Ageratum conyzoides (Asteraceae)

English: Goat weed, billy goat weed
Spanish (El Salvador): Mejorana , sunsumpate (Columbia): Yerba hemostatica
Portuguese: Mentrasto, Tropic ageratum
African vernacular names:
West Africa (Igbo): Nri-ewu (Yoruba): Imieshu , yarnigbei
Kianzi (Zaire): Nkaya bekia kwa nsey, Kikongo (Zaire): Mpota ka saku
India (Hindi): Uchunti Fidchi Islands: Botebotekoro
German: Mexikanischer Leberbalsam

The plant

The plant is widely spread over the world, especially in the tropical and subtropical regions. It is very common in West Africa and some parts of Asia and South America. It is an annual branching herb which grows up to 1 m in height. The stems and leaves are covered with fine white hairs; the leaves are ovate and up to 7.5 cm long. The flowers are purple to white, less than 6 mm across and arranged in a terminal inflorescence. The fruits are achaenes and easily dispersed.Because of its propagation it becomes a weed and causes problems for farmers and ecologists.It is not eaten by men because of its bad odour, like a male goat and is named goat weed or billy goat weed.The whole plant is only used for medicinal purposes and has a long history in the folk medicine of different countries.

Plant parts used

The whole plant, the leaves, more rarely the root

Constituents

The essential oil:

Mono- and sesquiterpenes

The oil content won by distillation varies randomly from 0.11 to 0.58 % for **leaves** and from 0.03 to 0.18 % for the **roots** depending on the seasons. From water distillation of the **fresh flowers**, the oil content was 0.2 %.The fatty oil yield of the **seeds** extracted by petrol ether was 26 %.An oil sample from plants collected from Nigeria brought 51 constituents analysed by GC-MS.It included 20 monoterpenes (6.4 %) and 20 sesquiterpenes (5.1 %).The quantities of the single substances were in the range of trace to 0.1 %. The monoterpenes (1 % of the oil) include sabinene and beta-pinene 1.6 %, beta phellandrene 1,8-cineole and limonene 2.9 %, terpinen-4-ol 0.6 % and alpha terpineol 0.5 %.

The major sesquiterpenes are beta-caryophyllene 1.9 %. 10.5 % from an oil obtained from Cameroon and 14-17 % in a Pakistani oil. Another sesquiterpene, cadinene occurred in aproximately 4.3 % in the oil from Indian plants. Sesquiphellandrene and caryophyllene epoxide have been obtained in 1.2 and 0.5 % (12).

Chromene, chromone, benzofurans, and coumarins

A further common component of the essential oil is precocene I (7-methoxy-2,2-dimethyl-chromene) and precocene, its 6,7-dimethoxy derivative with percentages between 30 % from a Vietnamese oil and 93 % from a Congolese oil together with further acetyl chromenes. Benzofuran and its derivatives are found in minor quantities and 1.24 % coumarin in oil from Brazil (12,16).

From the essential oil 12-6-methyl heptadecenoic acid was isolated. It shows an insecticidal and growth regulatory activity against the desert locust Schistocera gregaria (12).

Flavonoids and alkaloids
A.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 und their glycosides, too.
The two major common sterols sitosterol and stigmasterol together with minor sterol were isolated together with the triterpene friedelin.
From the pyrrolizidin alkaloids widely distributed in the plant familiy Asteraceae only lycopsamine and echinatine were found. Other common substances are sesamine, fumaric acid, caffeic acid, phytol, and long chain hydrocarbons (C_{27} H_{56} to C_{32} H_{66}) (12).

Ethnopharmacology

A.conyzoides is used in various parts of Africa, Asia and South America for curing various diseases in the folk medicine. It is used as a purgative, febrifuge, against colic, skin ulcers, as an antienteralgic and antipyretic, for cuts as a wound dressing. In some African countries the plant is indicated against infectious and mental diseases, against headache and dyspnoea. In Central Africa the plant is very common for skin diseases and wounds caused by burns. In Nigeria the decoction of the plant is taken internally to treat diarrhea and to relieve pain of the intestines. In Kenya it is applied against asthmatic, antispasmodic and haemostatic diseases. In Brazilian folk medicine teas of A.conyzoides are taken as anti-inflammatory, analgesic, anti-diarrhoeic medicines and in Vietnam against gynaecologic complaints. Other folk medicines include anti-itch, antitussive, vermifuge, against rheumatism and toothache. Additionally it is used as an prophylactic, as a tonic and to cure trachoma in cattle, finally (3). The most reliable application is in external wound healing, for disinfection and haemostyption (5).
A.conyzoides has magical and superstitious attributes. e. g. against snake bites. In West Nigeria incantations are said to help against witches and bad medicine. In Congo, if leaf sap is spread on the accused in a trial and when he is then pricked with a needle, pain will be felt only if guilty. Leaf sap on the hands of card players is believed to improve their luck (3).
In Nigeria traditional soft soaps are prepared from plant ashes like cocoa (Theobroma cacao) and from palm kernel shafts (Elaeis guinensis). Extractives from further medicinal plants together with A.conyzoides such as Aloe did not show any significant effect on the antimicrobial activities of the soaps against bacterial or fungal test organisms (10).

Results of experimental studies

Antibacterial effects and wound healing
Water and ethanol extracts of the shredded fresh collected plant were investigated for antibacterial activity. In an in vitro anti-methicillin resistant Staphylococcus aureus test (MRSA) the minimum inhibition concentration (MIC) 30.6 to 43.0 and 45.4 to 71.0 µg/kg were recorded for ethanol and water extracts. The minimum bactericidal concentration (MBC) was higher for both extracts (2).
Crude material from fresh leave extracted by petrolether yielded after column chromato-graphy on aluminium oxid (Brockman grade II) 60 fractions by extraction with petrolether/chloroform mixtures. Fraction 42 – 44, a whitish-brown crystallised material was effective against Staphylococcus aureus .Fraction 43 had wound healing properties. Burn wounds in rabbits treated with this compound healed in seven days while those of the control (vasline gauze) took 14 days for healing (3).
The aqueous residue of A.conyzoides showed a significant growth for the bacteria Alkaligenes viscolactis, Klebsiella aerogenes, Bacillus cereus and Streptococcus pyogenes (11).
Antiinflammatory effects

A hydroalcoholic extract was studied for antiinflammatory effects in rats. A group of rats, orally treated with 250 mg/kg extract had a 38.7 % reduction in the cotton pellet-induced granuloma ($p < 0.05$) .The development of chronically induced paw edema was also reduced significantly ($p < 0.05$) by the plant extract. The SGT activity in the blood of rats treated with 500 mg/kg was reduced to 30.2 % ($p < 0.05$).This should confirm the antiinflammatory properties of A.conyzoides according to the meaning of the authors. The biochemical and hematological analysis of the blood of rats treated with daily doses of 250 or 500 mg/kg extract for 90 days did not show any treatment–related abnormalities in the biochemical or haematological parameters towards toxicity. Therefore no indications were found for an apparent hepatoxicity (11).

Wound healing effects

The wound healing effect of the A.conyzoides methanolic extract was studied in Wistar rats (n=10). Wounds prepared in excised areas of the skin were packed with gauze soaked by the extracts and were determined histologically after 10 days. The Ageratum sections showed fewer inflammatory cells and more fibrosis than controls. The healed wounds from the Ageratum group had significantly fewer fibriblasts than the controls ($p < 0.036$) and than a combined application of Ageratum extract and honey ($p < 0.12$) (13).

Neurological effects

A lyophilized powder from leave juice of A.conyzoides was injected intraperitonealy in Wistar rats in doses of 25, 50, 100, 125, 150 mg/kg. Animal behaviour was observed macroscopically by the method of Martin et al. by measuring the spontaneous motor activity every ten minutes during30 minutes and by the hot plate method. All doses equal or over 125 mg/kg caused mortality of the rats. Only the doses of 50 and 100 mg/kg were selected for the experiments. The effects were a precocious ataxia, sedation and a slight ptosis. Six hours after injection, these effects disappeared. The spontaneous motor activity was reduced (1).

Oral administration of the water extract (0.1 to 0.5 g/kg) to rats and mice induced quietness and reduced the spontaneous motility. The sleeping time induced by sodium pentobarbital (50 mg/kg) in mice was not altered by previous treatment with water extract (2 g/kg), orally. In contradiction this treatment did not influence the paw edema induced by carrageenan or dextran, nor did it reduce the chronic paw edema induced by complete Freund`s adjuvant or formaldehyde in rats. The tail flick response in the immersion test and writhings induced by 0.8 % acetic acid in mice were not altered by water extract.

Spasmolytic effects and gastro protection

In the isolated guinea pig ilea 0.4 to 4 mg/ml water extract did not alter the EC 50 values of histamine or acetylcholine, but reduced the the maximal response to the agonists by 20 to 50 %. Proportional to the doses water extract (0.01 to10 mg/ml produced tonic contractions of the ileal smooth muscles, reaching a maximum of 75 % relatively to the maximum obtained with histamine. Those contractions were blocked by diphenhydramine (10 nM) and reduced by 32 % in presence of atropine (10 nM). The authors conclude that these results do not confirm the popular medicinal indications of the plant (19).

In order to evaluate the popular use of A.conyzoides as a spasmolytic medicine the water soluble fraction (WSF) was studied in the rat uterus and intestinal smooth muscles. The WSF (0.2 and 0.4 mg/ml) increased the EC 50 values and decreased the maximum responses to acetylcholine and calcium chloride. The WSF (0.5 - 3.3 mg/l) produced direct relaxant effect on smooth muscle preparations. Theophylline (10^{-3} M) potentiated the relaxant action of the WSF. Theophylline also prevented the decrease in maximum response promoted by the WSF in acetylcholine concentration-effect curves. These results seem to be partially linked to the calcium mobilisation. The data also suggest that the WSF can act synergistically with theophylline in the inhibition of cyclic AMP phosphodiesterase. According to the authors these results give support to the popular medicinal indication of A.conyzoides. That is in contradiction to (17,19).

The ethanol extract of A.conyzoides was evaluated for gastroprotection in rats using the ibuprofen, ethanol and cold restraint ulcer stress model. Efficacy was assessed by

determination of mean ulcer size, ulcer numbers and an ulcer index. In the ibuprofen model the ethanol extract orally administered at doses of 500 and 750 mg/kg significantly protected gastric lesions by 80.59 and 89.33 % as compared to misoprostol (74.43 %), in the cold stress model by 97.09 and 99.24 % compared to famotidine, and by 86.58 and 92.29 % in the alcohol model. The authors conclude that the sigificant gastroprotective activity can be mediated by the antioxidant activity, blocking of muscular calcium channels and antiserotogenic properties (18).

Effects on circulation

In the isolated guinea pig heart a leaf extract (no information about its preparation mentioned) changed the electrocardiogram, atrial impulse velocity and coronary vessels resistance. Alterations were:

a) the PR interval increased from 80 +/-1.4 ms to 105+/-14 ms ($p<0.01$)
b) the QT interval decreased from 170 +/-2 ms to 154 +/-7 ms ($p<0.01$)
c) the heart rate decreased from 170 +/-17 bpm to 152 +/-21 bpm ($p <0.01$)
d) the atrial impulse velocity decreased from 51 +/-2 cms to 45 +/-3 cms ($p <0.01$)
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 ($p <0.01$).

All these effects disappeared after a wash out (4).

Antitumour activity

In a murine ascites Dalton´s lymphoma in vivo the aqueous extract of A.conyzoides roots decreased glutathion in the liver and in the lymphoma cells of the tumour-bearing mice. In the opinion of the authors this could be one step producing the antitumour effect (14).

Analgesic effects

Three in vitro receptor radioligand binding assays (Bradykinin II expressed in Chinese hamster ovary ovary cells, Neurokinin1 expressed in astrocytoma cells, calcitonin gene related peptide) are implicated in the mediation of acute pain in the mammalian central nervous system. The A.conyzoides extract showed strong indications of biological activity for these assays.

According to the authors this could be congruent with the ethnomedicinal use of this plant against spasmodic pain (15).

Effects on Gamma radiation

The effects of various doses (0.25 to 900 mg/kg) of the alcoholic extract of A.conyzoides were tested on the mortality of mice exposed to 10 Gray of Gamma radiation. At a dose of 75 mg/kg extract the highest number of mice survived. It was considered the optimal dose for radio protection. This treatment reduced the severe symptoms of radiation sickness and mortality at all exposure doses of radiation and protected mice against the lethal gastrointestinal and bone marrow depressing effects, as revealed by the increased number of survivors at all radiation doses. The protectional effects against Gamma radiation may be caused by scavenging reactive oxygen molecules (8).

Allelopathic effects

Living whole plants of A.conyzoides show allelopathic potential against other plants. Under laboratory conditions the volatile oil of A.conyzoides inhibits other plants at 60 microgram/ml. The amount of 300 µg/ml was the lethal dose. Therefore A.conyzoides can dominate in natural environment as a weed (6). Flavones released by A.conyzoides possibly can control fungal pathogens in citrus orchids like a natural fungicide. It is comparable with Carbenzin, a commercial fungicide (7). In field studies an essential oil emulsion was sprayed in a citrus orchid. It decreased the population of mites and favoured the predators of the noxious parasites, maybe. But this could not be maintained beyond 48 hours because of the volatility of the essential oil (9).

Toxicity

lyophilised powder of the juice in rats: 125 mg/kg (1)
alcoholic extract of the whole plant in mice: > 3000 mg/kg (8)

hydroalcoholic extract of leaves in rats: no toxicity (8)

Results of clinical studies

The are no results available

Evaluation

The plant is known in many countries of Africa, South America and in Asia. It contains a lot of chemical components in the leaves and in the essential oil.
There are many reactions of the extracts with strong pharmacological effects.
Especially the compounds of the essential oil seem to be cytotoxic.The pyrrolizidin alkaloids in the plant extracts must be classified as cancerogens. Only the short time application of leaves on the skin can be judged positively.

Ageratum conyzoides

-leaves on the skin for wound healing	*** * ***
-tea from the whole plant against pain	**(*)**
-extracts (alcoholic, watery)	**- - -**

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