Ethno-botany and Pharmacognosy of *Ageratum conyzoides* L. (Compositae)

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Received: February 8, 2015, Accepted: March 7, 2015, Published: March 7, 2015.

**ABSTRACT**

Plants have been one of the important sources of medicines since the beginning of human civilization. Nowadays, there is a growing demand for plant based medicines, health products, pharmaceuticals, food supplements, cosmetics etc. *Ageratum conyzoides* L. is a multipurpose herb. *Ageratum conyzoides* L. is traditionally used as purgative, febrifuge, anti-ulcer and wound dressing. A review of its ethno-botany and pharmacognosy is given in the present article. The results revealed that *Ageratum conyzoides* L. is a multipurpose herb and will allow researchers to develop drugs of substitution (phytomedicines) at low cost for the local market, developed, manufactured and distributed in the difficult economic context. Because of its established hematopoietic properties, it is therefore necessary that this medicinal herb be included in our bio-prospection program and screened/assayed for the antisickling effects.

**Keyword:** Traditional Medicine, *Ageratum conyzoides*, ethno-pharmacological validation.

**INTRODUCTION**

Medicinal plants have been known as a rich source of pharmaceutical agents for the prevention and treatment of diseases and ailments. According to the WHO, 80% populations living in the developing countries rely almost exclusively on traditional medicine for their primary health care needs [1]. Exploration of the chemical constituents of the plants and pharmacological screening may provide to researchers in the field of ethno-pharmacology the basis for developing the leads/hits for development of novel agents of pharmaceutical relevance [2-7]. Many species of plants in African countries are widely used in the rural communities where there is little or no access to modern medicine [8, 9]. *Ageratum conyzoides* L. (Compositae) is an annual herbaceous plant with a large spectrum of traditional medicinal and agricultural uses [10]. *Ageratum conyzoides* L. has a long history of traditional medicinal uses in many countries in the world, especially in the tropical and subtropical regions. In African traditional medicine, *Ageratum conyzoides* has been used as purgative, febrifuge, anti-ulcer and wound dressing [11].

A wide range of chemical compounds including alkaloids, flavonoids, chromenes, benzofurans and terpenoids have been isolated from this species. *Ageratum conyzoides* was found to contain pyrrolizidine alkaloids, a class of hepatotoxic and carcinogenic phytochemicals. Extracts and metabolites from this plant have been found to possess pharmacological and insecticidal activities [12]. The comprehensive account of the biological activities presented in this review will help researchers to valorize the potential use of this herb either in pharmaceutics or as an agricultural resource.

**BOTANY**

*Ageratum conyzoides* L. belongs to the family Compositae/Asteraceae tribe Eupatoriae. A large majority of the plants in this family are herbaceous while trees and shrubs were comparatively rare. The genus *Ageratum* consists of approximately thirty species [13].

Height. The stems and leaves are covered with fine white hairs, the leaves are petiolate, ovate up to 7.5 cm long, the apex acute, the base truncate to rounded, rarely cordate, the margins crenate. The inflorescence is purple to white head, less than 6 mm across and arrange in close terminal corymb of 8-15 heads. Involucres are campanulate, the bracts are 2-3 seriate, linear, sub equal, acute, sparsely pilose outside; corollas are all tubular, 1-1.5 mm long, the limb 5-cleft. The fruits are linear-oblong black achene with 5-angled and are easily dispersed while the seed are photoblastic and often lost within 12 months; pappi are 5 short scales, the scales are often serrate below ending in a long awn [14].

*A. conyzoides* L. is native to tropical America. It is now found in all warm and subtropical areas of the world that is very common in West Africa and some parts of Asia and South America. It is usually found in waste places, rice fields, gardens, old cultivations, low secondary growth forests, forest-edges, roadsides, water courses etc., where there is ample exposure to sunlight [15].
PHARMACOGNOSY

INSECTICIDAL PROPERTIES

Fumigant activity

Essential oils (EOs) from Ageratum conyzoides L. were extracted and tested against Tribolium castaneum Herbst, the storage grain insect. The EOs were found effective against Tribolium castaneum during in vivo as well as in vivo fumigant testing. There was no adverse effect on seed germination as well as on seedling growth of EOs treated seeds showing non-phytotoxic nature of the oils. Hence, these EOs may be recommended as botanical insecticide against insect invasion of stored food commodities, thereby enhancing their shelf life [16].

- Pediculicidal activity

Eugenol from Ageratum conyzoides L. (Asteraceae) was found to possess in vitro pediculicidal activity [17].

TOXICOLOGICAL PROPERTIES

Toxicological properties

In a 90 days subchronic toxicity and in vitro toxicity bioassays, Ageratum conyzoides (at 500 and 1000 mg/kg) increased significantly (p<0.05) the relative weight of the liver, the spleen and kidney as compared to control rats group. Ageratum conyzoides increased also significantly (p<0.05) hematomal and biochemical parameters such as ALP, ALT, AST, blood glucose and the number of platelets associated with a normocytic and normochromic anaemia. The cytotoxicity, determined by the MTT [3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenylyterazolium bromide] test and neutral red assay, has shown that the cytotoxicity of hydroalcoholic extract of Ageratum conyzoides and its total alkaloids was very close. These toxic effects were attributed to its total alkaloids especially to pyrrolizidine alkaloids which are present in this plant [18]. In brine shrimp cytotoxic assay, the extracts of Ageratum conyzoides showed LC$_{50}$ values 508.86 ± 6.62 with reference to vincristine sulfate (LC$_{50}$ values 0.76±0.04) [19]. However, Antai et al. [20] reported that treatment of rats with Ageratum conyzoides (200, 400 and 600 mg/kg body weight of the extract daily for 21 days) did not significantly alter the serum and liver levels of total protein, ALT, AST and ALP in all test groups suggesting that ingestion of the extract may not be toxic at the doses investigated.

Anti-proliferative/anticancer activities

The anti-proliferative effect of Essential oils from A. conyzoides was assayed by the measurement of MTT on LNCaP and PC-3 prostate cancer cell lines, and SF-763 and SF-767 glioblastoma cell lines. These Essential oils displayed only bioactivity on LNCaP and SF-763 cell lines [21]. However, Adetutu et al. [22] reported that A. conyzoides leaves (ethanol extracts) were cytotoxic to SK-MES 1 cells, which to some extent may support their traditional inclusion in herbal preparations for treatment of cancer and providing evidence that the studied plant extracts might be potential sources of anticancer drug. Adebayo et al. [23] confirmed previously this assumption and reported also that ethylacetate extract of Ageratum conyzoides exhibited the highest cytotoxic activity on A-549 and P388 cancer cells with IC$_{50}$ values of 0.68 and 0.0003 μg/mL respectively.

ANTIOXIDANT ACTIVITY

The ethanol extract of the plant leaves have reported to possess a significant dose-dependent DPPH free radical scavenging activity with an IC$_{50}$ value of 18.91 μg/ml compared to ascorbic acid (IC$_{50}$: 2.937 μg/ml) and butylated hydroxyanisole (IC$_{50}$: 5.10 μg/ml). The IC$_{50}$ value of the extract for NO scavenging (41.81 μg/ml) was also found to be significant compared to the IC$_{50}$ value of ascorbic acid (37.93 μg/ml). Moreover, the extract showed reducing power activity and Fe$^{2+}$ ion chelating ability [24]. Adebayo et al. [23] reported that Kaempferol isolated from the ethylacetate extract of A. conyzoides rapidly scavenged DPPH at a concentration of 130.07 ± 17.36 g/kg. Ageratum conyzoides was also reported to possess tissues protective effect. Ogunlade et al. [25] reported that in the absence of Ageratum conyzoides extract (ACE), the rats treated with ethanol had significantly increased liver enzymes [alanine aminotransferase (AST), aspartate aminotransferase (ALT) and alkaline phosphatase (ALP)] and MDA levels but these were decreased in ethanol+ACE group compared to the ethanol group. The histologies of concurrent ethanol+ACE treated group were similar to control groups. They conclude that Ageratum conyzoides protects the liver against alcohol induced damage. Essential oil and methanol extract of A. conyzoides L. were assayed for their antioxidant activity. Methanol extract showed the highest antioxidant activity in FRAP and DPPH assay, whereas essential oil showed greater lipid peroxidation inhibition than methanol extract [26].

THROMBOLYTIC PROPERTIES

Using an in vitro thrombolytic model, Rahman et al. [19] reported that Ageratum conyzoides had no significant thrombolytic effect in term of clot lysis.

ANTIDIABETIC ACTIVITY

Aqueous extract of Ageratum conyzoides (500 mg/kg body weight) was reported to reduce fasting blood glucose of experimental animals by 39.1%. Agungiade et al. [27] reported that, the plant species Ageratum conyzoides displayed comparably weaker hypoglycaemic effect than exhibited by reference hypoglycaemic agent (glibenclamide). The hypoglycaemic and antihyperglycaemic properties of the aqueous extracts of the leaves of Ageratum conyzoides L. were also evaluated in normoglycemic and in streptozotocin-induced diabetic rats by Nyuani et al. [28], in order to validate its use in folk medicine. Tested animals were given the aqueous extracts of the plant at the doses of 100, 200 and 300 mg/kg. These doses were tested also on glucose loaded normal male rats (Oral Glucose Tolerance Test). Of all the doses, the aqueous extracts at 200 and 300 mg/kg showed statistically significant hypoglycaemic and antihyperglycaemic activities. For the oral glucose tolerance test, 100 mg/kg dose only attenuated significantly the rise of blood glucose in normal fasted rats. Consequently, these results confirmed the hypoglycaemic properties of the leaves of Ageratum conyzoides.
ANTIBACTERIAL ACTIVITY

The ethanolic extracts of A. conyzoides showed the best activity against E. coli, S. aureus and MRSA but no activity against P. aeruginosa [22]. The A. conyzoides essential oil displayed also strongest antibacterial activity against the bacteria Staphylococcus aureus and Bacillus subtilis in a disk diffusion bioassay [26].

WOUND HEALING PROPERTIES

Arulprakash et al. [29] reported that the A. conyzoides extract increased cellular proliferation and collagen synthesis. Wounds treated with the extract were found to heal much faster, based on the improved rates of epithelialization and wound contraction, and on the histopathological results. They reported also that a 40% increase in the tensile strength of the treated tissue was observed. Thus, topical application of A. conyzoides accelerates the rate of wound healing.

NEMATICIDAL ACTIVITY

Recent reports indicated that the aqueous and ethanolic extracts of Ageratum conyzoides leaves possess larvicidal activities on the eggs (unembryonated and embryonated), first and second larval stages of Heligmosomoides bakeri. The extract activities were dose dependent. The ethanolic extract was more potent against embryonation (39.6±2.9%) than the aqueous extract (53.3±10.9%) at the highest concentration (3.75 mg/mL). Both types of extracts killed larvae. The aqueous extracts displayed EC_{50} of 4.76 and 2.29 mg/mL respectively for L(1) and L(2) larvae. Although, the ethanolic extracts showed intermediate activity EC_{50} of 1.323 and 1.511 mg/mL respectively for L(1) and L (2) larvae [30]. Ageratum conyzoides contains pyrrolizidine alkaloids (PA) which are toxic for human and livestock. They undergo a metabolic toxification process in the liver which is the first target organ for PA poisoning [12].

SCHISTOSOMICIDAL ACTIVITY

The in vitro schistosomicidal effects of the essential oil of Ageratum conyzoides L. (Ac-EO) against adult worms of Schistosoma mansoni was assessed by de Melo et al. [31]. Ac-EO was considered to be active, but less effective than the positive control (praziquantel, PZQ) in terms of separation of coupled pairs, mortality, decrease in motor activity, and tegumental alterations. However, Ac-EO caused an interesting dose-dependent reduction in the number of eggs of S. mansoni. Precocene I (74.30%) and (E)-caryophyllene (14.23%) were identified as the two major constituents of Ac-EO. These compounds were tested individually and were found to be much less effective than Ac-EO and PZQ. A mixture of the two major compounds in a ratio similar to that found in the Ac-EO was also less effective than Ac-EO, thus revealing that there are no synergistic effects between these components. These results suggest that the essential oil of A. conyzoides is very promising for the development of new schistosomicidal agents.

ANTIAFLATOXIGENIC ACTIVITY

Aflatoxin B (1) is a highly toxic and carcinogenic metabolite produced by Aspergillus species on food and agricultural commodities. Inhibitory effects of essential oil of Ageratum conyzoides, on the mycelial growth and aflatoxin B (1) production by Aspergillus flavus were studied by Nogueira et al. [32]. The essential oil inhibited fungal growth to different extents depending on the concentration, and completely inhibited aflatoxin production at concentrations above 0.10 µg/mL. Comparison by transmission electron microscopy of the fungal cells, control and those incubated with different concentrations of essential oil, showed ultra-structural changes which were concentration dependent of the essential oil of A. conyzoides. Such ultra-structural changes were more evident in the endomembrane system, affecting mainly the mitochondria. Degradation was also observed in both surrounding fibrils. The ability to inhibit aflatoxin production as a new biological activity of A. conyzoides L. indicates that it may be considered as a useful tool for a better understanding of the complex pathway of aflatoxin biosynthesis. Patil et al. [26] reported also that essential oil from A. conyzoides L. inhibits completely the growth and aflatoxin production of the toxigenic strain Aspergillus parasiticus. The oil demonstrates also a reduction in mycelia growth and decreased production of different aflatoxins in fungi. Volatiles from macerated green leaf tissue of A. conyzoides were also effective against A. parasiticus. The inhibitory activity against the Aspergillus group of fungi and production of aflatoxins may add a new dimension to its usefulness in the protection of stored product.

ANTIPROTOZOAL ACTIVITY

Trypanocide, antileishmanial and antiplasmodial effects

The dichloromethane extract prepared from aerial parts of Ageratum conyzoides L. (Asteraceae), a plant commonly used in folk medicine for a number of illnesses including sleeping sickness, was found to exhibit a prominent activity (IC_{50}=0.78 µg/mL) against bloodstream forms of Trypanosoma brucei rhodesiense, the etiologic agent of East African Human Trypanosomiasis (East African Sleeping Sickness). This extract also exhibited noticeable activities against Leishmania donovani (Kala-Azar, IC_{50}=3.4 µg/mL) as well as Plasmodium falciparum (IC_{50}=8.0 µg/mL). This activity was attributed to flavonoids [33]

Anticoccidial effects

Ageratum conyzoides is traditionally used to treat diseases associated with bleeding. Nweze and Obiwalu [34] conducted a study to determine the efficacy of Ageratum conyzoides in treating caecal coccidiosis of broilers. Acute toxicity test was done using thirty 28 days old broiler chicks which were divided into six groups of five birds each. The birds were given 250-3000 mg of extract/kg body weight orally. Control group received equal volumes of distilled water. The birds were observed for 24 h for signs of toxicity. Twenty-five growing broilers were divided into five groups of five birds each. At 35 days of age, birds in groups A to D were each infected orally with 8000 oocysts of Eimeria tenella. Fifteen days post-infection, groups A and B were treated with 500 and 1000 mg/kg of the extract, respectively. Group C received Amprolium in drinking water as 0.012 and 0.006% solutions for 7 days, respectively. Groups D and E were the negative and positive controls. No signs of toxicity were observed during the acute toxicity test. The faecal oocyst per gram of faeces decreased steadily in all the treatment groups until it became zero. The packed cell volumes, weight and red blood cell counts of the treated birds were significantly (P<0.05) higher than those of the infected untreated control. This confirms its ethnoveterinary use in the treatment of coccidiosis.

ANTI-INFLAMMATORY EFFECT

Moura et al. [35] studied the hydro-alcoholic extract of Ageratum conyzoides leaves for its anti-inflammatory effect on subacute (cotton pellet-induced granuloma) and chronic (formaldehyde-induced arthritis) models of inflammation in rats. The absence or presence of toxicity by prolonged use of plant extract was also evaluated through biochemical and hematological analysis of rats’ blood samples using daily oral doses of 250 or
500 mg/kg body wt., during 90 days. The authors demonstrated that the group of rats treated with plant extract (250 mg/kg body wt.; p.o.) had a 38.7% (p < 0.05) reduction in cotton-pellet granuloma. The development of chronically induced paw edema was also reduced significantly (p < 0.05) by the plant extract. The toxicity study did not show any treatment-related abnormalities in biochemical and hematological parameters. The biochemical analysis from blood samples drawn from group of rats treated orally with 500 mg/kg body wt. did, however, present 30.2% (p < 0.05) reduction of SGPT activity as compared to the corresponding control group. These results confirm the anti-inflammatory properties of A. conyzoides, with no apparent hepatotoxicity.

** RADIO-PROTECTIVE EFFECT**

Jagetia et al. [36] evaluated the effect of various doses (0, 25, 50, 75, 100, 125, 150, 300, 600 and 900 mg/kg) of the alcoholic extract of the plant Ageratum conyzoides L., on the alteration of radiation-induced mortality in mice exposed to 10 Gy of gamma radiation was studied. The acute toxicity studies showed that the drug was non-toxic up to a dose of 3000 mg/kg, the highest dose that could be tested for acute toxicity. Administration of plant extract resulted in a dose-dependent decline in radiation-induced mortality up to a dose of 75 mg/kg, the dose at which the highest number of survivors (70.83%) was observed. Thereafter, the number of survivors declined with increasing doses of plant extract and a nadir was reached at 900 mg/kg. Since the number of survivors was highest for 75 mg/kg, this was considered by the authors as the optimum dose for radioprotection. In second experiment, mice were treated with 75 mg/kg of plant extract before exposure to 6, 7, 8, 9, 10 and 11 Gy of gamma radiation. The treatment of mice with plant extract at the dose of 75 mg/kg reduced the severity of symptoms of radiation sickness and mortality at all exposure doses, and a significant increase in survival was observed compared with the non-treated irradiated group. It was postulated that the plant extract treatment effectively protected mice against the gastrointestinal as well as bone marrow related death, as revealed by the increased number of survivors at all irradiation doses. The dose reduction factor was found to be 1.3. To understand the mechanism of action, the authors evaluated the various doses of the plant extract for their in vitro scavenging action on 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical. Extract from this plant was found to scavenge DPPH radicals in a concentration-dependent manner, indicating that the radioprotection afforded by this plant may be in part due to the scavenging of reactive oxygen species induced by ionizing radiation.

** GASTROPROTECTIVE EFFECT**

The ethanol extract of Ageratum conyzoides was evaluated for gastroprotection in rats using the Ibuprofen, ethanol and cold restraint stress ulcer models by Shirwaikar et al. [37]. The efficacy was assessed by determination of mean ulcer size, ulcer number and ulcer index. Oral administration of the ethanol extract at dose levels of 500 and 750 mg/kg significantly protected gastric lesions by 80.59 and 89.33%, respectively, as compared to Misoprostol (74.43%) in the Ibuprofen model; by 97.09 and 99.24%, respectively, in the cold stress model as compared to Famotidine (77.86 and 92.71%) and by 86.58 and 92.29%, respectively, in the alcohol model. The findings suggest that the significant gastroprotective activity could be mediated by its antioxidant activity, Ca^2+ channel blocking and antiserotopogenic properties.

**MYORELAXANT EFFECT**

The water soluble fraction of Ageratum conyzoides L. was studied in isolated rat uterus and intestinal smooth muscles by Sylva et al. [30] in order to evaluate its popular use as a spasmyloytic. Plant extracts (0.2 and 0.4 mg/mL) increased EC50 values and decreased maximum responses to acetylcholine and calcium chloride. The extract (0.5-3.3 mg/mL) also produced direct myorelaxant effect on smooth muscle preparations. These results seem to be partially linked to calcium mobilization. The results give support to the popular medicinal indications of the plant.

**ELECTROPHYSIOLOGICAL EFFECTS**

Garcia and Carvalho [39] demonstrated that an extract obtained from the leaves of Ageratum conyzoides L. changed the electrocardiogram, atrial impulse velocity, and coronary vessels resistance on isolated guinea-pig heart. Electrocardiographic alterations were: (a) PR interval increased from 80±1.4 ms to 105±14 ms (p < 0.01); (b) QT interval decreased from 170±2 ms to 154±7 ms (p < 0.01); (c) heart rate decreased from 170±17 bpm to 152±21 bpm (p < 0.01); (d) atrial impulse velocity decreased from 51±2 cm/s to 45±3 cm/s (p < 0.01); (e) the time spent for the impulse to be conducted from the atrium to the His bundle increased from 73±13 ms to 100±24 ms (p < 0.01). These effects disappeared after a washout.

**HAEMATOPOIETIC EFFECT**

The potential haematological effects associated with the administration of ethanolic leaf extract of Ageratum conyzoides was investigated by Ita et al. [40] in rats. The authors used 27 rats which were randomly divided into four groups. The first group had 6 rats and served as control, the remaining 3 experimental groups and had 7 rats each. These later groups were treated with the extract of Ageratum conyzoides in concentrations of 200 mg/kg, 400 mg/kg and 500 mg/kg respectively for 30 days at a dose of 0.1 ml/body weight. The control group was gavaged with 0.9% sodium chloride at a dose of 0.1 ml/body weight as placebo. The extract at the doses administered was found to increase in a dose-related fashion PCV and Hb (P < 0.01) for 200 mg/kg and P < 0.001 for 400 mg/kg and 500 mg/kg), RBC (P < 0.05) for 400 mg/Kg and 500 mg/kg) and marginal increases that were not significant for 200 mg/kg); MCH and MCV (P < 0.05) and [P < 0.01] for 400 mg/kg and 500 mg/kg respectively) 200 mg/kg was not significant. MCHC recorded no significant change. WBC recorded marginal increases that were not significant, similarly, the differential white blood cell recorded marginal increases that were not significant, except lymphocytes that recorded significant increase in group 4 [P < 0.05]. Marginal decreases in body weight were also observed, these decreases were however not significant. The result of this study thus indicates haematopoietic potentials of the extract and could possibly remedy anaemia.

**CONCLUSION**

The results of the present review revealed that Ageratum conyzoides L. is a multipurpose herb and will allow researchers to develop drugs of substitution (phytomedicines) at low cost for the local market, developed, manufactured and distributed in the difficult economic context. Because of its established hematopoietic properties, it is therefore necessary that this medicinal herb be screened/ assayed for the antisickling effects.

**Acknowledgments**

The authors are indebted to the International Foundation for Science (IFS, Stockholm, Sweden) and the Organization for the Prohibition of Chemical Weapons (OPCW) for research grant
REFERENCES:


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