in the range of 3.395–11.029 mg·kg⁻¹, and the herbes from Bozhou is the highest. Tongling, commonly known as Tongdu, has many copper mines. It is believed that MC has grown here with a high content of Cu, but in fact it is only 4.432 mg·kg⁻¹. The herbs of Wuhe got the highest Cd (0.778 mg·kg⁻¹) whereas other regions content was in the range of 0.070–0.448 mg·kg⁻¹. According to the regulations in the “Green Trade Standards of Importing & Exporting Medicinal Plants & Preparations” (WM2-2001), the maximum limits of Cu, Cd, Pb, Hg and As in CHMs are 20, 0.3, 5, 0.2 and 2 mg·kg⁻¹, respectively. Among all the herbs, Cu, Pb, Hg and As are below the limiting value. Some of herbs from Wuhe, Xuancheng and Chizhou were found to have excessive Cd levels, while the sample from Bozhou contains low level of Cd. This result should be related to the soil environment of producing area. The soil types in Wuhe, Xuancheng and Chizhou are mainly red (brown) soil, limestone soil and paddy soil in some areas. The soil is mostly acidic (Tao et al. 2011). The soil in Bozhou is developed from the parent material of yellow flood alluvium.
Fig. 2 Multi-elements distribution fingerprint map of MC herbs (WH—Wuhu, TL—Tongling, XC—Xuancheng, CZ—Chizhou, BZ—Bozhou). Heavy metals and toxic elements are excluded.
and mainly consists of yellow tide soil, which is alkaline (Ye et al. 2007). Studies have shown that the proportion of ion-exchangeable Cd in acidic soil is high, and that Cd bound with carbonate is released, increasing the fluidity and bioavailability of Cd. The pH of Bozhou soil is higher than 8, which reduces the solubility of Cd in soil, increases the

| Table 2 | Analytical results of the macro-elements in MC herbs. Sum (a): The sum of the concentrations of all macro-elements |
|---------|-------------------------------------------------------------------------------------------------------------|
| 8 Elements | Macro-elements content (mg.kg⁻¹ ± SD of the sampling sites, n = 5,5,4,4,4) |
|          | Wuhu | Tongling | Xuancheng | Chizhou | Bozhou | Mean | RSD% |
| Ca       | 9067 ± 2112 | 10,176 ± 1219 | 8370 ± 686 | 25,369 ± 2732 | 22,113 ± 7363 | 21,519 ± 54 |
| K        | 3728 ± 808 | 3364 ± 575 | 4363 ± 351 | 11,812 ± 1351 | 9841 ± 1828 | 8662 ± 59 |
| Mg       | 824 ± 138 | 882 ± 98 | 1288 ± 219 | 2132 ± 188 | 2832 ± 490 | 1591 ± 55 |
| P        | 805 ± 267 | 997 ± 460 | 1019 ± 103 | 2214 ± 223 | 2153 ± 573 | 1438 ± 48 |
| S        | 412 ± 62 | 435 ± 133 | 539 ± 70 | 1246 ± 108 | 1325 ± 314 | 791 ± 57 |
| Al       | 286 ± 105 | 350 ± 98 | 789 ± 205 | 1254 ± 219 | 1065 ± 305 | 749 ± 61 |
| Fe       | 170 ± 61 | 201 ± 53 | 452 ± 123 | 756 ± 129 | 744 ± 209 | 465 ± 61 |
| Na       | 111 ± 81 | 98 ± 29 | 109 ± 12 | 299 ± 23 | 890 ± 73 | 301 ± 113 |
| Sum (a)  | 15,401 | 16,503 | 16,929 | 45,081 | 40,963 | 26,976 |

| Table 3 | Analytical results of the rare earth elements in MC herbs. Sum (b): The sum of the concentrations of all rare earth elements |
|---------|-------------------------------------------------------------------------------------------------------------|
| 16 Elements | Rare earth element content (mg.kg⁻¹ ± SD of the sampling sites, n = 5,5,4,4,4) |
|          | Wuhu | Tongling | Xuancheng | Chizhou | Bozhou | Mean | RSD% |
| Sc       | 0.096 ± 0.04 | 0.133 ± 0.05 | 0.143 ± 0.05 | 0.081 ± 0.02 | 0.090 ± 0.02 | 0.109 ± 0.05 | 25 |
| Y        | 0.615 ± 0.34 | 0.380 ± 0.32 | 0.397 ± 0.10 | 0.350 ± 0.10 | 0.195 ± 0.07 | 0.387 ± 0.07 | 39 |
| La       | 1.210 ± 0.63 | 0.838 ± 0.32 | 1.010 ± 0.22 | 0.757 ± 0.14 | 0.340 ± 0.16 | 0.831 ± 0.16 | 39 |
| Ce       | 1.530 ± 0.85 | 1.147 ± 0.75 | 1.925 ± 0.39 | 1.008 ± 0.20 | 0.716 ± 0.34 | 1.265 ± 0.34 | 37 |
| Pr       | 0.218 ± 0.11 | 0.149 ± 0.12 | 0.201 ± 0.04 | 0.147 ± 0.03 | 0.079 ± 0.04 | 0.159 ± 0.04 | 34 |
| Nd       | 0.814 ± 0.40 | 0.565 ± 0.43 | 0.759 ± 0.16 | 0.321 ± 0.11 | 0.605 ± 0.14 | 0.605 ± 0.14 | 32 |
| Sm       | 0.155 ± 0.07 | 0.108 ± 0.08 | 0.144 ± 0.03 | 0.107 ± 0.02 | 0.067 ± 0.03 | 0.116 ± 0.03 | 30 |
| Eu       | 0.032 ± 0.02 | 0.018 ± 0.02 | 0.023 ± 0.01 | 0.014 ± 0.02 | 0.006 ± 0.01 | 0.019 ± 0.01 | 52 |
| Gd       | 0.162 ± 0.08 | 0.111 ± 0.09 | 0.139 ± 0.03 | 0.107 ± 0.02 | 0.066 ± 0.03 | 0.117 ± 0.03 | 31 |
| Tb       | 0.019 ± 0.01 | 0.012 ± 0.01 | 0.015 ± 0 | 0.011 ± 0 | 0.006 ± 0 | 0.012 ± 0 | 37 |
| Dy       | 0.106 ± 0.05 | 0.071 ± 0.06 | 0.082 ± 0.02 | 0.065 ± 0.01 | 0.046 ± 0.02 | 0.074 ± 0.02 | 30 |
| Ho       | 0.021 ± 0.01 | 0.014 ± 0.01 | 0.015 ± 0 | 0.012 ± 0 | 0.009 ± 0 | 0.014 ± 0 | 31 |
| Er       | 0.060 ± 0.03 | 0.042 ± 0.03 | 0.046 ± 0.01 | 0.038 ± 0.01 | 0.029 ± 0.01 | 0.043 ± 0.01 | 27 |
| Tm       | 0.008 ± 0 | 0.006 ± 0 | 0.007 ± 0 | 0.006 ± 0 | 0.005 ± 0 | 0.006 ± 0 | 22 |
| Yb       | 0.044 ± 0.02 | 0.031 ± 0.02 | 0.034 ± 0.01 | 0.028 ± 0 | 0.023 ± 0 | 0.032 ± 0 | 24 |
| Lu       | 0.005 ± 0 | 0.003 ± 0 | 0.003 ± 0 | 0.002 ± 0 | 0.001 ± 0 | 0.003 ± 0 | 43 |
| LREEs/HREEs | 3.807 ± 0.008 | 4.216 ± 0.006 | 5.504 ± 0.007 | 4.202 ± 0.006 | 4.024 ± 0.005 | 3.807 ± 0.006 | 4.351 |
| Sum (b)  | 5.094 ± 0 | 4.326 ± 0 | 4.944 ± 0 | 3.302 ± 0 | 2.000 ± 0 | 3.793 ± 0 | 43 |
negative charge of soil particles, reduces the exchangeable Cd in soil and reduces the mobility of Cd (Song et al. 2015; Li et al. 2013a, b). The exceedance ratios of Cd in the 66 samples were 59.09%, which pointed out that the Cd pollution is serious in MC herbs. Li et al. (2018) also reported that Cd content in MC from Daodi-producing areas exceeded the standard, which is consistent with the results of this study.

In the group (Table 5), due to the origin, the concentration of Si, U, Li, Be, Cr and Sr had remarkable difference, and the RSDs% varies from 54 to 77. There are a wide variety of Si in herb, ranging from 162 (Tongling) to 23.29 mg.kg⁻¹ (Bozhou). Sr in Xuancheng was the lowest at 21.034 mg.kg⁻¹ while it was the highest at 135.277 mg.kg⁻¹ in Bozhou. Cr content of the herbs was in the range of 2.302–8.280 mg.kg⁻¹ with the highest value from Xuancheng. The content of Si and Sr in MC in this study was higher than that in previous reports (Guo et al. 2008; Liu et al. 2017). Nevertheless, the concentrations of other elements in this group of samples from different origins display similar levels as the RSDs% are 8 and 43. Average content of Ti, Rb, B, Mo, Ni and Ba is 47.334 mg.kg⁻¹, 5.680 mg.kg⁻¹, 23.984 mg.kg⁻¹, 0.260 mg.kg⁻¹, 1.360 mg.kg⁻¹ and 35.208 mg.kg⁻¹, respectively. Br and I are typical non-metallic elements, Br level of all herbs is higher than I. They were determined the mean of 1.674 mg.kg⁻¹ and 0.154 mg.kg⁻¹, respectively. Zn in the herbs was ranged from 12.996 mg.kg⁻¹ (Xuancheng) to 25.041 mg.kg⁻¹ (Bozhou), which was consistent with Zn content in 32 batches of MC reported by Zhu et al. (2020).

### Chemical forms of Cd

Due to the phenomenon of Cd exceeding the standard detected in MC herbs, Cd chemical forms were further analyzed. The percentage of chemical forms of Cd in MC is shown in Table 6 and Fig. 4. The MC from Bozhou has the highest residue state Cd (P₉) in 6 chemical forms, accounting for 30.6%, while the other 4 producing areas have the highest integration with pectate and protein Cd (P₉NaCl). Owing to higher migration ability and higher biological activity, P₉E₉OH (inorganic Cd) and P₉H₂O (water-soluble Cd) are more harmful to plant cells than other Cd forms (Li et al. 2014; Wang et al. 2008; Qiu et al. 2011). The lowest sum

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### Table 4

Analytical results of the heavy metals and toxic elements in MC herbs. Sum(c): The sum of the concentrations of the heavy metals and toxic elements.

| Elements | Wuhu | Tongling | Xuancheng | Chizhou | Bozhou | Mean | Limiting value | RSD% |
|----------|------|----------|-----------|---------|--------|------|----------------|------|
| Cu       | 3.395 ± 0.70 | 4.432 ± 1.63 | 3.684 ± 0.23 | 9.472 ± 1.77 | 11.029 ± 2.14 | 6.402 ± 1.77 | 20 | 56 |
| As       | 0.080 ± 0.03 | 0.110 ± 0.05 | 0.223 ± 0.03 | 0.202 ± 0.04 | 0.187 ± 0.08 | 0.160 ± 0.04 | 2.0 | 39 |
| Cd       | 0.778 ± 0.76 | 0.287 ± 0.09 | 0.448 ± 0.21 | 0.358 ± 0.03 | 0.070 ± 0.01 | 0.388 ± 0.03 | 0.3 | 67 |
| Hg       | 0.004 ± 0.0 | 0.004 ± 0.0 | 0.004 ± 0.0 | 0.004 ± 0.0 | 0.004 ± 0.0 | 0.2 ± 0.0 | 5 | 5 |
| Pb       | 2.897 ± 2.63 | 0.936 ± 0.31 | 1.616 ± 0.52 | 1.241 ± 0.18 | 0.457 ± 0.11 | 1.429 ± 0.11 | 5 | 65 |
| Sum(c)   | 7.154 ± 4.15 | 5.769 ± 2.25 | 5.975 ± 2.25 | 11.277 ± 4.35 | 11.746 ± 4.75 | 8.384 ± 2.91 | - | - |

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Fig. 3 Distribution map of heavy metals and toxic elements in MC herbs (WH—Wuhu, TL—Tongling, XC—Xuancheng, CZ—Chizhou, BZ—Bozhou)
Table 5 Analytical results of 25 trace elements in MC herbs. Sum(d): The sum of the concentrations of 25 trace elements

| Elements | Trace elements content (mg.kg⁻¹ ± the sampling sites, n=5,5,4,4,4) |
|----------|---------------------------------------------------------------|
|          | Wuhan | Tongling | Xuancheng | Chizhou | Bozhou | Mean | RSD% |
| Ba       | 39.366±24.40 | 25.933±21.07 | 25.811±6.06 | 46.232±2.57 | 38.698±10.69 | 35.208±26 |
| Sr       | 72.153±15.64 | 64.902±41.89 | 21.034±7.93 | 107.723±18.38 | 135.277±40.52 | 80.218±54 |
| Zn       | 17.779±4.62 | 13.819±2.74 | 12.996±0.95 | 32.923±2.65 | 25.041±6.59 | 20.511±41 |
| Mn       | 19.416±9.31 | 12.908±3.50 | 26.252±4.10 | 23.370±4.59 | 14.799±3.30 | 19.349±29 |
| Si       | 105.906±66.56 | 161.997±86.41 | 25.607±12.34 | 64.435±49.93 | 23.286±16.66 | 76.246±77 |
| B        | 21.299±2.10 | 20.474±2.08 | 27.959±2.15 | 21.052±1.43 | 29.127±3.83 | 23.982±17 |
| Li       | 0.217±0.08 | 0.230±0.09 | 0.603±0.14 | 0.374±0.11 | 0.882±0.20 | 0.461±61 |
| Be       | 0.013±0.01 | 0.009±0.01 | 0.026±0.01 | 0.016±0.01 | 0.004±0.01 | 0.014±59 |
| Ti       | 43.962±10.43 | 53.223±5.70 | 47.557±6.18 | 44.357±9.78 | 47.570±7.46 | 47.334±8 |
| V        | 0.412±0.15 | 0.558±0.18 | 1.257±0.29 | 0.755±0.22 | 0.978±0.42 | 0.792±42 |
| Cr       | 2.346±0.83 | 2.302±0.68 | 8.280±1.21 | 4.178±0.99 | 3.952±1.18 | 4.211±58 |
| Co       | 0.187±0.06 | 0.167±0.06 | 0.316±0.04 | 0.194±0.04 | 0.233±0.09 | 0.220±27 |
| Ni       | 1.207±0.44 | 1.148±0.62 | 1.651±0.34 | 1.719±0.18 | 1.077±0.28 | 1.360±22 |
| Ge       | 0.008±0 | 0.012±0 | 0.007±0 | 0.004±0 | 0.005±0 | 0.007±40 |
| Br       | 1.995±0.87 | 1.334±0.43 | 1.897±0.17 | 1.551±0.21 | 1.593±0.34 | 1.674±16 |
| Rb       | 6.082±3.30 | 5.848±0.88 | 5.126±0.32 | 4.538±0.84 | 6.808±1.71 | 5.680±15 |
| Mo       | 0.301±0.10 | 0.195±0.10 | 0.302±0.04 | 0.203±0.02 | 0.297±0.06 | 0.260±21 |
| Sn       | 0.137±0.07 | 0.130±0.06 | 0.051±0.04 | 0.066±0.07 | 0.074±0.03 | 0.091±43 |
| Sb       | 0.134±0.14 | 0.152±0.07 | 0.185±0.04 | 0.156±0.04 | 0.123±0.03 | 0.150±16 |
| I        | 0.212±0.05 | 0.176±0.06 | 0.146±0.04 | 0.136±0.02 | 0.101±0.01 | 0.154±27 |
| Cs       | 0.048±0.02 | 0.063±0 | 0.117±0 | 0.078±0 | 0.100±0 | 0.081±34 |
| Tl       | 0.052±0.02 | 0.052±0.01 | 0.041±0.01 | 0.042±0.01 | 0.029±0.01 | 0.043±22 |
| Bi       | 0.007±0 | 0.007±0 | 0.011±0 | 0.008±0 | 0.007±0 | 0.008±23 |
| Th       | 0.071±0 | 0.080±0 | 0.177±0 | 0.100±0 | 0.127±0 | 0.111±38 |
| U        | 0.023±0 | 0.025±0 | 0.022±0 | 0.022±0 | 0.070±0 | 0.033±65 |
| Sum(d)   | 333.333±0 | 365.744±0 | 207.431±0 | 354.232±0 | 330.258±0 | 318.198±0 |
of inorganic Cd and water-soluble Cd in MC from Wuhu and Tongling is 18.4% and 19.7%, followed by that from Xuancheng and Chizhou, which is 29.8% and 27.7%, the highest is from Bozhou as 31.2%. The average percentage of PHAc (insoluble CdHPO4, Cd3(PO4)2), PHCl (Cd oxalate) and PR (residues) in all forms were 14.6% (8.0–21.3%), 5.4% (2.8–8.2%) and 19.4% (13.1–30.6%), respectively. The percentage of PNaCl (Cd integrated with pectate and protein) in herbs from Wuhu, Tongling, Xuancheng and Chizhou was the highest, accounting for 41.2% (25.2–56.4%) of all chemical forms. However, PNaCl percentage in MC from Bozhou is much lower than other regions, which only contained 9.1%. In terms of chemical form distribution, the herbs from Bozhou are quite different from those from other origins, and the proportion of PR, PH2O and PHAc is the highest top 3 among all samples. This is probably due to the geological environment where herbs are grown. Wuhu, Tongling, Xuancheng and Chizhou are hilly but Bozhou is plain.

Statistical analysis

Based on the content of 54 elements in MC samples from 22 sampling sites in 5 producing areas, the Fisher discriminant function general discriminant method was used to perform multivariate discriminant analysis through Statistical software, SPSS (Version23). Five elements (K, Na, Sc, Cr and Cd) with obvious regional distribution differences were taken as indicators as independent variables for judgment analysis to establish a discriminant model of MC origin, which is listed in S6. The discriminant function 1 and 2 cumulative explain ability of discriminant model is 94.8%, and the correlation coefficient was greater than 0.95, which shows that discriminant function 1 and 2 to five MC origins classification of main contribution, using the discriminant function score value of the discriminant function 1 and 2 as a scatter plot. It can be seen from Fig. 5. The group centroid of MC from Tongling and Wuhu is close to each other and overlap, which is also related to the special climate and soil conditions of Phoenix Mountain. The group centroid of MC from Xuancheng and Chizhou is closer to that of Wuhu and Tongling, and this may be due to their hilly terrain and location along the Yangtze River. It should be noted that the distance between Bozhou and other producing areas is far, so the distribution of inorganic elements is easy to distinguish the producing areas.

Health risk evaluation

The average Cd content of MC from Wuhu, Xuancheng and Chizhou was 0.778 mg.kg\(^{-1}\), 0.448 mg.kg\(^{-1}\) and 0.358 mg.kg\(^{-1}\), respectively. According to the maximum dose of 12 g for Chinese medicinal materials prescribed by the Chinese Pharmacopoeia 2020, the average weekly intake of Cd in MC (PTWI = Ci × 12 × 7)/62.5) from these three regions was 1.046 μg.kg\(^{-1}\), 0.602 μg.kg\(^{-1}\) and 0.481 μg.kg\(^{-1}\), respectively (Table 7). But in fact, oral Chinese medicine is mostly taken in the form of water decoction. Wang et al. (2019) reported that the dissolution rate of Cd in traditional Chinese medicine was 20.5%, so the actual weekly average intake of Cd in MC (PTWI\(_{\text{actual}}\) = PTWI × 20.5%) from Wuhu, Xuancheng and Chizhou was 0.215 μg.kg\(^{-1}\), 0.166 μg.kg\(^{-1}\) and 0.133 μg.kg\(^{-1}\), respectively. That’s less than 0.6 μg.kg\(^{-1}\) for Cd prescribed by WHO. Moreover, the highest migration and toxicity are PEtOH (inorganic Cd) and PH2O (water-soluble Cd) in 6 chemical forms of Cd, and the sum of the two percentage of Wuhu, Xuancheng and Chizhou was 18.4%, 29.8% and 27.7%, respectively. Corresponding to PIWI was 0.192 μg.kg\(^{-1}\), 0.180 μg.kg\(^{-1}\) and 0.133 μg.kg\(^{-1}\), which were

![Fig. 4 Chemical form of Cd in MC was expressed as percentage of total concentration](image-url)
also below limits (0.6 μg.kg⁻¹) as well. Therefore, in Wuhu, Xuancheng, Chizhou the residual amount of Cd in MC ingested by water decoction had little harm to human health.

Low doses of REEs are beneficial to human body, such as inhibiting tumors and protecting brain nerves (Xia et al. 2012; Jin et al. 2014), while high doses are opposite. The REEs that people consume accumulate in their internal organs, bones, brain, hair and blood and have significant effects on human digestive, respiratory, reproductive, nervous, blood and immune systems (Chen et al. 2005; Chen et al. 2008). The total amount of REEs in MC is in the range of 2.000–5.094 mg.kg⁻¹. Based on the maximum daily consumption of 12 g.person⁻¹ (Chinese Pharmacopoeia Commission 2020), the lifetime average daily pollutant intake (ADI = Ci × 12 × 90 × 70 / 62.5 × 365 × 70) is only 0.0947–0.241 ug.kg⁻¹.d⁻¹ (Table 7), and the REEs intake is 70 ug.kg⁻¹.d⁻¹, as the safe dose (Li et al. 2013a, b; Zhu et al. 1997). Judging from the amount of REEs in MC herbs, it is not harmful to human health.

### Conclusion

The multi-element fingerprint was established by determining the contents of 54 elements in MC from 5 producing areas, which is different from that of Baishao and other herbs, and can be used to distinguish herbs (Xue et al 2021; Lv et al. 2019). The content of macro-elements in MC from Bozhou is twice that from Wuhu and Tongling. The concentration of elements in MC from Wuhu, Tongling, Xuancheng and Chizhou are in the following order: Ca > K > Mg > Al > Fe > Na. The content of REEs in MC from 5 producing areas all conforms to the law of Oddo–Harkins, and the content in MC from Wuhu is the highest, and that from Bozhou is the lowest. Due to the origin, the contents of trace elements such as Si, U, Pb, Cu, Cd, Li, Be, Cr, Sr are significantly different. The distribution of chemical forms of Cd in MC from Bozhou is obviously different from that in the other 4 regions. In Bozhou MC, Cd mainly exists in residue state and water-soluble state, while in other 4 producing areas, Cd mainly exists in extracted NaCl states with low activity and low mobility. Cu, Hg, As and Pb in MC did not exceed the limits prescribed by Green Trade Standards of Importing & Exporting Medicinal Plants & Preparations (WM2-2001), while Cd in MC from Wuhu, Xuancheng and Chizhou exceeded the standard. Chinese medicine is mostly taken in the form of decoction. After reasonable assessment, taking the water decoction of MC does not pose a health risk to human health.

Based on the multi-element fingerprint, the MC from 5 producing areas was divided into 3 groups by statistical analysis: Tongling and Wuhu, Xuancheng and Chizhou, and Bozhou, providing a new method to trace the origin of herbs. Tongling and Wuhu are *Daodi*-producing areas of MC, and patterns of major and trace elements are highly similar. The climate, geology and soil conditions of Xuancheng and Chizhou are similar to those of Tongling and Wuhu, and both of them are hilly areas, so the element distribution in MC herbs has certain similarity with the *Daodi* origin. However, Bozhou is a typical great plain, and the distribution pattern of elements in MC herbs is quite different from the above 4 producing areas. Therefore, the next step should pay attention to the factors that cause the difference in the mineral element of herbs, such as soil, water and so on. This study provided a new method and idea for quality control of Chinese medicinal materials from the source.
Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s13762-022-04402-6.

Acknowledgements This work was supported by Natural Science Research Project of Universities in Anhui Province (KJ2020A0433) and Anhui Traditional Chinese Medicine Inheritance and Innovation Scientific Research Project (2020zczyb12).

Authors’ contributions Xuan Xue and Guijian Liu conceived the research idea and were responsible for the sample preparation, data interpretation and paper writing. Qian Tang and Hongyan Shi were responsible for sample handling and Cd speciation analysis by sequential extraction. Hongsu Zhao and Yunjing Zhang were responsible for the determination content of 54 elements in MOUTAN CORTEX (MC). Yong Wei was responsible for sample digestion; Deling Wu and Chuanshan Jin were responsible for sample collection. All authors participated in the paper writing and editing.

Funding This work was supported by Natural Science Research Project of Universities in Anhui Province (KJ2020A0433) and Anhui Traditional Chinese Medicine Inheritance and Innovation Scientific Research Project (2020zczyb12).

Availability of data and materials The result is clear, honest and free of falsified or inappropriate manipulation of data (including image-based manipulation). The authors follow discipline-specific rules when acquiring, selecting and processing data.

Code availability Software: Origin 9.0 and SPSS (Version23).

Declarations

Conflict of interest The authors declare that there are no conflicts of interest.

Ethics approval Not applicable.

Consent to participate Not applicable.

Consent for publication All authors agree to submit the manuscript to the journal.

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