

# Predicting the Potential Distribution of *Centaurea* balsamita Lam. in the world in current conditions and future climate change

### ARTICLEINFO

### Article Type Original Research

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# How to cite this article

Abbasian A., Asadi GhA., Naseri A. Predicting the Potential Distribution of Centaurea balsamita Lam. in the world in current conditions and future climate change. ECOP-ERSIA 2022;10(3): 217-229

### DOR:

20.1001.1.23222700.2022.10.3.5.2

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# Article History

Received: May 2, 2022 Accepted: August 23, 2022 Published: September 01, 2022

### ABSTRACT

**Aims:** An attempt was made to understand the effects of climate change on the potential future distribution of *Centaurea balsamita* In the world. *C. balsamita* is an annual herb in the Asteraceae family that invades fallow and slope areas worldwide. Climate change is causing extreme weather events that are having far-reaching effects on ecosystems across the globe, including Plant species distribution: CLIMEX software is used worldwide to analyze the potential distribution of species.

**Materials & methods:** The experiments were conducted in Mashhad, Khorasan Razavi Province. In the present study, CLIMEX software was used to study the potential distribution of this plant in the world at present and future climate conditions. The CLIMEX software requires five climate variables, including average, maximum, and minimum monthly temperature, precipitation, and relative humidity at 9 Am and 3 Pm. These data were obtained from various sources such as "CRU TS v.4.03" and used in model predictions. Literature data were used to gather information on biology and ecology needed to model the distribution of *C. balsamita* in Iran and worldwide under current and future climatic conditions.

**Findings:** Our results revealed that in current conditions, Europe, Asia, and North America are suitable locations for this invasive weed dispersal, and most parts of Europe have optimal conditions (20≤ EI) for the dispersal of *C. balsamita*. It is likely that the suitable *C. balsamita* habitat area will be wider in some parts of the world such as Asia, America, and Europe under future climatic scenarios as a result of the heat stress and will be limited in some areas such as Turkmenistan.

**Conclusion:** *C. balsamita* has global potential in both current and future climate scenarios. We have shown that entire regions are suitable for the establishment of *C. balsamita*, especially in Central Asia, Iran, Afghanistan, Turkey, and China. This is very consistent with its distribution at its origin.

Keywords: CLIMEX, Ecoclimatic Index, Invasive plant, Weed.

# CITATION LINKS

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# Introduction

Climate change is a major challenge for the international community [1]. Based on the IPCC, variations in temperature, precipitation, and evaporation occur in regions throughout the globe, resulting in various changes [2]. Plant invasiveness and climate change are two important issues in ecosystem disturbances and both threaten the status of biodiversity and the extinction of species [3, 4]. Climate change is affecting invasive plant management in many ways; For example, it can put pressure on native ecosystems, increase climatic disturbances and create new opportunities for introduced species to establish and thrive [5, 6]. The invasive plant causes high economic damages or losses. The economic damage from invasive species within the USA is calculable at USD 35 billion, Australia at USD four billion, Canada at USD 38 billion, Germany at USD 104 billion, and China at USD 14.45 billion annually [4, 8]. Invasive species will probably connect with climate change, requiring the administration to address both worldwide changes proactively [9]. Climate change also offers new opportunities for the successful prevention and management of invasive species. Therefore, the aggressive behavior of a plant in other parts of the world, especially in climate change, is an important predictor of the potential impact of invasive species. Prevention of new invasions is an effective technique for managing the invasive species, particularly if the emerging invaders are detected and addressed before their arrival. Climate change is projected to bring about a hundred new invasive plants to the northeastern United States [5]. The extraordinary temperatures and irregular precipitation patterns in numerous locales are expected to influence the dispersion of local and invasive species and the common warming trend is accepted to cause latitudinal and altitudinal shifts in the geographic ranges of a few species [10]. Various models are widely

used to predict the potential distribution of different species and to study the climate suitability of species under current and future climate-changing conditions. In this regard, CLIMEX is one of the most advanced soft to predict the distribution range of pest and weed species by focusing on the climatic effect on species inhabitation [11, 12]. CLIMEX is bioclimatic software that assesses the potential distribution of the flora, fauna, vector-borne diseases and crop pests, as well as the risk of their spread to new regions and the under conditions of climate change [13]. In the current and future climate, CLIMEX software is also employed in biological strategies, pest management, control quarantine, and epidemiology. CLIMEX uses organisms' biological and physiological characteristics to predict species dispersal [11]. The ability to predict the risk of new species entering an area could be essential to prevent invasive species from stabilizing. CLIMEX offers a beneficial tool to verify the probability of a introduced species establishing in a particular country or region and its possible distribution [14]. The thermos-hydrologic growth index (GI), which governs climate expertise and climate stress is effectively used to predict climate compliance and weed spread potential [15]. Centaurea has been identified from 400 to 700 species worldwide [16]. Also, it is native to Asia, Europe, North Africa and North America. Many species have been reported as problematic weeds, are C. diluta [17], C. solstitialis<sup>[18]</sup>, C. stoebe<sup>[20]</sup>, C. biebersteinii, C. melitensis<sup>[7]</sup>, C. repens [7], and C. diffusa<sup>[7]</sup>.C. balsamita is an annual plant that invades fallow and slope lands [22]. This plant species is reproduced by seed [23,25]. The distribution of C. balsamita has been reported in northern, northwestern, western, central, and eastern Iran. C. balsamita as an invasive weed in fields of winter wheat and barley fields in Iran has been observed. In addition, weeds are also

abundant in pastures, fallow farms, and roadside. Large thorns on the margins of the leaves and fruits of C. balsamita have made it difficult for manual weeding or hand picking in contaminated fields [26, 22] (Figure 1). C. balsamita has also been reported in wheat farms [28]. This study intended to assess the impact of climate change on the worldwide spread of *C. balsamita*. Thus, the primary purpose of this research was 1) to identify appropriate habitats and estimate global distribution of C. balsamita under the present climatic conditions 2) to estimate the effects of climate change on the geographic distribution of *C. balsamita* by 2050 and 2080 under various scenarios 3) Modeling the changing trend of *C. balsamita*'s appropriate habitat in response to climate change scenarios.





**Figure 1)** Invasion of *C. balsamita* Mashhad, Iran.

# Materials & methods Study area

The research was carried out in Mashhad, Iran, the capital of "Khorasan Razavi" province, approximately 850 km northeast of Tehran at 36.20 degrees north latitude and 59.35 degrees east longitude, in the valley of the Kashaf River between the mountain ranges of Binalood and Hezar-Masjed. A Steppe climate (Koppen BSk) with scorching summers and cold winters characterizes Mashhad. Summer time average temperatures exceed 30 °C. However, actual temperature extremes, like temperatures over 40 °C. The city barely receives roughly 250 mm of precipitation annually. Mashhad has less than 2900 h of annual sunlight [30].

# Potential distribution model

The computer software CLIMEX version 2.0 was used to assess the potential for the geographic spread of *C. balsamita* under current and future climatic conditions. CLIMEX can fit two different forms of data: location comparisons for species corresponding to the long-term climate of various locations and year comparisons for different climate years for the same location. Future climate change scenarios are based on a combination of SRES scenarios and GCM models available from the IPCC (Intergovernmental Panel on Climate Change and the Data Distribution Center). The parameter (growth index) for each species describes the response of that species to climate. The growth index (GI) describes the growth of the population over a favorable annual period.

# **CLIMEX** input

Long-term average weather data, i.e., long-term average maximum and minimum temperatures, precipitation, and relative humidity, are required as inputs to CLIMEX. We used data for the 1961 – 2000 periods [11]. There are two groups of geographically

restrictive variables for each species in this software:

1-Growth indices: The weekly growth index (GIW) and annual growth index (GIA) represent the temperature and humidity range (mainly temperature and soil moisture) for species growth and development, respectively.

Stress indicators are related geographically limited constraints. Cold Stress (CS), Heat Stress (HS), Dry Stress (DS), Wet Stress (WS) and stress interactions (Cold/Wet, Cold/Dry, Hot/Wet, Hot/Dry) are truly component indicators. Eco climatic Index (EI), which indicates the climatic suitability of a site for a particular species on a scale of 1 to 100. The Eco climatic Index (EI) combines the Yearly Increase Index (GI,), which indicates the potential for population growth, with the annual pressures that restrict survival during adverse seasons and any other limiting variables.

As is customary in CLIMEX modeling, the present model employs an EI value of 0 to label a region as climatically inappropriate. EI = 0 (unsuitable), (unsuitable),  $1 \le EI \le 4$  (marginal),  $5 \le EI \le 9$  (suitable),  $10 \le EI \le 29$  (highly suitable), and  $30 \le EI$  (optimal) [11]. EI is also subject to the restrictions of having sufficient degree-days to complete the lifecycle (PDD) and achieving the circumstances necessary to complete diapause.

The CLIMEX software needs biological, physiological and ecological information about each plant to determine potential distribution. All information about C. balsamita was obtained from the experiments conducted in our previous studies [31, 32] and entered into the CLIMEX software. After adjusting the parameter values, the data were used to run the model to predict the species' potential distribution. Then, based on the software prediction model, the distribution of each species was determined on various maps.

Potential distribution maps were prepared for the different continents for current and future climate situations. Prediction of the distribution of C. balsamita under climate change was based on the UK scenario for 2080 [11]. According to this scenario, by 2080, the Earth's temperature will rise to at least 2 °C and 3 °C in winter and at least 3 °C and 4 °C in summer. Precipitation will increase by 20% in winter and by 25% in summer. After preparing the map, the distribution of *C. balsamita* was described and analyzed. Based on the prediction model results, the constraints and barriers of distribution or factors of distribution of this species were discussed. The CLIMEX software requires five climate variables, including monthly average, maximum and minimum temperatures, precipitation and relative humidity at 9 AM and 3 PM. [33, 11].

In studies on C. balsamita, the lowest, optimum and maximum temperatures for germination were 1.44 °C, 15 °C, and 25 °C, respectively and the highest tolerance temperature in this species was 38.4°C. Based on our results [31], the lethal temperature of 50% of the populations of *C. balsamita* was set at -13 °C in the present study. It can be stated that it is one of the cold tolerant plants and it is foreseen that it is possible to spread and stabilize this invasive accumulation rate. Therefore, the cold stress threshold was set at -13 °C and zero weekly accumulation rates. Based on our study results [32] and the table in the CLIMEX guidelines (for semi-arid regions), the moisture stress threshold was set at 0.6, and the weekly accumulation rate was set at 0.005. The optimum germination temperature for *C. balsamita* was 15 °C to 25 °C, and the maximum temperature was 38.4 °C [31]. Therefore, the heat stress threshold for C. balsamita was 38.4 °C and the cumulative heat stress rate was 0.002 days a week. According to the distribution of *C. balsamita* under semi-arid conditions and the table

in the CLIMEX Guide, the drought stress threshold was set at 0.05 and the weekly accumulation rate was -0.005 (Table1). Based on the results of our studies [31] and the table in the CLIMEX guidelines (for semi-arid regions), the threshold of moisture stress was 0.6, and the weekly accumulation rate was considered 0.005.

Dormancy is an adaptation that enables it to withstand adverse climatic conditions. In

CLIMEX, this index refers to vernalization, where the plant needs a cooling period to create a flowering stem. In *C. balsamita*, usually in the early winter, the plant begins to grow slimy, and which dormancy induction day length lasts 12 h. Also, the phenomenon of vernalization in the plant is usually resolved by one to two weeks of planting at 1°C (Dormancy Induction temperature) to 7°C (Dormancy Termination temperature) [15].

**Table 1)** CLIMEX parameter values adjusted to *C. balsamita* base. Unitless values are dimensionless indices.

Index	Parameter	Abbreviation	Value
Temperature	Lower threshold	$DV_0$	°C1.44
	Lower optimum temperature	$DV_1$	°C15
	Upper optimum temperature	$\mathrm{DV}_2$	°C25
	Upper threshold	DV <sub>3</sub>	°C38.4
Dormancy index	Dormancy induction day length	$DPD_0$	12h
	Dormancy induction temperature	$DPT_0$	1 °C
	Dormancy termination temperature	$DPT_1$	7 °C
	Dormancy development days	DPD	14 Day
	Dormancy summer or winter indicator	DPSW	0
Moisture	Lower soil moisture threshold	$SM_0$	0.05
	Lower optimum soil Moisture	$SM_1$	0.1
	Upper optimum soil moisture	SM <sub>2</sub>	0.4
	Upper soil moisture threshold	$SM_3$	0.6
Cold stress	Temperature threshold	TTCS	-13°C
	Stress accumulation rate	THCS	0
	Degree-day threshold	DTCS	15 Days °C
	Degree-day stress	DHCS	-0.0002 (week <sup>-1</sup> )
Heat stress	Temperature threshold	TTHS	38.4
	Stress accumulation rate	THHS	0.002
Dry stress	soil moisture dry stress threshold	SMDS	0.05
	Stress accumulation rate	HDS	-0.005 (week <sup>-1</sup> )
Wet stress	Soil moisture wet stress threshold	SMWS	0.6
	Stress accumulation rate	HWS	0.005 (week <sup>-1</sup> )
Annual heat sum	Degree-day threshold	PDD	2476 Days °C

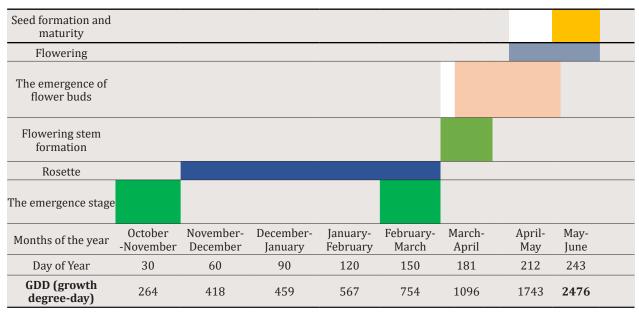


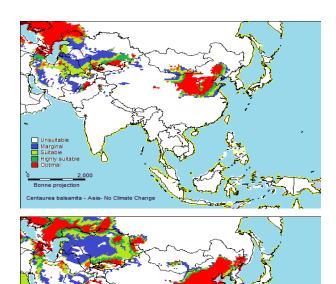
Figure 2) Phenological growth stages of C. balsamita in Mashhad, Iran [26, 27].

The index is the degree-day threshold (growth degree-day) during the growing season to create a new generation. A phenology study of *C. balsamita* was conducted in Mashhad weather conditions in 2014-2016<sup>[32]</sup>. Based on the study of phenology *C. balsamita* germinates in the autumn (especially November) and after 243 days. Seed falling happens, and the life cycle is completed (Figure 2).

# **Findings**

# The potential of *C. balsamita* distribution in Asia

Accordingly, the map fitted by CLIMEX was highly consistent with the researchers' reports, as shown by Climax's map of *C. balsamita* in Syria, Iran, Afghanistan, Transcaucasia (Georgia, Armenia, and Azerbaijan), Central Asia (Turkmenistan, Kazakhstan, Uzbekistan and Tajikistan), Mongolia and China were widely distributed. In some regions of China, Mongolia, Kyrgyzstan, and Uzbekistan, due to low temperatures, it is not possible to complete the life cycle of *C. balsamita* (Figure 3).



**Figure 3)** Distribution potential *of C. balsamita* in Asia under current and predicted climates (2080). Inappropriate areas for distribution of White *C. balsamita* (5> EI), Critical areas of blue (10> EI ≥5), areas of pale green ( $10 \le EI < 15$ ), areas of very green  $15 \le EI < 20$ ), and optimal areas are shown in red ( $20 \le EI$ ).

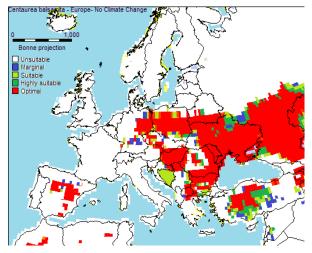
<sup>\*</sup>The emergence stage took place in November, but in the years when autumn rains are delayed germination occurs in late winter

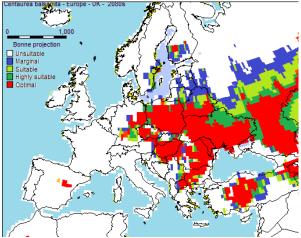
In some areas, such as India, parts of China, Japan, North, and South Korea, and Southwest Asia, there is a high degree of moisture stress and it is impossible to grow C. balsamita. In some parts of Russia, this species can't grow due to cold stress and an incomplete life cycle. The *C. balsamita* is not distributed in the Persian Gulf countries due to the high heat and drought stress. Based on CLIMEX's fitting map of C. balsamita parameters in climate change conditions, it was found that the spreading spots of this invasive plant increased in many areas (such as Kazakhstan, China, and Uzbekistan) and more dispersed to optimal areas (EI ≥20). It will move; however, the plant will be restricted in some areas, such as Turkmenistan.

# Potential of distribution of *C. balsamita* in Europe

C. balsamita has potential distribution in Turkey, southwestern Russia, Romania, Bulgaria, Ukraine, Spain, Hungary, the Netherlands, Belarus, Slovakia, Switzerland, Austria, Spain, Bosnia, and Herzegovina. Based on these results, these parts have optimal conditions for the growth and distribution of *C. balsamita* (EI ≥20) (Figure 4). Also, under current conditions, *C. balsamita* will not be distributed in much of Russia (due to the inadequate degree of growth required and the generation of very low temperatures). In northern Europe, stress distribution conditions are unavailable for this plant due to the lack of suitable temperature and high humidity. There is a high degree of moisture stress in Italy, France, England, and Ireland, so there are no conditions for C. balsamita growth. Based on a map of C. balsamita by Climax, it was determined that the spreading spots of this invasive plant in Europe would be greatly enhanced by climate change (such as Russia, Lithuania, Finland, Sweden, and the Netherlands) (Figure 4), as many

points Europe will find optimal conditions (EI  $\geq$ 20) for growth and distribution. In some regions, such as Spain and Bosnia and Herzegovina, the plant's growth will be limited.

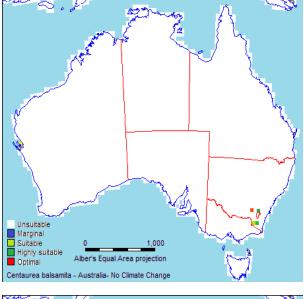


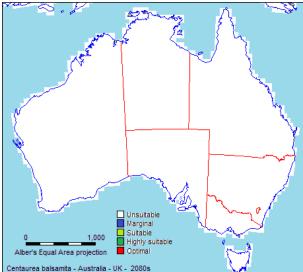


**Figure 4)** Distribution potential of *C. balsamita* in Europe under current and predicted climates (2080). Inappropriate areas for distribution of White of *C. balsamita* (5> EI), Critical areas of blue (10> EI  $\geq$ 5), areas of pale green (10 $\leq$ EI <15), areas of very green 15 $\leq$  EI <20) and optimal areas are shown in red (20 $\leq$ EI).

# The distribution potential of *C. balsamita* in Australia

According to CLIMEX's map of *C. balsamita*, this species won't be able to spread in Australia (except in a small part of the southeast) in current and predicted future climatic conditions. Drought and extreme heat will limit factor the growth of this

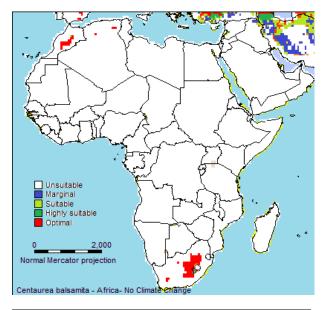


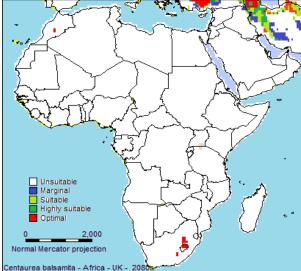


**Figure 5**) Distribution potential of *C. balsamita* in Australia under current and predicted climates (2080). Inappropriate areas for distribution of White of *C. balsamita* (5> EI), Critical areas of blue (10> EI ≥5), areas of pale green ( $10 \le EI < 15$ ), areas of very green  $15 \le EI < 20$ ) and optimal areas are shown in red ( $20 \le EI$ ).

# The potential of *C. balsamita* in Africa

*C. balsamita* will not be able to disperse in Africa (except in a small part of its southern part), and high heat stress is the limiting factor for the distribution of this species in Africa (Figure 6) in current and predicted future climates.





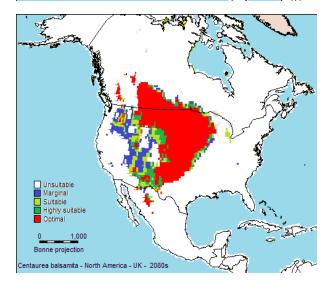
**Figure 6)** Distribution potential of *C. balsamita* in Africa under current and predicted climates (2080). Inappropriate areas for distribution of White of *C. balsamita* (5> EI), Critical areas of blue (10> EI ≥5), areas of pale green (10≤EI <15), areas of very green 15≤ EI <20) and optimal areas are shown in red (20≤EI).

# Potential of distribution of *C. balsamita* in North America

According to CLIMEX maps, under current conditions, *C. balsamita* has the potential to spread in the central west of America and parts of northern Mexico, while most of these areas have optimal conditions for the growth and distribution of this invasive

plant (Figure 7) (EI  $\geq$ 20). *C. balsamita* in Canada cannot spread because of the extreme cold. These maps also determined that the invasive plant in the United States would be widely dispersed with climate change so that many parts of North the US would find optimal conditions (EI  $\geq$ 15) for the growth and dispersal of *C. balsamita*.

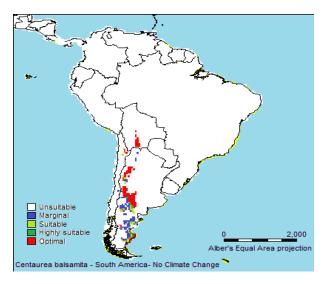
# Unsuitable Marginal Suitable Hignly suitable Optimal O\_\_\_\_\_\_1,000 Bonne projection Centaurea balsamita - North America- No Climate Change

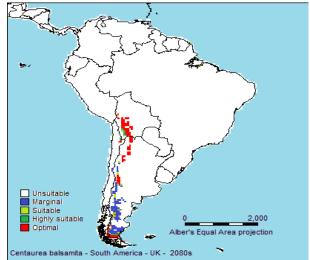


**Figure 7)** Distribution and potential of *C. balsamita* in North America under current and predicted climates (2080). Inappropriate areas for distribution of White of *C. balsamita* (5> EI), Critical areas of blue (10> EI ≥5), areas of pale green ( $10 \le EI < 15$ ), areas of very green  $15 \le EI < 20$ ) and optimal areas are shown in red ( $20 \le EI$ ).

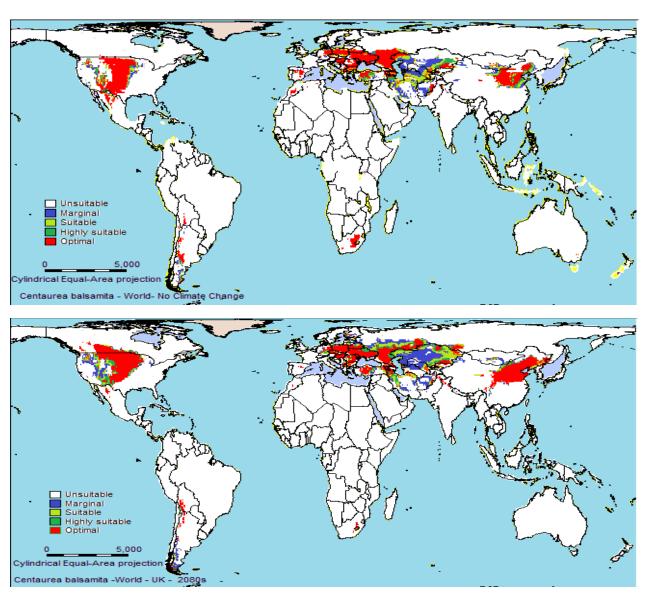
# Potential of distribution of *C. balsamita* in South America

*C. balsamita* has the potential to disperse in parts of Bolivia, Argentina, and Peru under present conditions (Figure 8). The maps showed that the distribution of this invader in South America would be much wider in future climate change.





**Figure 8)** Distribution potential of *C. balsamita* in South America under current and predicted climates (2080). Inappropriate areas for distribution of White of *C. balsamita* (5> EI), Critical areas of blue (10> EI ≥5), areas of pale green ( $10 \le EI < 15$ ), areas of very green  $15 \le EI < 20$ ) and optimal areas are shown in red ( $20 \le EI$ ).



**Figure 9)** Distribution potential *of C. balsamita* in the world under current and predicted climates (2080). Inappropriate areas for distribution of White of *C. balsamita* (5> EI), Critical areas of blue (10> EI ≥5), areas of pale green (10≤EI <15), areas of very green 15≤ EI <20) and optimal areas are shown in red (20≤EI).

# **Discussion**

Predicting the present and future distribution of species is essential for monitoring and assessment preparation. For this reason, species distribution modeling (SDM) is one of the most important methods for determining habitat suitability, species needs and ecosystem conservation, and recognition of biodiversity trends<sup>1</sup>.

In this study, CLIMEX was used to model the current and future (2050 and 2070) distribution of *C. balsamita*. Global studies show that temperatures have changed at

the global and regional levels over the past centuries [1, 2].

Temperature as an important climatic factor strongly influences the distribution of *C. balsamita*. The studied species (*C. balsamita*) is one of the most invasive species [26,22]. In the present study, the current distribution range of *C. balsamita* was investigated, and then it was predicted for the future based on a climate change scenario. Several studies have used CLIMEX Software to predict the possibility of different weed species in different countries (such as *Abutilon theophrasti*) [36],

Palmer amaranth<sup>[37]</sup>, Lantana camara<sup>[38]</sup>, hysterophorus [39], Parthenium Solanum carolinense [42]. Ophraella  $communa^{[43]}$ . Lolium rigidum[44] Climate condition also has an effect on plant invasion processes [45, 46, 47]. Climatic conditions determine the ability of an invasive plant to spread, survive and reproduce in a particular area. Non-native invasive plants are projected to migrate their range with climate change, creating hotspots where many new species grow and disperse [48].

Recognizing the factors anticipating the appropriate environments for invasive plants and how these appropriate environments are influenced by climate change are imperative for taking measures to restrain the spread of invasive plants [10]. In the United States, the distribution of *Centaurea solstitialis* was expected to increase, and the distribution of *Centaurea maculosa* changed slightly [5]. CLIMEX could be a special software program that can determine plant distribution based on climatic data and species physiological characteristics [12].

In the CLIMEX sensitivity analysis, varied primarily with factors related to temperature and humidity (TTCS, TTHS, DV0, DV1, SM0, and SM1). Temperature and humidity are precisely the main factors that determine plant development and thus climatic suitability:in the case of *U.* panicoides, constant values lower than the optimal temperature and humidity (25 • C and 0.2) prevent germination and growth by causing seed dormancy. In addition, U. panicoides has low cold tolerance, especially prolonged cold. Cold stress and accumulation rates are the reform the most susceptible factors. Climatic conditions influence the effectiveness of weed management.

The present study on *C. balsamita* showed that this weed species has the potential to invade worldwide in the current climate. This potential of invasion is even worth in

predicted climate. The distribution of this species would be broadened in some parts of the world. It was found that the spreading spots of this invasive plant will be greatly enhanced by climate change in Europe, Asia and North America, and many parts of Europe (EI ≥20). Several parts of China, Kyrgyzstan, and Uzbekistan Mongolia, would see a decline in suitability owing to low temperatures in 2050, 2080, and 2100, as a result of probable decreases in humidity and increases in stress during drought, as predicted by CLIMEX under the CSIRO SRES A2 scenario. Based on a map of *C. balsamita* by CLIMEX, climate change was projected to dramatically increase the spread of this invasive species across Europe (Figure 4). Climate change impacts precipitation patterns and water availability affects the physiological processes of weeds, resulting in an expansion of suitable areas in several European regions.

In this respect, CLIMEX software can be useful in identifying areas susceptible to invasive species. C. balsamita as an invasive weed showed high potential for dispersal and establishment (invasion) in current climate conditions and much higher potential in future predicted climate in most regions of the world. Although C. balsamita has invaded many regions, many areas still have good climatic conditions for its distribution. These results provide essential information needed to identify and highlight the potential of the areas at risk of invasion. Identifying these new areas can help prevent and manage the spread of the invasive plant. Predictive models for C. balsamita invasion could lead to quarantine measures and prevention strategies to prevent such invaders. It should also be emphasized that good projections are only future distributions based on climatic conditions, not future distribution projections. It can be suggested that future appropriate land projections based on CLIMAX should further consider non-climatic factors such as land use patterns, soil type, and soil drainage<sup>[50]</sup>.

# **Conclusion**

Species-occurrence modeling is an efficient predictive tool and helps identify priority areas for protection and restoration over time. In this study, we successfully modeled the potential spread of *C. balsamita* under current and future climatic conditions. Many predictive modeling systems, such as CLIMEX, gather information about the climate needs of target species from species geographic distribution data and use this knowledge to influence parameter fitting during model training. It was found that the spreading spots of this invasive plant will be greatly enhanced by climate change in Europe, Asia, North America and many parts of Europe (EI ≥20). Our findings indicate that future climate change will significantly impact the worldwide distribution of C. balsamita.

Maps of potential invasion risks could be a useful tool for public awareness campaigns, especially in countries identified as climatically suitable for *C. balsamita* under future climate scenarios. Conservation and management practices for C. balsamita should consider the expected consequences of climate change. It is recommended that the conservation and management practices of C. balsamita take into account the expected consequences of climate change. This research may give reliable information for developing adaptive responses for species' sustainable management. Further studies for prevention tools and management strategies to restrict spreading, establishment, development, and expansion should be conducted.

# **Conflict of Interest**

The author states that there are no conflicts of interest regarding the publication of this

manuscript.

# **Ethical Permissions**

Not declared by the authors.

# **Funding/Support**

This study received no specific grant from any funding agency.

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