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REVIEW ARTICLE

Chemical Composition and Medicinal Significance of *Ageratum conyzoides*: A Review

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ABSTRACT

The plant *Ageratum conyzoides* L. family Asteraceae is locally known as billygoat weed and Sadhandhi in India. It is used as traditional medicine for the treatment of numerous ailments such as analgesic, antifungal, wound healing, anti-inflammatory, hemostatic, smooth muscle relaxant, and anticoagulant activity. The plant has several phytoconstituents such as trans-cadina-1(6), 4-diene, hexanal, β-copaene, caryophylla-4(12), 8(13)-diene-5-β-ol and 1, 10-di-epi-cubenol. Evan through many of the investigational studies validated its traditional therapeutics uses, but unemployed uncharacterized crud extracts. Pharmacological activities of plant extracts and individual phytoconstituents have discovered analgesic, antifungal, wound healing, anti-inflammatory, hemostatic, smooth muscle relaxant, and anticoagulant activity. The results of few pharmacological studies and bioactive metabolites already reported in *A. conyzoides*. Hence, in the view of huge remedial worth of the plant, current review is therefore bringing together all the information related to the *A. conyzoides.*

Keywords: Wound healing activity, analgesic activity, muscle relaxant, hexanal, *Ageratum conyzoides* and medicinal significance

INTRODUCTION

Asteraceae is a large family of plant comprising approximately 1500 genera and 25,000 species in different habitats. This family's vegetation is rather different, ranging from herbs, subshrubs, shrubs to trees.[1] This vegetation, once environmentally friendly, is found in diverse habitats. Ageratum is one of those genera comprising 300 species in the Asteraceae family.[2] *Ageratum* is derived from the Greek words "*a geras,"* meaning non-aging, which refers to the entire plants longevity. On the other hand, *Conyzoides* derived from the greek name "*konyz"* of *Inulahelenium,* which the plant resembles.[3] Billy goat weed, catinga-de-bode, agerato, white weed and Mentrasto.[4-7] are commonly known as *Ageratum conyzoides* (Linn). In Shivalik range of India, Plant *A. conyzoides* grows around 30 to 80 cm in height and has been recorded to grow to 2 m.[8] *A. conyzoides* has its stems covered with white hairs. This species' leaves are opposite arranged, and its inflorescence is corymbing with purple or whitish at times. The fruits of this herb are achene, and wind and water disperse seeds.[9] Because of its abundant morphology) (variability this herb was adaptable in many climatic conditions. *A. conyzoides* is distributed worldwide at an altitude of 700–1660 meters above sea level (m.a.s.l) in pantropical regions.[10] In India, the plant becomes the dominant weed in various agricultural lands and leads to decline in crop yields.[11]

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Conyzoides are easily successful due to their wide adaptability in the environment, their superior reproductive capacity, and their allelopathy.[12] The species has a broad variety of secondary metabolites, including mono and sesquiterpenes, triterpenes, steroids, flavonoids, coumarins, tannins, and alkaloids.[13-17] Any of these metabolites are biologically active, as methoxy flavone isolated from a leaves hexane extract. *Conyzoides* having an insecticide activity.[15] Additional properties reported to the plant extracts are antibacterial,[18,19] antifungal,[20] antiparasitic,[21] anti-inflammatory,[22] curative[23] and cytotoxicity p.[24] Because of its structure and biological activities the essential oil of the leaves or aerial parts of the plant has been widely investigated. *A. conyzoides* has been determined to be the cheap adsorbent in the elimination of toxic pollutants in wastewater management. The use of *A. conyzoides* leaf powder (ACLP) has shown good results in removal from wastewater of methylene blue (MB) and hexavalent chromium Cr (VI). The powder was determined to act more effectively at low pH levels.[25] Despite the wide array of relevant studies on *A. conyzoides* chemical composition and activities. *Conyzoides*, there are few studies to describe the plant anatomically. This work thus aimed at describing the morpho-anatomical characteristics of root, stem, petiole, and leaf blade, contributing to the proper identification of this medicinal plant, as well as providing more information about the Ageratum genus.

PLANT DESCRIPTION

Synonyms

The plant has different synonyms like; Sadhandhi. Gotbilly weed.

Common Names

Sanskrit-, Marathi-, Hindi- Janglipudina, uchunti, Tamil-, English- Goat weed, Billy goat weed, Chicken weed, African Vernacular Names West Africa (Igbo): Nri-ewu (Yoruba): Imieshu, yarnigbei, Spanish (El Salvador): Mejorana, Portuguese: Mentrasto, Tropic ageratum, Sunsumpate (Columbia): Yerba hemostatica.

Taxonomic position, Kingdom- Plantae, Sub Kingdom- Angiosperm, Class- Eudicots, Order- Asterales, Family- Asteraceae, Genus- Ageratum, Species- *Ageratum conyzoides*.

Plant *Ageratum conyzoides*

Habitat and Geographical Distribution

A. conyzoides is a common herb distributed in tropical region of Brazil, America, and many other regions.

Phytochemistry

The medicinal properties of the plant *A. conyzoides* are ascribed to its numerous active phytochemical constituents.

Phytochemistry

A large percentage of the photochemistry publications relate to this plant's essential oil. The oil content for leaves ranges uniformly from 0.11 to 0.58% and for the roots from 0.03 to 0.18% depending on the time of year. The oil content was found to be 0.2% from the water distillation of the fresh flowers.[26] The oil yield from the seed extract petroleum ether was 26%.[27] The mono and the sesquiterpenes are obtained in minute quantities trace 0.1%. The monoterpenes obtained in approximately 1% of the oil include sabinene and pinene, 1.6%, phellandrene, 1, 8-cineole, and limonene, 2.9%, terpinen-4-ol, 0.6%, and terpineol, 0.5%. Ocimene which is found in trace amount in the oil from the Nigerian plant is found to be 5.3% of the oil from the plant collected in India.[28]

α-Pinene 6.6%, eugenol 4.4%, and methyleugenol 1.8% are also obtained from the Indian plant oil. The major sesquiterpenes are β-caryophyllene, 1.9%,[29] 10.5% from the oil obtained from Cameroon[30] and 14-17% in Pakistani oil.[31] δ -Cadinene is another sesquiterpene which has been reported to occur in approximately 4.3% of the oil from Indian plants.[32] Sesquiphellandrene and caryophyllene epoxide have also been obtained in 1.2 and 0.5%, respectively.[29]

Quantitative Phytochemical

Ageratum conyzoides have many secondary metabolites which include alkaloids, cumarins, essential oils, flavonoids and tannins. Many secondary metabolites are biologically active. Many of these are biologically active. 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 from water distillation of the fresh flowers, the oil content was found to be 0.2%. The yield of oil from the petroleum ether extract of the seed was 26%. Alarge number of constituents have been identified from the GC-MS analysis of the essential oil of Ageratum conyzoides. The largest so far, a total of 51 constituents have been reported from the analysis of an oil sample of the plant. The constituents identified include 20 monoterpenes 6.4% and 20 sequiterpenes 5.1%. The mono- and the sesquiterpenes are obtained in minute quantities trace-0.1%. The monoterpenes obtained in approximately 1% of the oil include sabinene and β-pinene, 1.6%, β-phellandrene, 1,8-cineole and limonene, 2.9%, terpinen-4-ol, 0.6%, and α- terpineol, 0.5%. Ocimene which is found in trace amount in the oil from the Nigerian plant is found to be 5.3% of the oil from the plant collected in India. α -Pinene 6.6%, eugenol 4.4% and methyleugenol 1.8% are also obtained from the Indian plant oil.The most common component of the essential oil of Ageratum conyzoidesis 7-methoxy2,2- dimethylchromene (precocene-I). Other related compounds obtained from the oil include encecalin, 6-vinyl-7-methoxy-2,2- dimethylchromene, dihydroencecalin, dihydrodemethoxyencecalin, demethoxyencecalin, demethylencecalin and 2(1-oxo-2-methylpropyl.-2-methyl-6,7-dimethoxychromene. The presence of these acetyl chromenes in Ageratum conyzoides is believed to be of chemotaxonomic significance 8.In addition to the chromenes obtained from the oil, seven other chromene derivatives are isolated from hexane extract of the aerial part of the plant. These are 2,2- dimethylchromene-7-O-glucopyranoside, 6-(1- methoxyethyl).-7-methoxy-2,2-dimethylchromene(3),6-(1-hydroxyethyl)-7-methoxy-2,2 dimethylchromene, 6-(1- ethoxyethyl).-7-methoxy-2,2-dimethylchromene, 6- angeloyloxy-7-methoxy-2,2-dimethylchromene and an inseparable mixture of encecanescins. Benzofuran derivatives, 2(2'-methylethyl)- 5,6dimethoxybenzofuran, 14-hydroxy-2H, β-3-dihydroeuparine as well as chromone derivatives, 3-(2-methylpropyl)-2-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. Ageratum conyzoides is rich in polyoxygenated flavonoids, 21 of them have been reported in the whole plant. Among them there are 14 polymethoxylated flavones. These polyhydroxyflavones include quercetin, kaempferol and their glycosides, too. The two major common sterols sitosterol and stigmasterol together with minor sterol wereisolated together with the triterpene friedelin. Other common substances are sesamine, fumaric acid, caffeic acid, phytol, and long chain hydrocarbons. The polyhydroxyflavones include scutellarein-5, 6, 7, 4- tetrahydroxyflavone, quercetin, quercetin-3- rhamnopiranoside, kaempferol, kaempferol -3- rhamnopiranoside and kaempferol 3,7- diglucopiranoside.

Ethnobotany and Traditionally Uses

A. conyzoides has been used in various parts of the world such as Asia, Africa, South America traditionally as folk medicine. It is used in West Africa, the USA, Australia, Fiji, Palau, Mauritius, Tonga, Vanuatu Solomon Islands, Papua New Guinea, Samoa, and South-East Asia (including India, China, Thailand, the Philippines, Singapore, Vietnam, Indonesia, Cambodia, and Malaysia), Brazil and Korea for curing various diseases.[33,34] The whole plant produces strong smelled volatile

oil which also possesses various pharmacological activates. It is used for as purgative, wound dressing, febrifuge, treatment of skin diseases, ophthalmic, ulcer, colic, and wound dressing.[35]

Pharmacological Properties

In South-Eastern parts of Nigeria the juice from *A. conyzoides* is useful in healing of wounds. In wastewater management, *A. conyzoides* has been determined to be the cheap adsorbent in removing toxic pollutants. The use of ACLP showed good results in removing MB and hexavalent chromium Cr (VI) from wastewater. The powder has been determined to work more effectively in low pH levels.[36,37] Ezech *et al*. findings showed that the leaf powder of Ageratum can successfully remove the effluent dye in optimum conditions (pH 4 and adsorbent concentration = 0.06 g).[25] therefore, understanding its spatial distribution pattern is necessary for medical and wastewater scientists.[37]

Insecticidal Activity

A. conyzoides has bioactivity that may have agricultural use. The insecticidal activity may in fact be the most important biological activity of this species. Both the essential oil as well as the major components of the oil, namely, the preciseness, have been reported to have ant juvenile hormonal activity. 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 to 10 µl/9.5 g beans with no adverse physiological effect. Precocene I was found to be 4 times as active as the oil.[38] Assays conducted in India showed high nymphal mortality 91%. of the oil to the Nymphs of *Schistocerca gregaria*.[39] Calle *et al*. showed that the hexane extract of the whole plant showed activity against *Musca domestica* larvae.[40] Methanolic extract from fresh leaves 250 and 500 ppm. also produced deficiency of juvenile hormone in the fourth instar of *Chilo partellus*, a sorghum pest.[41] Anti-juvenile hormonal activity of Precocenes I and II have been demonstrated on a variety of insects which include *Sitophilus oryzae*, *Thlaspida japonica*, *Leptocarsiachinesis*[42] and *Dysdercus flaidus*.[43] 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.[43] Preliminary study on the mode of action of precocene II on *Musa domestica* L. and *Luciliacaesar* L. have been carried out.[44] While the precocenes have been seen as fourth-generation insecticides, the drawback is that they have been shown to cause hepatotoxicity in rats.[45,46] This is an important factor bearing in mind the human health hazard in field applications of precocenes as large-scale insecticidal agents. The mechanism of action has been carried out by a number of researchers. 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.[45,47] Others, like Darvas *et al*.,[48] Casas *et al*.[49] 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.

Antimicrobial Activity

The antimicrobial effects of ethanolic extract of *A. conyzoides* against *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, and *Shigella dysenteriae* was determined using the Agar-well diffusion technique. The minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) as well as the phytochemical properties of the extract on the test isolates were also examined using the standard methods. The phytochemical components of the ethanolic extract of the *A. conyzoides* include tannin, alkaloids, steroids, saponin, phenol, flavonoids, triterpenes glycosides, and carbohydrate. All the test organisms were susceptible to ≥50 mg/ml of the extract. The MIC and MBC of the ethanolic extract of the *A. conyzoides* against *S. aureus* and

E. coli was 120 mg/ml, while that of *P. aeruginosa* and *S. dysenteriae* were 160 mg/ml and 200 mg/ml of the extract, respectively. The result of this study suggests that the ethanolic extracts of *A. conyzoides* could be suitable for the treatment of diseases/ infections caused by *S. aureus*, *P. aeruginosa,* and *E. coli* and *S. dysenteriae*.[51] Ethanolic extract of *A. conyzoides* leaves showed antibacterial activity with MIC against *Propionibacterium acnes* 5 mg/ml, *S. aureus* 10 mg/ml and *Staphylococcus epidermidis* 7.5 mg/ml.[50] Ethanolic extract of *A. conyzoides* leaves showed the strong fungicidal activity of all five fungi isolated from the rotted watermelon fruits. The mycelial inhibition of phytopathogenic fungi were as follows: *Fusarium verticillioides* (70.75%), *Botryodiplodia theobromae* (85.27%), *Aspergillus flavus* (83.29%), *Curvularia lunata* (86.56%) and *Alternaria cucumeria* (98.43%).[51] Aqueous extract of leaves of *A. conyzoides* showed the antifungal activity, 800 mg/ml was most effective concentration. *Aspergillus ustus* was most susceptible with 20.0 ± 0.6 mm zone of inhibition followed by *Aspergillus tamari* (15 ± 0.3) and *Aspergillus fumigatus* (8.0 ± 0.1 mm) at the least. The MIC values of extracts ranged from 50 mg/mL to 794 mg/mL.[52] Isolated compound of *A. conyzoides* leaves 60 and 120 μg/ml concentrations shown the antimicrobial activity of all 8 bacteria, zone of inhibition in between 20-36mm. MIC value against the bacteria ranged from 8 to 32 mg/ml.[53]

The essential oil of *A. conyzoides* leaves, root, and stem was the MIC ranged between 2.0 mg/ml and 4.0 mg/ml and these were recorded for *Bacillus subtilis, Klebsiella pneumoniae,* and *S. aureus* in the stem, leaves, and the root extracts. All the microbes tested were sensitive to the essential oils of *A. conyzoides* except *P. aeruginosa*.[54] Water and ethanolic extract of *A. conyzoides*, MIC, and MBC of the ethanol extracts range from 18.2 to 24.0 mcg/ml and 30.4 to 37.0 mcg/ml respectively. In contrast, MIC range of 30.6–43.0 mcg/ml and 55.4–71.0 mcg/ml was recorded for ethanol and water extracts of *A. conyzoides*.[55] The antimicrobial effects of ethanolic extract of *A. conyzoides* the MIC and MBC were against *S. aureus* and *E. coli* was 120 mg/ml, while that of *P. aeruginosa* and *S. dysenteriae* were 160 mg/ml and 200 mg/ml of the extract, respectively.[56] The leaf extract of the plant *A. conyzoides* Antibacterial effects, highest zone of inhibition was observed with the methanol extract at a concentration of 100 mg/ml for *Salmonella* Typhi and the lowest with the acetone extract at 25 mg/ml. The highest zone of inhibition was however observed for the hexane extract at a concentration 100 mg/ml for *Salmonella* Typhimurium and the least with methanol extract at 12.5 mg/ml.[57]

Anti-inflammatory Activity

The hydro-alcoholic extract of *A. 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.[22]

Antidiabetic Activity

Aqueous extract of *A. conyzoides* (500 mg/kg body weight) was reported to reduce fasting blood glucose of experimental animals by 39.1%. Agunbiade *et al*.[58] reported that, the plant species *A. 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 *A. conyzoides* L. were also evaluated in normoglycemic and in streptozotocin-induced diabetic rats by Nyunaï *et al*.,[59] 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 *A. conyzoides*.

Antioxidant Activity

The ethanolic leef extract of *A. conyzoides* possessed a significant dose-dependent DPPH free radical scavenging activity with an IC50 value of 18.91 mg/ml compared to ascorbic acid (IC50: 2.937 mg/ml) and butylated hydroxyanisole (IC50: 5.10 g/ml). The IC50 value of the extract for NO scavenging (41.81 mg/ml) was also found to be significant Compared to the IC50 value of ascorbic acid (37.93 mg/ml). Moreover, the extract showed reducing power activity and Feþþ ion chelating ability. The total phenolic value was also calculated (378.37 mg/g of gallic acid equivalents).[60] Alcoholic extract of leaves of *A. conyzoides* on higher concentration possesses better antioxidant potential when compare to reference standard ascorbic acid. DPPH free radical scavenging activity with IC50 value of 9.3 and 24.8 µg/ml for ascorbic acid and alcoholic leaves extract respectively. The absorbance for reducing power was found to be 0.0390, 0.0989 for ascorbic acid and alcoholic leaf extract, respectively.[61]

The ethanol extract of the plant leaves has reported to possess a significant dose-dependent DPPH free radical scavenging activity with an IC50 value of 18.91 µg/ml compared to ascorbic acid (IC50: 2.937 µg/ml) and butylated hydroxyanisole (IC50: 5.10 µg/ml). The IC50 value of the extract for NO scavenging (41.81 µg/ml) was also found to be significant compared to the IC50 value of ascorbic acid (37.93 µg/ml). Moreover, the extract showed reducing power activity and Fe++ ion chelating ability.[60] Adebayo *et al*. reported that Kaempferol isolated from the ethylacetate extract of *A. conyzoides* rapidly scavenged DPPH at a concentration of 130.07 ± 17.36 g/kg.[62] *A. conyzoides* was also reported to possess tissues protective effect. Ogunlade *et al*.[64] reported that in the absence of *A. conyzoides* extract (ACE), the rats treated with ethanol had significantly increased liver enzymes (alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase) and MDA levels but these were decreased in ethanol + ACE group compared to the ethanol group. The histologiesof concurrent ethanol + ACE treated group were similar to control groups. They conclude that *A. 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.[64]

Larvicides

Essential oil of *A. conyzoides* L. aerial parts at flowering stage exhibited strong larvicidal activity against the Asian tiger mosquito, *Aedesalbopictus*. A total of 32 components of the essential oil were identified and the principal compounds in the essential oil were precocene II (45.75%), precocene I (14.09%), and caryophyllene (12.13%) followed by germacrene D (4.18%) and caryophyllene oxide (4.06%). The essential oil had higher content (59.84%) of phenylpropanoids than monoterpenoids (3.70%) and sesquiternoids (33.01%). The essential oil of *A. conyzoides* aerial parts exhibited larvicidal activity against *Ae. Albopictus* with an LC50 value of 61.22 µg/ml while the two major constituents, precocene I and precocene II had LC50 values of 43.55 µg/ml and 41.63 µg/ml, respectively.[65]

Anti-anxiety

Methanolic leaves extract at both doses showed significant, when compared to vehicle control group, increase in time spent and number of entries in open arms of EPM confirming the anti-anxiety effects of *A. conyzoides*. Liquid-liquid partitioning of methanol extract gave two fractions (ethyl acetate and butanol) which were administrated at 25 and 50 mg/kg doses to mice in EPM, respectively. Results showed that ethyl acetate fraction was responsible for anxiolytic effects.[66] Wound healing effects, Analgesic activity, Anti-cancer, anti-radical scavenging activity and gastric properties, Spasmolytic effects, Gamma radiation effects, Anti-malarial properties, Anticoccidial activity, Schistosomicidal activity, Insecticidal property, Allelopathic property and Antitumour activity.[67-70]

CONCLUSION

Scientists needs to the further research on different weeds, one of which is *A. conyzoides*. Various environmental factors influence plant distribution and abundance, including soil, rainfall and temperature. There is a relationship between plant distribution and abundance, as well as variations in the environment and they must be determined. The distribution and abundance of plants can be influenced by environmental variables, such as nutrient status, soil texture and slope may affect the distribution and abundance of plants. *A. conyzoides* is an invader of Tanzanian farmlands and has become highly troublesome for crops. There are insufficient studies on the ecology of *A. conyzoides* in Tanzania. This study was therefore conducted to provide some vital information which can serve to control the weed. The main objective of this study was to find out the ecology of *A. conyzoides* in riverine and non-riverine habitats basis objectives to establish the spatial distribution pattern and abundance of *A. conyzoides* in riverine and non-riverine habitats to make comparisons of the abundance of *A. conyzoides* between the two sites (Riverine and non-riverine). We assumed that, in riverine and non-riverine habitats, *A. conyzoides s*is randomly distributed, in riverine and non-riverine habitats of and the abundance between the two sites is similar.

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