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REVIEW ARTICLE

Ageratum conyzoides L.: A review on its phytochemical and pharmacological profile

Anjoo Kamboj, Ajay Kumar Saluja[1]
Guru Gobind Singh College of Pharmacy, Yamuna Nagar - 135 001, Haryana, India, [1]A.R. College of Pharmacy, Vallabh Vidhyanagar - 388 120, Gujarat, India

Ageratum conyzoides L. (AC) is an annual herbaceous plant with a long history of traditional medicinal uses in many countries in the world, especially in the tropical and subtropical regions. The weed has been known since ancient times for its curative properties and has been utilized for treatment of various ailments, such as burns and wounds, for antimicrobial properties, for many infectious conditions and bacterial infections, arthrosis, headaches and dyspnea, pneumonia, analgesic, anti-inflammatory, antiasthmatic, antispasmodic and haemostatic effects, stomach ailments, gynaecological diseases, leprosy and other skin diseases. A wide range of chemical compounds including alkaloids, cumarins, flavonoids, chromenes, benzofurans, sterols and terpenoids have been isolated from this species. Extracts and metabolites from this plant have been found to possess pharmacological and insecticidal activities. This contribution provides a comprehensive review of its ethnomedical uses, chemical constituents and the pharmacological profile as a medicinal plant. Particular attention has been given to analgesic and anti-inflammatory, antibacterial and wound healing properties, radioprotective, antifungal, anthelmintic and nematicidal, insecticidal effects presented in this review such that the potential use of this plant either in pharmaceutics or as an agricultural resource can be evaluated.

Key words: *Ageratum conyzoides*, alkaloids, benzofurans, bioactivity, chromenes, flavonoids, terpenoids

INTRODUCTION

Ageratum is derived from the Greek words 'a geras', meaning non-aging, referring to the longevity of the whole plant. Conyzoides, on the other hand, is derived from 'konyz' the Greek name of *Inula helenium*, which the plant resembles.[1] The plant belongs to the family Asteraceae tribe Eupatorieae. This family is well marked in their characteristics and cannot be confused with any other. The genus Ageratum consists of approximately 30 species but only a few species have been phytochemically investigated.[2]

It is a tropical plant that is very common in West Africa, Australia, some parts of Asia and South America. It is an erect, annual, branched, slender, hairy and aromatic herb, which grows to approximately 1 m in height. The stems and leaves are covered with fine white hairs, the leaves are stalked, ovate, 4-10 cm long and 1-5 cm wide, with tip and base somewhat pointed and with round-toothed margins long. The flowers are purple to white, less than 6 mm across and arranged in close terminal inflorescences. The fruit is black and are easily dispersed while the seeds are photoblastic and often lost within 12 months.[3] The plant grows commonly in waste and on ruined sites. It has a peculiar odour likened in Australia to that of a male goat and hence its name 'goat weed' or 'billy goat weed'.

The essential oil obtained from plant has been reported to have a powerful nauseating odour[4] and found to be poisonous to rabbits due to the presence of HCN and coumarin.[5] The herb is not eaten by humans except for medicinal purposes, but in some cultures, it is a delicacy for domestic guinea-pigs, horses, cattle,[6] and also used to feed fish.[7] Presence of Pyrrolidine alkaloids are known to hepatotoxic and to cause lung cancer and other ailments[8] but of biological interest due to their association with Leptidoptera.[9]

ETHNOPHARMACOLOGY

Ageratum conyzoides (AC) has been used in various parts of Africa, Asia, and South America for curing various diseases. Githen, in his review[10], listed the uses of the plant as purgative, febrifuge, for ophthalmia, colic, treatment of ulcers, and wound dressing. The antienteralgic and the antipyretic properties of the plant were also indicated in a review on 'Medicinal plants from Senegal'.[11] In some African countries, the plant has been popular use for skin diseases, wound healing, mental and infectious diseases, headaches and dyspnea,[12,13] and used in traditional medicine for its anti-asthmatic, antispasmodic and haemostatic effects,[14] uterine troubles, pneumonia by rubbing them on the chest of the patient.[15] In Cameroon, it is a local remedy for craw-craw.[5]

In India, it is used in the treatment of leprosy and as an oil lotion for purulent ophthalmia.[16] The decoction or infusion

For correspondence: Anjoo Kamboj, GGS College of Pharmacy, Yamuna Nagar - 135 001, Haryana, India.
E-mail: anjoo73_kamboj@indiatimes.com
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of the herb is given in stomach ailments such as diarrhoea, dysentery, intestinal colic, flatulence, rheumatism, fever[17] and to relieve pain associated with navel in children.[15] In Brazil, medicinal tea plants are used as anti-inflammatory, analgesic and anti-diarrhoeic[18] and for gynaecological diseases (in Vietnam).[19] Other folk remedies include anti-itch, sleeping sickness, mouthwash for toothache, antitusive, vermifuge, tonic and killing lice (flowers).[20] The leaves are used for application on cuts, sores;[21-25] as anti-inflammatory agent, haemostatic;[26-30] as an insecticide;[31] in headache;[20,32] in boils;[33] skin diseases;[34] ringworm infection;[35] in typhoid, as an antidote to snake poison;[36,37] in malarial fever, as antitetanus; for uterine problems;[38,39] prolaps of anus;[40] for swollen piles;[41] in throat infection, painful gums; on abscess for early suppuration; in wound healing and leucorrhoea.[42-45] The root is used as an antilithic[21,26,38] and in infant diarrhoea.[46] It has been reported to have nematocidal activity and have potential use in controlling pests.[2,47] It is the only plant used in HIV/AIDS disease.[48]

Ageratum conyzoides also has a number of magical and superstitious attributes, e.g. in Ivory Coast, it has protective fetish properties for followers of Snake-Sect against snakebite. In Congo, the leaf sap on the hands of card players is believed to improve their luck. If sap is spread on the accused in a trial and is then pricked with a needle, pain will be felt only if guilty.[2]

PHYTOCHEMISTRY

The oil content varies randomly from 0.11 to 0.58% for leaves and from 0.03 to 0.18% for the roots depending on times of the year.[49] From water distillation of the fresh flowers, the oil content was found to be 0.2%.[4] The yield of oil from the petroleum ether extract of the seed was 26%.[50]

Mono and Sesquiterpenes

The GC-MS analysis of the essential oil showed that it is a complex mixture of 213 compounds of which 43-51 constituents have been reported. The constituents identified include 20 monoterpenes 6.4% [13 monoterpenoid hydrocarbons (5.0%), 7 oxygenated monoterpenoids (0.08-1.4%)], 20 sequiterpenes 5.1% [16 sesquiterpenoid hydrocarbons (4.3%), four oxygenated sesquiterpenoids (0.8%)] and three phenylpropanoids and benzenoids (2.33%). The most abundant monoterpenes include sabinene, β-pinene 1.6%, β-phellandrene, 1,8-cineole and limonene 2.9%, terpinen-4-ol 0.6%, α-terpineol, linalool 0.5%, α-pinene 6.6%, eugenol 4.4% and methyleugenol 1.8%. Sesquiterpenes hydrocarbons (26.48% of the oil) contain β-caryophyllene (19.79%), caryophyllene epoxide (0.5%), β-sesquiphellandrene (1.2-1.99%), δ-cadinene (4.3%) and τ-cadinene (1.44%) as the major components.[51-53] The major sesquiterpenes are β-caryophyllene 1.9%, 10.5% from the oil obtained from Cameroon[51,54] and 14-17% in Pakistani oil.[55] The oxygenated sesquiterpene hydrocarbons (69.29% of oil) comprised ageratochromene (32.90%), 6-methoxyquinoline-1-oxide (20.77%), β-caryophyllene oxide (7.29%) and β-sinensal (5.82%) as the major components.[51,52] Ocimene is found in trace amount in Nigerian plant and 5.3% of the oil from Indian plant.[53]

Chromene, Chromone, Benzofuran, and Coumarin

The most common components of the essential oil are 7-methoxy-2,2-dimethylchromene (precocene I) ranging from 30 (Vietnamese oil) to 93% (Congo oil), 6,7-dimethoxy derivative, ageratochromene (precocene II) ranges from 0.7 to 55%[49,56-58] and ageratochromene dimmer.[16-59] Other related compounds include encecalin, 6-vinyl-7-methoxy-2,2-dimethyl chromene, dihydroencecalin, dihydrodemethoxyencecalin, demethoxyencecalin, demethylencecalin and 2-(1′-oxo-2′-methylpropyl)-2-methyl-6,7-dimethoxychromene.[60,61] In addition, seven other chromene derivatives isolated from hexane extract of the aerial part of the plant are 2,2-dimethylchromene-7-O-β-glucopyranoside,[61,62] 6-acetyl-2,2′-dimethyl-3,4-dihydrochromene,[51] 6-(1-methoxy ethyl)-7-methoxy-2,2-dimethylchromene, 6-(1-hydroxy ethyl)-7-methoxy-2,2-dimethylchromene, 6-(1-ethoxyethyl)-7-methoxy-2,2-dimethyl chromene, 6-angeloyloxy-7-methoxy-2,2-dimethylchromene and an inseparable mixture of encecanescins.[63] Benzofuran derivatives, 2-(2′-methylethyl)-5,6-di methoxybenzofuran,[60,61] 14-hydroxy-2Hβ, 3-dihydroeuparine,[62] 6,7,6′,7′-tetramethoxy-2,2,2′, 2′-tetramethyl-3′(4′)-dehydro-3′-4S-bi chroman[16,59] as well as chromone derivatives, 3-(2′-methyl propyl)-methyl-6,8-dimethoxychrom-4-one and 2-(2′-methylprop-2′-enyl)-2-methyl-6,7-dimethoxychroman-4-one have also been reported from the plant.[60,61] The essential oil from Brazil has been reported to yield 1.24% of coumarin.[64] The ethanolic extract of the plant was found to be devoid of tannins.[65]

Flavonoids

Ageratum conyzoides is very rich in polyoxygenated flavonoids. A total of 21 polyoxygenated flavonoids have been reported. This includes 14 polymethoxylated flavones that are tricin derivatives, 3′,4′,5′-oxygenated flavones, which include ageconyflavone A, ageconyflavone B and ageconyflavone C, other flavonoids include 5′-methoxynobiletin, linderoflavone B, 5,6,7,3′,4′,5′-hexamethoxyflavone, 5,6,8,3′,4′,5′-hexamethoxyflavone, eupalestin, nobiletin, 5,6,7,5′-tetramethoxy-3′,4′-methylenedioxyflavone, sinensetin, 5,6,7,8,3′,5′-hexamethoxyflavone, 5,6,7,8,3′-pentamethoxy-4′-hydroxyflavone and 5,6,7,8,3′,5′-hexamethoxy-4′-hydroxyflavone. Conyzorigun originally believed to be a phenoxy chromone was found to be identical with eupalestin.[164] The polyhydroxyflavones

include scutellarein-5,6,7,4′-tetrahydroxyflavone, quercetin, quercetin-3-rhamanopiranoside, kaempferol, kaempferol-3-rhamnopiranoside and kaempferol-3,7-diglucopiranoside. A novel isoflavone glycoside, 5,7,2′, 4′-tetrahydroxy-6,3′-di-(3,3-dimethylallyl)-isoflavone 5-O-α-L-rhamnopyranosyl-(1→4)-α-L-rhamnopyranoside isolated from the stems.[57,63,66-74]

Triterpene and Sterols

The triterpenes isolated from plant are friedelin, and the major sterols are sterols-β-sitosterol (26.7%) and stigmasterol (59.9%). Other minor sterols isolated are brassicasterol (0.3%) and dihydrobrassicasterol (2.7%), spinasterol (5.2%), dihydrospinasterol (5.7%). The leaves also contain a rare sterol, stigmast-7-en-3β-ol.[75-79]

Alkaloids and Miscellaneous Compounds

Lycopsamine and echinatine, two isomeric pyrrolizidine alkaloids, are the only alkaloids isolated from this plant.[78] Other compounds isolated from plant include (+)-sesamin,[63] aurantiamide acetate,[79] fumaric acid, caffeic acid,[73] phytol, HCN and hydrocarbons, from nC_{27}-H_{56} to nC_{32}-H_{66},[9] (Z) 12-(6-methyl)-heptadecenoic acid.[80] The seed oil was found to contain oleic acid (25.52%),[81] palmitic, stearic, linoleic, linolenic and hexadecenoic acids.[50] The amino acid composition in the leaves and flowers are cystine, leucine, histidine, arginine, serine, alanine, tyrosine, valine, phenylalanine and threonine, glycine (trace).[82] The amino acid composition of the pollen was found to 0.5-4.0% of the total dry weight. They are amino-n-butyric acid, aspartic acid, cystine, isoleucine, methionine, proline, tryptophan, tyrosine, ornithine, glutamic acid and glycine.[83] The protein content found in the leaves is 4.69% and in flowers 9.37%. Leaves and flowers contain in addition fructose, ribose and glucose and vitamin B while vitamin A was reported to be present in the flowers.[84,85]

BIOACTIVITY

Ageratum conyzoides is a plant used in traditional medicine for mental and infection diseases, dyspnea, enteralgia and fever. The plant was reported to have significant antifungal and insecticidal properties. The biological activities of the plant are treated under two subheadings: (i) pharmacological properties and (ii) insecticidal and other biological properties.

PHARMACOLOGICAL PROPERTIES

Crude Extract

The crude extract of the whole plant has been reported to be superior to vaseline gauze as a wound dressing material.[70] It has been found to have neuromuscular blocking activity in isolated rat's phrenic nerve-diaphragm and also caused greater fall in diastolic pressure compared with that of systolic pressure in anaesthetized rats. It has calcium blocking activity similar to that of verapamil.[86] The leaf extract has been used in the treatment of chronic pain in osteoarthrotic patients.[87] It has antimicrobial and anticonvulsant activities.[14,88] Aqueous extract of the leaves has been reported to prevent coagulation of the whole blood while causing precipitation of some blood materials and the bleeding time was also decreased.[89]

Cardiovascular Activities

The water soluble portion of the plant potentiated pentobarbitone-induced hypnosis in mice in a dose of 1 g/kg. It produced hypotensive response in dog, which was not blocked by propranolol, anthisan or atropine. The extract revealed negative inotropic and chronotropic effects in doses of 10-40 mg on frog's perfused heart, which was not blocked by atropine. It showed a direct vasodilatory response in rats, and its smooth muscle activity similar to papaverine. The extract had no analgesic and anticonvulsant activity.[90] The essential oil in a concentration of 0.1 ml/ml caused contraction of the isolated frog rectus abdominis within 15 s after administration and showed a graded response up to a dose of 0.3 ml. The plant (leaves and root) was devoid of *in vivo* cholinesterase activity.[91]

The aqueous extract of leaves is reported to show haemostatic activity. The activity is observed probably due to vasoconstriction and the formation of an artificial clot that tend to produce a mechanical plug to arrest bleeding from small blood vessels. The plant extract exhibited muscle-relaxant activity on isolated rabbit ileum and cardio-depressant activity on isolated heart.[89,92] The leaves extract changes the electrocardiogram, atrial impulse velocity and coronary vessel resistance on isolated guinea-pig heart.[93]

Analgesic and Anti-inflammatory Activities

Clinical trials in patients with arthrosis have been conducted with the aqueous extract of the whole plant. Result shows analgesic effect in 66% of patients and improvement in articulation mobility in 24% without side effect.[94] In another study, the analgesic activity of the leaf extract was detected by hot plate method.[95] The extract decreased spontaneous motor activity and caused a fall in rectal temperature. *In vitro* receptor radio ligand assay was carried out on the extract to demonstrate its selectivity to a single receptor implicated in the mediation of pain. Result showed more than 50% inhibition in the bradykinin (BK II) assay, but the activity was lost after PVP treatment suggesting that phenolic compounds could be responsible for the initial bioactivity.[96] The extracts, however, did not produce positive effects in the neurokinin (NKI) and calcitonin gene-related peptide (CGRP) assays.

The antinoceptive properties were analyzed in the wistar rat by using Martin *et al.*, method slightly modified. The rectal temperature was sampled and analgesic activity evaluated by the hot plate method and by the writhing syndrome induced by acetic acid. The results obtained demonstrate that the doses of 50 and 100 mg/kg are selected for experiment it causes: a precocious ataxia, sedation and a slight ptosis for 6 h after injection.[18,95]

Aqueous extract of an association of AC, *Cymbopogon citrates* and *Lippia multiflora* produced a significant reduction in mouse of writhings induced by acetic acid and an increase of pain threshold in the hot plate test in mice. Presence of saponins and flavonoids supports the observed activities and suggests that this association of three plants could be used as traditional improved preparation.[97]

The water soluble fraction of the plant extract produces peripheral analgesic activity and an anti-inflammatory action, which seems to occur in leucocyte-dependent inflammatory events.[98,99] Silva *et al*., investigating the effect on smooth muscles using isolated rat uterus and intestine smooth muscles, concluded that the fraction possesses substances, which provoke direct relaxing effect on smooth muscles and inhibit contraction induced by several agonists possibly by blocking the entry of calcium and/or inhibiting cAMP phosphodiesterase.[100] These pharmacological characteristics could explain the popular use of AC to alleviate abdominal and menstrual pains. The aqueous extract of leaves was evaluated for their cytoprotective activity against ethanol-induced gastric lesions in rats. Microscopically, pretreated rats with aqueous extract or cimetidine showed significantly marked inhibition of gastric lesions and marked reduction of submucosal oedema compared to control group.[101]

The ethanolic root extract of plant in a dose of 100 and 300 mg/kg significantly reduced the carrageenin-induced hind pawoedema in rats with no acute toxic effect in mice.[102] The hydroalcoholic extract of leaves was studied for its anti-inflammatory effect on subacute (cotton pellet-induced granuloma) and chronic (formaldehyde-induced arthritis) models of inflammation in rats and evaluated by biochemical and haematological analysis of rats blood samples. The results confirm the anti-inflammatory properties with no apparent hepatotoxicity.[103] The ethanolic extract also showed significant gastroprotective activity that could be mediated by its antioxidant activity, Ca^{2+} channel blocking and antiserotogenic properties.[104] The ethanolic extract of roots possesses anti-inflammatory and analgesic properties.[102]

Antibacterial and Wound Healing Properties

The antibacterial properties of methanolic extract were studied against 11 wound isolates *S. aureus* (four strains), *E. coli* (two strains), *P. aeruginosa* (one strain), *Proteus* spp. (three strains) and *Shigella* spp. (one strain) using the well diffusion method. Wound healing properties were determined using the excision wound model. More than 90% wound healing was recorded in the extract, whereas 72% healing was observed in the distilled water-treated group.[105,106] The leaf extract was found to be active against *C. falcatum* and *R. solani*[107] and showed strong toxicity against the fungi causing ringworm, *E. floccosum*, *T. mentagrophytes* and *M. gypseum*, the inhibition of the mycelia being 80.28, 78.43 and 68.24%, respectively.[108] The extract of leaves, however, had no effect on the conidial germination of the fungus *D. oryzae*.[109] In a study, it was found that wounds treated with aqueous leaves extract in combination with honey and with solcosery ointment significantly accelerate wound healing process and the rates of wounds sterility compared to wounds treated with honey alone.[110,111]

The Nigerian traditional soft soaps prepared using varied locally sourced raw materials have been evaluated antimicrobial activities using standard pharmacopoeia protocols and an *in vitro* agar diffusion bioassay method. The incorporated medicinal plants used did not show any significant effect on the antimicrobial activities exhibited by the various soaps against the bacterial and fungal test organisms.[112]

Antibacterial activity of aqueous extract were tested against three Gram-positive bacteria and seven Gram-negative bacteria and evaluated by the filter paper disc diffusion method. Results showed a significant control of the growth of *A. viscolactis*, *K. aerogenes*, *B. cereus* and *S. pyogenes*.[113,114,161] In an investigation for *in vitro* anti-methicillin-resistant *Staphylococcus aureus* (MRSA) activity found that MIC range of 55.4-71.0 mcg/ml were recorded for ethanol and water extracts of AC. The concentrations were too high to be considered active and AC were found to be ineffective *in vitro* in the study; therefore, suggest the immediate stoppage of their traditional use against MRSA-associated diseases in Lagos, Nigeria.[115]

Radioprotective Activity

The effect of alcoholic extract of the plant on the alteration of radiation-induced mortality in mice exposed to 10 Gy of gamma radiation was studied. The mice were treated with 75 mg/kg (optimum dose) AC extract before exposure to 6, 7, 8, 9, 10 and 11 Gy of gamma radiation. The AC extract treatment effectively protected mice against the gastrointestinal as well as bone marrow-related death. In an *in vitro* study, AC extract was found to scavenge 1,1-diphenyl-2-picrylhydrazyl (DPPH) radicals in a concentration-dependent manner, indicating that the

radioprotection may be due to the scavenging of reactive oxygen species induced by ionizing radiation.[116]

Reproductive Problems

Many herbal remedies are traditionally used as contraceptives, abortifacients, emmenagogues or oxytocics. Forty-two plants are used for reproductive problems of men and women. AC is used to treat the prostate problems, unspecified female complaints and venereal disease. The AC extract inhibited uterine contractions induced by 5-hydroxy tryptamine suggesting that the extract exhibited specific antiserotonergic activity on isolated uterus but had no effect on uterine contractions induced by acetylcholine. The results support the popular use of the plant as a spasmolytic.[117,162]

Essential Oil

Essential oil of AC has been tested for anti-inflammatory, analgesic and antipyretic activities in mice and rats. The oil was found to have a significant anti-inflammatory cotton pellet granuloma activity and the antipyretic Brewer's yeast injection effect, whereas the analgesic tail-flick and writhing test activity with no gastric toxicity.[118]

Antibacterial and Antifungal Activities

The essential oil obtained from the plant showed antibacterial activity against *V. cholerae*, *S. shigae*, *S. pyogenes*, *C. diphtheriae* and *S. typhi*,[119,120] whereas it was devoid of any activity against the potato pathogenic bacteria viz., *B. polymyxa*, *E. carotovora* var. atroseptica, *E. carotovora*, *P. putida*, *P. solanacearum* and *X. vesicatoria*.[113] In other study, oil exhibit antibacterial and antifungal activities against 22 bacteria, including Gram-positive cocci and rods and Gram-negative rods and 12 fungi (three yeast-like and nine filamentous).[121] The total inhibition of growth was recorded against the four fungi, *C. albicans* SP-14, *C. neoformans* SP-16, *S. rolfsii* SP-5 and *T. mentagrophytes* SP-12. Rao[122] reported that the oil inhibited the growth of five bacteria as well as 10 fungi species and that the major component of the oil demethoxyageratochromene[1] was effective against two of the fungi, *P. chrysogenum* and *P. javanicum*.[51] The oil provided 100% inhibition of the mycelial growth and germination of spores of *Didymella bryoniae*.[123] The volatile oil extracted from the leaves possesses molluscicidal property.[51,124]

Industries have researched on the use of essential oils as an alternative for the treatment of some microbiologic pathologies. *A. flavus* is a fungus present in food and feeds and can produce aflatoxins under some environmental conditions. The effect of the essential oil and crude ethanolic extract on *A. flavus* growth was carried out by the disc diffusion method. The essential oil of AC was able to inhibit *A. flavus* growth, but crude ethanolic extract was not effective against the tested fungal in the concentration used. In another study, the essential oil of the plant showed antifungal activity against *H. turcicum*, *H. oryzae*, *C. capsici*, *P. setariae* and *F. moniliforme*.[114,125] At a concentration of 2000ppm, the oil exhibit strong antifungal activity against *E. floccosum*, *M. canis* and *T. mentagrophytes*.[126]

Anthelmintic and Nematicidal Activity

The essential oil of the plant exhibited anthelmintic activity against *T. solium* and *P. posthuma*.[127] The extract of the stem and leaves exhibited nematicidal activity against second stage juveniles of *Meloidogyne incognita* (kofoid and white) chitwood.[128,129]

Metabolites

Pharmacological activities of the most significant metabolites from this plant, responsible for the medicinal properties, have not been identified. There are however, a wide spectrum of pharmacological activities of the classes of compounds obtained from this plant. For example, simple chromenes and chromans, especially the 6-amino and 6-acetamido derivatives, have been reported to have anti-depressant, analgesic and antipyretic properties. Some of them possess activity against flat worms of the order of trematodes.[130] Other simple 2,2-dimethyl chromene derivatives, such as 6-(1-hydroxyethyl)-7,8-dimethoxy-2,2-dimethylchromene and 6-hydroxy-7,8-dimethoxy-2,2-dimethyl chromene, have been shown to have antimicrobial activities.[131]

The sterols, especially stigmasterol, have been shown to exert significant anti-inflammatory activity.[132] The flavonoids possess a wide range of biological activities that include effects on CVS, diuresis, spasmolytic, antiviral and anti-inflammatory properties.[15,19] The free radical scavenging and anti-cancer activities of the flavonoids are well known. Two polymethoxyflavones are found to have potent activity for inducing differentiation of human promyelocytic leukemia cells (HL-60). Although the biological activities of flavonoids isolated from AC have not been investigated, the polymethoxyflavones are important candidates for cancer-protective action.[133]

Insecticidal and Other Biological Properties

Insecticidal activity

Ageratum conyzoides has bioactivity that may have agricultural use. The crude plant extract also showed insecticidal and pesticidal activities against various types of insects and pests. The major components of the oil, namely the precocenes, have been reported to have antijuvenile hormonal activity.[163] The oil exerted acute toxicity on adults of cowpea weevil, *Callosobruchus maculatus* F., upon fumigation. Application of oil dressing on cowpea seed exhibited insecticidal activity against weevil. Significant oviposition deterrence and complete inhibition of emergence of adult insects F1 offspring from oil-treated

beans were evident at 2.5-10 µl/9.5 g beans with no adverse physiological effect. Precocene I was found to be four times as active as the oil.[134]

Assays conducted in India showed high nymphal mortality 91% of the oil to the Nymphs of *S. gregaria*.[61] Calle *et al*. showed that the hexane extract of the whole plant showed activity against *M. domestica* larvae.[135] Methanolic extract from fresh leaves (250 and 500 ppm) also produced deficiency of juvenile hormone in the fourth instar of *C. partellus*, a sorghum pest.[136] Antijuvenile hormonal activity of Precocenes I and II have been demonstrated on a variety of insects, which include *S. oryzae*, *T. japonica*, *L. chinensis* and *D. flavidus*.[137] The results from these assays include precocious metamorphosis of the larvae, production of sterile, moribund and dwarfish adults. The two chromenes have been reported to act synergistically and they survived metabolism for at least 12 days.[137] Preliminary study on the mode of action of precocene II on *M. domestica* L. and *L. caesar* L. has been carried out.[138] While the precocenes have been seen as fourth-generation insecticides, the drawback is that they have been shown to cause hepatotoxicity in rats.[139-141] This is an important factor bearing in mind the human health hazard in field applications of precocenes as large-scale insecticidal agents. Some workers demonstrated that the toxicity was due to a highly reactive precocene-3,4-epoxide, a metabolite produced in insect species from cytochrome P-450.[139,140] Others, like Darvas *et al.* and Casas *et al*.[142,143] reported that the 3,4 double bond played no significant role in the toxicity but that the oxidative dealkylation process at C7 position, as tocopherol-like antioxidants, might be responsible for the cytotoxicity.

The insecticidal activities of hexane and ethanol extract were evaluated against adults of *R. dominica*. Only the hexane extract showed insecticidal activity. 5,6,7,8,3′,4′,5′-Hepta methoxyflavone showed low activity against *D. hyalinata* and *R. dominica* and was not toxic to *M. domestica* or *P. americana*. In contrast, coumarin showed insecticidal activity against all four insect and pest species tested.[144] The extract of the plant was found to exhibit juvenilizing effect on *D. cingulatus* nymphs.[65]

The alcoholic extract of the plant possessed insecticidal activity against *M. domestica* and *T. castaneum*.[145] The petroleum ether and acetone extract of the plant showed juvenile hormone activity against *C. quinquefasciatus*, *A. aegypti* and *A. stephensi*.[146,147] The methanolic extract of the plant was found to suppress the population of the malaria vector *A. stephensi* in higher dosage, whereas in lower dosage it was found to induce several developmental defects and ultimately decrease the growth index to a considerable extent.[146] In another study, higher concentrations of the crude extract suppressed the vector population of *C. quinquefasciatus*, whereas the lower concentrations were found to induce developmental defects ultimately decreasing the growth index of the treated second and fourth instar larvae.[63,96,127,148]

The petroleum ether extract of the leaves, flowers and buds diluted in benzene and mixed with green gram seeds proved very repulsive, a potent oviposition inhibitor and a safe protectant against the infestation of pulse beetle *C. chinensis*.[149] The crude extract of the plant showed insecticidal activity against nymphs of mustard aphid *L. erysimi*.[150]

Allelopathy and Allelopathic Potential

Both the volatile oil and the aqueous extract of AC have been shown to have allelopathic effects on a number of cultivated crops. These include radish, mungbean and ryegrass.[151] The saturated aqueous solution of the isolated and purified precocenes I and II have been reported to have significant inhibitory effect on the seedling growth of radish, tomato and ryegrass.[152] The allelopathic potential of the aqueous extract from different organs of AC and from its different development stages, especially from different habitats, was different.[153,160]

The inhibitory effects of AC volatiles on peanut, redroot amaranth, cucumber and ryegrass increased when plants were grown under nutrient-deficient conditions or in competition with *B. pilosa*; however, there was no difference with physical damage or 2.4-D treatment. Phytoinhibitory effects decreased under fungal infection and aphid feeding. Volatiles from AC plants infected with *E. cichoracearum* or exposed to *A. gossypii* feeding inhibited or killed fungi and insects.[154]

Phytotoxic Action

Ageratum conyzoides showed strong inhibition on *R. sativus*, *L. germination* and growth in a bioassay. The leaves exhibited a greater suppression than the stem and root. Application of AC leaves at 2 t/ha in a paddy field 2 days after transplanting caused about 75% paddy weed reduction and increased yield by 14% compared with an herbicide treatment. The greater number of growth inhibitors (phenolic compounds) found in the leaves might result in the stronger inhibitory activity than the stem and root. AC might be a natural herbicide for weed control in paddy fields to reduce the dependence on synthetic herbicides.[155]

Toxicological Studies

The pollination season of the plant causing allergy has been found to be between November and January in Delhi. In another study, Ageratum (species not mentioned) pollen were reported to be cause of nasobronchial allergy in 5 out of 50 patients.[156]

CONCLUDING REMARKS

The genus *Ageratum* is a rapidly spreading plant and is presently a major problem for environmentalists, ecologists, farmers and animal scientists. A number of studies have been carried out on its control as a weed.[157,158] Of all the species, AC has been widely studied. It is believed that detailed information as presented in this review on its phytochemistry and various biological properties of the extracts and the constituents might provide incentive for proper evaluation of the use of the plant in medicine and in agriculture. Some small companies in Brazil are reported to be using AC as raw material for phytochemicals. Test conducted in mice and rats for anti-inflammatory, analgesic, antipyretic, antibacterial, antifungal, anti-ulcer, radioprotective activities have shown significant results without adverse side effects. Similarly, clinical trials with arthrosis patients conducted with the aqueous extract of the whole plant did not show any side effect.[87] The major constituents of the essential oil have been shown to produce precocious metamorphosis in insect larvae as well as sterility, moribund and dwarfishness in adult insects. Further work, however, still needs to be carried out on the toxicity of the plant and, especially on the precocenes, which have been shown in few cases to cause hepatotoxicity in rats.[139,140] The flavonoids possess wide range of biological activities like its effects on CVS, diuresis, antiviral, spasmolytic, anti-inflammatory properties of the flavonoids isolated from the plant need to be studied. Precocenes and coumarins have been seen as fourth-generation insecticides, also need to be studied. Germane to the pest control studies is the report that the plant extract induces morphogenetic abnormalities in the formation of mosquito larvae *C. quinquefasciatus*, *A. aegypti* and *A. stephensi*.[146,159] Further studies in this area could serve as a means of controlling the Anopheles mosquitoes and thus prevent human and economic losses caused by malaria.

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