BIDENS PILOSA L.: A COMPREHENSIVE REVIEW

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Summary

Plants used in traditional medicine represent a priceless tank of new bioactive molecules.*Bidens pilosa* L is one of the important plant from traditional system of medicine found all over the world. *Bidens pilosa* L., the largest flowering plant, a perennial herb having white 'petals' (rays) around a dense cluster of orange florets, has been reported to possess potent pharmacological properties like anti-hyperglycemic, anti-hypertensive, antiulcerogenic, hepatoprotective, anti-leukemic, anticancer, antipyretic, anti-virus, anti-angiogenic, anti-rheumatic, antibiotic, or antidiabetes. The various chemical constituents like alkaloids, saponins, tannins, phytosterols, ascorbic acid, carotene, essential oils, saponins, steroids polyacetylenes and flavonoids and many others were identified in this plant. This review gives a bird's eye view mainly on the pharmacognostic characteristics, traditional uses, phytochemistry and pharmacological actions.

KEYWORDS: - *Bidens pilosa* L., Spanish needle, phytochemistry, pharmacological actions.

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Introduction

The study of plants as therapeutic agents is of paramount importance to addressing health problems of traditional communities and third world countries as well as of industrialized societies. Herbal medicine is the root of various traditional medicine systems around the world. As well, a large number of studies have been conducted in the past few decades on the traditional pharmacopoeia of indigenous peoples and rural communities throughout the tropics. Many tribal people in the tropical regions use plants for their medicinal needs. In some cases, a number of tropical species have yielded substances that are pharmacologically important in the manufacture of ethical drugs (1, 2). Botanicals are a chemical source that directly provides around 25% of currently used crude drugs, with another 25% derived from chemically altered natural products. *Bidens pilosa* L., (Family Asteraceae) commonly known as 'Spanish needle' has respectable place in traditional literature because of its different uses.

Vernacular names

Hairy Beggarticks, cobbler's egs, black fellow, black jack in English; ko-sendan-gusa in Japanese; jin zhan yin pan in Chinese, ki nehe, ki pipilli in Hawaii, *Bidens adhaerescens, Bidens alausensis, Bidens chilensis, Bidens hirsuta, Bidens leucantha, Bidens montaubani, Biden reflexa, Bidens scandicina, Bidens sundaica, Coreopsis leucantha, Kerneria pilosa,*Picao preto, aceitilla, alfiler, clavelito de monte, romerillo, saltillo, yema de huevo, zaiguille, pau-pau pasir, Spanish needles (3,4).

Taxonomical Hierarchy of Bidens Pilosa L. (5)

Kingdom	:	Plantae
Subkingdom	:	Tracheobionta
Division	:	Magnoliophyta
Class	:	Magnoliopside
Subclass	:	Asteridae
Order	:	Asterales
Family	:	Asteraceae
Genus	:	Bidens L.
Species	:	Bidens Pilosa L.

Geographical distribution

Bidens pilosa L. is a plant native to South America which today is spread all over the world, particularly in tropical and subtropical regions (6). It is also found in the western part of Cameroon, South Africa, Taiwan, Mexico, Brazil (7-8).

Morphology

It is an erect annual or perennial herb with branching habit to about 1m high. Leaves are usually 2.5-13.5 cm long including petiole and deeply divided into three toothed lobes, with the terminal lobe larger than the other two. Individual flowers are yellow but are tiny and held in dense terminal clusters in a widely branching flowering head. Each flower cluster has four or five short, broad, white 'petals' (rays) around a dense cluster of orange florets (Figure 1). Heads 21-42 in compound cymes terminating main stem and lateral branches, discoid and 0.7-1 cm in diameter including ray florets, peduncles 1-9 cm long; outer

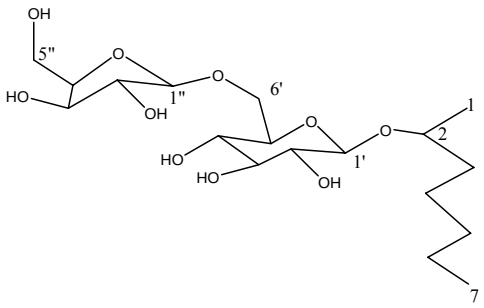
involucral bracts spatulate-tipped, 2.5-5 mm long; ray florets absent or 4-7 per head, rays white or yellowish, 2-8 mm long; disk florets 35-75 per head, perfect, corollas yellow; pappus of 2-3, barbed awns 1-2 mm long. The seeds are black, about 1 cm long, with 2 or 3 barbed awns at the tip. Its root has a distinctive aroma similar to that of a carrot (9).

Figure 1:- Image of *Bidens pilosa*

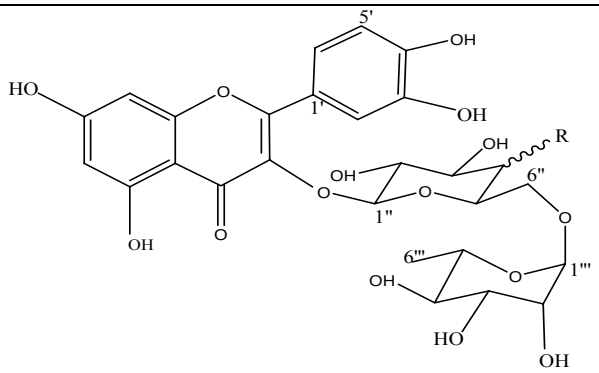
Phytochemistry

Bidens pilosa L. have revealed the presence of alkaloids, saponins, tannins, phytosterols, ascorbic acid, carotene, essential oils, anthocianins, saponins, steroids and sugars. From this species, groups of compounds with biological activity, mainly, polyacetylenes and flavonoids have been isolated and identified. Some types of flavonoids, mainly aurones and chalcones and aurone glucosides isolated from fresh leaves of *Bidens pilosa* were identified. Several polyacetylenes have been isolated from the aerial parts and from the roots of *Bidens pilosa* and the principal representative of this group of compounds being 1-phenylhepta-1, 3, 5-tryine. Other compounds with biological activities, such as terpenes, also have been isolated from this species (8-10). It also showed the presence of heptanyl 2-O-xylofuranosyl- (1→6)-glucopyranoside (**1**), along with eight known compounds, quercetin 3-O-rabinobioside (**2**), quercetin 3-O-rutinoside (**3**), chlorogenic acid (**4**), 3,4-di-O-caffeoylquinic acid (**5**), 3,5-di-O-caffeoylquinic acid (**6**), 4,5-di-O-caffeoylquinic acid **(7)**, jacein (**8**), and centaurein (**9**)(11). Also two methoxylated flavone glycosides were identified as the novel quercetin 3, 3'-dimethyl ether 7-O-α-L-rhamnopyranosyl- (1→6)-β-D-glucopyranoside and the known quercetin 3,3'-dimethyl ether 7-O-β-D glucopyranoside from the roots of *Bidens pilosa* L. (12). A new diterpene, phytyl heptanoate, has been isolated from *Bidens pilosa* L., and its structure confirmed by chemical synthesis (13). Five new flavonoids, named (Z)-6-O-(3",4",6"-triacetyl-β-D-glucopyranosyl)-6,7,3,4'-tetrahydroxyaurone (**10**),(Z)-6-O (2",4",6"-triacetyl-β-D-glucopyranosyl)-6,7,3',4' tetrahydroxyaurone (**11**),okanin4'-O-β-D(4",6"-diacetyl)-glucopyranoside (**12**), iso-okanin 7-β-D-(2",4",6"-triacetyl)-glucopyranoside (**13**) and quercetin-3,4'-dimethyl ether-7-O-rutinoside (**14**), respectively, together with six known constituents (Z)-6-O-(4",6"-diacetyl-β-D-glucopyranosyl) 6,7,3', 4' -tetrahydroxyaurone, okanin 4'-O-β-D-(3",4",6"-triacetyl)-glucopyranoside,luteolin,4-O-(2-O-acetyl-6-O-p-coumaroyl-β-D glucopyranosyl)-p-coumaric acid, butanedioic acid, and 1-phenyl-1,3,5-heptatriyne were isolated from the aerial parts of *Bidens pilosa vat. Radiata.* (14). Another novel polyacetyelene, namely cytopiloyne (**15**), two polyacetylenic glucosides, 2 D glucopyranosyloxy-1-hydroxy-5 (E)-tridecene-7, 9,11-triyne (**16**) and3-d glucopyranosyloxy-1-hydroxy-6 (E)-tetradecene-8, 10,12-triyne (**17**) were also reported (15).

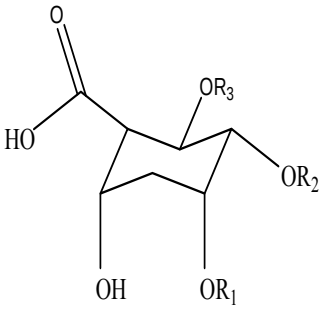
Table 1: Chemical constituents of *Bidens pilosa* Linn.



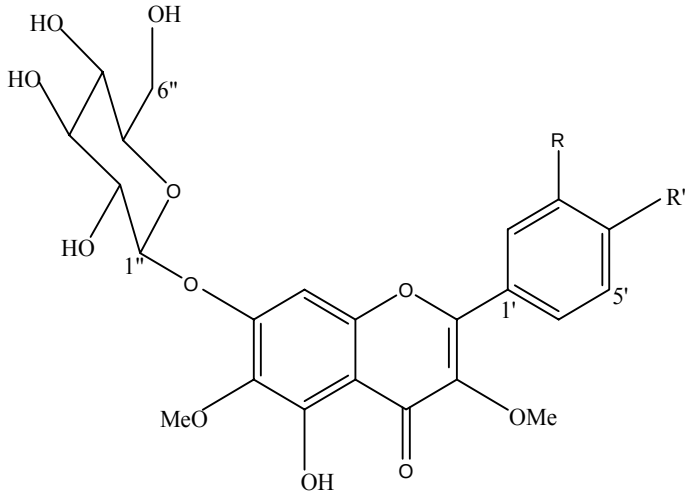
1:(Heptanyl2-O-xylofuranosyl-(1→6)-glucopyranoside)



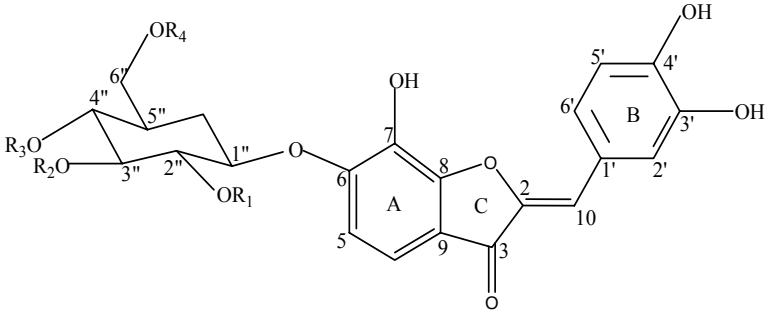
2 : R=b-OH (quercetin 3-O-rabinobioside)
3 : R=a-OH (quercetin 3-O-rutinoside)



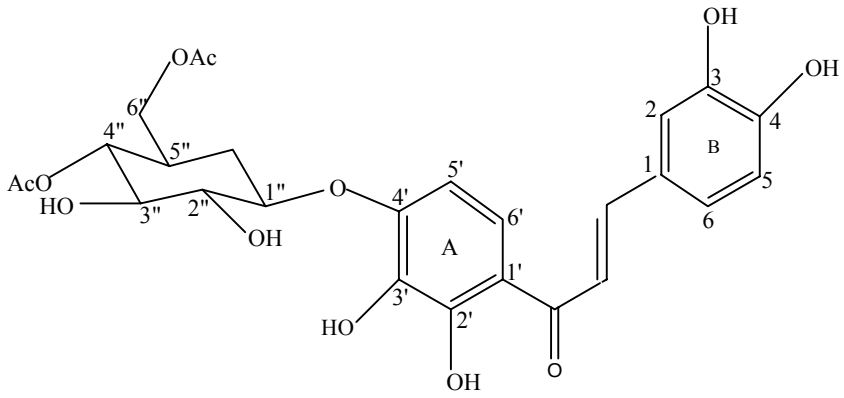
4: R1 = R2 = H, R3 = caffeoyl (chlorogenic acid)
5: R1 = R2 = caffeoyl, R3 = H (3,4-di-O-caffeoylquinic acid)
6: R1 = R3 = caffeoyl, R2 = H (3,5-di-O-caffeoylquinic acid)
7: R1 = H, R2 = R3 = caffeoyl (4,5-di-O-caffeoylquinic acid)



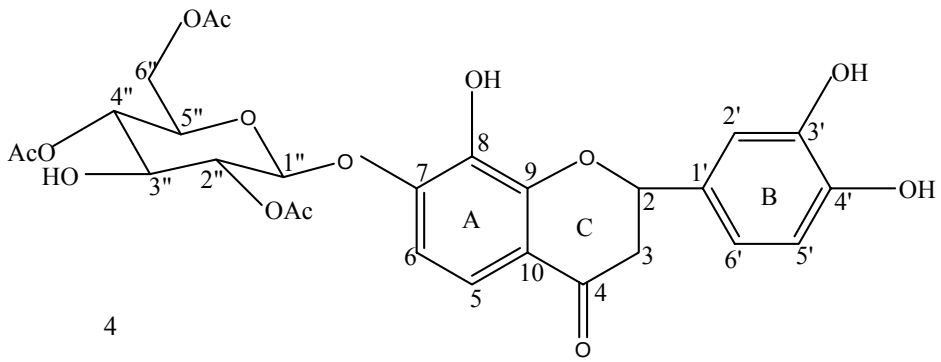
8: R = OMe, R' = OH(jacein)
9: R = OH, R' = OMe(centaurein)



10: R_2=R_3=R_4=Ac, R_1=H [(Z)-6-O-(3",4",6"-triacetyl-β-D-glucopyranosyl)-6,7,3,4'-tetrahydroxyaurone]
11: R_1=R_3=R_4=Ac, R_2=H [(Z)-6-O-(2",4",6"-triacetyl-β-D-glucopyranosyl)-6,7,3',4'-tetrahydroxyaurone]



12: okanin4'-O-β-D-(4",6"-diacetyl)-glucopyranoside



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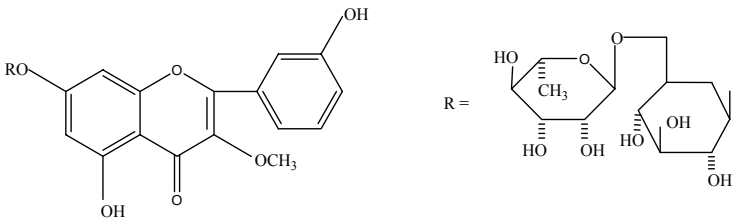
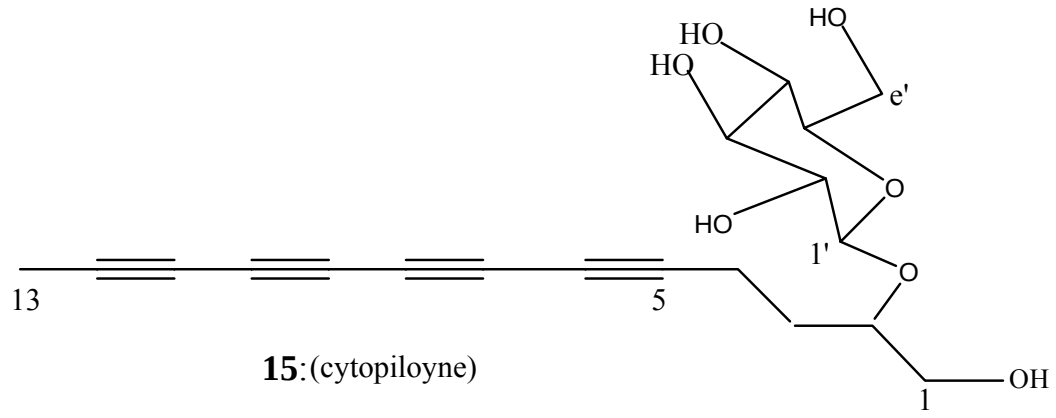
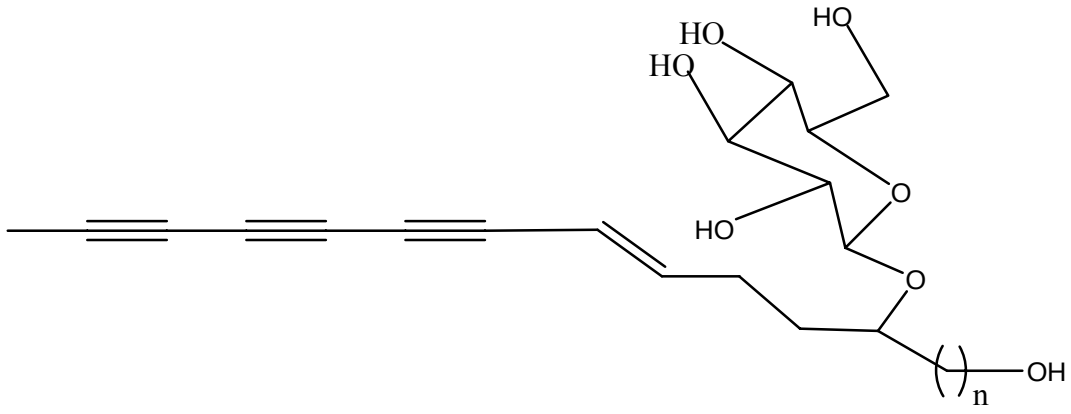
13: iso-okanin 7-β-D-(2",4",6"-triacetyl)-glucopyranoside



14: (quercetin-3,4'-dimethyl ether-7-O-rutinoside)



15:(cytopiloyne)



16: n=1 (2-dglucopyranosyloxy-1-hydroxy-5(E)-tridecene-7,9,11-triyne)
17: n=2 (3-d glucopyranosyloxy-1-hydroxy-6(E)-tetradecene-8,10,12-triyne)

Characterization of *Bidens pilosa*

Various methods were tried for the isolation and characterization of *Bidens pilosa* plant to know better about its phytochemistry. New polyacetylenic glucoside, namely cytopiloyne was isolated as an amorphous colorless solid. Its IR spectrum showed the presence of hydroxyl groups (3438 and 3271 cm−1) and acetylenic groups (2231 cm−1) (15). The major constituents in the BuOH fraction were isolated using several repeated procedures of RP-18 silica gel high performance liquid column chromatography. The structure of one new compound, heptanyl 2-*O*-xylofuranosyl- (1→6)-glucopyranoside along with eight known compounds, quercetin 3-*O* rabinobioside, quercetin 3-*O*-rutinoside, chlorogenic acid, 3,4-di-*O*-caffeoylquinic acid, 3,5-di-*O*-caffeoylquinic acid, 4,5-di-*O*-caffeoylquinic acid, jacein, and centaurein were determined mainly using IR, MS, and NMR analyses (9). Hydrolysable tannins were determined by HPLC and UV methods (15). It was demonstrated that crude extracts from roots prepared with 80% ethanol by percolation are active in vitro against *Plasmodium falciparum*. This extract was submitted to column chromatography with ether and ether methanol (1:1) and two fractions, enriched in polyacetylene and

flavonoids, respectively, were obtained. The extract and the fractions were assessed by HPLC/DAD analysis (16).

Pharmacological Action

Ethnical medicine for immunomodulatory activity: -

Bidens pilosa L. has been claimed as an immunomodulatory folk medicine. The immune efficacy of *Bidens pilosa* L., as evidenced in the up-regulation of IFN-γ, a potent cytokine in many immunomodulatory aspects. Moreover, identification of two bioactive flavonoids from *Bidens pilosa* L. with the ability to stimulate IFN-γ expression using a BGFI method was reported. Centaurein and centaureidin, which were synthesized from Bidens pilosa L. for the first time, manifested that centaurein and its aglycone, centaureidin, were able to modulate IFN-γ transcription. Also centaurein or centaureidin can in vitro boost IFN-γ production. It was also reported that a combination of IFN promoter, luciferase as a reporter gene, and T cells can be used to screen immunomodulatory phytochemicals from the *Bidens pilosa* L. plant, traditionally used as a folk medicine to improve immunity (17).

Antioxidant activity: -
The antioxidant effect of the infusion of *Bidens pilosa* L. on the hemolysis induced by AAPH [2, 2-azobis (2-amidinopropane) dihydrochloride]. The amount of *Bidens pilosa* L. infusion that halved the hemolysis induced by AAPH was 6µl, which corresponds to an IC_{50} of 1.19 mg of dry weight per milliliter of infusion. Thus, the oxidative hemolysis of erythrocytes induced by AAPH was suppressed by an aqueous infusion of *Bidens pilosa* L., which is a very active antioxidant and exerts its protective effect at low amounts (18).

Antimalarial Activity: -
In an *in vitro* study, the crude extracts from roots, prepared with 80% ethanol by percolation showed activity against *Plasmodium falciparum.* However the 80% ethanol extract and the fraction enriched in flavonoids (ether: methanol fraction) from *Bidens pilosa* L. roots also proved to be active against malaria *in vivo*. In the present study, the whole extract, however, containing both polyacetylenes and flavonoids, was more effective. The methoxylated aromatic compounds, like lignanes as well as the flavonoid showed moderate activity against the parasite *in vitro* (16).

Antibacterial Activity: -
In an *in vitro* study, the methanolic extract of *Bidens pilosa* L. leaves showed an antibacterial activity against *Staphylococcus aureus, Staphylococcus epidermis,* and *Bacillus subtilis* (19).

Pharmacological activities supported by experimental animal studies:

It was reported that this plant species had an anti-diabetic activity in NOD mice (an animal model for type I diabetes) db/db mice (an animal model for type II diabetes) and alloxan-treated mice, and it's the butanol fraction from hot water extract of *Bidens pilosa* L. could modulate the differentiation of human helper T cells and prevent autoimmune diabetes in NOD mice. The fraction of *Bidens pilosa* L. containing cytopiloyne caused a deterioration of Th2 cell-mediated airway inflammation induced by ovalbumin in BALB/c mice. It was concluded that cytopiloyne inhibited Th1 cell differentiation but increased Th2 cell differentiation in mouse Tcells. In vivo evidence revealed that cytopiloyne exhibited similar regulatory effect on both cytokines in NOD mice. The extracts or acetylenic constituents from *Bidens pilosa* L. showed anti-hyperglycemic effects in mouse models. Therefore, the bioactive fraction of *Bidens pilosa* L. containing polyacetylenic glucosides might risk aggravating allergy and asthma though this fraction and its derived polyacetylenes have a beneficial effect on Th1 cell-mediated autoimmune diseases such as diabetes (15).

Fructose is widely present in numerous foods. It has been commonly used as a sweetener and promoted as being useful for weight reduction, exercise endurance, and diabetes. It has been demonstrated that hypertension develops when normal rats are fed a fructose-enriched diet. The hypertension is accompanied by the metabolic abnormalities of hyperinsuline, insulin resistance and hypertriglyceridemia. We recently reported that the leaf methanol extract of *B. pilosa* decreases systolic blood pressure (SBP) in spontaneously hypertensive rats and salt-loading hypertensive rats and the extract contains compounds which, if taken in sufficient quantities, could conceivably be beneficial in the attenuation and prevention hypertension and hyperinsulinemia induced by high fructose diets in rats. The aqueous and methylene chloride extracts have also been shown to reverse the high blood pressure and hypertriglyceridemia developed due to fructose feeding in rats (20). It was reported that leaf aqueous extract of *B. pilosa* possesses smooth muscle relaxant activity, which is more potent on norepinephrine-induced contraction, compared with KCl-induced contractions (21).

The anti-ulcer property of the plant was studied using experimental rat models. This study reveals that of the three extracts tested, the methylene chloride extract of *B. pilosa* is the most potent inhibitor of gastric mucosal lesions caused by HCl: ethanol, but is not effective against absolute ethanol-induced lesions. The extract does not posses anti-secretory potential and would tend to increase gastric acidity if gastric outflow is obstructed by ligature. However, the cytoprotective action against irritant substances may be mediated by the cytoprotective action of endogenous prostaglandins (22). The study was conducted on Wistar rats and was found that *B. pilosa var. radiata Schult*. It possesses antiulcerogenic principles, which protect against gastric mucosal damage induced by indomethacin and ethanol, through inhibition of gastric acid and pepsin output (attenuation of aggresive factors) and stimulation of mucus secretion (potentiation of defensive factors). Probably the antiulcer effect is due, partly at least, to the presence of flavonoids in the ethanolic extract since quercetin has been identified by HPLC (23).

Medicinal uses

It is anti-hyperglycemic, anti-hypertensive, antiulcerogenic, hepatoprotective, anti-leukemic, anticancer, antipyretic, anti-virus, anti-angiogenic, diuretic, anti-rheumatic, antibiotic, or antidiabetes (11, 15). It is widely applied as an anti-inflammatory agent in hepatitis laryngitis, headache and digestive disorders (18). Also used in treatment of snakebites, insect stings, wounds, shock after accidents, lung troubles, fever and eye infections (24).

The leaves are used in the treatment of jaundice, threatened abortion, conjunctivitis, toothache, cough, intestinal helminthiasis and fever. The leaves with the flowers are used to treat flank pains, while the whole plant is used to treat fractures and febrile convulsion. The flower is used in the treatment of diarrhoea, dysentery and upset stomach in food poisoning. In the Peruvian Amazon, *Bidens pilosa* is used for aftosa, angina, diabetes, dysentery, dysmennorrhea, edema, hepatitis, water retention and dropsy. In the western region of Cameroon it is used for problems related to high blood pressure and the aqueous extract of the leaf possesses aortic smooth muscle relaxant activity (25). In the middle American islands the plant juice is used against ulcers and as a diuretic and choleretic. In some parts of Africa, it is used in the treatment of influenza, diarrhea, angina; paw edema, diabetes and conjunctivitis (20). In some parts of tropical Africa it is widely used by traditional healers in the treatment of diarrhoea, dysentery, influenza, otitis and ophthalmia (21).

Toxicity studies
Its potential toxicity after the oral administration of an infusion of this plant in an single and repeated dose (28 days) using in both cases limit doses and to assess if this preparation was a dermal irritant was studied. The infusion of *Bidens pilosa* L. does not produce acute oral toxicity at a limit dose of 2000 mg/ Kg does neither produce toxicity after the application of repeated doses of 1000 mg/ Kg during 28 days, being produced some beneficial changes on haematological and biochemical variables in the sentinel group. So much the gel as the cream prepared from the infusion of *Bidens pilosa* L. did not produce dermal irritation (26).

Drug Interactions
None clinically documented in humans; however, the use of this plant may potentiate antidiabetic, anticoagulant, and antihypertensive drugs (based on animal studies) (4).

Polyherbal formulations
A peculiarity of this unique herbalism is its richness in multi-species formulas that have been evolving across the centuries, some of which are labeled with specific denominations. These mixtures thus represent a social heritage, and their ethnobotanical investigation can add much to the understanding of local folk medical systems. While *Bidens pilosa* L. and *Cissus sicyoides* are principal in mixtures for respiratory problems, which form the major ethno-medical category in terms of number of preparations. Juice extract of *Bidens pilosa* L. (arial part) and Solanum *torvum* (leaves) was used to treat Catarrh. Decoction of (aerial part), *Cassia fistula* (fruits), *Cissus sicyoides* (fruits), *Crescentia cujete* (fruits), *Phyla scaberrima* (aerial part), *Ruellia tuberosa* (root) and bee's honey was used to provide coolness at the uterus and treat menstrual irregularity (27). *Bidens pilosa* L. with *Urtica dioica* can be used to treat gout (4).

Dosage
Bidens pilosa L. is available in crude plant material, decoction, capsules, tincture.

Decoction: ½ to 1 cup twice daily

Capsules: 2g twice daily

Tincture: 2-3ml twice daily

Generally the whole plant is uprooted and prepared in decoctions or infusions for internal use, and/or crushed into a paste or poultice for external use. In the Peruvian Amazon picão preto (*Bidens pilosa* L.*)* is used for aftosa (foot-and-mouth disease), angina, diabetes, menstrual disorders, hepatitis, laryngitis, intestinal worms and for internal and external inflammations. In Piura region of Peru, a decoction of the roots is used for alcoholic hepatitis and worms. The Cuna tribe mixes the crushed leaves with water to treat headaches. Near Pucallpa, Peru, the leaf is balled up and applied to a toothache; the leaves also are used for headaches. In other parts of the Amazon, a decoction of the plant is mixed with lemon juice and used to treat angina, hepatitis, sore throat, and water retention. The Exuma tribe grinds the sun-dried leaves with olive oil to make poultices for sores and lacerations and, in Tonga; an infusion of the flowers is used to treat upset stomach in food poisoning.

In Peruvian herbal medicine picão preto (*Bidens pilosa* L.*)* is employed to reduce inflammation, increase urination, and to support and protect the liver. It is commonly used there for hepatitis, conjunctivitis, abscesses, fungal infections, urinary infections, as a weight loss aid, and to stimulate

childbirth. In Brazilian herbal medicine it is used for fevers, malaria, hepatitis, diabetes, sore throat, tonsillitis, obstructions in the liver and other liver disorders, urinary infections, and vaginal discharge and infections. An infusion or decoction of the entire plant is often gargled for tonsilitis and pharyngitis. Externally it is used for wounds, fungal infections, ulcers, diaper rash, insect bites, and hemorrhoids. Brazilian herbalists also report using picão preto (*Bidens pilosa* L.*)* to normalize insulin and bilirubin levels in the pancreas, liver, and blood. In Mexico the entire plant or leaf is used to treat diabetes, stomach disorders, hemorrhoids, hepatitis, nervous problems, and fever. It is used as a gargle for mouth blisters, and the juice of the plant is used in an external poultice for kidney and liver inflammation. High doses can irritate bladder and kidneys. Do not use in cancer (4).

Discussion

Medicinal plants have provided copious leads to combat diseases, from the dawn of civilization. Herbal medicines are in great demand in the developed as well as developing countries for primary healthcare because of their wide biological and medicinal activities, higher safety margins and lesser costs (28-29).
The extensive survey of literature revealed that *Bidens pilosa* L. is important medicinal plant with diverse pharmacological spectrum. The plant shows presence of many chemical constituents, which are responsible of the various activities of the plant. *Bidens pilosa* L. embibing a tremendous potential deserves a special attention of the scientific fraternity to emerge as a milestone for medical science of this millennium due to its various medicinal uses. Further evaluation needs to be carried out on *Bidens pilosa* L. in order to explore the concealed areas and their practical clinical applications, which can be used for the welfare of the mankind.

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