Ageratum conyzoides: A Potential Source for Medicinal and Agricultural Products

Dipti Baral1,*, Manisha Chaudhary1,b, Ganga Lamichhane1,c, Binod Pokhrel1,d

1Agriculture and Forestry University, Rampur, Chitwan, Nepal
*Corresponding author

A B S T R A C T

Ageratum conyzoides is a widely spread weed, especially in the tropical and subtropical regions. It has been reported to be used as folk medicine in different countries for treating burns, wounds, skin disorders, headaches, fever, pneumonia, gynecological diseases, leprosy, snakebites, rheumatism, inflammations, stomach ailments like parasites, colic, diarrhea, dysentery, used as a painkiller during childbirth, and many more. It has been reported to contain active secondary metabolites such as alkaloids, tannins, phenols, saponins, coumarins, essential oils, and flavonoids, which support its medicinal uses in disease treatment and prevention. It can be a potential source of drugs for various diseases. In fact, pharmaceutical companies are using A. conyzoides as raw material with recommendations from the Brazilian Drug Centre. It is also used for agricultural purposes as manure, insecticide, pesticide, herbicide, nematicide, fodder, etc. In China, it is widely intercropped in the citrus orchard to control pests and weeds. The review attempts to bring together medicinal and agricultural usage of Ageratum conyzoides with scientific evidence to demonstrate its efficacy. This weed has a negative influence in agriculture and the ecosystem but after studying about its potential medical and agricultural uses, we now have a different viewpoint on this weed, and we believe that further harnessing it for such positive uses might be a management strategy for this weed.

Keywords: Ageratum conyzoides, Agricultural products, Medicinal use, Secondary metabolites

Introduction

Ageratum conyzoides (Compositae) is a weed of tropical and subtropical countries and is extremely difficult to eradicate (Dorga Kuldip, 2009). Ageratum conyzoides is derived from two Greek words ‘ageras’ and ‘konyz’ where ‘ageras’ means non-aging that signifies the longevity of the whole plant and ‘konyz’ is the Greek name of Inula helenium to which the plant resembles (Okunade, 2002a). It is named ‘Goat weed’ or ‘Billy goat weed’ as it has a distinctive odor that is compared to that of a male goat during childbirth, and many more. It has been reported to contain active secondary metabolites such as alkaloids, tannins, phenols, saponins, coumarins, essential oils, and flavonoids, which support its medicinal uses in disease treatment and prevention. It can be a potential source of drugs for various diseases. In fact, pharmaceutical companies are using A. conyzoides as raw material with recommendations from the Brazilian Drug Centre. It is also used for agricultural purposes as manure, insecticide, pesticide, herbicide, nematicide, fodder, etc. In China, it is widely intercropped in the citrus orchard to control pests and weeds. The review attempts to bring together medicinal and agricultural usage of Ageratum conyzoides with scientific evidence to demonstrate its efficacy. This weed has a negative influence in agriculture and the ecosystem but after studying about its potential medical and agricultural uses, we now have a different viewpoint on this weed, and we believe that further harnessing it for such positive uses might be a management strategy for this weed.
Mostly referred to as weed, *A. conyzoides* is also an annual herb with a long history of medicinal uses across the world. Studies show that the plant possesses a wide range of chemical compounds like alkaloids, flavonoids, and some constituents of flavonoids, tannins, saponins, glycosides, resins, phenols as phytochemicals while proteins, carbohydrate, and their reducing forms are present as nutrients along with some essential and non-essential amino acids (Amadi, Duru and Agomuo, 2012). These phytochemicals present in *Ageratum* confer antimicrobial and antioxidant properties that make them useful for the treatment of burns and wounds, skin disorders, diarrhea and giardiasis, headaches, and treatment of stomach ailments like parasites, colic, diarrhea, dysentery, rheumatism, and other inflammations, pneumonia, gynecological diseases, leprosy, to treat snakebites, used as an, used as analgesic and a painkiller during childbirth, more (Durodola, 1977; Okunade, 2002b). Free radicals, which are present everywhere in the environment, harm human health by causing oxidative stress. To protect the body from the effects of free radicals, it is vital to find exogenous sources of antioxidant activity. Antioxidants are the molecules that prevent the oxidation caused by free radicals and interact with and stabilize them (Salehi et al., 2019). In order to do so, these antioxidants are often reduced. So, antioxidants are mostly reducing agents such as thiols, ascorbic acid or polyphenols (Z, 2018).

In China, *A conyzoides* is intercropped in the citrus orchards for pests and weed management (Kong, 2010). In south China, *A. conyzoides* is traditionally used as green manure in fields to increase crop yields and control weeds. Along with this, it is used in vermicomposting. Although believed to be poisonous, it is also used as fodder for cattle, guinea pigs, horses, and goats. Hence, exploiting this weed for its medicinal and agricultural usage can render it less troublesome to agriculture and the environment. However, these uses may not compensate for its overall negative impact.

**Medicinal Uses**

*Ageratum conyzoides* is known as a weed but very little is known about its nutritional and medical potential. Plants belonging to the family Compositae show medicinal properties and contain numerous compounds, some of which may have potential as novel drug sources (*Ageratum Conyzoides - an overview | ScienceDirect Topics, n.d.*). Phytochemical screening of *A. conyzoides* has reported the presence of active secondary metabolites like alkaloids, tannins, phenols, saponins, coumarins, essential oils and flavonoids that support its excellent therapeutic uses in the treatment and prevention of diseases (Dele, Joshua and Jumoke, 2019). These phytoconstituents have shown diverse pharmacological properties including antimicrobial, anti-inflammatory, analgesic, antioxidant, anticancer, antiprotozoal, antiabetic, spasmylytic, and many more (Yadav et al., 2019). Because of its high caloric value and high content of crude protein and essential minerals (very rich in K, P, Ca, Fe, Mg, and Zn and a moderate amount of Cu and Mn), it may also be recommended as a supplement diet (Dele, Joshua and Jumoke, 2019).

It has been used as folk medicine in various parts of Africa, Asia, and South America. In Nigeria, rubbing the plant's leaves on a patient's chest is a cure for pneumonia; however, the leaves’ most popular medicinal use is for wound healing and burns (Kotta et al., 2020). In Nepal, leaf juice and leaf paste are applied to skin burns, cuts, wounds, boils, and muscular pain. The decocation of infusion of the herb is given in stomach ailments such as diarrhea, dysentery, and intestinal colic (Sharma and Sharma, 1995).

In Nigeria, female reproductive issues during antenatal conditions are dealt with insertion of crushed leaves into vagina while post-partum skin disease are cured with topical application of macerated leaves (Ogbie, Erugun and Uwagboe, 2009). In some parts of Africa, the plant is used for headaches, dyspnea, mental and infectious diseases (Sivakrishnan and Kavitha, 2017). Menstrual pain and other unspecified female complaints are also treated with *A. conyzoides* along with other herbs (Lans, 2007). The juice from the leaves and stems is used to treat wounds and various skin diseases, including leprosy, and is prescribed as a bath for eczhamosis patients (Sharma and Sharma, 1995). Eye lotion is made from the juice of the leaves and roots. It is also used for venereal disease in El Salvador (Hirschhorn, 1982). Paste of leaf with *Zingiber officinale* is used to treat snake bites in India (Nadu, 2020). The leaves are used along with salt as a vulnerary and are said to prevent tetanus (Sharma and Sharma, 1995). In Cameroon, it is a local remedy for craw-craw, but in Cameroon and Congo, it is used to treat fever, rheumatism, and colic (Sharma and Sharma, 1995). *A. conyzoides* is recommended by Brazilian Drugs Central as an antirheumatic (Ming, 1999). Some medicinal properties exhibited by *A. conyzoides* include:

**Wound healing property**

The crude plant extract of *A conyzoides* is considered significantly superior to Vaseline gauze as a wound dressing material (Durodola, 1977; Adesogan and Okunade, 1979). In research conducted to investigate the wound healing properties of methanolic extracts of *A. conyzoides* leaves compared with those of honey; inflammatory cells were found in lower numbers in *Ageratum* sections relative to honey and control sections. Healed scar parts of wounds dressed in the herb extract also showed increased fibrosis. *Ageratum*-healed wounds had significantly fewer fibroblasts than honey healed and control wounds (P = 0.012 and 0.036, respectively) (Oladejo et al., 2003).

Similarly, research conducted by Arulprakash et al., (2012) reported that *A. conyzoides* extract increased cellular proliferation and collagen synthesis in wound. Based on better rates of epithelialization and wound contraction, as well as histopathological findings, wounds treated with the *Ageratum* extract healed much faster. The treated tissue showed a 40% improvement in tensile strength (Arulprakash et al., 2012). As a result, topical application of *A. conyzoides* has been shown to hasten wound healing.

**Antimicrobial property**

Tests of antibacterial activity show that the essential oils from *A. conyzoides* have moderate antimicrobial activity against gram positive bacteria but are less effective against gram-negative bacteria (Kouame et al., 2017). A
crude material isolated from the petroleum ether extract of *A. conyzoides* leaves has been found to exhibit antibacterial activity against *Staphylococcus aureus* in vitro (Durodola, 1977; Sharma and Sharma, 1995). Similarly, a study conducted by Poné et al., (2011) reported that ethanolic extracts of *A. conyzoides* were effective against the intestinal worm *Heligmosomoides bakeri*.

Similarly, the efficacy of six forms of crude extracts, including those from leaves of white (LW), purple (LP), or white–purple flowered (LW–P) plants and flowers of white (FW), purple (FP), and white–purple flowered (FW–P) plants, as well as two types of essential oil from LW-P and FP plants, were investigated against pathogenic intestinal protozoa, *Giardia duodenalis* trophozoite. The *A. conyzoides* extracts LW–P and FP were more successful against *Giardia* than the other extracts examined (Pintong, Ruangsitichai, et al., 2020). Furthermore, the ultrastructure of *Giardia* trophozoites, such as flagella and ventral disks, which are the structures targeted by commercial anti-*Giardia* drugs, were altered by exposure to these extracts (Pintong, Ruangsitichai, et al., 2020). As a result, this study concluded that *A. conyzoides* may be a source of anti-*Giardia* drugs.

The extract of *A. conyzoides* had antibacterial activity against *Staphylococcus epidermidis* and *Propionibacterium acnes* with a Minimum Inhibitory Concentration (MIC) of 2.5% (Arif Budiman, Alfia Nur Azizah, 2018). Following physical examination, the formula containing 4% Sodium Carboxymethyl Cellulose (CMC) and 2.5% *A. conyzoides* extract produced the best results. The antibacterial activity of the *A. conyzoides* extract gel formulation occurs and inhibits *S. epidermidis* in a zone of 14.7 ± 2.3 mm and 15.43 ± 1.6 mm against *P. acnes* (Arif Budiman, Alfia Nur Azizah, 2018). As a result, a gel solution containing 4% Sodium CMC and 2.5% *A. conyzoides* extract has antibacterial activity against *S. epidermidis* and *P. acnes*.

In another research, the crude extract of *A. conyzoides* (100 mg ml⁻¹) was able to inhibit the growth of *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas putida*, *Salmonella enterica*, and *Streptococcus pyogenes* with the diameter of the zone of inhibition being 14mm, 18mm, 13mm, 12mm and 10 mm, respectively (Neelabh, Nahid and Navneet, 2017). In another study, the essential oil of the plant at a concentration of 2 000 ppm exhibited strong antifungal activity against *Epidermophyton floccosum* which causes skin and nail infection in humans, *Microsporum canis* that affects the upper dead skin of cats, and *Trichophyton mentagrophytes* causing ringworm in companion animals (Kamboj and Saluja, 2008). Hence, *A. conyzoides* inhibits several microorganisms including bacteria, protozoa, nematodes, and fungi.

**Anti-inflammatory property**

To investigate the anti-inflammatory activity of *A. conyzoides*, researchers used a carrageenan-induced anti-inflammatory paw edema model in Wistar albino rats. The extracts of *A. conyzoides* promoted 50.23% inhibition of carrageenan-induced paw edema at the 4th hour of administration in a time-dependent inhibition of carrageenan-induced paw edema model, and the results were statistically significant (P = 0.05) (Md. Atiar Rahman, 2012).

Also, the effect of *A. conyzoides* on acetic acid-induced colitis and indomethacin-induced enterocolitis models in rats were assessed. As compared to the disease-inducing population, pretreatment with ethanolic extract of *A. conyzoides* at doses of 500 and 750 mg kg⁻¹, p.o. (per oral) and a standard group of animals showed significant attenuated results in all of the studied parameters which included macroscopic evaluation (scoring of ulcers), microscopic evaluation (histopathology), estimation of biochemical parameters (myeloperoxidase and lipid peroxides) and measurement of physical parameters (change in body weight and colon weight) (Biradar et al., 2011). *A. conyzoides* pretreatment has protective and regeneration effects on colonic cells, according to a histopathological report. The finding of this study provides evidence that ethanolic extract of *A. conyzoides* may be beneficial in patients suffering from inflammatory bowel disease (Biradar et al., 2011).

**Analgesic property**

In Swiss albino mice, analgesic effects were studied using acetic acid-induced writhing model and a formalin-induced licking model. At the maximum dose of 2.0 g kg⁻¹ body weight, *A. conyzoides* extracts inhibited 49.85% of acetic acid-induced pain as compared to the reference drug, diclofenac sodium (40 mg kg⁻¹). Similarly, compared to morphine (0.5 mg kg⁻¹), *A. conyzoides* reduced 35.48% of formalin-induced pain by 2.0 g kg⁻¹. These effects were statistically significant (P<0.05) (Md. Atiar Rahman, 2012).

**Anticancer property**

Ethylacetate extract of *A. conyzoides* exhibited remarkable cytotoxic activity on A-549 cancer cells (lung carcinoma) and P-388 cancer cells (leukemia) with IC50 values of 0.68 and 0.0003 μg ml⁻¹ respectively (Adebayo et al., 2010), SF-767, LNCaP, PC-3, and SF-763 cancer cell lines were likewise suppressed by the leaf extract of *A. conyzoides* (Bayala et al., 2014). The presence of anticancer chemicals kaempferol, oxygenated terpenes, sesquiterpene hydrocarbons, and monoterpenic hydrocarbons was reported to be responsible for the anticancer action of *A. conyzoides* leaf extract (Bayala et al., 2014).

The ethanol extract of *A. conyzoides* was evaluated for gastroprotection in rats using the Ibuprofen, ethanol, and cold restraint stress ulcer models. In the Ibuprofen model, oral treatment of the ethanol extract at dose levels of 500 and 750 mg kg⁻¹ effectively prevented gastric lesions by 80.59% and 89.33%, respectively, as compared to Misoprostol (74.43%); by 97.09 and 99.24%, respectively, in the cold stress model as compared to Famotidine (77.86 and 92.71%) and by 86.58 and 92.29%, respectively, in the alcohol model (Shirwaikar et al., 2003).

**Reproductive property**

On the isolated sensitized virgin rat uterus, 5-HT and ACh (both 5 mg ml⁻¹ bath) induced uterine contractions. Treatment of the tissue with the *A. conyzoides* extract (200 μg ml⁻¹ bath) inhibited uterine contractions induced by 5-HT, indicating that the extract exhibits specific anti-serotonergic activity, while the plant extract did not affect uterine contractions induced by Ach (Achola and Munenge, 1998).
Agricultural uses

*A. conyzoides* has bioactivity that has agricultural uses as shown by various research across the globe. The plant extract shows insecticidal, antimicrobial, antifungal, herbicidal, nematicidal effects, and others as discussed below:

**Insecticidal / Pesticidal effect**

The insecticidal activity may be the most important biological activity of this species. It inhibited insects such as *Musca domestica, Sitophilus zeamais*, *Schistocerca gregaria*, mosquito larva of *Anopheles stephensi*, *Aedes aegypti*, *Anopheles gambiae* and *Culex quinquefasciatus*, *Platelia xylostella*, *Spodoptera litura*, *Sitophilus aemais*, *Thlaspi japonica*, *Leptocarsia chinesis*, *Dysdcurus flavidus*, *Lucilia caesar*, *Tribolium confusum*, *Mythimna separata*, *Culex pipienspallens* and others (Okunade, 2002a; Kong, 2015; Rioba and Stevenson, 2017). The terpenic compounds, mainly precocenes, with their antijuvenile hormonal activity are probably responsible for the insecticide effects of *A. conyzoides* (Ming, 1999).

Essential oil (EO) from *A. conyzoides* was extracted and tested as a fumigant against *Tribolium castaneum*, the storage grain insect where it showed 100% mortality at 250 ppm during in vitro testing and at 1 000 ppm it fully eliminated the insect’s damage to wheat grains in vivo testing (Jaya et al., 2014a). EO-treated seeds had no negative effects on seed germination or seedling growth, indicating that the oils are non-phytotoxic (Jaya et al., 2014a). As a result, this EO could be recommended as a botanical pesticide to protect stored food items from the insect invasion, extending their shelf life.

In another research, crude extracts and EOs were found effective against adult *Ae. aegypti* female mosquitoes (Pintong, Ampawong, et al., 2020). The mortality of adult *Ae. aegypti* females was higher from leaf extracts, particularly from purple flowered plant (median lethal dose, LD90 = 0.84%) (Pintong, Ampawong, et al., 2020). Histopathological alterations in adult *Ae. aegypti* females included compound eye degeneration, muscular damage with cellular infiltration, gut epithelial degeneration and necrosis, pyknotic nuclei in the malpighian epithelium and ovarian cell degeneration (Pintong et al., 2020).

The volatile oil of air-dried leaves of *A. conyzoides*, upon fumigation of artificially infested cowpea, exerted acute toxicity on adult cowpea weevil, *Callosobruchus maculatus* with maximal mortality of 95-97% by 60 μl oil (Jaya et al., 2014b). Further, significant oviposition deterrence and full prevention of adult insect (F1 progeny) emergence were observed with no negative consequences on the beans at doses ranging from 2.5 μl to 10 μl per 9.5 g of beans (Gboblade, Onayade and Ayinde, 1999). Evidence indicates that *A. conyzoides* is as effective as synthetic pesticides and is also economically viable, with a significantly lower impact on beneficial insects such as ladybirds, hoverflies, and spiders when compared to synthetics (Rioba and Stevenson, 2017).

**Allelopathic property**

*A. conyzoides* release many kinds of allelochemicals through leaching, volatilizing and residue decomposition into the environment. Ageratichromene and its derivatives, monoterpenes, and sesquiterpenes are major components of the volatiles from *A. conyzoides* along with ten flavones from residues and aqueous extract. These components significantly inhibit the germination and growth of various crops like rice, wheat, sesame, soybean, mungbean, radish, tomato, peanut, corn, cucumber, and others (Zohaib et al., 2017). *A. conyzoides* infests cultivated fields and lowers agricultural yields. It is, however, helpful to some crop plants in a variety of agro-ecosystems. In China, *A. conyzoides* is intercropped in citrus orchard, which quickly grows and covers the orchard to rule out other weeds like *Cyperus difformis*, *Bidens pilosa* and *Digitaria anguinalis* (Liang, 1994). Further, it stabilizes populations of *Amblyseius spp.*, an effective predatory natural enemy of the citrus red mite, *Panonychus citri* as its pollen provides alternate food for the natural enemies (Liang, 1994). Also, it reduces the spore germination of several fungal pathogens like *Phytophthora citrophthora*, *Pythium aphanidermatum*, and *Fusarium solani* through release of allelochemicals into the soil (Jianjun et al., 2002).

In addition to that, it is also used as a source of plant nutrients. Organic carbon is 42.11%, total nitrogen is 3.78%, and phosphorus is 0.21% in *A. conyzoides*, which has a C/N ratio of 11.15 and can be used as organic matter or compost (Anhare et al., 2018). *A. conyzoides* is traditionally used as green manure in fields in south China to boost crop yields and suppress weeds. *A. conyzoides* extract at 10% showed a positive impact on the germination of pea seeds (Naresh et al., 2018). The lower concentration of the weed extract stimulated growth and nodulation parameters whereas the higher percentage of weed extracts lowered the pH and cation-exchange capacity (CEC) values of soil in the pea field (Naresh et al., 2018). The finding of this research supports the use of *A. conyzoides* as green manure.

**Microbial effect**

In a research, *A. conyzoides* biomass was vermicomposted with cow dung in 25% (*Ageratum + CD*) (25: 75 v/v); 50% (*Ageratum + CD*) (50: 50 v/v); and 75% (*Ageratum + CD*) (25: 75 v/v). The result of this research showed that *Ageratum* with a 50-75% proportion in vermicomposts showed better results in waste mineralization, microbial enzymatic activities, and microbial population buildup (Gusain and Suthar, 2020). The ageratum with 50% and 70% proportion showed the highest fold increase in bacteria (2.09-2.51), fungi (1.48-2.41), and actinomycetes (1.52-1.79) population (Gusain and Suthar, 2020). In addition to this, vermicomposting caused a decrease in pH, but an increase in *N* (59.6-69.9%), *P* (53.8-148.7%), *K* (32.2-92.43%), and *Ca* (25.5-55.3%) (Gusain and Suthar, 2020). This result indicates that *Ageratum* could be bio-transformed into toxicfree manure through vermitecchnology.

**Anti-fungal effect**

In a research, water extracts of different weeds species (*Ageratum conyzoides*, *Oxalis corniculata*, *Phyllanthus debilis*) were assayed for their antifungal activity, where the extract from *A. conyzoides* inhibited the mycelial growth of *Rhizoctonia solani*, *Aspergillus niger* and *Phomopsis theae* at least by 70% (Iqbal et al., 2001). In another study, the essential oil of the plant showed
antifungal activity against *Helminthosporium turcicum*, *H. oryzae*, *Cercospora capsici*, *Pyricularia oryzae*, and *Fusarium moniliforme* (Kamboj and Saluja, 2008).

All the parts of *A. conyzoides* have fungitoxic chemicals against *Fusarium solani*, the wilt causing pathogen as reported by research where the target fungus was exposed to various concentrations (2, 4 and 6% w/v) of aqueous, methanolic and n-hexane extracts of inflorescence, leaf, stem and root. All the concentrations of extracts of four plant parts significantly suppressed the growth of the target fungal pathogen (Sidra Javed, 2012).

**Anthelmintic and Nematicidal effect**

The essential oil of the plant exhibited anthelmintic activity against *Taenia solium* and *Pheretima posthumae* and the extract of the stem and leaves exhibited nematicidal activity against second-stage juveniles of *Meloidogyne incognita* (Kamboj and Saluja, 2008).

In a research, six plants viz., *Ageratum conyzoides*, *Eichhornia crassipes*, *Ipomoea carnea*, *Nicotiana plumbaginifolia*, *Acalypha indica* and *Triannthera portulacastrum* were tested for their nematicidal effect, where the aqueous extracts of *A. conyzoides* showed the maximum damage amongst all the test plants to the eggs, reduced the hatching and caused paralysis and death of second stage juveniles (J2) of *Meloidogyne incognita* (Khan et al., 2017). Its effectiveness against *M. incognita* was further proved by another research in black gram (Pavaraj, Karthikairaj and Rajan, 2010).

**Herbicidal effect**

As per the research conducted in Thai Nguyen University of Agroforestry, Vietnam; the application of *A. conyzoides* leaves at 2 t ha⁻¹ in a paddy field 2 days after transplanting caused about 75% paddy weed reduction and increased yield by 14% compared with a herbicide treatment (Butachlor 3 kg ha⁻¹) (Xuan et al., 2004). This research suggests that *A. conyzoides* might be used as natural herbicide for weed control in paddy fields and reduce the dependency on synthetic herbicides.

In another experiment conducted in the Laboratory of Crop Science, Faculty of Agriculture, Miyazaki University, Japan in 2002, the application of *A. conyzoides* leaves at 2 t ha⁻¹ strongly decreased weed number of *Echinochloa crus-galli* (78.4% of inhibition) and completely inhibited the emergence of *Monochoria vaginalis* and *Aeschynomene indica* in calcareous soil condition (Xuan et al., 2004).

**Conclusion**

*Ageratum conyzoides* is popularly known to be an invasive weed but is hardly known for its medicinal and agricultural properties. It has been used as folk medicine for centuries in different countries. Different research has proved that the phytochemicals present in *A. conyzoides* are responsible for its medicinal effects on burns, wounds, diarrhea, fever, muscular pain, reproductive problems, skin diseases, etc. It is also used for agricultural purposes as insecticides, herbicides, manure, fodder, etc. The *Ageratum* genus is a fast-spreading plant and controlling them as a weed has been a significant concern for environmentalists, ecologists, farmers, and animal scientists. Having reviewed *A conyzoides* for its potential medicinal and agricultural usages presents a unique perspective to this weed that exploiting it further for such beneficial usage can be a management practice for this weed. In Brazil, some small pharmaceutical companies are being run using *A. conyzoides* as a raw material for phytochemicals. Further research in this area could serve as a means of treating several diseases and a biological approach for better agricultural production.

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