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REVIEW ARTICLE

Phytochemical, pharmacological and industrial application of *Chromolaena odorata* (Siam weed): An overview based on review of literature

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Abstract

Siam weed (*Chromolaena odorata* (L.) R.M. King & H. Rob.) of Asteraceae family, a perennial shrub with an invasive character, has been shown potential application in many of scientific communication. On the basis of broader geographical distribution across tropical and subtropical regions, research is mainly concentrated in ten countries of Africa, Asia and Oceania Australia. *C. odorata* has been largely studied for diverse phytochemical content including flavonoids, terpenoids and phenolic compounds responsible for many of its potential health and industrial application. In present work we reviewed several scientific literature and found antioxidant, anti-inflammatory, wound healing and anti-cancer application of *C. odorata*. Additionally, environmental applications of *C. odorata* as a phytoremediation and ecosystem restoration are in agricultural innovations are well established including natural pesticide and soil fertility enhancer. Moreover, several industrial applications including bioenergy and development of sustainable materials are also established. Finally based on balanced summary of available evidence on the ecological challenges and potential as a valuable biological resource for *C. odorata* and synthesizes current research knowledge that can help in the filling of knowledge gaps and defining of future research directions.

Keywords

bioactive properties; *Chromolaena odorata*; environmental utilization; pharmaceutical applications; phytochemicals

Introduction

Chromolaena odorata (L.) R.M. King & H. Rob., which belongs to the Asterac family, also known as Siam weed, Christmas bush, or devil weed is a fast-growing semi-lignified perennial shrub. *C. odorata* has differential distribution among regions and it is the most abundant plant in South America, with median approximately 60 %, then Africa with median around 50 %, Asia with median about 35 %, Australia with median roughly 20 % and North America got the least coverage with median about 15 %, therefore shows a definite geographical pattern of prevalence and establishment success, Fig. 1 which represents the Box Plot Representation of *C. odorata* Coverage in Various

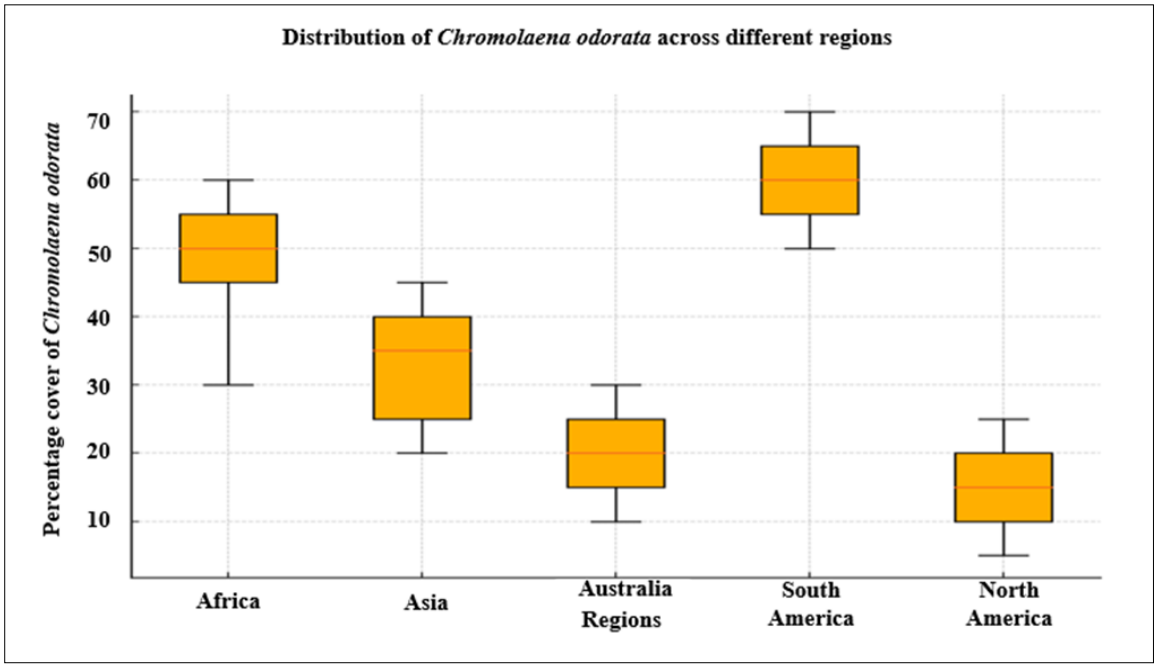

Fig. 1. Box plot representation of *C. odorata* coverage in various regions.

Regions. This aggressive colonizer is originally from South and Central America and it has naturalized all over the tropical and subtropical regions worldwide and it is very adaptable to various environmental conditions (1). Now common to those regions since its introduction in the mid-19th century, *C. odorata* has expanded rapidly and is found in disturbed places such as abandoned farmlands, forest edges and roadsides where it competes aggressively with native species and alters ecosystems. Distributed over Africa Nigeria, Ghana, South Africa; Asia (India, Thailand, Vietnam, Indonesia, Philippines, Malaysia); and Oceania Australia the worldwide research focus on *C. odorata* is conserved in 10 countries (Fig. 2).

C. odorata is the most important ethnomedicinal drug in Southeast Asia and in West Africa which demonstrated remarkable healing properties. It is said to have earned the nicknames 'Communist weed' or 'Freedom weed' – always in Vietnam, during the Vietnam War, a time it also received the moniker 'wound weed', because of its outstanding wound healing properties (2). Aqueous extract from the leaves of *C. odorata* has been used for the treatment of soft-tissue burns or skin infections (2). Though it holds an invasive reputation, *C. odorata* has been traditional used for the treatment of wounds, inflammation and infections (3, 4).

C. odorata with diverse biological activities and different potential applications in medicine, agriculture and environmental management (5) basically hold their biological activities on its chemical composition. Secondary metabolites, such as alkaloids, flavonoids, terpenoids, tannins, saponins, glycosides and phenolic acids (6, 7) are rich in the plant. Its antimicrobial, anti-inflammatory, antioxidant and wound healing properties are made possible by these compounds. Antimicrobial activity of alkaloids and tannins agrees well with traditional use as an infection control and as tissue regenerating agents (8) and flavonoids and phenolic acids exhibit strong antioxidant activity as potent mitigators of oxidative stress and inflammation (9).

What *C. odorata* offers beyond medicine, has also important potential applications in agriculture and the environment. In addition to suppressing weed growth via its allelopathic properties, this sorghum is rich in bioactive compounds that are acted as natural pesticides and increases the soil health as green manure (5). Additionally, the metabolites of the plant are also being explored as soil detoxification/ecosystem restoration (10). This has led to the interest of people in sustainable management practices which balance its advantages against its invasive property to extend its economic potential to pest management and even biofuel production (11).

This review critically examines the phytochemical composition and the biological activities of *C. odorata* which has been utilized for medicinal and agricultural purposes as well as for environmental sustainability and highlights the possible applications of the extract as well as its exploitation towards limiting some of the associated challenges and limitations. This paper highlights the knowledge gaps and proposes future research directions through synthesizing all research as a review aimed on balancing a view, understanding *C. odorata* as a source of valuable bioactive compounds and taking into account its ecological challenges at the same time.

Phytochemistry

Flavonoids and related compounds: *C. odorata* contains a rich array of flavonoids as its main bioactive compounds (12). It has also performed research which has revealed multiple quercetin derivatives with good antimicrobial properties, including quercetin-3-O-β-D glucoside, quercetin-3-O-rutinoside (rutin) and quercetin-4'-methyl ether. Kaempferol compounds (kaempferol-3-O-βD-glucoside and kaempferol-3,7-O-βD-glucoside) have been shown to improve wound healing by increasing proliferation of fibroblasts (2). Other flavonoids of *C. odorata*, such as rhamnetin, taxifolin, luteolin, apigenin and isorhamnetin also have potent antioxidant activity with IC 50 values between 23.7 and 52.4 µg/mL (13). Further detailed studies has to be conducted for assessing the chemical composition percentage.

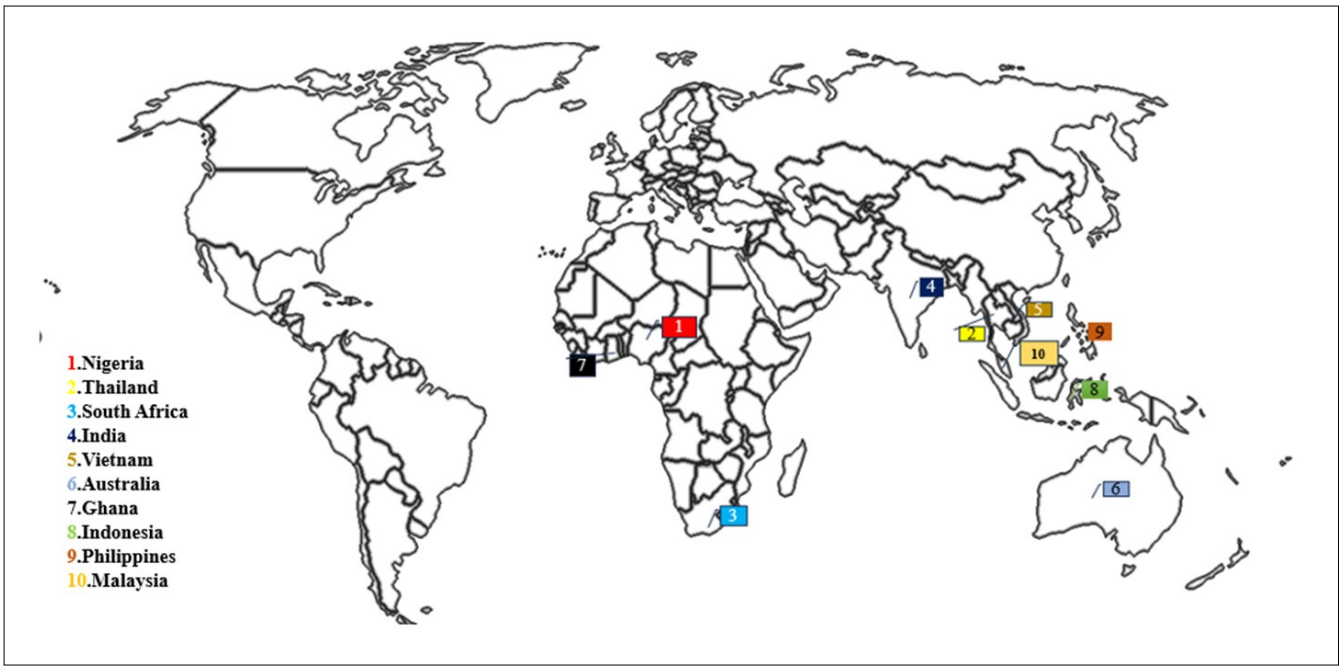

Fig. 2. Worldwide distribution of scientific research on *C. odorata* (1-10 ranking).

Terpenoids and essential oils: The terpenoid compounds that comprise the essential oil of *C. odorata* are presented. The concentrations of sesquiterpenes were found to be significant, with β-caryophyllene present in concentrations of 13.8-25.4 %, α-humulene 4.5-8.2 %, germacrene D 10.2-15.7 % and β-elemene 2.3-5.1 % (14). Monoterpenes (α-pinene, β-pinene, limonene and 1,8-cineole) are antimicrobial in properties and supplied by the plant according to (15).

Phenolic compounds and other constituents: Quantified different phenolic acids of *C. odorata* namely: protocatechuic acid (4.2 mg/g), p-coumaric acid (2.8 mg/g), ferulic acid (3.5 mg/g), vanillic acid (1.9 mg/g), gallic acid (2.3 mg/g) and caffeic acid (1.7 mg/g). Moreover, the plant is rich in complex phenolics with analgesic properties, tannins for wound healing, saponins that promote immune modulating and various steroids and phytosterols (16). Table 1 represents an overview of these extracted compounds organized into the broad categories, molecular formulas, as well as the plant parts from which these compounds were isolated and Fig. 3 is an effective depiction of *C. odorata* from wherein it was used traditionally for medicinal purposes and from which specific bioactive compounds that have been isolated from these plants and their properties.

Traditional Pharmacological Applications

In fact, Siam weed has been the focus of attention in the pharmaceutical area over the years thanks to its pharmacological profile highly laden of phytochemicals. The secondary metabolites of this plant, such as flavonoids,

Table 1. Chemical compounds identified in *C. odorata* and their extracted plant parts

Compound category	Specific compounds	Molecular formula	Extracted plant part	Reference
Flavonoids	Quercetin-3-O-β-D-glucoside	$C_{21}H_{20}O_{12}$	Leaves	(12)
	Quercetin-3-O-rutinoside (rutin)	$C_{27}H_{30}O_{16}$	Leaves	(12)
	Quercetin-4'-methyl ether	$C_{15}H_{10}O_7$	Leaves	(12)
	Kaempferol-3-O-β-D-glucoside	$C_{21}H_{20}O_{11}$	Leaves	(2)
	Kaempferol-3-O-rutinoside	$C_{27}H_{30}O_{15}$	Leaves	(2)
	Kaempferol-3,7-di-O-β-D-glucoside	$C_{21}H_{20}O_{12}$	Leaves	(2)
	Rhamnetin	$C_{16}H_{12}O_7$	Leaves	(59)
	Taxifolin	$C_{15}H_{12}O_7$	Leaves	(59)
	Luteolin and its glycosides	$C_{15}H_{10}O_6$	Leaves	(60)
	Apigenin	$C_{15}H_{10}O_5$	Leaves	(60)
	Isorhamnetin	$C_{16}H_{12}O_7$	Leaves	(59)
Sesquiterpenes	β-Caryophyllene	$C_{15}H_{24}$	Essential Oil (Leaves)	(14)
	α-Humulene	$C_{15}H_{24}$	Essential Oil (Leaves)	(14)
	Germacrene D	$C_{15}H_{24}$	Essential Oil (Leaves)	(14)
	β-Elemene	$C_{15}H_{24}$	Essential Oil (Leaves)	(14)
Monoterpenes	α-Pinene	$C_{10}H_{16}$	Essential Oil (Leaves)	(15)
	β-Pinene	$C_{10}H_{16}$	Essential Oil (Leaves)	(15)
	Limonene	$C_{10}H_{16}$	Essential Oil (Leaves)	(15)
	1,8-Cineole	$C_{10}H_{18}O$	Essential Oil (Leaves)	(15)
Phenolic acids	Protocatechuic Acid	$C_7H_6O_4$	Leaves	(48)
	p-Coumaric Acid	$C_9H_8O_3$	Leaves	(48)
	Ferulic Acid	$C_{10}H_{10}O_4$	Leaves	(48)
	Vanillic Acid	$C_8H_8O_4$	Leaves	(48)
	Gallic Acid	$C_7H_6O_5$	Leaves	(48)
	Caffeic Acid	$C_9H_8O_4$	Leaves	(48)

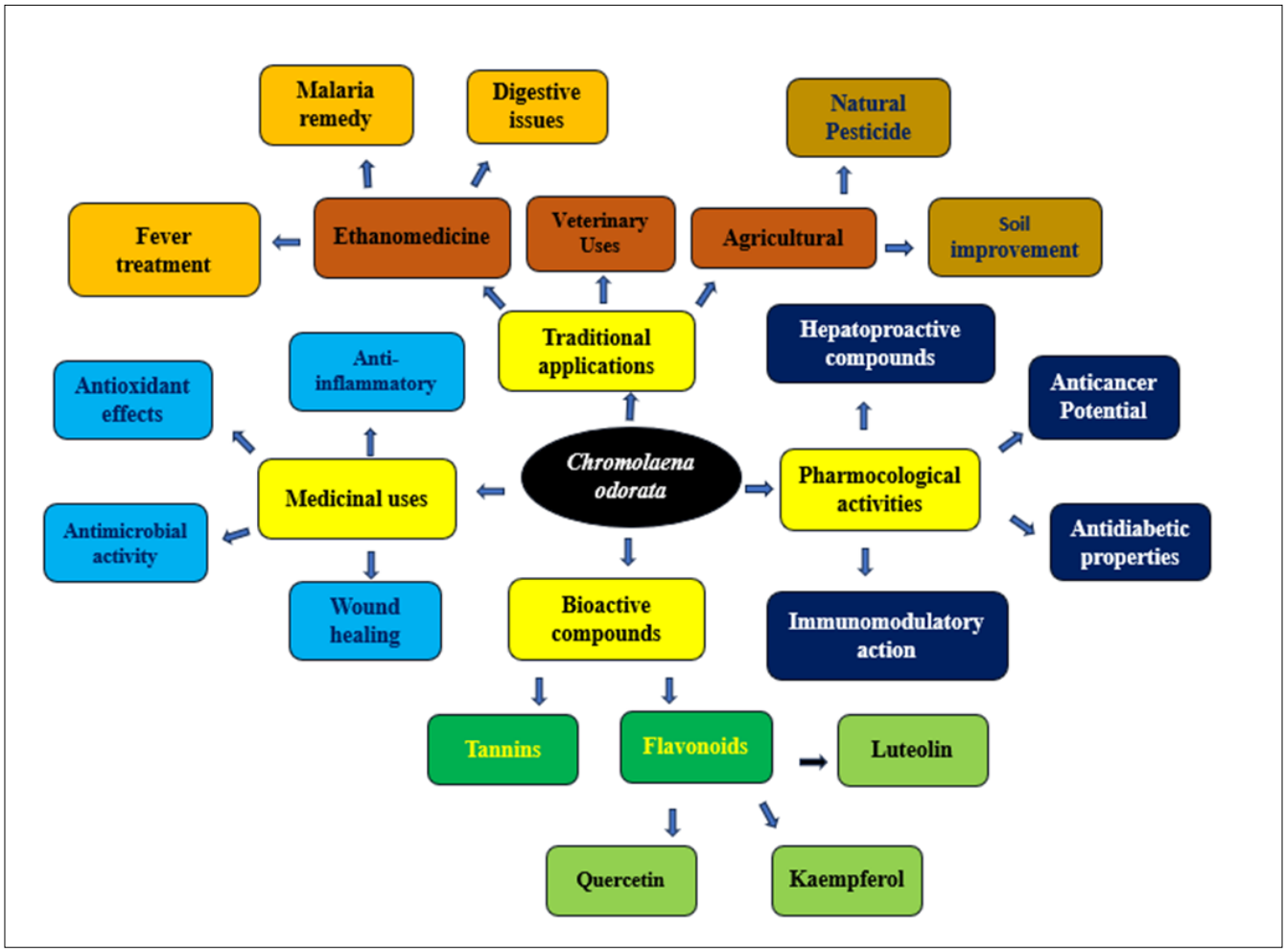

Fig. 3. *C. odorata* applications and compounds.

alkaloids, terpenoids, tannins and phenolic acids are claimed to have a variety of biological activities (17, 18) and are therefore taking into consideration a potential drug. These compounds have their potential as the drugs to combat infections and prevent the chronic diseases. Flavonoids and phenolic acids found in *C. odorata* play a vital role in preventing the oxidative stress and metabolizing the free radicals produced; also reducing the amount of oxidative stress (19). Chronic diseases such as cardiovascular conditions, neurodegenerative disorders, diabetes (20), are due to oxidative stress. *C. odorata* scavenges free radicals and protects the cellular components to prevent these conditions. Moreover, it also shows its anti-inflammatory mechanism through inhibiting of pro inflammatory cytokines and enzymes like cyclooxygenase (COX) and can be used to treat arthritis and inflammatory bowel disease (21). Alkaloids, terpenoids and tannins of *C. odorata* have antimicrobial properties that inhibit microbial growth and survival (22). For inhibition of enzymatic activity and impairing replication of pathogens (23, 24) consider these compounds to be these compounds. Due to the fact, *C. odorata* is a source for the development of natural antibiotics particularly against bacteria resistant to antibiotics. Its broad-spectrum activity against gram-positive and gram-negative bacteria, as well as fungi, underscores its utility in infection control. It has been proved by research that some of the compounds in *C. odorata* these are flavonoids, terpenoids have shown cytotoxicity to cancer (25, 26). Activation of such pathways such as the mitochondrial apoptosis pathways and caspase cascades lead these compounds to induce apoptosis (programmed cell death) of cancer cells. In addition, they inhibit angiogenesis, the process that makes tumors fed by developing new blood vessels as a way to starve cancer cells to death. *C. odorata* is therefore a source for novel anticancer agents with a potential dual action (27).

Scientifically Validated Pharmacological Applications

Antioxidant activity

C. odorata has been extensively characterized with regard to its antioxidant properties in both *in vitro* and *in vivo* studies. Comprehensive analyses of the plant's free radical scavenging were conducted and showed the plant having very good activities against various reactive oxygen species. The IC 50 used by their research was particularly potent at 32.5 µg/mL DPPH radical scavenging activity, being higher than a number of standard antioxidant compounds. In addition, the study also noted wide spectrum of antioxidant properties of the plant as the ABTS radical neutralization (IC 50 = 28.7 µg/mL) was found to be significant (28).

Investigated cellular antioxidant mechanisms that *C. odorata* extracts significantly increased the exogenous antioxidant defense systems. They demonstrated that superoxide dismutase (SOD) activity upregulates 175 % of control conditions and increases for catalase. This also documented a 230 % increase of cellular glutathione levels, giving a complete protection against oxidative stress via multiple pathways (26).

The groundbreaking study on the relationship between the antioxidant properties of *C. odorata* and its therapeutic uses in age related disorders. Examining regular administration of the extracts against oxidative damage in neurons indicated potential application in neurodegenerative conditions. The mitochondrial function in this study was revealed to be remarkable promising anti-aging properties under oxidative stress conditions (29).

Anti-inflammatory properties

Molecular mechanisms: Studies of late have elucidated many pathways of anti-inflammatory action of *C. odorata*. The extract administration brings down tumor necrosis factor alpha (TNF-α) levels by 65 % and interleukin 1β (IL-1β) production (1). Significant cyclooxygenase-2 (COX-2) inhibition with an IC 50 value of 45 µg/mL via both direct enzyme interaction and gene expression modulation and also found large reduction in inducible nitric oxide synthase (iNOS) activity and in the levels of prostaglandin E2 (PGE2) (30). The plant's extracts, particularly scutellarein tetramethyl ether (STE), have been shown to suppress the expression of cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS). These enzymes are pivotal in producing pro-inflammatory mediators like prostaglandin E2 (PGE2) and nitric oxide (NO). By downregulating COX-2 and iNOS, *C. odorata* reduces the levels of these mediators, thereby mitigating inflammation (10). The anti-inflammatory efficacy of *C. odorata* is also attributed to its impact on the Nuclear Factor kappa-light-chain-enhancer of activated B cells (NF-κB) signaling pathway. STE inhibits the phosphorylation of IκB kinase complex alpha/beta (IKKα/β) and the degradation of Inhibitory-kappa-B-alpha (IκBα), preventing the translocation of NF-κB to the nucleus. This inhibition leads to decreased transcription of pro-inflammatory genes, contributing to the plant's anti-inflammatory effects (10).

Wound healing properties: Wound management using *C. odorata* has been widely described among different cultures as a traditional practice. Crushed leaf paste was successfully employed in direct wound application by local communities (2). Also found a significant improvement of wound contraction and a rise in wounded tissue tensile strength (31) and showed the speed of epithelialization through histological studies (32).

Biochemical and protective effects: Wound healing of the plant is accomplished through multiple biochemical pathways showed that stimulation of angiogenesis by upregulation of vascular endothelial growth factor (33). *C. odorata* as a traditional practice showed enhanced collagen synthesis and deposition (2, 31). It improved clot formation due to tannin mediated protein precipitation (13), whereas the significant reduction in wound exudate by virtue of the astringent properties (32). In addition, the plant has broad spectrum antimicrobial activity (34) and cell membrane stabilization (31).

Anticancer properties

Studies related to *C. odorata* has an advantageous effect for use as anticancer agent by showing cytotoxicity against different cancer cells through cell apoptosis and cell cycle arrest. Studies in which minimal toxicity of the normal cells was shown to also suppress tumor metastasis had demonstrated its ability to inhibit angiogenesis (6, 35).

Metabolic and diabetes management

Also revealed is that *C. odorata* has a great ability to enhance insulin sensitivity and glucose tolerance in the control of diabetes. It also shows protection of the pancreatic β cells and increased glucose uptake. Furthermore, in studies it is also proven effective in the management of diabetic complications such as nephropathy and cardiovascular complications (5, 36).

Hepatoprotective functions

Hepatoprotective use of the plant has been recorded widely in the control of rise of liver enzymes and protection of tissues. Studies and clinical trials demonstrate that it is able to manage alcoholic liver disease, viral hepatitis and an effective viral clearance rate as well as slowed progression of fibrosis (36, 37).

Imunomodulatory effects

C. odorata is well known to possess complex immunomodulatory properties like increased natural killer cell activity as well as improvement in macrophage function. In addition, it can be used to treat autoimmune diseases as a modulator of T helper cell response to reduce the autoantibody production (39).

Neurological applications

Studies have shown *C. odorata* to have neuroprotective effects with possible benefits with respect to cognition. This research showed spatial memory and learning capacity increase, up regulation of brain derived neurotrophic factor (BDNF) levels and increase in hippocampal neurogenesis (40).

Respiratory applications

In fact, plant appears to have good potential in the treatment of respiratory diseases due to its anti-asthmatic property and management of chronic obstructive pulmonary disease (COPD). The respiratory function parameter improved and frequency of asthmatic episode was diminished (41).

Agriculture and Industrial Application

C. odorata is a plant of high invasive features, however it is becoming a valuable resource in sustainable agriculture (42). The main allelopathic properties of the plant are mainly the secondary metabolites such as phenolics and terpenoids, involving natural herbicidal effects that stop the competing vegetation (25). As synthetic herbicide alternatives remain in great demand in the context of organic farming systems, this natural weed control mechanism has garnered great attentions (43).

It has complex profile of alkaloids and flavonoids that renders the plant pesticidal properties to use in different agricultural pests (44). *C. odorata* which is effective to control common crop pests with similar efficiency to conventional pesticides with reduced environmental impact (45). Consequently, these findings have made *C. odorata* a basket star of the integrated pest management strategies for a region which has agreed to have sustainable agriculture (46).

A study on the erosion control and soil moisture conservation effectiveness of the plant is well documented (47). Its dense foliage is used as mulch which as a good barrier to soil erosion and evaporation of water to improve water use efficiency in an agricultural system. Furthermore, it's natural weed suppressing properties are an additional sustainable approach to the weed management without mechanical and chemical intervention (48).

Due to the unique biological characteristics of *C. odorata*, they provide a tool for dealing with environmental challenge. This is an exceptional plant for an ecosystem restoration and an environmental remediation efforts (49).

Therefore, the use of *C. odorata* as soil contaminant phytoremediator of heavy metals (50), because of its high phytoremediation efficiency, is being exploited. The studies provide results indicating that its biomass removed greater than 70 % of lead, cadmium and zinc from contaminated soils (51). This is supplemented at the same time by a special ability to stimulate the activity of soil microbes and promote the natural recovery processes (15).

The plant has been well documented in ecosystem restoration of the degraded landscapes (52). As this plant has a good developed root system with a robust root system providing good soil stabilization and also rapid biomass production, its root system also helps in the accumulation and improvement of soil organic matter and soil structure (53). Research has been pursued into the successful utilization in mine site rehabilitation and erosion control but with the caution to prevent unwanted spread.

Recently, *C. odorata* has been studied as a renewable energy source (54). Due to the high biomass yield of the plant, biochar and biogas production based on it represents an alternative to a conventional fuel (55). However, results from anaerobic digestion of *C. odorata* for biogas production and biochar from *C. odorata* to be used as soil amendment for carbon sequestration have indicated the potential of the species in biogas production and carbon sequestration through soil amendment.

It has been discovered in recent research that there is great potential of *C. odorata* in various areas of industrial application and provides high value (56). Because of its high biomass yield and efficient conversion rates, it is very useful for the utilisation to generate bioethanol, biodiesel and bio gas (biodiesel and bioethanol are the most common types of bio fuels). It has been shown to be successfully enzymatically hydrolysed and the lignocellulosic structure hydrolysed to ethanol at similar yields as conventional feedstocks.

One of the highly versatile applications of biochar production from *C. odorata* has emerged (57). There have been recent studies documenting its effectiveness both in agricultural and in industrial processes such as strengthening of concrete and pollutant filtration. For optimal environmental remediation applications, the material should have a high carbon content and a porous structure (58).

Conclusion

C. odorata, a plant with a rich phytochemical profile, is a versatile species with potential applications in agriculture, industry and environmental management. Its antioxidant, anti -inflammatory, antimicrobial and anticancer properties have been scientifically validated in wound healing traditions. *C. odorata*'s value in sustainable farming practices is highlighted by its natural herbicidal and pesticidal capabilities, soil fertility enhancement, erosion control capabilities and effectiveness in phytoremediation, ecosystem restoration and as a renewable energy source. Bioenergy production, sustainable materials development and biochar applications have revolutionized the value of *C. odorata*. This review of human interaction and utilization of *C. odorata*, coupled with scientific understanding of its global distribution and the role of insects, shows that species classification need not deter invasive species. However, its invasive nature must be balanced with careful management, ensuring its beneficial properties are not spread uninvited. Future research should focus on optimizing these applications and creating efficient controls to prevent uninvited species.

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Authors' contributions

PD and KK helped in choosing the review topic and its overall outline. KB, PS, PR, PH, RR, MV, MM, SK and VK participated in giving ideas related to the topic and drafted the manuscript. All authors read and approved the final manuscript.

Compliance with ethical standards

Conflict of interest: Authors do not have any conflict of interests to declare.

Ethical issues: None

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