WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Unveiling The Health Benefits Of Ageratina Adenophora: A Detailed Review

Nidhi Bisht [a], Diksha Sharma [b]

[a]University Institute of Pharma Sciences, Chandigarh University, Mohali 140413, Punjab India
[b] University Institute of Pharma Sciences, Chandigarh University, Mohali 140413, Punjab India
[a-] nidhibisht2228@gmail.com
[b-] dikshasharma121121@gmail.com

ABSTRACT :

Ageratina adenophora, also called crofton weed, is a perennial plant that belongs to family Asteraceae, native to Mexico and Cost 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 alleopathic 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 rewiew 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 sunflowerfamily, is a flowering plant which is a perrenial herabaceous 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*

Kingdom	Plantae
Sub-kingdom	Viridiplantae
Infra-kingdom	Streptophyta
Superdivision	Embryophyta
Division	Tracheophyta
Sub-division	Spermatophytina
Class	Magnoliopsida
Superorder	Asteranae
Order	Asterales
Family	Asteraceae
Genus	Ageratina
Species	*Ageratina adenophora*

Figure1: A. Adenophora

Figure 2: Flowering in A. adenophora

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 Cost Rica, *A. adenophora* aggressively invades several countries throughout the world and flourishes in many tropical and sub tropical regions like India ,China, South Africa, Australia, Nepal, New Zealand, Malaysia, Phillipines, 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 invade within the Limpopo province in 1958 and later spreads to Mpumalanga, Western Cape,and Guateng provinces(6,7). In India, this plant spreads over the Western Ghats and North – Himalayan regions.

1.3. Phtyochemicals

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).

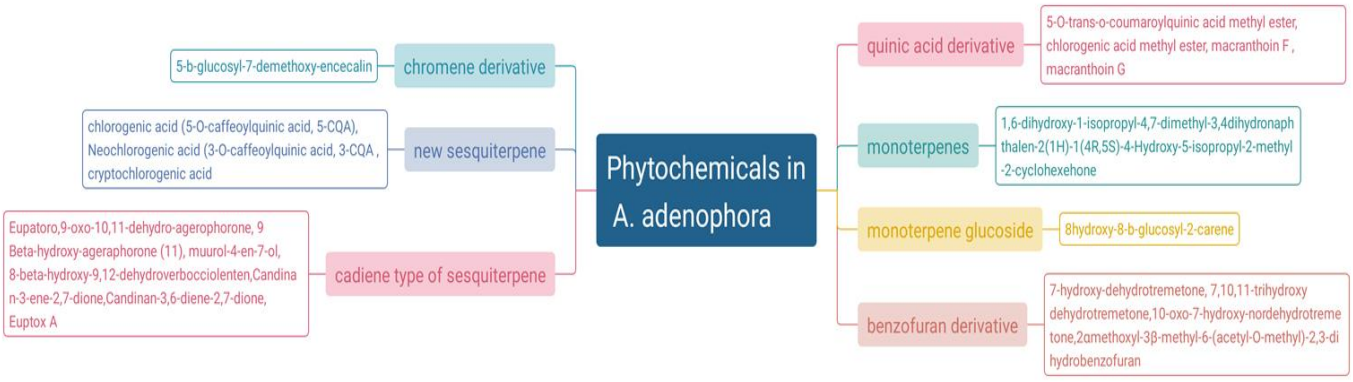

Figure 3: Phytochemicals present in *A. adenophora*

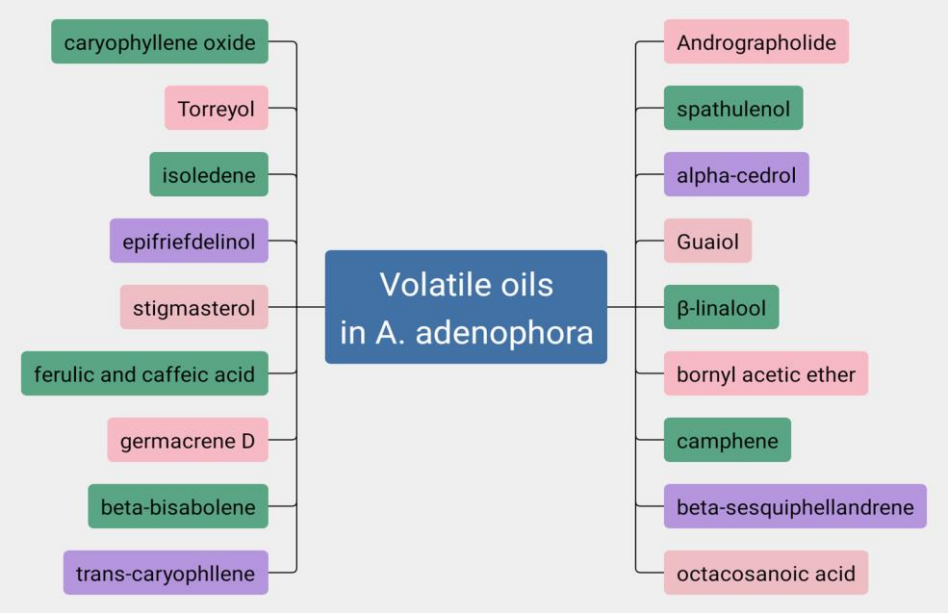

Figure 4: Volatile oils present in *A. Adenophora*

2. TOXICITY TOWARDS CATTLES

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. PHARMCOLOGICAL IMPORTANCE

In addition to the toxicity of A. Adenophora toward cattles , this plant possess different pharmacological benefits as summarised in fig.5. It is greately 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.

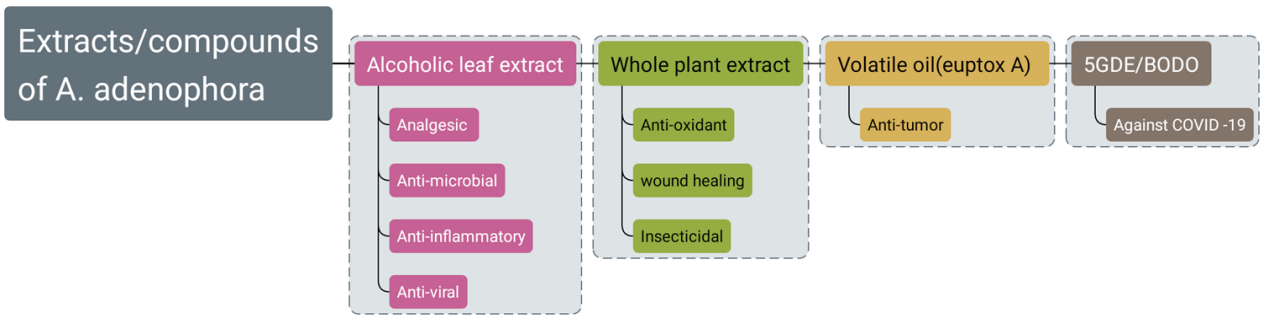

Figure 5: Pharmacological importance of *A. adenophora*

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, coumarins, 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 (pt0.01) 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 tumour 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 tumour 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 new anti 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 rufimanus Boheman, maize weevil S. zeamais Motschulsky,* and rice weevil *Sitophilus oryzae (L.)*. The results showed that handling the four species with a fumigant concentration of 44.44mg/L resulted in a 100.00% 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. Anti-viral 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 remedisivir 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 remedesivir 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 eupatorone, 2-deoxy-2-(acetyloxy)-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 :

1. Parsons, W.T., & Cuthbertson, E.G. (1992). Noxious weeds of Australia. Inkata Press, Melbourne, Vol II.
2. Heystek, F., Wood, A.R., Neser, S., & Kistensamy, Y. (2011). Biological control of two Ageratina species (Asteraceae: Eupatorieae) in South Africa. African Entomology, 19(2), 208-217.
3. Muniappan, R., Reddy, G.V., & Raman, A. (2009). Biological control of tropical weeds using arthropods. Cambridge University Press, Cambridge, Edition 1, 1-16.
4. Wan, F., Liu, W., Guo, J., Qiang, S., Li, B., Wang, J., & Jiang, Z. (2010). Invasive mechanism and control strategy of Ageratina adenophora (Sprengel). Science China Life Sciences, 53(11), 1291-128.
5. Henderson, L. (2001). Alien weeds and invasive plants. Plant Protection Research Institute, Agricultural Research Council, Cape Town, First Edition.
6. Kluge, R.L. (1991). Biological control of crofton weed, Ageratina adenophora (Asteraceae), in South Africa. Agriculture, Ecosystems & Environment, 37(1-3), 187-191.
7. Henderson, L. (2006). Comparisons of invasive plants in southern Africa originating from southern temperate, northern temperate and tropical regions. Bothalia, 36(2), 201-222.

8. Zhang, X.W., Liu, W.X., & Wan, F.H. (2007). Allelopathy of aqueous leachates of Ageratina adenophora and the identification of the allelo-chemicals. Journal of Agricultural University Hebei, 30, 68-71, 76.
9. Niu, H.B., Liu, W.X., Wan, F.H., & Liu, B. (2007). An invasive aster (Ageratina adenophora) invades and dominates forest understories in China: altered soil microbial communities facilitate the invader and inhibit natives. Plant and Soil, 294(1-2), 73-85.
10. Niu, H.B., Liu, W.X., & Wan, F.H. (2007). Invasive effects of Ageratina adenophora Sprengel (Asteraceae) on soil microbial community and physical and chemical properties. Acta Ecologica Sinica, 27(7), 3051-3060.
11. Li, H., Liu, W., Wan, F., & Cao, Y. (2009). Invasive impacts of Ageratina adenophora (Asteraceae) on the changes of microbial community structure, enzyme activity and fertility in soil ecosystem. Scientia Agricultura Sinica, 42(11), 3964-3971.
12. Fuller, T.C. (1981). Introduction and spread of Eupatorium adenophorum in California. In Proceedings of the Eighth Asian-Pacific Weed Science Society Conference, held in Bangalore, 277-280.
13. Subba, B., & Kandel, R.C. (2012). Chemical composition and bioactivity of essential oil of Ageratina adenophora from Bhaktapur district of Nepal. Journal of Nepal Chemical Society, 30, 78-86.
14. Li, Y., Li, Z., & Ye, M. (2008). The chemical compositions and their bioactivities in the different parts of Eupatorium adenophorum Spreng. Journal of Yunnan Agricultural University, 23(1), 42-72.
15. Shi, W., Luo, S., & Li, S. (2012). Defensive sesquiterpenoids from leaves of Eupatorium adenophorum. Chinese Journal of Chemistry, 30(6), 1331-1334.
16. Qiansheng, Y., Jie, Y., Huamin, L., Aocheng, C., Qinghua, C., Yongqi, W., & Lan, H. (2006). Advances in the studies on the chemical components and bioactivity of Eupatorium adenophorum Spreng as an intruding species. Journal of Beijing Normal University Natural Science Edition, 42(1), 70.
17. Luo, B., Dong, L.M., Xu, Q.L., Zhang, X., Zhang, Q., Liu, W.B., & Tan, J.W. (2018). A new monoterpene and a new sesquiterpene from the roots of Ageratina adenoph
18. Zhao, X., Zheng, G.W., Niu, X.M., Li, W.Q., Wang, F.S., & Li, S.H. (2008). Terpenes from Eupa-torium adenophorum and their allelopathic effects on Arabidopsis seeds germination. *Journal of Agricultural and Food Chemistry*, 57(2), 478-82.
19. Pala-Paul, J., Perez-Alonso, M.J., Velasco-Negueruela, A., & Sanz, J. (2002). Analysis by gas chromatography–mass spectrometry of the volatile components of Ageratina adenophora Spreng, growing in the Canary Islands. *Journal of Chromatography A*, 947(2), 327-331.
20. Sasikumar, J.M., Doss, A.P.A., & Doss, A. (2005). Antibacterial activity of Eupatorium glandu-losum leaves. *Fitoterapia*, 76(2), 240-43.
21. Kurade, N.P., Jaitak, V., Kaul, K., & Sharma, O.P. (2010). Chemical composition and antibacterial activity of essential oils of Lantana camara, Ageratum houstonianum and Eupatorium adenophorum. *Pharmaceutical Biology*, 48(5), 539-44.
22. Pandey, A.K., Mohan, M., Singh, P., Palni, U.T., & Tripathi, N.N. (2014). Chemical composition, antibacterial and antioxidant activity of essential oil of Eupatorium adenophorum Spreng. from Eastern Uttar Pradesh, India. *Food Bioscience*, 7, 80-87.
23. Samuel, L., Muthukumaran, R.B., Gurusubramanian, G., & Senthilkumar, N. (2014). Larvicidal activity of Ipomoea cairica (L.) Sweet and Ageratina adenophora (Spreng.) King & H. Rob. plant extracts against arboviral and filarial vector, Culex quinquefasciatus Say (Diptera: Culicidae). *Experimental Parasitology*, 141, 112-21.
24. Hill, R.L. (1989). Ageratina adenophora (Sprengel) R. King & H. Robinson, Mexican devil weed (Asteraceae). *Technical Communication (Commonwealth Institute of Biological Control)*, 317-20.
25. Oelrichs, P.B., Calanasan, C.A., Macleod, J.K., Seawright, A.A., & Ng, J.C. (1995). Isolation of a compound from Eupatorium adenophorum (Spreng.) [Ageratina adenophora (Spreng.)] causing hepatotoxicity in mice. *Natural Toxins*, 3(5), 350-54.
26. Sun, W., Zeng, C., Yue, D., Liu, S., Ren, Z., Zuo, Z., & Hu, Y. (2019). Ageratina adenophora causes spleen toxicity by inducing oxidative stress and pyroptosis in mice. *Royal Society Open Science*, 6(7), 190127.
27. Ringmichon, C.L., & Gopalkrishnan, B. (2017). Antipyretic activity of Eupatorium adenophorum leaves. *International Journal of Applied Biology and Pharmaceutical Technology*, 8.
28. Mandal, S.K., Boominathan, R., Parimaladevi, B., Dewanjee, S., & Mandal, S.C. (2005). Analgesic activity of methanol extract of Eupatorium adenophorum Spreng. leaves. *Indian Journal of Experimental Biology*, 43, 662-63.
29. Ramya, N., Mayuri, P.K., Santny, A.S., & Angayarkanni, T. (2015). Antimicrobial efficacy of silver nanoparticles conjugated with Ageratina adenophora leaf extract. *Asia Pacific Journal of Research*, 1, 170-76.
30. Ahluwalia, V., Sisodia, R., Walia, S., et al. (2014). Chemical analysis of essential oils of Eupatorium adenophorum and their antimicrobial, antioxidant, and phytotoxic properties. *Journal of Pest Science*, 87, 341-349.
31. Chakravarty, A.K., Mazumder, T., & Chatterjee, S.N. (2011). Anti-inflammatory potential of ethanolic leaf extract of Eupatorium adenopho-rum Spreng. through alteration in production of TNF-α, ROS, and expression of certain genes. *Evidence-Based Complementary and Alterna-tive Medicine*.
32. Khazeo, P., Mazumder, M.U., Puro, K.N., Jyrwa, R., Jamir, N., & Sailo, L. (2018). In-vitro antioxidant activity of methanolic extracts of Ageratum conyzoides and Ageratina adenophora leaves. *Mizoram Science Congress 2018 (MSC 2018). Atlantis Press*, 178, 169-72.
33. Kumar, N., Singh, A., Sharma, D.K., & Kishore, K. (2017). Evaluation of wound healing activity of Ageratina adenophora (Spreng.) R. M. King & H. Rob. *International Journal of Pharma Research and Health Sciences*, 5(5), 1873-76.
34. Chen, H., Zhou, B., Yang, J., Ma, X., Deng, S., Huang, Y., & Yang, X. (2018). Essential oil derived from Eupatorium adenophorum Spreng. mediates anticancer effect by inhibiting stat3 and akt activation to induce apoptosis in hepatocellular carcinoma. *Frontiers in Pharmacology*, 9, 483.
35. Liao, F., Hu, Y., Wu, L., Tan, H., Mo, Q., Luo, B., He, Y., Deng, J., & Wei, Y. (2014). Antitumor activity in-vitro by 9-Oxo-10,11-dehy-droageraphorone extracted from Eupatorium adenophorum. *Asian Journal of Chemistry*, 26, 7321-23.

36. Li, Y., Zou, H., Wang, L., Nai, Z., Li, W., Na, X., & Yang, Y. (2001). Insecticidal activity of extracts from Eupatorium adenophorum against four stored grain insects. *Kunchongzhishi*, 38(3), 214-16.
37. Jin, Y., Hou, L., Zhang, M., Tian, Z., Cao, A., & Xie, X. (2014). Antiviral activity of Eupatorium adenophorum leaf extract against tobacco mosaic virus. *Crop Protection*, 60, 28-33.
38. Neupane, N.P., Karo, A.K., Mukeri, I.H., Pathak, P., Kumar, P., Singh, S., Qureshi, I.A., Jha, T., & Verma, A. (n.d.). Molecular dynamics analysis of phytochemicals from Ageratina adenophora against COVID-19 main protease (MPRO) and human angiotensin-converting enzyme 2 (ACE2).
39. Tripathi, Y.C., & Singh, S. (2003). Phytomedicinal Research: Towards New Perspectives Based on Indigenous Knowledge System. In: Potentials of Living Resources (Tripathi, G., & Kumar, A. eds.). India: Discovery Publishing House (DPH), New Delhi, 276-315.
40. Zheng, & Guowei. (2018). Specialized Metabolites from Ageratina adenophora and their inhibitory activities against pathogenic fungi. *Phytochemistry*, 148, 57-62.
41. Weyerstahl, P., Marschall, H., Seelmann, I., & Kaul, V.K. (1997). Constituents of the flower essential oil of Ageratina adenophora (Spreng.) K. et R. from India. *Flavour and Fragrance Journal*, 12(6), 387-96.
42. Libbey, L.M. (1991). A paradox database for GC/MS data on components of essential oils and other volatiles. *Journal of Essential Oil Research*, 3(3), 193-94.
43. Padalia, R.C., Bisht, D.S., Joshi, S.C., & Mathela, C.S. (2009). Chemical composition of the essential oil from Eupatorium adenophorum Spreng. *Journal of Essential Oil Research*, 21(6), 522.
44. Wang, Y., Zhao, B., Fan, Z., Fan, Y., & Tan, C. (2005). The advance in Eupatorium adenophorum Spreng and its damage. *Dongwuyixuejinzhan*, 26(5), 45-48.
45. Katoch, R., Sharma, P., Dawra, R.K., & Kurade, N.P. (2000). Hepatotoxicity of Eupatorium adenophorum to rats. *Toxicon*, 38(2), 309-14.
46. O'Sullivan, B.M. (1985). Investigations into Crofton weed (Eupatorium adenophorum) toxicity in horses. *Australian Veterinary Journal*, 62(1), 30-32
47. Bais, H.P., Vepachedu, R., Gilroy, S., Callaway, R.M., & Vivanco, J.M. (2003). Allelopathy and exotic plant invasion: from molecules and genes to species interactions. *Science*, 301(5638), 1377-80.
48. Sheng, Q. (1998). The history and status of the study on Crofton weed (Eupatorium adenophorum Spreng.) a worst worldwide weed. *Journal of Wuhan Botanical Research*, 4.
49. Buckley, Y.M., Downey, P., Fowler, S.V., Hill, R., Memmot, J., Norambuena, H., & Wittenberg, R. (2003). Are invasives bigger? A global study of seed size variation in two invasive shrubs. *Ecology*, 84(6), 1434-40.
50. Dodd, A.P. (1961). Biological control of Eupatorium adenophorum in Queensland. *Australian Journal of Science*, 23(11), 356-65.