Unveiling The Health Benefits Of Ageratina Adenophora: A Detailed Review

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ABSTRACT:

Ageratina adenophora, also called crofton weed, is a perennial plant that belongs to family Asteraceae, native to Mexico and Costa Rica and an introduced species in many countries like China, India, New Zealand, South Africa etc. This plant, often called noxious weed because of its allelopathic competition over other plant species and its phytotoxicity towards livestock causing chronic pulmonary diseases in horses. Despite being a destructive plant, it signifies high indications of secondary metabolites possessing several pharmacological activities like anti-tumor, anti-pyretic, anti-inflammatory, anti-fungal, anti-viral, anti-oxidant, anti-microbial, wound healing properties and analgesic activity. Recently, this plant is also found to be an aid for COVID-19. This review will highlight all the therapeutic uses and value of Ageratina adenophora.

Keywords: Ageratina adenophora, introduced species, secondary metabolites, pharmacological activity

1. INTRODUCTION:

Ageratina adenophora (crofton weed), belonging to Asteraceae as shown in Table 1, relative of sunflower family, is a flowering plant which is a perennial herbaceous shrub developing to top of one-2m tall. It is usually known as crofton weed but has various vernacular names like catweed, eupatory, Mexican devil, sticky eupatorium, sticky snakeroot, white thoroughwort and hemp agrimony.(1)

Table 1- Taxonomical classification of Ageratina adenophora

<table>
<thead>
<tr>
<th>Kingdom</th>
<th>Plantae</th>
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<tbody>
<tr>
<td>Sub-kingdom</td>
<td>Viridiplantae</td>
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<tr>
<td>Infra-kingdom</td>
<td>Streptophyta</td>
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<td>Superdivision</td>
<td>Embryophyta</td>
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<td>Division</td>
<td>Tracheophyta</td>
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<tr>
<td>Sub-division</td>
<td>Spermatophytyina</td>
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<td>Class</td>
<td>Magnoliopsida</td>
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<tr>
<td>Superorder</td>
<td>Asteranae</td>
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<tr>
<td>Order</td>
<td>Asterales</td>
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<tr>
<td>Family</td>
<td>Asteraceae</td>
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<td>Genus</td>
<td>Ageratina</td>
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<td>Species</td>
<td>Ageratina adenophora</td>
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1.1. Description

*Ageratina adenophora* is an evergreen plant with a height range of 3.3 to 6.6 feet. It has opposing, trowel-shaped, serrated leaves that range in length from 6 to 10 cm (2.4 to 3.9 in) and width from 1.2 to 6 cm (2.4 in). The tiny compound plants appear in bunches at the ends of branches in the late spring and early summer. Every flower head is creamy white and up to 0.5 cm in diameter. Each tiny blossom is accompanied by a small brown seed that resembles a dandelion and has a white feathery “parachute” that can be scattered by the wind (2,3).

1.2. Distribution

Native to Mexico and Costa Rica, *A. adenophora* aggressively invades several countries throughout the world and flourishes in many tropical and subtropical regions like India, China, South Africa, Australia, Nepal, New Zealand, Malaysia, Philippines, Thailand, and Pakistan(2). First brought in China in the 1940s from Myanmar, firstly as an ornamental plant into the Yunnan province. Later, it spreads to the Hainan and Guangxi provinces. As China passed through an economic growth, there may be a growth in worldwide alternate and invasive plant introductions, due to this, this plant invades the South and East Asia(4). *A. adenophora* invades Australia at some stage in 1900s inside the Queensland coastal regions and on the new South Wales Northern Coast and as far south as Wollongong. And this species spreads in many areas of Australia like Sydney, Gosford, and Queensland border. It is also discovered within the California and Hawaii. It thrives over ten countries in California, from Marin to San Bernardino(5). In South Africa, it first invades within the Limpopo province in 1958 and later spreads to Mpumalanga, Western Cape, and Gauteng provinces(6,7). In India, this plant spreads over the Western Ghats and North Himalayan regions.

1.3. Phytochemicals

*A. adenophora* mostly contains mono-, sesqui-, di-, and tri-terpenes. In addition to terpenoids, phenylpropanoids, flavonoids, coumarins, and essential oils, *A. adenophora* has also been shown to contain sterols, phenolic acids, and alkaloids as secondary metabolites. In fig. 3 there are some of the principles phytochemicals that have been found in this plant, along with their classifications. Also, it has been discovered that *A. adenophora* leaves and aerial parts are abundant in several essential oils, some of which are presented in fig.4(9,14-23).

Figure 3: Phytochemicals present in *A. adenophora*
2. TOXICITY TOWARDS CATTLE

The invasive herb *Ageratina adenophora* has significant toxicological effects on cattle. *A. adenophora* consumption on a daily basis results in persistent pulmonary illness in horses, which is marked by lung interstitial fibrosis, emphysema, alveolar epithelization, and decreased exercise tolerance. This horse ailment, which is a common adverse effect of *A. adenophora*, is known as "blowing disorder" in Hawaii, U.S.A., and "Numimbah horse illness" in Queensland and New South Wales, respectively. It takes time to develop and become visible, but it is always fatal. Similar to this, a recent study found that giving mice intragastric injections of *A. adenophora*’s freeze-dried leaf powder or methanol extract caused localised parenchymal necrosis and liver degeneration. Rats fed chow with 25% (w/w) freeze-dried meat. Advanced jaundice caused by *A. adenophora* leaf powder is characterised by an increase in plasma bilirubin, alanine and aspartate transaminases, and alkaline phosphate (ALP). Instead of the lungs, the liver was shown to have a variety of abnormalities using the electron microscope. The focal necrosis of the parenchyma in multiple areas, along with deterioration and damage of the epithelium lining the small bile ducts, were used to characterise the hepatic injury in those animals, and the active principle 9-oxo-10,11-dehydroagerophorone was found to be responsible for those lesions.

Additionally, cattle were the cause of rumination suspension and photosensitization. Additionally, the harmful effects of *A. adenophora* intake on goat liver, spleen, and kidney have been proven; dose-dependent apoptosis and autophagy are evident in goat tissues. Another study examined whether *A. adenophora* causes mice to experience oxidative stress, which is shown by an upregulation of the mRNA levels of antioxidants such glutathione, catalase, and superoxide dismutase (SOD) (GSH). Due to its toxicity, this plant damages local native plants as it spreads there, and it also indirectly harms local wildlife.(25,26)

3. PHARMACOLOGICAL IMPORTANCE

In addition to the toxicity of *A. Adenophora* toward cattle, this plant possess different pharmacological benefits as summarised in fig.5. It is greatly effective in humans. This plant has many therapeutic activities like anti-microbial, anti-fungal, anti-viral, anti-pyretic, anti-inflammatory, anti-tumour, analgesic and can help in wound healing. It also has ability to fight against COVID-19.
3.1. Anti-pyretic

In numerous studies, it has been discovered that aqueous extract of leaves of A. adenophora act as a great anti-pyretic agent. The aqueous extract at doses of 300 and 400 mg/kg bodyweight showed a symbolic decline within the pyretic temperature during the second hour of treatment and its effect are similar to that of trendy drug (Paracetamol). At dose of 500 mg/kg weight, the pyretic temperature got reduced within one hour. So, the aqueous extract is determined to be more powerful than the standard drug without any harmful effect (27).

3.2. Analgesic activity

The results of a study show that the methanolic extract of A. adenophora leaves has analgesic properties. The activity is tested using the tail immersion, tail-flick, and acetic acid-induced writhing test models and contrasted with pentazocine and diclofenac sodium, two common medications. Additionally, the methanol extract-treated mice exhibited considerable analgesic activity in the tail-flick and tail immersion tests and displayed tremendous development within the required induction time to induce the writhing movements. As a result, A. adenophora’s methanolic extract can be utilised as a pain reliever (28).

3.3. Anti-microbial activity

The antibacterial potential of the silver nanoparticles created using the methanolic leaf extract of Ageratina adenophora was examined by Ramya N. et al. When tested at a 10 g concentration based on zone of inhibition, the silver nanoparticles were found to be more effective against Proteus vulgaris, Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, and Salmonella typhi, while only being marginally useful against Klebsiella pneumoniae and Shigella flexneri. Aspergillus niger, Aspergillus flavus, and Candida albicans were all completely destroyed by their antifungal activity when evaluated using the agar plug method, while Rhizopus indicus, Aspergillus fumigatus, and Mucor oryzae were all partially destroyed (29).

Another study claimed that A. adenophora has antibacterial properties since it included several compounds such terpenoids, phenylpropanoids, flavonoids, coumarns, sterols, and alkaloids. Its extract has significant MIC values against gramme positive bacteria compared to gramme negative bacteria and has antibacterial activity against S. aureus, MRSA, and S. typhi. Consequently, it was demonstrated as a viable alternative to combat the bacterial infection (30).

3.4. Anti-inflammatory activity

In accordance with the most recent study conducted by Chakravarty et al., the ethanolic leaf extract of A. adenophora was administered intravenously & in various cases topically on the site of a delayed type allergy (DTH) reaction in a mouse foot paw triggered by dinitrofluorobenzene to examine its anti-inflammatory effect. A lot sooner than the controls, the leaf extract was observed to block the DTH response and restore normalcy to the paw. Intravenous treatment of the leaf extract increased serum levels of tumour necrosis factor (TNF-) and the variety of CD4 T lymphocytes in the spleen of DTH mice. Additionally, the leaf extract increased the expression of the TNF- gene, the TGF- gene that encodes a cytokine involved in the restoration of tissues, and the serum level of the cytokine. Additionally, it inhibits the production of the COX-2 gene, which is responsible for the metabolism of inflammatory mediators such prostaglandins, and another pro-inflammatory cytokine gene, IL-1. However, there has been no change in the expression of many genes related to inflammation, such as IL-6, IL-10, and IKK (31).

3.5. Anti-oxidant activity

The in-vitro antioxidant activity of Ageratina adenophora and Ageratum conyzoides leaves was evaluated in the recent study by Khazeo P. et al. (2018) using DPPH and hydrogen peroxide radical scavenging capacity. The extracts shown a considerable DPPH activity in the scavenging experiments when compared to the conventional butylated hydroxyl toluene (IC50 for A. conyzoides was 70.489, for A. adenophora was 92.791 and for butylated hydroxyl toluene was 68.043). Similar to the standard ascorbic acid, they also demonstrated H2O2 scavenging activity (A. conyzoides = 63.15%, A. adenophora = 79.32%, Ascorbic acid = 86.84%) (32).

3.6. Wound healing activity

In a study led by Kumar N. et al., the gel-formulated alcoholic extract of Ageratina adenophora was tested on excision and incision wound models, and the results were monitored for 13 days. At the same time, in the incision model, the plant extract demonstrated significant rise (37.86%) in tensile strength on the 13th day in comparison with pure gel control. The ethanolic extract consistently meets important (p<0.01) wound recuperation potential in excision as 90.98% wound closure and 36.16% decrease in epithelialization time. Therefore, our research offered the experimental support for the popular wisdom that this species of plants is a potent wound healer (33).

3.7. Anti-tumour activity

In a recent study, it was found that A. adenophora essential oil increased HCC (hepatocellular carcinoma) apoptosis by triggering the apoptotic signalling pathway in the mitochondria and endoplasmic reticulum, as well as by suppressing STAT3 (sign transducer and activator of transcription 3) and AKT (protein kinase B) activity in HCC cells (34).
The raw 9-oxo10,11-dehydroageraphorone (euptox A), a cadenine from A. adenophora, was discovered to have significant anti-tumor potential against the three tumor cell lines in vitro in a dose-based manner, according to another study by Liao F et al. The 4,5-dimethylthiazol-2-(yl)-2,5-diphenyltetrazolium bromide (MTT) assay was used to determine its cytotoxicity against human lung cancer A549 cells, Hela cells, and Hep-2 cells in vitro. Human lung cancer A549 cells, Hela cells, and Hep-2 cells were all inhibited to varying degrees at 500 ng/mL, with the percentage inhibition being 76.42, 68.30, and 79.05%, respectively. However, the 50% inhibitory concentration (IC50) of euptox A for the three tumor cell strains was 369, 401, and 427 ng/mL (A549, Hela and Hep-2 cells, respectively). This finding indicates that euptox A can be produced as a new tumor agent (35).

3.8. Insecticidal activity

In a study conducted by Yunshou et al., the insecticidal activity of A. adenophora crude extract was estimated against the adults of the Chinese bean weevil Callosobruchus chinensis (L.), European bean weevil Bruchus rafanus Boheman, maize weevil Sitophilus oryzae (L.). The results showed that handling the four species with a fumigant concentration of 44.44mg/L resulted in a 100.0% mortality rate. The bioassay also revealed that the LC50 (median lethal dose) after giving the 4 species for 24 hours was 14.65, 12.80, 25.07, and 12.20mg/L, respectively, while the LC50 (median lethal dose) after treating them for 48 hours was 11.79, 9.67, 13.29, and 9.76mg/L, respectively (36).

3.9. Antiviral activity

The local lesion assay approach was used to test the extract from A. adenophora for antiviral activity against the tobacco mosaic virus (TMV), and it was also described. The TMV infection was significantly inhibited by the A. adenophora leaf extract, and electron microscopy examinations revealed that the virus debris had been broken up. This finding—the first discoveries of antiviral activity from A. adenophora leaf extracts—indicates that this species offers a wonderful array of antiviral compounds for use in medicine (37).

3.10. Activity against COVID-19

Netra Prasad Neupane et al. recently conducted a study in which the phytochemicals of A. adenophora were in-silico tested against Mpro and ACE2 receptor. The docking computation also revealed that the phytochemical 5GDE has significant equivalent interactions with the chosen protein as do reference chemicals. However, the binding capacity was only slightly greater than that of the common medications remdesivir and hydroxyl-chloroquine. The MD study of the Mpro complex shape revealed that it maintained a similar degree of compactness to that of its apo structure throughout the simulation, but with increased structural stability and residue fluctuation in contrast to the apo shape. In contrast, the phytochemical BODO demonstrated high binding affinity (rating), nearly constant interaction with the ACE2 receptor, maintenance of comparable compactness, and movement of residues similar to that of its apo structure, but with increased structural stability throughout the simulation. This finding demonstrated that A. adenophora herbal substances have a binding affinity that is comparable to or greater than that of the generic inhibitors remdesivir and hydroxychloroquine. As a result, 5GDE and BODO could develop as therapeutic candidates against the coronavirus responsible for the ongoing epidemic and its Mpro and ACE2 receptor (38).

4. CONCLUSION

In conclusion, this plant is one of the most dangerous invasive plants having severe negative effects on farm animals (particularly horses and mice). Instead of those undesirable characteristics, this plant has been at the forefront of the research field because it has been shown to contain a variety of novel components, including euptaporne, 2-deoxy-2-(acetyloyl)-9-oxoageraphorone (DAOA), 7,10,11-trihydroxy dehydrotremetone, and 10-oxo-7-hydroxy-nordehydrotremetone. With potential medical applications including analgesic, larvicidal, anti-pyretic, anti-viral, anti-tumor, etc. Similar to how it is used as a folk medicine to treat fever, sleeplessness, and dysentery, more research is required to confirm its safety and efficacy because the most recent findings are based solely on a small sample size.

REFERENCES:


