



Original Article

Towards a scientific rationale for traditional properties of Chinese medicinal plants: “natures” and “flavors”

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ABSTRACT

Objective: According to theory of Chinese medicine property, the ecological environment shapes properties (natures and flavors) of Chinese materia medica (CMM) and there are close relationships between certain natures and flavors. However, to date these observations have not been validated scientifically in the context of the whole flora of a region. The present study aims to address this gap.

Methods: We collected geographical distributions of 3637 vascular plant species native to the Xinjiang region of northwest China, of which around 812 are medicinal plants. The CMM property characters of these medicinal plants were also collected. All medicinal plants were then analyzed in the occurrence of their natures (*cold, cool, neutral, warm, and hot*) and flavors (*sweet, bitter, sour, salty, and pungent*). Possible correlations between these properties and environmental factors, notably climate, as well as correlations with plant species richness of the wider native flora of Xinjiang were then investigated using permutation test and regression.

Results: *Cold* species (38.5%) were more numerous than *warm* (21.0%) and *neutral* (22.3%), while *bitter* species (43.3%) were more numerous than *pungent* (25.6%), *sweet* (22.4%) and *sour* (6.7%) ones. Species with *bitter* flavor were most commonly also *cold* (48.6%) in nature, *sour* flavor usually coincided with *cold* (44.2%) or *cool* nature (26.0%), whereas *pungent* or *sweet* species tended to be *warm* (34.4%, 28.4%) or *neutral* (27.8%, 28.4%). The percentages of species of *cold/cool* nature, *bitter* flavor were higher in mountainous regions, and the percentages of *warm/neutral* and *pungent/sweet/sour* were higher in basins. The percentages of species of *cold/cool*, *bitter* were positively correlated with actual evapotranspiration (AET), and also plant species richness but had a bell-shaped relationship with potential evapotranspiration (PET), whereas the inverse situation was shown for *warm/neutral* and *pungent/sweet/sour* species.

Conclusion: Analysis of the data in Xinjiang region of China supports the qualitative observations concerning natures and flavors in traditional theory of Chinese medicine property. Specifically, (i) certain natures and flavors co-occur more frequently than if randomly distributed; (ii) correlations between proportions of natures and flavors and climatic variables suggest a role for the environment in shaping the properties of CMM.

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1. Introduction

According to theory of Chinese medicine property, the classification of Chinese materia medica (CMM) into various flavors and natures, jointly referred to here as natural properties or

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NPs, reflects their medical actions and therapeutic efficacy (Han et al., 2018; Wang, 2011). Previous research (Tang, Yang, & Huang, 2010a,b; Zhai, Wang, Meng, & Wang, 2011a) suggests that such NPs are influenced by the ecological environment and there is a relationship between the expression of natures and flavors. For example, a CMM having a *cold/cool* nature is associated with having a *bitter/sweet* flavor (Zhai, Wang, Hong, & Ma, 2011b), while a CMM having *warm/hot* nature is likely to have a *pungent* flavor (Zhai, Wang, Liu, Meng, & Ma, 2012a). However, such relationships have rarely been the subject of scientific quantification. The causal associations between environment and CMM property characters were also rarely studied. Tian, Chen, and Lian (2010) and Tian, Jiao, Chen, and Lian (2013) published some of the first such scientific studies using a plant dataset from the Gansu Province of China. They researched the percentage composition of the flavors and natures of CMM and analyzed the relationship of medicine properties and actions with altitude at which the source plants grew (an indirect environmental variable). Findings indicated that most of the 802 endemic medicinal plant species studied were classified as having *cold/cool* natures, and a *bitter* flavor (Tian et al., 2010). A number of plants classified as *bitter* flavor was found to correlate positively with altitude whereas those with *sour*, *salty*, or *pungent* flavors correlated negatively with altitude (Tian et al., 2010, 2013).

Using a much larger dataset and direct environmental variables (temperature and precipitation), we conducted the present study to obtain results with greater statistical significance. The study area chosen for the present work is the Xinjiang region of far north-western China occupying an area of 1.6 million km². The region is characterized by its huge range of environmental and climatic extremes. These extremes may be reflected in the range of NPs to be encountered across this region and as such Xinjiang provides an ideal area for research on environmental determinants of medicinal plant NPs. Furthermore, recent research based on the whole region has generated the structured datasets of the native plant species and medicinal plant species (Li, Yin, & Tang, 2011; Li et al., 2013, 2015).

2. Materials and methods

2.1. Data sources

The vascular plant, medicinal plant and distribution data used in this study have been sourced from the database constructed by Li et al. (2011, 2013, 2015) with a resolution of 0.1° × 0.1° which in turn was compiled from the following sources: *Florae Xinjiangensis* (Commissione Redactorum Florae Xinjiangensis, 1992–2011), two databases of <http://www.csdb.cn> and Network Query System on “Classification and Codes of Traditional Chinese Medicine Resource” (Wang, Sun, Chen, Lin, & Li, 2012), respectively, and *Records of Chinese Medicinal Resources* (China National Corporation of Traditional & Herbal Medicine, 1994). The NPs of the medicinal plants followed those of the *Chinese Materia Medica* (State Administration of Traditional Chinese Medicine – Chinese Materia Medica Editorial Board, 1999), the *Pharmacopoeia of the People’s Republic of China* (Volumes I) (Chinese Pharmacopoeia Commission, 2015), and *Chinese Medicinal Plants, Herbal Drugs and Substitutes: an identification guide* (Leon & Lin, 2017).

The two main climatic variables used throughout our study, actual evapotranspiration (AET) and potential evapotranspiration (PET), were calculated according to the monthly temperature and precipitation with the resolution of 0.0083 arc degree sourced from the World Climate Database (Hijmans, Cameron, Parra, Jones, & Jarvis, 2005). AET is an indicator of water that plants utilize, and PET is an indicator of thermal efficiency.

2.2. Definitions of NPs

The terms nature and flavor have a long history of usage in traditional Chinese medicine and, according to theory of Chinese medicine property, NPs reflect the characters of each CMM (dried, processed plant part or *Yin pian*) (Dan et al., 2010). Flavors are traditionally defined in CMM as *sweet*, *bitter*, *sour*, *salty* or *pungent* while natures are *cold*, *cool*, *neutral*, *warm* or *hot*. Excluded from this study are CMM classified as *hot*, owing to their scarcity within CMM; in Xinjiang region the only CMM with a *hot* nature is sourced from species of *Aconitum*. We also excluded from the later stages of this study all CMM classified with the flavor *salty* as they represent less than 4% of CMM in each grid cell in the dataset. Omitted for purposes of simplicity, are *Paozhi*; this is the further traditional processing involving heat (e.g. steaming, dry-frying) or the addition of adjuvants (e.g. yellow rice wine). The central focus of this study is to quantify the relationships of flavors and natures and to investigate the environmental drivers of the NP characters expressed in each CMM.

2.3. Data analyses

NP data were collected for all the medicinal plants of Xinjiang region. For single CMM plant species exhibiting more than one character, for example, *Ferulae Resina* (sourced from *Ferula fukanensis* K. M. Shen) has both *bitter* and *pungent* flavors, then *bitter* and *pungent* were both scored as the flavor of the species (Fig. 1). In cases where different parts of a plant species were used to make different CMM, all the NPs of these CMM were scored as for that species. Essentially the underlying data for this study were as inclusive as possible of the natures and flavors of plants in this region.

To correlate data between natures and flavors, a presence–absence test was used. This assesses the probability of co-occurrence by means of permutation ($P < 0.05$ indicating significant probability of co-occurrence). The test was conducted with the function “test.a” (Borcard, Gillet, & Legendre, 2018) in software R 3.5.0 (R Core Team, 2018).

The percentages of the NP characters were geographically mapped in 0.1° × 0.1° grid cells. Then the climatic variables were evaluated for the impacts on the medicinal plant NPs with the method of ordinary least square (OLS) regressions (linear and quadratic). Partial regressions were conducted to find the independent effects of each variable using “varpart” function in Vegan package (Oksanen et al., 2018) in software R 3.5.0 (R Core Team, 2018). We used the whole dataset for analyses. For clarity of visualization, 5% randomly selected data of the entire dataset, i.e. ca. data of 870 grid cells were used for Figs. 5–8.

3. Results

3.1. A general view of herbal medicine properties and their relationships

Medicinal plants native to Xinjiang had NP characters in the following proportions: *cold* (38.5%), *warm* (22.3%), *neutral* (21.0%), and *cool* (18.3%), respectively in nature; *bitter* (43.3%), *pungent* (25.6%), *sweet* (22.4%), *sour* (6.7%), and *salty* (2.0%), respectively in flavor (Table 1).

Bitter and *sour* flavors were more frequently associated with a *cold* nature, *pungent* and *sweet* flavors were more frequently associated with *warm* and *neutral* natures, and a *salty* flavor was most frequently associated with a *warm* nature (Fig. 2, Table 2).

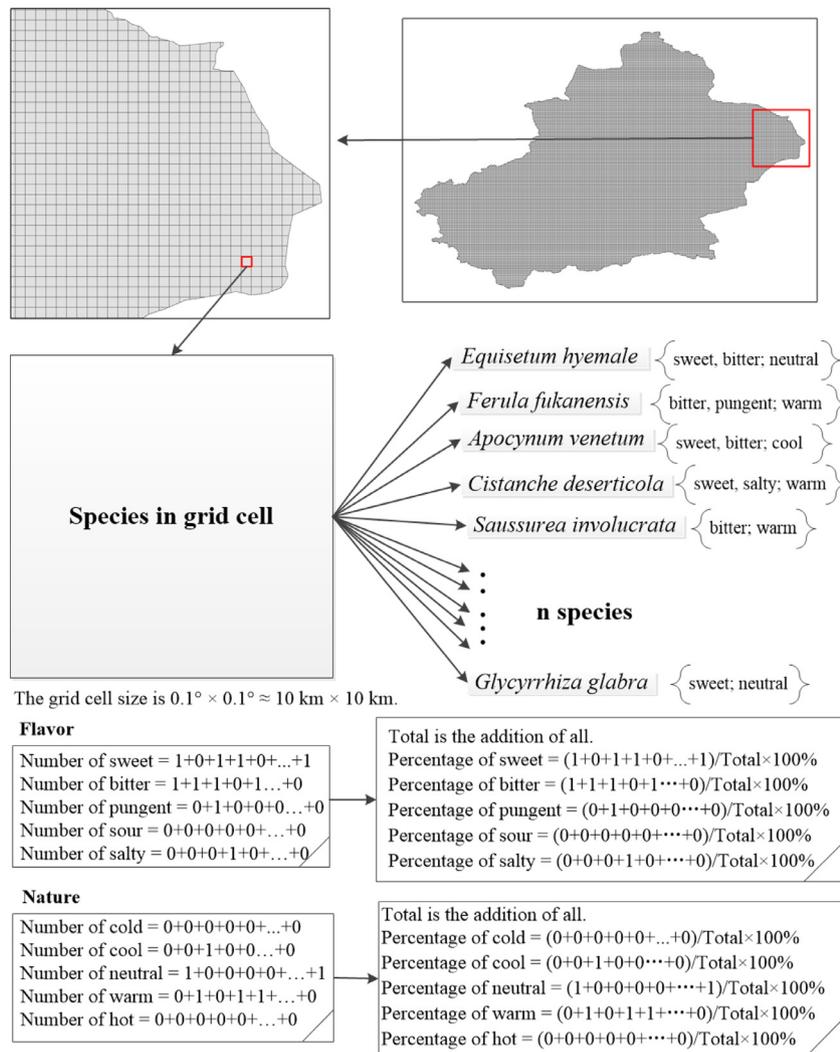


Fig. 1. Mapping processes of medicinal plant properties in Xinjiang, China.

Table 1
Basic statistics of medicine properties in Xinjiang, China.

| Natures | Number | Percentage/% | Flavors | Number | Percentage/% |
|---------|--------|--------------|---------|--------|--------------|
| Cold | 288 | 38.5 | Bitter | 490 | 43.3 |
| Cool | 137 | 18.3 | Pungent | 289 | 25.6 |
| Neutral | 157 | 21.0 | Sweet | 253 | 22.4 |
| Warm | 167 | 22.3 | Sour | 76 | 6.7 |
| | | | Salty | 23 | 2.0 |

Note: Nature of hot was found only for genus *Aconitum* in this region, data were not shown. Most of plants have one nature whereas most of plants have more than one flavor.

Table 2
P values of correlations between flavor and nature.

| Natures | Flavors | | | | |
|---------|---------|---------|-------|------|-------|
| | Bitter | Pungent | Sweet | Sour | Salty |
| Cold | <0.01 | 1.00 | 1.00 | 0.05 | 0.99 |
| Cool | 0.10 | 0.89 | 0.29 | 0.02 | 0.78 |
| Neutral | 1.00 | <0.01 | <0.01 | 1.00 | 1.00 |
| Warm | 0.99 | <0.01 | <0.01 | 0.51 | <0.01 |

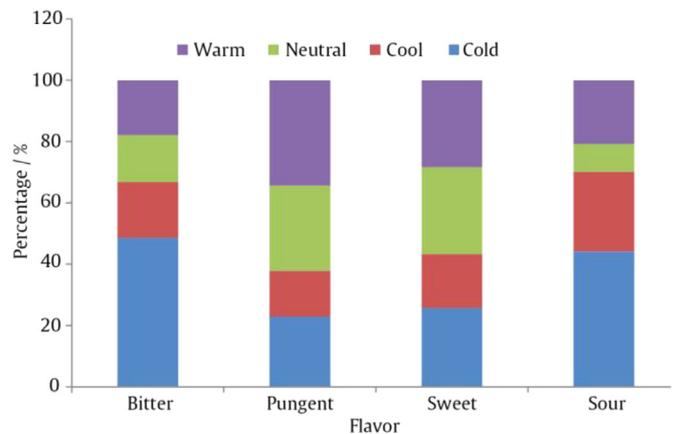


Fig. 2. Correlates of medicinal plant properties (nature and flavor).

3.2. Distribution patterns of percentages of NPs

Cold and cool natures were most frequently associated with plant species growing in northern Xinjiang mountain ranges such as, the Tianshan, Altay, and west Jungar. In contrast, plants associ-

ated with warm or neutral natures were at lower altitudes such as Tarim and Jungar basins. However, in Altun mountains, percentages of medicines with nature of warm or neutral were also relatively high (Fig. 3).

Bitter flavor was most frequently found in plant species growing in the mountains of northern Xinjiang and less common in the lower altitude in basins and Altun mountains. The opposite pattern

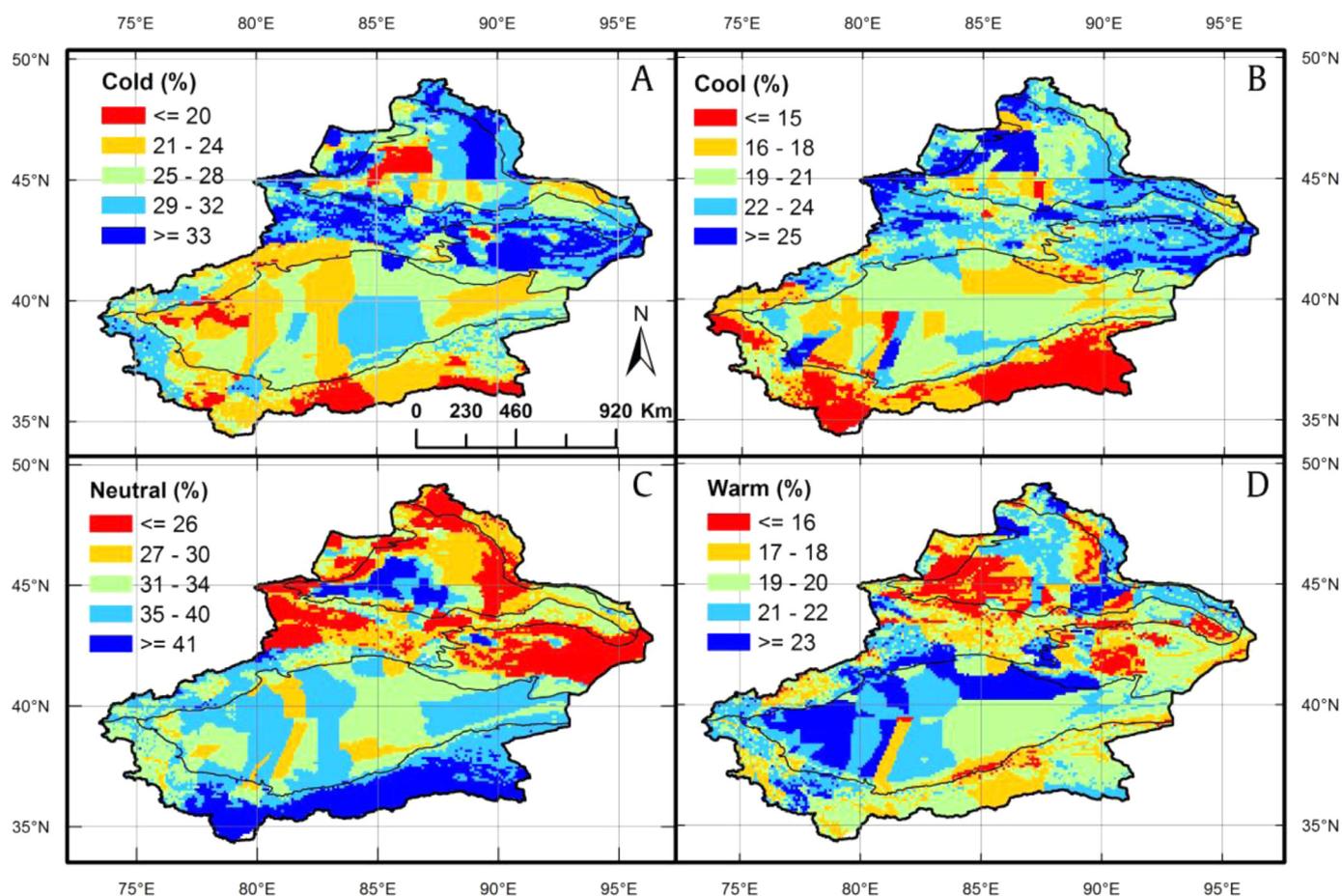


Fig. 3. Distribution patterns of percentages of nature (A: cold, B: cool, C: neutral, D: warm. Hot nature was only found in genus *Aconitum* and it was omitted from our analysis) in Xinjiang, China.

Table 3
Relationship (R^2 values) of NPs and climate / plant species richness.

| Natures | AET | PET | Plant species richness | Flavors | AET | PET | Plant species richness |
|---------|------|-------|------------------------|---------|------|-------|------------------------|
| Cold | 0.30 | -0.34 | 0.87 | Bitter | 0.37 | -0.36 | 0.91 |
| Cool | 0.28 | -0.37 | 0.81 | Pungent | 0.32 | -0.41 | 0.82 |
| Neutral | 0.26 | -0.32 | 0.61 | Sweet | 0.30 | -0.38 | 0.82 |
| Warm | 0.20 | -0.30 | 0.73 | Sour | 0.02 | -0.42 | 0.31 |

Note: linear regression for AET and Plant richness, quadratic regression for PET.

was observed for percentages of *pungent*, *sweet* and *sour*. Percentages of *sour* flavor were quite low (Fig. 4).

3.3. Determinants of percentages of NPs

Numbers of species with particular NPs showed similar patterns to total vascular plant numbers in terms of their relationships with climatic variables. Numbers of species with each NP character increased with AET and showed a bell-shaped relationship with PET (Table 3). The percentages of NPs were differently correlated with the climatic variables (Figs. 5 and 6). The percentages of *cold* and *cool* natures increased significantly with AET (Fig. 5A and B) whereas the percentages of *warm* and *neutral* de-

creased with AET (Fig. 5C and D). The percentages of *cold* and *cool* had a bell-shaped relationship with PET (Fig. 5E and F) whereas those of *warm* and *neutral* had an inverse bell-shaped relationship with PET (Fig. 5G and H). The percentage of *bitter* flavor increased with AET whereas those of *pungent*, *sweet* and *sour* all decreased with AET (Fig. 6A–D). The percentage of *bitter* had a bell-shaped relationship with PET whereas proportions of *pungent*, *sweet* and *sour* showed an inverse bell-shaped relationship with PET (Fig. 6E–H).

Numbers of species with particular NPs were positively correlated with the background vascular plant richness with high R^2 values (Table 3), but patterns changed when the percentages were considered (Figs. 7 and 8). The percentages of *cold* and *cool*

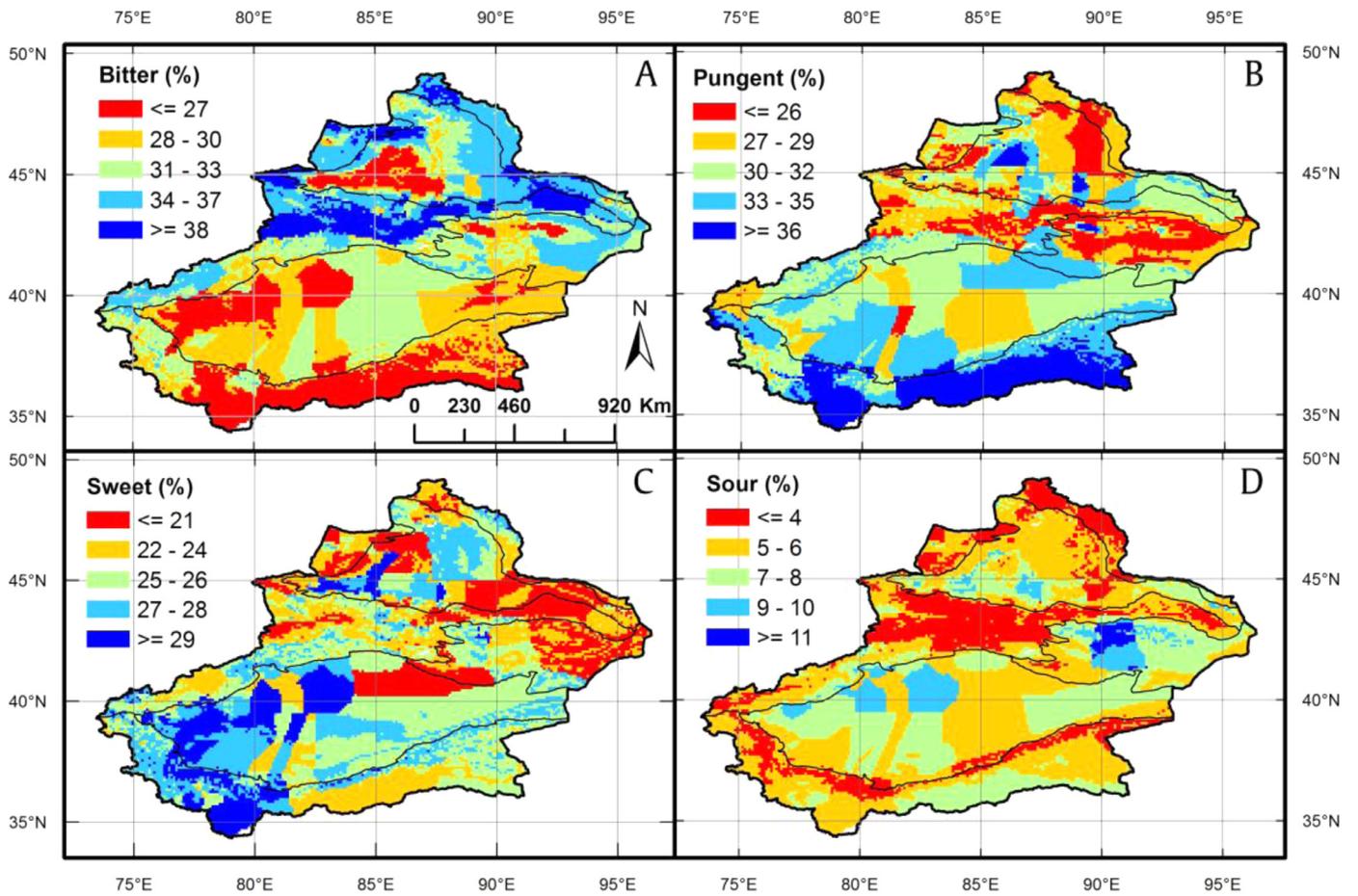


Fig. 4. Distribution patterns of percentages of flavors (A: bitter, B: pungent, C: sweet, D: sour. Salty flavor is locally very rare and it was omitted in our analysis.) in Xinjiang, China.

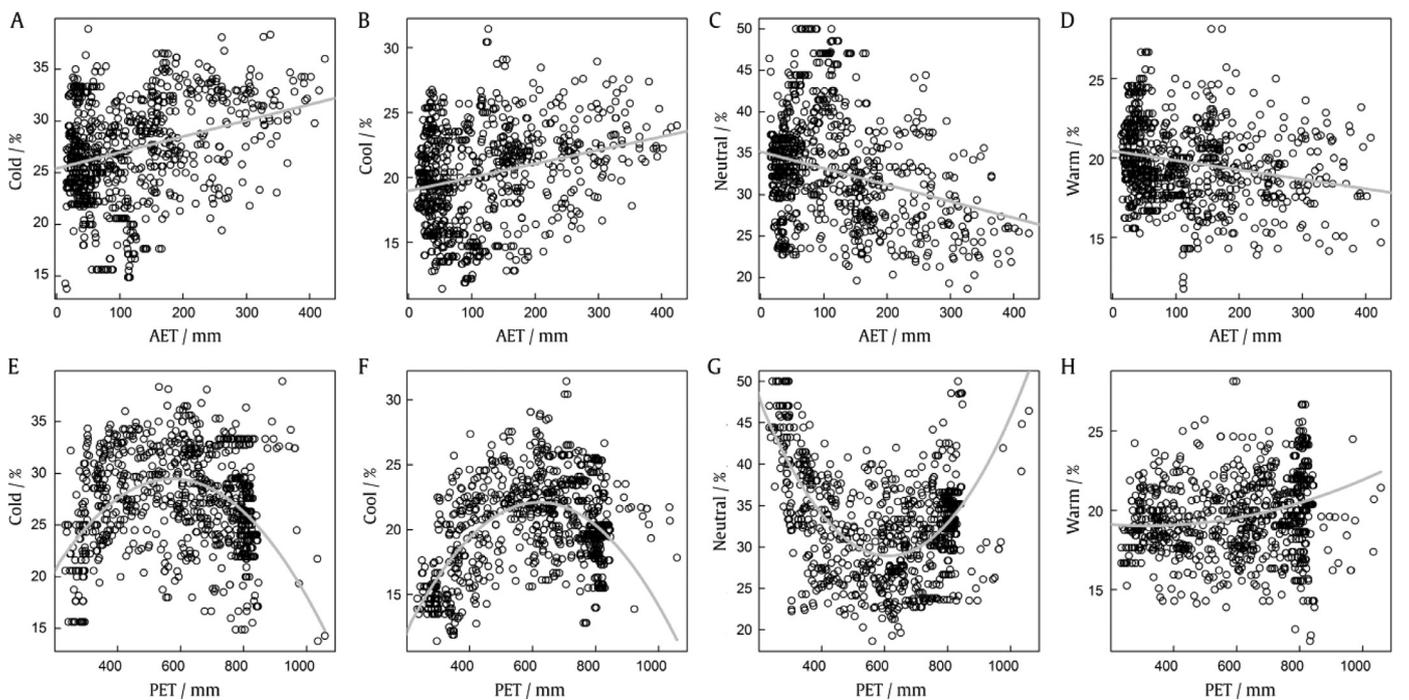


Fig. 5. Relationship of percentages of each nature with climatic variables.

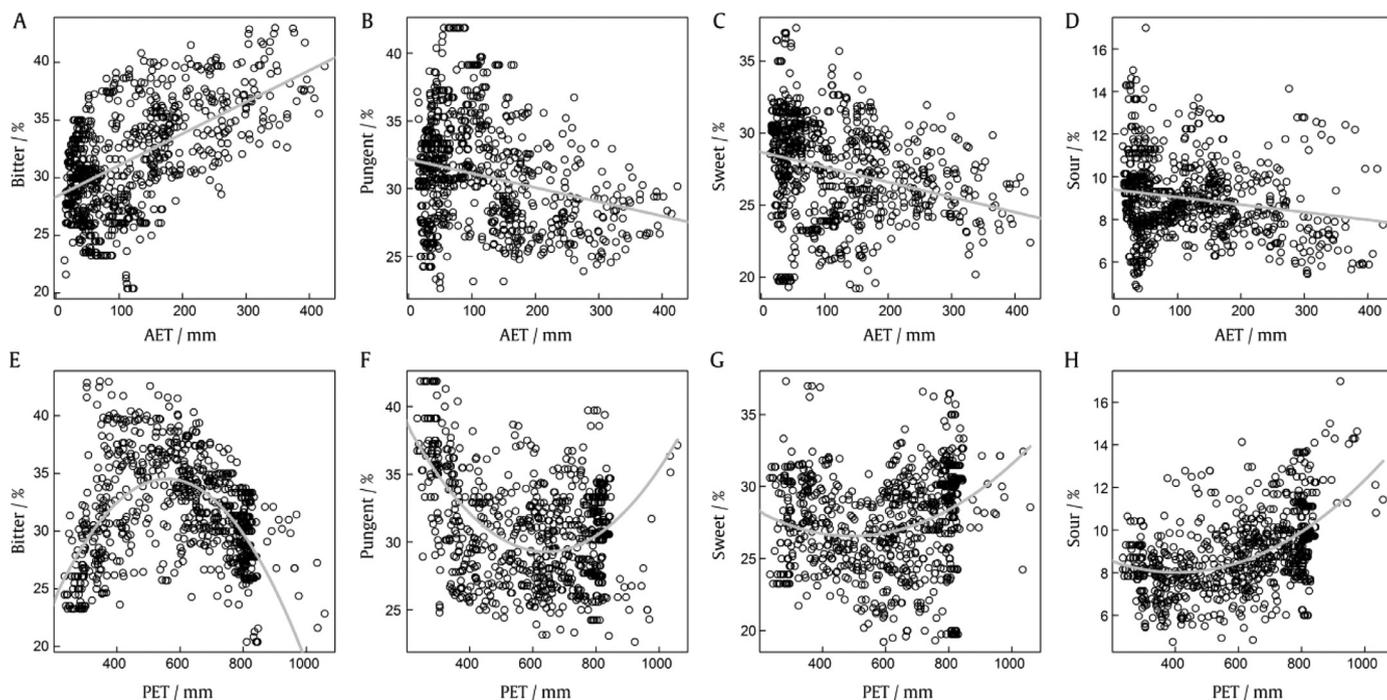


Fig. 6. Relationship of percentages of each flavor with climatic variables.

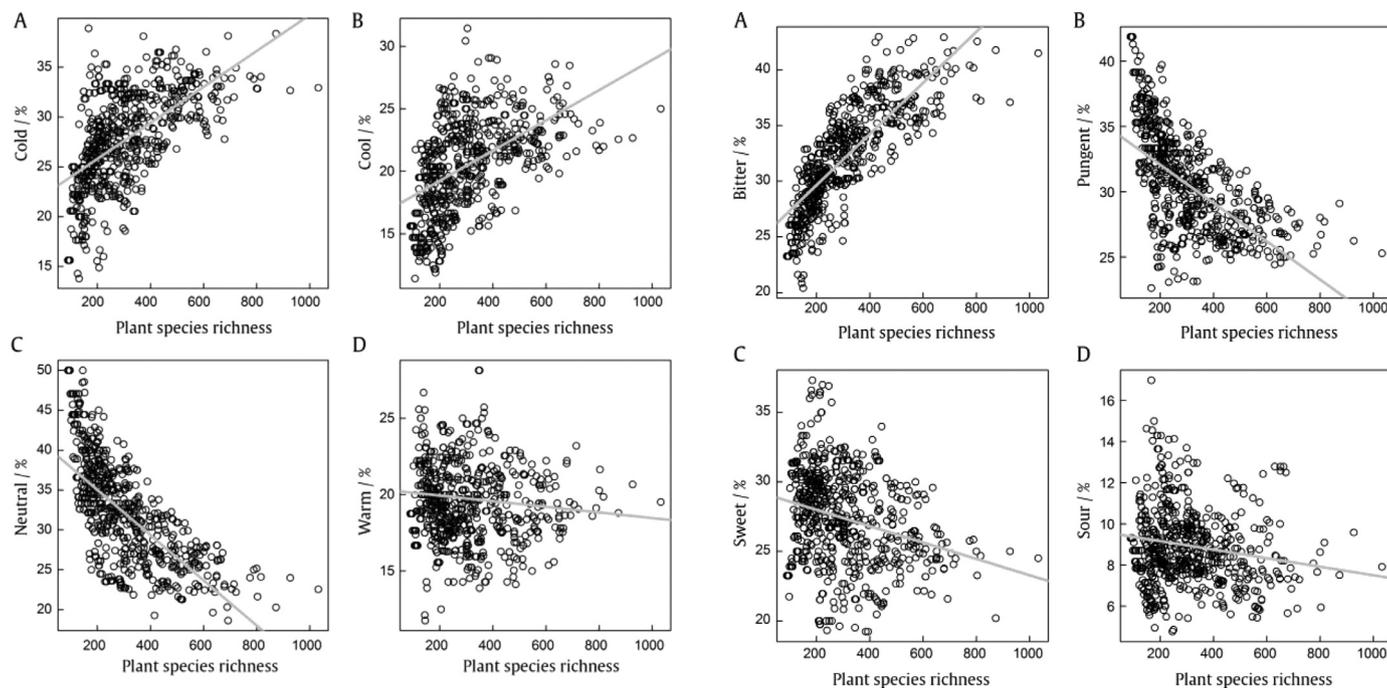


Fig. 7. Relationship of percentages of each nature with plant species richness.

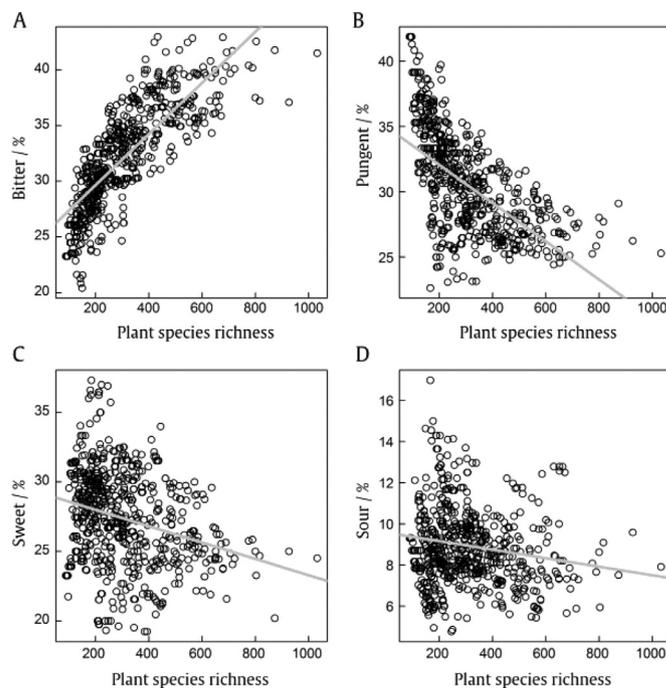


Fig. 8. Relationship of percentages of each flavor with plant species richness.

Table 4

Independent effects of climate (energy and water availability) and plant species richness on percentages of medicinal plant NPs.

| Effects | | Nature percentages | Flavor percentages |
|-----------------|---------------------|--------------------|--------------------|
| Climate + Plant | Independent climate | 0.12 | 0.12 |
| | Independent plant | 0.21 | 0.08 |
| | Shared | 0.12 | 0.07 |
| | Residuals | 0.55 | 0.73 |
| Water + Energy | Independent energy | 0.16 | 0.09 |
| | Independent water | 0.18 | 0.09 |
| | Shared | – | 0.01 |
| | Residuals | 0.76 | 0.81 |

natures increased with plant species richness whereas those of *warm* and *neutral* decreased with plant species richness. The percentage of *bitter* flavor increased with plant species richness whereas those of *pungent*, *sweet* and *sour* decreased with plant species richness.

3.4. Independent effects of plant species richness, water and energy availability on percentages of NPs

Climate and plant species richness independently explained 12% and 21% of the variation in nature percentage respectively, and 12% and 8% of the variation in flavor percentage, respectively. Energy and water independently explained 16% and 18% of the variation in nature percentage respectively, and 9% and 9% of the variation in flavor percentage, respectively (Table 4).

4. Discussion

4.1. Certain NPs are tightly coupled

In Xinjiang region, our results showed that proportions of medicinal plants having the nature of *cold* or *cool* (combined total 56.7%) and flavor of *bitter* (43.3%) were greater than those having other natures or flavors, consistent with previous studies (Tian et al., 2010; Yan, 1981). Yan (1981) showed that 42.4% of 459 commonly used CMM had the nature of *cold* or *cool* followed by 24.2% of *neutral* and 33.4% of *warm* or *hot*. Of 802 endemic medicinal plant species in Gansu Province of China, Tian et al. (2010) found that 50.2% had the nature of *cold* or *cool* followed by 21.3% of *neutral* and 28.4% of *warm* and *hot*; 46.1% had the flavor of *bitter*. Further studies are needed to establish whether medicinal plants of *cold*, or *cool* nature and *bitter* flavor are usually most frequent.

It is traditionally considered that there are correlations among nature and flavor in CMM. Previous studies of the inter-correlations of medicinal plant properties were based on specific taxa, on medicines with similar NP characters (Zhai et al., 2011b, 2012a; Zhai, Wang, Wuyun, Meng, & Ma, 2012b), or on medicinal species and their close relatives (Yang, Tang, Huang, & Xiao, 2008). Relationships were not reported for a broad region. Here, we statistically showed that in the large Xinjiang region, *cold* nature was more closely associated with *bitter* flavor than with other flavors, *cool* with *sour*, *neutral* with *pungent* or *sweet*, *warm* with *pungent*, *sweet* or *salty*. Our results are one of the first attempts to provide

a scientific rationale for the classification of CMM properties assigned to medicinal plants. However, the results need more verification in several respects. First, the processing of crude drugs was not considered, for example, different processing methods including stir-frying or steaming, could influence the properties of medicines. Second, only the properties of nature and flavor were considered, the characters of meridian tropism and action were not included. Third, the conclusions were based only on data for plant species in Xinjiang region. More studies including more variables should be conducted. Data across larger ranges are needed for validating the relationships of NP characters.

4.2. Environmental variables influence distribution patterns of NPs

Until now, few studies mapped the distribution patterns of NPs, and the relationship of medicinal properties with the environment has not been quantified. Studies at the regional level about NPs are mostly basic description of medicinal property characters of the plants in a region, for example, the summary of the actions of herbal medicines in Yunnan Province, China (Pu & Chen, 2010). The influences of environment on NPs were mostly reported as descriptive summaries based on ancient books (Tang et al., 2010a,b), and these descriptions were not readily amenable to statistical tests. With 90 representative CMM, Xin, Liu, Yin, and Deng (2011) identified the causal associations of “ecological factors → chemical components → herbal properties”. Our research statistically verified environmental effects on the property characters of medicines.

We correlated herbal medicine properties with environmental variables and found that the proportions of species of *cold* or *cool* natures and *bitter* flavor increased significantly with AET and with plant species richness, and had a bell-shaped relationship with PET. These patterns mirrored those for total vascular plants and for medicinal plants in the region (Li et al., 2013, 2015). However, the percentages of *neutral*, *warm*, *pungent*, *sweet* and *sour* showed the opposite patterns. To differentiate the impacts of climate and plant species richness on NP distribution patterns, we conducted the analysis of variance partitions. Both climate and plant species richness significantly influenced the percentages of NPs but neither of the two dominated.

Besides the environment, the NPs might be associated with or based on the chemicals in the medicinal plants or crude drugs. Many studies were conducted in the 1980s on the possible correlations of Chinese medicinal properties, e.g., nature, flavor, meridian tropism, chemical component and action

(Wu & Yan, 1988; Yan, 1981; Yan & Wu, 1987a,b, 1988). These studies were focused on inorganic components. The production of organic compounds in plants is highly influenced by the climate or soil conditions (Tian et al., 2010). In particular, the content of secondary compounds in plants is highly influenced by the environmental stresses, such as drought, freezing, soil nutrient deficiencies (Gershenzon, 1984). Influences of organic chemicals, for example, phenols, saponin, and polysaccharides on the NPs should be addressed in future research. In addition, the characters of action and therapy will also provide the focus for future studies.

4.3. Quantitative analysis validates aspects of CMM property theory

Properties of CMM have long been believed to be correlated with and influenced by their environment. However, how they are correlated and to what extent they are impacted by the environment were not statistically verified, leading to debates and criticisms on the theory of Chinese medicine property. Statistical analysis and tests on these opinions are rare. However, these difficulties can be overcome due to the availability of big datasets such as that for Xinjiang region.

Unlike most studies about individual species or genera, this study provided a detailed analysis of the correlates of NPs, the relationship of the environment and NPs in Xinjiang based on well-documented characters of NPs of hundreds of medicinal plant species. Furthermore, this study included a wider analysis of the relative effects of plant species richness and main climatic variables on NPs. Our conclusions could be highly relevant and complementary to the theory of pharmacophylogeny as an aid to finding new medicinal plants from the wilderness.

Conflict of interest

The authors declare no conflict of interest.

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