

**REVIEW ARTICLE** 

# An overview of the Multi-Utility Potential of a Tropical American Herb: *Ageratum houstonianum* Mill.

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**Abstract** The demand for plant-based metabolites, pharmaceuticals, food supplements, cosmetics etc. keeps on increasing day by day. For that purpose, our quest for finding novel uses of plants is never ending. Among a large number of useful species of plants, some are generally overlooked, or underestimated. In this paper, such a species from the genus *Ageratum* of family Asteraceae is being discussed, which is claimed to have high therapeutic potential to treat various diseases, yet ignored largely as a weed. It is a multipurpose herb with many ethno-medicinal and pharmacological characteristics, with a long history of traditional medicinal use. Extract of young leaves is said to be effective against skin problems, and a study of the literature revealed many other pharmacological activities of this plant. The current review is an attempt to provide pharmacological and biological reports on *A. houstonianum*.

Keywords: Ageratum houstonianum, antimicrobial, medicinal plants, phytoconstituents

#### Introducation

Herbal drug practitioners have been engaged in using traditional or folk medicine from ancient times for treatment of various ailments like irritation, artery diseases, cancer as well as for their antimicrobial activities (Kumar et al. 2007). Herbal plants or their uses are less demonstrated and, therefore, scientifically inadequately assessed by the followers of modern medicine for their properties. Herbal medicine has been used extensively in many countries and has become part of primary health care as the herbal products are used to treat various skin conditions, skin irritation, burns, indigestion, infections, lesion, trims, ulcers and swellings. They are also effective as antibacterial, antifungal, antiviral, and antiprotozoal agents (Tennyson et al. 2011). In general terms, out of approximately 400,000 species of plants known to exist, bioactivity has been studied in only 6% and around 15% plant compounds have been examined. Phytochemicals

are really very useful in protecting humans from various disorders. They generally have curative, protective, or disease preventive properties for the host (Kanase and Shaikh 2018). Ageratum houstonianum is herbaceous plant, often known as blue mink. It is very useful in curing fever, paste of leaves is useful in wound healing, essential oil shows cytotoxic effect (Hadidyet al. 2019), and it is also examined for antimicrobial and mosquitocidal effects (Tennyson et al. 2011). The screening of literature regarding biological assets of A. houstonianum revealed negligible data and seems almost silent on this aspect as very fewreports are present on activity of this plant (Chandrekar et al. 2020). Oil of this plant is having insecticidal activity (Kurade et al. 2010). A. houstonianum is widely used as a fodder and to protect soil (Menut and Lamaty 1993). The essential oil has very strong smell and has been tested for different biological activities. Chemical constituents of A. houstonianum essential oil include: flavonoids, triterpenoids (Chandra et al. 1996), benzofuran derivatives and steroids (Menut and Lamaty 1993). This study is aimed to summarize pharmacological and biological activities of this valuable herb.

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#### **Taxonomical Information**

The accepted name of the taxon is *Ageratum houstonianum* Mill (http://powo.science.kew.org/) with native range from Mexico to Central America. As per the same database, it has 19 synonyms. The genus *Ageratum* L. with around 40 species worldwide is included in family *Asteraceae* Bercht. & J. Presl.

#### Vernacular Names

Floss flower, Blue mink, Blueweed, Pussyfoot, Mexican paintbrush, Bluebilly goat weed. It is referred to as "Yerba de Zopilote" and "Flor de Garrapata" in Vera Cruz, its native habitat (Johnson, 1971). A few more regional names are being provided below:

Table 1: Showing Vernacular Names

Language	Vernacul ar Names		
English	Floss flower, Mexican paintbrush		
Nepali	Nilogandhe, Buko bon,		
	Gandhejhaar		
Malayalam	Michanga, Niloappa		
Bengali	Nak ful, Dochunty, Elamejhar		
Kannada	Amanpathri		
Aruna chal Pradesh	Eehgaarh		

#### Habitat and Distribution

In 1731, Vera Cruz was the first place from where *Ageratum houstonianum* was collected and placed in the tribe Eupatorieae, which is characterized by its tubular flowers. The family Asteraceae includes more than 1650 genera globally, which are distributed across tropical and subtropical regions. This species usually grows wild near habitation on fallow lands, along the sides of roads, in disrupting regions, and banks of the river in Mexico, Central America, the Caribbean, South and East Africa (Hadidy*et al.* 2019, Menut and Lamaty1993). It is present mainly up to 1300 m above sea level.

#### **Botanical description**

It is an annual, herb 30-70 cm in height. It emerges from Peru, Mexico, and Central America (Devkota and Sahu 2019). Stems glandular, densely hairy, usually purple to reddish, round. Leaves opposite, ovate to triangular, 2-7 cm long, margins serrated. Bluish-pink, homogamous flower heads or capitulate appear in umbellate clusters. Florets tubular with 5 sepals reduced to pappus. The brown to black 'seeds' (achenes) are topped with five whitish awn-tipped scales resembling short bristles or hairs, which are modified sepals (pappus). Seeds are dispersed with the help of air. According to a study by Lamsal *et al.* (2019) *A. houstonianum* plants are not drought tolerant and grow better in



Figure 1: Ageratum houstonianum

neutral to alkaline soil conditions.

#### **Cultivation and General Phenology**

Flowering: April-November; Fruiting: September-December

It is often grown for showy heads, as an ornamental, attracted by a number of butterflies and other insects. For cultivation (not much popular in India), the propagules are seeds, which can be sown from March to September. The preferred soil type is neutral to slightly alkaline, and the shady, moist areas are the habitats which promote its growth well. Being a tropical climate plant, it can flourish at a variety of temperatures. When in cultivation, the removal of dead flowering heads extends its flowering season.

#### Cytology and Morphology

In *A. houstonianum*, white flower plants have diploid number n=10, whereas tetraploid number (n=20)were reported in plants having blue flowers (Gill and Garg 2016). The cultivated varieties usually include tetraploids as well as hybrids.

### Differences between A. houstonianum and A. conyzoides

*A. houstonianum* is common in plains while *A. conyzoides* is naturally distributed in high altitude areas. *A. houstonianum* has a better invader strategy due to low LCC resulting in use of energy more effectively (Singh *et al.* 2011). (Table 1).

#### Pyrrolizidine alkaloids

*A. houstonianum* was found to inhibit the growth of nematodes. Some *Crotalaria* species are known to be used for inhibiting nematodes, because they produced pyrrolizidine alkaloids. But it is also to be noted that these alkaloids were commonly produced by *A. houstonianum*. Wiedenfeld and Cetto (2001) isolated four Pyrrolizidine alkaloids which were determined with the help of GC–MS and homo- as well as hetero-nuclear 2D NMR spectroscopy. They stated that only one was reported previously that belongs to retronecine-typeO<sup>9</sup>-(-)-viridiflorylretronecinewhile other three were characterised by them, which show retronecine-O<sup>9</sup> and retronecine-O<sup>7</sup> structure.

## Polymethoxy flavones and Benzofuran derivatives

Quijano *et al.* (1982) collected aerial parts of *A. houstonianum*, its petroleum extract resulted in isolation of lucidin dimethyl ether, eupalestin, and agecorynin C that are already known but they demonstrate new flavones that are highly oxygenated, named as agehoustin A and B According to them, it was the first report of these flavones. In Asteraceae family, the first octamethoxyflavone reported was Agehoustin A and the third compound reported from *A. houstonianum*roots are of phytochemical and taxonomic interest due to their unusual pattern (Breuer *et al.* 1987).

S. No.	A. houstonianum	A. conyzoides
1.	Plants more vigorous and grows	Plant less vigorous and grows not above 30
	up to 60 cm in height	cm in height
2.	Branches more and dense, purple.	Branches few and sparse, green.
3.	Ovate to triangular leaves, simple	Egg-shaped leaves with the broad end at the
	and opposite	base
4.	Leaf base is generally cordate to	Leaf base is obtuse or broadly cuneate
	truncate	
5.	Numerous sticky hairs on the	Few hairs on the bracts
	bracts	
6.	Diameter of capitulum up to 6mm	Capitulate up to 4 mm wide
	wide	
7.	Involucre bracts pubescent	Involucre bracts are less pubes cent

 Table 2: Differences Between A. houstonianum and A. conyzoids

Table 3: Showing Phytoconstituents of A. houstonianum

Compounds	Class	Source	References	
Agerarin		Plant extract	Shin et al., 2017	
Precocene I,	Chromenes	Plant extract	Lu et al., 2014, Kuradeet al., 2010	
Precocene II				
2,2- di met hyl	Chromenes	Plant extract, Oil extract	Hadidyet al., 2019	
chromenes				
β-caryophyllene	Sesquiterpenes	Plant extract, Oil extract	Lu et al., 2014	
β- sesquiphellandrene	Sesquiterpenes	Leaves oil	Menut and Lamaty, 1993	
3,7- Dimethyl-2,6-		Plant extract	Zeeshanet al., 2012	
octadi en yl a cetate				
Ageratochrome	Chromenes	Oil extract	Adebisiet al., 2019, Lu et al., 2014	
(Precocene II)				
Benzofuran		Roots	Breuer et al., 1987	
derivatives				
α-Bisabolo		Leaves oil	Hadidyet al., 2019	
Exoticin	Flavones	Aerial parts extract	Quijanoet al., 1982.	
Geranial	Terpenes	leaves	Chandra et al., 1996	
Camphene	Terpenes	leaves	Chandra et al., 1996	
Myrcene	Terpenes	Leaves oil	Menut and Lamaty, 1993	

Table 4: Showing Traditional Uses of A. houstonianum

Countries	Used plant part	Plant properties	References
China	Whole plant	To clear away heat and toxic material	Devkota and Sahu, 2019
Central America	Wholeplant	Used as an antiphlogisticto relieve swelling and throat pain	Devkota and Sahu, 2019
Nepal, India, Mexico, Southern America	Whole plant	Used as an ornamental plant	Sharma, 2020
India	Wholeplant	Antimicrobial, antifungal, and mosquitocidal activity	Devkota and Sahu, 2019
Mexico, India	Aerial parts	Antimicrobial, antibacterial, antioxidant, antifungal, anti-inflammatory, wound healing	Lu <i>et al.</i> , 2014
Mexico	Aerial parts	Plant infusion is given in most of the stomach problems such as diahorrea, dysentery, and indigestionas well as rheumatism and fever	Hadidyet al., 2019
India	Aerial parts	The paste of the leaves is applied to the wound to stop bleeding and quick healing	Wangpanet al., 2019
India	Aerial parts	Treat skin infections and sore throat	Hadidyet al., 2019
India	Leaves extract	Treatment of diabetes	Sharma, 2020
	Leaves extract	Treat conjunctivitis, ophthalmics, and skin problems	Adebisiet al., 2019

#### **Chromenesprecocene I and II**

Siebertz*et al.* (1990) separated plants into different organs (leaves, flowers, stems, and roots) to analyze the accumulation of precocene. The most prevalent amounts have been identified in leaves (12.45  $\mu$ mol per plant) then in flowering heads (9.14  $\mu$ mol per plant), followed by small concentration in stalks and roots (0.069- 0.63  $\mu$ mol per plant). Precocene I

and II have been found to be present in highest concentration in involucral bracts and in receptacles(34 and 31.5  $\mu$ mol g<sup>-1</sup> fresh weight respectively). Precocene aromatic ring biosynthesis wasconducted by feeding stable isotopesand <sup>14</sup>C-labelled compound, inhibitors of PAL, to the seedling of *A. houstonianum*. With this study, it was concluded that chromene is the biogenetic precursor of precocene II.



Precocene I



Precocene II



**Beta carophyllene** 



Exoticin



3,7-dimethyl-2,6-octadienal acetate



2,2-dimethylchromenes

Figure 2: Phytoconstituents structure found in major amount in A. houstonianum

#### Ethnopharmacological Activities (Table 3)

#### a. Adulticidal activity and Antidiabetic activity

The absorption of the different levels of plant extract was recorded by the  $\alpha$ -amylase inhibition activity. The results demonstrate that extracts of plant found to be a potent  $\alpha$ -amylase enzyme inhibitor similar to standard acarbose. A dose dependent increase in  $\alpha$ -amylase inhibitory activity of plant extract is reported by Sharma (2020). Reddy *et al.* (2012)conducted an experiment in alloxane-induced diabetic rats and regular rats to monitor blood glucose levels at two doses 200 and 400 mg/kg. It was shown that hydro-alcoholic

extract of *A. houstonianum* with 400 mg/kg was more impactful than 200 mg/kg in the treatment of diabetes as this dose was found to reduce blood glucose concentration between 2-4 hours.

#### b. Antimicrobial activity

Tennyson *et al.* (2011) studied the *A. houstonianum* leaf extracts to analyse the antimicrobial effect with different solvents (hexane, ethyl acetate and methanol) by disc diffusion method. Test organisms included *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Vibrio fischeri*, *Klebsiella pneumoniae*, *Yersinia enterocolitica*,

*Erwinia amylovora, Salmonella typhi, Enterobactera erogens, Proteus vulgaris* and *Candida albicans*. The highest activity (19 mm) against *P. aeruginosa* was given by ethyl acetate extract followed by *S. typhi*(18 mm). *P. aeroginosa* was inhibited by all three extracts but *E. aerogens* was not inhibited by any of the solvent extracts.

#### c. Antioxidant and Antifungal activity

Hadidvet al. (2019) revealed potential cosmetic and medicinal uses of A. houstonianum. The herb is very useful source of naturally occurring antioxidants. The free radical scavenging action against radicals of DPPH and hydroxyl was assessed using methanolic leaf extracts, ethyl acetate and hexane. Ethyl acetate gave better results as compared to hexane and extract of methanol (Tennyson et al. 2012). If compared with the standard ascorbic acid IC<sub>50</sub> 5.38 µg/mlthe plant showed mild antioxidant potential with IC<sub>50</sub>123.67 µg/ml (Sharma, 2020).Devkota and Sahu (2019)have demonstrated high fungicidal potential of A. houstonianum against five strains Sclerotium rolfsii, Phytophthora capsici, Alternaria brassicae, Fusarium oxysporum and Botrytis cinerea. Highest antifungal activity had been shown by methanolic extracts against P. capsici, S. rolfsii, and F. oxysporum at various concentrations. At higher concentrations of about 150-250 mg/mL, the plant extracts might have better fungicidal properties as they were more efficient than the chemical fungicides.

#### d. Wound healing

Panicke ret al. (2017) performed wound healing experiment on wistar rats with leaf extract of A. houstonianum by using methanol as a solvent. A. houstonianum treated group was recovered more quickly and the wound width was considerably reduced in comparison with control. Moreover, microscopic examination of rat's scar tissue showed reduction when medicated with 10% to 20% concentration of extract in a dose dependent manner. The reason behind this is the presence of antioxidant molecule i.e., flavonoids which scavenge free radicals and thereby contributing in wound healing property of the extract.

#### e. Oviposition deterrent activity

Tennyson et al. (2012) have shown the impact of A.

*houstonianum* leaf extract against oviposition activity of *Anopheles stephensi*, *Aedes aegypti*, and *Culex quinquefasciatus*. They conducted site analysis, planning, ovitraps placement, field observation, and finally natural breeding monitoring at the study site. They concluded that *A*. *houstonianum* leaf extract has the potential of oviposition deterrent property that is observed in both field and laboratory results.

#### f. In vitro organogenesis

The combination of Auxin and IAA activates the root and shoot regeneration for *A. houstonianum*. Various concentrations of Kin and IAA (0.4-0.4, 1-1, 2-2, 4-4, 0.4, 1-0.4, 2-4, 4-2) (mg L<sup>-1</sup>) were used in induction of callus shoot, root multiplication, and plantlet formation. At 2-4 (mg L<sup>-1</sup>) concentration, the maximum results for root and shoot formation in epicotyl explants were observed. Shoot apical meristems were found to be responding best for regeneration of plantlets at 4- 2 (mg L<sup>-1</sup>) Kin-IAA combination (Mohammadi, 2017).

#### g. Heavy metal stress tolerant

Cadmium (Cd) is causing high toxicity as it is a heavy metal pollutant of the environment. Milusheva et al. (2019) performed experiments to examine the Cd stress physiological response, shown by ornamental A.houstonianum. The stress effect was assessed by examining different indicators like changes in height and width of the plant, diameter and length of roots, biomass, and the electrolyte discharge of micro plant. Visual observations, including delayed growth and necrosis, leaf chlorosis and root tip browning, withering and severe stress effect death were observed as symptoms of toxicity. The effects of Cd toxicity on the plant's development and explant height were more severe in young plants according to biometrical indices of in vitro cultivated A. *houstonianum*. In the presence of Cd up to  $10 \text{ mg l}^{-1}$ , the height of explants remained unaffected as compared to control (non-treated) (5x MPC). The height of 20-day-old explants was found to have decreased significantly. They claim that using in vitro models of ornamental plants is a reliable method for analysing and predicting yearly tolerance to Cd and other heavy metal.

#### **Essential oil**

In the plant essential oil, almost 35 components were identified. Precocene II (62.68%), Precocene I (13.21%), and  $\beta$ -caryophyllene (7.92%) were present in major amount. Oil and its constituents have better ability to develop insecticides and resist stored grain insects (Lu *et al.* 2014). According to Kurade *et al.* (2010), precocene-II (43.99%), precocene-I (23.34%), and  $\beta$ -caryophyllene (9.16%) were the main constituents. Flavonoids, triterpenoids, steroids and benzofuran derivatives were present (Chandra *et al.* 1996).

#### a. Antimicrobial activity

Agar well diffusion method was assessed for the antimicrobial effect of leaves and flowers essential oil of A. houstonianum (Hadidyet al. 2019). Both Gram positive and negative strains of bacteria including Staphylococcus aureus, Bacillus subtilis and Methylene resistance Stapylococcusaureus clinical isolate, Klebsiellapneumoniae, Salmonella typhimurium, and Escherichia coli were used. In comparison with Gentamycin, the flower oil sample was shown to be highly efficient against *B*. subtilis and S. aureus having 50% potency. The antibacterial effect of essential oils was observed and better results were shown against gram positive bacteria as compared to gram negative bacteria. They suggested that due to the presence of chromenes the essential oil of the flowers of A. *houstonianum* showed the antibacterial effect.

#### b. Acaricidal activity

Leaf essential oil of *A.houstonianum* containing foam soap shown the acaricidal properties against *Rhipicephalus lunulatus*. Four replications of different doses ranging from 0.00, 0.02, 0.025, and 0.03 ml/g were observed *in vitro* and 10 ticks were placed in each of the petriplate having different concentration with the foam soap on the bottom. Mortality rates observed *in vitro* vary from 0 to 50% when treated with control and when compared 95% with the lowest dose on 8<sup>th</sup> day and 100% on the 3<sup>rd</sup> day after treatment. The result indicates the high efficiency of this medicated oil soap as it is highly toxic to *R. lunulatus* (Pamo *et al.* 2004).

#### c. Repellent Activity and Contact Toxicity

Aerial part essential oil of *A. houstonianum* evaluated for booklice to commercial repellent dimethyl phthalate, at a concentration of  $0.8 \text{ nL/cm}^2$  after 4 hours of exposure. Results showed that essential oil exhibited strong repellent activity.Furthermore, the essential oil bioactive constituents also showed contact cytotoxityagainst *L. bostrychophila* with an LC<sub>50</sub> value of 50.8 µg/cm<sup>2</sup>.Stronger acute toxicity was shown by Precocene II than precocene I (Lu *et al.* 2014).

#### d. Insecticidal activity

Fresh *A. houstonianum*aerial parts were extracted by steam distillation and characterized by GCMS analysis. Main compounds were precocene I and Precocene II and beta- caryophyllene. The isolated constituentswere agetochrome and 1- heptadecene. *Plutellaxylostella* and *Aphiscraccivora* were used against essential oil, hexane/methanol fractions. Hexane fraction, essential oil, agetochrome and 1heptadecenewas toxic to P. *xylostella* larvae whileagainst *A. craccivora* methanol fraction was effective. Essential oil showed repellent activity against *P. xylostella* (Adebisi *et al.* 2019).

#### e. Antifungal effect

Seven fungal species viz., Aspergillus flavus, A. fumigatus, A. niger, Candida albicans, Epidermophyton floccosum, Fusarium oxysporous, Trichophyton rubrum were isolated from infected human nails. There was co-dominance of Candida and Trichophyton and these were seen to be present in both sterilized as well as unsterilized infected nails. A. houstonianum essential oil was found as most potent toxicant as it inhibits the mycelialgrowth at 500 ppm against the test fungi. For both Candida albicans and Trichophyton rubrum the minimal inhibitory concentration was 400 ppm, and it was fungicidal at 500 ppm for both the test fungi (Kumar 2014).

#### f. Anticancerous activity

Hadidy *et al.* (2019) performed an experiment using three cancer cell lines HepG-2, HCT-116 and MCF-7 to assess cytotoxicity test on *A. houstonianum* essential oil. For leaves and flower oil sensitivity of human cancer cell was performed with the help of MTT assay test. The principle behind the MTT assay depend on the fact that, a compound of yellow colour is converted into purple derivative i.e. formazan by viable cells. Flowers and leaves derived oil showed *in vitro* cytotoxicity against colon (HCT-116) carcinoma cell line with  $IC_{50}$  (11.1 %, 14.2 %) µg/ml sample, respectively. According to them, it may be due to the presence of  $\beta$ -caryophyllene as it is a major constituent in leaves derived oil and exerted significant cytotoxicity.

#### g. Anti-Dermatophytic activity

The oil was obtained from the leaves of A. houstonianum by hydro distillation method and the test was performed against two clinical dermatophytic isolates Microsporum gypseum and Trichophyton mentagrophytes. The potentization of griseofulvin's activity with essential oil has been assessed. For testing essential oil/griseofulvin were taken in the ratio 8:2 and 10:1 respectively. On guinea pigs (Cavia porcellus), oil dermal toxicity was assessed by using the Agar dilution method used for anti-dermatophytic tests. When compared with the control group, no diarrhoea, change in treated skin, and appearance of fur was observed by the workers. On the contrary, with the increase in the dose concentration, noise sensitivity, pinch reaction, locomotion and reactivity decreased. The LD<sub>50</sub> was 5g kg-1 body weight. These results suggested that A. houstonianum leaves oil when used topically may not be toxic and having antidermatophytic compounds (Njatenget al. 2010).

#### Conclusion

A. houstonianum is very useful in pathogenic infection treatment. The research has shown that A. houstonianum have antioxidant, analgesic, antimicrobial, mosquitocidal, insecticidal, wound healing, and antifungal activity. The chemical constituents such as phenolic acids, flavonoids, phenolic compounds, and some other active compounds are responsible for these activities. A literature review found that A. houstonianumis rightly recognised as a useful natural herbal plant.

#### Acknowledgement

The author is grateful to the CSIR-UGC,

Government of India for providing the financial support for my Ph.D. research work as a Junior Research Fellow.

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