A Review on Phytochemistry and Pharmacological Aspects on Heliopsis longipes

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Abstract:
Heliopsis longipes is a rare species of flowering plant fall in the family Asteraceae. The geographical locations for the H.longipes is states of Guanajuato, sanluispotosi, and Queretaro in north-central Mexico. chilcuague is a local name and other names include Aztecs gold root. In Mexico the prehispanic populations believed it is a powerful medicine. The origin of chilcuague word is in the Nahuatl because this plant was recognized as Chilcoatl (chil means spicy and coatl for the shape of its roots that's looks like a snake).The photochemical constituents present in the plant include sterols, tannins, phenolic compounds (Hydroxybenzoic acid, Caffeic acid, Coumaric acid), Flavanoids (Rutin, Apigenin, Genistein, Quercetin, Naringenin) and N-alkamides (Affinin). Pharmacological studies reported analgesic, anesthetic, antimicrobial, anti-arthritic, anti inflammatory, antimutagenic, antinociceptive, insecticidal, larvacidal, molluscicidal, proangiogenic effect and thermal hyperalgesia(mouse) properties of Heliopsis longipes. The main aspect of this review article includes the detailed Information of the morphological characters, phytochemicals , and pharmacological aspects of Heliopsis longipes in an attempt to provide a direction to the researcher for further research.

Keywords: chilcuague, Affinin, anti-arthritic, antimutagenic, antinociceptive, proangiogenic effect.

Introduction:

Heliopsis longipes (A. Gray) Blake (Asteraceae) is a Mexican Traditional Medicine. In south America the rural peoples are used inDental pain management [3]because of its analgesic, anti-inflammatory, and anti-ulcerative properties. The plant extract on investigating revealed its ability of preventing Writhing constrictions on testing with Acetic acid I.P
Injection in pain paradigm in mice.[5]Heliopsis longipes[7], often known as "chilcuague" or "chilcuan," is an indigenous plant in Mexico[6][8][9][10].

Acree, Jacobson, and Haller conducted the initial analyses on this plant in 1945 and 1947. H.longipes Blake was discovered as the source of Affinin, which was assumed to come from Erigeron affinis D. C[12]. Because of the existence of the chemical constituent (affinin), numerous organizations have undertaken chemical analyses on this plant to explore its bacteriostatic, anti-hyperalgesic, fungistatic [13], analgesic, antinociceptive, and anti-inflammatory capabilities. They have a significant role as anesthetic for oral use and antiparasitic, analgesic (local) and anesthetic due to the presence of substances with similar activity.After some investigestions on this plant. They concluded that the presence of Affinin [N-isobutyl-2E,6Z,8E-decatrienamide] also known as [spilanthol] is the major chemical component found in the roots which shows the analgesic activity.

Massive amounts of wild plant material must be collected in order to extract this chemical, which depletes the native population of those plants [14]. Wide genetic diversity found in wild medicinal plants can be used to create crops that are more productive, nutrient-rich, and disease-resistant. The availability of wild plants for pharmacological, building, nutritional, culinary, industrial, and therapeutic uses, as well as their conservation status in their environment, is still being researched [15].

TAXONOMY :

Kingdom	:	Plantae
Clade	:	Tracheophytes
Clade	:	Angiosperms
Clade	:	Eudicots
Clade	:	Asterids
Order	:	Asterales
Family	:	Asteraceae
Genus	:	Heliopsis
Species	:	longipes

COMMON NAMES
Ayurveda:Heliopsis longipes S.F. Blake, Philactislongipes A. Gray.
Mexico: Chilcuague, Azteca gold root.

MORPHOLOGY:
A Rhizomatous herbaceous perennial, Heliopsis longipes can reach heights of 40–150 cm (16–59 in). Oval to triangular or lance-shaped, the serrated leaf blades can have a smooth, hairy, or rough texture. The blooming period (flowering season) is from July to early fall. One to many composite flower heads are present in the inflorescence. Yellow ray florets, which are typically 2-4 cm (34-1+12 in) long, are present in each head. The little forked pistil at the base of the fertile rays sets them apart from actual sunflowers and serves as a sign of their fertility. Numerous yellow to brownish disc florets can be found in the middle. An achene measuring 5 mm (0.20 in) in length is the fruit.

PHYTOCHEMISTRY

FLAVANOIDS
Flavanoids from Heliopsis longipes, include rutin (2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-3-[(2S,3R,4S,5S,6R)-3,4,5 trihydroxy-6-[[(2R,3R,4R,5R,6S)-3,4,5-trihydroxy-6-methyloxan-2-yl]oxymethyl]oxan-2-yl]oxychromen-4-one), Apigenin (5,7-dihydroxy-2-(4-hydroxyphenyl)chromen-4-one), Genistein(4′,5,7-Trihydroxyisoflavone), Quercetin(2-(3,4-Dihydroxyphenyl)-3,5,7-trihydroxy-4H-1-benzopyran-4-one), Naringenin((2S)-5,7-Dihydroxy-2-(4-hydroxyphenyl)-2,3-dihydro-4H-1-benzopyran-4-one).[16]

PHENOLIC ACIDS
Hydroxybenzoic acid, Chlorogenic acid((1S,3R,4R,5R)-3-[(E)-3-(3,4-dihydroxyphenyl)prop-2-enoyl]oxy-1,4,5-trihydroxycyclohexane-1-carboxylic acid), Caffeic acid((2E)-3-(3,4-Dihydroxyphenyl)prop-2-enoic acid), Coumaric acid((2E)-3-(4-Hydroxyphenyl)prop-2-enoic acid). [16]

OTHER CHEMICAL CONSTITUENTS
The major alkamide present in Heliopsis longipes is Affinin (spilanthol).which have many biological activities, N-2-methylbutyldeca -2E,GZ,8E trienamide, N-isobutyl-dodeca-2E,4E,8Z,l OE-tetraenamide[17], tannins and sterols.

PHARMACOLOGICAL STUDIES:
ANALGESIC:

Traditional medicine use the stem of Heliopsis longipes as an analgesic for toothaches.[18] The GABA system is crucial for the analgesic effect. Affinin boosted GABA release because of increasein the GABA concentrations in cerebral cortex,long-term analgesic effect is felt byenhancing descending regulation of spinal nociceptive neurons. This plant's dichloromethane extract at 10g/ml revealed analgesic effect in mouse brain slices through releasing GABA. G_1, G_2, G_4, and G_6 fractions were isolated using a bioassay and were all active at the same concentration. At a concentration of 1 x 104 M, Affinin was the single and most prevalent active component, causing GABA release 0.5 minutes after treatment. Hinokinin, 2-hydroxyhinokinin, 13(18)-ursen-3-ol, 13(18)-ursen-3-acetate, undeca-2E-en-8,10-dyinoic acid isobutylamide 3-sn-glyceroyl-(1-palmitoxy)-sitosterol and stigmasterolUrs-12-ene and hinokinin were both inactive. Heliopsis longipes' analgesic action could be attributed to Affinin.[19]

ANAESTHETIC :
The anesthetic action of Heliopsis longipes is caused by the presence of spilanthol. One of the most significant medical advances, local anesthetics are chemical compounds that block nerve conduction near the application site and result in a temporary loss of sensation. Anesthetics are used topically in various medical departments such as, including dentistry, otorhinolaryngology, urology, ophthalmology and anesthetic surgery, to alleviate the symptoms such as anxiety, pain, discomfort associated with certain treatments. This is due to the fact that they cause a temporary sensational loss of conjunctiva, mucous membrane, skin. Yamamoto and colleagues synthesized via a convergent approach, with the combining allyltitanium species with aldehyde being a critical step. A GC-FID examination revealed that spilanthol has an 88% purity level.[20,21]They described a novel method for producing N-alkylamidespilanthol, to offer a more easy analog that required one fewer step than spilanthol, a Z-alkene was swapped with an alkyne. In vitro, both drugs showed equivalent patterns of penetration into dermatomed pig ear skin. When tested in vivo utilizing the tail flick model, analogue 8 exhibited a better anesthetic profile than spilanthol and the commercial anesthetic EMLA. These findings paved a way for further investigation of compound 8 as a potential medical help, as well as the investigation of new spilanthol derivatives.[22]

ANTI-INFLAMMATORY:

Heliopsis longipes root crude ethanolic extract considerably reduces inflammation produced by arachidonic acid (AA) and Phorbol Myristate Acetate (PMA). The crude extract of Heliopsis longipes is effective in managing AA-Induced oedema with an

effective dose of 0.8 mg/ear. Both Affinin and Isobutyl-decanamide (Alkamides) were effective in preventing irritant induced inflammation. The ED50 of Affinin, Isobutyl-decanamide are 1.2mg/ear, 0.9 mg/ear respectively were found to exhibit same effect. H. longipes (91.3%), Spilantholol (72.6%), and isobutyl-decanamide (81.4%) all demonstrated the greatest advantages at 2 to 3 mg/ear when compared to the reference medication, nimesulide (1 mg/ear).Acute PMA-induced inflammation in the ears of mice was reduced by topical application of tested items. The extract of Heliopsis longipes was effective in decreasing the inflammation at doses of greater than 1.0 mg/ear. Whereas alkamides, Spilantholol and Isobutyl-decanamide were effective at 1.3 mg/ear, 1.1 mg/ear respectively.The combination of Heliopsis longipes (80.3%), Spilantholol (72.4%) , Isobutyl-decanamide (82.9%) was effective at 2 - 3 mg/ear on comparing with Indomethacin (3 mg/ear). Affinin and other alkamides components present in H. longipes extract is responsible for inhibiting COX, LOX enzymes. According to their maximum effects, the extract and alkamides had anti-inflammatory effects comparable to indomethacin and stronger than nimesulide.[23]

ANTI ARTHRITIC

In a Freund adjuvant-induced arthritis model in mice, an affinin-rich hexane extract of Heliopsis longipes roots showed anti-arthritic efficacy. The extract was administered orally at dosages of 2, 6.6, or 20 mg/kg; substantial edema-inhibitory activity was observed in both the acute and chronic phases at doses of 2 and 20 mg/kg, respectively. In terms of anti-inflammatory and anti-arthritic qualities, the extract performed better than the reference medication phenylbutazone (80 mg/kg).Heliopsislongipes hexane extract was more effective than the reference drug phenyl butazone.[24]

ANTIMICROBIAL:

The bioactive amide Affinin, isolated from the roots of Heliopsis longipes, was investigated for its capacity to suppress the growth of suspension cultures of Escherichia coli, Pseudomonas solanacearum, Bacillus subtilis, and Saccharomyces cerevisiae. The roots of Heliopsis longipes are used to create an ethanolic extract with antibacterial characteristics.At dosages as low as 25 ug/ml, the alkamideAffinin reduced E. coli and S. cerevisiae. The growth of P. solanacearum and B. subtilis was inhibited by high doses of Affinin.[25]

ANTI MUTAGENIC :

The main component Affinin in H. longipes extract was found with antimutagenic and antiradical activity so it finds its use in pain management (Neuropathic pain). His+ reverent mutations were induced by using mutagen in S. typhimurium strains TA98, TA100, TA102 with and without metabolic activation. The preliminary toxicity assessment was performed as a result there was no toxicity manifested. His+ reverent bacterial colonies were reduced, where asAuxotropic background growth was found to be increased. Previously it was discovered that H. longipes extract has no effect on S. typhimurium strains. But Affinin reduced free radical mutations, Frame shift mutations caused by 2AA treatment S. typhimurium TA98.[26]

ANTI HYPERALGESIA :

Heliopsis longipes is a Mexican herbaceous plant that has traditionally been utilized because of its anesthetic, analgesicactivity. The extract of H. longipes when combined with other synthetic drugs it evidenced better therepeutic outcomes at low doses and reducing the unwanted effects in pain management. So, this paves a way to study th pharmacological interactions of H.longipes extract (Ethanolic extract) and synthetic drugs (Diclofenac) by using Hargreaves model of heat hyperalgesia in mice. Diclofenac, HLEE (Heliopsis longipes Ethanolic Extract) , or a fixed-dose ratio are all options. The thermal hyperalgesia test was performed to evaluate the antihyperalgesic effect of systemically administered HLEE-diclofenac combinations in mice. All of the medicines exhibited an antihyperalgesic effect that was dose dependant. Isobologram was obtained by ED_{30}values for each therapy. The predicted and experimental ED30 value of HLEE-diclofenac combination were 54.479.4 mg/kg body weight, 8.674.0 mg/kg body weight respectively.These finding supports the Hargreaves model of thermal hyperalgesia, which predicts an interaction effect between HLEE and diclofenac which is synergistic. The synergistic effect of HLEE and diclofenac is applied therapeutically in Inflammatory pain treatment.[27]

ANTINOCICEPTIVE :

The H. longipes ethanolic exatract has Affinin is a major component that causes antinociceptive action.The writhing and hot-plate tests, two widely used pain models, were used to measure the analgesic activity in mice. According to reports, the writhing test is helpful for examining peripheral anti-nociceptive activity, but the hot-plate test is excellent for identifying analgesics that act on the central nervous system.[28] The hot-plate and writhing tests showed that HLEE has analgesic effect in mice, according to the results. Acute peritoneal inflammation caused by acetic acid has been shown to occur [29]; the nociceptive response that is induced may also involve the production of inflammatory mediators in addition to nociceptive afferent fibers direct stimulation as a result of the pH lowering.[30]These findings imply that the lipoxygenase and/or cyclooxygenase systems may play a role in the mechanism of action of HLEE, especially in light of the fact that acetic acid elevates prostaglandin levels (PGE2 and PGF2alpha) in peritoneal fluid. H. longipes is said to include a number of alkamides. The most prevalent alkamide found in the plant has been identified as affinin (N-isobutyl-2E,6Z,8E-decatrienamide) [31]. In this

regard, it has been discovered that alkamides prevalent in other species can prevent lipopolysaccharide-stimulated RAW264.7 murine macrophage cells from producing prostaglandin E2.[32] HLEE had a sizable antinociceptive effect in the hotplate test. This experiment demonstrates activity in and C fibers as well as temperature sensitive afferent fibers.[33]The response latency after 15 minutes was significantly lengthened (56.6-58.9%) by maximum dosages of HLEE (30 and 100 mg/kg). Therefore, it is inferred that HLEE revealed spinal cord-level actions. This theory is supported by the description of Affinin's GABA release-mediated analgesic effect in mouse brain slices (Ros et al., 2007). As a result, the spinal cord levels may be where the analgesic effect of HLEE is mediated. This study offers proof that HLEE, when given systemically, exhibited antinociceptive effects on mice suffering from acute heat and acute inflammation-induced nociception. Both acute thermal-induced and chemical-induced nociception were equally responsive to HLEE's anti-nociceptive efficacy. This shows that HLEE may be a viable option for treating pain without running the risk of genotoxic or cytotoxic harm..[34]

ANTI INSECTICIDAL :

The isolation of an amide poisonous to some insects from the roots of Heliopsis longipes (A. Gray) Blake native of Mexico[35]. .Heliopsis longipes roots were dried using the soxhlet equipment and solvents such as petroleum ether, ethyl ether, and chloroform. The extractives were mixed into kerosene sprays at a concentration of 25 mg per milliliter of spray. Acetone was utilized as an additional solvent when it was necessary to completely dissolve the substance. Because the extract contains pyrethrins, which are poisonous to insects.[36]

ANTI LARVACIDAL :

Diseases such as Encephalitis, Dengue fever, Filariasis and malaria includes mosquitoes as there major vectors[37]. Worldwide, around 3500 mosquito species in the Culicidae family, which includes the genera Anopheles and Aedes, serve as vectors of serious sickness.[38] Four malaria-causing parasites, the most severe of which is Plasmodium falciparum, can be transmitted by Anopheles species.[39] The arbovirus that causes dengue and dengue hemorrhagic fever is transmitted by the species Aedes. In tropical regions such as Asia, Africa, Latin America experiences high morbidity and mortality ratesconcerning to Malaria and Dengue fever because of altered socio-economical status. The alkamides of H.longipes is found to be exhibiting insecticidal properties. A crude extract of H.longipes roots and Spilanthalol were produced to test the insecticidal activity of H.longipes against Anopheles albimanus and Aedes aegypti. The metabolites of catalytic reduction of affininproduced two alkamides (N-isobutil-2E-decenamide and N-isobutil-decanamide) which also exhibit insecticidal properties .These Crude extracts were tested on third instar An. albimanus and Aedes aegypti larvae. The results revealed larvicidal efficacy of crude extract againstAn.albimanus and Aedes aegypti larvae. This effect could be attributed to Affinin, whose conjugated double bonds in the molecule's structure are essential for larvicidal activity to be maintained. The ability of H.longipes to inhibit the larval stages of An. albimanus and Aedes aegypti, was demonstrated in this study.[41]

ANTI MULLOSCIDAL:

Unsaturated aliphatic isobutylamidesof Asteraceae, Rutaceae, and Piperaceae families have been used to treat schistosomiasis.

Affinin (1) root extract of H. longipeswas tested using HPLC against the freshwater snail Physa occidentalis Tryon and the mollusk's Leptocercous cercariae. Above 50 mg/l in water, 21 snails became inactive after 60 minutes and perished after 18 hours.Cercarial emergence stopped at 150 mg/l (the solubility limit for 1), after 30 minutes, the snails stopped moving. L. cercariae convulsed after 1 minute and stopped moving after 5 sets. These results are equivalent to damsin (14 mg/l), but indicate that the amide is likely less efficacious than saponins. H. longipes crude crushed root with molluscicidal action.[42]

PROANGIOGENIC EFFECT

Heliopsis longipes ethanolic extract possesses proangiogenic properties. Heliopsis longipes roots have been extensively researched for therapeutic purposes, with a wide range of extraction and analytical procedures employed to investigate the primary phytochemicals, alkamides. In terms of extraction, maceration combined with UAE increased HLEE yield by a factor of two (54.7 g/kg roots dry weight) over prior studies that simply employed maceration extraction (17 g/kg roots dry weight). Using HPLC and TLCtechniques, it was discovered that phytochemical affinin was most abundant in HLEE. Despite the increasing amount of HLEE collected, Affinin extraction did not rise, indicating that the UAE prefers to extract phytochemicals other than Affinin.Several animal models have been used to create tests for measuring the angiogenic process. The rat aortic ring assay has several advantages such as less expensive, only a small number of animals were sufficient, and the development of new vascular sprouts can be followed by representative images of the angiogenesis steps, allowing successful evaluation of angiogenesis inhibitors and analysis of potential molecular factors involved. This test's key shortcoming is that it cannot explore the relation between angiogenesis and other processes in vivo model can. Affinin and HLEE enhanced the development of new blood vessel sprouts at concentrations of 1 and 10 g/mL, but inhibited it at 100 g/mL.The root organic extract of H.longipes and Spilanthalolevidenced to be a part of molecular

pathways in angiogenesis process, the most recent discovery was their vasodilation mechanism. This study identifies the role of Spilanthalol and HLEE in promoting Angiogenesis. The former and latter has increased vascular expansion in aortic ring rat experiment in a dose dependent manner (Ex viviapproach) whenangioreactors were placed in CD_1 mice. This is the first study to indicate that H.longipes can produce angiogenesis. The studies on mechanism of action and therapeutic application in adequate angiogenesis were to be encouraged.[48]

CONCLUSION

As a treatment for a number of illnesses, Heliopsis longipes has been utilized in traditional medicine. Numerous studies on experimental animals have also demonstrated its usefulness outside of ethnomedicine. These plant's pharmacological properties may be attributed to alkaloids and flavonoids that were isolated from it. Identifying individual bioactive chemicals that may be to blame for these activities is the next step. Consequently, Heliopsis longipes has to be grown, collected, and subjected to additional pharmacological research.

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