Original Research

Conservation of Medicinal plants by sustainable aquaponics approach for novel drug development

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Abstract
Medicinal plants are one of the significant elements of global population that play a pivotal role in healthcare and other sectors. The cultivation and trade of medicinal plants hold considerable economic value for a country. However, the interplay of climate change, intensive harvesting, and other stress factors has resulted in a decline in the availability of medicinal plants, leading to a loss of their medicinal properties and, in extreme cases, species extinction. Despite the existence of numerous recommendations aimed at conserving and sustainably utilizing medicinal plant resources, only a limited number of these initiatives have successfully safeguarded some medicinal plant species. This review aims to highlight the significance of conservation of medicinal plants by aquaponics, a sustainable approach integrating aquaculture and hydroponics. The review discusses stress factors affecting the survival of medicinal plants and various applications of medicinal plants in new drug development. Studies providing evidence of aquaponics grown medicinal plants with enhanced performance and medicinal properties were discussed. Future research work can focus more on expanding the scope of utilizing aquaponics to grow and protect a wider array of medicinal plant species. Such an approach will potentially conserve medicinal plants from climate change, exploitative practices, species extinction and can be utilized for novel drug development.

Keywords: Medicinal plants, stress factors, conservation, sustainability, aquaponics, drug development

INTRODUCTION

Medicinal plants serve as a significant contribution to the healthcare sector worldwide, representing nature's bestowed gift upon humanity.[1] The research and documentation surrounding the role of medicinal plants in both traditional and modern medicine have extensively examined their prominence. These plants serve as a valuable resource for the development of novel drugs, thus enabling their commercial production. In developing nations, medicinal plants constitute the primary healthcare source for approximately 80% of the population, with a growing demand observed in developed countries. Additionally, medicinal plants play a pivotal role in the production of herbal drugs, secondary metabolites, and natural health products.[2,3,4] Their utilization in veterinary medicine contributes to economic benefits for livestock owners, owing to their easy accessibility and cost-effectiveness in treating animal diseases. Moreover, many people in various countries derive their livelihoods from traditional healing practices or the trade using medicinal plants. The harvesting and trading activities associated with medicinal plants provide a substantial source of income for countries, estimated to exceed US$32.6 billion annually.[5,6] Consequently, medicinal plants are regarded as highly valuable resources for human sustenance. According to the International Union for Conservation of Nature (IUCN) and the World Wildlife Fund (WWF), an estimated 50,000 to 80,000 species of flowering plants around the world are used for medicinal purposes. Unfortunately, 15,000 of these species face the threat of extinction due to overharvesting and habitat destruction, primarily in countries such as China, Nepal, India, Kenya, Tanzania, and Uganda.[7,8,9,10,11] Numerous medicinal plant species remain unexplored, particularly in countries like the United Arab Emirates (UAE), where habitat destruction of medicinal plants due to climate change stress factors such as salinity and extreme temperature are escalating at an alarming pace.[12]

The global phenomenon of climate change poses an additional

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threat to medicinal plants, leading to a decrease in their availability and even the complete extinction of certain plant species. The Intergovernmental Panel on Climate Change (IPCC) has unequivocally declared the reality of climate change. Projections indicate a future temperature increase ranging from 1.4 to 5. 8̊ C on a global scale, will be accompanied by the occurrence of extreme and unpredictable weather events by 2033. The primary causes of climate change are currently observed to be elevated levels of greenhouse gas (GHGs) emissions, particularly carbon dioxide (CO_2), followed by methane and ozone gas. These alterations exert stress on plants and disrupt their medicinal properties.[13,14,15] Notably, arid zone medicinal plants are among the biomes experiencing the most rapid rates of climate change.[16] For example, the desert steppe habitat, which is used in Chinese medicine and exemplified by *Glycyrrhiza uralensis* Fisch., has undergone significant degradation in recent decades, mainly due to the intensification of climate change and human activities.[17] Climate change factors have profound effects on medicinal plants, influencing their productivity, quality, bioactivity, and chemical composition.[18-22]

Medicinal plants are recognized for producing a diverse array of bioactive compounds. that serve as the foundation for drug production and herbal remedies.[23,24] Moreover, these compounds are utilized in a variety of industries, including food, cosmetics, and agrochemicals.[25,26,27] Climate change and other stress factors impact the production of bioactive compounds in medicinal plants, rendering them less suitable for various uses and applications Table 1.

IMPACT OF CLIMATE CHANGE AND OTHER STRESS FACTORS ON MEDICINAL PLANTS

Some studies have highlighted the positive and negative impacts of climate change on medicinal plants, such as phenological changes, affecting the timing of events such as bud burst, leaf unfolding, flowering, fruit setting, and leaf drop.[62] Shifting ranges results in the displacement of medicinal plants to new habitats, leading to habitat loss and, in some cases, extinction.[63] Elevated levels of carbon dioxide (CO_2) have been found to have beneficial effects on the productivity and quality of certain medicinal plants. For example, studies have demonstrated that cultures of Oregano (*Origanum vulgare* L.), Peppermint (*Mentha piperita*), Lemon basil (*Ocimum basilicum* L.), Thyme (Thymus vulgaris L.), and Spearmint (*Mentha spicata* L.), show increased fresh weight, as well as a greater number of leaves and roots, compared to cultures grown under ambient air conditions.[64] The effects of ultraviolet (UV) radiation can cause metabolic and cellular damage in plants Table 2. This damage includes DNA mutation, harm to proteins and other biopolymers.[62] Elevated ozone (O_3) levels activates the metabolic pathways, including the jasmonic acid and salicylic acid pathways, which play a role in the production of bioactive compounds.[65]

Variations in light intensities also play a significant role in the growth and development of medicinal plants. Both high and low light intensities can inhibit photosynthesis and reduce plant growth.[66] Research has shown that light intensity and photoperiod significantly influence the synthesis and storage

Table 1. Various applications & uses of medicinal plants

Author [Reference]	**Application & Plant source**	**Uses**
	Herbal medicine	
Firenzuoli, F. and Gori, L., 2007[23]	Bergamot (*Citrus bergamia*)	Fragrance, disinfectant, healer
	Coltsfoot (*Tussilago fanfara* L.)	Cough sedative
	Germander (*Teucrium chamaedrys* L.)	Depurative, slimming, digestive
	Marigold (*Calendula officinalis* L)	Hemmenagogus, dysmenorrea
	Greater celandine (*Chelidonium majus*)	Hepatobiliary diseases, liver depurative gastric ulcer
	Pharmaceuticals	
Pasierski, M. and Szulczyk, B., 2022[28]	*Capsicum annum*	Pain relievers
Bahmani, Mahmoud, et al.,2016[29]	*Trigonella foenum-graceum* L	Anti-diabetic, anti-conception
Wen, Ming-Chun, et al.,2005[30]		
Lone, S.H., Bhat, K.A. and Khuroo, M.A., 2015[31]		
Flora, Kenneth, et al.,1998[32]	*Glycyrrhiza uralensis*	Anti-asthma
	Artemisia glabella	Anti-tumor
	Silybum marianum	Hepatoprotective activities
	Cosmetics	
Shah, G.M. and Khan, M.A., 2006[33]	*Achyranthes aspera* L.	Pimples & Boils
Ahmed, M., et al.,2007[34]		
Ahmad, S.S. and Husain, S.Z., 2008[35]		
Jan, G., Khan, M.A. and Jan, F., 2009[36]		

Shah, G.M. and Khan, M.A., 2006[33]	*Cannabis sativa* L.	Skin care
Husain, S.Z., 2008[35]		
Muhammad Arshad, M.A. and Saadia Akram, S.A., 1999[37]		
Dastagir, G., 2001[38]		
Zabihullah, Q., Rashid, A. and Akhtar, N., 2006[39]		
Qureshi, Rahmatullah, et al.,2009[40]		
Shah, G.M. and Khan, M.A., 2006[33]	*Datura stramonium* L.	Boils & Warts
Dastagir, G., 2001[38]		
Haq, I. and Shah, M., 1986[41]		
Badshah, L., Hussain, F. and Mohammad, Z., 1996[42]		
Arshad, M. and Akram, S., 1999[43]		
Zabihullah, Q., Rashid, A. and Akhtar, N., 2006[39]	*Ipomoea nil* (L.) *Roth.*	Hair care
Husain, S.Z., 2008[35]		
Zabihullah, Q., Rashid, A. and Akhtar, N., 2006[39]	*Solanum miniatum*	Scabies, pimples
Haq, I. and Hussain, Z., 1995[44]		
Ali, Muhammad S., et al.,1998[45]		
	Veterinary medicine	
Russo, R., Autore, G. and Severino, L., 2009[46]	*Vaccinium macrocarpum*	Urinary disease treatment
Severino, Lorella, et al.,2008[47]		
Russo, R., Autore, G. and Severino, L., 2009[46]		
Severino, Lorella, et al.,2008[47]	*Thymus vulgaris*	Respiratory disease treatment
Tresch, Milena, et al.,2019[48]	*Artemisia annua*	Immunostimulant, treatment of gastrointestinal diseases
Zitterl-Eglseer, K., et al.,2004[49]	*Calendula officinalis*	Treatment for wound, skin disease
Carrió, Esperança, et al.,2012[50]	*Rosmarinus officinalis*	Treatment for gastrointestinal diseases, parasite repellent
	Food industry	
Figueirinha, Artur, et al.,2008[51]	*Cymbopogon citratus* (D.C.) Stapf. (Lemongrass)	Flavor enhancer, antimicrobial
Kasali, A.A., Oyedeji, A.O. and Ashilokun, A.O., 2001[52]	*Geranium mexicanum* Kunt (Geranium)	Antioxidant, antimicrobial
Calzada, F., Cervantes-Martínez, J.A. and Yépez-Mulia, L., 2005[53]		
Alanis, A. D., et al.,2005[54]		
Calzada, F. and Alanís, A.D., 2007[55]	*Helianthemum glomeratum* Lag (Clustered frostweed)	Additives, regulate appetite & weight loss
Nielsen, S.V.S. and Teisen-Simony, C., D xign Ltd, 2014[56]		
Rojas, Gabriela, et al.,2001[57]		
Kumar, R., Mishra, A.K., Dubey, N.K. and Tripathi, Y.B., 2007[58]	*Gnaphalium oxyphyllum* DC. (Gordolobo)	Antibacterial
	Chenopodium ambrosioides L (Wormseed)	Antioxidant
	Agrochemicals	
Pitarokili, D., Tzakou, O. and Kalamarakis, A., 2002[59]	*Salvia pomifera* L. ssp.	Inhibits mycelial growth
	calycina (Sm.) Hayek	
Bi, Yang, et al.,2012[60]	*Origanum syraicum*	Strong antifungal activity
	Cymbopogon martini,	
Erdoğan, O., Celik, A. and Zeybek, A., 2016[61]	*Thymus vulgaris*	Inhibits mycelial growth
	Mentha piperita L.,	
	Thymus vulgaris L.,	
	Lavandula angustifolia Mill.	

Table 2. Stress factors and its effects on medicinal plants

Author [Reference]	Plant species	Stress factors	Effects
Shibata, M., et al.,1988[111]	*Chrysanthemum*	Temperature	Decreased level of anthocyanin and delayed flowering
Neffati, M. and Marzouk, B., 2008[85]	*Coriandrum sativum*	Soil Salinity	Decreased level of oil contents
Baatour, Olfa, et al.,2010[86]	*Origanum majorana*	Soil Salinity	Decreased level of Trans-sabinene Hydrate; γ-Terpinene
Rahimi, S. and Hasanloo, T., 2016[112]	*Silybum marianum* (L.) Gaertn	Temperature	Decreased level of Silymarin
Souther, S. and McGraw, J.B., 2014[87]	*Panax quinquefolius L.*	Unsustainable harvest	Decline in plant species abundance and average stature
McElhaney, Janet E., et al.,2011[88]			
Seida, J.K., Durec, T. and Kuhle, S., 2011[89]			
Barton, Debra L., et al.,2013[90]			
Mucalo, Iva, et al.,2013[91]			
McGraw, J.B., 2001[92]			
Case, Martha A., et al.,2007[93]			
Mulligan, M.R., 2003[94]	*Hydrastis canadensis* L.	Unsustainable harvest	Decline in size or abundance
Law, W. and Salick, J., 2005[95]			
Applequist, Wendy L., et al.,2020[96]			
Yuan, Yingdan, et al.,2020[113]	*Dendrobium officinale* Kimura & Migo	Temperature	Decreased total alkaloids and total flavonoids
Sharma, Shikha, et al.,2020[114]	*Hypericum perforatum* L.	Elevated CO_2 level	Decrease level of hypericin
Zhang, L. X., et al.,2015[115]	*Glechoma longituba* (Nakai) Kuprian	Light intensity	Decrease level of ursolic and oleanolic acid
Bortolin, Rafael Calixto, et al.,2016[116]	*Capsicum baccatum* L. var. Pendulum	Elevated ozone	Decrease level of capsaicin and dihydrocapsaicin
Rastogi, Shubhra, et al.,2019[117]	*Ocimum tenuiflorum* L.	Drought	Decrease level of eugenol
Alhaithloul, Haifa A., et al.,2019[118]	*Mentha* piperita L.	Drought	Decrease level of phenol and flavonoid
Valifard, M., Mohsenzadeh, S. and Kholdebarin, B., 2017[119]	*Salvia macrosiphon* Boiss	Salinity	Decrease level of phenol
Dar, Tariq Ahmad, et al.,2016[120]	*Trigonella* foenumgraecum L.	Soil fertility	Decrease level of alkaloid

of various compounds, including flavonoids, phenolic acids, terpenes, vitamins, saponins, and minerals.[67,68,69] Furthermore, high light intensity has been reported to have positive effects on plant growth and development.[70] For instance, *Erigeron breviscapus* leaves grown in shaded environments contain lower levels of flavonoid glycosides compared to those grown in sunlight.[71] The light spectrum encompasses a range from ultraviolet (UV) radiation to infrared radiation, spanning wavelengths of 295-2500nm. Although only a small fraction of UV radiation from sunlight reaches the Earth's surface, it has a substantial impact on plant growth and the synthesis of bioactive compounds. While UV radiation can naturally stimulate the synthesis of bioactive compounds, excessive amounts can cause damage to the photosynthetic system, DNA, RNA, and proteins.[62] For instance, in *Chrysanthemum* plants, the production of flavonoids and phenolic acids was enhanced under the influence of UV-B radiation.[72] However, most studies have shown that high levels of UV radiation negatively affect plant growth, development, and medicinal activity.[73]

Temperature, a crucial factor that undergoes variation due to climate change, plays a significant role in plant development and growth. The impact of temperature variation on plants can be either beneficial or detrimental, depending on the plant species and various other factors.[74] Furthermore, low temperatures can induce alterations in physiochemical and molecular processes within plants.[75] To explore the effect of temperature on bioactive constituents, a research study analyzed five medicinal plants, *Echinacea purpurea* L., *Thymus vulgaris* L., *Matricaria chamomilla* L., *Cynara cardunculus* L., and *Hypericum perforatum* L., grown at two different locations. The study found variations in the bioactive constituents, such as phenols and flavonoids, across these plants. Notably, H. perforatum and M. chamomilla showed higher levels of phenols, xanthophylls, and proline. This suggests that certain medicinal plants can adapt to temperature changes, while others experience a decrease in the production of bioactive compounds, subsequently affecting their medicinal properties.[76]

Drought stress, regarded as a prominent factor associated with climate change, exerts a substantial influence on the growth and physiological activity of medicinal plants.[77] Notably, under drought conditions, plants have shown an increased concentration of alkaloids, tannins, and terpenoids, while experiencing decreased level of phenols, flavonoids, and saponins.[78] For instance, *Trachyspermum ammi* L., a medicinal plant, exhibited an elevation in its total phenolic content in response to drought stress.[79] Conversely, the leaves of *Ocimum tenuiflorum* L. demonstrated a decline in the accumulation of the phenolic compound eugenol when subjected to drought conditions.[80] Furthermore, an investigation focusing on *Scutellaria baicalensis* Georgi, commonly referred to as Baikal Skullcap employed in traditional medicine, showed a reduction in flavonoid production due to drought stress.[81] Similarly, *Withania somnifera* (L.) Dunal, popularly known as Ashwagandha, displayed a substantial decrease of up to 65% in its bioactive terpenoid content under drought conditions.[82] It is crucial to acknowledge that varying levels of drought severity, such as mild, moderate, and severe conditions, elicit distinct effects on different plant species Figure 1. Thus, drought stress can enhance the concentration of secondary metabolites in medicinal plants compared to other plants, although it negatively impacts their growth and yield.[83]

Elevated soil salinity levels instigate salinity stress in plants, thereby causing nutritional imbalances, hyper-osmotic stress, and impeding photosynthesis and growth.[84] A study conducted on Tunisian coriander (*Coriander sativum* L.) leaves cultivated in a hydroponic medium, exposed to salinity levels of 25 and 50mM NaCl, revealed a significant increase of 18% and 43%, respectively, in essential oil yield. However, as the salinity level continued to rise, a notable decrease in essential oil yield was observed. Moreover, increased salinity levels also resulted in a reduction of unsaturated to saturated fatty acid ratio, leading to the formation of more rigid cell membranes.[85] In the case of marjoram (*Origanum majorana*), the influence of varying NaCl concentrations (0, 50, 100, 150 mM) on growth, mineral nutrition, essential oil yield, and composition was examined. The findings indicated the accumulation of NaCl in the roots and leaves at salinity levels of 50mM and 150mM, respectively. Additionally, a decrease in essential oil yield was observed when the NaCl concentration reached 100mM.[86] The conservation and sustainable use of medicinal plants are currently receiving increased attention, driven not only by the climate change stress factors but also by the challenges posed by unsustainable harvesting practices.[87] High-value medicinal plants like *Panax quinquefolius* L., commonly known as American ginseng, utilized for treating fatigue, upper respiratory infections, and hypertension, have faced unsustainable harvesting practices and are being sold in bulk quantities to meet the high demand in the Chinese market.[87-93] The patterns of decline in size and abundance have been observed in other herbs such as *Hydrastis canadensis* L. (goldenseal) and *Saussurea laniceps Hand.-Mazz*. (snow lotus).[94,95,96]

Furthermore, the commercial harvesting of medicinal plants in North Africa has led to the complete extinction of *Ferula* sp., an exceptionally valuable medicinal plant.[97,98] The fragmentation of habitats has impeded the migration of medicinal plant species, thereby exacerbating the risk of extinction. Certain medicinal plants, which rely on interactions with pollinators or commensal organisms, encounter phenological disruptions.[99,100,101] The proliferation of pollution resulting from excessive usage of fertilizers and chemicals further exacerbates the risk of extinction for medicinal plant species. Notably, a study conducted in North America revealed that the warming climate has led to an increase in insect populations, which, coupled with fungal infections like blister rust, has destroyed vast expanses of medicinal plants within coniferous forests, spanning millions of hectares.[102,103] As temperatures continue to rise, medicinal plants become increasingly susceptible to infections and invasive insect pests. Additionally, factors such as drought, fire, pests, and pathogens also exert significant impacts on the conservation of medicinal plants.[104-108] For example, *Tylophora hirsuta* (Wall.), used for treating asthma and urinary retention in parts of northern Punjab, Pakistan, and Baluchistan, is at imminent risk of complete extinction due to habitat loss.[109] Despite the limited scope of research investigating the impact of climate change and other factors on medicinal plants, the conservation efforts directed towards these plants remain relatively insignificant in comparison to commercial crops.[110]

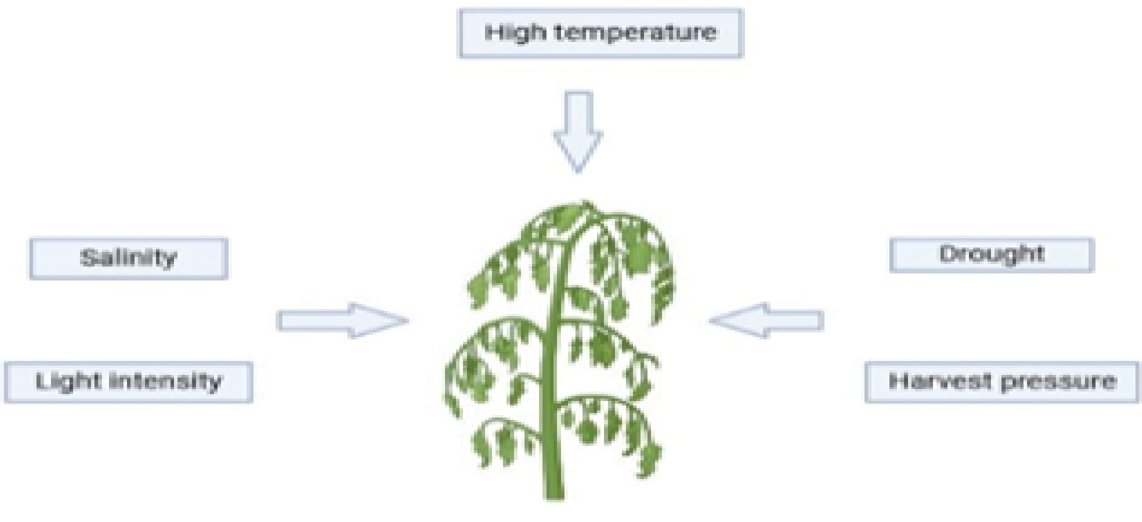


Figure 1. Stress factors affecting medicinal plants survival

CONSERVATION OF MEDICINAL PLANTS BY AQUAPONICS

Many conservation strategies are employed to ensure the sustainable production of medicinal plants. Among these, aquaponics emerges as an ecologically sound and sustainable approach that integrates aquaculture with hydroponics to facilitate the cultivation of medicinal plants Table 3. Aquaponics is an alternative way of modern agriculture which uses water from fish waste and utilizes it as nutrients for plant growth under controlled conditions. In the recirculating aquaponics system (RAS), key growth parameters for both plants and fish, including pH, temperature, nitrate, nitrite, ammonia levels, and overall water quality, will be continuously monitored. The environmental impact from aquaponics systems is much lower when compared to other conventional farming systems. In countries with scarce water and land resources, aquaponics offers a sustainable solution for the conservation of plants. As plant and fish growth parameters are continuously monitored and maintained in aquaponics it serves as a valuable tool in the conservation of medicinal plants, offering protection against the negative effects of climate change, unsustainable harvesting practices, and illicit trade. The research study conducted on *Ocimum basilicum* (basil) demonstrated that cultivating medicinal plant in an aquaponics system led to improved growth and enhanced medicinal properties, specifically increased antioxidant activity, compared to its cultivation in a greenhouse system. The aquaponics system provided better growth parameters, as well as improved quality and quantity of *Ocimum basilicum.*[121] Another study focused on analyzing the performance of four medicinal plants—*Peumus boldus* (boldu chilanum), *Alternanthera brasiliana* (Brazilian joyweed), *Mentha x piperita* (peppermint), and *Origanum vulgare* (oregano)—in an aquaponics system. The results demonstrated that both Boldu Chilanum and peppermint exhibited notable growth across multiple parameters, including dissolved oxygen, pH, temperature, ammonia, nitrate, and nitrite levels. Boldu Chilanum achieved an average final height of more than 63.00cm over 91 days, whereas a previous study reported heights more than 64.00 cm for the same plant when grown in soil. In contrast, peppermint showed an average total biomass weight of 262.5 ± 96.05 g per planter, equating to 65.62 g per plant.[122,123] In another study where peppermint was grown in pots with soil prepared, shaded with different colored screens, and exposed to a 50% light intensity, the average weight per plant reached 31 g over a 120-day experiment. At the end of the experiment, the number of leaves in three of the four species studied—Boldu Chilanum, peppermint, and Brazilian joyweed—was significantly higher. [124] Since this parameter is closely related to the plant parts used for producing drugs, it indicates that aquaponics can be a valuable method for maximizing the production of these important plant products.[125]

Aquaponics has received considerable attention in sustainable vegetable cultivation, as demonstrated by numerous prior studies.[126-128] Moreover, recent findings indicate its potential for producing high-quality medicinal plants.[129] A medicinal plant species *Helichrysum odoratissimum* (L.), which is widely harvested and marketed in South Africa faces threat due to the spread of the pathogen *Fusarium oxysporum*, which causes *Fusarium* wilt disease. *Helichrysum odoratissimum* (L.), belonging to the Asteraceae family, has been used for treating catarrh, abdominal pains, heartburn, headache, fever, urinary tract infections, menstrual problems, and wounds. The study compared the performance of *Helichrysum odoratissimum* (L.) in aquaponics and hydroponics system. The aquaponics system grown plants outperformed hydroponics in terms of essential micronutrients (Mn, Cu, Zn) and improved antifungal activity with a MIC value of 0.37 mg/mL, followed by hydroponics. Hydroponic grown plants showed higher phenol and flavanol contents. The study suggests that aquaponics and hydroponics could be potential alternatives to soil cultivation for *Helichrysum odoratissimum* (L.). By utilizing these soilless cultivation methods, the spread of diseases like *Fusarium* wilt can be prevented, reducing the risk of crop loss and economic damage.[130] In a separate study evaluating spinach yields across

Table 3. List of medicinal plants in aquaponics

Author [Reference]	Plant source	Aquaponics
Manjula, D, Raja, S, 2019[138]	*Trigonella foenum-graecum*	Aquaponics system integrated with liquid biofertilizer showed improved morphological properties of *Trigonella foenum-graecum*
Albadwawi, Maryam AOK, et al.,2022[121]	*Ocimum basilicum*.	Aquaponics grown *Ocimum basilicum* showed improved antioxidant properties, increased height, weight (fresh and dry) compared to greenhouse grown plants
Manjula, D. and Raja, S., 2019[139]	*Solanum nigrum* Linn.	Higher growth of *Solanum nigrum* Linn. were observed in aquaponics system using seaweed as liquid biofertilizer, an ecofriendly approach
Abdel-Rahim, Mohamed M., et al. 2019[140]	Rose mary *(Rosmarinus officinalis),* Marjoram *(Origanum majorana L.),* Mint *(Mentha spicata L.),* Thyme *(Thymus vulgaris L.)*	Study proved the four medicinal plants Rose mary, Mint, Marjoram and Thyme can be produced efficiently and economically by aquaponics system
Nuwansi, K. K. T., et al.,2019[141]	*Centella asiatica* L.	Aquaponics provided favourable growing environment for the cultivation of *Centella asiatica* L. in addition to greenhouse
Castro-Mejía et al.,2020[142]	*Coriander sativum* L.,	Study showed *Coriander sativum* L.,*Anethum graveolens* & *Petroselinum crispum* can be adequately produced in aquaponics system
	Anethum graveolens &	
	Petroselinum crispum	

aquaponic, hydroponic, and traditional soil-based cultivation systems, it was reported that spinach grown aquaponically produced higher yields compared to both hydroponic and conventional soil-based methods.[131]

A wide variety of essential oil products sourced from Helichrysum sp. are commercially available for both medicinal and non-medicinal uses. When comparing the cultivation strategies of hydroponics, aquaponics, and field-grown plants, no statistically significant differences were observed in the total number of volatile constituents in *Helichrysum* sp. However, it is noteworthy that the aquaponic plants exhibited higher concentrations of α-terpineol, a potent antioxidant and antifungal agent.[132-135] Additionally, other important compounds, namely o-ethyltoluene, α -phellandrene, tetradecane, palustrol and α-curcumene, were found to occur at significantly higher levels in aquaponically grown plants compared to hydroponic and field grown plants.[136] One of the studies presented findings regarding the comparative analysis of aquaponic basil and organic soil-grown crops. The authors observed significant differences ($p < 0.001$) in both the total phenolic content and antioxidant capacity between the two cultivation methods. Aquaponic basil exhibited higher levels of total phenolic content compared to organic soil-grown crops. Similarly, the antioxidant activity of aquaponic basil (28.04 mol AAEqg^{-1}DW) was higher than the organic soil-grown crops (20.33 mol AAEqg^{-1}DW). Furthermore, the antifungal activity of the aquaponic plants was assessed through minimum inhibitory concentration (MIC) measurements, specifically targeting the growth of *F. oxysporum.* The results showed a significant inhibition of *F. oxysporum* growth after 18 hours of incubation. Notably, the aquaponically grown plants had higher concentrations of volatile compounds, such as α-curcumene and α-terpineol, both of which have demonstrated antifungal properties. These findings imply the increased presence of some volatile compounds in aquaponic grown plants that may contribute to their enhanced medicinal properties.[130]

Another study on improving the quality of medicinal plants analyzed the growth performance and alteration of bioactive compounds in *Cuphea hyssopifolia* and *Cuphea cyanea*. No statistically significant differences were observed in the growth performance of the two *Cuphea spp.* For *C. hyssopifolia*, aquaponically grown plants retained more than 50% of their phenols and over half of their flavonoids in the dry biomass, compared to those grown conventionally. Additionally, apigenin content increased by over 50%. For *C. cyanea*, aquaponic cultivation resulted in phenolic content remaining elevated, while apigenin and flavonoid levels decreased by 50%. These findings suggest that aquaponics can enhance the bio stimulation of medicinal plants and boost their bioactive compounds, though the effects vary between plant species.[137]

Cultivation technology like aquaponics will limit the exploitation and extinction of medicinal plants, reducing water wastage, and enhancing the commercialization of medicinal plants.[143] Medicinal plants grown in aquaponics act as a biofiltration removing toxic compounds from water and recirculating it for the growth of fishes.[144,145] Cultivation of medicinal plants and fish in an aquaponics system is a feasible, eco-friendly, and sustainable approach.[146] High value medicinal plants and fishes can be grown with more density making aquaponics system more profitable.

MEDICINAL PLANTS FOR NOVEL DRUG DEVELOPMENT

Plants are a valuable source of natural products with a range of therapeutic properties, and they continue to be explored for the development of new drugs. For centuries, traditional medicines have relied on these natural products to treat a wide range of diseases. Today, most pharmaceutical drugs are sourced from these natural origins. These products are rich in bioactive compounds that exhibit biological activity against various disease-causing agents. So far, numerous secondary metabolites with diverse structures and pharmacological properties have been identified in medicinal plants.[147,148] These medicinal plants, which offer significant health benefits, are threatened by climate change stress factors and unsustainable harvesting practices. These combined factors lead to a decline in biomass production and alterations in chemical content, potentially affecting the quality and safety of medicinal plant use.[149] Cultivating and preserving medicinal plants in carefully regulated environments, such as aquaponics, boosts their quality, bioactivity, and biomass on a commercial scale. The aquaponics method is especially advantageous in regions facing consistent environmental challenges like extreme cold, heat, or drought. The potential to use aquaponics systems to optimize the production of secondary metabolites in high-value medicinal plants is highly promising. Aquaponics is an innovative technology to produce food that can be implemented in unconventional spaces like rooftops, abandoned industrial sites, and areas that are typically non-arable or contaminated, thereby reducing the need for deforestation.[150,151] The cultivation of medicinal plant species using aquaponics systems is rare, making it crucial to explore these systems for the production of medicinally valuable species (Figure 2).[177] Significantly, many secondary metabolites produced by medicinal plants are valuable resources for the pharmaceutical industry in developing new drugs.[152]

Medicinal plants continue to be a crucial source of new drugs, drug leads, and novel chemical entities (NCEs).[153,154] Arteether, a powerful antimalarial drug, is derived from artemisinin, a sesquiterpene lactone extracted from *Artemisia annua* L. (Asteraceae), a plant traditionally used in Chinese medicine. Other artemisinin derivatives are also being used or are currently undergoing clinical trials as antimalarial drugs in Europe.[155,156] Galantamine, a natural compound identified through ethnobotanical research, was first isolated from *Galanthus woronowii* Losinsk. (Amaryllidaceae). It is approved for the treatment of Alzheimer's disease, where it slows neurological degeneration by inhibiting acetylcholinesterase (AChE) and modulating the nicotinic acetylcholine receptor (nAChR).[157,158] Nitisinone, derived from *Callistemon citrinus* Stapf. (Myrtaceae), is a novel drug used to treat the rare genetic disorder tyrosinaemia, highlighting the value of

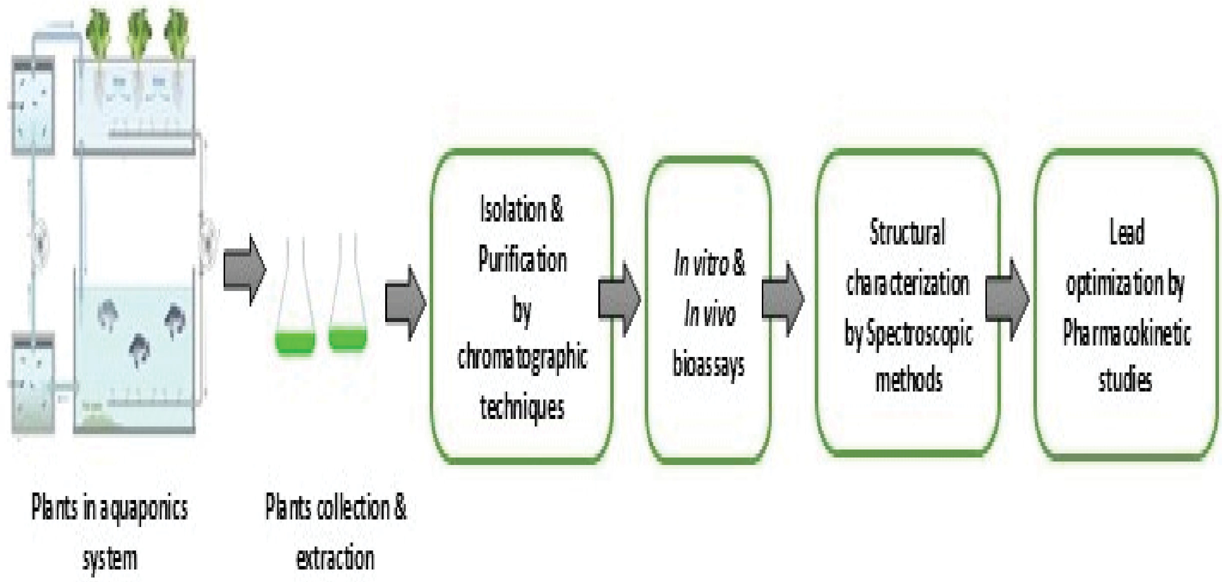
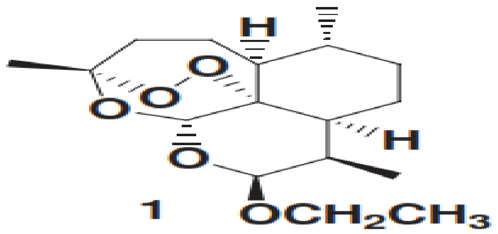


Figure 2. Medicinal plants in aquaponics system for drug development

natural products as lead compounds for drug development.[159] Tiotropium, an inhaled anticholinergic bronchodilator derived from ipratropium, is based on atropine, which is extracted from *Atropa belladonna* L. (Solanaceae) and other members of the Solanaceae family. Tiotropium has shown greater efficacy and longer-lasting effects compared to other medications used for treating chronic obstructive pulmonary disease (COPD).[160-162] Morphine-6-glucuronide, a metabolite of morphine obtained from *Papaver somniferum* L. (Papaveraceae), is being used as an alternative pain medication with fewer side effects than morphine. Vinflunine, a modified form of vinblastine from *Catharanthus roseus* (L.) G. Don (Apocynaceae), is an anticancer agent with enhanced efficacy.[164,165] Exatecan, derived from camptothecin is being developed as an anticancer drug which is found in *Camptotheca acuminata* Decne. (Nyssaceae).[166,167] Calanolide A, a dipyranocoumarin isolated from *Calophyllum lanigerum* var. *austrocoriaceum* (Whitmore), is an anti-HIV drug that functions as a non-nucleoside reverse transcriptase inhibitor (NNRTI) targeting type-1 HIV. It is also effective against AZT-resistant strains of the virus.[168-170] Figure 3 illustrates the chemical structures of few lead compounds from medicinal plants used in drug development.[178]



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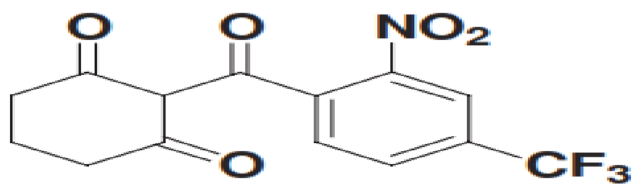
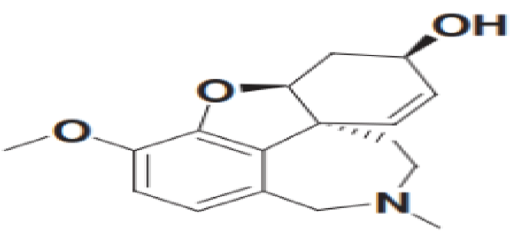
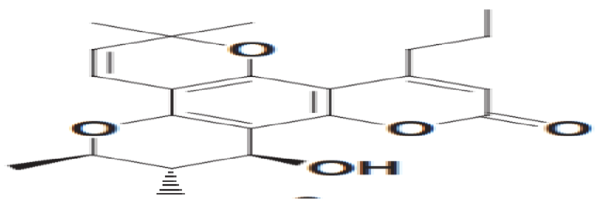


Nitisinone



Galantamine



Calanolide A

Figure 3. Examples of highly potent drug compounds from medicinal plants

Certain plant-derived compounds, including resveratrol from Cassia quinquangulata Rich., ixocarpalactone A from the edible plant *Physalis philadelphica* Lam. (Solanaceae), and isoliquiritigenin from the seeds of Dipteryx odorata Willd. (Fabaceae), serve as natural inhibitors of carcinogenesis.[171-173]Additionally, plant-based compounds are used in cosmetics and nutrition, including the production of drugs, fragrances, dietary supplements and dyes.[174] Plant extracts rich in bioactive secondary metabolites have proven effective in controlling plant pathogens and predatory insects. Consequently, creating cultivation protocols to maximize secondary metabolite content and thereby boost the medicinal value of plants is an important and valuable research area.

CONCLUSION

Medicinal plants are widely recognized as invaluable natural resources, holding significant potential for the development of drugs, bioactive compounds, food additives, veterinary medicine, and agrochemicals. However, they currently face a multitude of threats, predominantly caused by climate change factors such as high temperatures, salinity, drought, and altered light intensity. These stress factors severely impact the growth, development, and medicinal properties of plants. Moreover, unsustainable harvesting, illegal trade, and habitat destruction further exacerbate the problem by causing the complete loss and extinction of medicinal plant species. To address these challenges, various conservation strategies have been established, such as natural reserves, botanic gardens, wild nurseries, seed banks, and Good Agricultural Practices (GAP). One of the promising conservation approaches discussed in the review is aquaponics, which combines hydroponics and aquaculture. In this aquaponics system, medicinal plants can be grown alongside fish by recycling water and nutrients, creating a sustainable and efficient environment for both. Aquaponics offers an innovative solution by providing a controlled, resource-efficient environment to grow medicinal plants while conserving water and reducing waste. This method not only safeguards endangered species but also protects biodiversity, ensuring a steady, sustainable supply of medicinal plants for future research. By integrating aquaponics, we can promote sustainable farming practices, preserve valuable plant species, and foster collaborations in drug development. Additionally, aquaponic systems offer educational and economic benefits, making them accessible to local communities while contributing to the conservation of vital plant species at risk of extinction. Research has shown that aquaponics can improve the growth and enhance the medicinal properties of plants, enabling the extraction of precursor or lead compounds for the development of new drugs. Furthermore, aquaponics offers a sustainable solution with high productivity, profitability, global adaptability, and the ability to protect medicinal plants from the negative impacts of climate change, excessive harvesting, and other threats. Overall, aquaponics holds great promise for the sustainable conservation and utilization of these valuable natural resources. The combination of preserving valuable medicinal plants and using an innovative, sustainable farming method could play a vital role in both conservation and novel drug development, addressing the need for immediate action to protect these plants.

AUTHOR CONTRIBUTION

RM: data curation, writing—original draft preparation

CSN: methodology, data curation

RS, DN: writing—original draft preparation

AJ, MR, XX: Conceptualization, validation, supervision

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