

Original Research

Predicting Potential Habitat of *Aconitum carmichaeli* Debeaux in China Based on Three Species Distribution Models

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Abstract

Aconitum carmichaeli Debeaux is a perennial herb and medicinal plant, which has the effects of warming Yang and dispelling cold, warming meridians and relieving pain, dispelling wind and dehumidification, supplementing fire and helping Yang. In recent years, affected by the destruction of shrubs and climate warming, the habitat of *A. carmichaeli* wild resources has been seriously damaged, indicating of great significance to the artificial protection and cultivation of *A. carmichaeli* to predict its potential suitable habitat using species distribution models (SDMs). In this paper, 14 environmental variables and 449 specimen distribution records were applied to three models, i.e. MaxEnt, GARP and Bioclim to simulate the distribution of *A. carmichaeli*. Our results showed that, the AUC average values of the three models were all above 0.85 and the Kappa average values were above 0.75, justifying their applications for predicting the potential areas of *A. carmichaeli*. Furthermore, simulation of MaxEnt showed that, the highly suitable habitats were concentrated in the middle east of Sichuan ($17.07 \times 10^4 \text{ km}^2$), western Hubei ($7.34 \times 10^4 \text{ km}^2$), southern Shaanxi ($7.2 \times 10^4 \text{ km}^2$), north central Guizhou ($6.74 \times 10^4 \text{ km}^2$), eastern Chongqing ($5.62 \times 10^4 \text{ km}^2$) and western Hunan ($5.21 \times 10^4 \text{ km}^2$) and scattered in the middle of Zhejiang ($3.07 \times 10^4 \text{ km}^2$), the southwest Anhui ($1.87 \times 10^4 \text{ km}^2$) and western Henan ($1.43 \times 10^4 \text{ km}^2$). Jackknife test and response curves determined that the key variables affecting the distribution of *A. carmichaeli* were annual precipitation (751.25-1580.72 mm), precipitation of warmest quarter (422.71-717.21 mm), min temperature of coldest month (-6.85-3.12°C), temperature annual range (24.83-31.97°C), elevation (145.87-2769.22 m) and human footprint (<4.01).

Keywords: *Aconitum carmichaeli* Debeaux, MaxEnt, GARP, Bioclim, suitable habitat

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Introduction

Species distribution models (SDMs) simulate current and future geographical distribution habitats of species and the changes through certain algorithms according to the geographical coordinate data and environmental variables of target species [1-3]. The accuracy of the simulation results of SDMs is mainly affected by the type of environmental variables, the migration ability of species and the richness of species distribution data [4-6]. At present, the commonly used SDMs include CLIMEX, GARP, MaxEnt, Bioclim and Domain [7, 8]. The modeling concept of MaxEnt model is to find out the maximum entropy of species distribution probability through calculation, and then simulate the geographical distribution of species in the specified area [9]. Based on the principle of genetic algorithm, GARP uses the known distribution point data and environmental data of species to generate sets of different rules, and takes the result of the optimal set as the potential distribution of species [10]. Bioclim is a framework model that extracts the limited range of environmental factors from the known species distribution area, and then summarizes the environmental needs of species into environmental envelope [11]. In recent years, SDMs have been applied in the study of the geographical distribution of medicinal plants, including *Fritillaria cirrhosa* [12], *Panzerina lanata* [13], *Paris verticillata* [14], *Sinopodophyllum hexandrum* [15], *Berberis aristata* [16].

Aconitum carmichaelii Debeaux is a perennial herb and medicinal plant, which grows on hillsides, under forests and meadows at an altitude of 150-3500 m, with warm and humid climate, sufficient sunshine, loose soil surface, good drainage and medium fertility [17-20]. The stem height of aconitum can reach 200 cm, the leaf blade is thin and pentagonal, the terminal raceme, and the root tuber is obconical (Fig. 1). Underground tuber is the medicinal part of *A. carmichaelii* (Fig. 1d), in which the processed product of the mother root is *Radix Aconiti* and the processed product of the daughter root is *Aconiti Lateralis*, which has the effects of warming Yang and dispelling cold, warming meridians and relieving pain, dispelling wind and dehumidification, supplementing fire and helping Yang [21]. *Aconitum carmichaelii* is mainly distributed in Sichuan, Shaanxi, Yunnan, Gansu, Guizhou, Hubei, Jiangxi, Hebei, Hunan and other provinces [22, 23]. In particular, Jiangyou and Mianyang in Sichuan and Hanzhong in Shaanxi have a long cultivation history and large-scale planting area [24]. In recent years, affected by policies, a large number of economic forests such as Chinese fir have been planted in mountainous areas of China, resulting in the destruction of shrubs [25, 26]. Coupled with the impact of climate warming, the habitat of *A. carmichaelii* wild resources has been seriously damaged, indicating that it should be protected [27, 28].

Recently, some scholars have focused on the relationship between the distribution of medicinal

plants and environmental factors, but the research on *A. carmichaelii* mainly focuses on biological characteristics [27, 29], chemical composition [30, 31], pharmacological action [32, 33], quality control [34, 35] and molecular biology [36, 37], while there is no research on its geographical division in China. In this paper, GIS technology and SDMs were selected to predict the distribution of *A. carmichaelii*, obtain the key environmental variables determining its geographical distribution, and delimit the its suitable grade and range.

Materials and Methods

Occurrence Data

Occurrence data of *A. carmichaelii* in China were acquired from various sources, including the Chinese Virtual Herbarium (CVH), the National Specimen Information Infrastructure (NSII) the Global Biodiversity Information Facility (GBIF), and our field survey, as well as literature reports [18, 21, 26-28, 30-32, 35, 37, 38]. Referring to the methods in literature [39, 40], we processed the distribution records of *A. carmichaelii*. Firstly, Baidu coordinate picking system was used to determine the longitude and latitude of records accurate to the town level. Second, Microsoft Excel (2010) was used to remove duplicate records. Third, the distance between each point and the center of the cell grid was calculated, and the point closest to the center in each cell grid was retained. After the above procedures, 449 distribution points of *A. carmichaelii* were retained for the establishment of SDMs (Fig. 2).

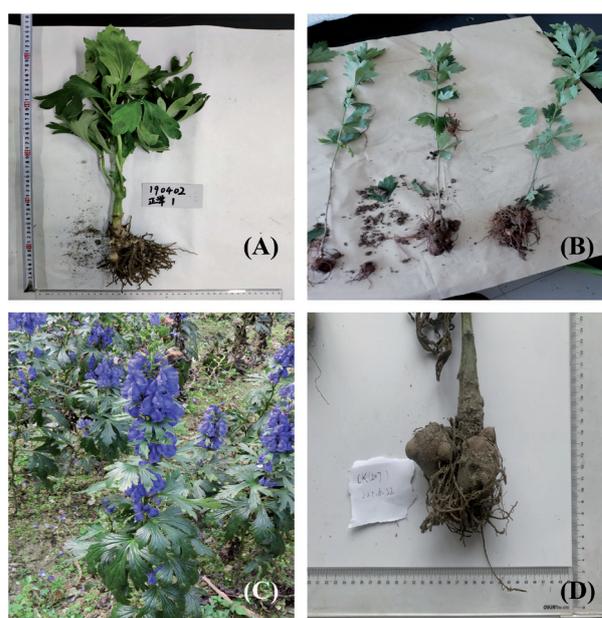


Fig. 1. The plant morphology, flowers and medicinal organs of *A. carmichaelii*.

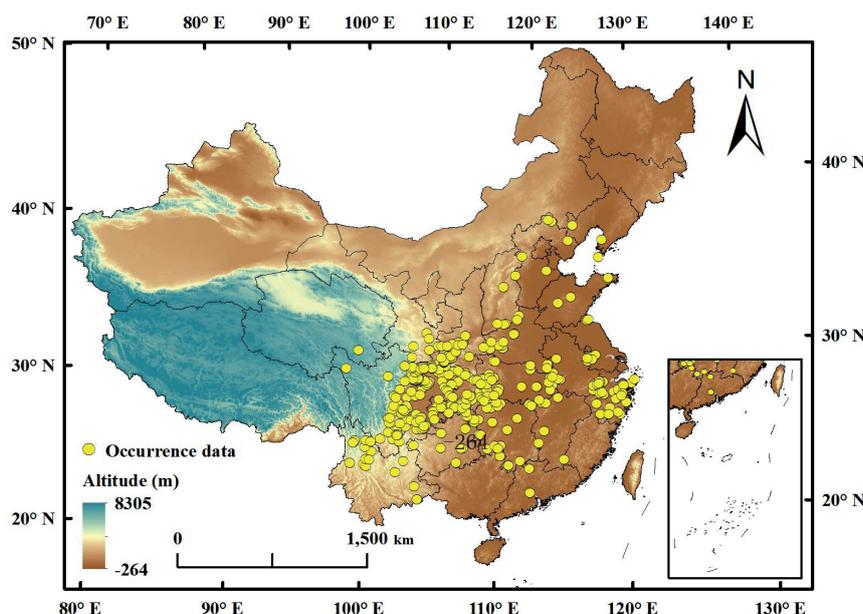


Fig. 2. Occurrence data of *A. carmichaeli*.

Environmental Data

Four types of environmental variables were selected in this study (Table S1). We pretreated the bioclimatic variables according to the following procedure. Firstly, MaxEnt was used to calculate the percent contributions of 19 variables, and whose percent contribution rate was greater than 0 were retained (Table S2). Thereafter, the Pearson’s coefficients between two variables with percent contributions greater than 0 corresponding to 449 occurrence data of *A. carmichaeli* were analyzed using SPSS. Thirdly, by comparing the percentage contribution of the variables with the absolute value of the coefficient greater than 0.85, the higher one was retained. Finally, 8 variables were obtained from 19 bioclimatic variables. In addition to abiotic climate variables, a total of 14 variables were selected to establish the prediction model of *A. carmichaeli* (Table 1) [41-43].

MaxEnt, GARP and Bioclim Modelling Process

MaxEnt software operation procedure was as follows. 1) The occurrence data of *A. carmichaeli* in “CSV” format and the environmental variables in “ASC” format (including bioclimatic variables, soil factors, elevation, UV-B3 and human footprint) were imported into the “sample” and “environmental layers” data boxes of MaxEnt software (V3.4.4) respectively. 2) “Create response curves” and “Do jackknife to measure variable importance” were selected respectively to analyze the relationship between variables and presence probability of *A. carmichaeli* and measure the importance of variables. 3) In the initial model, “Random test percentage” was set to 25 %, while in the

reconstructed model, “random seed” was selected, and the “replicates” was set to 10 [4, 44].

Desktop GARP (v1.1.6, <http://www.lifemapper.org>) was used for data analysis. 75% of the distribution data were randomly selected as the training data set and the remaining 25% as the test data set. The number of runs was set to 20, and other basic settings were set

Table 1. Environmental variables retained to build the MaxEnt model of *A. carmichaeli*.

Code	Variable	Resolution	Unit
Bio2	Mean Diurnal Range	2.5°	°C
Bio3	Isothermality	2.5°	/
Bio5	Max Temperature of Warmest Month	2.5°	°C
Bio6	Min Temperature of Coldest Month	2.5°	°C
Bio7	Temperature Annual Range	2.5°	°C
Bio12	Annual Precipitation	2.5°	mm
Bio15	Precipitation Seasonality	2.5°	/
Bio18	Precipitation of Warmest Quarter	2.5°	mm
El	Elevation	2.5°	m
PH	Potential of hydrogen	2.5°	/
T-C	Organic carbon pool topsoil	2.5°	%
Depth	Reference soil depth	2.5°	m
UV-B3	Mean UV-B of Highest Month	2.5°	kJ/m ²
Hf	Human footprint index	2.5°	/

to the default values, that was, the convergence limit was set to 0.01 and the max iterations was set to 1000 [7, 10]. According to Anderson's [45] method, 10 optimal models were superimposed in ArcGIS to obtain the grid map of range value [0~10], that was, the geographical distribution prediction map of *A. carmichaeli*.

DIVA-GIS software running Bioclim model was downloaded free from DIVA-GIS official website. Firstly, the training data set in shp format was added to DIVA-GIS, and then 14 environmental variables were converted into grd format to generate stack data set. A stack file was added in the modeling Bioclim/Domain module and selected the Bioclim model for prediction [46].

Evaluation of SDMs

Receiver operating characteristic (ROC) and Kappa statistics were commonly chosen to evaluate the accuracy of SDMs. With reference to methods of predecessors [46, 47], DIVA-GIS software was used to convert prediction map into grd file and establish corresponding stack data set, then import test point layer to create evaluation file, and finally output ROC and Kappa values.

ROC curve is a highly recognized diagnostic test evaluation index, and the value range of area value under ROC curve, i.e. AUC value, is 0.5-1 [40]. Kappa statistics is a consistency test method, which comprehensively considers the species distribution rate, sensitivity and specificity, and is widely used in model evaluation. The value range of kappa is -1~1. $Kappa \geq 0.75$ indicates that the prediction of the model is ideal, while $Kappa < 0.4$ indicates that the effect is poor [48].

Results and Discussion

Model Performance

In this paper, 10 groups of repetitions were used to test the ROC curve and kappa consistency of the three models. The average AUC of MaxEnt, GARP and Bioclim were 0.937, 0.881 and 0.922, which were higher than random models (Table 2). The average Kappa values of MaxEnt, GARP and Bioclim were greater than 0.75, indicating that the prediction consistency of the models was significant (Table 2).

Bioclim extracts the limited range of environmental factors of the study species from the existing species distribution data, and explores the suitability of the species in the study area [11]. However, the environmental variables used by Bioclim are independent of each other, which is contrary to the actual situation and may promote the inaccuracy of the scope of the environmental envelope [6]. In this study, Bioclim's prediction results was smaller than MaxEnt and GARP, which may be related to this. Compared with MaxEnt and Bioclim, the geographical distribution range of *A. carmichaeli* predicted by GARP was the most wider. GARP model automatically searches the environmental factors related to species distribution through genetic algorithm, selects the optimal rule set and map it to the study area [7, 10]. GARP focuses on the analysis of the geographical environment space that species may occupy under the ideal conditions without the interference of other factors, that is, the basic niche [49]. MaxEnt's prediction result was more accurate than other models (AUC = 0.937, Kappa = 0.822). Relevant literature has proved that MaxEnt has better prediction ability than other SDMs under the condition of small sample size [50, 51]. Therefore, this paper mainly refers to the suitable area predicted by MaxEnt model for subsequent analysis.

Table 2. The AUC and Kappa values of the three models.

Groups	AUC			Kappa		
	MaxEnt	GARP	Bioclim	MaxEnt	GARP	Bioclim
1	0.926	0.891	0.911	0.806	0.813	0.735
2	0.946	0.885	0.923	0.831	0.821	0.754
3	0.944	0.861	0.915	0.83	0.78	0.725
4	0.947	0.899	0.907	0.821	0.794	0.846
5	0.943	0.875	0.933	0.814	0.811	0.769
6	0.931	0.849	0.945	0.827	0.805	0.754
7	0.915	0.901	0.906	0.859	0.828	0.777
8	0.942	0.879	0.922	0.842	0.794	0.768
9	0.937	0.887	0.915	0.8	0.757	0.815
10	0.937	0.886	0.943	0.79	0.792	0.787
Average	0.937	0.881	0.922	0.822	0.799	0.773

Potential Distribution of *A. carmichaeli* Simulated by SDMs

The ASC file generated by MaxEnt model was imported into ArcGIS and divided into 4 grades (Fig. 3a). According to the statistics, the areas of highly, moderately and poorly suitable habitat were $60.82 \times 10^4 \text{ km}^2$, $57.26 \times 10^4 \text{ km}^2$ and $114.91 \times 10^4 \text{ km}^2$ respectively. The highly suitable habitat were concentrated in the middle east of Sichuan ($17.07 \times 10^4 \text{ km}^2$), western Hubei ($7.34 \times 10^4 \text{ km}^2$), southern Shaanxi ($7.2 \times 10^4 \text{ km}^2$), north central Guizhou ($6.74 \times 10^4 \text{ km}^2$), eastern Chongqing ($5.62 \times 10^4 \text{ km}^2$) and western Hunan ($5.21 \times 10^4 \text{ km}^2$) and scattered in the middle of Zhejiang ($3.07 \times 10^4 \text{ km}^2$), the southwest Anhui ($1.87 \times 10^4 \text{ km}^2$) and western Henan ($1.43 \times 10^4 \text{ km}^2$) (Fig. 3a).

For the 10 layers selected according to the principle of optimal model by GARP, ArcGIS was used to overlay the prediction results to obtain the overlay value (OV). According to the OV value, the prediction map of *A. carmichaeli* was divided into four grades: unsuitable habitat ($OV < 50\%$), poorly suitable habitat ($50\% \leq OV < 70\%$), moderately suitable habitat ($70\% \leq OV < 90\%$) and highly suitable habitat ($OV \geq 90\%$). According to the statistics, the areas of highly, moderately and poorly suitable habitat were

$153.56 \times 10^4 \text{ km}^2$, $82.52 \times 10^4 \text{ km}^2$ and $61.42 \times 10^4 \text{ km}^2$ respectively. Fig. 2b) showed that the suitable habitat of *A. carmichaeli* simulated by GARP was much wider than MaxEnt. The highly suitable habitat were mainly distributed in $24.01^\circ\text{N} \sim 36.65^\circ\text{N}$, $98.05^\circ\text{E} \sim 122.07^\circ\text{E}$, including eastern and southern Sichuan ($22.69 \times 10^4 \text{ km}^2$), most of Hunan ($18 \times 10^4 \text{ km}^2$), central and northern Yunnan ($16.64 \times 10^4 \text{ km}^2$), Guizhou ($15.45 \times 10^4 \text{ km}^2$), most of Hubei ($15.16 \times 10^4 \text{ km}^2$), central and western Jiangxi ($9.28 \times 10^4 \text{ km}^2$), central and southern Anhui ($8.35 \times 10^4 \text{ km}^2$), southern Shaanxi ($7.21 \times 10^4 \text{ km}^2$), Southern Henan ($6.43 \times 10^4 \text{ km}^2$), most of Zhejiang ($6.04 \times 10^4 \text{ km}^2$), northern Guangxi ($5.56 \times 10^4 \text{ km}^2$) and southeastern Shandong ($5.26 \times 10^4 \text{ km}^2$) (Fig. 3b).

Bioclim model calculates the suitable index (SI) of species, which is divided into 6 grades by default. We imported the file into ArcGIS and reclassified it into unsuitable habitat ($SI < 5\%$), poorly suitable habitat ($5\% \leq SI < 20\%$), moderately suitable habitat ($20\% \leq SI < 40\%$) and highly suitable habitat ($SI \geq 40\%$) to the proportion of SI. According to the statistics, the areas of highly, moderately and poorly suitable habitat were $12.97 \times 10^4 \text{ km}^2$, $42.1 \times 10^4 \text{ km}^2$ and $70.71 \times 10^4 \text{ km}^2$ respectively. Fig. 3c) showed that among the three models, the suitable area of *A. carmichaeli* predicted by Bioclim was the smallest. The highly suitable area

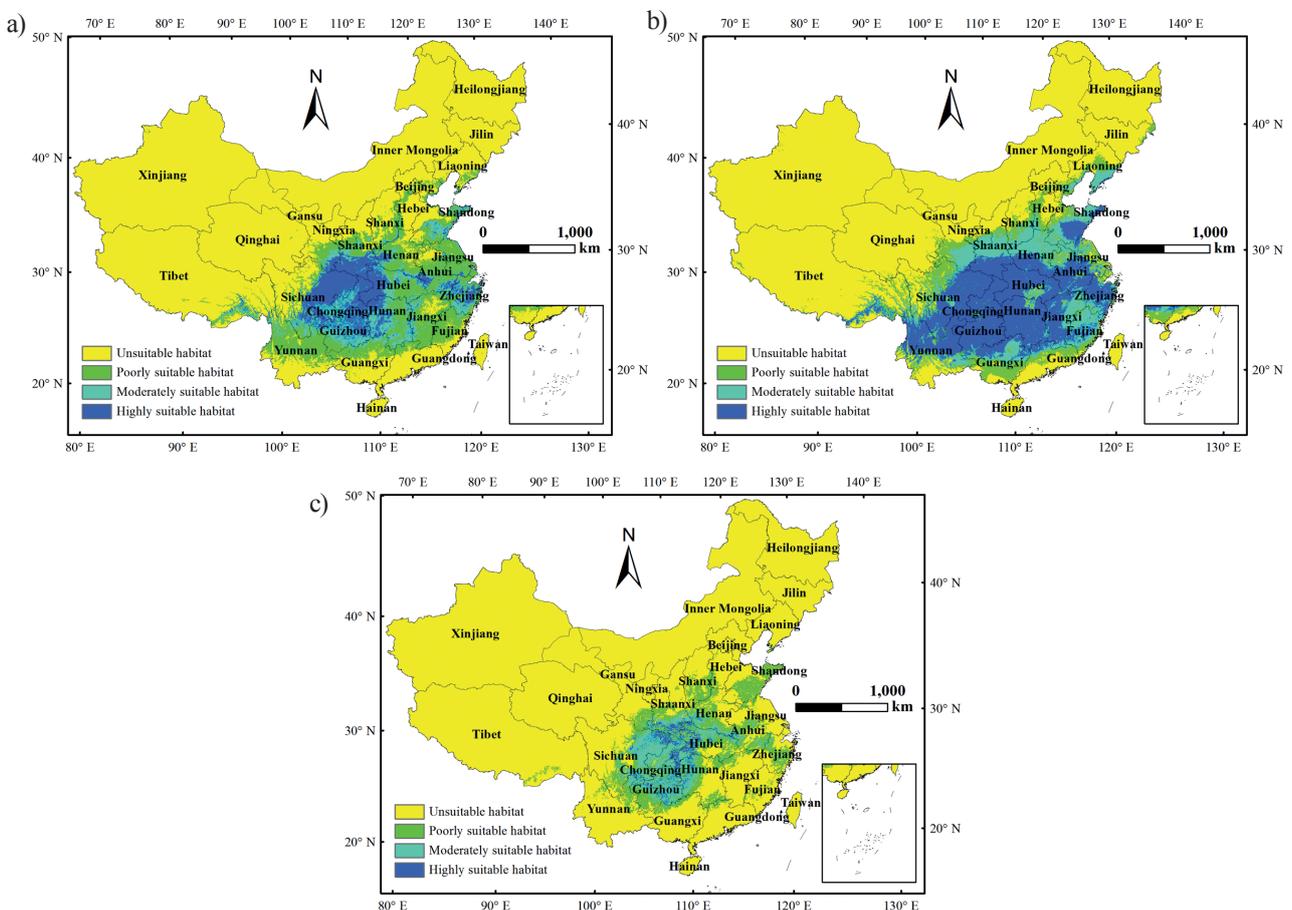


Fig. 3. Potential distribution of *A. carmichaeli* simulated by three models. a) MaxEnt; b) GARP; c) Bioclim.

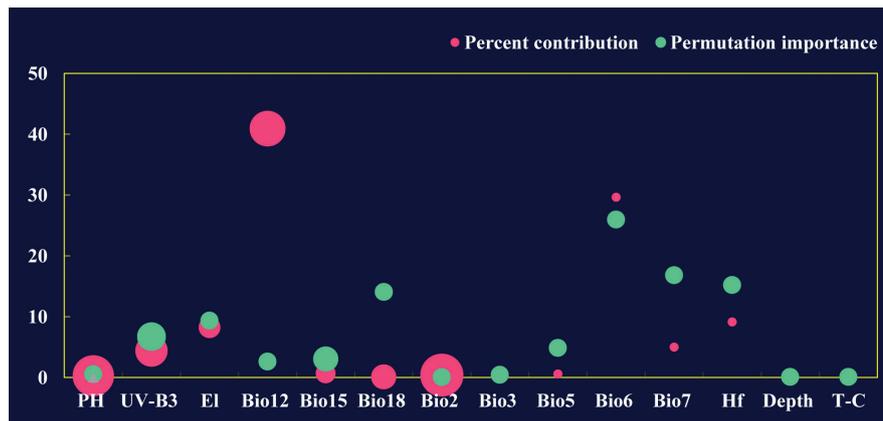


Fig. 4. Percent contribution and permutation importance of 14 environmental variables.

was mainly located in western Hubei ($3.78 \times 10^4 \text{ km}^2$), northeastern Sichuan ($2.21 \times 10^4 \text{ km}^2$), central and northern Guizhou ($2.01 \times 10^4 \text{ km}^2$), southern Shaanxi ($1.87 \times 10^4 \text{ km}^2$) and eastern Chongqing ($1.4 \times 10^4 \text{ km}^2$).

Simulation of MaxEnt showed that the highly suitable habitats of *A. carmichaeli* were concentrated in the middle east of Sichuan ($17.07 \times 10^4 \text{ km}^2$), western Hubei ($7.34 \times 10^4 \text{ km}^2$), southern Shaanxi ($7.2 \times 10^4 \text{ km}^2$), north central Guizhou ($6.74 \times 10^4 \text{ km}^2$), eastern Chongqing ($5.62 \times 10^4 \text{ km}^2$) and western Hunan ($5.21 \times 10^4 \text{ km}^2$). According to the literature, *A. carmichaeli* has been cultivated in more than 20 provinces such as Chongqing, Guangxi, Hunan and Hubei [27, 28, 34]. However, due to climate, environment, diseases and pests, many areas have been eliminated by the market and have stopped cultivation [27, 28]. Based on the field investigation, the main cultivation areas of *A. carmichaeli* include Jiangyou and Butuo in Sichuan, Hanzhong in Shaanxi and Weishan in Yunnan [17, 28]. Compared with Fig. 2a), the highly suitable habitat we simulated includes the current main cultivation areas of *A. carmichaeli*, which confirmed our results. Zhao et al. used TEMGIS-I system to analyze the suitability of *A. carmichaeli* producing area, and they found the suitable habitat includes 336 counties and cities in 10 provinces and regions, indicating that *A. carmichaeli* can be cultivated in a wide area from the perspective of climate conditions [38], which was consistent with the conclusion of this paper.

Widrechner [52] used the annual average minimum temperature as an index to draw the Plant Hardiness Zone Map (PHZM) in China, and divided 11 grades. Combined with our prediction, the distribution range of *A. carmichaeli* was grade 8~11 ($-12.2 \sim 4.5^\circ\text{C}$). According to the cold resistant temperature standard of PHZM, some areas of Hebei, Jiangsu, Anhui, Henan, Yunnan, Guangdong, Guangxi and Taiwan in this range, which may be suitable for introduction and cultivation of *A. carmichaeli*. Combining the potential distribution map predicted by SDMs with PHZM can improve the understanding of *A. carmichaeli* habitat and distribution area, and provide a theoretical basis for its introduction.

Although the above discussion was based on MaxEnt, the prediction results of different models can complement each other. For example, on the distribution map predicted by MaxEnt, Hebei, Jiangsu and Shandong belong to the poorly suitable habitat of *A. carmichaeli*, while this area in GARP model was the highly suitable habitat. By consulting the literature, we found that there were records of large-scale cultivation in the above areas [27].

Contributions of Environmental Variables

Comparing the percent contribution rate (Fig. 4), the order of variables was annual precipitation (40.94%), min temperature of coldest month (29.66%), human footprint (9.14%) and elevation (8.27%), with a cumulative rate of 87.99%. Comparing the permutation importance, the ranking of variables was min temperature of coldest month (25.97%), bio7 (16.82%), human footprint (15.21%), precipitation of warmest quarter (14.09%), and elevation (9.34%) with a cumulative rate of 81.43%.

Fig. 5 showed the Jackknife test of the modeling variables. Comparing the regularization training gain of each variable modeled separately, the min temperature of coldest month (1.2), annual precipitation (1.02) and temperature annual range (1) were significantly higher than others, indicating their unique role in the geographical distribution of *A. carmichaeli*.

Suitable Value Range of Main Environmental Variables

The response curves of 6 important environmental variables drew by MaxEnt demonstrated that the suitable ranges of annual precipitation, precipitation of warmest quarter, min temperature of coldest month, temperature annual range, elevation and human footprint index were 751.25-1580.72 mm (Fig. 6a), 422.71-717.21 mm (Fig. 6b), $-6.85 \sim 3.12^\circ\text{C}$ (Fig. 6c), $24.83 \sim 31.97^\circ\text{C}$ (Fig. 6d), 145.87-2769.22 m (Fig. 6e), <4.01 (Fig. 6f), respectively.

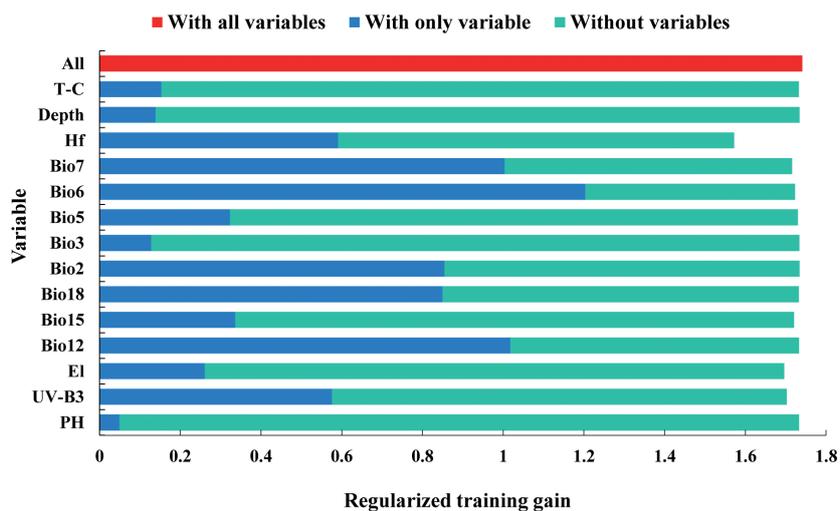


Fig. 5. Import of environmental variables for prediction based on jackknife test.

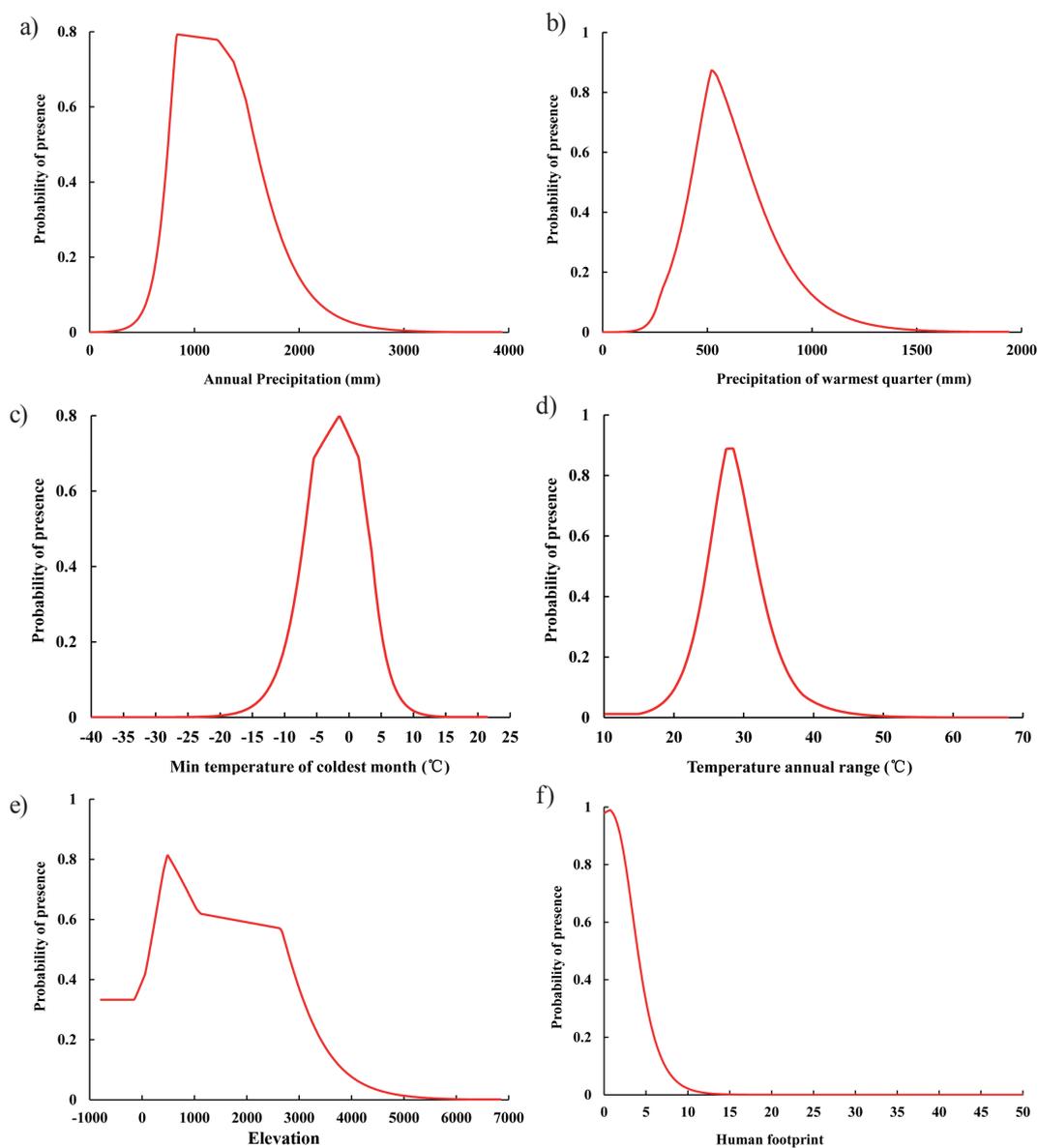


Fig. 6. Response curves of *A. carmichaeli* to key variables.

The impact of climate factors on species is a comprehensive and long-term process, especially temperature and precipitation, which affect the physiological process of plants, and finally form the distribution pattern suitable or unsuitable for today's species [53]. In this study, the temperature variables affecting the geographical distribution of *A. carmichaeli* were min temperature of coldest month and temperature annual range. Research showed that the climate conditions of the genuine producing area of *A. carmichaeli* were close to the climate characteristics of subtropical zone, and there was no real cold area [27, 38]. Our study found that the suitable ranges of min temperature of coldest month was $-6.85-3.12^{\circ}\text{C}$, which was consistent with the winter temperature conditions in its genuine producing area. Here, we boldly speculate that the low temperature in winter restricts *A. carmichaeli* from crossing the Qinling Huaihe line and the northern boundary of subtropical zone. According to the analysis results of Jackknife, temperature annual range was another temperature variable affecting the geographical distribution pattern of *A. carmichaeli*. In a certain range, with the increase of temperature annual range, the adaptability of *A. carmichaeli* to habitat will increase, which may be because the temperature difference is one of the most important factors for plant growth, development and flowering. The growth characteristics of *A. carmichaeli* are as follows: the seedlings emerge and form seed roots in mid February, the seed roots expand rapidly from May to June, the plants moss into reproductive growth in mid July, blossom in mid September, and the fruits mature in mid November [17, 31, 38]. Most plants need to experience warm-cold-warm during these important growth and development periods. Chen et al. found that the germination of *A. carmichaeli* seeds was closely related to temperature, and the effect of variable temperature treatment ($10-20^{\circ}\text{C}$) was better than that of constant temperature treatment [33]. The increase of temperature range in a certain range may contribute to the growth and development of *A. carmichaeli* and increase its adaptability to the environment.

In addition to temperature, the simulation results showed that the precipitation of warmest quarter was an dominant variable affecting the geographical distribution of *A. carmichaeli*. In mid July, the leaf area, number of sub roots and fibrous roots of *A. carmichaeli* reached the maximum in the growth cycle, and in mid August, the total biomass of sub roots and plants reached the maximum in the growth cycle [29, 34, 38]. These reveal that the warmest quarter (July to September) is the most vigorous growth period of *A. carmichaeli*, that is, the period with high water demand. The precipitation between 422.71-717.21 mm (Fig. 6b) can not only meet the water demand of *A. carmichaeli*, but also will not cause root rot due to excessive water, which plays a key role in its growth and distribution. Many scholars have pointed out that temperature restricts the change of North-South latitude of plants, while precipitation

affects the change from coastal to inland, and the two jointly restrict the geographical distribution pattern of plants [54-56].

Many studies have proved that the use of climate factors separately will lead to a wider predicted niche than the actual niche of species [57, 58]. Now the most viewpoints are that even in the suitable distribution area of species, the high fragmentation of natural habitat caused by human excessive activities will hinder the expansion of species [59-61]. Xu et al. found that there was a negative correlation between human activities and narrow-ranged plants [62], and Cao et al. obtained the similar conclusion on the study of *Swertia przewalskii* [63]. Considering these, in addition to the commonly used bioclimatic variables, elevation, soil factors and human activity intensity were also supplemented as environmental data in this study, so as to more comprehensively reflect the ecological environment of *A. carmichaeli* and obtain more accurate prediction results. In this paper, Jackknife test showed that the percent contribution (9.14%) and permutation importance (15.21) of human footprint in affecting the growth suitability of *A. carmichaeli* was high. Based on the above results, it can be inferred that a series of human activities such as land use, infrastructure construction, population density, roads and railways will have a certain impact on the growth, habitat and reproduction of *A. carmichaeli*.

Conclusions

Based on SDMs and GIS technology, this paper studied the suitability zoning of *A. carmichaeli*, analyzed the main environmental variables affecting its growth and the range of suitable values, and divided its suitability grade, which can provide a scientific theoretical guidance and basis for the selection of *A. carmichaeli* wild tending and artificial standardized planting base. In this study, we analyzed the effects of environmental variables on the geographical distribution of *A. carmichaeli*, but the effects of variables on its pharmacodynamic components still need to be further analyzed to make the study more complete.

Author Contributions

Ting Li, Yanli Xia and Rulin Wang planned and supervised the project. Yuxia Yang and Rulin Wang performed the experiments, analyzed the data, contributed reagents/materials/analysis tools.

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Conflicts of Interest

The authors declare no conflicts of interest.

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Supplementary Materials

Table S1. 27 initial environmental variables used in this study.

	Variables and description	Unit
Bio1	Annual Mean Temperature	°C
Bio2	Mean Diurnal Range(Mean of monthly (max temp - min temp)	°C
Bio3	Isothermality (BIO2/BIO7) (* 100)	/
Bio4	Temperature Seasonality (standard deviation *100)	°C
Bio5	Max Temperature of Warmest Month	°C
Bio6	Min Temperature of Coldest Month	°C
Bio7	Temperature Annual Range (BIO5-BIO6)	°C
Bio8	Mean Temperature of Wettest Quarter	°C
Bio9	Mean Temperature of Driest Quarter	°C
Bio10	Mean Temperature of Warmest Quarter	°C
Bio11	Mean Temperature of Coldest Quarter	°C
Bio12	Annual Precipitation	mm
Bio13	Precipitation of Wettest Month	mm
Bio14	Precipitation of Driest Month	mm
Bio15	Precipitation Seasonality (Coefficient of Variation)	/
Bio16	Precipitation of Wettest Quarter	mm
Bio17	Precipitation of Driest Quarter	mm
Bio18	Precipitation of Warmest Quarter	mm
Bio19	Precipitation of Coldest Quarter	mm
El	Elevation	m
PH	Potential of hydrogen	/
T-C	Topsoil organic carbon	%
T-sand	Topsoil sand fraction	
USDA	Topsoil USDA texture classification	name
Depth	Reference soil depth	m
UV-B3	Mean UV-B of Highest Month	kJ/m ²
Hf	Human footprint index	/

Table S2. Percent contribution of 19 bioclimatic variables.

Variable	Percent contribution (%)
Bio12	42.5
Bio6	29.2
Bio9	10.0
Bio5	5.6
Bio7	4.0
Bio14	2.0
Bio10	1.3
Bio11	1.0
Bio19	0.9
Bio4	0.7
Bio15	0.7
Bio3	0.6
Bio18	0.5
Bio8	0.4
Bio2	0.3
Bio1	0.1
Bio17	0.1
Bio16	0.1
Bio13	0.0