Asian Journal of Research in Botany

Volume 9, Issue 1, Page 46-63, 2023; Article no.AJRIB.98474

Review of the Phytochemistry, Ethno-medicinal, and Pharmacological Properties of *Ageratum conyzoides* L. (Billygoat Weed)

Oluwasayo Esther Ogunjinmi [a*], Olumayowa Vincent Oriyomi [b], Peter Ifeoluwa Adegbola [b,c] and Adewale Adetutu [c]

[a] Department of Industrial Chemistry, Faculty of Natural and Applied Sciences, First Technical University, Ibadan, Nigeria.
[b] Department of Biochemistry and Forensic Science, Faculty of Natural and Applied Sciences, First Technical University, Ibadan, Nigeria.
[c] Department of Biochemistry, Faculty of Basic Medical Sciences, Ladoke Akintola University of Technology, Ogbomoso, Nigeria.

Authors' contributions

This work was carried out in collaboration among all authors. Author OEO conceptualized the study, developed the outline, sourced the materials and wrote the original draft, authors OVO and PIA sourced the materials and edited the original draft. Author AA developed the outline and proof read the manuscript. All authors read and approved the final manuscript.

Article Information

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/98474

Review Article

Received: 30/01/2023
Accepted: 01/04/2023
Published: 08/04/2023

ABSTRACT

Medicinal plants are natural resources, yielding valuable herbal products, which could be used in the treatment of various ailments. Natural products, such as plant extract, either as pure compounds or as standardized extracts provide unlimited opportunities for new drug discoveries

**Corresponding author: E-mail: oluwasayoesther@yahoo.com, oluwasayo.ogunjinmi@tech-u.edu.ng;*

because of their unmatched availability of chemical diversity. *Ageratum conyzoides* has been known since antiquity for its medicinal properties and effectiveness in the treatment of various ailments ranging from skin disease, fever, to relief colic, flatulence, dysentery, and diarrhea. A wide range of chemical compounds, belonging to the phytochemical classes namely; alkaloids, cumarins, flavonoids, chromenes, benzofuran, sterols, and terpenoids have been identified in this specie. *Ageratum conyzoides* extracts and their metabolites have been found to possess significant pharmacological properties. In this review, the phytochemistry and medicinal benefits of this plant was reported.

Keywords: Ageratum conyzoides; phytochemicals, medicinal plant; pharmacological uses; traditional uses.

1. INTRODUCTION

Medicinal plants have a long-dated history of their many beneficial purposes including their contribution to the growth of many economies [1, 2]. "Since ancient times, medicinal plants have been used for treating various human disorders such that many pharmaceutical and research institutes are adopting and investing in plants and other natural products as a reliable source for drug development and discovery" [3-5]. Despite the availability of synthetic drugs, plants are yet recognized as a significant contributor to the healthcare program and system of many countries [6].

Based on empirical evidences, many of the available scientific studies have documented one or more biological activities attributable to herbal plants [7]. Further to this, the mechanisms of action as well as the active principles contributing to the pharmacological activities have been elucidated [8]. Therefore, medicinal plants are the repository of biological agents capable of curing and treating numerous human diseases. Aside from the efficacy of medicinal plants, the advantage owns to them include their cheap and ready availability, and their presumed safety [9]

"Ageratum conyzoides L. is a popular invasive weed known as billy goat weed. Being a member of the Asteraceae family, the plant is herbaceous and is found throughout the tropic and subtropic regions around the world" [10]. "*Ageratum conyzoides* is capable of producing extensive number of seeds and is highly prolific, it could spread to distant places thus enhancing its encroachment to wider areas" [11]. Goat weed as popularly called, has much application in traditional medicine and have been proven effective in many scientific studies as antimicrobial, anti-parasitic, antimalarial, and in gastroprotection [12-15]. The current review intends to profile the medicinal application of *A. conyzoides* with emphasis on recent pharmacological findings.

2. BOTANICAL DESCRIPTION AND DISTRIBUTION

Ageratum conyzoides sometimes called *Eupatorium conyzoides* is a plant of the tropical and sub-tropical, locally known as Billygoat weed. The plant belongs to the Asteraceae family one of the largest plant families with over 1000 genera and 25,000 species [16]. The name Ageratum was coined from Ancient Greek "a geras" which means stay young and conyzoides derived from "konyz" means plants [17].

As an annual branching herb, *Ageratum conyzoides* grows to approximately 1 m in height with wide adaptability. The stems and leaves are covered with fine white hairs, the leaves are ovate and up to 7.5 cm long while the stem is erect and branching with soft hairs (pubescent) (Fig. 1) and grow to a height of approximately 3 feet [18, 19].

In addition, the roots are shallow and fibrous, usually about 4 inches deep. The leaves of goat weed are lanceolate to broadly ovate, usually opposite, 0.25 to 4 inches long, 0.2 to 2 inches wide, on 0.2 to 3-inch-long hairy petioles (Fig. 1c). Margins of the leaf are serrated with coarse teeth, rough surfaces, and lightly hairy with prominent veins ((Fig. 1d) which when crushed, produces a strong, rancid odor [18]. The flowers are purple to white, less than 6 mm across, and arranged in close terminal inflorescences. It flowers all year round when the condition is favorable. The fruits are achene, brown, and easily dispersed [18, 19]. The plant grows commonly in the proximity of habitation, thrives in any garden soil, and is very common in waste places and on ruined sites [20]. Goat weed can complete its life cycle in approximately two

months, grows particularly well, and forms dense populations where soil fertility is high. It could also survive and reproduce in low-fertility soils. Although, the plant prefers moist soil it also grows in dry areas. The plant is native to the warmer parts of the southeastern United States, Mexico, the Caribbean, and tropical South America [18, 21].

2.1 Proximate and Phytochemical Composition

Although there is a dirt of literature on extensive studies of the phytochemicals and biological properties of *Ageratum conyzoides*, the review has shown that most of the report on the phytochemistry has to do with the essential oil. The oil content, which although varied randomly ranged from 0.11 to 0.58 % in the leaves and 0.03 to 0.18% in the roots ([10]. Some compounds identified as a major component of *Ageratum conyzoides*' essential oil include Bicyclo [3.1.0] hexane, 6-methylene, 1,5-Heptadiyne, N-Methyl-7-azabicyclo (2,2,1) hept-2, 4-Oxo-4,5,6,7-tetrahydrobenzofurazan, and Tricyclo [3.2.2.0] nonane-2-carboxylic acid [22]. The proximate analysis of *Ageratum conyzoides* whole plant showed that it contains 17.7% total ash, and 7.3 % crude fiber [23]. In the plant stem powder, moisture content was 4.21±0.26 %, and 4.21±0.26 % in the flower. The total ash content in both organs was 1.78±0.61 and 1.61±0.53 respectively [24]. Carbohydrate was also detected in the ethanol whole plant extracts [25]. The chemical constituents identified in different morphological organs of *Ageratum conyzoides* are in the class of alkaloids, flavonoids, terpenoids, tannins, and saponins. Qualitative phytochemical analysis of the ethanol leaf, flower, and stem extracts showed the presence of tannins, alkaloids, flavonoids, phenols, steroids, saponins, and anthraquinones. In the ethanol root extract, alkaloids, flavonoids, and anthraquinones were not detected. In the aqueous extracts, the majority of the phytochemicals were not detected. Only the phenol and anthraquinones were detected in the flower extract. In the stem extracts, alkaloids, saponins, and anthraquinones were the identified phytochemicals while flavonoids and steroids were the identified phytochemicals in the root extract [26]. Similar qualitative phytochemical studies of the plant showed that alkaloids, phenols, saponins, tannins, steroids, and triterpenes were present in the ethanol extract [25]. Qualitative screening comparing the phytochemical components of the methanol extracts and ethyl acetate fraction of the aerial part of *Ageratum conyzoides* showed that alkaloids, terpenoids, anthraquinones, tannins, and saponins which were detected in the methanol extract were absent in the ethyl acetate fraction [27]. Interestingly, in the study conducted by Patil *et al.* [28], tannins were identified in the methanol, hexane, and aqueous extracts of the plant, whereas flavonoid was only identified in the hexane extracts and steroid in the aqueous extracts. Phytochemicals such as flavonoids, steroids, triterpenoids, anthraquinones, and alkaloids previously identified in the methanol extract were absent. GC-MS profiling of the aqueous and methanol leaf extract of the plant showed the presence of biological essential compounds. In the aqueous extract, the compounds included; 1,2,4-Trizol 4-amine N-(2-thienylmethyl)-ester (2.54%), 2-Pentadecenone 6,10,14-trimethyl ester (3.05%), n-Hexadecanoic acid (17.77%), 9,12,15-Octadecatrienoic acid (Z,Z,Z)- (9.12%), 9,12-Octadecadienoic acid (Z,Z)- (48.01%), Phytol (12.63%) and Methyl stearate (6.90%). The methanol extract on the other hand contains more of the volatile compounds such as 1,7-dibromoheptane (3.73%), 2,6,6-trimethyl bicyclo-3,1,1-heptane (6.87%), 3,7,11,15-tetramethyl-2-hexadecen-1-ol (2.65), Hexadecanoic acid methyl ester (14.00%), n-Hexadecanoic acid (12.73%), Thiophene-2-acetic acid dodec-9-ynyl ester (3.39%), cyclohexylmethyl pentadecyl ester (2.60%), 2-Methoxybenzoic acid (4.57%), 2- Furanmethanol (5.96%), 9,12-Octadecadienoic acid (4.50%), 9-Octadecenoic acid (9.72%), 5-Eicosene (4.41%), Dioctyl disulphide (2.22%), Octadecanoic acid, methyl ester (7.40%), 9,17-Octadecadienal (0.91%), Docosane (3.31%), Cyclohexane, 1-(1,5-dimethylhexyl)-4-(4-methylpentyl)-ester (6.73%) and Octacosane (4.30%) [29].

Pyrrolone (5-ethoxy-1H-pyrrol-2(5H)-one) a yellowish oily compound was isolated from the CH_2Cl_2 extract of the aerial part of the plant [30] (Fig. 2). Recently, Ahuchaogu and Echeme, [31], isolated and characterized a pentacyclic triterpenoid from the stem bark. The isolation was preceded by initial partitioning of the crude extracts into solvents of varied polarity and from the chloroform fraction, column fractionation yielded Lupeol; the pentacyclic triterpenoid which was structurally characterized by NMR spectroscopy.

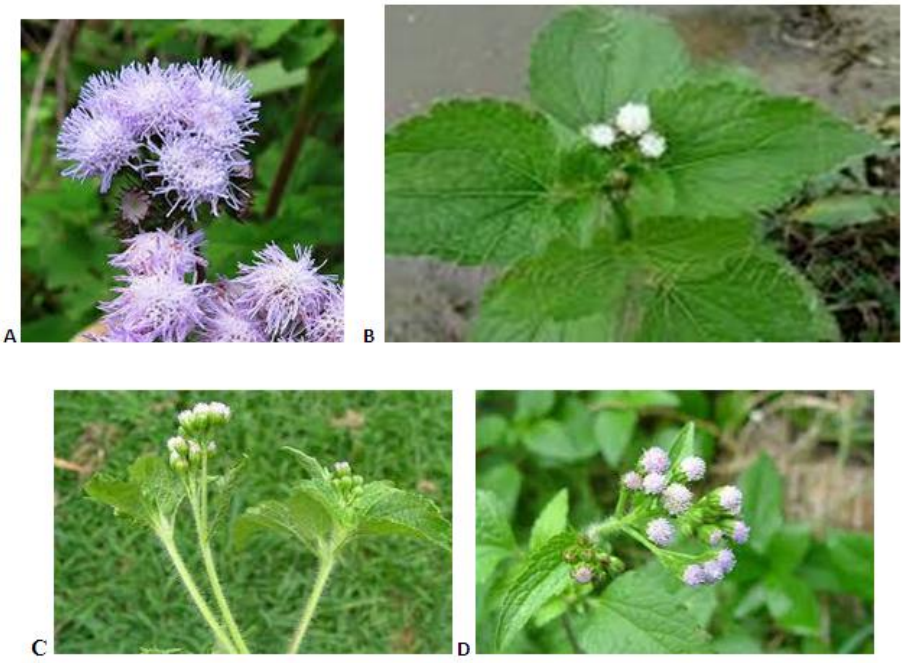
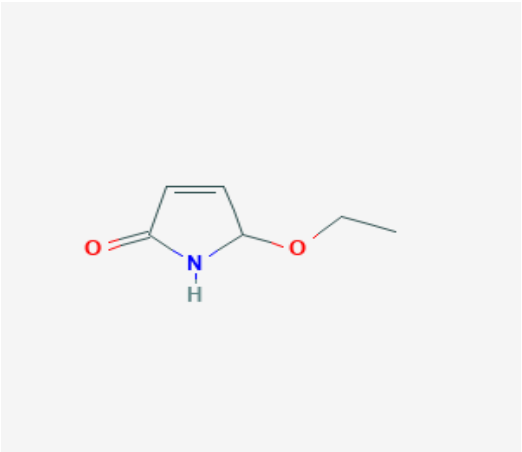
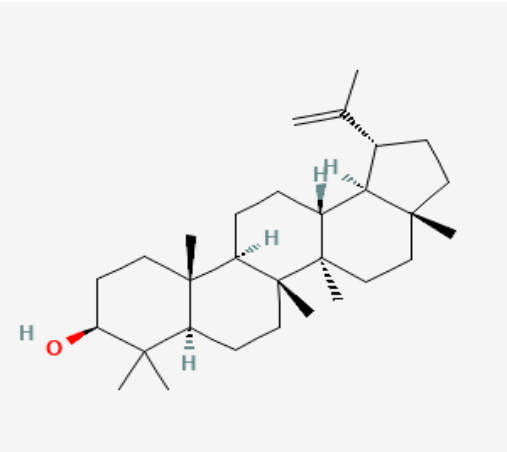


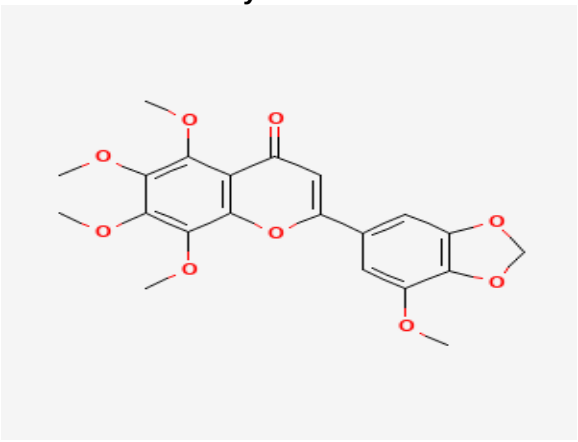
Fig. 1. *Ageratum conyzoides:* Flower (A), Leave (B), Stem (C)



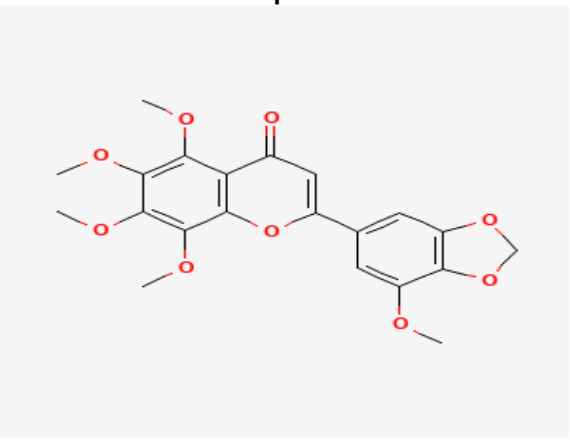
Pyrrolone



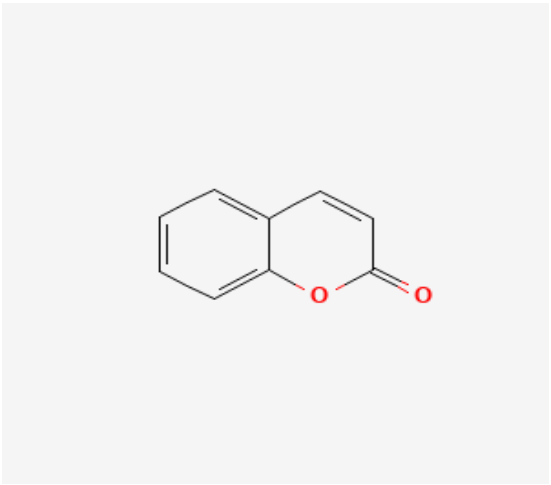
Lupeol



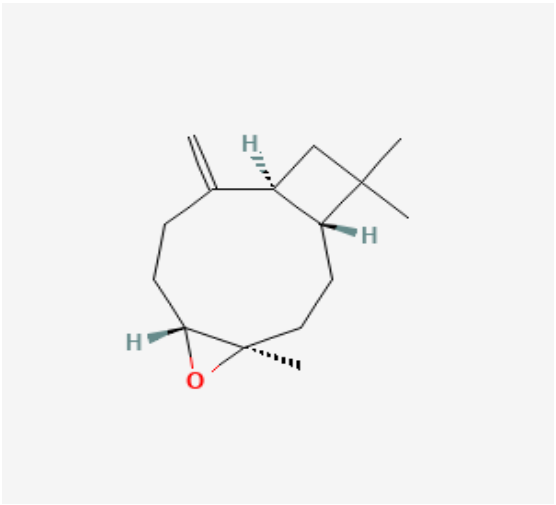
Eupalestin



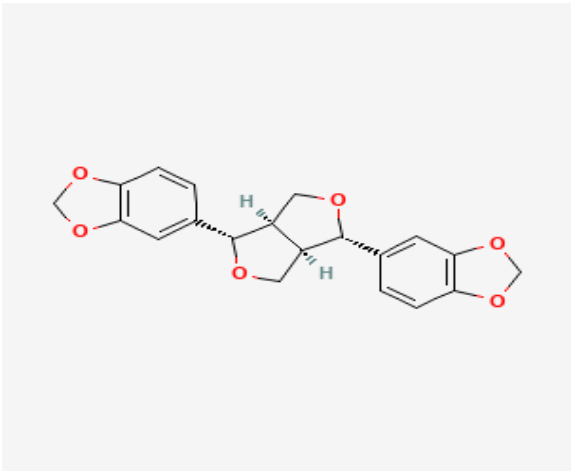
Inderoflavone B



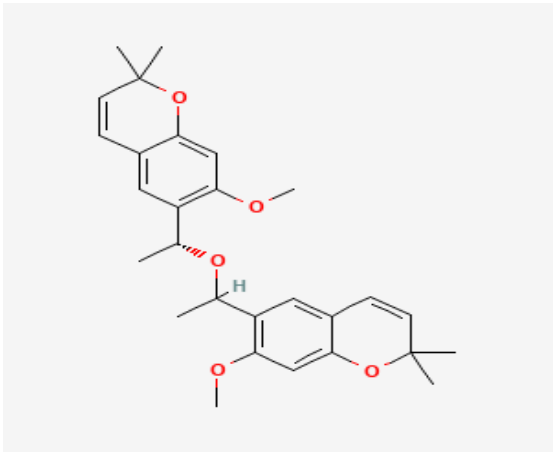
Coumarin



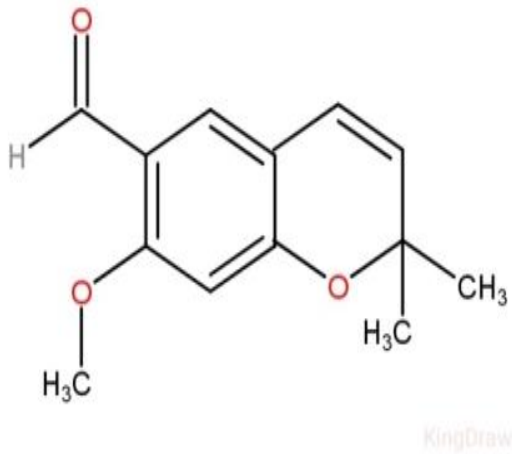
Caryophyllene Oxide



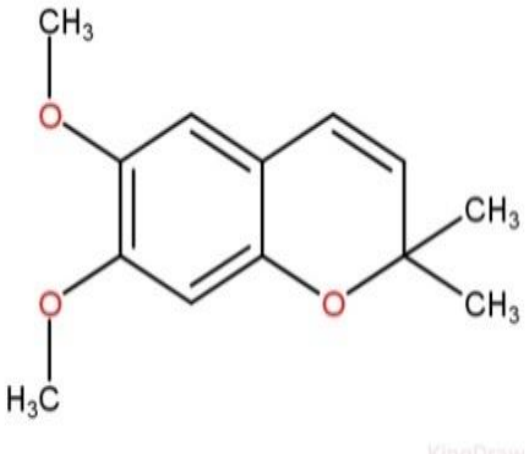
(+) Sesamin



Ecnecanescins



Precocene I



Precocene II

Fig. 2. Chemical Compounds characterized from *Ageratum conyzoides*

Eupalestin, encecalol, demethoxyencecalol, 2-hydroxydihydrocinnamic acid, 2,2-dimethylchromane, linderoflavone B, coumarin, ageconyflavone C, precocene II are some of the known phenolics specifically methoxylated flavonoids and chromenes already identified in the plant [32]. Gonzalez *et al.* [33] characterized 11 chromenes after fractionation of the n-hexane extract of the plant's aerial part. Lignin; (+) sesamin, and sesquiterpene; caryophyllene oxide (figure 2) were among the characterized compounds. Others included; precocene (I), precocene II, 6-(I-methoxyethyl)-7-methoxy-2,2-dimethylchromene, 6-(I-hydroxyethyl)-7-methoxy-2,2-dimethylchromene, 6-(1-ethoxyethyl)-7-melhoxy-2,2-dimethylchromene, encecaline, 6-vinyl-7-methoxy-2,2-dimethylchromeneromene, and encecanescins (Fig. 2).

2.2 Traditional and Ethno-botanical Uses

Traditional usage of *Ageratum conyzoides* cut across the region such as Asia, Africa, and South America where is it commonly used in wound dressing, ulcer treatment, and treatment of skin disease [34, 35]. The decoction or infusion is applied for the relieve of colic, flatulence, dysentery, and diarrhea [36]. Other traditional uses include mouthwash to relieve toothache, antitussive, management of sleeping sickness, an antidote for snake poison, treatment of fever, and vermifuge [37-39].

There is no doubt about the utility of *Ageratum conyzoides,* the traditional application, however varied widely across regions and cultures. In Africa, it is commonly used to relieve constipation, fever, as an antiulcer agent, and as a wound dressing agent. In Togo, the herb is used to treat measles and snake bites, whereas, in Nigeria, the plant is used for the treatment of skin diseases, diarrhea, wound healing, and to relieve pain around the navel in children [40]. The leaves are sometimes consumed as vegetables to prevent tetanus [41]. It is used as a medication against pneumonia, antitoxin of snake venom, sore throat, typhoid fever, candidiasis, and malaria fever. The flower and roots are also useful for treating tumors, lithiasis, and diarrhea in babies, to relieve itching, insomnia, cough, and antibug parasite [42]. Invariably all the morphological organs are of traditional value. Traditional communities in India use goat weed as a bactericide, anti-dysenteric, and antilithic. The aqueous extract is also utilized as a bactericide in Asia, South America, and Africa, whereas in Central Africa it is used to treat pneumonia [43]. *Ageratum conyzoides* is used medicinally in China to treat a variety of conditions, including colds, headaches, boils, eczema, bleeding wounds, and burns [44].

2.3 Pharmacological Uses

The antioxidant, anti-inflammatory, anti-malaria, antimicrobial, anti-parasitic, and anti-diabteic potentials of *Ageratum conyzoides* were the pharmacological properties reviewed in this article. A summary of different studies is given in Table 1.

Table 1. Summary of the pharmacological activity of *Ageratum conyzoides*

Pharmacological uses	Plant part used	Extract	References
Antioxidant	Leaf, root, flower, stem	Ethanol, ethyl acetate, hexane, methanol, chloroform	[14, 56]
Antimicrobial	Leaf, whole plant, flower	Methanol, ethanol, hexane	[12, 25, 74, 76]
Anti-inflammatory	Aerial part, leaf	Methanol, ethanol	[63, 79, 80]
Anti-diabetic, Anti-hyperglycaemia	The whole plant, leaf	Aqueous, ethanol	[99, 101, 105]
Gastroprotective activity	Leaf	Methanol, aqueous	[29, 86, 94]
Anti-parasitic	Leaf, flower, stem, root	Methanol, ethyl acetate, hexane	[107]
Anti-malaria	Leaf	Aqueous, ethyl acetate, chloroform, hexane	[111, 112]

2.4 Antioxidant Properties of *Ageratum conyzoides*

Oxidative stress is a condition characterized by increased production of reactive oxygen species (ROS) parallel with an imbalance in the antioxidant defense system [45, 46]. Some of these radicals are generated via endogenous processes while some are acquired from exogenous sources. For instance, superoxide radicals (O_2*) and hydrogen peroxide (H_2O_2) are by-products of mitochondrial electron transport and other metabolic processes [47]. Whereas, exposure to environmental pollutants such as air pollution, cigarette smoking, excessive alcohol consumption, and ultraviolet radiation can bring about a generation of high amounts [48]. ROS are implicated in the etiopathology of many human diseases such as cancer, atherosclerosis, and Parkinson and Alzheimer's disorders [49]. Interestingly, fruit, vegetables, and numerous medicinal plants are the repository of important metabolites capable of quenching or chelating free radicals, or able to stimulate the antioxidant defense mechanism of the living cell thereby counteracting radical-induced tissue damage and protecting the biological molecules [50, 51]

In-vitro and in-vivo, *Ageratum conyzoides* demonstrated significant antioxidant efficacy, which was attributed to the high phenolic content of the extract and fractions. The antioxidant efficacy of the extract contributed to the organ protection against CCl_4-induced damage. This observation of Sarfo-Antwi *et al.* [14] conforms well with that of Acheampong et al. [52] who reported the antioxidant properties of the hydroethanolic extract of *A. conyzoides* and further attributed the effect to the phenol and flavonoids constituent of the extract. The authors confirmed this by FTIR analysis, which showed the presence of phenols, alcohols, and aromatics. The antioxidant compounds are well-recognized scavengers of free radicals with potentials such as anticancer [53], enhancing male fertility [54] and improving cardiovascular health [51, 55]. According to Sarfo-Antwi *et al.* [14], DPPH inhibition by *A. conyzoides* (0.14±0.010 mg/ml) measured by the concentration (µg/ml) of extracts that scavenged 50 % of DPPH radicals was found to be almost equal that of ascorbic acid (0.18±0.06 mg/ml). On a similar note, the DPPH radical inhibition by the leaf and root extracts of ethyl acetate, n-Hexane, and ethanol gave credence to the strong antioxidant capacity of *Ageratum conyzoides.* The ethanol extract with the strongest radical inhibition had IC_{50} value of 7.34 and 9.18 µg/mL for the root and leaf extract respectively while for the ethyl acetate extract, the value was 11.63 and 12.97 µg/mL respectively. The n-hexane extract, which showed the weakest inhibition, has the value to be 14.62 and 15.88 µg/mL for the root and leaf respectively [56]**.** Patel and Modi, [57] combined the DPPH inhibition, reducing power assay, ferric reducing antioxidant power, and phosphomolybdenum assay to determine the antioxidant potential of a different morphological organ of the plant. From indication, concentration-dependent increase in DPPH radical inhibition was observed for the aqueous and ethanol extract of the flower, leaf, stem, and root of the plant with the plant flower having the strongest inhibition capacity. In addition, the aqueous and ethanol flower extracts exhibited the most significant ferric-reducing antioxidant power and phosphomolybdenum inhibition. This observation was also supported by another study where the stems and flowers of *A. conyzoides* exhibited strong antioxidant activity due to the rich flavonoids and phenolic content [58].

The antioxidant activity of the methanol, ethyl acetate, chloroform, and hexane extract was measured by the ability to scavenge DPPH and ABTS free radicals. It was observed that ethyl acetate extract had higher DPPH radical scavenging activity (56.35±1.79) and hexane extract showed a higher ABTS radical scavenging activity (65.85±00) [59]. Sutjiatmo *et al.* [60] reported the IC_{50} of the ethanol extract as 80.7 µg/mL. Similarly, the results from the study reported by Neelabh *et al.* [61] showed that the antioxidant activity of *A. conyzoides* increased with an increase in the concentration of plant extract. The methanol extract had IC_{50} value of 213.57 µg/ml against the IC_{50} value of reference ascorbic acid with IC_{50} value of 6.82 µg/ml. The reducing power of the extract was found to be equivalent to 41 µg of garlic acid per milligram of extract. The total antioxidant activity of the methanol extract was determined to be equivalent to 316 µg of ascorbic acid per milligram of extract. In another investigation, extracts of various solvents (ethanol 70%, ethyl acetate, and chloroform) showed the DPPH radical inhibition with the extracts having IC_{50} values of 126.4871 g/mL, 90.2554 g/mL, and 93.2538 g/mL respectively, the antioxidant activity correlate with the total phenol and total flavonoid content of the extract [62].

Furthermore, from the results of a study conducted by Vikasari *et al.* [63], the extract had an IC_{50} of 153.63 g/mL with moderate DPPH inhibitory activity, while vitamin C had an IC_{50} of 5.53 g/mL with very strong antioxidant activity. Based on the observation, the antioxidant effect of the extract is in line with the research of Neelabh *et al.* [64] which stated that the methanol extract of the leaves had an IC_{50} of 213.57 µg/ml. Nevertheless, contradicts that of Shekhar and Anju, [65], which obtained an IC_{50} value of 24.8 g/ml for the alcoholic extract of *A. conyzoides* leaves. The difference may however be due to differences in the growing locations, which will cause differences in the content of secondary metabolites possessed by these plants [66].

The essential oil in the leaves of *A. conyzoides* reported by Quoc *et al.,* [22] showed a somewhat high IC_{50} value when compared to the value obtained for the crude extracts in other studies. Although the DPPH inhibition was concentration-dependent, IC_{50} value was approximately 8 mg/mL and quite higher than those of some previous studies, such as EOs of *Piper betle* L. and *Thymus caramanicus* Jalas whose IC_{50} values were 4 and 263 µg/mL, respectively [67, 68].

Observation from the study reported by Adetuyi *et al.* [69] showed that the methanol extract have higher DPPH and hydrogen peroxide scavenging activities over the aqueous extract but the aqueous extract had a higher reducing power. The methanol extract exhibited a greater inhibition against lipid peroxidation induced by Fe^{2+} in rat pancreas and penile tissue homogenate exemplified by their least IC50 (94.21 µg/ml in the pancreas) and (75.95 µg/mL in penile tissue). In rat brain homogenate, the aqueous extract exhibited a greater inhibition against lipid peroxidation induced by Fe^{2+} with the least IC_{50} of 91.74 µg/mL. Hence, these extracts can be used as a potent natural antioxidant against free radicals and as a natural source of combating disease caused by oxidative stress. A summary of the investigations on the antioxidant activity of the plant is shown in Table 2.

2.5 Antimicrobial Properties of *Ageratum conyzoides*

Diseases caused by microorganisms are responsible for approximately 66.67% of all deaths in tropical countries [25] and the increases in this trend have resulted in renewed interest in the medical and public health communities for strategies on treatment and prevention through the development of new antimicrobials. Going by history, medicinal plants have provided a good source of anti-infective agents with compounds that are highly effective instruments in the fight against microbial infections.

Among important plants with antibacterial activity is *Ageratum conyzoides* L. A study reported the methanol extract and oil to inhibit 20 bacteria and four fungi strains**.** Although Martins *et al.* [70] reported that the oil exhibited weak activity against *Staphylococcus epidermidis*, *Staphylococcus aureus,* and *Cladosporium cladosporioides*, the extract inhibited the growth of *Staphylococcus aureus*, *Escherichia coli, Pseudomonas aeruginosa,* and *Bacillus subtilis*. In support of this observation**,** Budiman and Aulifa, [12] showed that the ethanol extract of *Ageratum conyzoides* and *Piper betle* L extract have activity against *S. aureus.* A previous article reported that *Piper betle* L. contains fatty acid compounds, hydroxy fatty acid ester, and hydroxychavicol, which have antibacterial activity. Fatty acids at low pH acts as antibacterial and antifungal by targeting the structure and function of cell walls and bacterial membranes. Whereas, a flavonoid contained in the extract can form complex connections with extracellular and bacterial cell walls [71]. From observation, "the extract of *Ageratum conyzoides* showed a broad spectrum of antibacterial activities, inhibiting *P. aeruginosa, E. coli, S. dysenteriae* and *S. aureus* at a concentration of 50 mg/ml. The extract at 25 mg/ml was observed to have some activities on *S. dysenteriae* and *S. aureus* with the zone of inhibition at 6.0 mm for both. The Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) for the ethanol extract of the plant on *S. aureus* and *E. coli* was 120 mg/ml, while the MIC and MBC of *P. aeruginosa* was 160 mg/ml and *Shigella dysenteriae* has 200 mg/ml of the plant extract. The observation suggested that the ethanol extracts of *A. conyzoides* could be suitable for the treatment of diseases/infections caused by *S. aureus*, *P. aeruginosa*, *E. coli,* and *Shigella dysenteriae"* [25].

"The comparative anti-microbial study involving different solvent extracts of the plant against *Staphylococcus aureus* and E*. coli* was performed using the agar well diffusion method. The antimicrobial potential of the methanol

Table 2. Summary of the antioxidant properties of *Ageratum conyzoides*

Antioxidant Method	Plant part used	Extract	References
DPPH	Leaf, root, flower, stem	Ethanol, ethyl acetate, hexane,	[14, 56, 57, 62]
Phosphomolybdenum inhibition	Flower, stem, root, and leaf	Aqueous, ethanol	[57]
ABTS radical scavenging	Leaf	Ethyl acetate, methanol, chloroform, and hexane	[59]
Ferric reducing antioxidant power	Flower, stem, root and leaves	Aqueous, ethanol	[57]
Hydrogen peroxide scavenging	Leaf	Methanol, aqueous	[69]

extracts was greater with the largest zone diameter of inhibition (14.5 mm and 13.7 mm) for *S. aureus* and E*. coli* respectively. While comparatively least activity was recorded with a 9.5 mm zone of inhibition in hexane extract at a concentration of 50 micro litters against S*. aureus*. The aqueous extract inhibited *E. coli* with an inhibition zone of 9.1 mm. The study indicated that methanol extract of *Ageratum conyzoides* had the maximum ability to restrict the growth of infectious bacteria. These types of therapeutic properties of plant bioactive components have good antimicrobial efficiency to provide cures against many pathogenic diseases of human beings" [28].

In another study, "the efficacy of *Ageratum conyzoides* when compared with other plant extracts was demonstrated against various test organisms. The result indicated that a high proportion of test organisms were all susceptible to *Piper betle*, *Ageratum conyzoides* and *Curcuma domestica*. However, for *Muntinga calabura*, only *S. simulans*, *S. chromogens*, *S. dysagalactiae* and *S. sanguinis* were susceptible, whereas *S. mitis*, *S. agalactiae,* and *S. uberis* were resistant. Ethanol extract of *Piper betle* had inhibition zones ranging from 14.2 to 28.7 mm, *Ageratum conyzoide*s extract had inhibition zones ranging from 10.4 to 21.5 mm, *Curcuma domestica* extract had inhibition zones ranging from 7.0 to 21.0 mm, whereas *Muntinga calabura* extract had inhibition zone ranging from 8.0 to 17.4 mm. The minimum inhibitory concentrations of all extracts were 12.5 mg/ml" [72].

Chemically modified and unmodified oil of *Ageratum conyzoides* were compared for improved activity against some selected strains of pathogenic microbes. The oil from a fresh flowers of the plant was extracted by steam distillation. A portion of the extracted oil was modified by rapid bromination and its activity against *Staphylococcus aureus, Klebsiella aerogenes. Streptococcus spp, Escherichia coli, Bacillus anthracis, Candida parapsilosis, Candida albicans*, which causes genital infection, and *Trichophyton mentagrophytes*, which causes athlete's foot, a skin disease in men, were compared against those of the pure oil. The results obtained showed that the chemically modifie oil of A*. conizoides* exhibited increased antifungal properties than the pure oil. *C. parapsilosis* and *K. aerogenes* were totally resistant to the modified oil. *T. mentagrophytes* and *S. aureus*, which is pathogenic skin microbes, was totally resistant to the pure oil but were sensitive to the chemically modified oil making this type of oil a good active ingredient in ointments against the microbes. *E. coli* and *B. anthracis* were both sensitive to the oils with the organisms being more sensitive to the pure oil than the brominated one. The sensitivity of *Streptococcus spp* to the two oils was low with a better effect shown by the brominated oil. *5. aureus* which is a bacterium that causes skin infection was resistant to the pure oil but showed some sensitivity to the brominated oil. These results show that the sensitivity of some bacteria strains can possibly be improved by the modification of the oil [73]. *A. conyzoides* leaves essential oil demonstrated some antibacterial activity against *S. enteritidis* (inhibitory zone of 15.33 mm). From the inhibition zones recorded for *S. enteritidis*, the bacterial was considered "very sensitive" (inhibition diameter was observed in a range of 15 to 19 mm [74]. The oil did not inhibit *B. subtilis, E. coli* and *S. aureus*. Thus contradicting the observation of that of Patil *et al*. [75], where *A. conyzoides* plants essential oil was recorded against the bacteria *S. aureus, B. subtilis* and *E. coli*. In addition, *A. conyzoides* flowers essential oil in the study of Kouame *et al*. [76] inhibited the growth of *S. aureus* and *E. coli*.

The difference in antibacterial activity between other studies can be attributed to the difference in the chemical composition of essential oil.

2.6 Anti-inflammatory Activity of *Ageratum conyzoides*

Inflammation as a complex biological response to harmful stimuli can be protective in nature when the organism attempts to remove injurious stimuli and initiate the healing process. It becomes harmful on another end when it is chronic and can result in the pathogenesis of various inflammatory-related human diseases [51]. Many diseases management strategies involve regulation of the inflammatory processes in the living cell and several herbal medicinal efficacies have been associated with their anti-inflammatory potentials [51, 77, 78].

Galati *et al.* [79]; Saputri *et al.* [80]; VikasarI *et al.,* [15] used the carrageenan-induced swelling assay to evaluate the acute anti-inflammatory potentials of *Ageratum conyzoides.* Vikasari *et al.* [15] found that the extract showed the same onset of the anti-inflammatory effect starting at minute 90 minutes, with diclofenac sodium. From observation, the percentage of inflammation inhibition, of the extract gave a faster onset of action as an anti-inflammatory agent, which was stable for 3 hours, in contrast to diclofenac sodium, which anti-inflammatory effect increased over time. Also by the carrageenan-induced paw edema test in the hind paw of a rat, Rahman *et al.* [81] found *A. conyzoides* (50.23 %) as a more effective anti-inflammatory plant than *E. sonchifolia* which promoted 48.11% of inhibition. Both extracts demonstrated a time-dependent anti-inflammatory action with the highest action after the 4^{th} hour of administration. The opinion based on the study conducted by Hassan *et al[82]* supports the time-dependent anti-inflammatory action of *A. conyzoides,* which reduced the paw volume between 1 hour to 4 hours after administration at a percentage of 59.15 % and maximum effect at 4^{th} hour. Inflammation is a complex series of events that result from a complex network of interactions among the cells, tissue, and some mediators released locally at the site of inflammation and can enhance the signs and symptoms of inflammation. Among others, a very important consequence of inflammatory stimulus is the perturbation of the neutrophil membrane, which stimulates highly reactive oxygen products, including superoxide, and the release of lysosomal enzymes or release of histamine by basophil and mast cells [79]. The anti-inflammatory effect of *A. conyzoides* is thought to be due to the presence of flavonoids that can stabilize membranes and inhibit protein denaturation [83]. It could also be linked to their ability to reduce myeloperoxidase (MPO), inhibit leukocyte influx, and adenosine deaminase (ADA). They could also reduce pro-inflammatory mediators such as nitric oxide metabolites (NOx), interleukin 17A (IL-17A), tumor necrosis factor (TNF), interleukin 10 (IL-10), interleukin 6 (IL-6), and interferon-gamma (IFN-γ). The plant could inhibit phosphorylation of p65 subunit of NF-B (p-p65 NF-κB) and p38 mitogen-activated protein kinases (p-p38 MAPK) as demonstrated by (VigildeMello *et al.,* [844]. The canonical activation of NF-κB pathways is a major pathway for the activation of inflammation in the presence of oxidation [15].

2.7 Gastro-protective Properties of *Ageratum conyzoides*

“Any factor that alters the balance between the aggressive factors that can disrupt the mucosal integrity and the protective factors can affect the gastric mucosal health. The alteration in the gastric mucosal integrity may lead to injury or ulceration” [85]. “The gastric mucosal aggressive factors could include the endogenous factors; increased gastric acid secretion, ischemia and bile acids, and exogenous factors; bacteria, ethanol, non-steroidal anti-inflammatory drugs, and even oxidative stress” [86, 87]. “The protective machinery on the other hand is are the mucus and bicarbonate ions produced by mucous and parietal cells in the gastric mucosa, respectively. The mucus and bicarbonate ions create a viscous layer of gel that helps ensure a near-neutral pH at the gastric mucosal surface protecting mucosal cells from the activity of digestive enzymes (such as pepsin) and the erosive effect of acidic gastric secretions” [88]. “Other factors may also include the mucosal microcirculation, nitric oxide, prostaglandins, epidermal growth factors, and cyclooxygenase” [89-91]. In general, exogenous factors that stimulate the protective factors of gastric mucosa and their protective effects and/or down-regulate the aggressive factors and their erosive effects contribute to gastric mucosal protection.

The histochemical observation of the mucous cells in the gastric mucosa, revealed prominence of mucous cell population in the gastric tissues after treatment with various doses of *A. conzyzoides* methanol leaves extracts. The

author also reported a corresponding increase in the mucous cell count in the gastric tissues of animals. The animals treated with 100, 300, and 500 mg/kg extract recorded mucous cell counts (9.88±0.40), (9.63±0.86), and (9.75±0.80) respectively. "The increased gastric mucous cell population implied increased secretion of viscous and alkaline mucus which constitutes a vital part of primary gastric mucosal protective factors. The mucus forms a protective layer of gel on a gastric mucosal surface which protects it against the digestive action of pepsin and the erosive effect of acidic gastric juice" [86]"Two types of this mucus are secreted by mucous cells of gastric mucosa i.e. mucus secreted by neck mucous cells which neutralizes gastric contents and insoluble mucus secreted by surface mucous cells after exposure to chemical or physical irritants" [86, 87]. According to Olaibi *et al.* [92], "induction of gastric mucosal injury involves disruption of mucus production by the gastric mucous cells, and the preservation of same i.e. mucus-secreting cells in stomach tissue is vital in gastric mucosal protection". Ige *et al.* [93] from their study, demonstrated an increase in mucus secretion as one mechanism of gastric mucosa protection from gastric mucosal injury. Omotoso *et al.* [94] therefore ascribed a similar mechanism to the gastroprotective activity of methanol extracts of *Ageratum conyzoides* L.

In another vein, a shift in the equilibrium between the protective and aggressive factors towards cell survival or death will respectively maintain or disrupt the gastric mucosal integrity. The tumor suppressor (p53) protein is one key factor that projects cells towards cell death. The study by Arab *et al.* [95] opined that "gastroprotective mechanisms involve down-regulation of apoptotic triggers such as p53 protein expression so as to shift the balance of gastric mucosal cells toward survival". From the report of Omotoso *et al.* [94], "the gastro-protective effects of *A. conzyzoides L.* were exhibited through suppression of pro-apoptotic signals generated by p53 upon exposure to gastric mucosal aggressive factors".

Both the aqueous methanol leaf extracts of *A. conyzoides* L were protective against erosive effect of acidic gastric secretions. The histological appearance of gastric tissues was showed relatively normal gastric mucosal histo-architecture with densely packed gastric glands. An observation, by Omotoso *et al.* [29] said "might directly be associated with the protective effects of leaf extracts of *A. conyzoides* L. on gastric mucosa from the corrosive action of gastric juice since the non-treated animals showed prominent mucosal surface erosion". Observations from similar studies have associated these effects with the anti-oxidant efficacy of *A. conyzoides.* Shirwaikar *et al.* [96] who demonstrated "the protective effects of the ethanol extract of *A. conyzoides* against ibuprofen-, ethanol, and stress-induced gastric ulceration" and Mahmood *et al.*[97], who used "the aqueous extract of *A. conyzoides* against ethanol-induced gastric ulcers linked the gastro-protection with anti-oxidant properties of the plant extract".

"The prominent and intense mucosa erosion upon pyloric-ligation, which was revered to mild mucosal erosion upon treatment with the plant extracts, was also accompanied by an increase in mucous cells, a significant increase in Bcl-2 expression without a significant increase in p53 expression in gastric mucosa. The gastric mucosa compromised tissue was on the other hand characterized by decrease in mucous cell count and Bcl-2 expression with a significant concomitant increase in p53 expression. The increased mucous cell population and reciprocal expressions of Bcl-2 and p53 proteins in the gastric mucosa of animals highlighted the sub-cellular mechanisms of gastroprotective activity of *A. conyzoides"* [98]. As a way of demonstrating the gastro-protective effect of *A. conyzoides,* [99]**,** showed a dose dependent decrease in castor oil induced diarrhoea as well as inhibition of barium sulphate induced gastro-intestinal motility in albino rats. Summarily of all the pharmacological investigation is the validation of the traditional usage of the plants to relieve colic, diarrhea, and relieve pain around the navel in children.

2.8 Anti-diabetic Properties of *Ageratum conyzoides*

Medicinal plants such as anti-diabetics have been in existence since time immemorial. Different preparations are often engaged in the traditional system of medicine to manage diabetics, and its complication. Diabetes is a critical health burden responsible for high rate of morbidity and mortality. According to the World Health Organization (WHO) 25% of the currently available drugs are of plant origin [100]. *Ageratum conyzoides* is a potential plant to source for effective anti-diabetic agents. For instance, the aqueous extract significantly lowered the blood glucose of diabetic rats and

improved significantly the insulin level in serum [101]. In the same vein, short-term hypoglycaemic effect after oral administration to diabetic rats was reported [102, 103]. Dyslipidaemia accompanying diabetes development in the experimental rats was also abrogated showing the hypolipidemic potentials of the extract [101]. In the rats' diabetic model, the ethanol whole plant extracts demonstrated significant hypoglycaemic effects. Rahman *et al.* (2013) attributed this effect to the terpenoids, tannins, and coumarin constituents of the plant. In normoglycemic rats, the extract exhibited some glycemic control that was attributable to the phytochemicals inherent in the plant sample [104]. A dose-dependent decline in blood glucose of normoglycemic rats administered the leave extract of *Ageratum conyzoides* was in line with the reported utilization of the plant for diabetes management in Nigeria and Cameroon [105, 106].

2.9 Anti-parasitic Properties of *Ageratum conyzoides*

Extracts of *Ageratum conyzoides* have been shown to exhibit anti-parasitic potentials. For instance, various extracts of the plant showed different levels of efficacy against viable *Giardia duodenalis* trophozoites [107]. The parasite is a common enteric protozoan known to be the causative agents for giardiasis in humans and animals. The symptoms of giardiasis vary from asymptomatic cases to chronic diarrhea [108]. In cases of severe infection especially in children, malnutrition and alteration in mental and physical development may be seen [109]. The extract was also reported to demonstrate larvicidal activity against *Anopheles gambiae.* The methanol, ethyl acetate, and n-Hexane extracts of the leaves, flowers, stem, and root showed varying degrees of bioactivity against the adult, third, and fourth instar larvae of the parasite. The observation indicates the potentials of the plant in malaria control, as it serves as an inhibitor of plasmodium vector responsible for malaria [110].

2.10 Anti-malarial Properties of *Ageratum conyzoides*

"The water extract of *Ageratum conyzoides* can increase the anti-malaria efficacy of chloroquine and artesunate in the plasmodia-induced mice. The result also showed no antagonistic effect produced by the herb-drug combination in all the combination doses used. The increase in parasitemia clearance with increase in dose of *A. conyzoides* in each combination gave credence to this observation" [111]. "The leaves extract as well as its fraction similarly demonstrated significant inhibitory effects in-vitro and in mice infected with *Plasmodium berghei"* [112].

3. CONCLUSION

It could be deduced from the current review that *Ageratum conyzoides* is a repository of important beneficial bioactive principles with known biological efficacies that can be annexed for managing different human ailments. It could also be deduced that there is sdirt of literature information on the basic mechanism of some of the pharmacological activities of the plant and therefore necessitate further investigation to substantiate some of the acclaimed pharmacological potentials and establish the likely mode of activity. The traditional application also varied widely across regions and cultures, and this might be due to differences in the phytochemical constituents across the different regions. It is noteworthy to state that the chemical composition of *Ageratum conyzoides* varies in the different studies and the variation may be attributed to differences in the site and time of collection.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Mehmood A, Naveed K, Azeem K, Khan A, Ali N, Khan SM. Sowing time and nitrogen application methods impact on production traits of Kalonji (*Nigella sativa* L.). Pure Appl Biol. 2018;7(2):476-85.
   DOI: 10.19045/bspab.2018.70060.
2. Shahzad Q, Sammi S, Mehmood A, Naveed K, Azeem K, Ahmed Ayub MH et al. Phytochemical analysis and antimicrobial activity of Adhatoda vasica leaves. Pure Appl Biol. 2020. 43;9(2):1654-61.
   DOI: 10.19045/bspab.2020.90174.
3. Mehmood A, Naveed K, Jadoon N, Ayub Q, Hussain M, Hassaan M. Phytochemical screening and antibacterial efficacy of black cumin (*Nigella sativa* L.) seeds. FUUAST J Biol. 2021a;11(1):23-8.
4. Olasunkanmi AA, Fadahunsi OS, Adegbola PI. Gas chromatography-Mass Spectroscopic, high performance liquid

chromatographic and In-silico characterization of antimicrobial and antioxidant constituents of Rhus longipes (Engl). Arab J Chem. 2022;15(2):103601.
DOI: 10.1016/j.arabjc.2021.103601.

5. Olorunnisola OS, Adetutu A, Owoade AO, Ajayi FA, Ajibade AA, Adegbola P. Acute and sub-acute toxicity assessment of *Euphorbia lateriflora* (Schum and Thonn) in Wistar albino rats. EJMP. 2019;29(1):1-10.
DOI: 10.9734/ejmp/2019/v29i130147.
6. Fadahunsi O, Adegbola PI, Olorunnisola SO, Akinloye OA. Phytochemistry, nutritional composition, and pharmacological activities of *Thaumatococcus daniellii* (Benth): A review. Biotechnologia. 2021a;102(1):101-17.
DOI: 10.5114/bta.2021.103766
7. Mehmood A, Naveed K, Ayub Q, Alamri S, Siddiqui MH, Wu C et al. Exploring the potential of Moringa leaf extract as bio stimulant for improving yield and quality of black cumin oil. Sci Rep. 2021b;11(1): 24217.
DOI: 10.1038/s41598-021-03617-w
8. Fadahunsi OS, Adegbola PI, Olorunnisola OS, Subair TI, Adepoju DO, Abijo AZ. Ethno-medicinal, phytochemistry, and pharmacological importance of *Hunteria umbellate* (K. Schum.) Hallier f. (Apocynaceae): A useful medicinal plant of sub-Saharan Africa. Clin Phytosci. 2021b; 7(1):54.
DOI: 10.1186/s40816-021-00287-z.
9. Rehman AU, Mehmood A, Naveed K, Haq NU, Ali S, Ahmed J et al. Integrated effect of nitrogen and sulphur levels on productive traits and quality of black cumin (*Nigella sativa* L.). J Xi'an Shiyou Uni Nat Sci Edi. 2022;18(10):38-58.
10. Okunade AL. Ageratum conyzoides L. (Asteraceae). Fitoterapia. 2002;73(1):1-16.
DOI: 10.1016/s0367-326x(01)00364-1
11. Negi B, Bargali SS, Bargali K, Khatri K. Allelopathic interference of *Ageratum conyzoides* L. against Rice varieties. Curr Agri Res Jour. 2020;8(2):69-76.
DOI: 10.12944/CARJ.8.2.01.
12. Budiman A, Aulifa DL. A study comparing antibacterial activity of Ageratum conyzoides L. extract and Piper BetleL. Extract in gel dosage forms against Staphylococcus aureus. Pharmacogn J. 2020;12(3):473-7.
DOI: 10.5530/pj.2020.12.73.
13. Omotoso DR, Ajeigbe KO, Owonikoko WM, Okwuonu UC, Akinola AO, Daramola OO et al. Role of mucous cell and p53 protein in gastroprotective activity of methanolic extracts of Ageratum conyzoides Linn in rats. Afr J Biotechnol. 2019c;18(27):640-6.
DOI: 10.5897/AJB2019.16851.
14. Sarfo-Antwi F, Larbie C, Babatunde D. Extracts of *Ageratum conyzoides* L. protects against carbon tetrachloride-induced toxicity in rats through inhibiting oxidative stress. J Adv Med Pharm Sci. 2018;19(2):1-14.
15. Vikasari SN, Sukandar EY, Suciati T, Adnyana IK. Anti-inflammation and antioxidant effect of ethanolic extract of *Ageratum conyzoides* Leaves. 2nd annual conference on health and food. Sci Technol. 2022;1104:01202.
16. Del-Vechio-Vieira G, de Sousa OVd, Miranda MA, Senna-Valle L, Kaplan MAC. Analgesic and anti-inflammatory properties of essential oil from *Ageratum fastigiatum*. Braz Arch Biol Technol. 2009;52(5):1115-21.
DOI: 10.1590/S1516-89132009000500008.
17. Kotta JC, Lestari ABS, Candrasari DS, Hariono M. Medicinal effect, in silico bioactivity prediction, and pharmaceutical formulation of *Ageratum conyzoides* L.: a review. Scientifica. 2020;2020:6420909.
DOI: 10.1155/2020/6420909
18. Kanissery R, Sellers B, Futch S. Biology and Management of Tropical White Weed (Ageratum conyzoides) in Citrus Groves. Horticultural Sciences Department, UF/IFAS Extension; 2019 [cited Jan 12, 2023].
Available: https://edis.ifas.ufl.edu.
19. Shekhar TC, Anju G. A comprehensive review on Ageratum conyzoides linn. (Goat weed). Int J Pharm Phytopharmacol Res. 2012;1(6):391-5.
20. Vaidyaratnam, varier, P.S. 2002. Indian Medicinal Plants-A Compendium of 500 species, I. Kottakkal, India: Orient longman publishing house. 146.
21. Wunderlin RP, Hansen BF, Franck AR, Essig FB. "Atlas of Florida Plants; 2018. Available from: http://florida.plantatlas.usf.edu/.
22. Quoc T. Physicochemical properties and antibacterial activity of essential oil of Ageratum conyzoides L. Leaves. Agric Conspec Sci. 2020;85(2):139-44.

23. Janarthanan L, Karthikeyan V, Jaykar B, Balakrishnan BR, Senthilkumar KL, Anandharaj G. Pharmacognostic studies on the whole plants of *Ageratum conyzoides* Linn. (ASTERACEAE). Eur J Pharm Med Res. 2016;3(5):618-26.
24. Warsinah W W, Baroroh HN. Pharmacognostic profile of Ageratum conyzoidesL plant and Simplicia. Pharmacogn J. 2020;12(5):1072-6. DOI: 10.5530/pj.2020.12.151.
25. Odeleye OP, Oluyege JO, Aregbesola OA, Odeleye PO. Evaluation of preliminary phytochemical and antibacterial activity of *Ageratum conyzoides* (L.) on some clinical bacterial isolates. Int J Eng Sci (IJES). 2014;3(6):1-5.
26. Enerijiofi KE, Isola OB. Preliminary Phytochemical screening and in vitro antibacterial activities of aqueous and ethanol extracts of *Ageratum conyzoides* L. Leaf, Stem, Flower and Root on some Bacterial isolates associated with diarrhoea. Nig J Pure Appl Sci. 2019;32(2).
27. Razafindrakoto ZR, Tombozara N, Ramanitrahasimbola D, Raoelihajaina DF, Rakotondramanana DA. Vaso-relaxing activity of Ageratum conyzoides linn. (Asteraceae) aerial parts on isolated rat aorta. Am J Innov Res Appl Sci. 2020;10(4):165-71.
28. Patil A, Kishore K, Arya M, Shivani. Phytochemical screening of *Ageratum conyzoides* and Its antimicrobial activity against *Staphaylococcus aureus* and *Escherichia coli*. Int J Res Anal Rev. 2019;6(2):312-20.
29. Omotoso DR, Akinola AO, Daramola O, Uwagbor V, Onyewotu O. Assessment of gastroprotective activity of leaf extracts of *Ageratum conyzoides* Linn. using pyloric-ligation method in animal model. Int J Biol Med Res. 2019a;10(07):e5214.
30. Hussien TA, Mohamed NS, Moustafa MFM, El-Sayed MA. A new natural pyrrolone from the Egyptian Ageratum species. Eur J Chem. 2010;1(2):140-1. DOI: 10.5155/eurjchem.1.2.140-141.17.
31. Ahuchaogu AA, Echeme JO. Isolation and NMR Characterisation of a Pentacyclic triterpenoid from chloroform fraction of Ageratum conyzoides Linn stem bark. J Phytopharmacol. 2019;8(6):291-4. DOI: 10.31254/phyto.2019.8604.
32. Bosi CF, Rosa DW, Grougnet R, Lemonakis N, Halabalaki M, Skaltsounis AL et al. Pyrrolizidine alkaloids in medicinal tea of Ageratum conyzoides. Braz J Pharmacogn. 2013;23(3):425-32. DOI: 10.1590/S0102-695X2013005000028.
33. Gonzalez AG, Aguiar ZE, Grillo TA, Luis JG, Riverat A, Calle J. Chromenes from Ageratua *conyzozdes*. Phyrochemisfry. 1991;30(4):I137-1139.
34. Girthen TS. Drug plants of Africa. Afr Handb. 1948;8:59.
35. Singh SB, Devi WR, Marina A, Devi WI, Swapana N, Singh CB. Ethnobotany, phytochemistry and pharmacology of *Ageratum conyzoides* Linn (Asteraceae). J Med Plants Res. 2013;7.
36. Chopra RN, Nayar SL, Chopra IC. Glossary of Indian medicinal plants. New Delhi: NISCIR. 2002;9.
37. Kapur SK. Ethnomedico plants of Kangra valley (Himachal Pradesh). J Econ Tax Bot. 1993;17:395-408.
38. Neogi B, Prasad MNV, Rao RR. Ethnobotany of some weeds of Khasi and Garo hills, Meghalaya, Northeastern India. Econ Bot. 1989;43(4):471-9. DOI: 10.1007/BF02935921.
39. Rajwar GS. Low altitude medicinal plants of south Garhwal (Garhwal Himalaya). Bull Ethnobot Res. 1983;4:14-28.
40. Diallo A, Eklu-Gadegkeku K, Agbono A, Aklikokou K, Creppy EE, Gbeassor M. Acute and sub-chronic (28-day) oral toxicity studies of hydroalcohol leaf extract of Ageratum conyzoidesL. (Asteraceae). Trop J Pharm Res. 2010;9(5).
41. Kaur R, Dogra NK. A review on traditional uses, chemical constituents and pharmacology ofAgeratum conyzoidesL. Asteraceae,"International Journal of Pharmaceutical and Biological Science Archive. 2014;5(5):33-45.
42. Yadav N, Ganie SA, Singh B, Chhillar AK, Yadav SS. Phytochemical constituents and ethnopharmacological properties ofAgeratum conyzoides L. Phytother Res. 2019;33(9):2163-78. DOI: 10.1002/ptr.6405
43. Annonymous. The Wealth of India- Raw materials, I(A), Revised Edn, NISCAIR, New Delhi. 2003;2003:108-109.
44. Flora of China. Ageratum conyzoides Linnaeus. 2023;20-21: 879. Available:http://www.efloras.org/volume_page.aspx?volume_id=2020&flora_id=2. Accessed 05/01/2023, 06:20
45. Bhattacharya S. Reactive oxygen species and cellular defense system. [in:] Free

radicals in human health and diseases. Ed. Rani V, Yadav UCS. Springer India. 2015;17–29.

46. Stamati K, Mudera V, Cheema U. Evolution of oxygen utilization in multicellular organisms and implications for cell signaling in tissue engineering. J Tissue Eng. 2011;2(1):20417314114-32365.
DOI: 10.1177/2041731411432365
47. Shinde A, Ganu J, Naik P. Effect of free radicals & antioxidants on oxidative stress: a Review. J Dent Allied Sci. 2012;1(2):63-6.
DOI: 10.4103/2277-4696.159144.
48. Lobo V, Patil A, Phatak A, Chandra N. Free radicals, antioxidants and functional foods: impact on human health. Pharmacogn Rev. 2010;4(8):118-26.
DOI: 10.4103/0973-7847.70902
49. Parihar MS, Parihar A, Fujita M, Hashimoto M, Ghafourifar P. Alpha-synuclein over expression and aggregation exacerbates impairment of mitochondrial functions by augmenting oxidative stress in human neuroblastoma cells. Int J Biochem Cell Biol. 2009;41(10):2015-24.
DOI: 10.1016/j.biocel.2009.05.008
50. Adegbola PI, Adetutu A, Olaniyi TD. Antioxidant activity of Amaranthus species from the Amaranthaceae family-A Review. S Afr J Bot. 2020;133:111-7.
DOI: 10.1016/j.sajb.2020.07.003.
51. Adegbola P, Aderibigbe I, Hammed W, Omotayo T. Antioxidant and anti-inflammatory medicinal plants have potential role in the treatment of cardiovascular disease: a review. Am J Cardiovasc Dis. 2017;7(2):19-32.
52. Acheampong F, Larbie C, Appiah-Opong R, Arthur FKN, Tuffour I. In-vitro antioxidant and anticancer properties of hydroethanolic extracts and fractions of *Ageratum conyzoides*. Eur J Med Plants. 2015;7(4):205-14.
DOI: 10.9734/EJMP/2015/17088.
53. Spatafora C, Tringali C. Natural-derived polyphenols as potential anticancer agents. Anti Cancer Agents Med Chem. 2012;12(8):902-18.
DOI: 10.2174/187152012802649996
54. Seddiki Y, DaSilva FM. Antioxidants properties of polyphenols and the potential use in improving male fertility: a review. Biomed J Sci Tech. 2017;1:1.
55. Tangney CC, Rasmussen HE. Polyphenols, inflammation and cardiovascular disease. Curr Atheroscker rep 15. Curr Atheroscler Rep. 2013;15(5): 324.
DOI: 10.1007/s11883-013-0324-x
56. Omole OA, Oladipo JO, Orimolade BO, Ajetomobi OO, Olorunmaiye KS, Dosumu OO. Antioxidant and antimicrobial activities of the Root and leaf extracts of *Ageratum conyzoides* L. *2019*;84(3):295-304.
57. Patel FR, Modi NR. Antioxidant activity and FTIR analysis of Ageratum conyzoides L. International Journal of Botany Studies. 2021;6(5):1152-61.
58. Ajetomobi OO, Omole OA, Elasoru SE. Evaluation of antioxidant activity of stem and flower extracts of *Ageratum conyzoides*. International Journal of Advance Research. Ideas Innov Technol. 2018;4(3):891-7.
59. Rajput D, Saikia LR, Borkataky M, Agarwalla S. *Ageratum conyzoides L.*: *In vitro* antimicrobial, antioxidant, and phytochemical study. Eco Environ Cons. 2022;28:S255-61.
60. Sutjiatmo AB, Edriayani N, Mulyasari TE, Hermanto F, Fahrauk M, Sukandar EY et al. Antioxidant and antiaging assays of *Ageratum conyzoides* (L.) ethanolic extract. Pharm Sci Res (PSR). 2020; 7(3):145-52.
DOI: 10.7454/psr.v7i3.1061.
61. Neelabh C, Nahid A, Navneet K. Study on methanolic extract of Ageratum conyzoides for its ability to act as an antioxidant and to suppress the microbial growth. The Pharma. Innov J. 2017;6(11):170-3.
62. Mulyani Y, Nabhani SR, Sukmawat IK. Antioxidant and antibacterial activity test of bandotan (Ageratum conyzoides L.) Extract on Streptococcus pyogenes bacteria. World J Pharm Res. 2021; 10(14):81-100.
63. Vikasari SN, Sukandar EY, Suciati T, Adnyana IK. Anti-inflammation and antioxidant effect of ethanolic extract of *Ageratum conyzoides* Leaves. 2nd annual conference on health and food. Sci Technol. 2022;1104:01202.
64. Neelabh C, Nahid A, Navneet K. Study on methanolic extract of *Ageratum conyzoides* for its ability to act as an antioxidant and to suppress the microbial growth. J Pharm Innov J. 2017;6(11):170-3.
65. Shekhar T, Anju G. Antioxidant activity by DPPH radical scavenging method of *Ageratum conyzoides* Leaves L. Orient. 2014;1(4):244-9.

66. Li Y, Kong D, Fu Y, Sussman MR, Wu H. The effect of developmental and environmental factors on secondary metabolites in medicinal plants. Plant Physiol Biochem. 2020;148:80-9. DOI: 10.1016/j.plaphy.2020.01.006
67. Prakash B, Shukla R, Singh P, Kumar A, Mishra PK, Dubey NK. Efficacy of chemically characterized Piper betle L. Essential oil against fungal and aflatoxin contamination of some edible commodities and its antioxidant activity. Int J Food Microbiol. 2010;142(1-2):114-9. DOI: 10.1016/j.ijfoodmicro.2010.06.011
68. Safaei-Ghomi J, Ebrahimabadi AH, Djafari-Bidgoli Z, Batooli H. GC/MS analysis and in vitro antioxidant activity of essential oil and methanol extracts of Thymus caramanicusJalas and its main constituent carvacrol. Food Chem. 2009;115(4):1524-8.
DOI: 10.1016/j.foodchem.2009.01.051.
69. Adetuyi FO, Karigidi KO, Akintimehin ES, Adeyemo ON. Antioxidant properties of Ageratum conyzoides L. Asteraceae leaves. Bangladesh J Sci Ind Res. 2018;53(4):265-76.
DOI: 10.3329/bjsir.v53i4.39190.
70. Martins AP, Salgueiro LR, Gonçalves MJ, Vila R, Cañigueral S, Tomi F et al. Essential oil composition and antimicrobial activity of Ageratum conyzoides from S. Tomé and Príncipe. J Essent Oil Res. 2005;17(3):239-42.
DOI: 10.1080/10412905.2005.9698888.
71. Nalina T, Rahim ZHA. The crude aqueous extract of Piper betle L. and its Antibacterial Effect Towards Streptococcus mutans. Am J Biochem Biotechnol. 2007;3(1):10-5.
DOI: 10.3844/ajbbsp.2007.10.15.
72. Harjanti DW, Ciptaningtyas R, Wahyono F. Phytochemical properties and antibacterial activity of *Ageratum conyzoides*, *Piper betle*, *Muntinga calabura* and *Curcuma domestica* against mastitis bacteria isolates. IOP Conf S Earth Environ Sci. 2019;247:012049.
DOI: 10.1088/1755-1315/247/1/012049.
73. Duru lA, Duru CE, Ibe FC, Nweze CA. Comparison of antimicrobial properties of chemically modified and unmodified flower oil of *Ageratum conyzoides*. Res Gate. 2013:88-93.
74. Ponce AG, Fritz R, Del Valle C, Roura SI. Antimicrobial activity of essential oils on the native microflora of organic Swiss chard. LWT Food Sci Technol. 2003; 36(7):679-84.
DOI: 10.1016/S0023-6438(03)00088-4.
75. Patil RP, Nimbalkar MS, Jadhav UU, Dawkar VV, Govindwar SP. Antiaflatoxigenic and antioxidant activity of an essential oil from Ageratum conyzoidesL. J Sci Food Agric. 2010; 90(4):608-14.
DOI: 10.1002/jsfa.3857
76. Kouame BKFP, Toure D, Kablan L, Bedi G, Tea I, Robins R et al. Chemical constituents and antibacterial activity of essential oils from flowers and stems of *Ageratum conyzoides* from Ivory Coast. Rec Nat Prod. 2018;12(2):160-8.
DOI: 10.25135/rnp.22.17.06.040.
77. Adetutu A, Owoade AO, Adegbola PI. Inhibitory effects of ethyl acetate and butanol fractions from *Morinda lucida* benth on benzeneinduced leukemia in mice. Arab J Chem. 2022;15(6):103802.
DOI: 10.1016/j.arabjc.2022.103802.
78. Adegbola PI, Fadahunsi OS, Ajilore BS, Akintola AO, Olorunnisola OS. Combined ginger and garlic extract improves serum lipid profile, oxidative stress markers and reduced IL-6 in diet induced obese rats. Obes Med. 2021;23:100336.
DOI: 10.1016/j.obmed.2021.100336.
79. Galati EM, Miceli N, Taviano MF, Sanogo R, Raneri E. Antiinflammatory and antioxidant activity of Ageratum conyzoides. Pharm Biol. 2001;39(5): 336-9.
DOI: 10.1076/phbi.39.5.336.5891.
80. Saputri MP, Utami R, Fadila J, Handayani SN. Anti-inflammation activity of Ageratum conyzoides Leaf ethanol extract on Rattus norvegicus. Walisongo J Chem. 2020; 3(1):46-51.
DOI: 10.21580/wjc.v3i1.6136.
81. Rahman A, Akter N, Rashid H, Ahmed NU, Uddin N, Shahidul Islam S. Analgesic and anti-inflammatory effect of whole Ageratum conyzoides and Emilia sonchifolia alcoholic extracts in animal models. Afr J Pharm Pharmacol. 2012;6(20):1469-76.
82. Hassan M. Shahid-Ud-Daula, A.F.M., Jahan;I(A)., Nimmi:I., Adnan, T., Al-Mansur, A., Hossain, H. (2012). Anti-inflammatory Activity, Total Flavonoids and Tannin Content from the Ethanolic Extract of Ageratum conyzoides Linn. Leaf. International Journal of Pharmaceutical and Phytopharmacological Research. 1(5): 234-241.

83. Kumar A, Ghosh S, Vaishali V. An experimental evaluation of Ageratum conyzoides on membrane stabilization and protein denaturation during acute inflammation and arthritis. Biomed Pharmacol J. 2011;4(2):313-7.
DOI: 10.13005/bpj/302.
84. Vigil de Mello SVG, da Rosa JS, Facchin BM, Luz ABG, Vicente G, Faqueti LG et al. Beneficial effect of Ageratum conyzoides Linn (Asteraceae) upon inflammatory response induced by carrageenan into the mice pleural cavity. J Ethnopharmacol. 2016;194:337-47.
DOI: 10.1016/j.jep.2016.09.003
85. Omotoso DR, Uwagbor V, Lawal OS, Olatomide OD, Okojie IG. Gross and histo-morphological study of antiulcerogenic effects of *Cissampelos owariensis* (P. Beauv.) methanolic extract in Wistar rats. J Biomed Sci. 2019b;8(3):1-5.
86. Sembulingam K, Sembulingam P. Essentials of medical physiology. 5th ed. St Louis: Jaypee Brothers Medical Publishers Ltd, USA. 2010;218-26.
87. Rhoades RA, Tanner GA. Medical Physiology. 2nd ed. Lippincott Williams & Wilkins. 2004;2004;484-88.
88. Johnson LR. Essential Medical Physiology. 3rd ed. Carlifonia, USA: Academic Press. 2003:502-12.
89. Sun WH, Tsuji S, Tsujii M, Gunawan ES, Kawai N, Kimura A et al. Induction of cyclooxygenase-2 in rat gastric mucosa by rebamipide, a mucoprotective agent. J Pharmacol Exp Ther. 2000;295(2):447-52.
90. Bongu S, Vijayakumar S. Animal models in experimental gastric ulcer screening-a review. Int J Pharmacol Screen Methods. 2012;2(2):82-7.
91. Brzozowski T, Konturek PC, Konturek SJ, Brzozowska I, Pawlik T. Role of prostaglandins in gastroprotection and gastric adaptation. J Physiol Pharmacol. 2005;56;Suppl 5:33-55.
92. Olaibi OK, Ijomone OM, Olawuni IJ, Adewole SO, Akinsomisoye SO. Mucus secreting activity and nitric oxide concentrations of ethanol-induced pylorus and duodenum of rats pretreated with *Moringa oleifera*. J Exp Integr Med. 2014;4(2):123-30.
DOI: 10.5455/jeim.260214.or.097.
93. Ige AO, Adewoye EO, Okwundu NC, Alade OE, Onuobia PC. Oral magnesium reduces gastric mucosa susceptibility to injury in experimental diabetes mellitus. Pathophysiology. 2016;23(2):87-93.
DOI: 10.1016/j.pathophys.2016.04.003
94. Omotoso DR, Ajeigbe KO, Owonikoko WM, Okwuonu UC, Akinola AO, Daramola OO et al. Role of mucous cell and p53 protein in gastroprotective activity of methanolic extracts of Ageratum conyzoides Linn in rats. Afr J Biotechnol. 2019c;18(27):640-6.
DOI: 10.5897/AJB2019.16851.
95. Arab HH, Salama SA, Omar HA, Arafa EA, Maghrabi IA. Diosmin protects against ethanol-induced gastric injury in rats: novel Anti-ulcer actions. PLOS ONE. 2015;10(3):e0122417.
96. Shirwaikar A, Bhilegaonkar PM, Malini S, Kumar JS. The gastroprotective activity of the ethanol extract of Ageratum conyzoides. J Ethnopharmacol. 2003; 86(1):117-21.
DOI: 10.1016/s0378-8741(03)00050-3
97. Mahmood AA, Sidik K, Salmah I, Suzainur KAR, Philips K. Antiulcerogenic activity of *Ageratum conyzoides* leaf extract against ethanol induced gastric ulcer in rats as animal model. Int J Mol Med Adv Sci. 2005;1(4):402-40.
98. Omotoso DR, Eze GK. Assessment of gastroprotective activity of aqueous leaf extract of Ageratum conyzoidesL: role of mucous cells, anti-apoptotic (Bcl-2) and tumor suppressor (p53) proteins. J HerbMed Pharmacol. 2022;11(2):245-52.
99. Rahman A, Sultana R, Akter R, Islam SI. Antidiarrheal and antidiabetic effect of ethanol extract of whole Ageratum conyzoides L. in albino rat model. Afr J Pharm Pharmacol. 2013;7(23):1537-45. DOI: 10.5897/AJPP12.325.
100. Wasana KGP, Attanayake AP, Jayatilaka KAPW, Weerarathna TP. Antidiabetic activity of widely used medicinal plants in the Sri Lankan traditional healthcare system: new insight to medicinal flora in Sri Lanka. Evid Based Complement Alternat Med. 2021;2021:6644004. DOI: 10.1155/2021/6644004
101. Nyunaï N, Abdennebi EH, Bickii J, Manguelle-Dicoum MA. Subacute antidiabetic properties of Ageratum conyzoides leaves in Diabetic rats. Int J Pharm Sci Res. 2015;6(4):1378-87.
102. Nyunaï N, Njifutié N, Abdennebi EH, Mbafor JT, Lamnaouer D. Hypoglycaemic and antihyperglycaemic activity of Ageratum conyzoides Linn. in rats. Afr. J

Trad Complement Altern Med. 2009;6:123-30.
103. Nyunaï N, Manguelle-Dicoum A, Njifutié N, Abdennebi EH, Cros G. Antihyperglycaemic effect of Ageratum conyzoides L. fractions in normoglycemic and diabetic male Wistar rats [international journal] of Biomedical and Pharmaceutic al Sciences. 2010;4:38-42.
104. Gnagne AS, Coulibaly K, Fofie NBY, Bene K, Zirihi GN. Hypoglycemic Potential of Aqueous Extracts of Ageratum conyzoides L., Anthocleista Djalonensis A. Chev. and *Bidens pilosa* L., Three Plants fromthe Ivorian Pharmacopoeia. Eur Sci J. 2018;14(12):360-73.
DOI: 10.19044/esj.2018.v14n12p360.
105. Kamboj A, Saluja AK. Ageratum conyzoides L.:A eview on its phytochemical and pharmacological profile. Int J Green Pharm. 2008;2(2):59-68.
DOI: 10.4103/0973-8258.41171.
106. Nyunai A, Dicoum M, Njifutie N, Abdennebi E, Gerard C. Antihyperglycemic effect of Ageratum conyzoides L. Fraction in normoglycemic and diabetic male Wistar rat. Int J Biomed PharmSci. 2006;4(1):38-42.
107. Pintong AR, Ruangsittichai J, Ampawong S, Thima K, Sriwichai P, Komalamisra N et al. Efficacy of Ageratum conyzoides extracts against Giardia duodenalis trophozoites: an experimental study. BMC Complement Med Ther. 2020;20(1):63.
DOI: 10.1186/s12906-020-2860-6, PMID 32111225.
108. Sahagún J, Clavel A, Goñi P, Seral C, Llorente MT, Castillo FJ, et al. Correlation between the presence of symptoms and the *Giardia duodenalis* genotype. Eur J Clin Microbiol Infect Dis. 2008;27(1): 81-3.
DOI: 10.1007/s10096-007-0404-3
109. Hotez PJ, Brooker S, Bethony JM, Bottazzi ME, Loukas A, Xiao S. Hookworm infection. N Engl J Med. 2004;351(8):799-807.
DOI: 10.1056/NEJMra032492
110. Suwaiba H, Barde AA, Mao PM, Aliyu AO. Larvicidal activity of Ageratum conyzoides L. extracts on Anopheles gambiae complex, GSC Biological and Pharmaceutical Sciences. 2018;03(03): 001-5.
111. Ukwe CV, Obinna E, Epueke EA, Ubaka CM. Antimalarial activity of Ageratum conyzoides in combination with chloroquine and artesunate. Asian Pac J Trop Med. 2010a:943-7.
112. Ukwe CV, Epueke EA, Ekwunife OI, Okoye TC, Akudor GC, Ubaka CM. Antimalarial activity of aqueous extract an fractions of leaves of Ageratum conyziodesin mice infected with *Plasmodium berghei*. Int J Pharm Sci. 2010b;2(1):33-8.

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/98474